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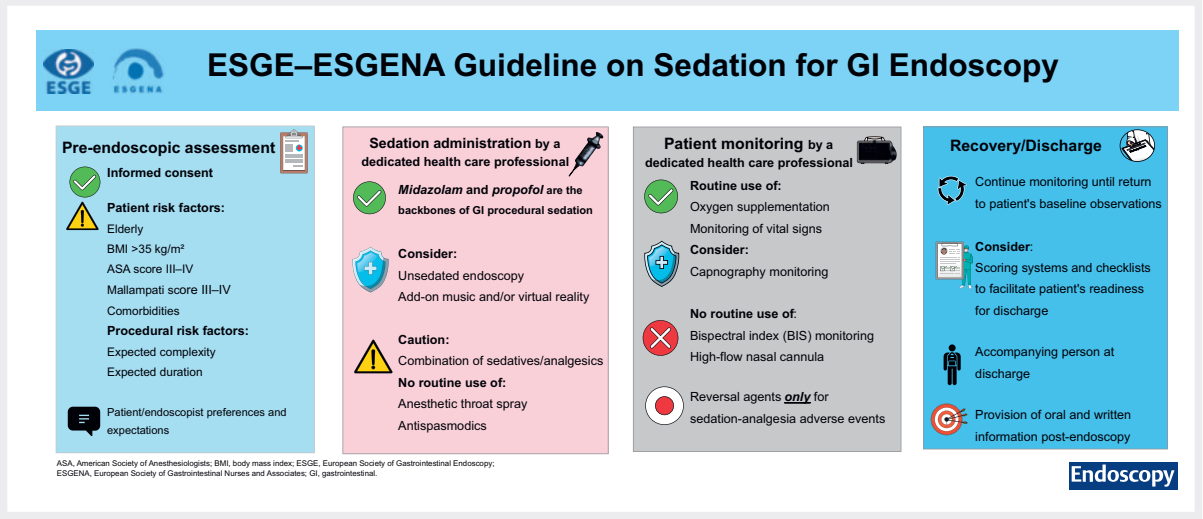
Sedation for gastrointestinal endoscopy: European Society of Gastrointestinal Endoscopy (ESGE) and European Society of Gastroenterology and Endoscopy Nurses and Associates (ESGENA) Guideline

GRAPHICAL ABSTRACT



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MAIN RECOMMENDATIONS

ESGE and ESGENA recommend that informed consent for gastrointestinal endoscopic procedures should include consent for sedation and cover best practice as outlined in the ESGE Position Statement for informed consent.
Strong recommendation, very low certainty of evidence.

ESGE and ESGENA recommend pre-assessment, a specific sedation regimen, and enhanced periprocedural monitoring in high-risk patients undergoing gastrointestinal procedures with sedation, to reduce the risk of sedation-related adverse events.
Strong recommendation, very low certainty of evidence.

ESGE and ESGENA recommend that pre-assessment, sedation regimen, and periprocedural monitoring should be determined by the complexity (duration, invasiveness) of the endoscopic procedure.
Strong recommendation, very low certainty of evidence.

ESGE and ESGENA suggest that the management of sedation in patients on glucagon-like peptide-1 receptor agonists should be individualized.
Conditional recommendation, very low certainty of evidence.

ESGE and ESGENA suggest offering the option of diagnostic colonoscopy and gastroscopy without sedation, based on the patient's and endoscopist's preference.
Conditional recommendation, very low certainty of evidence.

ESGE and ESGENA recommend that sedation should be provided by a dedicated healthcare professional trained in sedation administration and patient monitoring.
Strong recommendation, very low certainty of evidence.

ESGE and ESGENA recommend propofol for procedural sedation, as first line, depending on the country's human resources, service framework, and legislation.
ESGE and ESGENA recommend midazolam for procedural sedation, in combination with opiates when analgesia is required.
Strong recommendation, very low certainty of evidence.

ESGE and ESGENA suggest the provision of the ultrashort-acting sedative remimazolam in elderly patients and patients with cardiovascular and/or respiratory comorbidities.
Conditional recommendation, low certainty of evidence.

ESGE and ESGENA suggest exercising caution when combining ultrashort-acting sedatives with other sedatives or analgesics.
Conditional recommendation, low certainty of evidence.

ESGE and ESGENA suggest capnography monitoring for patients undergoing sedated gastrointestinal endoscopy who are at higher risk of hypoxemia.
Conditional recommendation, very low certainty of evidence.

ESGE and ESGENA recommend that the use of reversal agents should be restricted to managing sedation-analgesia adverse events that do not improve with non-pharmacological intervention.
Strong recommendation, very low certainty of evidence.

ESGE and ESGENA recommend that patients be monitored after endoscopy by trained and qualified staff until the return of the patient's baseline observations.
Strong recommendation, very low certainty of evidence.

ESGE and ESGENA suggest using scoring systems and standardized discharge checklists to facilitate patient readiness for discharge. Assessments should include a detailed record of vital signs, pain levels, and psychomotor performance.
Conditional recommendation, very low certainty of evidence.

ESGE and ESGENA suggest that the performing endoscopist holds the overall medicolegal responsibility for the patient's treatment, including safe recovery, but may delegate the assessment and discharge to trained and qualified personnel based on standardized discharge criteria.
Conditional recommendation, very low certainty of evidence.

ESGE and ESGENA recommend that patients receive oral and written information regarding the post-endoscopy period. Contact details should be provided for potential delayed complications, emergencies, or readmission.

ESGE and ESGENA recommend that patients undergoing sedated endoscopy have an accompanying person at discharge.
Strong recommendation, very low certainty of evidence.

ESGE and ESGENA recommend performing emergency endoscopy under moderate sedation in hemodynamically stable patients. Alternatively, emergency endoscopy without sedation in cooperative patients is feasible.

ESGE and ESGENA recommend sedation administration by an anesthesiology specialist in emergency endoscopy in patients at increased risk of aspiration, or with hemodynamic instability or significant comorbidities.
Strong recommendation, very low certainty of evidence.

ESGE and ESGENA recommend consultation with anesthetic and obstetric teams involved in the pregnant patient`s care, together with the patient's choice for the appropriateness and choice of sedation during gastrointestinal endoscopy.
Strong recommendation, very low certainty of evidence.

ESGE and ESGENA recommend improving and expanding educational offerings on sedation strategies and the principles of airway management, using structured training.
Strong recommendation, low certainty of evidence.

ESGE and ESGENA recommend the development and implementation of a quality improvement program with performance indicators to monitor the quality of sedation practices in gastrointestinal endoscopy.
Strong recommendation, very low certainty of evidence.

ESGE and ESGENA recommend a rational use of sedatives to reduce the environmental impact of endoscopy.
Strong recommendation, moderate certainty of evidence.

Introduction

The volume of gastrointestinal (GI) endoscopy has increased exponentially over the last few decades. There is an increase in the complexity and number of procedures with a closer bridge to the surgical interface, such as with the resection of neoplasia. With these advancements comes an inherent increase in the amount of sedation utilized. Our understanding of patient comfort and experience has also altered our clinical practice, ensuring better patient tolerability and satisfaction.

The provision and use of sedation across Europe is widely varied and governed by national legislation, legal frameworks, and various healthcare systems. Minimal to moderate sedation is the norm in several countries, such as the United Kingdom and Greece, and the combination of midazolam and an opioid remains the backbone for most endoscopies carried out. In others, such as Germany, Denmark, and Switzerland, propofol sedation is more commonly utilized. The delivery of propofol is also varied; whilst it can be administered by endoscopists or appropriately trained individuals in some countries, its use is restricted to anesthetist-only administration in countries such as France and the UK [1]. However, the overarching principles in the delivery of safe sedation for GI endoscopy are similar, regardless of the choice of sedative used. This ESGE–ESGENA Guideline provides up-to-date and evidence-based recommendations on the delivery of sedation, from the pre-assessment of the patient to post-procedure recovery and discharge. This Guideline is intended to complement existing guidelines from national societies, rather than to compete with, replicate, or replace recently published national guidance, namely the British, German, Greek, and Spanish society guidelines [2, 3, 4, 5]. The aim is to inform practicing clinicians, endoscopists, and all staff

ABBREVIATIONS

ADR	adenoma detection rate
AE	adverse event
AP	anesthesiologist provision
ASA	American Society of Anesthesiologists
BIS	bispectral index
BMI	body mass index
CAPS	computer-assisted personalized sedation
DAE	device-assisted enteroscopy
ECG	electrocardiography
EGD	esophagogastroduodenoscopy/upper gastrointestinal endoscopy
ERCP	endoscopic retrograde cholangio-pancreatography
ESGE	European Society of Gastrointestinal Endoscopy
ESGENA	European Society of Gastroenterology and Endoscopy Nurses and Associates
EUS	endoscopic ultrasound
GA	general anesthesia
GI	gastrointestinal
GLP-1RA	glucagon-like peptide-1 receptor agonist
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HFNC	high-flow nasal cannula
HR	hazard ratio
MD	mean difference
mPADSS	modified post-anesthesia discharge scoring system
NAAP	nonanesthesiologist administration of propofol
OR	odds ratio
PICO	population/patient, intervention/indicator, comparator/control, outcome
RCT	randomized controlled trial
RR	risk ratio
SAE	serious adverse event
SMD	standardized mean difference
TCI	target-controlled infusion
TNE	transnasal endoscopy

involved in the delivery of sedation for endoscopy across Europe on the recently published evidence. Rigorous methodology has been applied, and a comprehensive literature search for key evidence over the last 5 years has been conducted to cover the different clinical needs across Europe.

Methods

This Guideline was commissioned by the Governing Boards of the European Society of Gastrointestinal Endoscopy (ESGE) and the European Society of Gastroenterology and Endoscopy Nurses and Associates (ESGENA) to provide an update on the previous publication in 2015 [6]. The Guideline leader (K.T.) invited a co-leader (R.S.) who developed a draft outline of the entire guideline. Several ESGE members, pertinent stakeholders (ESGENA representatives), and other key contributors (anesthetists) were invited to join the task forces.

An initial meeting was arranged at ESGE Days 2024 for a review of the outline of the guideline. The two leaders agreed on the guideline domains, namely: (i) pre-assessment; (ii) sedation administration; (iii) monitoring; (iv) safe discharge; (v) special situations; (vi) training and environmental impact; and (vii) research gaps. The guideline co-leader (R.S.) developed draft PICO questions (where P stands for population/patient; I for intervention/indicator; C for comparator/control; and O is outcome) for all guideline domains and MESH (Medical Subject Headings) terms to aid literature searches. Task force leaders were invited, and the different topics were assigned within each task force group with a balanced distribution of clinicians (endoscopists and anesthetists) and endoscopy nurses. All task force members were required to disclose potential financial and intellectual conflicts of interest, in line with ESGE policy.

All task force members met in May 2024. Task force leaders and assigned members further refined the PICO questions according to the respective sections of the Guideline, to inform searches for available evidence to support the development of statements. Details are included in the Supplementary Material available online. Task forces conducted a systematic search of literature published in the English language (listed in the Supplementary Material for each PICO) over the last 5 years, focusing on meta-analyses and prospective studies, particularly randomized controlled trials (RCTs) involving humans. Where literature was lacking, the searches were extended beyond this timeframe. Retrospective analyses and case studies were also included if they addressed topics not covered in the prospective studies. A library of literature and references was also provided to task force members, and a methodologist (G.T.) assisted each task force with the grading of the literature evidence. Thereafter, evidence tables were generated for each key question summarizing the evidence from the available studies. The assessment of the literature by the task force members and the development of recommendations have been done according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system [7], with the assistance of the methodologist who pooled the data using meta-analytic tools and – when feasible – providing the effect measure (odds ratio, risk ratio, mean difference, standardized mean difference, etc., and their respective 95%CI), and evaluated the quality of the studies and the certainty of evidence. When pooling of study results was not possible and/or quantitative data were lacking, the certainty of evidence was rated as very low a priori. Each task force proposed recommendations based on the GRADE criteria. (▶ **Table 1, Table 2**), which were discussed during an online meeting in September 2024. As patients are at the heart of every endoscopy service, the recommendations have been carefully weighed to incorporate a patient perspective. There is a special note in the text for

▶ **Table 1** Interpretation of the certainty of evidence of effects using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework.

Certainty	Description
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the estimate of effect. The true effect is likely to be close to the estimate of effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.
Very low	We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

cases where the perspectives of the clinicians or policymakers were considered.

Following discussions and modifications by all task force members during this meeting, the final draft was discussed and approved by the Guideline leaders after critical review. Two further meetings were organized on September 24th, 2025, and on December 9th, 2025, where all task force members finalized the Guideline document. Key recommendations are presented in the Main Recommendations section at the beginning of this Guideline, and the patient's journey from the initial evaluation to sedated endoscopy to discharge is highlighted in ▶ **Fig. 1**. The Guideline was reviewed by the Chair of the ESGE Publications Working Group, a member of the ESGE Governing Board, an external reviewer, and members of the ESGE Member Societies, as well as individual ESGE members. Comments received have been incorporated accordingly. All authors approved the final version of the manuscript.

This Guideline will be reviewed for updates when new relevant evidence becomes available. Any updates to the Guideline will be noted on the ESGE website: http://www.esge.com/esge-guidelines.html.

1. Pre-endoscopic assessment

1.1 Informed consent for sedated endoscopic gastrointestinal (GI) procedures

RECOMMENDATION

1.1 ESGE and ESGENA recommend that informed consent for GI endoscopic procedures should include consent for sedation and cover best practice as outlined in the ESGE Position Statement for informed consent.

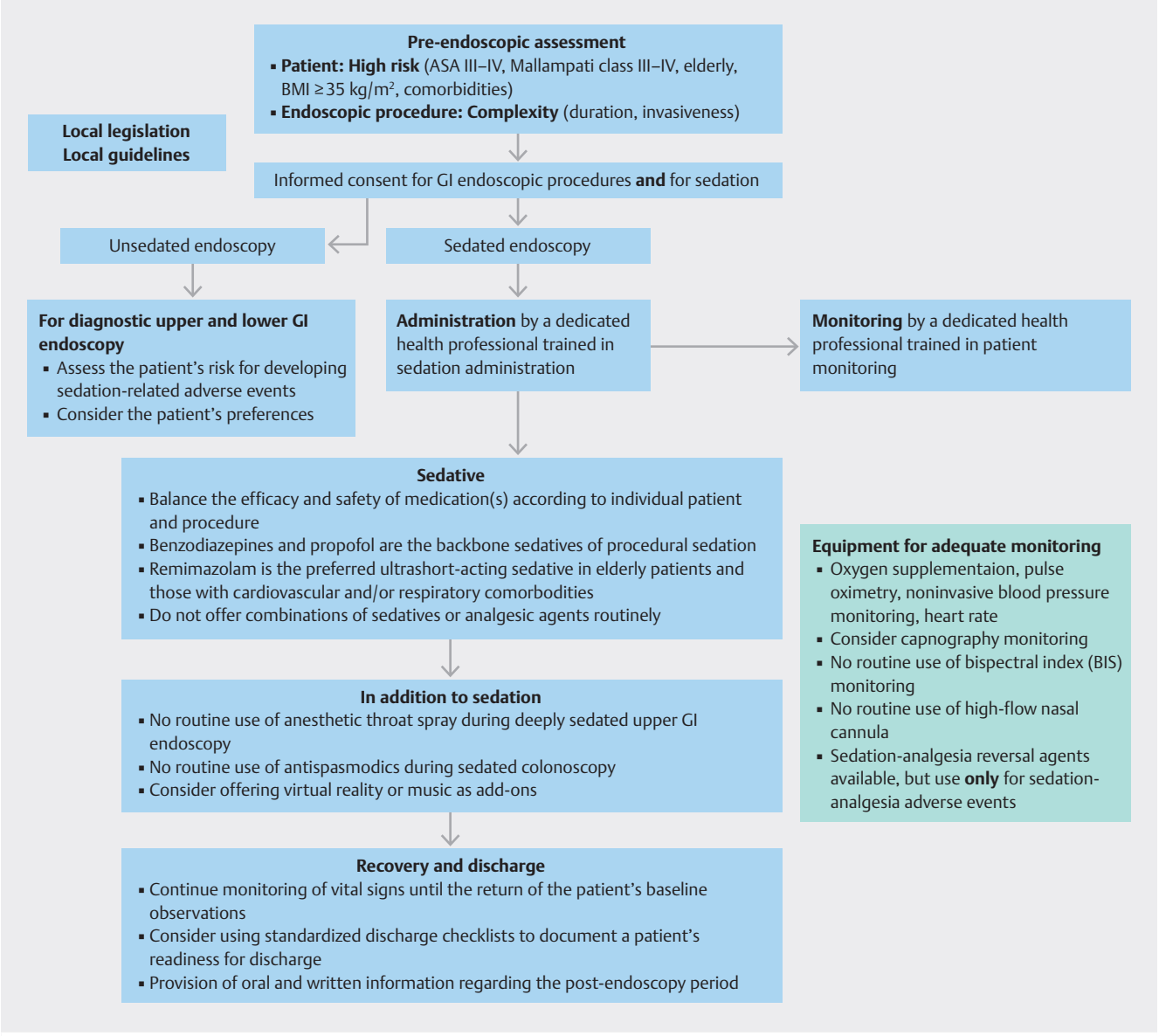
Strong recommendation, very low certainty of evidence.

▶ **Table 2** Implications of strong and conditional recommendations using the GRADE framework.

	Implications of strong and conditional recommendations	
	Strong recommendation	**Conditional recommendation**
For patients	Most individuals in this situation would want the recommended course of action, and only a small proportion would not.	Most individuals in this situation would want the suggested course of action, but many would not.
For clinicians	Most individuals should receive the intervention. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	Different choices will be appropriate for individual patients, consistent with their values and preferences. Use shared decision-making. Decision aids may be useful in helping patients make decisions consistent with their individual risks, values, and preferences.
For policymakers	The recommendation can be adapted as a policy or performance measure in most situations.	Policy-making will require substantial debate and involvement of various stakeholders. Performance measures should assess whether decision-making is appropriate.

Summary of the evidence

The principles of informed consent for patients undergoing endoscopic GI procedures are outlined in the ESGE Position Statement [8]. The benefits and risks of sedation vary according to the complexity of the procedure and the patient's comorbidities. Patients may, however, have strong preferences for sedation or anesthesia. The requirement of an additional consent form for sedation and/or anesthesia depends on local legislation. ESGE recommends that informed consent for nonanesthesiologist administration of propofol (NAAP) may be incorporated into the main body of the endoscopy consent form [8], and UK guidelines for general anesthesia state that a separate form is not required where anesthesia is used to facilitate another treatment [2]. However, practitioners should be aware of local legislation and use an additional consent form if required.



▶ **Fig. 1** Sedation algorithm for gastrointestinal endoscopy. ASA, American Society of Anesthesiologists; BMI, body mass index; GI, gastrointestinal

1.2 Patient risk factors

RECOMMENDATION

1.2 ESGE and ESGENA recommend pre-assessment, a specific sedation regimen, and enhanced periprocedural monitoring in high-risk patients undergoing GI procedures with sedation, to reduce the risk of sedation-related adverse events.

Strong recommendation, very low certainty of evidence.

Summary of the evidence

Specific patient factors may predict failure of endoscopy under moderate sedation. The most recent evidence is presented in one prospective observational study of 766 adult patients undergoing colonoscopy: risk factors for failed colonoscopy with conscious sedation were younger age (odds ratio [OR] 0.98, 95%CI 0.96–0.99), and opiate or benzodiazepine use (OR 1.71, 95%CI 1.03–2.84, and OR 1.72, 95%CI 0.98–3.01, respectively) [9].

ESGE deems that patients who are at high risk for developing sedation-related adverse events (AEs) are those with American Society of Anesthesiologists (ASA) score III–IV, in Mallampati class III–IV, elderly, having body mass index (BMI) ≥35 kg/m², and those with specific comorbidities, e. g. obstructive sleep apnea, and chronic cardiovascular, renal, and liver diseases (▶ **Table 3**).

A recent study analyzed retrospective data of 23 788 upper and lower GI endoscopies, ERCPs, and endoscopic ultrasounds, all including interventional procedures with anesthetist-

▶ **Table 3** Pre-assessment and patients at high risk for developing sedation-related adverse events.

High-risk patients	Preassessment
ASA score III-IV	Safety checklist
Mallampati class III-IV	Clinical examination
Elderly	Patient history
BMI ≥35 kg/m²	Clinical examination
Comorbidities	
▪ Cardiovascular disease (e. g. ischemic or congestive heart failure)	Echocardiogram (ECG) on indication Spirometry on indication Laboratory tests
▪ Chronic lung disease/apnea	
▪ Chronic kidney disease	
▪ Chronic liver disease	

administered propofol. It was found that age >75 yielded 46% more AEs than age <66 years; BMI ≥27 yielded 27% more AEs than BMI <21 kg/m^2, and emergency endoscopy 11% more AEs than routine endoscopy [10]. Any 1-point increment in the ASA score or the Mallampati class was associated with a 42% and a 16% increment in AEs, respectively. Similarly, a cross-sectional study by Lieber et al. [11], using national registry-enrolled data from 428 947 endoscopic procedures in adults, reported that risk of sedation-related adverse events increased with older age (OR 2.12, 95%CI 1.75–2.56), ASA score III (OR 1.65, 95% CI 1.47–1.86), ASA score IV/V (OR 4.10, 95%CI 3.49–4.81), procedure type, and case complexity. These results were also corroborated in prospective studies that followed. In a prospective observational study by Choe et al. [12] which enrolled 446 patients who underwent upper and lower GI endoscopy sedated by NAAP, the authors identified high BMI (OR 1.44, 95%CI 1.26–1.64), greater neck circumference (OR 2.05, 95%CI 1.64–2.45), and Mallampati class II, III or IV (OR 1.55, 95%CI 0.59–4.07; OR 3.32, 95%CI 1.24–9.0, and OR 4.70, 95%CI 0.85–25.94, respectively) as independent risk factors for hypoxia. In this context, patient pre-assessment is important before an endoscopic intervention with sedation.

A pre-assessment is a structured process conducted before an endoscopic procedure to evaluate a patient's suitability and ensure that logistical and clinical elements are in place to support a safe and efficient experience. It ensures that there is a balance between the indication and intended aim of the procedure as against the patient's comorbidities and risks. A thorough clinical evaluation, including patient history, comorbidities, and physical examination, should be performed for risk stratification and prompt identification of high-risk patients. When patients are referred through an open-access route, the referring physician must complete a pre-assessment at the time of referral. The ASA score provides a general evaluation of a patient's physical condition, with higher ASA class scores associated with increased risk of sedation-related adverse events [13]. However, ASA classification is imperfect, as disagreement has been reported regarding ASA class designation between healthcare providers evaluating the same patient. This disagreement is higher among physicians of different medical specialties [14]. Gastroenterologists performing preprocedural assessment of ASA scores have fair agreement with anesthesiologists, poor agreement with other gastroenterologists, and only moderate agreement with themselves. Given this inaccuracy, ESGE and ESGENA strongly recommend the implementation of safety checklists as part of the standard practice for all GI endoscopy procedures. In this checklist, assessment of patient risk factors (correct preparation, ASA score, Mallampati class, medical/surgical comorbidities, medication use, documented drug allergies, dental status, and history of sedation-related adverse events) is included in the sign-in phase of the checklist [15].

It is advisable to select in advance the type and depth of sedation, as well as the medication to be used, according to a comprehensive sedation plan. This plan should consider the type, duration, and complexity of the procedure, as well as the patient's risk profile. It is essential to assess patients for risk factors before sedation and to implement specific strategies to mitigate the risks associated with sedation, particularly during advanced and prolonged therapeutic procedures [16]. In this regard, patients may be offered the option of unsedated endoscopy or may benefit from the use of newer sedatives, e. g. remimazolam, with accumulating lines of evidence supporting their safe and effective use for procedural sedation. These may reduce the risk of respiratory compromise and thus, avoid the use of medications that are known to cause significant respiratory depression, particularly in patients with respiratory problems.

Similarly, patient monitoring during the procedure as well as in the recovery phase should be based on the individual patient's health status, the invasiveness of the endoscopic procedure, and the type of sedation/analgesia used. Extending monitoring due to the increased risk of respiratory depression, such as in patients with obstructive sleep apnea and desaturation post-sedation, should be clearly detailed. There should be a concrete plan for managing potential airway obstruction or respiratory complications, including advising patients to bring their own continuous positive airway pressure machine, the availability of emergency airway management equipment, and trained staff to manage the recovery period. The section **4. Safe patient discharge** covers this element in greater detail.

Certainty of evidence

The risk of bias assessment for each study is provided in **Table 1.2.3s**, (**Supplementary material**, available online-only). The recommendation was based on qualitative data review only; thus, the quality of the studies was rated as low, and the certainty of evidence was very low.

RECOMMENDATION

1.2.1 ESGE and ESGENA suggest that the management of sedation in patients on glucagon-like peptide-1 receptor agonists should be individualized. There should be shared medical decision-making after a multidisciplinary discussion, taking into account patient symptoms as well as procedure-related factors.

Conditional recommendation, very low certainty of evidence.

Summary of the evidence

Glucagon-like peptide-1 receptor agonists (GLP-1RAs) are potent treatments for diabetes mellitus. However, they also impair GI motility by inhibiting gastric peristalsis and increasing pyloric contractions in a dose-dependent manner. This effect has raised safety concerns about delayed gastric emptying and retention of gastric contents, with a risk of pulmonary aspiration and airway compromise in patients undergoing GI endoscopy.

The summary of the 11 published meta-analyses [17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27] shows that use of GLP-1RAs is associated with increased retention of gastric contents and more frequent aborted procedures during upper endoscopy, but no significant difference in terms of adverse event and aspiration rates. In particular, the number needed to scope to observe one event of aspiration has been estimated to be 794 [26].

Despite recommendations on the preoperative management of such patients [28, 29, 30], evidence regarding the optimal sedation approach remains scant. A large population-based, retrospective cohort study using a health insurance database (enrolling ~800 000 patients undergoing endoscopy) reported significantly higher risk of aspiration pneumonia associated with propofol-assisted endoscopies (hazard ratio [HR] 1.49, 95%CI 1.08–2.06), but not in the group without propofol (HR 1.31, 95%CI 0.78–2.20) [31]. In another large comparative cohort study analyzing outcomes from 24 817 adults with type 2 diabetes who used a GLP-1RA within 30 days before upper GI endoscopy, no difference in risk of pulmonary aspiration was observed between GLP-1RAs in subgroup analyses according to the type of anesthesia used [32]. Similarly, Firkins et al. [33] in a single-center retrospective analysis of 1512 EGDs performed on adults taking GLP-1RAs, did not identify any association between retained gastric content risk and type of sedation/anesthesia (conscious sedation, anesthesia-directed sedation without intubation, anesthesia-directed sedation with intubation). The robustness of evidence is impaired by their limited number and the inherent caveats in the design of the above-mentioned studies summarized in **Table 1.2.1.2s**, namely, retrospective nature, single-center, populations with various endoscopy indications, poorly powered, and lack of sedation-related AEs as a primary endpoint. Thus, a cautious interpretation of these findings is required. To date, well-designed and powered large prospective studies to identify risk of sedation-related adverse events among GLP-1RA users are absent.

Endoscopists are encouraged to perform a thorough pre-procedural evaluation for GI symptoms (i. e., nausea, vomiting, regurgitation, abdominal bloating, abdominal distention), which may be indicative of delayed gastric emptying in patients on GLP-1RAs. In addition, the setting of the procedure (i. e., inpatient, outpatient) as well as endoscopic procedure-related factors (i. e., type, complexity, emergency endoscopy, time-sensitive, or elective endoscopy) require close evaluation before endoscopy. The decision to proceed or to reschedule should balance the benefits against the potential risks and be individualized as part of shared clinical decision-making.

Certainty of evidence

Although the included studies were considered of good quality (**Table 1.2.1.3s**), the certainty of evidence was deemed very low, given the nature and drawbacks in the design of the discussed studies, the number of participants involved, and the number of events reported.

1.3 Procedure risk factors

RECOMMENDATION

1.3 ESGE and ESGENA recommend that pre-assessment, sedation regimen, and periprocedural monitoring should be determined by the complexity (duration, invasiveness) of the endoscopic procedure.

Strong recommendation, very low certainty of evidence.

Summary of the evidence

According to the British Society of Gastroenterology sedation guidelines [2] and one recent narrative review [34], identified procedural risk factors that should guide the sedation regimen as well as the monitoring strategy include the following: upper and lower GI polypectomy/resection of neoplasia; prolonged procedure time of more than 60 minutes; endoscopic bariatric surgery; large variceal bleed with significant gastric contents; foreign body retrieval; therapeutic endoscopic ultrasound (EUS) or endoscopic retrograde cholangiopancreatography (ERCP, pancreatic fluid collection drainage; and small-bowel device-assisted enteroscopy.

Similarly, in a retrospective safety study of 23 788 GI endoscopies performed under propofol alone or in combination with either opioids or benzodiazepines, every hour that prolonged the endoscopy procedure increased the overall AEs by 41%. In relation to sedation with propofol, the addition of opioids to propofol increases overall AEs by 43%, and the addition of benzodiazepines by 51%. The risk for respiratory AEs was higher during emergency endoscopy, for inpatients, and for prolonged procedures [10].

Certainty of evidence

The recommendation was based on qualitative data review; thus, the quality of the studies was rated as low, and since no meta-analysis could be performed, the certainty of evidence was very low.

2. Type of sedation

2.1 Diagnostic colonoscopy without sedation

RECOMMENDATION

2.1 ESGE and ESGENA suggest offering the option of diagnostic colonoscopy without sedation, based on the patient's and endoscopist's preference.

Conditional recommendation, very low certainty of evidence.

Summary of the evidence

Due to the anticipated discomfort of the examination, sedation is routinely planned for many GI endoscopic procedures. However, some patients prefer to undergo the procedure without any sedation to avoid the potential hazards of sedation and to resume their daily activities immediately after the completion of the examination [35]. There is evidence that diagnostic colonoscopy outcomes, such as cecal intubation rate, adenoma miss rate, and adenoma detection rate (ADR) are not compromised if the procedure is performed without sedation [36, 37, 38]. The task force recommends careful consideration of colonoscopy without sedation on a case-by-case basis, recognizing that it may require advanced technical skills to manipulate and advance the scope. Techniques to minimize discomfort, such as water intubation, should also be considered as useful adjuncts to colonoscopy without sedation [35, 39, 40].

Benefits

A total of 8 (6 retrospective cohort, 1 RCT, and 1 cross-sectional) studies [36, 37, 38, 41, 42, 43, 44, 45] examining the efficacy and safety of unsedated colonoscopy compared to colonoscopy under sedation were retrieved (**Table 2.1.2s**). The pooled results of these studies showed no differences regarding the quality measures for colonoscopy, ADR (**Fig. 2.1.1s**, OR 0.97, 95%CI 0.84–1.13, $I^2 = 71\%$) and cecal intubation rate (**Fig. 2.1.2s**, OR 1.65, 95%CI 0.45–6.01, $I^2 = 91\%$).

Harms

In the pooled results of the studies, unsedated endoscopy was not related to higher rates of discomfort compared to sedated procedures (**Fig. 2.1.3s**, OR = 0.45, 95%CI 0.11–1.83, $I^2 = 100\%$), whilst information directly comparing unsedated versus sedated procedures in terms of other adverse events (tachycardia, desaturation, pain, etc.) is scanty and heterogeneous, preventing further analysis.

Certainty of evidence

The risk of bias assessment for each study is presented in **Tables 2.1.3s**, **2.1.5s**, and **2.1.7s**. Overall, the quality of the studies was good. In the absence of RCTs, the certainty of evidence due to indirectness (heterogeneity in the endoscopic expertise) and imprecision (broad confidence interval crossing 1.0) was downgraded to very low for all benefits and harms outcomes, as shown in **Tables 2.1.4s**, **2.1.6s**, and **2.1.8s**.

2.2 Unsedated transnasal or ultrathin peroral gastroscopy

RECOMMENDATION

2.2 ESGE and ESGENA suggest offering diagnostic gastroscopy without sedation based on the patient's and endoscopist's preferences, preferably with an ultrathin or transnasal gastroscopy, where available.

Conditional recommendation, very low certainty of evidence.

Summary of the evidence

Three meta-analyses [46, 47, 48] indicate that ultrathin transnasal endoscopy exhibits sensitivity and specificity comparable to those of conventional gastroscopy for detecting esophageal lesions, whilst also being better tolerated by patients.

All ultrathin transnasal endoscopy procedures were performed without sedation, and some conventional gastroscopies were also performed without sedation; therefore, it is impossible to evaluate the impact of sedation. Using an ultrathin gastroscope or the transnasal approach during unsedated gastroscopy allows examination of the entire upper GI tract without reducing lesion detection rates. Additionally, this approach resulted in higher levels of patient satisfaction [41, 49].

Benefits

Three RCTs [41, 49, 50] evaluating the efficacy of unsedated ultrathin or transnasal gastroscopy compared to standard endoscopy under sedation were retrieved (**Table 2.2.2s**). The pooled results of these studies showed marginal, nonsignificant improvement in procedure completion with the use of unsedated ultrathin or transnasal gastroscopy (**Fig. 2.2.1s**, RR 0.98, 95%CI 0.96–1.00, $I^2 = 100\%$). Ultrathin or transnasal gastroscopy results in lower distress rates (**Fig. 2.2.4s**, MD –1.01, 95%CI –1.60 to –0.42, $I^2 = 0\%$) compared to conventional gastroscopy.

Harms

In our pooled results analysis, no difference in reported patient comfort was detected (**Fig. 2.2.3s**, MD –0.72, 95%CI –4.31 to 2.86, $I^2 = 99\%$).

Certainty of evidence

Tables 2.2.2s and **2.2.4s** provide the risk of bias assessment for each study. Overall, the included studies were considered of high quality. The certainty of the evidence was downgraded

due to indirectness, specific heterogeneity in endoscopic expertise, inconsistency, and imprecision, as indicated by a broad confidence interval that crossed 1.0. This resulted in a very low certainty for all benefits and harm outcomes (**Tables 2.2.3s**, **2.2.4s**, and **2.2.5s**).

2.3 Sedation provider during endoscopy

RECOMMENDATION

2.3 ESGE and ESGENA recommend that sedation should be provided by a dedicated healthcare professional trained in sedation administration and patient monitoring. Strong recommendation, very low certainty of evidence.

Summary of the evidence

Most studies comparing nonanesthesiologist (endoscopists, nurses) versus anesthesiologist procedural sedation have been performed using propofol for deep sedation. In actual practice, the delivery of propofol-based sedation by nonanesthesia personnel remains controversial [51]. Several guidelines developed by many international societies support nonanesthesiologist-delivered propofol for sedation [6, 52, 53], but there remains a reluctance from anesthetics societies to support training and education for nonanesthesiologist-delivered propofol sedation. In fact, the European Society of Anaesthesiology retracted their support for the previous ESGE–ESGENA Guideline supporting nonanesthesiologist delivery of propofol sedation [54]. Regardless of the type of sedation used, all clinical staff involved in sedation practice need to be appropriately trained in the pharmacology of the regimens used as well as other structural requirements for endoscopy sedation, including medication options, patient monitoring, and discharge [6].

In 2015, a comparative meta-analysis was conducted to evaluate the safety of nonanesthesiologist administration of propofol (NAAP) versus anesthesiologist provision in advanced GI endoscopic procedures [55]. The total numbers of procedures in the NAAP and AP groups were 3018 and 2374 (patients were ASA I–IV in both groups), respectively. The pooled hypoxia rates, defined as oxygen saturation rates of less than 90%, were similar for the NAAP and anesthesiologist groups (0.13% [95%CI 0.12%–0.15%], vs. 0.14% [95%CI 0.13%–0.16%], respectively). The pooled airway intervention rates were higher in the patient groups where propofol was administered by anesthesiologists (0.13% [95%CI 0.12%–0.15%, vs. 0.04% [95%CI 0.03%–0.05%]). Patient and endoscopist satisfaction rates were higher with propofol administered by an anesthesiologist. The mean dose of propofol given by anesthesiologists was also higher, averaging 340 mg (95%CI 327–353 mg) compared to 251 mg (244–258 mg) for NAAP. The specific nature and complexity of the performed procedures were unknown.

One comparative meta-analysis indicated that NAAP did not increase airway interventions (OR 1.07, 95%CI 0.3–3.9) or hypotension (OR 1.5, 95%CI 0.4–5.4) rates in low-risk patients who underwent nonadvanced GI endoscopies. However, it was associated with higher rates of bradycardia (OR 3.7, 95%CI 1.6–8.1). Nonanesthesiologists administered lower doses of propofol than anesthesiologists (MD –61.8, 95%CI –114.5 to –9.1), and their patients were more likely to experience awareness with recall (OR 20, 95%CI 7.9–50.8). Nevertheless, NAAP did not prolong the total procedure time (MD –0.08, 95%CI –3.5 to 3.3) [56].

Similarly, the pooled safety results of another meta-analysis indicated extremely low pooled rates of hypoxia (0.014%, 95%CI 0.008%–0.023%), airway interventions (0.002%, 95%CI 0.001%–0.006%), and airway complications (0.001%, 95%CI 0–0.001%) in patients undergoing nonadvanced gastrointestinal endoscopic procedures with NAAP sedation [57].

Evidence from comparative and noncomparative studies accumulated following publication of the three meta-analyses confirms the safety of NAAP during advanced and nonadvanced GI procedures. There is also zero heterogeneity in low-risk patients, as discussed in the following *Benefits* and *Harms* sections below. Evidence from colonoscopy studies [58, 59, 60, 61] suggests that NAAP does not compromise the efficacy of the procedure in terms of ADR, cecal intubation rate, and total procedural time.

Patient-controlled sedation (PCS) has been built on patient-controlled analgesia, which is frequently used in postoperative pain management. Although PCS appears safe and efficient, these patients were sedated more slowly, at lower sedation levels, and with lower satisfaction compared to physician-directed sedation [62].

Computer-assisted personalized sedation mainly relies on target-controlled infusion (TCI) based on pharmacokinetic models of specific sedative drugs. Recently, NAAP using TCI has been shown to reduce the dose of propofol (8.2 mg/min vs. 9.3 mg/min) without impact on procedural time or adverse events [63].

Benefits

A total of 18 studies (16 cohort and 2 RCTs) [58, 59, 60, 61, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77] comparing the efficacy and safety of sedation delivered by nonanesthesiologists versus anesthesiologists during various GI endoscopy procedures were retrieved (**Table 2.3.3s**). Regarding colonoscopy outcomes, the pooled results of two studies [58, 59] showed no differences regarding ADR (**Fig. 2.3.1s**, RR 1.06, 95%CI 0.94–1.19, $I^2 = 0\%$) and cecal intubation rate (**Fig. 2.3.2s**, RR 1.01, 95%CI 0.98–1.04, $I^2 = 10\%$). Overall procedure length did not differ as assessed in five studies [58, 59, 60, 61, 77] enrolling various endoscopic procedures (**Fig. 2.3.3s**, MD (minutes) –0.94, 95%CI –2.79 to 0.91, $I^2 = 74\%$).

Harms

In addition to the meta-analyses discussed above, the task force has identified 1 RCT [58] and 10 cohort studies [61, 69, 70, 71, 72, 73, 74, 75, 76, 77] that measured AEs related to NAAP.

In low-risk (ASA I–II) outpatients undergoing nonadvanced GI endoscopic procedures (gastroscopy, colonoscopy), the pooled rate of major AEs (endotracheal intubation, hospitalization, permanent neurologic impairment, or death) was 0.00%

▶ **Table 4** In low-risk (ASA I–II) patients undergoing either low-risk (gastroscopy, colonoscopy) or advanced GI endoscopic procedures, the rates of major adverse events associated with nonanesthesiologist administration of propofol (NAAP) were extremely low.

	Type of adverse event (AE)	Pooled rates of AEs with NAAP (1 RCT and 10 cohort studies)	
		Pooled rate, % (95%CI)	I^2
Low-risk procedures and low-risk patients	Major AE	0.00 (0–0.01)	0%
	Non-major AE	11.60 (4.01–27.20)	100%
	▪ Respiratory	1.26 (0.73–1.78)	100%
	▪ Cardiovascular	9.82 (4.54–24.18)	100%
Advanced procedures and low-risk patients	Major AE	0.05 (0–0.10)	98%
	Non-major AE	14.74 (6.28–35.77)	100%
	▪ Respiratory	5.28 (0.70–9.85)	100%
	▪ Cardiovascular	11.30 (5.84–28.45)	100%

▶ **Table 5** In low-risk (ASA I–II) patients, the pooled results analysis of comparative studies found no significant difference in the rates of major and non-major AEs overall, between NAAP and anesthesiologist provision (AP), regardless of the endoscopic procedure risk.

	Type of adverse event (AE)	Comparison of AEs between NAAP and AP (1 RCT and 3 cohort studies)	
		OR (95%CI)	I^2
Low-risk procedures and low-risk patients	Major AE	Not estimable	Not estimable
	Non-major AE	0.91 (0.54–1.52)	5%
	▪ Respiratory	1.37 (0.59–3.18)	0%
	▪ Cardiovascular	0.59 (0.15–2.31)	59%
Advanced procedures and low-risk patients	Major AE	0.50 (0.07–3.59)	
	Non-major AE	1.03 (0.79–1.36)	
	▪ Respiratory	1.69 (0.75–3.83)	68%
	▪ Cardiovascular	0.31 (0.18–0.54)	NA

ASA, American Society of Anesthesiologists; GI, gastrointestinal; NA, not applicable; NAAP, nonanesthesiologist administration of propofol; OR, odds ratio; RCT, randomized controlled trial.

(95%CI 0–0.01%, I^2 = 0%) (**Fig. 2.3.4s**), whereas the pooled rate for non-major AEs (transient oxygen saturation 75%–90%; transient apnoea; transient airway obstruction; allergic reaction; failed sedation; bradycardia or tachycardia [>25% change from baseline]; hypo- or hypertension [>25% change from baseline]) was 11.60% (95%CI 4.01%–27.20%, I^2 = 100%) (**Fig. 2.3.5s**).

In low-risk patients undergoing advanced GI endoscopic procedures, the pooled rate of major AEs was 0.05% (95%CI 0.01%–0.10%; I^2 = 98%) (**Fig. 2.3.4s**), and for non-major AEs it was 14.74% (95%CI 6.28%–35.77%, I^2 = 100%) (**Fig. 2.3.5s**).

Regarding the type of AEs, the pooled safety results of the aforementioned studies indicated low rates of non-major respiratory AEs (hypoxia, airway interventions, and airway complications) in patients undergoing both nonadvanced and advanced GI endoscopic procedures with NAAP sedation (1.26%, 95%CI 0.73%–1.78%, I^2 = 100%, and 5.28%, 95%CI 0.70%–9.85%, I^2 = 100%, respectively (▶ **Table 4** and **Fig. 2.3.6s**). The pooled results of the studies in relation to non-major cardiovascular AEs (bradycardia or tachycardia, hypo- or hypertension) in patients undergoing nonadvanced or advanced gastrointestinal endoscopic procedures with NAAP sedation were 9.82% (95%CI 4.54%–24.18%, I^2 = 100%) and 11.30% (95% CI 5.84%–28.45%, I^2 = 100%, respectively) (▶ **Table 4** and **Fig. 2.3.7s**).

The task force also compared the AE rates detected in the two arms (NAAP vs. anesthetist-provided) in the one RCT and three cohort studies [58, 61, 76, 77], which included 21 223 low-risk patients (▶ **Table 5**). In total, there were 82 AEs in the intervention (NAAP) group and 907 AEs in the control group. There was no significant statistical difference between the two intervention groups regarding major adverse events in low-risk patients undergoing advanced GI endoscopic procedures (OR 0.50, 95%CI 0.07–3.59, I^2 = 0%, ▶ **Table 5**, **Fig. 2.3.8s**). Regarding non-major AEs in low-risk patients, there was no statistically significant difference between the two groups, either for non-advanced or advanced GI endoscopic procedures (OR 0.91, 95% CI 0.54–1.52, I^2 = 5%; and OR 1.03, 95%CI 0.79–1.36, I^2 = 0%) (▶ **Table 5**, **Fig. 2.3.9s**).

Analysis regarding the non-major respiratory AEs showed no statistically significant difference between the two intervention groups, for low-risk patients undergoing either nonadvanced or advanced GI endoscopic procedures (OR 1.37, 95%CI 0.59–3.18, I^2 = 0%, and OR 1.69, 95%CI 0.75–3.83, I^2 = 25%, respectively (▶ **Table 5**, **Fig. 2.3.10s**). For non-major cardiovascular AEs, the task force detected no statistically significant difference between the two intervention groups for low-risk patients undergoing nonadvanced GI endoscopic procedures (OR 0.59, 95%CI 0.15–2.31, I^2 = 59%). There was a statistical difference regarding AEs in favor of anesthetist provision compared to NAAP for advanced procedures, based on a single study (OR 0.31, 95% CI 0.18–0.54, I^2 = NA, ▶ **Table 5**, **Fig. 2.3.11s**). Combining the

▶ **Table 6** Levels of sedation and anesthesia.

	Minimal sedation	Moderate sedation	Deep sedation	General anesthesia
Responsiveness	Normal response to verbal stimuli	Purposeful response to verbal or tactile stimuli	Purposeful response after repeated or painful stimuli	Unarousable even with painful stimuli
Airway	Not affected	No intervention required	Intervention may be required	Intervention often required
Spontaneous ventilation	Not affected	Adequate	Maybe inadequate	Frequently inadequate
Cardiovascular function	Not affected	Usually, unaffected	Usually, unaffected	May be impaired

results of two non-RCTs, NAAP sedation has not been linked to a higher rate of endoscopic complications compared to anesthetist provision (**Fig. 2.3.12s**, OR 1.24, 95%CI 0.59–2.61, I^2 = 0%). It is important to interpret the above results with caution, as there is significant variability amongst the studies in the definition and seriousness of AEs. Furthermore, the designs of the studies prevent a direct association between the observed adverse events and the administration of sedation.

Regarding computer-assisted propofol sedation, meta-analysis of two studies [78, 79] showed that its implementation results in a similar sedation success rate (**Fig. 2.3.13s**, OR 0.94, 95%CI 0.63–1.39, I^2 = 0%), but lower – albeit nonsignificant – recovery time compared to standard sedation (**Fig. 2.3.14s**, MD –13.44, 95%CI –27.65 to 0.77, I^2 = 100%).

Regarding TCI, the task force pooled the AEs detected in two RCTs [80, 81] and three cohort studies [82, 83, 84] assessing NAAP using TCI or NAAP-bolus propofol infusion. The pooled rate of hypoxia (SaO_2 <90%) was 7.02% (95%CI 5.10%–8.95%, I^2 = 100%) in the TCI arm compared to 21.59%, (95%CI 10.29–32.89, I^2 = 100%) (**Fig. 2.3.15s**) with the bolus infusion. Similarly, TCI also resulted in a lower hypotension rate (<90/60 mmHg or fall >20% of the blood pressure) compared to bolus infusion (14.19%, 95%CI 4.32%–24.05%, I^2 = 100% vs. 27.06%, 95%CI 26.53%–27.59%, I^2 = 0% (**Fig. 2.3.16s**), with the effect being more profound during ERCP procedures.

The task force compared the AEs detected in the two arms (TCI NAAP and bolus propofol infusion, total 322 patients) in two RCTs [80, 81] and one cohort study [84]. There were significantly fewer hypoxia episodes with TCI implementation (20 vs. 41; RR 0.53, 95%CI 0.34–0.82, I^2 = 0%, **Fig. 2.3.17s**. However, the difference regarding hypotension episodes did not reach significance (43 vs. 45; RR 0.90, 95%CI 0.44–1.86, I^2 = 75%) (**Fig. 2.3.18s**).

Certainty of evidence

The risk of bias in the included studies is detailed in **Tables 2.3.4s**, **2.3.8s**, and **2.3.12s**, respectively. Overall, all the included studies were of good quality, and the included RCTs were well-designed with a low risk of bias. The certainty of evidence for all clinical outcomes in this PICO question was downgraded due to the inclusion of noncomparative observational studies. Further downgrading was applied due to high inconsistency (high heterogeneity), resulting in a very low overall certainty of evidence (**Table 2.3.15s**).

2.4 Pharmacological sedation

From minimal sedation to general anesthesia, there is a continuum (▶ **Table 6**) that the healthcare professional administering sedative and analgesic medications must master. Thus, knowledge of the pharmacology of the available medications, their indications and differences, and the management of potential adverse reactions are prerequisites for safe and effective sedation and analgesia administration. Ideally, there should be a dedicated individual with the aforementioned knowledge and skills able to administer sedation with minimal interruptible tasks, which is particularly pertinent for deep sedation. This varies according to country and the local endoscopy unit setup.

Midazolam and propofol are essential components of sedation for GI endoscopic procedures, and according to a recent ESGE survey, propofol is the most frequently used drug [1] due to its rapid onset of action, brief duration of effect, and short recovery time. However, propofol is associated with side effects, including hypotension and hypoxia [85]. In a meta-analysis, midazolam monotherapy had similar efficiency and side effects as propofol, but was associated with a slower onset of sedative effect and longer recovery time [86]. Extensive evidence and guidance on how to use the two backbones of sedation administration are available in the British and German guidelines recently published [2, 3]. There is increasing evidence on the use of benzodiazepines in combination with opiates with or without propofol, and new ultrashort-acting sedatives have been recently introduced into the armamentarium, promising better efficacy and safety compared to the traditional sedatives (▶ **Table 7**) [87, 88, 89, 90, 91, 92].

RECOMMENDATION

2.4.1 ESGE and ESGENA recommend propofol for procedural sedation, as first line, depending on the country's human resources, service framework, and legislation.

ESGE and ESGENA recommend midazolam for procedural sedation, in combination with opiates when analgesia is required.

Strong recommendation, very low certainty of evidence.

▶ **Table 7** Pharmacokinetics of sedative and analgesic drugs that are commonly used for sedation in gastrointestinal procedures.

Type of medication	Medication [references]	Onset, s	Clinical effect, minutes
Sedative	Propofol [87, 88]	15–60	3–15
	Ciprofol [89]	30–60	5–10
	Remimazolam [87, 90]	30–120	3–8
	Etomidate [88, 90]	30–60	3–5
	Esketamine [88, 90]	30–120	15–60
	Midazolam [87]	120–300	20–80
	Dexmedetomidine [88]	180–300	15–30
Analgesic	Remifentanil [90, 91]	30–60	2–6
	Alfentanil [92]	45	5–10
	Sufentanil [92]	60	30
	Fentanyl [88, 92]	60–120	30–60

Summary of the evidence

Midazolam and propofol are the backbones of sedation for GI endoscopic procedures; however, propofol is associated with cardiorespiratory depression, which can be prevented and managed by a well-trained sedation provider. Given the significant variation in sedative use according to local legislation, service framework, and restriction of propofol administration to anesthetists in many countries, midazolam administration, with or without narcotics, is the standard for moderate sedation that is widely used for colonoscopy. There are several lines of evidence demonstrating equal efficiency and comparable safety between midazolam and propofol for GI procedural sedation, especially for procedures that do not require deep sedation, and that the addition of a narcotic analgesic to the sedative regimen alleviates pain and discomfort.

Benefits of midazolam (with or without opioids)

The task force identified one meta-analysis [86] incorporating the most recent evidence from 9 RCTs comparing safety, satisfaction, and efficiency outcomes between midazolam with or without short-acting opioids versus propofol for sedation during lower GI endoscopic procedures, as well as one additional RCT [93], which was not included in the aforementioned meta-analysis. In detail, the meta-analysis included 9 studies enrolling 1427 outpatients undergoing colonoscopy [86]. Midazolam plus fentanyl was the most prevalent combination, while propofol, along with opioids (fentanyl, remifentanil, alfentanil), was used in 4 of 9 studies. Notably, no significant differences in cardiorespiratory outcomes (hypotension, hypoxia, bradycardia) were evident between the sedative groups. Although patients sedated with propofol had greater satisfaction than those sedated with midazolam (with or without short-acting opioids) (SMD 0.54, 95%CI 0.30–0.79), there was considerable heterogeneity.

Harms

According to the meta-analysis [86] of the RCTs, patient satisfaction was lower with the combination of midazolam (with or without short-acting opioids) compared to propofol (SMD 0.93, 95%CI 0.46–1.41, I^2 = 95%; **Fig. 2.4.2s**), while endoscopists favored the use of propofol (SMD 0.59, 95%CI 0.34–0.85, I^2 = 11%) resulting in higher satisfaction scores. Additionally, total procedure time and recovery/discharge time were longer with midazolam (SMD −0.57, 95%CI −1.10 to −0.03, I^2 = 96%; and SMD −0.72, 95%CI −1.25 to −0.19, I^2 = 96%, respectively; **Fig. 2.4.3s**).

When pooling all 10 RCTs, the total cardiorespiratory adverse event rate was similar between the two groups (RR 0.94, 95%CI 0.62–1.41, I^2 = 55%, **Fig. 2.4.1s**). This effect was consistent for hypotension (RR 1.20, 95%CI 0.55–2.59, I^2 = 49%), bradycardia episodes (RR 1.07, 95%CI 0.68–1.69, I^2 = 0%), and hypoxia episodes (RR 0.63, 95%CI 0.29–1.35, I^2 = 55%) (**Fig. 2.4.1s**).

Certainty of evidence

Table 2.4.3s provides the risk of bias assessment for each study. Overall, the included studies were considered of good quality, despite concerns about the lack of blinding in many of them. The certainty of evidence for all clinical outcomes was downgraded due to indirectness (variability in sedative doses administered, outcome definitions, discharge policies, and no report on insufflation technique, air vs. CO2 vs. water), while including only studies on colonoscopy raises doubts about the generalizability of the results for procedural sedation overall. Further downgrading was applied for the main outcome, i. e., adverse events, due to high inconsistency (high heterogeneity) and imprecision (broad CI crosses 1.0), resulting in a very low overall certainty of evidence, as shown in **Table 2.4.3s**.

RECOMMENDATION

2.4.2 ESGE and ESGENA suggest the provision of the ultrashort-acting sedative remimazolam in elderly patients and patients with cardiovascular and/or respiratory comorbidities.

Conditional recommendation, low certainty of evidence.

Summary of the evidence

Remimazolam is a newer water-soluble ultrashort-acting benzodiazepine that enhances gamma-aminobutyric acid-A (GABA-A) receptor activity, leading to sedation and anxiolysis. It is broken down by tissue esterases. The efficacy and safety of remimazolam have been intensively investigated in RCTs for procedural sedation. Remimazolam achieves more stable perioperative hemodynamics with a lower incidence of side effects. Individual studies and meta-analyses indicate a lower incidence of sedation-related side effects in patients sedated with remimazolam compared to propofol [94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121].

Ciprofol, a 2,6-disubstituted phenol analog, is a new intravenous anesthetic with a similar chemical structure to propofol that binds with the GABA-A receptor [122].

Benefits of remimazolam and ciprofol

Propofol, remimazolam, and ciprofol are the available ultrashort-acting sedatives (▶ **Table 7**). The task force panel identified that the most recent evidence evaluating the efficacy and safety of remimazolam compared to other sedatives, including propofol and ciprofol, is summarized in one network meta-analysis [123], one meta-analysis with trial sequential analyses [124] and two meta-analyses aiming to clarify the efficacy and safety of remimazolam versus propofol in patients aged 60 years and older who underwent upper and lower GI endoscopic procedures [119, 120]. More precisely, in the network meta-analysis that included 42 studies (34 for GI endoscopic procedures) with 10 540 patients, 31 studies compared propofol with remimazolam, 10 compared ciprofol with propofol, and one was a comparison of the three drugs.

A total of 31 studies were assessed as having a low risk of bias [123]. In the pairwise comparisons, although propofol had the shortest sedation induction time, there was no statistically significant mean difference among the three drugs: remimazolam versus propofol 0.16 min (95%CI 0.14–0.46); remimazolam versus ciprofol –0.04 min (95%CI –0.57 to 0.47); ciprofol versus propofol 0.20 min (95%CI –0.21 to 0.63). Similarly, no statistically significant mean difference regarding sedation recovery time was detected amongst the three drugs: remimazolam versus propofol 0.24 min (95%CI –0.86 to 1.33); remimazolam versus ciprofol 0.79 min (95%CI –1.10 to 2.70); ciprofol versus propofol 1.02 min (95%CI –0.55 to 2.61). In the pairwise analyses of the 34 GI endoscopy studies included in the network meta-analysis, the rate of respiratory AEs was statistically lower for remimazolam and ciprofol compared to propofol (RR 0.38, 95%CI 0.27–0.50, and RR 0.52, 95%CI 0.3–30.76, respectively), while no difference between remimazolam and ciprofol (RR 0.74, 95%CI 0.45–1.20) was detected. Regarding cardiovascular safety, remimazolam was superior to propofol and ciprofol (RR 0.49, 95%CI 0.38–0.61, and 0.60, 95%CI 0.38–0.92), respectively). No difference between ciprofol and propofol (RR 0.82, 95%CI 0.56–1.20) was detected. Given that remimazolam has a 56% cardiovascular relative risk reduction compared to propofol sedation, the authors state that remimazolam is a safer alternative for high-risk patients [123]. Although promising results are available, there are currently insufficient data to prioritize remimazolam over propofol in patients with hepatic encephalopathy [125].

In the systematic review with meta-analyses and sequential analyses [124], authors evaluated 63 RCTs (54 in GI endoscopy) with 84 comparisons (including a placebo arm) involving 13 953 patients. Remimazolam was compared to propofol as a single drug in 43 RCTs, and its administration was associated with a similar sedation success rate (RR 0.98, 95%CI 0.97–1.00) and with higher patient mean satisfaction compared to the active comparators (MD 0.3 points, 95%CI 0.0–0.5). Remimazolam had a lower risk of respiratory complications compared to propofol (RR 0.38, 95%CI 0.28–0.51) and a similar risk compared to ciprofol (RR 0.64, 95%CI 0.29–1.41). Remimazolam administration was also associated with a lower risk of cardiovascular complications compared to propofol (RR 0.40, 95%CI 0.33–0.49) and with a similar risk compared to ciprofol (RR 0.55, 95%CI 0.21–1.44) [124].

The first meta-analysis comparing remimazolam to propofol [119] included 7 RCTs involving 1466 patients aged 60 years and older who underwent GI endoscopic procedures. Remimazolam exhibited a significantly lower risk of bradycardia (OR 0.43, 95%CI 0.22–0.86), hypoxemia (OR 0.20, 95%CI 0.11–0.39), and pain on the injection site (OR 0.17, 95%CI 0.09–0.23). No statistically significant differences in sedation time, number of supplemental doses, procedural parameters, and other adverse outcomes were observed.

Similarly, in the other meta-analysis addressing this issue [120], remimazolam exhibited a significantly lower risk of AEs, including hypoxemia, respiratory depression, hypotension, bradycardia, and injection pain, compared to propofol in elderly patients undergoing GI endoscopy.

The task force panel also identified 14 RCTs [94, 95, 96, 101, 102, 105, 106, 108, 110, 113, 114, 116, 126, 127] evaluating the efficacy of remimazolam as monotherapy compared to propofol, which were not included in the aforementioned meta-analyses (**Table 2.4.2s**). The meta-analysis of these 14 RCTs showed that remimazolam led to a shorter sedation induction time (MD –0.41, 95%CI –0.70 to –0.12, I^2 = 97%, **Fig. 2.4.4s**) compared to propofol. On further analysis, the reported procedural time, sedation success, and patient satisfaction were similar between the two medication treatments (MD 0.69, 95%CI –0.74 to 2.13, I^2 = 54%, **Fig. 2.4.5s**; RR 0.99, 95%CI 0.90–1.09, I^2 = 98%, **Fig. 2.4.6s**; and MD 0.77, 95%CI –0.22 to 1.76, I^2 = 55%, **Fig. 2.4.7s**; respectively). The task force panel identified eight RCTs reporting on major AEs in trials comparing remimazolam and propofol in monotherapy. Remimazolam demonstrated a significantly lower total rate of AEs compared to pro-

pofol (RR 0.66, 95%CI 0.56–0.78, I^2 = 73%, **Fig. 2.4.8s**). This effect was consistent for hypotension (RR 0.40, 95%CI 0.29–0.54, I^2 = 75%, **Fig. 2.4.9s**), bradycardia episodes (RR 0.46, 95%CI 0.32–0.67, I^2 = 0%, **Fig. 2.4.10s**), and respiratory AE rate (RR 0.44, 95%CI 0.27–0.74, I^2 = 42%, **Fig. 2.4.11s**).

Regarding ciprofol, the task force panel identified six RCTs [127, 128, 129, 130, 131, 132] evaluating the efficacy and safety of ciprofol as monotherapy compared to propofol (**Table 2.4.2s**). The reported pooled sedation success rates were similar between the two medication treatments (RR 1.01, 95%CI 0.97–1.04, I^2 = 31%, **Fig. 2.4.12s**). Ciprofol resulted in a comparable total AE rate (RR 0.47, 95%CI 0.14–1.54, I^2 = 99%, **Fig. 2.4.13s**), hypotension (RR 0.86, 95%CI 0.72–1.04, I^2 = 32%, **Fig. 2.4.14s**), and bradycardia episodes (RR 1.28, 95%CI 0.79–2.08, I^2 = 0%, **Fig. 2.4.15s**). While the incidence of respiratory AEs was lower for ciprofol, this difference did not achieve statistical significance (RR 0.46, 95%CI 0.20–1.04, I^2 = 66%, **Fig. 2.4.16s**). Ciprofol is only marketed in China so far; thus, it is questionable whether the evidence can be generalized to other populations.

Harms of remimazolam

One scoping review [124] raises concerns about rare but serious adverse events detected in 73 trials and 36 case reports, involving 6740 patients who received remimazolam in the context of either sedation or general anesthesia. Delayed emergence of sedation was reported in 68 cases, anaphylaxis in 10, and re-sedation in 8 cases. These reactions are uncommon during procedural sedation but are more common in the elderly. Among those cases, there was only one of delayed emergence of sedation with remimazolam during endoscopy. Moreover, in one meta-analysis in patients aged 60 years or older remimazolam demonstrated a significantly longer time to loss of consciousness and lower sedation success after the first dose compared to propofol [119]. There is also a report [133] of two cases of anaphylaxis associated with remimazolam use for procedural sedation among the 15 anaphylactic episodes associated with remimazolam administration. Anaphylactic reactions are rare during sedation, but they might be associated with significant morbidity and mortality.

The underlying mechanism for remimazolam remains unclear; it might be an IgE-mediated reaction after midazolam exposure, or a non-IgE-mediated reaction to one excipient (e. g., dextran-40). The high cost of remimazolam as compared to midazolam may limit its widespread use.

Certainty of evidence

For remimazolam, studies included in the network meta-analysis were of good quality, and the certainty of evidence, as assessed using the GRADE approach, was very low to low [123]. All trials included in the systematic review with meta-analyses and trial sequential analyses were deemed at high risk of bias, and the certainty of the evidence was very low to low [124]. Overall, the studies included in the third meta-analysis were of a high quality and low risk of bias, with a certainty of evidence ranging from low to moderate [119]. The assessment of bias risk for each study not included in the two meta-analyses conducted by the task force is shown in **Table 2.4.3s**; the studies were of high quality. The certainty of evidence for the benefits and harms of remimazolam, shown in **Tables 2.4.7s–2.4.14s**, was downgraded to low due to inconsistency (moderate heterogeneity) and imprecision (broad CI crossing 1.0).

For ciprofol, the assessment of bias risks for each study is shown in **Table 2.4.3s**. Overall, the included studies were considered of high quality. The certainty of evidence was downgraded due to inconsistency (moderate heterogeneity) and imprecision (broad CI crossing 1.0). Thus, the certainty of evidence was downgraded to low (**Tables 2.4.15s–2.4.19s**).

RECOMMENDATION

2.4.3 ESGE–ESGENA suggest exercising caution when combining ultrashort-acting sedatives with other sedatives or analgesics.

Conditional recommendation, low certainty of evidence.

Summary of the evidence

Addition of other sedatives and/or analgesics (especially those with a short half-life) to short-acting sedatives such as propofol, remimazolam, and ciprofol has been proposed. The aim is to lower the dose of the primary sedative and to increase the safety of the sedation regimen, and patient and endoscopist satisfaction, without compromising efficacy during GI endoscopic procedures. There are several RCTs – even meta-analyses, concerning the combination of short-acting sedatives with short-acting analgesics – that favor these combinations. Notably, almost all data derived from these studies include mainly low-risk patients undergoing low-risk procedures.

For ERCP, the best evidence for the combination of sedatives originates from a network meta-analysis that included 42 RCTs evaluating different sedative–analgesic combinations in ASA I–III patients [134]. The results indicate that midazolam plus pethidine plus dexmedetomidine, propofol plus oxycodone, and dexmedetomidine plus fentanyl exhibited lower rates of adverse events compared with propofol. The value of this publication is limited by several factors: the inclusion of studies that evaluate long-acting sedatives and analgesics that are rarely used in endoscopy (such as oxycodone); the limited availability of certain outcomes; the potential bias introduced by comparisons based on a single study; and lack of detailed information regarding dosage combinations and administration methods.

The number and quality of the studies, the underrepresentation of high-risk ASA classification patients, the administration of these combination regimens in low-risk endoscopic procedures in different dosages, and the fact that all studies have been conducted in Asia highlight the low certainty of evidence for this recommendation.

Benefits of the addition of dexmedetomidine to propofol

Dexmedetomidine is an α2-adrenergic agonist acting in several parts of the brain. It reduces sympathetic nervous system activity, leading to a relaxing and sleep-inducing effect. The task

force identified five RCTs [135, 136, 137, 138, 139] informing the AE outcomes related to dexmedetomidine in combination with propofol compared to propofol monotherapy (**Table 2.4.2s**). Addition of dexmedetomidine resulted in significantly fewer hypotension (**Fig. 2.4.17s**, RR 1.75, 95%CI 1.09–2.83, I^2 = 0%) and bradycardia episodes (**Fig. 2.4.18s**, RR 3.44, 95%CI 1.73–6.84, I^2 = 0%) as well as lower total respiratory AE rate (**Fig. 2.4.19s**, RR 0.35, 95%CI 0.17–0.71, I^2 = 0%) compared to propofol monotherapy.

Harms of the addition of dexmedetomidine to propofol

Delayed discharge readiness has been associated with addition of dexmedetomidine to propofol [135, 136, 137, 138, 139, 140].

Certainty of evidence

The bias risk assessment for each study is detailed in **Table 2.4.3s**, and all included studies were deemed of high quality overall. The level of certainty for the evidence presented in **Tables 2.4.20s**, **2.4.21s**, and **2.4.22s** was reduced to low. This downgrade is due to the limited number of RCTs and the small number of studies, all conducted in Asia and involving no high-risk patients. These patients underwent low-risk procedures under sedation, and the studies did not use a standardized dosage scheme for the drug combination.

Benefits of the addition of lidocaine to propofol

The most recent meta-analysis investigating the effects of adding lidocaine to propofol sedation in patients undergoing colonoscopy included eight RCTs with 520 patients [141]. Compared with propofol monotherapy, intravenous lidocaine reduced propofol consumption (MD −42.93 mg, 95%CI −62.89 to −22.97), shortened awakening time (MD −3.38 minutes, 95%CI −5.92 to −0.84), reduced post-procedural pain scores (MD −1.38, 95%CI −2.72 to −0.04), and increased patient satisfaction scores (MD 0.50, 95%CI 0.30–0.70). No significant differences were detected between the groups regarding hypoxia or hypotension rates, procedure duration, and endoscopist satisfaction.

The task force pooled the results of two RCTs [142, 143], not included in the meta-analysis, regarding the rate of respiratory AEs (**Table 2.4.2s**). Addition of lidocaine led to a significantly lower rate of respiratory AEs compared to propofol monotherapy (**Fig. 2.4.20s**, RR 0.48, 95%CI 0.25–0.92, I^2 = 0%).

Certainty of evidence

The quality of the studies included in the meta-analysis [141] was deemed high. The studies primarily involved ASA physical status I and II patients. Two of the eight trials included patients younger than 18 years. Additionally, significant heterogeneity was observed between studies for some outcomes. Thus, the certainty of evidence was rated as low to moderate. The bias risk assessment for the two RCTs is detailed in **Table 2.4.3s**, and all included studies were deemed of high quality overall. The certainty of evidence detailed in **Tables 2.4.23s** was downgraded to low, as explained above.

Benefits of the addition of etomidate to propofol

Etomidate is a short-acting intravenous hypnotic. It has a rapid onset of action with advantages in terms of hemodynamics and respiration as compared to propofol. It has been investigated as monotherapy and in combination with propofol, benzodiazepines, and opiates. One meta-analysis (15 studies, 2973 participants) showed that using etomidate in combination with propofol, compared to propofol alone, was safer in terms of sedation-related AEs, including hypoxia (OR 0.16, 95%CI 0.08–0.33, I^2 = 0%), hypotension (OR 0.05, 95%CI 0.01–0.19, I^2 = 79%), and injection site pain (OR 0.14, 95%CI 0.07–0.26, I^2 = 70%); no difference was detected regarding heart rate in patients undergoing gastroscopy [144].

The task force identified two RCTs [145, 146] evaluating the efficacy and safety of etomidate-propofol combination in patients undergoing gastroscopy, which were not included in the meta-analysis (**Table 2.4.2s**). Due to differences in study design and outcomes reporting, the results of these RCTs could not be pooled. However, both studies confirmed the benefits of the combination regimen.

Harms of the addition of etomidate to propofol

According to the meta-analysis [144], the combination slightly increases the recovery time (MD 0.14, 95%CI 0.04–0.24, I^2 = 0%), the risk for myoclonus (OR 3.07, 95%CI 1.73–5.44, I^2 = 0%), and the nausea/vomiting rate (OR 1.46, 95%CI 1.04–2.03, I^2 = 0%). No more harms were reported in the two RCTs [145, 146].

Certainty of evidence

The quality of the studies included in the meta-analysis ranged from low to moderate. These studies primarily focused on patients with ASA I and II undergoing low-risk procedures. Additionally, significant variability in outcomes across the studies, indicated considerable heterogeneity. Hence, the overall certainty of evidence was assessed as very low to low.

Benefits of the addition of esketamine to propofol

Esketamine is an antagonist of the N-methyl-D-aspartate receptor, which has analgesic and anesthetic effects. In combination with propofol, it has demonstrated improved safety, particularly regarding cardiorespiratory side effects. Four RCTs [147, 148, 149, 150] listed in **Table 2.4.2s** reported the outcomes of SAEs between esketamine combined with propofol as compared to propofol monotherapy. Addition of esketamine resulted in significantly fewer hypotension episodes (**Fig. 2.4.21s**, RR 0.46, 95%CI 0.23–0.94, I^2 = 36%) compared to propofol. Although bradycardia episodes and total respiratory AE rate were lower in the esketamine group, the difference failed to reach significance for both outcomes (**Fig. 2.4.22s**, RR 0.33, 95%CI 0.10–1.12, I^2 = 35%, and **Fig. 2.4.23s**, RR 0.47, 95%CI 0.21–1.05, I^2 = 70%, respectively).

Harms of the addition of esketamine to propofol

Esketamine should be used with caution, considering the possibility of its psychotomimetic effects [147, 148, 149, 150].

Certainty of evidence

The risk of bias assessment for each study is detailed in **Table 2.4.3s**. Overall, the included studies were considered of high quality. The certainty of evidence for all outcomes was downgraded to low due to inconsistency (moderate heterogeneity) and imprecision (broad CI crossing 1.0) (**Tables 2.4.24s**, **2.4.25s**, and **2.4.26s**).

Harms of the addition of midazolam to propofol

The addition of midazolam to propofol sedation did not result in a difference in cognition, quality of recovery, or discharge times [151]. In patients with advanced cirrhosis, no difference in safety profile or cognitive impairment was observed, but adding midazolam to propofol was associated with higher endoscopist satisfaction [152]. However, the addition of propofol to a midazolam and fentanyl combination has been associated with a lower dose of midazolam, leading to improved post-procedural cognition [153]. Overall, midazolam-based regimens with propofol are associated with a lower sedation success rate and longer recovery times and, therefore, they are no longer recommended [154].

Benefits of the addition of short-acting opioids to short-acting sedatives

New short-acting analgesic agents such as alfentanil and sufentanil might be combined with sedatives such as propofol, remimazolam, and ciprofol with an additive analgesic effect. The task force summarized the most recent evidence on this topic by discussing three recent meta-analyses [118, 155, 156].

Addition of alfentanil to propofol versus propofol monotherapy

The meta-analysis of 13 RCTs involving 1762 patients undergoing GI endoscopic procedures [155] showed that compared with propofol alone, alfentanil combined with propofol had, for the primary analysis endpoints, a more stable mean arterial pressure (MD 5.38, 95%CI 1.97–8.80, I^2 = 91%), heart rate (MD 3.78, 95%CI 1.30–6.26, I^2 = 80%), and pulse oxygen saturation (MD 1.90, 95%CI 0.93–2.78, I^2 = 97%) with lower propofol dose (MD −2.82, 95%CI −3.70 to −1.94, I^2 = 98%), and shorter awakening time (MD −3.23, 95%CI −4.01 to −2.45, I^2 = 98%). Regarding AEs, there was a lower incidence of hypotension (RR 0.23, 95%CI 0.12–0.46, I^2 = 0%), respiratory depression (RR 0.37, 95%CI 0.15–0.89, I^2 = 0%), nausea and vomiting (RR 0.32, 95%CI 0.14–0.71, I^2 = 0%), and cough reflex (RR 0.33, 95%CI 0.12–0.89, I^2 = 0%).

These results suggest that combining propofol with alfentanil might provide greater efficacy than utilizing propofol alone, with a lower rate of adverse reactions in patients undergoing GI endoscopy [155].

Addition of short-acting analgesics to remimazolam versus addition of short-acting analgesics to propofol

This meta-analysis [118] included 15 trials with 4516 patients who underwent upper and lower GI endoscopies (one RCT included ERCP only). The meta-analysis examined the efficacy and safety of remimazolam combined with opioid analgesics (RCTs analyzed: alfentanil, 5; sufentanil, 5; fentanyl, 4; and remifentanil, 1) compared pairwise to propofol combinations with the same analgesics.

Remimazolam combinations resulted in a marginally lower sedation success rate (RR 0.99, 95%CI 0.98–1.00, I^2 = 0%) and a slightly longer induction time (MD 9 s, 95%CI 4–13, I^2 = 93%), whereas there was no significant difference between the sedative combinations in other time-related outcomes (total sedation time, and time to discharge). Remimazolam combinations were associated with significantly lower rates of respiratory depression (RR 0.41, 95%CI 0.30–0.56, I^2 = 46%), hypotension (RR 0.43, 95%CI 0.35–0.51, I^2 = 65%), and bradycardia (RR 0.42, 95% CI 0.30–0.58, I^2 = 0%).

There was no difference in patient and endoscopist satisfaction between the combinations. These results indicate that the combination of remimazolam with a short-acting opioid offers similar efficacy and enhanced safety compared to a propofol-based combination for sedation during GI endoscopies [118].

Addition of short-acting analgesics to ciprofol vs. addition of short-acting analgesics to propofol

This meta-analysis [156] included 17 RCTs and 2800 patients who underwent upper or lower GI endoscopy (ciprofol arms 1450, propofol arms 1350 patients, in total). In pairwise comparisons, in 10 RCTs sulfentanil was combined with ciprofol or propofol, in 3 RCTs no opioid was added to ciprofol or propofol, and, in 1 RCT each, alfentanil, remifentanil, butorphanol or nalbuphine were combined with ciprofol or propofol.

The meta-analysis showed no statistically significant difference in the sedation success rate or recovery time between the two groups across all age categories. The incidences of hypotension (OR 0.48, 95%CI 0.32–0.72, I^2 = 59%), bradycardia (OR 0.66, 95%CI 0.49–0.87, I^2 = 19%), respiratory depression (OR 0.21, 95%CI 0.15–0.30, I^2 = 0%), and injection pain (OR 0.08, 95%CI 0.05–0.15, I^2 = 58%), in the ciprofol group were lower than those in the propofol group. The results were consistent across all age groups, including the elderly, and indicate that ciprofol combinations with short-acting opioid analgesics had a higher safety profile than those of propofol [156].

Certainty of evidence

One common concern of all the meta-analyses is that almost every study involved patients originating from China, thus limiting the generalizability of the results. The task force raised questions about the risks of bias of the studies included in the first meta-analysis [155]. There was heterogeneity regarding the results for the primary endpoints results and indirectness due to the inclusion of patients with undefined ASA physical status who underwent only low-risk procedures. Thus, the certainty of evidence was rated very low.

Regarding the remimazolam meta-analysis [118], the risk of bias for each included study was low. Some outcomes had a significant between-study heterogeneity, and indirectness was detected due to the inclusion of ASA physical status I and II patients who underwent mainly low-risk procedures. Thus, the certainty of the evidence was rated low for this meta-analysis [118].

The task force raised questions about the risks of bias in the studies included in the ciprofol meta-analysis [156]. There were differences in the definition of anesthesia protocol and of some outcome indicators in the study, which led to high heterogeneity in some results, and all studies involved patients originating from China, thus limiting the generalizability of the results. The certainty of evidence of the results of the ciprofol meta-analysis was rated as very low.

RECOMMENDATION

2.4.4 ESGE and ESGENA do not suggest routine use of an anesthetic throat spray (xylocaine) during gastroscopy under deep sedation.

Conditional recommendation, very low certainty of evidence.

Summary of the evidence

Topical pharyngeal anesthesia can enhance patient tolerance during procedures without sedation or under moderate sedation. It also aids in esophageal intubation, improves endoscopist satisfaction, and reduces side effects, such as the gag reflex, pain, and discomfort. Xylocaine (lidocaine) is the most often used agent, administered as a spray, nebulized, viscous fluid, lozenge, lollipop, or ice popsicle.

Benefits

The task force identified eight recent RCTs [157, 158, 159, 160, 161, 162, 163, 164]; six evaluated the administration of xylocaine topical throat anesthetic during sedated gastroscopy with propofol, while no sedation was administered in the remaining two (**Table 2.4.4.2s**).

No difference was reported concerning mean propofol dose when topical anesthetic xylocaine was administered, compared to placebo (MD –29.82, 95%CI –92.33 to 32.68, I^2 = 100%; **Fig. 2.4.4.1s**). Evaluation of procedures under propofol sedation showed that endoscopist and patient satisfaction were also similar between the two groups (MD 0.53, 95%CI –2.13 to 3.18, I^2 = 0%, **Fig. 2.4.4.2s**; and MD 3.44, 95%CI –4.05 to 10.92, I^2 = 0%, **Fig. 2.4.4.3s**; respectively).

Harms

The pooling of RCTs with procedures performed under propofol sedation showed no difference in discomfort/tolerance (MD –9.75, 95%CI –22.88 to 3.39, I^2 = 99%, **Fig. 2.4.4.4s**). In contrast, coughing was more likely to occur when a topical xylocaine anesthetic was administered (RR 0.46, 95%CI 0.28–0.76, I^2 = 49%, **Fig. 2.4.4.5s**).

Certainty of evidence

The risk of bias assessment for each study is detailed in **Table 2.4.3s**. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to inconsistency (moderate heterogeneity), imprecision, and indirectness, so the quality of evidence was downgraded to very low as shown in **Tables 2.4.4.3s–2.4.4.7s**.

RECOMMENDATION

2.4.5 ESGE–ESGENA do not suggest routine use of antispasmodics during sedated colonoscopy.

Conditional recommendation, very low certainty of evidence.

Summary of the evidence

Hyoscine butylbromide, hyoscyamine, scopolamine, and other antispasmodic agents are used in gastrointestinal endoscopic procedures, mostly for colonoscopy. While there is some evidence that their use is associated with higher ADR, their benefit in reducing the need for sedation cannot be established.

Benefits

Two RCTs published in 2014 and 2016 randomly assigned patients to receive intravenous hyoscine butylbromide (n = 116) versus placebo (n = 121), in combination with propofol [165, 166] (**Table 2.4.5.2s**). Pooling the results of these two RCTs showed that addition of hyoscine butylbromide reduces neither the total dose of propofol (MD 0.11, 95%CI –0.35 to 0.56, I^2 = 0%, **Fig. 2.4.5.1s**) nor total procedure time (MD 0.83, 95%CI –0.58 to 2.24, I^2 = 0%, **Fig. 2.4.5.2s**). Moreover, the use of antispasmodics other than hyoscine butylbromide also does not improve either cecal intubation time (MD 1.29, 95%CI –0.55 to 3.12, I^2 = 0%; **Fig. 2.4.5.3s**) or technical difficulty of the examination (MD 0.01, 95%CI –0.24 to 0.22, I^2 = 54%; **Fig. 2.4.5.4s**). In addition, there was no difference in pain reported by the patients (MD –0.16, 95%CI –0.59 to 0.27, I^2 = 60%; **Fig. 2.4.5.5s**).

In a 2020 meta-analysis that included six studies, spraying of peppermint oil during colonoscopy resulted in lower spasticity. The cecal intubation time was similar, as well as the report of pain. The use of sedation and technical difficulty were not evaluated [167].

Harms

The pooling of results from RCTs evaluating hyoscine butylbromide as an adjunct to propofol during colonoscopy showed a significant effect on heart rate (MD 21.53, 95%CI 16.63–26.43, I^2 = 44%; **Fig. 2.4.5.6s**). However, no serious AEs were reported.

Certainty of evidence

The risk of bias assessment for each study is detailed in **Table 2.4.3s**. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to inconsistency (moderate heterogeneity), imprecision, and indirectness, so the quality of evidence was downgraded to very low as shown in **Tables 2.4.5.3s–2.4.5.8s**.

2.5 Nonpharmacological adjuncts to sedation

RECOMMENDATION

2.5 ESGE and ESGENA suggest offering nonpharmacological techniques (virtual reality or music) as complementary options to sedation administration during gastrointestinal endoscopy based on patient and endoscopist preference.

Conditional recommendation, very low certainty of evidence.

Summary of the evidence

Nonpharmacological interventions such as a virtual reality experience or music can be offered to patients undergoing GI endoscopy, in addition to pharmacological sedation. Evidence indicates some benefits in terms of subjective outcomes, such as patients' pain levels and overall satisfaction [168].

Benefits

The task force identified a recent meta-analysis [168] incorporating evidence from 12 RCTs assessing the effect of nonpharmacological techniques, such as virtual reality and music as adjuncts to sedation administration, on patients' reported pain during GI endoscopic procedures. Compared to standard sedation groups, the addition of nonpharmacological techniques resulted in significantly lower pain (MD −1.02, 95%CI −1.64 to −0.41, I^2 = 64%), and reduction in patient anxiety levels (MD −1.07, 95%CI −1.75 to −0.39, I^2 = 20%) with significantly higher patient satisfaction (MD 1.67, 95%CI 0.50–2.84), I^2 = 94%).

Addition of nonpharmacological techniques led to lower, albeit nonsignificant, mean doses of midazolam and analgesia compared to standard sedation alone (MD −0.43, 95%CI −0.88 to 0.02, I^2 = 93%; and MD −1.41, 95%CI −4.14 to 1.32, I^2 = 51%; respectively).

Another systematic review and meta-analysis [169] also detected a positive role for music (total 11 RCTs, 9 sedation plus music; 1590 patients) and task distraction (12 RCTs, 4 sedation plus distraction task; 1163 patients) to reduce pain and anxiety for patients undergoing colonoscopy.

With music intervention, there was a significant weighted mean pain score reduction of 1.50 (95%CI 0.69–2.31, I^2 = 83.5%). For anxiety, the weighted mean reduction was 3.56 (95%CI 0.86–6.27, I^2 = 66.7%), which was also significant. Among the studies that reported sedation, six studies reported a significant pain reduction, and four reported no significant pain reduction. Five studies measured anxiety and sedation use, with only one study reporting a significant reduction.

A significant improvement in pain scale reporting was found for 14 of the 16 distraction techniques. Weighted mean pain score reduction was 1.59 (95%CI 0.79–2.39, I^2 = 91.8%). In studies with sedation, there was a significant mean pain score reduction (1.23, 95%CI 0.68–1.78, I^2 = 9%). A significant improvement in anxiety scale scoring was found for 3 out of 9 distraction techniques. Overall, there was a significant weighted mean anxiety score reduction of 7.49 (95%CI 3.64–11.35, I^2 = 96%). In studies with sedation, no significant mean anxiety score reduction was detected.

Harms

No significant differences were evident in the vital signs with the use of the nonpharmacological techniques compared to standard sedation alone (systolic blood pressure, MD −3.10, 95%CI −8.15 to 1.96), I^2 = 75%; oxygen saturation, MD 0.32, 95%CI −0.68 to 1.32, I^2 = 36%; and pulse/min, MD −3.52, 95%CI −9.49 to 2.45), I^2 = 88%) [168]. The meta-analysis of Ahmed et al. [169] did not evaluate any objective measures, as outlined above.

Certainty of evidence

The overall quality of evidence was downgraded due to risks of performance and detection bias in most studies, inconsistency (serious heterogeneity), and indirectness. Thus, the certainty of evidence was downgraded to very low in the meta-analysis by Roelandt et al. [168] Similarly, the certainty of evidence of the Ahmad et al. [169] meta-analysis was downgraded to very low due to high heterogeneity, imputed missing data during statistical analysis, the variety of distraction techniques, and the impact of distraction overall versus a specific type of distraction technique being utilized.

3. Requirements for safe sedation administration

3.1 Who should monitor the sedated patient?

RECOMMENDATION

3.1 ESGE and ESGENA recommend the provision of sedation by a dedicated healthcare professional trained in the administration of sedation and patient monitoring.

Strong recommendation, very low certainty of evidence.

Summary of the evidence

The task force concluded that the topic had been thoroughly addressed by the task force panel for section **2. Type of sedation**, and supports their Recommendation 2.3 on *Sedation provider during endoscopy*.

3.2 Equipment required for monitoring patients undergoing GI endoscopy under sedation

To reduce the risk of sedation-related complications, appropriate patient monitoring is crucial. Recent societal guidance from the United Kingdom and from Germany indicates that safe sedation requires monitoring of vital signs to reduce the risk of hypoxia, bradycardia, or hypotension. This includes oxygen supplementation, continuous pulse oximetry, noninvasive blood pressure monitoring, and heart rate monitoring for the entire duration of the procedure [2,3]. Furthermore, specific recommendations include using continuous capnography to measure end-tidal carbon dioxide, employing bispectral index

(BIS) monitoring to assess sedation depth, and administering high-flow oxygen to enhance patient safety in targeted patient cohorts.

3.2.1 Capnography monitoring

RECOMMENDATION

3.2.1 ESGE and ESGENA suggest capnography monitoring for patients undergoing sedated gastrointestinal endoscopy who are at higher risk of hypoxemia.

Conditional recommendation, very low certainty of evidence.

Summary of the evidence

One systematic review and meta-analysis [170] included nine sets of data from eight RCTs (one pediatric) involving 3088 patients who underwent upper and lower GI endoscopies, ERCP, EUS, and other interventional procedures. These were primarily performed under propofol (five studies), and the rest used fentanyl, midazolam, meperidine, ketamine, or combinations of the sedatives/analgesics.

The evidence showed that the addition of capnography to standard monitoring significantly reduced the incidence of hypoxemia, the primary endpoint, defined as SpO_2 <90% or <95% (OR 0.61, 95%CI 0.49–0.77, I^2 = 43%), and severe hypoxemia, the secondary endpoint, defined as SpO_2 <85% (OR 0.53, 95%CI 0.35–0.81, I^2 = 53%). On the other hand, for the rest of the secondary outcomes, namely apnea episodes, incidences of bradycardia or hypotension, assisted ventilation oxygen supplementation, early procedure termination rate, patient satisfaction, and cooperation, there was no advantage to incorporating capnography into the standard monitoring process. The overall quality of the studies was moderate to low, using the GRADE approach (**Table 3.2.1.1s**).

The evidence accumulated following the publication of the above meta-analysis shows that the advantage of capnography monitoring in reducing the risk of hypoxemia is consistent among RCTs and non-RCT studies, regardless of either the invasiveness of the endoscopic procedures or the administered sedation regimen. However, the benefit appears greater in patients at higher risk of respiratory compromise or undergoing deeper sedation. On the other hand, the positive effect of capnography monitoring regarding the rest of the safety parameters (death, need for assisted ventilation, termination of the procedure, among them) is either absent or inconsistent (regarding ability to lower the amount of propofol).

Benefits

The task force panel identified three RCTs [171, 172, 173] evaluating the efficacy of capnography monitoring in addition to standard monitoring in reducing the incidence of sedation-related adverse events (**Table 3.2.1.1s**). Two RCTs [171, 173] involved high-risk procedures (percutaneous endoscopic gastrostomy tube placement, ERCP, and EUS) performed under either propofol [171] or nonpropofol-based regimens [173], and one involved low-risk upper and lower GI endoscopies done under propofol sedation [172]. The panel also identified four service evaluation studies (before and after implementation of capnography monitoring) [174, 175, 176, 177] and one prospective cohort study [178], which included high- and low-risk procedures performed under different sedation regimens. Two of the service studies also included patients who underwent bronchoscopy [174, 176] and cardiology interventions [176]. Pooling of the results of the above eight studies showed a significantly lower risk ratio for oxygen desaturation (the definition varied across the studies) with the addition of capnography to standard monitoring (RR 0.61, 95%CI 0.46–0.82, I^2 = 74%; **Fig. 3.2.1.1s**) This effect was significant for the RCTs (RR 0.57, 95%CI 0.35–0.93, I^2 = 70%; **Fig. 3.2.1.1s**) and the non-RCT studies (RR 0.64, 95%CI 0.43–0.96, I^2 = 80%; **Fig. 3.2.1.1s**). In studies that analyzed non-GI endoscopy patients, the risk ratio of oxygen desaturation was numerically lower in the capnography group (RR 0.74, 95%CI 0.30–1.83, I^2 = 89%), specifically among the non-RCT studies.

The panel also pooled the incidence of oxygen desaturation in the three RCTs [171, 172, 173] with that of five adult RCTs included in the meta-analysis by Kim et al. [170]. Analysis showed that the addition of capnography to standard monitoring significantly reduced the incidence of oxygen desaturation (definitions vary across studies), as shown in **Fig. 3.2.1.2s**, (RR 0.74, 95%CI 0.63–0.85, I^2 = 61%). Notably, the positive impact of capnography was consistently significant for both low- and high-risk procedures in terms of oxygen desaturation (**Fig. 3.2.1.2s**). Regarding the type of sedation (propofol vs. nonpropofol vs. mixed regimens), the addition of capnography was related to a lower risk ratio of oxygen desaturation; nevertheless, statistical significance was detected only in propofol studies (**Fig. 3.2.1.3s**).

It has been published [179] that capnography may have a clinically significant positive impact on hypoxia detection only during long-lasting procedures. The task force attempted to assess how the duration of procedures affected the outcomes in the studies referenced earlier. However, the exact duration of the procedures was reported in only two of these studies, making it impossible to draw meaningful conclusions from the analysis. In a before-and-after service evaluation study [174] subanalysis, among the patients monitored with capnography, the risk ratio for AE incidence during recovery was almost 5-fold lower compared to that during the procedure, indicating the value of capnography during recovery.

Harms

The task force panel did not find any evidence that adding capnography to standard monitoring results in lower amounts of propofol administration. They also did not detect any positive impact of capnography monitoring on major AEs, such as death and hospitalization. While the effects of this monitoring method vary in the literature regarding other outcomes, including endoscopist and patient satisfaction, the overall findings have shown no significant benefits.

From the policymakers' perspective, the cost of implementing capnography in all patients has been calculated as minimal [174, 176], although this may vary locally. However, it is considered to be cost-saving, bearing in mind the overall costs of monitoring and the management of AEs. Whilst the implementation of capnography would require staff to be trained to use and interpret it, this could be included in safe sedation courses as a short module. The recommendation currently is that capnography be used in patients at higher risk of hypoxemia. Such patient groups include, amongst others, those with respiratory or neuromuscular disorders, with morbid obesity or comorbidities, elderly or frail patients, and also those undergoing prolonged endoscopic procedures with a higher requirement for procedural sedation [1, 2].

Certainty of evidence

Tables 3.2.1.2s and **3.2.1.3s** provide the risk of bias assessment for each study. Overall, the included studies were considered of high quality.

The certainty of evidence was downgraded due to indirectness (heterogeneity in the endoscopic expertise), and to low due to inconsistency for the benefits regarding hypoxemia, as shown in **Table 3.2.1.4s**. Due to the absence of evidence regarding major AEs and propofol dose reduction, as well as the inconsistent effects on other secondary outcomes, we further downgraded the certainty of evidence to very low.

3.2.2 Bispectral index (BIS) monitoring

RECOMMENDATION

3.2.2 ESGE and ESGENA do not recommend routine bispectral index monitoring for patients undergoing gastrointestinal endoscopic procedures with propofol.
Strong recommendation, very low certainty of evidence.

Summary of the evidence

Bispectral index (BIS) monitoring is a noninvasive method used to assess the depth of sedation. It measures brain activity by analyzing electroencephalogram and electromyogram signals, providing a numerical score (0–100) that correlates with the patient's level of consciousness. It has been used to determine the appropriate level of sedation or anesthesia for a patient, with the expectation of enhanced sedation safety and a lower amount of administered sedative. One systematic review and meta-analysis [180] included 13 sets of data from 12 articles (including 1 each on bronchoscopy and endobronchial ultrasound) with 1372 patients; propofol was administered either as monotherapy or in combination with other sedatives in 11 sets. The meta-analysis showed that the addition of BIS to standard monitoring significantly reduced the incidence of intraprocedural hypoxia (RR 0.76, 95%CI 0.62–0.93, I^2 = 37%); however, the subsequent trial sequential analysis did not confirm this finding. Another meta-analysis [181] of 12 datasets from 11 RCTs showed that although the mean propofol dose was not significantly lower in the BIS arm, the total amount of propofol administered was lower in the BIS arm (pooled SMD −0.15, 95%CI −0.28 to −0.01, I^2 = 28%). In both meta-analyses, none of the secondary surrogates for safety outcomes and patient satisfaction were significantly higher in the BIS arms (**Table 3.2.2.1s**).

The accumulated evidence following the publication of the two meta-analyses has not changed the effects for outcomes, indicating that no significant relevant advantages for the use of BIS monitoring in GI endoscopy exist, apart from the potential for lowering the total dose of propofol. Therefore, the use of such monitoring cannot be routinely recommended.

Benefits

The task force panel identified three RCTs [182, 183, 184], and one prospective [185] and one retrospective [186] study, in addition to the two aforementioned meta-analyses evaluating the effect of BIS in addition to standard monitoring. Regarding the dose of propofol, pooling the effects of one set [183] and two sets [184, 185], among the studies evaluated in the meta-analyses, did not change the overall size and direction effect (SMD −0.25, 95%CI −0.47 to −0.04, I^2 = 61%, and SMD −0.41, 95%CI −1.37 to 0.55, I^2 = 97%) as shown in **Figs. 3.2.2.1s** and **3.2.2.2s**, respectively, indicating a significant reduction in total but not in mean propofol dose.

Harms

The studies reported inconsistent effects of BIS monitoring on the surrogate outcomes of safety and patients' satisfaction [182, 183, 184, 185, 186]. Thus, these results could not be pooled with the results of the two meta-analyses.

Certainty of evidence

Table 3.2.2.2s provides the risk of bias assessment for each study. Overall, the included studies were considered of high quality. The certainty of evidence for the outcome of total propofol dose was downgraded due to inconsistency (moderate heterogeneity); hence, the quality of evidence was downgraded to moderate, and a conditional recommendation was proposed. For the outcome of mean propofol dose, further downgrading was applied due to imprecision (broad CI crossing 1.0); thus, the quality of evidence was downgraded to very low, and a conditional recommendation was proposed.

3.2.3 Oxygen supplementation with high-flow nasal cannula (HFNC)

RECOMMENDATION

3.2.3 ESGE and ESGENA do not recommend routine oxygen supplementation via high-flow nasal cannula for patients undergoing gastrointestinal endoscopic procedures with propofol.
Strong recommendation, very low certainty of evidence.

Summary of the evidence

High-flow nasal cannula (HFNC) promises better oxygenation than conventional ventilation devices and can be considered as an option in GI endoscopy. The device's unique feature is delivery of humidified oxygen at flows of up to 60–80 L/min, allowing for adjustable titration of the inspired oxygen fraction, reaching up to 100%. Furthermore, HFNC enables the application of positive end-expiratory pressure of up to 7.5 cmH_2O, preventing collapse of the upper airways and reducing dead space to decrease the work of ventilation through CO2 washout [187].

There is evidence from three meta-analyses that HFNC oxygen supplementation decreases the risk for hypoxemia during sedated GI endoscopy [188, 189, 190]. However, high heterogeneity potentially attributed to variances of the endoscopic procedures (small sample, inadequate representation of colonoscopy, sedation agents, depth of sedation, duration of endoscopy), and HFNC flow characteristics (flow rate, fraction of inspired oxygen), as well as inability to identify patient and procedure specifics which may benefit more from this modality, may limit the clinical value of this observation.

Benefits

The task force panel identified three meta-analyses [188, 189, 190], published between 2022 and 2024, that evaluated the potential benefits of administering oxygen via HFNC compared to standard nasal cannula during sedated GI endoscopy. The meta-analyses included 5, 7, and 11 studies [188, 189, 190], respectively, with up to 3726 participants, evaluating patients undergoing mainly sedated (with varying agents) gastroscopy and ERCP. All meta-analyses showed that HFNC reduced the odds for hypoxemia (the definition varied across studies) compared to standard cannula oxygen administration, with ORs ranging from 0.12, 95%CI 0.03–0.59, $I^2 = 82.5\%$ [188] to 0.39, 95%CI 0.29–0.53, $I^2 = 46\%$ [189]. One of the three meta-analyses [190] showed that the benefit was restricted only to patients with low risk of hypoxemia (arbitrarily defined as BMI <30, or without obstructive sleep apnea syndrome, or ASA physical status I or II), and a further meta-analysis [189] showed that the benefit was equal for patients undergoing either gastroscopy or ERCP, with very low heterogeneity [191, 192] (**Table 3.2.3.1s**). Only one meta-analysis examined the effect of HFNC on the unexpected termination of the procedure, showing a positive effect. The meta-analyses also reported inconsistent effects on the need for airway intervention (one study neutral [188] and two studies [189, 190] positive effects). One meta-analysis showed that HFNC use had no impact on the incidence of hypercapnia [190] (**Table 3.2.3.1s**).

Harms

No clinical harms have been detected in the literature. Neither cost–effectiveness data analysis nor evaluation of the setting burden for HFNC have been published yet.

Certainty of evidence

The quality of the studies included in the meta-analyses was low to moderate, with multiple risks of bias for the RCTs. The certainty of evidence for the hypoxemia outcome was downgraded, due to heterogeneity, indirectness, and inconsistency, to very low for all the meta-analyses.

3.3 Reversal agents should be restricted to the management of sedation-analgesia adverse events only

RECOMMENDATION

3.3 ESGE and ESGENA recommend that the use of reversal agents should be restricted to managing sedation-analgesia adverse events that do not improve with nonpharmacological intervention.

Strong recommendation, very low certainty of evidence.

Summary of the evidence

The evidence that routine use of reversal agents (flumazenil and naloxone) has been associated with fast resolution of baseline psychomotor skills, improved levels of consciousness, and shorter discharge time, without significant differences in patient satisfaction, psychological status, or procedure-related discomfort has been extensively discussed in the recently issued guidance documents [2, 3]. Administration of reversal agents (especially flumazenil) has been associated with AEs, and patients may exhibit residual sedation with increased recovery time, and thus implications for the procedure cost. Cardiopulmonary sedation-related AEs are the most common sedation-related complications, with hypoxia, hypotension, or bradycardia being the common complications during GI endoscopy. Almost all these complications can be managed without reversal agents. Despite the relatively common sedation-related complications during GI endoscopy, the need for reversal agents is relatively rare. A recent study involving 119 860 patients found that only 26 individuals (0.02%) required reversal agents [193]. The most common reason for administering these agents was hypoxia. Additionally, flumazenil demonstrated effectiveness in achieving complete endoscopy amongst patients who experienced paradoxical reactions to midazolam, with a success rate of 93.3% [194].

Currently, there is no evidence for using reversal agents for all patients undergoing endoscopy, and we recommend the use of a relevant reversal agent only in patients with opiate or benzodiazepine-induced respiratory depression, during or following endoscopy, that cannot be managed by other means (higher oxygen flow supplementation, chin-lift maneuver, etc.).

Benefits and harms

The task force panel did not identify any comparative study evaluating the use of reversal agents restricted for respiratory depression management only, compared to the routine use of these agents during GI endoscopy.

Certainty of evidence

Without comparative studies, the certainty of this recommendation is very low.

4. Safe patient discharge

4.1 Personnel and minimum equipment required for monitoring patients during the post-endoscopy period

RECOMMENDATION

4.1.1 ESGE and ESGENA recommend that patients be monitored after endoscopy by trained and qualified staff until the return of the patient's baseline observations.

Strong recommendation, very low certainty of evidence.

Summary of the evidence

Several national and European guidelines provide consistent statements concerning the post-endoscopy phase/recovery phase until the patient is discharged. This broadly includes three stages: (i) return to baseline consciousness levels with protective reflexes restored; (ii) the patient has resumed normal activities, i.e., eating and drinking, and is ready to leave after receiving all necessary discharge information, including clear follow-up plans; and (iii) the patient has left the department. Patients should be continuously monitored by specially trained staff throughout all three stages. [2,3,6]. Complications related to sedation, or the procedure itself, may become evident in any of the abovementioned stages. Staff in recovery areas should have the same training in sedation and emergency management as the endoscopy staff who monitor patients during procedures to manage potential AEs and complications effectively [2,3].

Benefits and harms

The task force panel retrieved very little data regarding the optimal number of personnel needed in recovery rooms to ensure safe monitoring. A descriptive international cross-sectional study in anesthesia nursing found that one nurse can effectively handle 3–4 patients in the second stage of the post-endoscopic phase [195]. Personnel in recovery areas should always be present, with minor interruptive tasks only. In a retrospective observational study, where patients were observed in the recovery area by technical monitoring, with nurses going to the patients only when an alarm bell rang, it showed that there were more AEs after moderate sedation with benzodiazepines in the recovery area compared to the endoscopy suite (1.1% vs. 0.51% for hypoxemia, respectively) [196]. An audit in an endoscopy tertiary center in Shanghai, China, demonstrated that a formalized organizational discharge policy and a continuous cycle of audit and re-audit of quality criteria on patient care and safe recovery could be improved when adequate staff and equipment were available in the recovery room [197]. Moreover, in a retrospective study [198] occurrence of desaturation during recovery correlated with desaturation during the procedure ($P<0.001$), higher ASA scores (OR 1.86, 95%CI 1.01–3.46), ischemic heart disease (OR 1.81, 95%CI 0.65–5.08), hypertension (OR 1.30, 95%CI 0.47–3.52), and diabetes mellitus (OR 2.41, 95%CI 0.95–6.09). This underlines the need for increased and continuous monitoring by specially qualified personnel, especially in patients with ASA scores ≥II or with comorbidities.

Certainty of evidence

The recommendation was based on qualitative data review only; thus, the quality of the studies was rated as low, and the certainty of evidence was very low.

RECOMMENDATION

4.1.2 ESGE and ESGENA recommend that recovery areas include equipment for monitoring vital signs along with supplemental oxygen and the capability to address potential cardiorespiratory adverse events and complications.

Strong recommendation, very low certainty of evidence.

Summary of the evidence

Guidelines require the same level of safety during and after endoscopic procedures, as AEs and complications can also occur in the post-endoscopy phase [2,3,6]. Recovery areas should be equipped to monitor vital signs and to treat cardiopulmonary complications [3]. These principles of best practice are equivalent to those in Post-Anesthesia Care Unit II settings of anesthesiology [195].

Benefits and harms

The task force panel did not retrieve individual studies specifically addressing this issue. There is scant evidence showing that pulse oximetry allows prompt recognition of disturbances of circulation and oxygenation, facilitating action to prevent or treat them. Dossa et al. [199] established that a minimum of noninvasive blood pressure monitoring and pulse oximetry is required for all sedated patients.

Certainty of evidence

The recommendation was based solely on a qualitative data review; therefore, the quality of the studies was rated as low, and the certainty of the evidence was rated as very low.

4.2 Discharge criteria

RECOMMENDATION

4.2.1 ESGE and ESGENA suggest using scoring systems and standardized discharge checklists to facilitate patient readiness for discharge. Assessments should include a detailed record of vital signs, pain levels, and psychomotor performance.

Conditional recommendation, very low certainty of evidence.

Summary of the evidence

There is moderate evidence that existing scoring systems may be valuable in everyday clinical practice, standardizing the discharge process and shortening recovery time, as they are relatively simple to use and incorporate clinical parameters, regardless of the physician's expertise level, status of previous training, or access to the patient's medical file. However, the effect of different sedation regimes on psychomotor performance and cognitive judgement cannot be measured using the existing discharge scoring systems. and a responsible person to escort the patient is necessary, especially for elderly and patients with comorbidities [2, 3, 200, 201, 202, 203, 204, 205, 206, 207].

Benefits

The task force panel identified one recent systematic review [208] summarizing the evidence from five studies evaluating different discharge scoring systems and from 45 studies of various designs, focusing on discharge after administration of different types of sedatives during ambulatory GI endoscopy. In this systematic review, included studies were arbitrarily classified according to the scoring system used for safe patient discharge into: (a) Aldrete scoring system; (b) modified postanesthesia discharge scoring system (mPADSS); or (c) other discharge criteria. The presence of statistical and clinical heterogeneity among the studies precluded meta-analysis of study results. Nevertheless, there is evidence that implementation of scoring discharge systems, namely the Aldrete and mPADSS, by trained nurses after sedation with different regimes resulted in standardization of the discharge process and shortening of recovery time [209, 210, 211].

Harms

Literature highlights that the performance of existing discharge scoring systems in assessing overall psychomotor performance remains suboptimal [209, 210]. Beyond the shorter discharge time using the Aldrete score, data suggest that patients may still show more drowsiness. Hence, the patient's consciousness level should be assessed carefully when using the modified Aldrete score, especially in those who visit the hospital alone [210], and considering that patients under midazolam sedation may need more time for recovery with a prolonged phase of amnesia and impaired psychomotor skills.

One RCT found a shorter recovery time and quicker return of psychomotor skills for propofol sedation compared to midazolam (values are mean [SD]; 14 [9] vs. 25 [8] min, and 8.7 [1.3] vs. 6.3 [1.1] points, respectively; $P<0.01$ for both) [200], and one prospective cohort study confirmed these results, identifying midazolam dosage >3 mg ($P<0.006$) and fentanyl dosage >50 µg ($P<0.009$) as predictors of poorer neurocognitive function [207]. Based on these results, differing advice on fitness to drive after sedation with midazolam or propofol should be offered. Prospective studies on propofol sedation found that patients return to baseline after 30–45 minutes [201, 202], suggesting that passive participation in traffic (e. g., taking a taxi or tram) may be possible in healthy patients [201]. The task force panel detected three studies [203, 204, 205] assessing driving performance as measured using a driving simulator after endoscopy under sedation. Lois et al. [203], in a prospective observational study on a simulator showed that patients should not drive home after sedated endoscopy because they crossed the midline significantly more frequently than their escort drivers (3 vs. 2 crossings, $P=0.015$) and drove over the speed limit for a higher proportion of the distance travelled (mean [SD], 37% [20] and 24% [17], respectively, $P=0.029$). In another prospective pilot study evaluating patients after sedated endoscopy [204], driving ability (defined as mean acceleration, lane deviation, and number of deviations on a driving simulator) was found to return to baseline at 4 hours after propofol sedation.

Certainty of evidence

The recommendation was based solely on a qualitative data review; therefore, the quality of the studies was rated as low, and the certainty of the evidence was rated as very low.

RECOMMENDATION

4.2.2 ESGE and ESGENA suggest that the performing endoscopist holds the overall medicolegal responsibility for the patient's treatment, including safe recovery, but may delegate the assessment and discharge to trained and qualified personnel, based on standardized discharge criteria.

Conditional recommendation, very low certainty of evidence.

Summary of the evidence

Guidelines underline the medicolegal responsibility of the endoscopist for patients' safe recovery and discharge [2, 6]. Endoscopists are responsible for their patients not only during the endoscopy procedure but also throughout the entire recovery period. Since the responsible endoscopist may leave the unit for other clinical duties before all patients are discharged, the responsibility for safe patient discharge can be delegated to a qualified and adequately trained staff member. This individual should be capable of promptly recognizing and managing any complications that may arise from the procedure or sedation.

Benefits and harms

Studies with different sedation regimes showed that trained nurses can use various scores safely and effectively to assess patients for discharge. Research has shown that using standardized scores can lead to shorter discharge times [209, 210, 211].

Certainty of evidence

The task force panel issued a conditional recommendation highlighting the legal component of the responsibility for patient safe discharge and the absence of solid data; therefore, the certainty of evidence was rated very low.

RECOMMENDATION

4.2.3 ESGE and ESGENA recommend that patients receive oral and written information regarding the post-endoscopy period. Contact details should be provided for potential delayed complications, emergencies, or readmission.

ESGE and ESGENA recommend that patients undergoing sedated endoscopy have an accompanying person at discharge.

Strong recommendation, very low certainty of evidence.

Summary of the evidence

Guidelines recommend that both oral and written information should be provided regarding the post-endoscopy period. This information should cover topics such as nutrition, the ability to return to work, participation in road traffic (both active and passive), and the capacity to make legally binding decisions. Additionally, it should include contact details or a telephone number for emergencies and readmissions [2, 3].

Certainty of evidence

The recommendation was based almost exclusively on existing guidance documents. Thus, the certainty of evidence was rated very low.

5. Special situations

5.1 Sedation in emergency GI endoscopy

RECOMMENDATION

5.1.1 ESGE and ESGENA recommend performing emergency endoscopy under moderate sedation in hemodynamically stable patients. Alternatively, emergency endoscopy without sedation in cooperative patients is feasible.

Strong recommendation, very low certainty of evidence.

RECOMMENDATION

5.1.2 ESGE and ESGENA recommend sedation administration by an anesthesiology specialist in emergency endoscopy in patients at increased risk of aspiration, or with hemodynamic instability or significant comorbidities.

Strong recommendation, low certainty of evidence.

Summary of the evidence

For this Guideline, emergency endoscopy is defined as endoscopy ≤6 hours after presentation, for lower/upper endoscopy due to GI bleeding, lower/upper endoscopy due to foreign body, and ERCP and/or EUS due to acute cholangitis. Emergency endoscopy without sedation is considered good clinical practice for hemodynamically stable and cooperative patients who agree to undergo the procedure without sedation.

On the other hand, in the case of hemodynamic instability, involvement and monitoring by the anesthesia team is recommended. In situations with a higher risk of aspiration, such as suspected gastric retention (when the patient is not fasting, has gastric outlet obstruction, or has large-volume hematemesis), it is strongly advised that tracheal intubation be performed for airway protection, with anesthesia administered by an anesthesiologist.

Benefits

All evaluated studies involved patients who underwent endoscopic hemostasis for upper GI bleeding. Pooling the results of two retrospective studies with more than 300 patients, each evaluating hemostasis success rate [212, 213], did not show a significant benefit of performing the procedure with or without sedation (OR 1.19, 95%CI 0.81–1.76, $I^2 = 0\%$; **Fig. 5.1.1s**). However, sedation administration has been associated with shorter duration of the procedure [212, 213] (MD −1.60 min, 95%CI −2.60 to −0.61, $I^2 = 0\%$: **Fig. 5.1.2s**). Another retrospective study involving 703 patients who underwent sedated endoscopic hemostasis demonstrated an almost 100% success rate. [214].

Harms

The pooled results of the two aforementioned studies [212, 213] did not detect any harm of providing sedation during emergency hemostasis, regarding either aspiration pneumonia (OR 1.53, 95%CI 0.80–2.89, $I^2 = 0\%$; **Fig. 5.1.3s**) or 30-day mortality (OR 0.90, 95%CI 0.62–1.32, $I^2 = 0\%$; **Fig. 5.1.4s**). Pooling the results of two retrospective [215, 216] and one prospective [217] nonrandomized, cohort studies that evaluated potential advantages of tracheal intubation for emergency upper GI endoscopy for bleeding peptic ulcer (**Table 5.1.2s**) did not detect a significant benefit of tracheal intubation in terms of aspiration pneumonia (OR 3.05, 95%CI 0.07–139.26, $I^2 = 81\%$; **Fig. 5.1.5s**) or mortality (OR 1.30, 95%CI 0.68–2.49, $I^2 = 54\%$; **Fig. 5.1.6s**). Finally, in one nationwide study involving 3097 patients undergoing emergency EGD for bleeding, an increased 30-day mortality (10.4% vs. 5.6%) was detected in patients when anesthesia staff were involved during the procedure.

However, shock at admission and ASA score IV were more prevalent among patients receiving anesthesia care [218].

Certainty of evidence

The risk of bias assessment for each study is provided in **Tables 5.1.3s–5.1.13s**. Overall, all the included studies were considered of good quality. However, the certainty of evidence was downgraded because only noncomparative observational studies were included. For the outcome of hemostasis efficacy, further downgrading was applied due to indirectness (heterogeneity regarding the use of endoscopic modalities for hemostasis) and imprecision (broad CI crossing 1.0), so the quality of evidence was downgraded to very low.

5.2 Sedation for GI procedures during pregnancy and lactation

RECOMMENDATION

5.2 ESGE and ESGENA recommend consultation with anesthetic and obstetric teams involved in the pregnant patient's care, together with the patient's choice for the appropriateness and choice of sedation during GI endoscopy.

Strong recommendation, very low certainty of evidence.

Summary of evidence

A team that may include an endoscopist, obstetrician, anesthesiologist, and/or a surgeon is required to ensure the best outcome for women undergoing GI endoscopy during pregnancy. The careful choice of sedatives for endoscopy in the first trimester is important due to the teratogenicity of specific drugs (such as diazepam). Cautious sedative choices are also needed in the late third trimester or in the case of impending delivery because of the risk of premature delivery. Both high-risk pregnancies and high-risk endoscopic procedures, such as ERCP for acute cholangitis or gastroscopy for significant GI bleeding in the pregnant patient, require a multidisciplinary approach and planning with the respective team members. Information on the safety of sedative medications during pregnancy and lactation can be found elsewhere [2].

Benefits

The task force did not identify any studies on specific benefits of administering sedation for GI endoscopy during pregnancy.

Harms

Most available data originate from six single-center [219, 220, 221, 222, 223, 224] and one multicenter [225] ERCP studies, that included 1–65 patients. All endoscopic procedures were performed under moderate or deep sedation with propofol [219, 220, 221, 222, 223, 225, 226] (**Table 5.2.2s**). In the largest cohort, none of the 65 pregnancies were terminated due to ERCP or sedation administration during the procedure [220]. In another report of 48 various endoscopic diagnostic and therapeutic procedures performed during pregnancy, there was one case of miscarriage 24 hours after esophageal stricture dilation [224]. Two more cases required cesarean section, and one intrauterine death was reported. The task force found no data for lactation in the scanned literature.

Certainty of evidence

We did not conduct a formal evaluation of bias risk for each study because we could not pool the data using meta-analytic tools. Considering the nature of the studies, the participant count, and the significant number of reported events, we concluded that the certainty of evidence was very low.

5.3 Sedation for GI procedures in patients premedicated with mucolytic and defoaming agents

RECOMMENDATION

5.3 ESGE and ESGENA do not recommend withholding sedation administration in patients premedicated with mucolytic and defoaming agents before esophagogastroduodenoscopy.

Strong recommendation, moderate certainty of evidence.

Summary of evidence

The rate of missed esophageal and gastric cancers during esophagogastroduodenoscopy (EGD) is estimated to be 6%–11% [227, 228]. It has been observed that the ability to detect upper GI pathologies is related to the cleanliness of the upper GI tract [229]. To improve visibility, premedication with antifoaming and mucolytic agents such as simethicone, N-acetylcysteine, or pronase is effective [230, 231]. This approach has been widely used and is recommended by Asian Societies [232]. Despite the low volume of premedication (approximately 100 ml), the administration of additional fluids approximately 30 minutes before the procedure may cause concerns about adverse events such as aspiration.

Benefits

The task force identified two meta-analyses [230, 231], eight RCTs [233, 234, 235, 236, 237, 238, 239, 240], and one cohort study [241] (not included in the above two meta-analyses) evaluating the efficacy and safety of premedication with antifoaming agents with or without mucolytic substances in patients undergoing sedated upper GI endoscopy (**Table 5.3.2s**). Various premedication regimens were administered in volumes not exceeding 100 ml. The regimen mainly contained simethicone only or in combination with other substances such as pronase or sodium bicarbonate or N-acetyl-cysteine/peppermint oil.

Harms

Available literature provided indirect evidence on the AE rates (secondary outcomes in all studies) of patients who underwent gastroscopy under sedation with or without mucosal cleansing premedication. One of the two meta-analyses reported no AEs potentially linked to the premedication. In the other meta-analysis, there was no significant difference between the simethicone group and the water group, with a risk ratio of 0.45 (95%CI 0.2–1.0, $I^2 = 0\%$).

The task force pooled the AEs detected in the two arms in the eight RCTs and the cohort study, namely intervention (up to 100 ml of antifoaming-mucolytic solution) and comparator (either up to 100 ml of water or nil per mouth). Altogether, 18 sets of data in nine studies with 10 283 patients were analyzed. There were 27 and 39 AEs in the intervention and in the control groups, respectively, with a pooled AE rate of 0%, 95%CI 0–0.01, $I^2 = 93\%$ (**Fig. 5.3.1s**). Focusing only on studies with nil per mouth, as a comparator [233, 238, 241], the task force detected no excess AE rate in the premedication group (OR 0.55, 95%CI 0.11–2.72, $I^2 = 86\%$; **Fig. 5.3.2s**). It must be highlighted that in one sophisticated RCT of patients sedated with propofol, oxygen saturation measured at different landmarks of the upper GI tract was not different between patients premedicated with simethicone and pronase and compared to patients who fasted only [233]. The results should be interpreted with caution, as only a limited number of studies used oxygen saturation as a surrogate marker to associate AEs with sedation administration. Additionally, the design of these studies makes it impossible to definitively link the identified AEs to the use of sedation.

Certainty of evidence

The risk of bias of the studies included in the two reviewed meta-analyses was low. The bias assessment of the studies that the task force pooled is detailed in **Table 5.3.3s**. The quality of the cohort study was good, while overall, the included RCTs had a low risk of bias, as shown in **Table 5.3.3s**. Notably, participating physicians were not blinded in three studies, while most of the studies (7 out of 8) were deemed to be potentially at risk of detection bias. The certainty of evidence in the reviewed meta-analyses was downgraded to low due to high heterogeneity in one study and due to indirectness in both studies. The evidence from the studies that the task force pooled in **Table 5.3.4s** was rated as moderate, due to significant heterogeneity.

6. Training, quality, and environmental impact

6.1 Training for sedation administration for GI procedures

RECOMMENDATION

6.1 ESGE and ESGENA recommend improving and expanding educational offerings on sedation strategies and the principles of airway management, using structured training.

Strong recommendation, very low certainty of evidence.

Summary of the evidence

In 2013, ESGE and ESGENA published the European curriculum for sedation training during GI procedures [242]. It focused on training in all types of sedation practices in GI endoscopy, aiming to set standards for the training of nonanesthesiologist physicians and nurses, to understand the levels of sedation-anesthesia [243] (▶ **Table 6**), to administer sedation during GI endoscopy, and to expand the specific knowledge, competence, and skills necessary for endoscopists and nursing staff for managing sedation within endoscopy. The curriculum encompassed management of sedation complications, putting the patient first to ensure patient comfort and safety, and aimed to support individual endoscopy departments, national societies, and official bodies in developing local or national recommendations and curricula.

The impact of training in the ESGE and ESGENA curriculum has been measured in one study conducted on over 12 000 procedures (80% under deep sedation with propofol-based regimens) [244]. All staff members, including physicians and nurses, completed the ESGE–ESGENA sedation course. The results showed no sentinel AEs, 5 moderate-risk AEs (0.05%), and 18 minor-risk AEs (0.17%). All of these events were managed by the endoscopy team without requiring additional sedation, following the integration of the ESGE–ESGENA training program into the staff curriculum [244]. Similar training guidance has been successfully implemented in other European countries [245, 246]. This ESGE–ESGENA curriculum for sedation training in GI procedures is currently being updated by the ESGE Curricula Working Group and is expected to complement this Guideline.

Certainty of evidence

The recommendation was based on good clinical practice recommendations; thus, the certainty of evidence was very low.

6.2 Measuring quality in sedation and implementation of an improvement program for sedation in GI endoscopy

RECOMMENDATION

6.2 ESGE and ESGENA recommend the development and implementation of a quality improvement program with performance indicators to monitor the quality of sedation practices in gastrointestinal endoscopy.
Strong recommendation, very low certainty of evidence.

Summary of the evidence

Quality metrics for sedation administration have not yet been clearly defined, but at least three distinct domains linked to quality of sedation can be identified: patient safety (including preprocedural risk stratification, identification and management of intraprocedural and post-procedural sedation-related AEs); technical outcome of the procedure (i.e., successful completion of the endoscopic procedure at the planned level of sedation, and lack of complications driven by inadequate sedation); and patient comfort [247].

The quality of the endoscopic procedure (i.e., completion of the procedure, adenoma detection rate) has been linked to the quality and availability of sedation [9, 248, 249], although recent evidence questions the effects of deep sedation on colonoscopy outcomes [250, 251]. Similarly, the link between patient safety and the technical outcome of the endoscopic procedure is not straightforward. For example, one study evaluating the impact of extensive monitoring and implementation of a national society guideline did not show improved clinical outcomes [252]. Also, some interventions aiming for safer sedation practices, such as drug dose reduction, were linked to worsening technical outcomes of the endoscopic procedure, leading to an increased incomplete procedure rate [253]. On the other hand, studies have shown that auditing and feedback of anesthesiology practices [254] or nursing staff involvement in quality improvement [255] can result in a lower rate of sedation-related AEs.

In relation to patient comfort, assessing this factor before, during, and after endoscopic procedures is recognized as a quality measure supported by various society guidelines. However, there are currently no patient-reported experience measures specifically designed to evaluate the quality of sedation during endoscopy [2]. To this extent, specific tools have been validated for assessing the tolerability of endoscopic procedures performed using conscious sedation [256], but they were designed to measure the overall experience of the endoscopic procedure rather than the quality of sedation itself.

The task force panel recognizes that developing specific sedation quality performance indicators, not confounded by the overall quality assessment of the endoscopic procedure, requires scientific strength and rigor. As advancements in GI endoscopy progress, the development and systematic review of quality measures for sedation will remain critically important. Recognizing existing gaps in guidance, the ESGE Quality Improvement Committee has established a task force to create a quality improvement program focused on sedation administration for GI procedures.

Certainty of evidence

The recommendation was based on good clinical practice recommendations and indirect evidence, due to the absence of comparative data; thus, the certainty of evidence was very low.

6.3 Environmental impact of sedation during GI endoscopy

RECOMMENDATION

6.3 ESGE and ESGENA recommend a rational use of sedatives to reduce the environmental impact of endoscopy.
Strong recommendation, very low certainty of evidence.

Summary of the evidence

Anesthesiology and GI endoscopy departments significantly contribute to waste generation, both directly and indirectly, and have been identified as being among the top three highest producers of hazardous waste in a hospital [257]. Currently data examining the specific cost and environmental impact of GI-related sedation are limited [258], and no studies directly compare the environmental impact of the different sedation strategies available for GI endoscopy (i.e., no sedation, conscious sedation, monitored anesthesia care, or general anesthesia). In their recent Position Statement, ESGE and ESGENA recommend a rational use of peri- and intraprocedural medication (including sedatives) to reduce the environmental impact of endoscopy [259]. Indirect evidence from interventional cardiology suggests that intravenous sedation may have less environmental impact than inhalation anesthesia. Significant efforts are also underway to reduce nitrous oxide use [260]. Despite some limited and indirect evidence suggesting that simple, audit-based interventions at a unit level might help streamline sedation procedures for GI procedures [261] and for anesthesia in general [262], there is currently a research gap in this field that should be addressed through further studies.

Certainty of evidence

In the absence of comparative studies, the recommendation was based on good clinical practice recommendations; thus, the certainty of evidence was very low.

7. Future development and research

The recommendations outlined in this current ESGE Guideline are based on studies that provide the highest level of evidence available. However, most of these recommendations are grounded in low-quality evidence. Consequently, there is a significant need for further research in various aspects of sedation practices for GI endoscopy.

The impact of preprocedural risk stratification in patients at higher risk of sedation-related complications (for example, considering age, comorbidities, and BMI) and of tailored approaches based on patient-specific factors such as anxiety levels and previous sedation history, requires further evaluation. Additionally, choice of sedation type, and whether to sedate or not, should be based on procedure complexity, whether it is an ambulatory or emergency setting, and who administers the sedation (anesthetist or nonanesthetist provider). This aspect also requires further evaluation. In this context, new sedatives promising improved efficacy, shorter recovery times, and fewer side effects need further assessment and implementation within the sedation algorithm.

Standardization of monitoring during procedures is crucial for different sedation regimens, as is the identification and management of sedation-related AEs. It is important to determine the optimal regimen for minimal/moderate sedation, deep sedation, or general anesthesia, as well as post-procedure observation and discharge criteria (monitoring, recovery duration, and regarding driving). Additionally, development of an endoscopy-specific recovery and discharge score is needed to be developed, as existing scores such as Aldrete and mPADSS are not tailored for GI endoscopy. There is also a lack of evidence regarding the number of staff required for patient observation during recovery.

A comprehensive risk analysis of postoperative complications is necessary. This analysis will identify high-risk patients, provide data on the types and frequency of complications, and potentially inform recommendations for the equipment needed during post-procedure observation. There is also low-quality evidence that sedation-related complications, such as infections, thromboembolic or circulatory events, may occur late after the endoscopy. We need more well-structured studies focused on hard endpoints and delayed complications after sedated endoscopy. More evidence is required to measure their incidence accurately and reduce their occurrence.

The development of standardized training programs for endoscopists and nursing staff on sedation administration is greatly needed. Given the emergence of newer drugs for specific patient populations, education on who would benefit most from them, and on monitoring, prevention, and treatment in sedation-related emergency scenarios is needed. There are currently no patient-reported experience measures specifically designed to assess the quality of sedation during endoscopy. Several questions can be addressed, such as what additional interventions/techniques may reduce discomfort during endoscopy (e. g. xylocaine throat spray, spasmolytics, acupuncture, use of virtual reality glasses, music).

Artificial intelligence (AI) is being increasingly integrated into sedation practices. However, there are unanswered questions regarding where AI can provide the most benefit in the patient journey, from pre-assessment to recovery. It is essential to determine the most effective areas for initial implementation, particularly for units that are not yet familiar with its use.

Finally, there is a limited understanding of the environmental impact of GI sedation. Data examining its specific effects are scarce, and no direct studies compare the environmental impacts of various sedation strategies (e. g., no sedation, conscious sedation, monitored anesthesia care, or general anesthesia).

Disclaimer

The legal disclaimer for ESGE publications [263] applies to this Guideline.

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Conflict of Interest

M. Hollenbach has received honoraria for lectures from Fujifilm (2018–2024). P. Roelandt's department has received research support from Medtronic (2019– present). M. Romanczyk has received consulting fees and a device loan from Odin Vision (2024– ongoing); he has received consulting fees from Olympus (2025– ongoing) and Medtronic (2025–2026). M.T. Soria San Teodoro has provided services to Medtronic (Medtronic capnography in sedation segmentation playbook, 3 hours in 2021; Virtual Medtronic Advisory Board, 5 hours in 2020). N. Abu-Freha, A. Becq, U. Beilenhoff, E. Coron, K. Garborg, B. Kovacevic, V. Lorenzo-Zúñiga, M. Manno, A. Parrella, S. Pontone, R. Pouw, R. Sidhu, P.A. Sá, T.C. Tham, K. Triantafyllou, D. Turnbull, G. Tziatzios, H. van Malenstein, P. Vilmann, and T. Voiosu have no competing interests.

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Supplement to the ESGE-ESGENA Guideline on Sedation for Gastrointestinal Endoscopy

Index

Endoscopy | DOI 10.1055/a-2898-6540 |

TASK FORCE 1: Pre-endoscopic assessment

Leader: Hannah Van Malenstein

Members: Mauro Manno, Maria Soria San Teodoro, Tony Tahm, Marcus Hollenbach, Bojan Kovacevic

Q1.1: Informed consent for sedated endoscopic GI procedures

Clinical Question: Should all sedated patients provide informed consent before the procedure?

No PICO

Ref. Everett et al. Position statement on informed consent – Endoscopy 2023

Q1.2: Patient risk factors

Clinical Question: Which patient factors (age, co-morbidities, preferences, etc.) should guide the type of sedation? Obesity, Liver disease, renal failure, neuromuscular disorders, respiratory disease, cardiovascular disease etc.

Table 1.2.1s PICOs

PICO	Population	Intervention	Comparator	Outcome
1.2	High-risk patients scheduled for GI endoscopy	Moderate sedation	No sedation	Patient safety and satisfaction
1.2	High-risk patients scheduled for GI endoscopy	Deep sedation	Moderate sedation	Patient safety and satisfaction
1.2	High-risk patients scheduled for GI endoscopy	General anesthesia	Deep sedation	Patient safety and satisfaction
1.2	High-risk patients scheduled for GI endoscopy	Moderate sedation	No sedation	Procedure outcomes
1.2	High-risk patients scheduled for GI endoscopy	Deep sedation	Moderate sedation	Procedure outcomes
1.2	High-risk patients scheduled for GI endoscopy	General anesthesia	Deep sedation	Procedure outcomes

BIBLIOGRAPHIC SEARCH

Endoscopy | DOI 10.1055/a-2898-6540 |

Bibliographic search strategies were performed in **Medline, Embase** and **Cochrane** from 2019 to 2024 using the following search strategies:

Keywords: minimal, moderate sedation, comorbidity, patient experience in GI endoscopy, patient satisfaction GI endoscopy

Gi endoscopy in renal failure, liver disease, neuromuscular disorders, cardiovascular disease, obesity, OSA, pre-assessment GI endoscopy, malampati, STOPBANG scoring Gi endoscopy

MeSH Terms: Conscious Sedation; Deep Sedation; Anesthesia; Endoscopy, Gastrointestinal; Patients

a. PubMed- Search (July 18th, 2024)

("endoscopy, digestive system"[MeSH Terms]) AND ("Conscious Sedation"[MeSH Terms] OR "Anesthesia"[MeSH Terms] OR "Deep Sedation"[MeSH Terms] OR "Propofol"[MeSH Terms] OR "Midazolam"[MeSH Terms] OR "Anesthetics, Intravenous"[MeSH Terms] OR "Nurse Anesthetists"[MeSH Terms]) AND ("Obesity"[MeSH Terms] OR "Renal Insufficiency"[MeSH Terms] OR "Neuromuscular Diseases"[MeSH Terms] OR "Comorbidity"[MeSH Terms] OR "Liver Cirrhosis"[MeSH Terms] OR "Cardiovascular Diseases"[MeSH Terms] OR "Aged"[MeSH Terms] OR "Respiratory Tract Diseases"[MeSH Terms] OR "malampati" OR "assessment" OR "sedation choice" OR "STOPBANG") AND 2019/01/01:3000/12/31[Date - Publication] AND "English"[Language]

Results: 231 studies

b. Embase + Cochrane - Search 2019-2024

(endoscopy/ or nasal endoscopy/ or colon capsule endoscopy/ or gastrointestinal endoscopy/ or intestine endoscopy/ or digestive tract endoscopy/)

AND

(deep sedation/ or conscious sedation/ or sedation/ or propofol/ or midazolam/)

AND

(obesity/ or renal insufficiency/ or neuromuscular diseases/ or comorbidity/ or liver cirrhosis/ or cardiovascular diseases/ or aged/ or respiratory tract diseases/ or (malampati or assessment or sedation choice or STOPBANG).mp)

AND

limit to (human and english language and "remove medline records" and yr="2019 -Current")

Results: 554 studies

c. Results of the bibliographic searches

Results Total 231 + 554 = 785 studies

After removing duplicates (n=51), 734 articles were found. 53 studies were considered potentially relevant and acquired in full text.

Excluded studies (23 studies)

- Aminnejad R et al. Comparing the Efficacy and Safety of Dexmedetomidine/Ketamine with Propofol/Fentanyl for Sedation in Colonoscopy Patients: A Doubleblinded Randomized Clinical Trial. 2022 CNS & neurological disorders drug targets (No mention of risk factors)
- Chen L et al. The Effect of Different Doses of Ciprofol in Patients with Painless Gastrointestinal Endoscopy. 2023 (No mention of risk factors)
- Chen SH et al. Remimazolam tosilate in upper gastrointestinal endoscopy: A multicenter, randomized, non-inferiority, phase III trial. 2021. Journal of Gastroenterology and hepatology (No mention of risk factors)
- Cummings et al. Incidence of sedation-related adverse events during ERCP with anesthesia assistance: a multicenter observational study. 2022. Gastrointestinal endoscopy
- Gao SH et al. The efficacy and safety of ciprofol and propofol in patients undergoing colonoscopy: A double-blind, randomized, controlled trial. 2024. Journal of Clinical Anesthesia (No mention of risk factors)
- Haher R.K. et al. Intermittent Manually Controlled versus Continuous Infusion of Propofol for Procedural Sedation during Interventional Endoscopic Procedures: A Single-blinded Randomised Study. 2022. Journal of Clinical and Diagnostic Research (No mention of risk factors)
- Han SJ et al. Etomidate Sedation for Advanced Endoscopic Procedures. 2019. Digestive diseases and sciences (No mention of risk factors)
- Kim J.H. et al. Efficacy and safety of etomidate in comparison with propofol or midazolam as sedative for upper gastrointestinal endoscopy. 2020. Clinical Endoscopy (No mention of risk factors)
- Lin Y, Zhang X, Li L et al. High-flow nasal cannula oxygen therapy and hypoxia during gastroscopy with propofol sedation: a randomized multicenter clinical trial. 2019. Gastrointestinal endoscopy (No mention of risk factors)
- Liu W et al. Safety and efficacy of dexmedetomidine vs. midazolam in complex gastrointestinal endoscopy: A systematic review and meta-analysis. 2024. Clinics and research in hepatology and gastroenterology (No mention of risk factors)
- Liu W et al. Comparison of clinical efficacy and safety between dexmedetomidine and propofol among patients undergoing gastrointestinal endoscopy: a meta-analysis. 2021 The Journal of International Medical Research (No mention of risk factors)

- Mazzeffi et al. High-Flow Nasal Cannula Oxygen in Patients Having Anesthesia for Advanced Esophagogastroduodenoscopy: HIFLOW-ENDO, a Randomized Clinical Trial. 2021. Anesthesia and analgesia (No mention of risk factors)
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- Sato M. Safety and Effectiveness of Nurse-Administered Propofol Sedation in Outpatients Undergoing Gastrointestinal Endoscopy. 2019. Clinical gastroenterology and hepatology (No mention of risk factors)
- Shao LJ et al. Sedation strategy for gastroscopy in obese patients. 2022 Journal of anesthesia (Letter to the editor)
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- Wang LL et al. A comparative study on the efficacy and safety of propofol combined with different doses of alfentanil in gastroscopy: a randomized controlled trial. 2023 Journal of Anesthesia (No mention of risk factors)
- Zhang CC et al. A Sedation-related complications during anesthesiologist-administered sedation for endoscopic retrograde cholangiopancreatography: a prospective study. 2020 BMC anesthesiology (No mention of risk factors)
- Zhang K et al. Safety and efficacy of propofol alone or in combination with other agents for sedation of patients undergoing colonoscopy: an updated meta-analysis. 2020 European review for medical and pharmacological sciences (No mention of risk factors)
- Zhang W et al. A prospective, randomized, single-blinded study comparing the efficacy and safety of dexmedetomidine and propofol for sedation during endoscopic retrograde cholangiopancreatography. 2024. BMC anesthesiology
- Zhaxi D et al. High-flow nasal cannula oxygen reduced hypoxemia in patients undergoing gastroscopy under general anesthesia at ultra-high altitude: a randomized controlled trial. 2024 BMC anesthesiology (No mention of risk factors)
- Zhou Y et al. Safety and efficacy of etomidate in combination with oxycodone in painless gastroscopic procedures in the elderly: A prospective randomized controlled trial study. 2023 (No mention of risk factors)

Included studies (30 studies)

1 meta-analysis

- Ahmer W et al. Remimazolam versus propofol for sedation in gastrointestinal endoscopy and colonoscopy within elderly patients: a meta-analysis of randomized controlled trials. 2024. European journal of clinical pharmacology

16 RCTs

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- Liu Y et al. Sedation with a 1:1 mixture of etomidate and propofol for gastroscopy in hypertensive elderly patients. 2023 Journal of Clinical Hypertension
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- Zhang K. et al. Effects of opioid-free propofol or remimazolam balanced anesthesia on hypoxemia incidence in patients with obesity during gastrointestinal endoscopy: A prospective, randomized clinical trial 2023 Frontiers in Medicine
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- Zheng L et al. Efficacy and Safety of a Subanesthetic Dose of Esketamine Combined with Propofol in Patients with Obesity Undergoing Painless Gastroscopy: A Prospective, Double-Blind, Randomized Controlled Trial. 2023 Drug design, development and therapy

3 prospective observational studies

- Alam L et al. Safety of balanced propofol and midazolam in upper gastrointestinal endoscopy for sedation in cirrhotic patients. 2021 JPMA. The Journal of the Pakistan Medical Association
- Choe J.W. et al. Development of a predictive model for hypoxia due to sedatives in gastrointestinal endoscopy: a prospective clinical study in Korea. Clin Endosc. 2024 Jul;57(4):476-485.
- Wahab E.A et al. Conscious sedation using propofol versus midazolam in cirrhotic patients during upper GI endoscopy: A comparative study. 2019 JGH Open

10 retrospective studies

- Garg S. et al. Patient characteristics and procedural outcomes of moderate sedation for endoscopic procedures in patients with obesity: A retrospective, propensity score-matched study. 2021 Endoscopy International Open
- Gemma M et al. Risk of adverse events in gastrointestinal endoscopy: Zero-inflated Poisson regression mixture model for count data and multinomial logit model for the type of event. 2021 PloS one
- Jeong J et al. Propofol alone prevents worsening hepatic encephalopathy rather than midazolam alone or combined sedation after esophagogastroduodenoscopy in compensated or decompensated cirrhotic patients. 2020 European journal of gastroenterology & hepatology
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- Pozin I.E. et al. Respiratory complications during recovery from gastrointestinal endoscopies performed by gastroenterologists under moderate sedation, 2023 Clinical Endoscopy
- Sneyd JR et al. Hypotension during propofol sedation for colonoscopy: a retrospective exploratory analysis and meta-analysis. 2022 British journal of anaesthesia

- Tokmak S et al. Efficacy and safety of endoscopic retrograde cholangiopancreatography in the very elderly by using a combination of intravenous midazolam, ketamine and pethidine. 2021 Geriatrics & gerontology international
- Wang Y et al. Postoperative Complications Associated with Moderate Sedation in Endoscopic Procedures Among Patients with Cirrhosis. 2021 Medical Science Monitor

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Table 1.2.2: Evidence: Characteristics of the included studies

RISK FACTORS

Study (Author, year)	Country	Study design	No. of subjects	Age (y)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm	Conclusions
Choe J.W., 2024	Korea	Prospective observational	446	55.3 (12.6)	63.2	Observational	n/a	In multivariate models following risk factors: Neck circumference 2.048(1.642–2.454) p<0.001 BMI 1.438 (1.263–1.636) p<0.001 Mallampati score 2 1.548 (0.589–4.074) p=0.376; 3: 3.325 (1.243–8.896) p=0.017; 4: 4.697(0.850–25.944) p=0.026	In multivariate models following risk factors: Neck circumference 2.048(1.642–2.454) p<0.001 BMI 1.438 (1.263–1.636) p<0.001 Mallampati score 2 1.548 (0.589–4.074) p=0.376; 3: 3.325 (1.243–8.896) p=0.017; 4: 4.697(0.850–25.944) p=0.026	
Gemma M, 2021	Italy	Retrospective	23788			Observational	n/a	Age >75 years (1.44; 95% CI 1.28-1.62) BMI >27 (1.25; 95% CI 1.06-1.45) ASA score (IV vs I 3.54; 95% CI 3.07-4.00)	n/a	Age, BMI, ASA score, Mallampati score, in-hospital procedure duration, and other sedatives with propofol increase the risk for AEs during sedation for GI endoscopy.
Lieber SR, 2020	USA	Retrospective	428947	59.1 (15.6)	45.1	Observational	n/a	Age 65 – 79 OR 1.58 (1.35, 1.84) Age≥80 OR 2.12 (1.75, 2.56) Male sex OR 1.29 (1.16, 1.43) ASA score III OR 1.65 (1.47, 1.86) ASA score IV/V OR 4.10 (3.49, 4.81) EGD OR 1.63 (1.43, 1.85) colonoscopy ref ERCP 8.83 (7.70, 10.12) colonoscopy ref	n/a	Risk of ADS complications increased with older age, more severe disease, procedure type, and case complexity.
Nishizawa T, 2021	Japan	Retrospective	3898	57.3 (14.1)	40.4	Observational	n/a	For upper endoscopy: Age OR 1.025 95% CI 1.014–1.036 p<0.001 Sex (Female) OR 1.657 95% CI 1.220–2.249 p<0.001 For colonoscopy: Age OR 1.024 95% CI 1.012–1.036 p<0.001	n/a	Old age, female sex, and midazolam dose were independent risk factors for prolonged hospital stay after endoscopy.

								Sex (Female) OR 1.935 95% CI 1.357–2.761 p<0.001		
Pozin I.E., 2023	Israel	Retrospective	657	63.0 (15.3)	54.8	Observational	n/a	During the procedure Sex (male vs. female) OR 0.778 (0.543–1.115) p=0.295 Age OR 1.004 (0.992–1.016) p=0.200 ASA score OR 1.314 (1.024–1.688) p=0.027 Pulmonary disease OR 1.754 (1.030–2.985) p=0.026 Length of procedure OR 1.014 (1.002–1.027) p=0.008 Fentanyl OR 1.011 (1.000–1.022) p=0.057	During the post-procedure recovery period Sex (male vs. female) OR 0.494 (0.206–1.183) p=0.480 Age OR 1.005 (0.971–1.040) p=0.102 ASA score OR 1.867 (1.008–3.458) p=0.002 Ischemic heart disease OR 1.815 (0.649–5.080) p=0.006 Hypertension OR 1.289 (0.472–3.516) p=0.037 Diabetes mellitus OR 2.406 (0.950–6.095) p<0.001	We found no major complications during recovery after balanced propofol-based sedation administered by a gastroenterologist-nurse team. Patients with the identified risk predictors must be monitored carefully.
Sneyd JR, 2022	USA	Retrospective, combined individual data from multiple studies	939	50.0 (15.0)	47.0	Observational	n/a	Total dose of propofol (mg kg1) OR 1.079 (1.01-1.52) p=0.023 Duration of propofol administration (min) OR 1.021 (1.012-1.030) p<0.001 Age (yr) OR 0.998 (0.988-1.008) p=0.665 Male sex OR 0.94 (0.709-1.247) p=0.668 ASA physical status 1 reference ASA physical status 2 OR 1.045 (0.744-1.468) p=0.799 ASA physical status 3 OR 1.269 (0.784-2.053) p=0.332	Total dose of propofol (mg kg1) OR 1.079 (1.01-1.52) p=0.023 Duration of propofol administration (min) OR 1.021 (1.012-1.030) p<0.001 Age (yr) OR 0.998 (0.988-1.008) p=0.665 Male sex OR 0.94 (0.709-1.247) p=0.668 ASA physical status 1 reference ASA physical status 2 OR 1.045 (0.744-1.468) p=0.799 ASA physical status 3 OR 1.269 (0.784-2.053) p=0.332	Hypotension is common during propofol sedation for colonoscopy and of a magnitude and duration associated with harm in surgical patients.
Cassell, 2020	USA	Prospective observational	766	58.3 (11.5)	50.4 %	Adult patients undergoing colonoscopy	-	Risk factors for failed conscious sedation: Younger age (OR 0.98, 0.96-0.99, p < 0.001), female gender (OR 1.2, 0.83-1.75, p = 0.024), use of adjunct sedation medications (OR 3.34, 1.94-5.73, p < 0.001),, outpatient opiate use (OR 1.71, 1.03-2.84, p0.006), outpatient benzodiazepine use (OR 1.72, 0.98-3.01, p = 0.002) were associated with failed CS.		
King, 2021	USA	Retrospective, propensity score	46	41.1 (14.2)	21.7 %	Cannabis use	No use of cannabis	Amount of sedation: Propofol, mg (200; 150-260) Fentanyl, no and % (13; 56.5%), Ketamin, no and % (3, 13%)		Propofol, mg (200; 150-250) Fentanyl, no and % (10; 43.5%), Ketamin, no and %

		matched							(1, 4.3%)	

OBESE/OBSTRUCTIVE SLEEP APNEA PATIENTS

Study (Author, year)	Country	Study design	No. of subjects	Age (y)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm	Conclusions
Cukierman DS, 2023	USA	RCT	109	60.0 (52-66)	51.4	nasal CPAP	Face mask	AE rate 3.6%	AE rate5.6%	Nasal CPAP does not improve oxygenation in obese patients
Garg S, 2021	USA	Retrospective, propensity score matched	5746	57.1 (16.0)	38.3%	Obese (BMI≥30)	Non-obese (BMI<30)	7-day all-cause hospitalization: 23 (1.69%) for EGD and 28 (1.61%) for colonoscopy	7-day all-cause hospitalization: 27 (1.99%) for EGD and 33 (1.90%) for colonoscopy	Similar outcomes for obese patients compared to non-obese patients
Kang S, 2021	China	RCT	115			Conscious sedation	Deep sedation	SpO2 <95%: n=25 SpO2 <90%: n=4 Emergency airway management: n=14 Hypotension: n=6 Bradycardia: n=7	SpO2 <95%: n=39 SpO2 <90%: n=11 Emergency airway management: n=47 Hypotension: n=19 Bradycardia: n=16	Conscious sedation with propofol and sufentanil reduced the incidence of hypoxic events without affecting the gastroscopy procedure and satisfaction of the patients and endoscopists compared with the deep sedation in obese patients.
Li X, 2020	China	RCT	90	44.4 (7.13)	57.8	i.v. Lidocain + propofol	Propofol	The number of hypoxemia episodes was 1.49±1.12 The number of apnea episodes was 1.62±0.49 Intraoperative bradycardia 10 (22) Intraoperative hypotension 4 (9)	The number of hypoxemia episodes was 2.11±1.32 The number of apnea episodes was 2.16±0.37 Intraoperative bradycardia 9 (20) Intraoperative hypotension 3 (7)	Intravenous infusion of lidocaine could significantly decrease the number of oxygen desaturations and apnea episodes in obese patients during colonoscopy.
Riccio CA, 2019	USA	RCT	59	59.0 (7.0)	13.6	High-flow nasal cannula	Standard nasal cannula	Desaturation episode < 90%: 11 (39.3) Number of desaturation episodes: 0(0,2) Airway interventions: 5	Desaturation episode < 90%: 14 (45.2) Number of desaturation episodes: 0(0,1)	At similar FiO2, HFNC was not significantly different from SNC for the prevention of arterial oxygen desaturation in morbidly obese patients undergoing propofol

								(17.9)	Airway interventions: 10 (32.3)	sedation for colonoscopy.
Zhang K, 2023	China	RCT	264	45 (IQR 39-50)	53.3	remimazolam + esketamine	propofol + esketamine	Mild hypoxemia, no. (%) 37 (14.2) Severe hypoxemia, no. (%) 11 (4.2) Bradycardia, no. (%) 10 (7.6) Tachycardia, no. (%) 8 (6.1) Hypotension, no. (%) 15 (11.5) Hypertension, no. (%) 4 (3.1) Dizziness, no. (%) 8 (6.1) Headache, no. (%) 1 (0.8) PONVc, no. (%) 2 (1.5)	Mild hypoxemia, no. (%) 30 (11.5) Severe hypoxemia, no. (%) 24 (9.2) Bradycardia, no. (%) 12 (9.2) Tachycardia, no. (%) 4 (3.1) Hypotension, no. (%) 13(10) Hypertension, no. (%) 1 (0.8) Dizziness, no. (%) 9 (6.9) Headache, no. (%) 2 (1.5) PONVc, no. (%) 0 (0)	Compared with propofol combined with esketamine, remimazolam combined with esketamine, can reduce the incidence of severe hypoxemia during gastrointestinal endoscopy in obese patients.
Zheng L, 2023	China	RCT	104	41.1 (7.9)	63.5	Propofol + esketamine	Propofol	Injection pain 16 (30.8) Hypoxemia 9 (17.3) Hypotension 4 (7.7) Bradycardia 2 (3.8) Choking 17 (32.7) Body movement 19 (36.5) Nausea 0 (0) Vomiting 0 (0) Dizziness 0 (0) Delirium 0 (0)	Injection pain 42 (80.8) p<0.0001 Hypoxemia 21 (40.4) p=0.009 Hypotension 12 (23.1) p=0.029 Bradycardia 9 (17.3) p=0.026 Choking 44 (84.7) p<0.0001 Body movement 48 (92.3) p<0.0001 Nausea 0 (0) Vomiting 0 (0) Dizziness 0 (0) Delirium 0 (0)	The combination of propofol and esketamine (0.25 mg/kg) improves the safety and reduces the incidence of adverse events in patients with obesity during painless gastroscopy. Thus, this method is worthy of clinical application.

LIVER CIRRHOSIS

Study (Author, year)	Country	Study design	No. of subjects	Age (y)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm	Conclusions
Alam L,	Pakistan	Prospective	500	50.3	59.8	Patients with	Controls (no	Minor bradycardia (1.2%), hypoxemia	Minor bradycardia (1.2%), hypoxemia	Propofol and midazolam are safe for cirrhotic patients

2021		observational		(18.1)		cirrhosis	cirrhosis)	(0.8%), grade II HE	(0.8%)	
Jeong J, 2020	Korea	Retrospective	67	55.8 (9.9)	73.1	Propofol	Midazolam	n=4.0 (18.2)	n=8.0 (40.0)	Cirrhotic patients undergoing propofol sedation score better (NCT number connection test) compared to those sedated with midazolam or a combination of the two. However, no apparent difference in the worsening of HE is observed.
Jung J.H, 2020	Korea	RCT	126	54.2 (10.8)	70.6	Etomidate	Propofol	54.1 [43.8]	85.1 [111.9]	Etomidate-based sedation exacerbates neither subclinical nor overt hepatic encephalopathy. It guarantees efficacies similar to those of propofol regarding rapid sedation, fast recovery, and early discharge, with no increased risk of adverse respiratory or cardiovascular events in patients with LC.
Wahab EA, 2029	Egypt	Prospective comparative (or retrospective?)	90	53.1 (7.9)	78.9	Propofol	Midazolam (or combination)	Enodoscopy time (min.) 3.59 (0.93) Recovery time (min.) 6.06 (2.13) Hypoxia (% of Pts) 0 OAAS scale Score 5: 18 (60%) Score 3–4: 9 (30%) 3: 3 (10%)	Enodoscopy time (min.) 3.18 (1.14) Recovery time (min.) 31.1 (6.25) Hypoxia (% of Pts) 23% OAAS scale Score 5: 7 (23.3%) Score 3–4: 6 (20%) 3: 17 (56.7%)	Considering safety and efficacy issues, propofol is better than midazolam in gastrointestinal endoscopy, especially in patients with liver cirrhosis.
Wang Y, 2021	China	Retrospective	232	median 57	69.8	Observational	n/a	Among a total of 40 complications (17.2%), the most common type of complication was postpro-cedural (35/40; 87.5%), including postprocedural pain, nausea, or vomiting. 8 serious complications (3.4%), a majority of which were cardiovascular (7/8, 87.5%), including 6 of transfusions and 1	n/a	Moderate sedation-associated postoperative complications were relatively high among cirrhotic patients un-undergoing endoscopic procedures. Complications were associated with sicker patients who underwent endoscopic procedures in the evening, suggesting the potential need for more intensive care of perioperative management in this population, including anesthesia monitoring.

								clinically significant hypotension.		
Yoo JJ, 2019	Korea	RCT	60	52.6 (10.1)	80.0	Propofol	Midazolam	Stroop test (cognitive performance): Off-time (seconds) Pre 74.7 (57.0–85.8) Post 70.1 (59.9–91.0) Δ Post-Pre −2.8 (−13.0–13.2) On-time (seconds) Pre 90.0 (72.2–144.4) Post 91.7 (64.8–113.8) Δ Post-Pre −11.8 (−52.5–17.3) Off-time + On-time (seconds) Pre 166.5 (137.0–227.5) Post 159.9 (116.2–231.5) Δ Post-Pre −18.9 (−62.5–25.6)	Stroop test (cognitive performance)Off-time (seconds) Pre 80.1 (64.4–96.9) Post 73.9 (63.8–100.6) Δ Post-Pre 1.6 (−15.0–22.5) On-time (seconds) Pre 97.7 (71.7–123.3) Post 84.4 (73.6–118.3) Δ Post-Pre −15.8 (−57.8–11.5) Off-time + On-time (seconds) Pre 180.7 (139.2–226.2) Post 161.4 (116.0–197.9) Δ Post-Pre −10.5 (−51.5–9.7)	All sedative methods using midazolam, propofol, or combination therapy showed a similar safety profile in advanced cirrhosis and were not associated with increased risk of cognitive impairment.

ELDERLY

Study (Author, year)	Country	Study design	No of subjects	Age (y)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm	Conclusions
Ahmer W, 2024	Pakistan	Meta-analysis of RCT	1466	n/a	n/a	Remimazolam	Propofol	5 studies (n=1,323) reported bradycardia and superiority of remimazolam in comparison to propofol (OR: 0.43; 95% CI: 0.22 to 0.86; P=0.02). 5 studies (n=1,271) reported nausea and vomiting with no difference (OR:1.28; 95% CI: 0.76 to 2.17; P=0.36). Four studies (n=822) reported dizziness and headache with no difference (OR: 0.65; 95% CI: 0.32 to 1.33; P=0.24). Five studies (n=1,184) reported respiratory depression with no difference (OR: 0.44; 95% CI: 0.12 to 1.65; P=0.22). Six studies (n=1,389) reported hypoxemia with remimazolam being superior (OR: 0.20; 95% CI: 0.11 to 0.39; P < 0.0001; Fig. 5). Five studies (n=1,184) reported pain on injection, revealing superiority of remimazolam (OR: 0.17; 95% CI: 0.09 to 0.32; P < 0.00001)		Remimazolam demonstrated superiority in terms of bradycardia, hypoxemia, and reduced pain on the injection site in comparison to propofol. However, there were no significant differences between remimazolam and propofol in terms of nausea and vomiting, dizziness and headache, respiratory depression, and hypotension.
Breazu CM, 2022	Romania	RCT	83	74.7 (7.92)	48.8	i.v. Lidocain + propofol	Propofol	Desaturation <94%: 0% Desaturation <90%: 0%	Desaturation <94%: 33% Desaturation <90%: 0%	i.v. Lidocaine is safe and is associated with lower propofol requirement and lower risk of desaturation in elderly patients
Chen M, 2020	China	RCT	92	71.4 (5.1)	44.3	i.v. Lidocain + propofol	Propofol	Brief apnea (n=2)	Brief apnea (n=0)	i.v. Lidocaine is safe and is associated with lower initial propofol and bolus requirements
Guo P, 2021	China	RCT	193	69.1 (4.51)	53.4	Oxycodone + propofol	Fentanyl + propofol	Hypotension: n=7 Bradycardia: n=3 SpO2 < 90%: n=0	Hypotension: n=6 Bradycardia: n=4 SpO2 < 90%: n=7	Both regimens are safe. Oxycodone combined with propofol surpasses

								Nausea: n=1 Vomiting: n=0	Nausea: n=8 Vomiting: n=5	traditional fentanyl and propofol anesthesia due to milder respiratory depression and a lower incidence of perioperative adverse events.
Hu S, 2022	China	RCT	140	70.7 (4.21)	59.3	i.v. Lidocain + propofol	Propofol	Hypoxaemia: n=9 Severe hypoxaemia: n=1 Emergency airway management: n=2 Hypotension: n=7 Bradycardia: n=1	Hypoxaemia: n=19 Severe hypoxaemia: n=3 Emergency airway management: n=12 Hypotension: n=11 Bradycardia: n=2	i.v. lidocaine can significantly reduce the amount of propofol, the incidence of hypoxia, and postoperative pain during gastroscopy in elderly patients, with a higher patient and gastroscopist satisfaction.
Kim SY, 2020	Korea	Retrospective	1943150	57.3 (10.6)	43.7	GI endoscopy with or without sedation	n/a	Older age (70-99 years vs 40-69 years) (OR 1.69; 95% CI, 1.65-1.73; P < .001) and sedation during endoscopy (OR 1.12; 95% CI, 1.09-1.14; P < .001) were identified as independent risk factors for CCD AE Chronic diseases (hypertension: OR, 1.24; 95% CI, 1.22-1.27; P < .001; DM: OR, 1.06; 95% CI, 1.04-1.09; P < .001; valvular disease: OR, 1.37; 95% CI, 1.16-1.61; P < .001; hyperlipidemia: OR, 1.05; 95% CI, 1.03-1.08; P < .001; COPD: OR, 1.06; 95% CI, 1.04-1.09; P < .001; renal disease: OR, 1.15; 95% CI, 1.07-1.23; P < .001) and use of antiplatelet agents (OR, 1.40; 95% CI, 1.37- 1.44; P < .001) were independent risk factors for CCD adverse events	n/a	CCD adverse events after diagnostic endoscopy were significantly more frequent in individuals with older age (70-99 years) and/or sedation during endoscopy.
Li M, 2022	China	RCT	87	69.0 (66.0-71.2)	59.8	i.v. Lidocain + propofol	Propofol	Dizziness: 11 Nausea/vomiting: 1	Dizziness: 4 Nausea/vomiting: 0	Intravenous lidocaine can reduce propofol consumption in elderly patients undergoing colonoscopy, with quicker time to loss of

										consciousness.
Li YP, 2022	China	RCT	120	47.7 (7.31)	50.0	Propofol + oxycodone	Propofol	Hypotension: n=4 Bradycardia: n=1 Respiratory depression: n=3 Nausea and/or vomiting: n=1	Hypotension: n=6 Bradycardia: n=8 Respiratory depression: n=5 Nausea and/or vomiting: n=6	0.05 mg/kg oxycodone in combination with propofol can be used safely and effectively for painless gastroscopy, with the advantages of a low propofol dose, maintenance of hemodynamic stability, and few adverse effects.
Liu Y, 2023	China	RCT	328	66.6 (5.3)	45.4	Etomidate	Propofol	Oxygen desaturation 16(14.8) Hypotension 0 (0)	Oxygen desaturation 37(33.6) Hypotension 18 (16.4)	Combined use of etomidate and propofol appeared to maintain cardiopulmonary stability with minimal side effects in older hypertensive patients scheduled for gastroscopy, which further implied that this sedation strategy could be a safe and pain-free option for managing patients undergoing gastroscopy, particularly those at a higher risk of adverse cardiovascular events
Tokmak S, 2021	Turkey	Retrospective	232	Group A: 87.3 (4.1) Group B: 46.2 (11.0)	40.1	Age ≥ 80 years	Age ≤ 65 years	Post-ERCP pancreatitis Mild 2 (2.7) Moderate 0 (0) Severe 0 (0) Perforation 2 (2.7) Cardiopulmonary Hypoxia 1 (1.3) Hypotension 0 Hypertension 27 (36) Bradycardia 2 (2) Tachycardia 24 (32) Cholangitis 1 (1.3)	Post-ERCP pancreatitis Mild 2 (1) Moderate 0 (0) Severe 1 (0.5) Perforation 1 (0.5) Cardiopulmonary Hypoxia 0 (0) Hypotension 0 (0) Hypertension 60 (30) Bradycardia 5 (2) Tachycardia 55 (28) Cholangitis 1 (1.5)	ERCP can be safely performed in elderly patients using a combination of midazolam and ketamine without propofol. The incidence of complications is comparable with that observed in younger patients
Zhang	China	RCT	120	66.2	38.3	Remimazolam	Propofol +	Hiccups (n, %) 8 (13.3%) Hypoxia (n, %) 1 (1.7%)	Hiccups (n, %) 0 p=0.003 Hypoxia (n, %) 3 (5.0%)	The safety and efficacy of remimazolam besylate are

Q, 2024	(3.7)		etomidate	Depression of respiration (n, %) 1 (1.7%) Tongue falling (n, %) 1 (1.7%) Total respiratory-related adverse events (n, %) 3 (5.0%) Choking cough (n, %) 3 (5.0%) Movement of the body (n, %) 1 (1.7%) Low blood pressure (n, %) 24 (40%) Nausea (n, %) 1 (1.7% Dizziness (n, %) 0 (0%)	p=0.310 Depression of respiration (n, %) 6 (10.0%) p=0.051 Tongue falling (n, %) 2 (3.3%) p=0.559 Total respiratory-related adverse events (n, %) 11 (18.3%) p=0.047 Choking cough (n, %) 0 (0.0%) p=0.080 Movement of the body (n, %) 2 (3.3%) p=0.559 Low blood pressure (n, %) 22 (36.7%) p=0.851 Nausea (n, %) 1 (1.7%) p=1.000 Dizziness (n, %) 1 (1.7%) p=1.000	not inferior to those of etomidate combined with propofol, rendering it a safe option for sedation during gastrointestinal endoscopy in ASA I-II elderly patients, but care should be taken to monitor the occurrence of hiccup

Table 1.2.3s: Risk of bias assessment for studies

Study	Selection (max 4 stars)	Comparability (max 2 stars)	Outcomes (max 3 stars)	Quality (Total 9/9)
		RISK FACTORS		
Choe J.W., 2024	***	**	***	**Good**
Gemma M, 2021	***	**	***	**Good**
Lieber SR, 2020	***	*	**	**Good**
Nishizawa T, 2021	***	**	**	**Good**
Pozin I.E., 2023	***	**	***	**Good**
Sneyd JR, 2022	***	*	**	**Good**
Cassell, 2020	***	**	**	**Good**
King, 2021	**	*	**	**Fair**

Good quality: 3 or 4 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain.

Fair quality: 2 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain.

Poor quality: 0 or 1 star in selection domain OR 0 stars in comparability domain OR 0 or 1 stars in outcome/ exposure domain

Certainty of evidence

The risk of bias assessment for each study can be found in the **Supplemental Table 1.2.3**. The certainty of evidence for all clinical outcomes in this PICO question was downgraded because only observational studies were included. Therefore, the panel rated the certainty of the evidence as very low.

CLINICAL QUESTION

Q1.2.1 Peri-endoscopic sedation management of patients on glucagon-like peptide-1 receptor agonists/sodium-glucose cotransporter-2 inhibitors

Clinical Question: Should glucagon-like peptide-1 receptor agonists (GLP-1RAs) AND/OR sodium-glucose cotransporter-2 (SGLT-2) inhibitors guide the type of sedation?

Table 1.2.1.1s PICOs

PICO	Population	Intervention	Comparator	Outcome
1.1	Patients receiving glucagon-like peptide-1 receptor agonists (GLP-1RAs) AND/OR sodium-glucose cotransporter-2 (SGLT-2) inhibitors scheduled to GI endoscopy	Moderate sedation	No sedation	Patient safety (aspiration pneumonia, hypoxia, adverse events)
1.2	Patients receiving glucagon-like peptide-1 receptor agonists (GLP-1RAs) AND/OR sodium-glucose cotransporter-2 (SGLT-2) inhibitors scheduled to GI endoscopy	Deep sedation	Moderate sedation	Patient safety (aspiration pneumonia, hypoxia, adverse events)
1.3	Patients receiving glucagon-like peptide-1 receptor agonists (GLP-1RAs) AND/OR sodium-glucose cotransporter-2 (SGLT-2) inhibitors scheduled to GI endoscopy	General anesthesia	Deep sedation	Patient safety (aspiration pneumonia, hypoxia, adverse events)
1.4	Patients receiving glucagon-like peptide-1 receptor agonists (GLP-1RAs) AND/OR sodium-glucose cotransporter-2 (SGLT-2) inhibitors scheduled to GI endoscopy	Moderate sedation	No sedation	Procedural outcomes (gastric residual content (GRC), inadequate bowel preparation (IBP), aborted procedures)
1.5	Patients receiving glucagon-like peptide-1 receptor agonists (GLP-1RAs) AND/OR sodium-glucose cotransporter-2 (SGLT-2) inhibitors scheduled to GI endoscopy	Deep sedation	Moderate sedation	Procedural outcomes (gastric residual content (GRC), inadequate bowel preparation (IBP), aborted procedures)
1.6	Patients receiving glucagon-like peptide-1 receptor agonists (GLP-1RAs) AND/OR sodium-glucose cotransporter-2 (SGLT-2) inhibitors scheduled to GI endoscopy	General anesthesia	Deep sedation	Procedural outcomes (gastric residual content (GRC), inadequate bowel preparation (IBP), aborted procedures)

BIBLIOGRAPHIC SEARCH

Bibliographic search strategies were performed in **PubMed**, using the following search strategies:

d. PubMed- Search August 31th 2025

Search: **conscious sedation OR deep sedation OR anesthesia AND glucagon-like peptide-1 receptor agonists** Sort by: **Most Recent**

("conscious sedation"[MeSH Terms] OR ("conscious"[All Fields] AND "sedation"[All Fields]) OR "conscious sedation"[All Fields] OR ("deep sedation"[MeSH Terms] OR ("deep"[All Fields] AND "sedation"[All Fields]) OR "deep sedation"[All Fields]) OR ("anaesthesia"[All Fields] OR "anesthesia"[MeSH Terms] OR "anesthesia"[All Fields] OR "anaesthesias"[All Fields] OR "anesthesias"[All Fields])) AND ("glucagon like peptide 1 receptor agonists"[Pharmacological Action] OR "glucagon like peptide 1 receptor agonists"[Supplementary Concept] OR "glucagon like peptide 1 receptor agonists"[All Fields] OR "glucagon like peptide 1 receptor agonists"[All Fields] OR "glucagon like peptide 1 receptor agonists"[MeSH Terms] OR ("glucagon like"[All Fields] AND "peptide 1"[All Fields] AND "receptor"[All Fields] AND "agonists"[All Fields]))

Translations

conscious sedation: "conscious sedation"[MeSH Terms] OR ("conscious"[All Fields] AND "sedation"[All Fields]) OR "conscious sedation"[All Fields]

deep sedation: "deep sedation"[MeSH Terms] OR ("deep"[All Fields] AND "sedation"[All Fields]) OR "deep sedation"[All Fields]

anesthesia: "anaesthesia"[All Fields] OR "anesthesia"[MeSH Terms] OR "anesthesia"[All Fields] OR "anaesthesias"[All Fields] OR "anesthesias"[All Fields]

glucagon-like peptide-1 receptor agonists: "glucagon-like peptide-1 receptor agonists"[Pharmacological Action] OR "glucagon-like peptide-1 receptor agonists"[Supplementary Concept] OR "glucagon-like peptide-1 receptor agonists"[All Fields] OR "glucagon like peptide 1 receptor agonists"[All Fields] OR "glucagon-like peptide-1 receptor agonists"[MeSH Terms] OR ("glucagon-like"[All Fields] AND "peptide-1"[All Fields] AND "receptor"[All Fields] AND "agonists"[All Fields])

Results: 124 studies

b. Cochrane Central Register of Controlled Trials (CENTRAL)- Search August 31th 2025

#1	("conscious sedation OR deep sedation OR anesthesia") (Word variations have been searched)	105306
#2	("glucagon-like peptide-1 receptor agonists") (Word variations have been searched)	1030
#3	#1 AND #2	**10**

Results: 10 studies

c. <u>Results of the bibliographic searches</u>

Results Total 124 + 10 = 134 studies

After removing duplicates (n=14), 120 articles were found. 13 studies were considered potentially relevant and acquired in full text.

Included studies (4 studies)

4 Cohort studies

1) *Panchal S, Mahmud N, Atkins JH, Kang H, Leto A, Goebel A, Trivedi N, Chatila A, Hsu WW, Ginsberg GG, Pickett-Blakeley O, Zandvakili I. Endoscopy and anesthesia outcomes associated with glucagon-like peptide-1 receptor agonist use in patients undergoing outpatient upper endoscopy. Gastrointest Endosc. 2025 Aug;102(2):216-222. doi: 10.1016/j.gie.2025.01.004. Epub 2025 Jan 15. PMID: 39824444*
2) *Alkabbani W, Suissa K, Gu KD, Cromer SJ, Paik JM, Bykov K, Hobai I, Thompson CC, Wexler DJ, Patorno E. Glucagon-like peptide-1 receptor agonists before upper gastrointestinal endoscopy and risk of pulmonary aspiration or discontinuation of procedure: cohort study. BMJ. 2024 Oct 22;387:e080340. doi: 10.1136/bmj-2024-080340. PMID: 39438043*
3) *Yeo YH, Gaddam S, Ng WH, Huang PC; Motility and Metabolic Pharmacoepidemiology Group; Ma KS, Rezaie A. Increased Risk of Aspiration Pneumonia Associated With Endoscopic Procedures Among Patients With Glucagon-like Peptide 1 Receptor Agonist Use. Gastroenterology. 2024 Jul;167(2):402-404.e3. doi: 10.1053 /j.gastro.2024.03.015. Epub 2024 Mar 27. PMID: 38552724.*
4) *Firkins SA, Yates J, Shukla N, Garg R, Vargo JJ, Lembo A; Cleveland Clinic Obesity Medicine and Bariatric Endoscopy Working Group. Clinical Outcomes and Safety of Upper Endoscopy While on Glucagon-Like Peptide-1 Receptor Agonists. Clin Gastroenterol Hepatol. 2025 Apr;23(5):872-873.e3. doi: 10.1016/j.cgh.2024.03.013. Epub 2024 Apr 3. PMID: 38574832.*

Table 1.2.1.2s: Evidence related to Sedation AEs in patients on GLP-1RA: Characteristics of the included studies.

Author, year	Country	Study design	No. of subjects	Intervention	Comparator	Findings
Panchal S 2025	USA	Single-center, retrospective cohort	598	360	298	Solid RGC in the GLP-1RA group in multivariate analysis (odds ratio, 3.80; 95% confidence interval, 1.57-9.21; Patients in the GLP-1RA group had procedures aborted (1.3% vs 0%; P = .021) .003) Rate of hypoxia was similar (.2% vs .3%; P = .341). There were no cases of pulmonary aspiration.
Alkabbani W 2024	USA	Comparative cohort	43 365	24 817	18 537	Among users of GLP-1 receptor agonists and SGLT-2 inhibitors, the weighted risk per 1000 people was, respectively, 4.15 and 4.26 for pulmonary aspiration GLP-1 receptor agonist use was not associated with an increased risk of pulmonary aspiration (pooled risk ratio 0.98, 95% CI 0.73 to 1.31), although it was associated with a higher risk for discontinuation of endoscopy (1.99, 1.56 to 2.53).
Yeo 2024	USA	Retrospective cohort	916,249	20,099	778,253	GLP-1RA use showed a higher incidence rate of aspiration pneumonia (0.83% vs 0.63%), associated with a significantly higher risk of aspiration pneumonia (hazard ratio [HR], 1.33; 95% confidence interval [CI], 1.02–1.74; P ¼ .036) compared to the nonuser group Higher risk of aspiration pneumonia was observed in patients with propofol-assisted endoscopies (HR, 1.49; 95% CI, 1.08–2.06; P = .014) but not in the group where propofol was not used (HR, 1.31; 95% CI, 0.78–2.20; P = .310).
Firkins 2025	USA	Single-center, retrospective cohort	1512	1512	NA	2.0% incidence of procedure abortion among patients taking GLP-1RAs,

Table 1.2.1.3s: Risk of bias assessment for studies

Study	Selection (max 4 stars)	Comparability (max 2 stars)	Outcomes (max 3 stars)	Quality (Total 9/9)
Panchal S 2025	***	**	***	**Good**
Alkabbani W 2024	***	*	***	**Fair**
Yeo 2024	***	*	**	**Good**
Firkins 2025	***	**	**	**Good**

Good quality: 3 or 4 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain.

Fair quality: 2 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain.

Poor quality: 0 or 1 star in selection domain OR 0 stars in comparability domain OR 0 or 1 stars in outcome/ exposure domain

Certainty of evidence

The risk of bias assessment for each study can be found in the **Table 1.2.1.3s**. The certainty of evidence for all clinical outcomes in this PICO question was downgraded because only observational studies were included. Therefore, the panel rated the certainty of the evidence as very low.

Peri-endoscopic management of patients on glucagon-like peptide-1 receptor agonists/sodium-glucose cotransporter-2 inhibitors

BIBLIOGRAPHIC SEARCH

Bibliographic search strategies were performed in **PubMed**, using the following search strategies:

a. PubMed- Search August 28th 2025

Search: **Glucagon-like peptide-1 receptor agonists OR sodium-glucose cotransporter-2 (SGLT-2) inhibitors AND gastrointestinal endoscopy** Sort by: **Most Recent**

("glucagon like peptide 1 receptor agonists"[Pharmacological Action] OR "glucagon like peptide 1 receptor agonists"[Supplementary Concept] OR "glucagon like peptide 1 receptor agonists"[All Fields] OR "glucagon like peptide 1 receptor agonists"[All Fields] OR "glucagon like peptide 1 receptor agonists"[MeSH Terms] OR ("glucagon like"[All Fields] AND "peptide 1"[All Fields] AND "receptor"[All Fields] AND "agonists"[All Fields]) OR ("sodium glucose transporter 2 inhibitors"[Pharmacological Action] OR "sodium glucose transporter 2 inhibitors"[Supplementary Concept] OR "sodium glucose transporter 2 inhibitors"[All Fields] OR "sglt2 inhibitors"[All Fields] OR "sodium glucose transporter 2 inhibitors"[MeSH Terms] OR ("sglt2"[All Fields] AND "inhibitors"[All Fields]))) AND ("endoscopy, gastrointestinal"[MeSH Terms] OR ("endoscopy"[All Fields] AND "gastrointestinal"[All Fields]) OR "gastrointestinal endoscopy"[All Fields] OR ("gastrointestinal"[All Fields] AND "endoscopy"[All Fields]))

Translations

Glucagon-like peptide-1 receptor agonists: "glucagon-like peptide-1 receptor agonists"[Pharmacological Action] OR "glucagon-like peptide-1 receptor agonists"[Supplementary Concept] OR "glucagon-like peptide-1 receptor agonists"[All Fields] OR "glucagon like peptide 1 receptor agonists"[All Fields] OR "glucagon-like peptide-1 receptor agonists"[MeSH Terms] OR ("glucagon-like"[All Fields] AND "peptide-1"[All Fields] AND "receptor"[All Fields] AND "agonists"[All Fields])

Sodium-glucose cotransporter-2 (SGLT-2) Inhibitors: "sodium-glucose transporter 2 inhibitors"[Pharmacological Action] OR "sodium-glucose transporter 2 inhibitors"[Supplementary Concept] OR "sodium-glucose transporter 2 inhibitors"[All Fields] OR "sglt2 inhibitors"[All Fields] OR "sodium-glucose transporter 2 inhibitors"[MeSH Terms] OR ("sglt2"[All Fields] AND "inhibitors"[All Fields])

gastrointestinal endoscopy: "endoscopy, gastrointestinal"[MeSH Terms] OR ("endoscopy"[All Fields] AND "gastrointestinal"[All Fields]) OR "gastrointestinal endoscopy"[All Fields] OR ("gastrointestinal"[All Fields] AND "endoscopy"[All Fields])

Results: 108 studies

b. Cochrane Central Register of Controlled Trials (CENTRAL)- Search August 28th 2025

#1	("glucagon-like peptide-1 receptor agonists") (Word variations have been searched)	1030

#2	("glucagon-like peptide-1 receptor agonists") (Word variations have been searched)	81
#3	#1 AND #2	**56**

Results: 56 studies

c. Results of the bibliographic searches

Results Total 108 + 56 = 164 studies

15 studies were considered potentially relevant and acquired in full text. After removing duplicates (n=2), 13 articles were found. 12 studies were considered relevant.

Included studies

11 Meta-analyses

1. *Singh S, Rahman SH, Khan N, Rajagopal A, Shafique N, Tawde P, Bhardwaj V, Suresh Kumar VC, Aswath G, Inamdar S, Dutta S, Hurairah A, Mohan BP. Effects of glucagon-like peptide-1 receptor agonists on endoscopy outcomes: systematic review and meta-analysis. Gastrointest Endosc. 2025 Feb;101(2):343-349.e5. doi: 10.1016/j.gie.2024.10.011. Epub 2024 Oct 12. PMID: 39401599.*
2. *Elkin J, Rele S, Sumithran P, Hii M, Thuraisingam S, Spelman T, Phan T, Choong P, Dowsey M, Shadbolt C. Association between glucagon-like peptide-1 receptor agonist use and peri-operative pulmonary aspiration: a systematic review and meta-analysis. Anaesthesia. 2025 Jul;80(7):846-858. doi: 10.1111/anae.16601. Epub 2025 Apr 15. PMID: 40230298*
3. *Ahmed Z, Iqbal A, Arif SF, Campbell C, Fehlman J, Allen DJ, Bowel Preparation Quality in Patients Using Glucagon-Like Peptide-1 Agonists: A Systematic Review and Meta-Analysis. Gastrointest Endosc. 2025 Aug 20:S0016-5107(25)01931-5. doi: 10.1016/j.gie.2025.08.027. Epub ahead of print. PMID: 40846241.*
4. *Abdulraheem A, Abujaber B, Ayers L, Al-Zureikat Q, Bashiri K, Impact of GLP-1 receptor agonists on upper gastrointestinal endoscopy: an updated systematic review and meta-analysis. Surg Endosc. 2025 Aug;39(8):5135-5151. doi: 10.1007/s00464-025-11962-4. Epub 2025 Jul 9. PMID: 40634731.*

5. *Tarar ZI, Farooq U, Chaudhry A, Gandhi M, El Alayli A, Ayoub M, Singh B, Evidence Report on the Safety of Gastrointestinal Endoscopy in Patients on Glucagon-like Peptide-1 Receptor Agonists: A Systematic Review and Meta-Analysis. Diagnostics (Basel). 2025 Mar 19;15(6):770. doi: 10.3390/diagnostics15060770. PMID: 40150111; PMCID: PMC11941505.*
6. *Tan Y, Zhang X, Lv XH, Sun YN, Yang JL, Xiao X. Glucagon-like peptide-1 receptor agonists increase the risk of residual gastric content and pulmonary aspiration on upper endoscopy: A meta-analysis. Dig Liver Dis. 2025 Jul;57(7):1377-1385. doi: 10.1016/j.dld.2025.03.002. Epub 2025 Mar 24. PMID: 40133086.*
7. *Chiu YT, Chen YT, Lee FJ, Chang CY. The impact of glucagon-like peptide-1 receptor agonists on the quality indicators of colonoscopy - a systematic review and meta-analysis. Dig Liver Dis. 2025 Jul;57(7):1386-1392. doi: 10.1016/j.dld.2025.03.004. Epub 2025 Mar 22. PMID: 40121157.*
8. *Beran A, Nayfeh T, Akhras A, Ramai D, Mohamed M, Guardiola JJ, Al-Haddad M, Rex DK. Effect of Glucagon-Like Peptide-1 Receptor Agonists on Bowel Preparation for Colonoscopy: A Systematic Review and Meta-Analysis. Am J Gastroenterol. 2025 Feb 12;120(7):1653-1656. doi: 10.14309/ajg.0000000000003362. PMID: 39933910.*
9. *Baig MU, Piazza A, Lahooti A, Johnson KE, Rangwani S, Gouda Z, Mahadev S, Newberry C, Hanscom M, Sampath K, Kumar S, Anca D, Schulman AR, Carr-Locke DL, Sharaiha RZ. Glucagon-like peptide-1 receptor agonist use and the risk of residual gastric contents and aspiration in patients undergoing GI endoscopy: a systematic review and a meta-analysis. Gastrointest Endosc. 2025 Apr;101(4):762-771.e13. doi: 10.1016/j.gie.2024.12.019. Epub 2024 Dec 16. PMID: 39694296.*
10. *Facciorusso A, Ramai D, Dhar J, Samanta J, Chandan S, Gkolfakis P, Crinò SF, Maida M, Anderloni A, Boskoski I, Triantafyllou K, Dinis-Ribeiro M, Hassan C, Fuccio L, Arvanitakis M. Effects of Glucagon-Like Peptide-1 Receptor Agonists on Upper Gastrointestinal Endoscopy: A Meta-Analysis. Clin Gastroenterol Hepatol. 2025 Apr;23(5):715-725.e3. doi: 10.1016/j.cgh.2024.07.021. Epub 2024 Aug 12. PMID: 39142543.*
11. *do Nascimento TS, Pereira ROL, Maia E, Ohnuma T, da Costa MG, Slawka E, Galhardo C Jr, Krishnamoorthy V. The impact of glucagon-like peptide-1 receptor agonists in the patients undergoing anesthesia or sedation: systematic review and meta-analysis. Perioper Med (Lond). 2024 Jul 22;13(1):78. doi: 10.1186/s13741-024-00439-y. PMID: 39039540; PMCID: PMC11264430.*

1 Retrospective cohort study

11. *Panchal S, Mahmud N, Atkins JH, Kang H, Leto A, Goebel A, Trivedi N, Chatila A, Hsu WW, Ginsberg GG, Pickett-Blakeley O, Zandvakili I. Endoscopy and anesthesia outcomes associated with glucagon-like peptide-1 receptor agonist use in patients undergoing outpatient upper endoscopy. Gastrointest Endosc. 2025 Aug;102(2):216-222. doi: 10.1016/j.gie.2025.01.004. Epub 2025 Jan 15. PMID: 39824444; PMCID: PMC12260032.*

Evidence of the effect of GLP-1RAs AND/OR SGLT-2 inhibitors on procedural and clinical outcomes in patients undergoing gastrointestinal endoscopy

Author, year PMID	Study design	No. of studies	Endoscopy type	Findings
Singh S 2025 PMID: 39401599	Systematic review and meta-analysis	23	EGD, Colonoscopy	GLP-1RAs exposure was associated with an increased risk of RGCs (OR, 15.39; 95% CI, 4.65-50.99; P < 0.01) and aborted procedures (OR, 13.86; 95% CI, 4.42-43.43; P < 0.01) No significant differences were observed between the 2 groups in terms of aspiration events (OR, 21.06; 95% CI, 0.13-3379.01; P = 0.24) and bowel preparation quality (OR, 0.94; 95% CI, 0.67-1.31; P = 0.83).
Elkin J 2025 PMID: 40230298	Systematic review and meta-analysis	28	EGD, Colonoscopy	GLP-1RAs exposure was associated with an increased risk of residual gastric contents despite appropriate fasting (OR 5.96, 95%CI 3.96–8.98) GLP-1RAs exposure was not associated with pulmonary aspiration (OR 1.04, 95%CI 0.87–1.25)
Ahmed Z 2025 PMID: 40846241	Systematic review and meta-analysis	6	Colonoscopy	No difference in the pooled rate of inadequate bowel preparation events (OR 1.00, 95% CI: 0.73-1.37, P = 0.99, I2 = 33%). Mean BBPS score reported in three studies was significantly lower in the GLP-1 RA group (mean difference -0.36, 95% CI: -0.44 to -0.28, P < 0.001, I2 = 91%).
Abdulraheem A, 2025 PMID: 40634731	Systematic review and meta-analysis	20 retrospective studies, 207,708 patients	EGD	Higher rates of gastric residual content compared to non-users (OR: 5.57; 95% CI: 4.07-7.62), higher aborted EGDs with GLP-1 RA use (OR 4.90; 95% CI: 2.94-8.18) No difference in aspiration events between the two groups (OR 1.75; 95% CI: 0.64-4.77)
Tarar ZI, 2025 PMID: 40150111	Systematic review and meta-analysis	12 studies with 105,515 patients	EGD	Higher rates of RGC compared to the control group (OR 6.30, 95% CI 5.30-7.49, I2 0%). Higher aborted (OR 5.50, 95% CI 3.25-9.32, I2 0%) and repeated procedures (OR 2.19, 95% CI 1.42-3.38, I2 0%) No increased odds (1.26, 95% CI 0.86-1.87, I2 34%) of aspiration in GLP-1 users compared to the non-GLP-1 group.
Tan Y, 2025 PMID: 40133086	Systematic review and meta-analysis	39 studies of 1,253,498 subjects	EGD	Increased risk of RGC (OR 4.86, 95 % CI 3.85-6.14; adjusted OR 5.24, 95 % CI 3.49-7.87), Increased risk of pulmonary aspiration (OR 2.29, 95 % CI 1.36-3.87), Increased risk of interrupted endoscopic procedures (OR 3.22, 95 % CI 1.65-6.29), Increased risk of repeated endoscopy (OR 2.16, 95 % CI 1.14-4.11), delays in gastric transit time VCE (MD 45.51, 95 % CI 1.33-89.68).
Chiu YT, 2025 PMID: 40121157	Systematic review and meta-analysis	6 studies of 16000 subjects	Colonoscopy	Higher rate of inadequate bowel preparation (RR = 0.06, 95 % CI 0.05-0.08, p < 0.001, I^2 = 39 %). Total BBPS is lower in GLP-1 RA users (mean difference = -0.31, 95 % CI -0.39--0.23, p < 0.001, I^2 = 0 %).

Beran A, 2025 PMID: 39933910	Systematic review and meta-analysis	5 studies of 16000 subjects	Colonoscopy	IBP was higher in the GLP-1RAs group compared to the control group (odds ratios 2.10, 95% CI 1.41-3.13, P = 0.0003). Mean BBPS lower in GLP1-RAs vs. control group (MD -0.34; 95% CI -0.51, -0.17; P = 0.0001).
Baig MU, 2025 PMID: 39694296	Systematic review and meta-analysis	23 studies of 262,018 subjects	EGD	Increase in risk of RGCs ([OR], 4.54; 95% confidence interval [CI], 3.30-6.24; P < .00001, I2 = 68%) Premature endoscopy termination (OR, 4.54; 95% CI, 3.05-6.75; P < .00001, I2 = 0%). No difference in the risk of aspiration pneumonia (OR, .96; 95% CI, .53-1.75; P = .90, I2 = 70%).
Facciorusso A, 2024 PMID: 39142543	Systematic review and meta-analysis	13 studies, 84,065 patients	EGD	Higher rates of RGC (OR, 5.56; 95% CI, 3.35 to 9.23), Higher rates of aborted and repeated procedures in GLP-1RA (OR, 5.13; 95% CI, 3.01 to 8.75; and OR, 2.19; 95% CI, 1.43 to 3.35; respectively). No significant differences in AE and aspiration rates (OR, 4.04; 95% CI, 0.63 to 26.03; and OR, 1.75; 95% CI, 0.64 to 4.77; respectively).
do Nascimento, 2024 PMID: 39039540	Systematic review and meta-analysis	14 studies 2143 patients	elective surgeries and procedures	Higher rates of RGC residual gastric content (OR 6.08; 95% CI 2.86, 12.94; p < 0.00001; I2 = 0%) No significant differences in AE and aspiration rates (OR, 4.04; 95% CI, 0.63 to 26.03; and OR, 1.75; 95% CI, 0.64 to 4.77; respectively).
Panchal S, 2024 PMID: 39824444	Single-center, retrospective cohort study	598 patients	elective surgeries and procedures	RGC was higher in the GLP-1RA group (odds ratio, 3.80; 95% confidence interval, 1.57-9.21; P =0 .003), but odds were not in patients undergoing concurrent colonoscopy. More in the GLP-1RA group had procedures aborted (1.3% vs 0%; P = 0.021), Rates of hypoxia were similar (.2% vs .3%; P = .341). no cases of pulmonary aspiration.

Q1.3: Procedure risk factors

Clinical Question: Which procedure-related risk factors should guide the type of sedation?

Table 1.3.1 PICOs

PICO	Population	Intervention	Comparator	Outcome
1.3	Patients scheduled for low-risk GI endoscopy	Moderate sedation	No sedation	Patient safety and satisfaction
1.3	Patients scheduled for low-risk GI endoscopy	Deep sedation	Moderate sedation	Patient safety and satisfaction
1.3	Patients scheduled for low-risk GI endoscopy	General anesthesia	Deep sedation	Patient safety and satisfaction
1.3	Patients scheduled for low-risk GI endoscopy	Moderate sedation	No sedation	Procedure outcomes
1.3	Patients scheduled for low-risk GI endoscopy	Deep sedation	Moderate sedation	Procedure outcomes
1.3	Patients scheduled for low-risk GI endoscopy	General anesthesia	Deep sedation	Procedure outcomes
1.3	Patients scheduled for high-risk GI endoscopy	Moderate sedation	No sedation	Patient safety and satisfaction
1.3	Patients scheduled for high-risk GI endoscopy	Deep sedation	Moderate sedation	Patient safety and satisfaction
1.3	Patients scheduled for high-risk GI endoscopy	General anesthesia	Deep sedation	Patient safety and satisfaction
1.3	Patients scheduled for high-risk GI endoscopy	Moderate sedation	No sedation	Procedure outcomes
1.3	Patients scheduled for high-risk GI endoscopy	Deep sedation	Moderate sedation	Procedure outcomes
1.3	Patients scheduled for high-risk GI endoscopy	General anesthesia	Deep sedation	Procedure outcomes

BIBLIOGRAPHIC SEARCH

a) Bibliographic search strategies were performed in **PubMed** and **Cochrane**, from June 2024 to March 2025, using the following search strategies:

d. PubMed- Search June 15th 2025

Search: **complex endoscopic AND sedation** Filters: **from 2019 - 3000/12/12** Sort by: **Most Recent**

(("complex"[All Fields] OR "complex s"[All Fields] OR "complexant"[All Fields] OR "complexants"[All Fields] OR "complexated"[All Fields] OR "complexation"[All Fields] OR "complexations"[All Fields] OR "complexe"[All Fields] OR "complexed"[All Fields] OR "complexes"[All Fields] OR "complexing"[All Fields] OR "complexities"[All Fields] OR "complexity"[All Fields] OR "complexs"[All Fields]) AND ("endoscope s"[All Fields] OR "endoscoped"[All Fields] OR "endoscopes"[MeSH Terms] OR "endoscopes"[All Fields] OR "endoscope"[All Fields] OR "endoscopical"[All Fields] OR "endoscopically"[All Fields] OR "endoscopy"[MeSH Terms] OR "endoscopy"[All Fields] OR "endoscopic"[All Fields]) AND ("sedate"[All Fields] OR "sedated"[All Fields] OR "sedating"[All Fields] OR "sedation"[All Fields] OR "sedations"[All Fields])) AND (2019:3000/12/12[pdat])

Translations

complex: "complex"[All Fields] OR "complex's"[All Fields] OR "complexant"[All Fields] OR "complexants"[All Fields] OR "complexated"[All Fields] OR "complexation"[All Fields] OR "complexations"[All Fields] OR "complexe"[All Fields] OR "complexed"[All Fields] OR "complexes"[All Fields] OR "complexing"[All Fields] OR "complexities"[All Fields] OR "complexity"[All Fields] OR "complexs"[All Fields]

endoscopic: "endoscope's"[All Fields] OR "endoscoped"[All Fields] OR "endoscopes"[MeSH Terms] OR "endoscopes"[All Fields] OR "endoscope"[All Fields] OR "endoscopical"[All Fields] OR "endoscopically"[All Fields] OR "endoscopy"[MeSH Terms] OR "endoscopy"[All Fields] OR "endoscopic"[All Fields]

sedation: "sedate"[All Fields] OR "sedated"[All Fields] OR "sedating"[All Fields] OR "sedation"[All Fields] OR "sedations"[All Fields]

Results: 86 studies

e. Cochrane Central Register of Controlled Trials (CENTRAL)- Search June 15th 2025

#1	("gastrointestinal endoscopy") (Word variations have been searched)	2117
#2	("complex procedure ") (Word variations have been searched)	823
#3	#1 AND #2 AND #3	**7**

Results: 7 studies

f. Results of the bibliographic searches

Results Total 86 + 7 = 93 studies

After removing duplicates (n=12), 81 articles were found. 6 studies were considered potentially relevant and acquired in full text. None of these studies (n=0) answering this question could be found. The BSG guidelines on sedation in gastrointestinal endoscopy seem to share the same conclusions: there is no cited reference on procedural factors to be considered in the choice of sedation in this guideline, and only a narrative review provided insights. The level of evidence is very low.

REFERENCES

1. Sidhu R, Turnbull D, Haboubi H et al. British Society of Gastroenterology guidelines on sedation in gastrointestinal endoscopy. Gut 2024; 73: 219-245. doi:10.1136/gutjnl-2023-330396
2. Godoroja-Diarto D, Constantin A, Moldovan C, Rusu E, Sorbello M. Efficacy and Safety of Deep Sedation and Anaesthesia for Complex Endoscopic Procedures-A Narrative Review. Diagnostics (Basel). 2022 Jun 22;12(7):1523. doi: 10.3390/diagnostics12071523. PMID: 35885429; PMCID: PMC9323178.

Certainty of evidence

No formal risk of bias assessment has been done. The certainty of evidence for all clinical outcomes in this PICO question was downgraded to very low in the absence of quantitative data

TASK FORCE 2: Type of sedation

Leader: Philip Roelandt

Members: Paula Alexandra Sa, David Turnbull, Aymeric Becq, Kjetil Garborg, Emmanuel Coron, Naim Abu Freha

Q2.1: Diagnostic colonoscopy without sedation

Table 2.1.1s PICOs

PICO	Population	Intervention	Comparator	Outcome
1	Patients scheduled for GI endoscopy	No sedation	Moderate sedation	Procedure outcomes, safety, satisfaction, cost-effectiveness
2	Patients scheduled for GI endoscopy	No sedation	Deep sedation	Procedure outcomes, safety, satisfaction, cost-effectiveness

BIBLIOGRAPHIC SEARCH

Bibliographic search strategies were performed in **PubMed** and **Cochrane,** from 2014 to 2024 using the following search strategies:

e. PubMed- Search August 7th 2024

((("gastrointestinal endoscopy"[all fields]) OR ("gastrointestinal endoscopy"[MeSH Terms])) AND ("unsedated"[all fields])) AND ((((("moderate sedation"[all fields]) OR ("moderate sedation"[MeSH Terms])) OR ("deep sedation")) OR ("deep sedation"[MeSH Terms]))

Results: 28 studies

f. Cochrane Central Register of Controlled Trials (CENTRAL)- Search August 7th 2024

#1	("gastrointestinal endoscopy") (Word variations have been searched)	1136
#2	("unsedated") (Word variations have been searched)	158

#3	#1 AND #2	**19**

Results: 19 studies

g. Results of the bibliographic searches

Results Total 28 + 19 = 47 studies

After removing duplicates (n=1), 46 articles were found. 11 studies were considered potentially relevant and acquired in full text.

Excluded studies

- Sui Y et al. Comparison of three sedation models for same-day painless bidirectional endoscopy: A multicenter randomized controlled trial. J Gastroenterol Hepatol. 2022 Aug;37(8):1603-1609. doi: 10.1111/jgh.15901. Epub 2022 Jun 2. (All three groups had sedation in some form)
- Catinean A et al. The advantages of water immersion colonoscopy in ambulatory service. Turk J Gastroenterol. 2019 Jul;30(7):636-640. doi: 10.5152/tjg.2019.18784. (Compared two colonoscopy techniques).
- Ramalingam R et al. Effect of Premedication with Glycopyrrolate on Patient Tolerance and Procedure Outcomes in Patients Undergoing Unsedated Upper Gastrointestinal Endoscopy: a Randomized Placebo-controlled Trial. Euroasian journal of hepato-gastroenterology, 2023, 13(2), 55-60 | added to CENTRAL: 29 februar 2024 | 2024 Issue 2 (Compares two groups of unsedated upper endoscopy, no comparison with sedated procedures).

Included studies (8 studies)

1 RCT

- Chen D et al. Comparing blind spots of unsedated ultrafine, sedated, and unsedated conventional gastroscopy with and without artificial intelligence: a prospective, single-blind, 3-parallel-group, randomized, single-center trial. Gastrointest Endosc. 2020 Feb;91(2):332-339.e3. doi: 10.1016/j.gie.2019.09.016. Epub 2019 Sep 18

6 cohort studies

- Sui Y et al. Comparison of missed adenomas in deep-sedated and unsedated colonoscopy: A multicenter retrospective study. Eur J Intern Med. 2023 Apr;110:48-53. doi: 10.1016/j.ejim.2023.01.019. Epub 2023 Jan 27.
- Sui Y et al. Comparison of adenoma detection in different colorectal segments between deep-sedated and unsedated colonoscopy. Sci Rep. 2022 Sep 12;12(1):15356. doi: 10.1038/s41598-022-19468-y.

- Khan F et al. Unsedated Colonoscopy: Impact on Quality Indicators. Dig Dis Sci. 2020 Nov;65(11):3116-3122. doi: 10.1007/s10620-020-06491-0. Epub 2020 Jul 22.
- Robertson AR et al. Colonoscopy quality with Entonox vs intravenous conscious sedation: 18608 colonoscopy retrospective study. World J Gastrointest Endosc. 2017 Sep 16;9(9):471-479. doi: 10.4253/wjge.v9.i9.471.
- Quinn L et al. Sedation for gastroscopy: Is it an adequately understood and informed choice? Ir J Med Sci. 2016 Nov;185(4):785-789. doi: 10.1007/s11845-015-1354-x. Epub 2015 Sep 10.
- Lee TJ et al. Colonoscopic factors associated with adenoma detection in a national colorectal cancer screening program. Endoscopy. 2014 Mar;46(3):203-11. doi: 10.1055/s-0033-1358831. Epub 2014 Jan 28.

1 Cross-sectional study

- Bugajski M et al. Modifiable factors associated with patient-reported pain during and after screening colonoscopy. Gut. 2018 Nov;67(11):1958-1964. doi: 10.1136/gutjnl-2017-313905. Epub 2017 Sep 28.

Table 2.1.2s: Characteristics of the included studies

Study (Author, year)	Country	Study design	No. of sites (no. of subjects)	Age (y)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm	Follow-up
Sui, 2023	China	Retrospective cohort	7 (n=3710)	50 (Median)	52.3	Colonoscopy with deep sedation (left lateral position)	Unsedated colonoscopy (dynamic position change)	Adenoma miss rate 19.14%	Adenoma miss rate 16.15%	-
Sui, 2022	China	Retrospective cohort	7 (n=4500)	35-60	51.8	Colonoscopy with deep sedation (left lateral position)	Unsedated colonoscopy (dynamic position change)	Average number of segmental adenomas: splenic flexure 0.01, descending colon 0.16. Other segments non-significant ADR 45.4% Adenomas per positive patient 1.76	Average number of segmental adenomas: splenic flexure 0.02, descending colon 0.24. Other segments non-significant ADR 46.3% Adenomas per positive patient 2.00	-
Khan, 2020	USA	Retrospective cohort	1 (n=24795; 179 unsedated, 24616 sedated)	17-97	43.3	Colonoscopy with sedation	Unsedated colonoscopy	ADR 27.4% CIR 95.8%	ADR 21.2% CIR 85.5%	-
Chen, 2020	China	RCT	1 (n=437)	≥18	47.2	Unsedated ultrathin transoral endoscopy +/- AI	Unsedated conventional EGD +/- AI Sedated conventional EGD +/- AI	Blind spot rate (BSR) (+ AI) 21.77% Tachycardia 22 (31.4%) O2 desaturation 9 (12.9%)	BSR (+ AI) 31.23% Tachycardia 26 (36.6%) O2 desaturation 7 (9.9%)	BSR (+ AI) 3.42% Tachycardia 0 (0%) O2 desaturation 14 (19.2)	-

									Willingness to repeat 44 (62.9%) Comfort score (VAS-10), mean (SD) 6.9 (2.39)	Willingness to repeat 41 (57.8) Comfort score 5.79 (2.3)	Willingness to repeat 66 (90.4) Comfort score 9.45 (1.47)	
Robertson, 2017	UK	Retrospective cohort (Three arms; Entonox, i.v. sedation and no sedation. Entonox arm and the no sedation arm were not compared; the Entonox arm was excluded from this table.	4 (n=13259; 1893 unsedated)	≥18	45.1	Unsedated colonoscopy	Colonoscopy with i.v. sedation		Moderate-to-extreme discomfort 11.4% CIR 94.2% PDR 37.4%	Moderate-to-extreme discomfort 18.8% CIR 93.7% PDR 33.1%		-
Bugajski, 2018	Poland	Cross-sectional	23 (n=22725; 63.4% unsedated)	Mean 59.9 (SD 2.7)	48.5	Unsedated colonoscopy	Colonoscopy w/moderated sedation	Colonoscopy w/deep sedation	Severe/moderate (S/M) pain 21.9%	S/M pain 19.2%	S/M pain 1.6%	-
Quinn, 2016	Ireland	Prospective cohort (Patients chose sedation or no sedation)	1 (n=111)	Range from <30 to >60	38.8	Unsedated gastroscopy	Sedated gastroscopy		48 (43.2%) chose no sedation Satisfied with decision (no sedation) 73%	63 (56.8%) chose sedation Satisfied with decision (sedation) 90%		-
Lee, 2014	England	Retrospective cohort	? (n=31088; 13.1% unsedated)	60-74	60.3	Unsedated colonoscopy	Colonoscopy with sedation		ADR 49.1% Advanced ADR 30.3% Right-sided ADR 20.9%	ADR 46.0% Advanced ADR 28.7% Right-sided ADR 19.1%		-

Fig. 2.1.1s Effect of no sedation on adenoma detection rate (ADR)

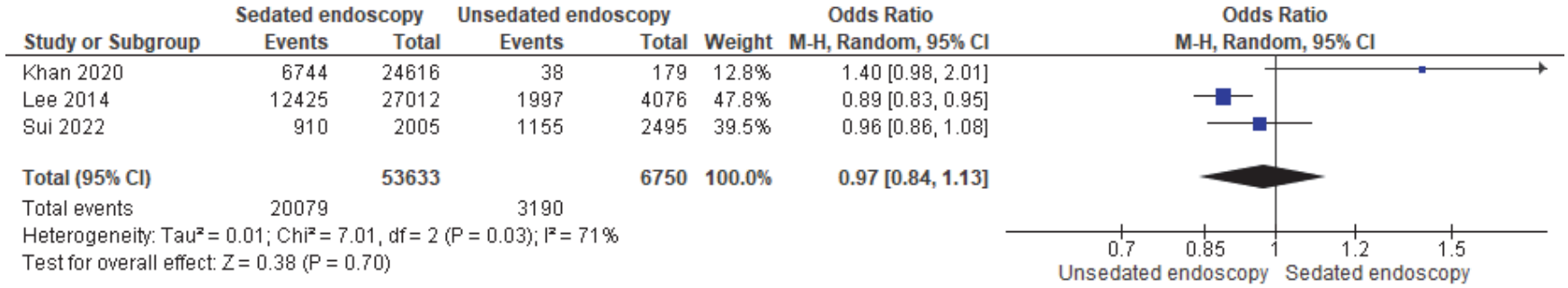


Table 2.1.3s: Risk of bias assessment for studies

Study	Selection (max 4 stars)	Comparability (max 2 stars)	Outcomes (max 3 stars)	Quality (Total 9/9)
Sui, 2022	***	*	**	**Good**
Khan, 2020	***	*	**	**Good**
Lee, 2014	***	*	**	**Good**

Table 2.1.4s Certainty of evidence

The risk of bias assessment for each study can be found in **Table 2.1.3s**. Overall, the included studies were considered of good quality. The certainty of evidence for this outcome was downgraded because the evidence was based only on three non-randomized observational studies in the absence of RCTs. For the outcome of efficacy of ADR, further downgrading was applied due to indirectness (heterogeneity in the endoscopic expertise) and imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to very low, and a conditional recommendation was proposed.

Fig. 2.1.2s Effect of no sedation on Cecal Intubation Rate (CIR)

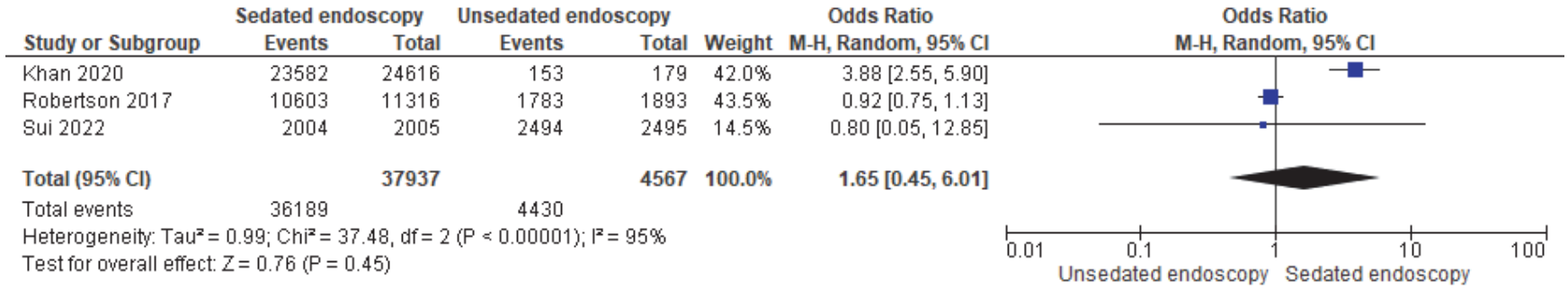


Table 2.1.5s: Risk of bias assessment for studies

Study	Selection (max 4 stars)	Comparability (max 2 stars)	Outcomes (max 3 stars)	Quality (Total 9/9)
Sui, 2022	***	*	**	**Good**
Khan, 2020	***	*	**	**Good**
Robertson, 2017	***	*	**	**Good**

Table 2.1.6s Certainty of evidence

The risk of bias assessment for each study can be found in **Table 2.1.5s**. Overall, the included studies were considered of good quality. The certainty of evidence in this PICO question was downgraded because the evidence was based only on three non-randomized observational studies in the absence of RCTs. For the outcome of efficacy of hemostasis, further downgrading was applied due to indirectness (heterogeneity in the endoscopic expertise) and imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to very low

Endoscopy | DOI 10.1055/a-2898-6540 |

Fig. 2.1.3s Effect of no sedation on patient discomfort

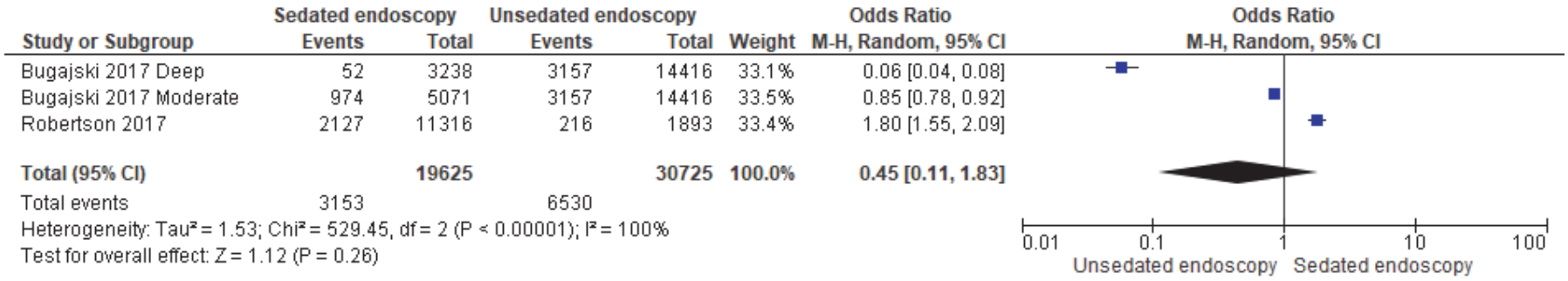


Table 2.1.7s: Risk of bias assessment for studies

Study	Selection (max 4 stars)	Comparability (max 2 stars)	Outcomes (max 3 stars)	Quality (Total 9/9)
Bugajski, 2018	***	*	**	**Good**
Robertson, 2017	***	*	**	**Good**

Table 2.1.8s Certainty of evidence

The risk of bias assessment for each study can be found in **Table 2.1.7s**. Overall, the included studies were considered of good quality. The certainty of evidence in this PICO question was downgraded because the evidence was based only on two non-randomized observational studies in the absence of RCTs. For the outcome of efficacy of hemostasis, further downgrading was applied due to indirectness (heterogeneity in the endoscopic expertise) and imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to very low

Endoscopy | DOI 10.1055/a-2898-6540 |

Table 2.1.4s, 2.1.6s, 2.1.8s Certainty of evidence

Bibliography:. TF 2 for Q1. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With placebo	With Q1a		Risk with placebo	Risk difference with Q1a
ADR											
60383 (3 non-randomised studies)	serious[a]	serious[b]	serious[c]	serious[a]	none	⨁◯◯◯ Very low[a,b,c]	3190/6750 (47.3%)	20079/53633 (37.4%)	**OR 0.97** (0.84 to 1.13)	3190/6750 (47.3%)	**8 fewer per 1.000** (from 43 fewer to 31 more)
CIR											
42504 (3 non-randomised studies)	serious[a]	serious[b]	serious[c]	serious[a]	none	⨁◯◯◯ Very low[a,b,c]	4430/4567 (97.0%)	36189/37937 (95.4%)	**OR 1.65** (0.45 to 6.01)	4430/4567 (97.0%)	**12 more per 1.000** (from 34 fewer to 25 more)
Discomfort											
50350 (3 non-randomised studies)	serious[a]	serious[b]	serious[c]	serious[a]	none	⨁◯◯◯ Very low[a,b,c]	6530/30725 (21.3%)	3153/19625 (16.1%)	**OR 0.45** (0.11 to 1.83)	6530/30725 (21.3%)	**104 fewer per 1.000** (from 184 fewer to 118 more)

Q2.2: Unsedated transnasal or ultrathin peroral gastroscopy

Table 2.2.1s. PICOs

PICO	Population	Intervention	Comparator	Outcome
1	Patients scheduled for GI endoscopy	Unsedated transnasal or ultrathin peroral endoscopy	Sedated upper endoscopy	Procedure outcomes, safety, satisfaction

BIBLIOGRAPHIC SEARCH

Bibliographic search strategies were performed in **PubMed** and **Cochrane** from 2019 to 2024 using the following search strategies:

a. PubMed- Search August 30th 2024

(((gastrointestinal endoscopy[all fields]) OR (gastrointestinal endoscopy[MeSH Terms])) AND (transnasal[all fields])) OR (ultrathin[all fields])

Results: 8434 studies

b. Cochrane Central Register of Controlled Trials (CENTRAL)- Search August 30th 2024

#1	("gastrointestinal endoscopy") (Word variations have been searched)	2498
#2	("transnasal") (Word variations have been searched)	271
#3	("ultrathin") (Word variations have been searched)	197
#3	#1 AND (#2 OR #3)	18

Results: 18 studies

c. Results of the bibliographic searches

Results Total 8434 + 18 = 8452 studies

After removing duplicates (n=12), 8440 articles were found. 11 studies were considered potentially relevant and acquired in full text.

Excluded studies

5 studies were excluded

- van Tilburg L et al. Endoscopic screening of the upper gastrointestinal tract for second primary tumors in patients with head and neck cancer in a Western country. Endoscopy. 2023 Nov;55(11):981-990. (No control group, irrelevant for PICO)
- Takahashi K et al. Nasal breathing is superior to oral breathing when performing and undergoing transnasal endoscopy: a randomized trial. Endoscopy. 2023 Mar;55(3):207-216. (No standard control group, irrelevant for PICO)
- Sugimoto M et al. Efficacy of high-vision transnasal endoscopy using texture and colour enhancement imaging and narrow-band imaging to evaluate gastritis: a randomized controlled trial. Ann Med. 2022 Dec;54(1):1004-1013. (No standard control group, irrelevant for PICO)
- Nakamura M et al. Novel ultrathin double-balloon endoscopy for the diagnosis of small-bowel diseases: a multicenter nonrandomized study. Endoscopy. 2021 Aug;53(8):802-814. (All patients sedated, irrelevant for PICO)
- Wellenstein DJ et al. Cost analysis of office-based transnasal esophagoscopy. Eur Arch Otorhinolaryngol. 2019 May;276(5):1457-1463. (No endoscopy control group, irrelevant for PICO).

Included studies

3 Meta-analyses

- Huibertse LJ et al. Unsedated transnasal endoscopy for the detection of Barrett's esophagus: systematic review and meta-analysis. Dis Esophagus. 2023 Jan 28; 36(2):doac045. doi: 10.1093/dote/doac045.
- Wong MCS et al. Performance of screening tests for esophageal squamous cell carcinoma: a systematic review and meta-analysis. Gastrointest Endosc. 2022 Aug;96(2):197-207.e34. doi: 10.1016/j.gie.2022.04.005. Epub 2022 Apr 9.
- Wickremeratne T et al. Systematic review with meta-analysis: ultra-thin gastroscopy compared to conventional gastroscopy for the diagnosis of oesophageal varices in people with cirrhosis. Aliment Pharmacol Ther. 2019 Jun;49(12):1464-1473. 3 RCTs
- Matsumoto K et al. Acceptability, Safety, and Feasibility of Transnasal and Peroral Ultrathin Endoscopy Using GAGLESS Mouthpieces: A Prospective Randomized Trial. In Vivo. 2024 Mar-Apr;38(2):826-832. doi: 10.21873/invivo.13507.
- Chen D et al. Comparing blind spots of unsedated ultrafine, sedated, and unsedated conventional gastroscopy with and without artificial intelligence: a prospective, single-blind, 3-parallel-group, randomized, single-center trial. Gastrointest Endosc. 2020 Feb;91(2):332-339.e3. doi: 10.1016/j.gie.2019.09.016. Epub 2019 Sep 18.
- Kang D et al. An Operable, Portable, and Disposable Ultrathin Endoscope for Evaluation of the Upper Gastrointestinal Tract. Dig Dis Sci. 2019 Jul;64(7):1901-1907. doi: 10.1007/s10620-019-5478-0. Epub 2019 Jan 25.

Table 2.2.2s: Evidence: Characteristics of the included studies

Outcomes, safety, satisfaction

Study (Author, year)	Country	Study design	No. of sites (no. of subjects)	Age (y)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm	Follow-up
Matsumoto, 2024	Japan	RCT	? (n=101)	≥20	100	Transnasal endoscopy, unsedated	Peroral ultrathin endoscopy with a gagless mouthpiece, unsedated	Completed procedure 47/49 Degree of distress during EGD (VAS-10), Mean (SD) Overall 2.722 (2.174)	Completed procedure 52/52 Degree of distress during EGD (VAS-10), Mean (SD) Overall 3.569 (2.389)	-
Chen, 2020 NB! Only half of the patients are accounted for in table 1	China	RCT (three arms: unsedated ultrathin peroral, unsedated conventional EGD, and sedated conventional EGD)	1 (n=437)	≥18	47.2	Unsedated ultrathin peroral endoscopy +/- AI	1.Unsedated cEGD +/- AI 2. Sedated cEGD +/- AI	Values are mean (SD) Blind spots w/AI: 5.66 (2.59) Comfort score (VAS-10): 6.9 (2.39)	Values are mean (SD) Blind spots w/AI: 1) 8.12 (3.55) 2) 0-89 (1.49) Comfort score (VAS-10): 1) 5.79 (2.3) 2) 9.45 (1.47)	-
Kang, 2019	South Korea	RCT (crossover, all patients had both procedures)	1 (n=40 for maneuverability and diagnostics, n=10 for comfort scores (crossover))	20-65	40.8	Transnasal endoscopy	Standard EGD	Overall discomfort (VAS-10), mean (SD) 3.2 (1.19	Overall discomfort (VAS-10), mean (SD) 4.4 (0.7)	-

Fig. 2.2.1s Effect of unsedated transnasal or ultrathin peroral endoscopy on procedure success

Study or Subgroup	unsedated transnasal or ultrathin peroral endoscopy Events	Total	Conventional upper endoscopy Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Chen 2020	141	145	142	146	33.6%	1.00 [0.96, 1.04]
Chen 2020 Sedated	141	145	146	146	54.2%	0.97 [0.94, 1.00]
Kang 2019	10	10	10	10	1.5%	1.00 [0.83, 1.20]
Matsumoto 2024	47	49	52	52	10.6%	0.96 [0.90, 1.03]
Total (95% CI)		**349**		**354**	**100.0%**	**0.98 [0.96, 1.00]**
Total events	339		350			

Heterogeneity: Tau² = 0.00; Chi² = 1.73, df = 3 (P = 0.63); I² = 0%
Test for overall effect: Z = 1.72 (P = 0.09)

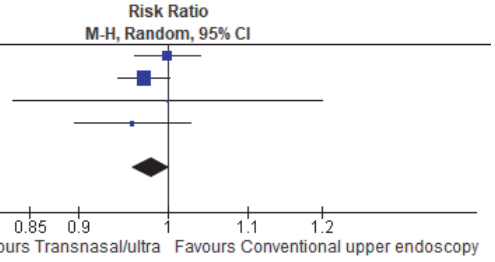
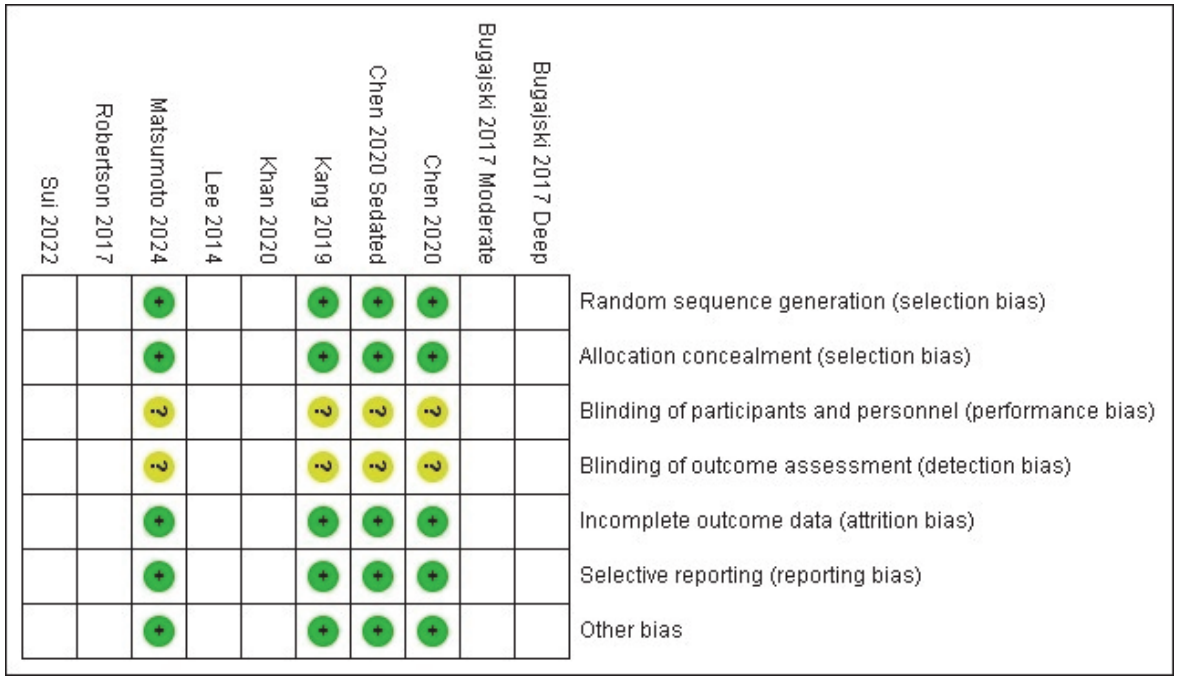


Fig 2.2.2s: Risk of bias assessment for studies



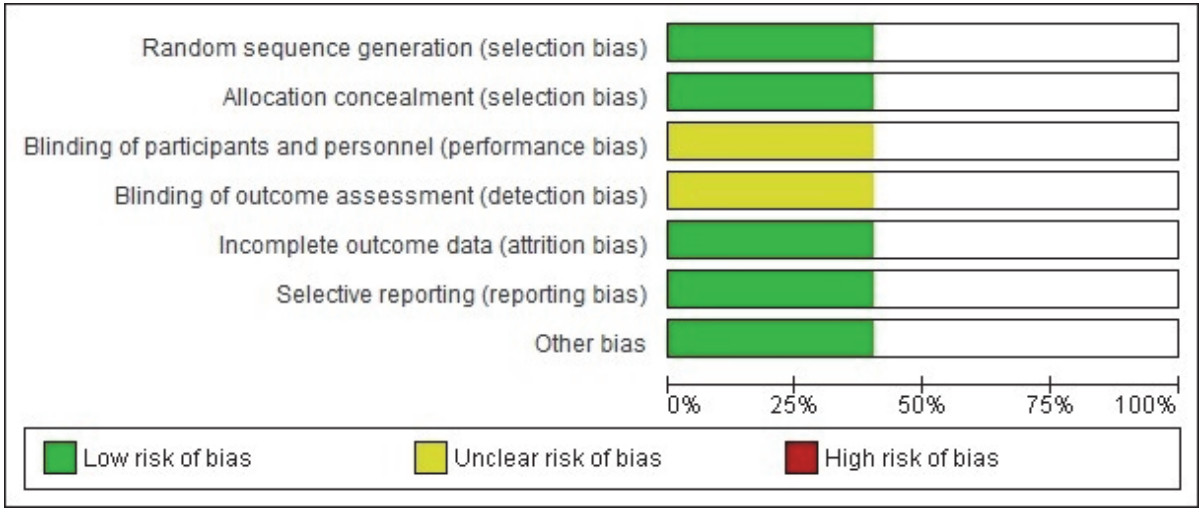


Table 2.2.3s Certainty of evidence

The risk of bias assessment for each study can be found in **Fig 2.2.2s**. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to indirectness (heterogeneity in the endoscopic expertise), inconsistency, and imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to very low

Fig. 2.2.3s Effect of unsedated transnasal or ultrathin peroral endoscopy on comfort score

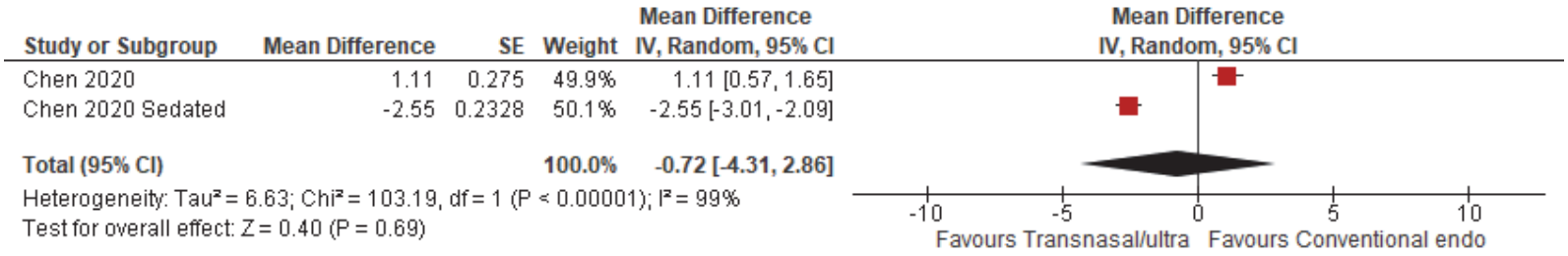


Table 2.2.4s Certainty of evidence

The risk of bias assessment for each study can be found in **Fig 2.2.2s**. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to indirectness (heterogeneity in the endoscopic expertise), inconsistency and imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to very low

Fig. 2.2.4s Effect of unsedated transnasal or ultrathin peroral endoscopy on distress

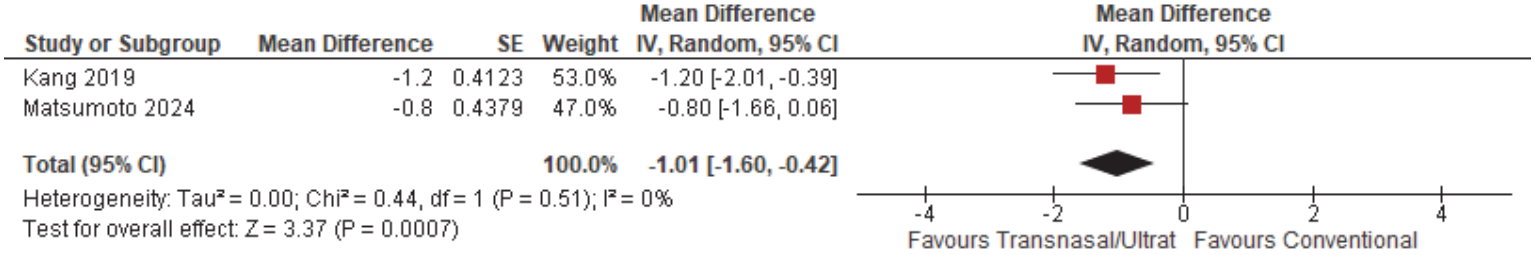


Table 2.2.5s Certainty of evidence

The risk of bias assessment for each study can be found in **Fig 2.2.2s**. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to indirectness (heterogeneity in the endoscopic expertise), inconsistency and imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to very low

Table 2.2.3s – 2.2.5s Certainty of evidence

Q1a compared to placebo for unsedated endoscopy
Bibliography: TF 2 for Q1. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With placebo	With Q1a		Risk with placebo	Risk difference with Q1a
ADR											
60383 (3 non-randomised studies)	serious[a]	serious[b]	serious[c]	serious[a]	none	⨁◯◯◯ Very low[a,b,c]	3190/6750 (47.3%)	20079/53633 (37.4%)	**OR 0.97** (0.84 to 1.13)	3190/6750 (47.3%)	**8 fewer per 1.000** (from 43 fewer to 31 more)
CIR											
42504 (3 non-randomised studies)	serious[a]	serious[b]	serious[c]	serious[a]	none	⨁◯◯◯ Very low[a,b,c]	4430/4567 (97.0%)	36189/37937 (95.4%)	**OR 1.65** (0.45 to 6.01)	4430/4567 (97.0%)	**12 more per 1.000** (from 34 fewer to 25 more)
Discomfort											
50350 (3 non-randomised studies)	serious[a]	serious[b]	serious[c]	serious[a]	none	⨁◯◯◯ Very low[a,b,c]	6530/30725 (21.3%)	3153/19625 (16.1%)	**OR 0.45** (0.11 to 1.83)	6530/30725 (21.3%)	**104 fewer per 1.000** (from 184 fewer to 118 more)

Q2.3: Sedation provider during endoscopy

2.3.1 Who administers minimal-moderate sedation?

Table 2.3.1s: PICOs

PICO	Population	Intervention	Comparator	Outcome
1	Patients undergoing GI endoscopy under mild-moderate sedation	Non-anaesthesiologists	Anaesthesiologist	Completeness of procedure, quality, patient safety and satisfaction, endoscopist satisfaction, cost-effectiveness, time management

BIBLIOGRAPHIC SEARCH

Bibliographic search strategy was performed in **PubMed** using the following search strategies:

a. **PubMed- Search 24.09.2024 & 04.10.2024**

("conscious sedation"[Title/Abstract] OR "no sedation"[Title/Abstract] OR "Anesthesia"[Title/Abstract] OR "Analgosedation"[Title/Abstract] OR "Sedation"[Title/Abstract] OR "nitrous oxide"[Title/Abstract] OR "midazolam"[Title/Abstract] OR "remimazolam"[Title/Abstract] OR "fentanyl"[Title/Abstract] OR "remifentanyl"[Title/Abstract])

AND ("endoscopy"[Title/Abstract] OR "gastroscopy"[Title/Abstract] OR "colonoscopy"[Title/Abstract] OR "esophagogastroduodenoscopy"[Title/Abstract] OR "EUS"[Title/Abstract] OR "endoscopic ultrasound"[Title/Abstract] OR "ERCP"[Title/Abstract] OR "endoscopic retrograde cholangiopancreatography"[Title/Abstract] OR "enteroscopy"[Title/Abstract])

AND ("endoscopist"[Title/Abstract] OR "non-anesthesiologist"[Title/Abstract] OR "nurse" [Title/Abstract])

Results: 755 results, including 206 RCTs, 230 clinical studies, and 9 meta-analyses

b. <u>Results of the bibliographic searches</u>

After removing duplicates (n=0), 0 articles were found. No studies were considered potentially relevant and acquired in full text.

No specific studies or meta-analyses answering this question could be found. The BSG guidelines on sedation in gastrointestinal endoscopy[1] seem to share the same conclusions: there is no cited reference on non-anaesthesiologist versus anaesthesiologist for mild/moderate sedation in this guideline. The level of evidence is very low.

REFERENCES

1. Sidhu R, Turnbull D, Haboubi H et al. British Society of Gastroenterology guidelines on sedation in gastrointestinal endoscopy. Gut 2024; 73: 219-245. doi:10.1136/gutjnl-2023-330396
2. Goudra BG, Singh PM, Gouda G et al. Safety of Non-anesthesia Provider-Administered Propofol (NAAP) Sedation in Advanced Gastrointestinal Endoscopic Procedures: Comparative Meta-Analysis of Pooled Results. Dig Dis Sci 2015; 60: 2612-2627. doi:10.1007/s10620-015-3608-x
3. Barbosa EC, Espírito Santo PA, Baraldo S et al. Remimazolam versus propofol for sedation in gastrointestinal endoscopic procedures: a systematic review and meta-analysis. Br J Anaesth 2024; 132: 1219-1229. doi:10.1016/j.bja.2024.02.005
4. Johnson KL, Meyers JS, Mortensen GN et al. Remimazolam: A Retrospective Study of Initial Safety and Recovery Data in Diverse Procedural Sedation. Clin Ther 2024; 46: 90-95. doi:10.1016/j.clinthera.2023.11.004

2.3.2 Who administers deep sedation?

Table 2.3.2s. PICOs

PICO	Population	Intervention	Comparator	Outcome
1	Patients scheduled for GI endoscopy under deep sedation	Deep sedation provided by trained non-anaesthesiologists (physicians)	Deep sedation provided by anaesthesiologists	Procedure outcomes, safety, and satisfaction
2	Patients scheduled for GI endoscopy under deep sedation	Deep sedation provided by a trained nurse	Deep sedation provided by anaesthesiologists	Procedure outcomes, safety, and satisfaction

BIBLIOGRAPHIC SEARCH

Bibliographic search strategies were performed in **PubMed** and **Cochrane** from 2019 to 2024 using the following search strategies.

a. PubMed- Search (August 2024)

(("propofol"[MeSH Terms] OR "propofol"[All Fields] OR "endoscopy"[All Fields]) AND “deep sedation”[All Fields]

Results: 372 studies

(("deep sedation"[All Fields] AND "endoscopy"[All Fields] AND "nurse"[All Fields]), no date restriction

Results: 72 studies

b. Cochrane Central Register of Controlled Trials (CENTRAL)- Search (August 2024)

Results: 222 studies

C. Results of the bibliographic searches

Results Total 372 + 72 + 222 = 666 studies

#1	("propofol") (Word variations have been searched)	9,396
#2	("upper GI endoscopy") (Word variations have been searched)	4533
#3	("patient experience") (Word variations have been searched)	47087
#4	("Endoscopy") (Word variations have been searched)	196,895
#5	("deep sedation") (Word variations have been searched)	2,534
#6	#1 AND #4 AND #5	**222**

After removing duplicates, 129 articles were found. 16 studies were considered potentially relevant and acquired in full text.

Excluded studies

3 publications were excluded; the articles were narrative discussions or related to paediatrics.

Included studies

3 meta-analyses

- Goudra BG et al. Safety of Non-anesthesia Provider-Administered Propofol (NAAP) Sedation in Advanced Gastrointestinal Endoscopic Procedures: Comparative Meta-Analysis of Pooled Results. Dig Dis Sci 2015; 60: 2612-2627.
- Gouda B, et al. Safety of non-anesthesia provider-administered propofol sedation in non-advanced gastrointestinal endoscopic procedures: A meta-analysis. Saoudi J Gastroenterol 2017; 23(3):133-143.
- Daza Jf, et al. Propofol administration by endoscopists versus anesthesiologists in gastrointestinal endoscopy: a systematic review and meta-analysis of patient safety outcomes. Can J Gastroenterol 2018; 61(4):226-236.

2 RCTs

- Ferreira AO, Torres J, Barjas E, Nunes J, Glória L, Ferreira R, Rocha M, Pereira S, Dias S, Santos AA, Cravo M. Non-anesthesiologist administration of propofol sedation for colonoscopy is safe in low risk patients: results of a noninferiority randomized controlled trial. Endoscopy. 2016 Aug;48(8):747-53. doi: 10.1055/s-0042-105560. Epub 2016 Apr 21. PMID: 27100716.
- Molina-Infante J et al. Nonanesthesiologist-administered propofol versus midazolam and propofol, titrated to moderate sedation, for colonoscopy: a randomized controlled trial. Dig Dis Sci 2012; 57: 2385-2393. ***(off target, propofol vs. midazolam + pethidine)***

16 observational studies

- de Paulo GA et al. Sedation in gastrointestinal endoscopy: a prospective study comparing nonanesthesiologist-administered propofol and monitored anesthesia care. Endosc Int Open 2015; 3: E7-E13.
- Jensen JT et al. Moderate and deep nurse-administered propofol sedation is safe. Dan Med J 2015; 62: A5049.
- Ooi M & Thomson A. Morbidity and mortality of endoscopist-directed nurse-administered propofol sedation (EDNAPS) in a tertiary referral center. Endosc Int Open 2015; 3: E393-397.
- Jensen JT et al. High efficacy with deep nurse-administered propofol sedation for advanced gastroenterologic endoscopic procedures. Endosc Int Open 2016; 4: E107-111.
- Buxbaum J et al. Anesthetist-Directed Sedation Favors Success of Advanced Endoscopic Procedures. Am J Gastroenterol 2017; 112: 290-296. (moderate sedation).
- Tiankanon K et al. Nurse Administered Propofol Sedation (NAPS) versus On-call Anesthesiologist Administered Propofol Sedation (OAPS) in Elective Colonoscopy. J Gastrointestin Liver Dis 2020; 29: 579-585.
- Gururatsakul M et al. Prospective audit of the safety of endoscopist-directed nurse-administered propofol sedation in an Australian referral hospital. J Gastroenterol Hepatol 2021; 36: 490-497.
- Heron V, Golden C, Blum S et al. Endoscopist-Directed Propofol as an Adjunct to Standard Sedation: A Canadian Experience. Journal of the Canadian Association of Gastroenterology 2019; 3: 141-144.
- Medina-Prado L et al. Safety of endoscopist-administered deep sedation with propofol in ASA III patients. Rev Esp Enferm Dig 2022; 114: 468-473.
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- Patel J, Fang J, Taylor LJ, Adler DG, Gawron AJ. Safety and efficacy of non-anesthesiologist administration of propofol sedation during esophagogastroduodenoscopy in the intensive care unit. Endosc Int Open. 2019 Apr;7(4):E625-E629. doi: 10.1055/a-0829-6284. Epub 2019 Apr 12. PMID: 30993168; PMCID: PMC6461546.
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- Riesco-López JM, Rizo-Pascual J, Díaz-Sánchez A, Manzano-Fernández R, Martín-Saborido C, Varillas-Delgado D, Rivero-Fernández M, González-Alonso R, Moya-Valverde E, García-Fernández P, Campos-Cantero R. Endoscopist-directed propofol is more efficient than anesthesiologist-administered propofol in patients at low-intermediate anesthetic risk. Eur J Gastroenterol Hepatol. 2020 Nov;32(11):1440-1446. doi: 10.1097/MEG.0000000000001820. PMID: 32925498.
- Alburquerque M, Smarrelli A, Montesinos JC, Carreño SO, Fernandez AZ, García AV, Frontado CL, Vidal L, Francesch MF, Lladó FG. Outcomes of colonoscopy with non-anesthesiologist-administered propofol (NAAP): an equivalence trial. Endosc Int Open. 2021 Jul;9(7):E1070-E1076. doi: 10.1055/a-1452-9242. Epub 2021 Jun 17. PMID: 34222632; PMCID: PMC8211490.
- Monsma-Muñoz M, Romero-García E, Montero-Sánchez F, Tevar-Yudego J, Silla-Aleixandre I, Pons-Beltrán V, Argente-Navarro MP. Retrospective observational study on safety of sedation for colonoscopies in ASA I and II patients performed by a nurse and under the supervision of anesthesiology. Rev Esp Anestesiol Reanim (Engl Ed). 2022 Jun-Jul;69(6):319-325. doi: 10.1016/j.redare.2021.05.012. Epub 2022 Jun 24. PMID: 35760692.

Table 2.3.3s: Evidence: Characteristics of the included studies

Study (Author, year)	Country	Study design	No. of sites (no. of subjects)	Age (y)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm
Goudra, 2015	-	Meta-analysis				NAAP	AAP	Hypoxia rate 0.133 (0.117-0.152) Airway intervention rate 0.035 (0.026-0.047) Patient satisfaction 7.22 (7.17-7.27) Endoscopist satisfaction 6.03 (5.94-6.11) Propofol 251.44 mg (244.39-258.49)	Hypoxia rate 0.143 (0.128-0.159) Airway intervention rate 0.133 (0.118-0.150) Patient satisfaction 9.82 (9.76-9.88) Endoscopist satisfaction 9.06 (8.91-9.21) Propofol 340.32 mg (327.30-353.33)
Gouda 2017		Meta-analysis Non-advanced procedures The risk of bias was not officially measured	25 studies 137078 pts			NAAP	AP	Pooled airway intervention rate, %: 0.002, 0.001-0.006 Pooled airway complication rate, %: 0.001, 0-0.001 Pooled hypoxia rate, %: 0.014, 0.008-0.023	
Daza, 2018		Meta-analysis Low risk of bias Non advanced procedure ASA 1-II pats	5/21054			NAAP	AP	Airway intervention, OR, 95%CI: 1.07, 0.3-3.9 Hypotension, OR, 95%CI: 1.5, 0.4-5.4 Bradycardia, OR, 95%CI: 3.7, 1.6-8.1 Propofol dose, difference, MD, 95%CI: -61.8, -114.5- -9.1 Procedure time, Difference, MD, 95%CI: -	

								0.08, -3.5 – 3.3
de Paulo, 2015	Brazil	Observational	2 (2000)	All	51.4	NAAP + ANE	ANE	Anaesthesiology uses more propofol, and patients are frequently under deep sedation. Procedures are statistically significantly longer, but this is only one or two minutes.
Ferreira, 2016	Portugal	RCT	1 (277)			NAAP	ANE	NAAP is equivalent to anaesthesiologist-administered sedation in the rate of adverse events in a low-risk population.
Jensen, 2015	Denmark	Observational	1 (6840)	> 13	38.6	NAAP moderate/deep	-	Hypoxia 3.2% Hypotension 3.1% Ventilation 0.5% Higher rate complications ASA III
Ooi, 2015	Australia	Observational	1 (33539)	>18		EDNAPS	-	0.07% complications requiring Medical Emergency Team calls
Jensen, 2016	Denmark	Observational	1 (1899)	> 16	43.4	NAAP deep	-	Hypoxia 4.3% Ventilation 1.1%
Buxbaum, 2017	USA	Observational	1 (1171)	>11	36	Anesthesist-directed sedation	Endoscopist-directed sedation	Less sedation failure in ADS
McVay 2017	USA	Observational	130 EGD obese		36	NAAP		
Maestro Antolin 2018	Portugal	Observational	ERCP			NAAP		
Patel 2019	USA	Observational	EGD (ICU)			NURSE AAP		
Facciorusso 2020	Italy	Observational	EUS			NURSE AAP		
Riesco Lopez 2020	Spain	Observational	EGD+Colono+ EUS					
Alburquerque 2021	Spain	Observational	Colonoscopy					
Monsma-Munoz 2022	Spain	Observational	Colonoscopy					

Tiankanon, 2020	Thailand	Observational	1 (252)	18-90	57.5	NAPS	OAPS (on-call anesthesiologist administered propofol sedation	Propofol 180.2 ± 102 mg Adverse events 2.1% Procedural time 17.2 ± 16 min	Propofol 248.4 ± 88 mg Adverse events 4.8% Procedural time 16.3 ± 6 min
Gururatsakul, 2021	Australia	Observational	1 (24958)	>18	52.3	EDNAPS	-	0.26% complications (hypoxia, arrhythmia, hypotension)	
Molina-Infante, 2012	Spain	RCT	1 (119)	> 18	46.2	NAAP propofol + midazolam	NAAP propofol	Pain 0.3 Satisfaction 9.8 Deep sedation 4 min 16% Early recovery 6.8 min	Pain 1.03 Satisfaction 9.4 Deep sedation 4 min 1% Early recovery 5.3 min
Heron, 2019	Canada	Observational	1 (4930)	All	?	NAAP propofol	NAA standard sedation		
Medina-Prado, 2021	Spain	Observational	1 (562)	>18	49.1	NAAP (endoscopist) ASA III	NAAP (endoscopist) ASA I-II	Adverse events (hypotension, bradycardia, desaturation) 23.8%	Adverse events (hypotension, bradycardia, desaturation) 14.5%

Fig. 2.3.1s. NAAP vs. Anesthetists regarding Adenoma Detection Rate (ADR)

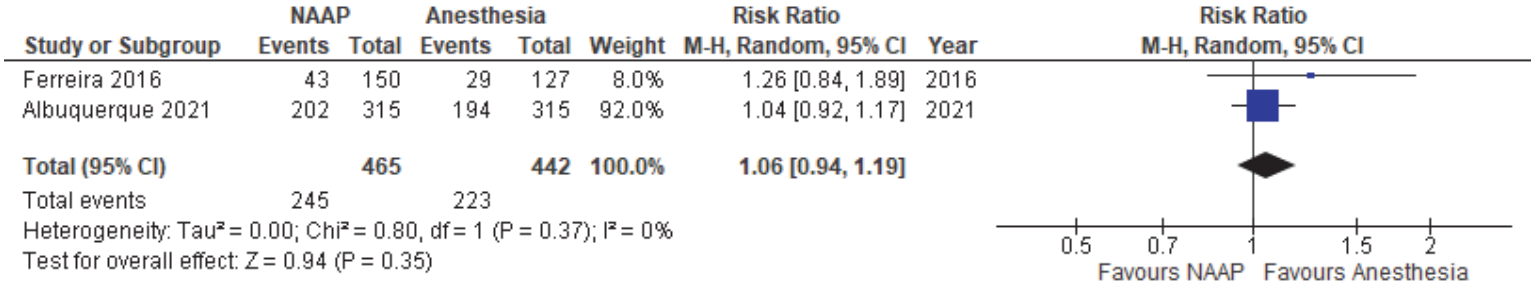
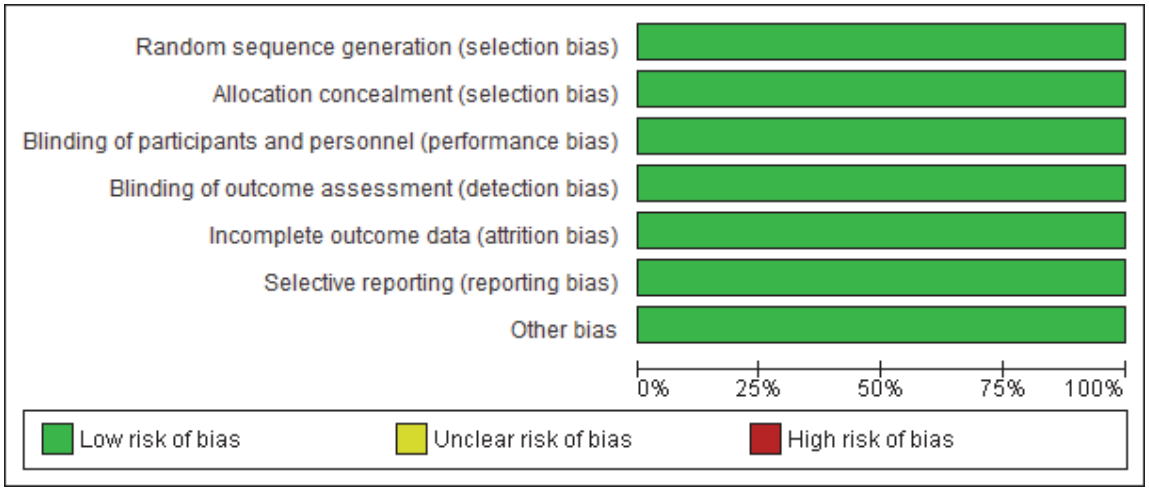
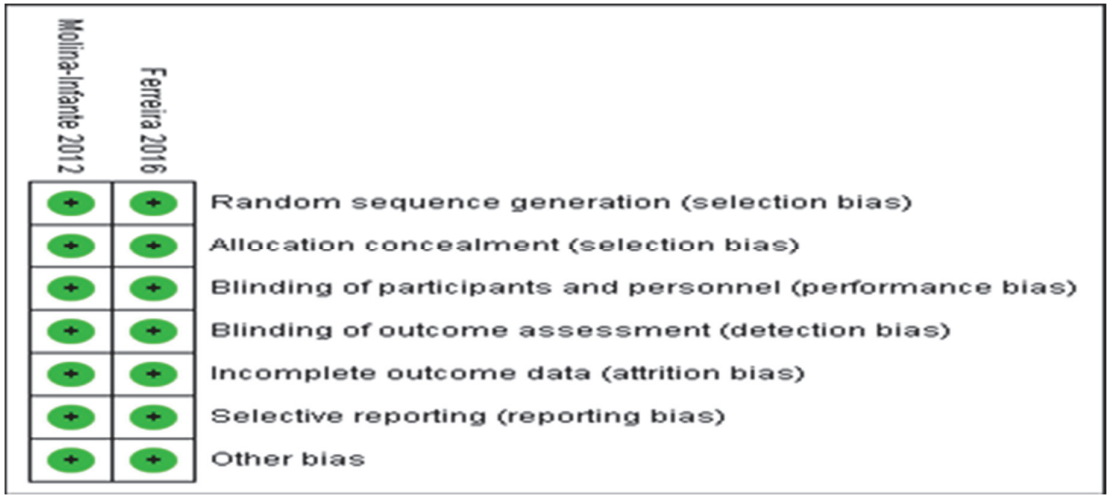


Table 2.3.4s: Risk of bias assessment for studies





Endoscopy | DOI 10.1055/a-2898-6540 |

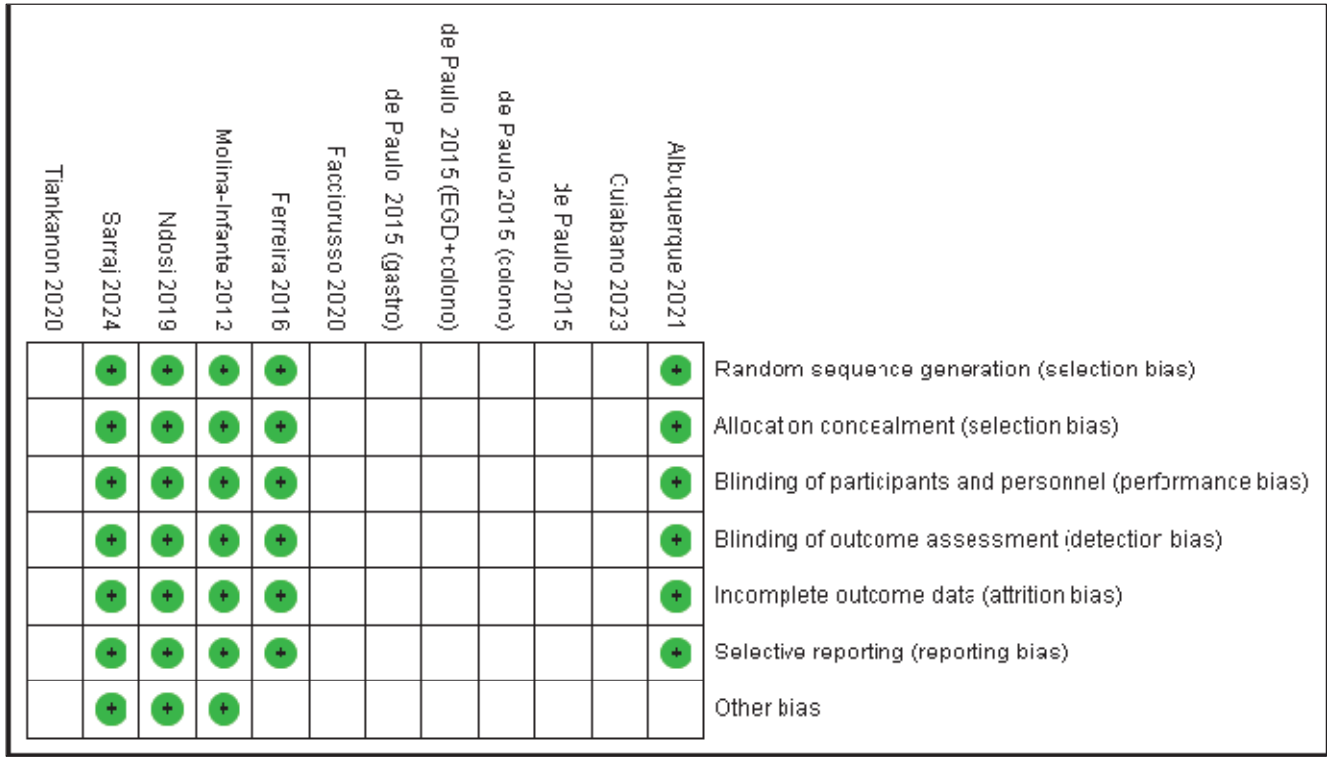


Table 2.3.5s Certainty of evidence

The risk of bias assessment for each study can be found in **Table 2.3.4s**. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded because the evidence was based only on two randomized trials, inconsistency, and imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to very low

Fig. 2.3.2s. NAAP vs Anesthetists regarding Cecal intubation rate (CIR)

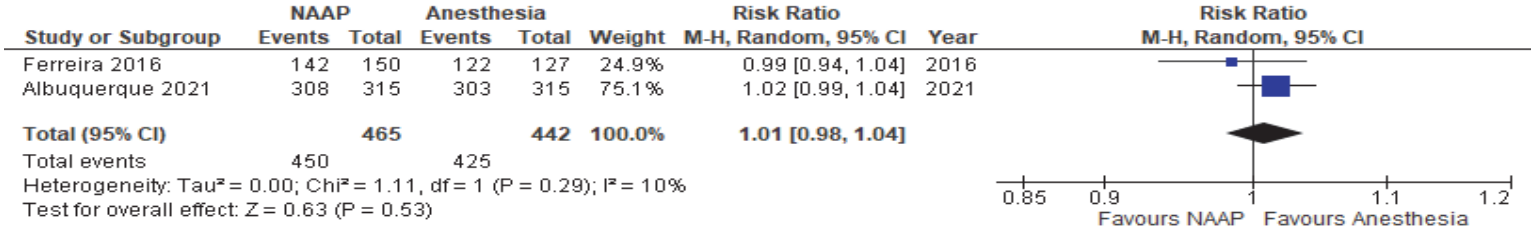


Table 2.3.6s Certainty of evidence

The risk of bias assessment for each study can be found in **Table 2.3.4s.** Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded because the evidence was based only on two randomized trials, inconsistency, and imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to very low.

Fig. 2.3.3s. NAAP vs Anesthetists regarding procedure length per endoscopy type

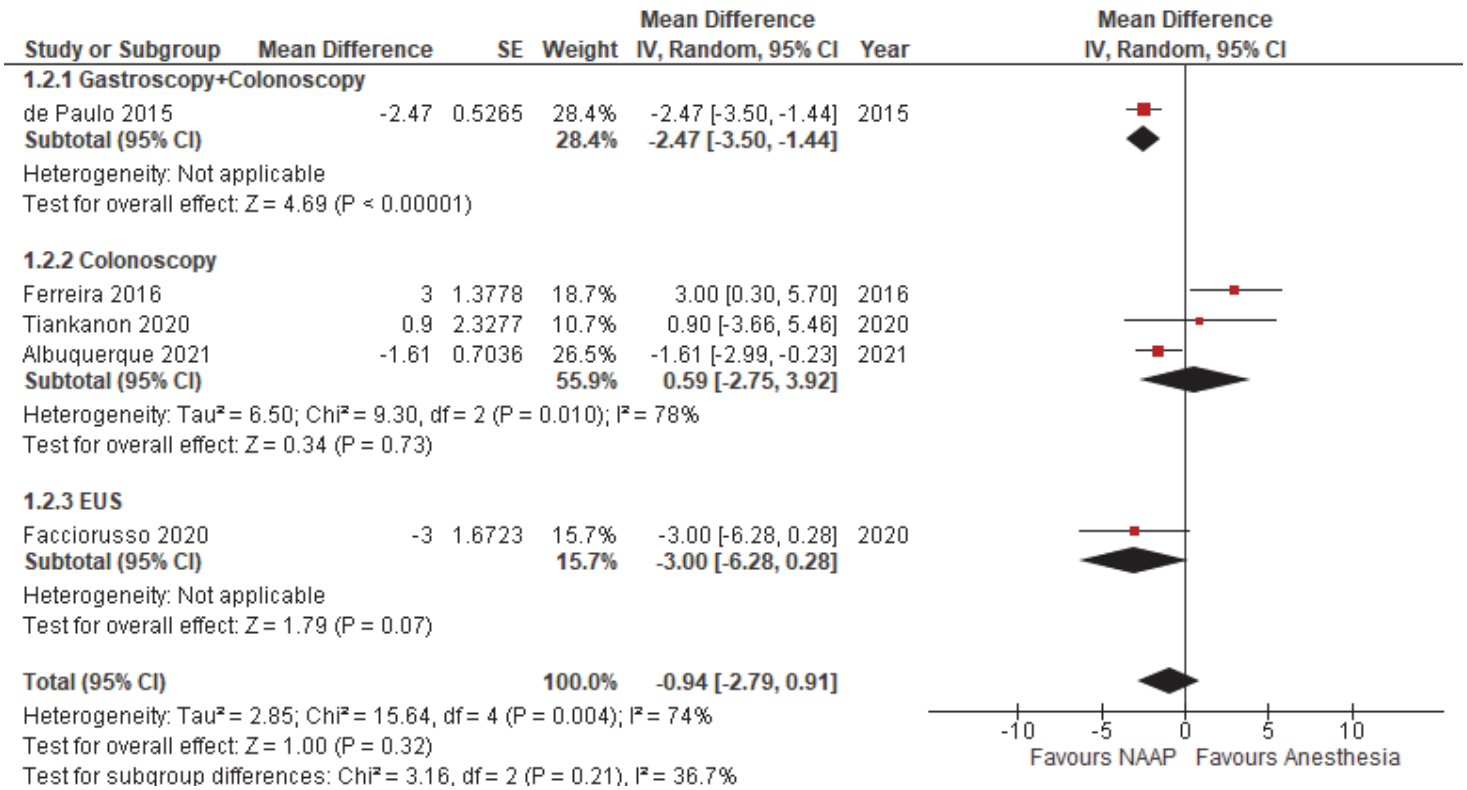

Study or Subgroup
Mean Difference
SE
Weight
Mean Difference IV, Random, 95% CI
Year
Mean Difference IV, Random, 95% CI
1.2.1 Gastroscopy+Colonoscopy
de Paulo 2015 -2.47 0.5265 28.4% -2.47 [-3.50, -1.44] 2015
Subtotal (95% CI) 28.4% -2.47 [-3.50, -1.44]
Heterogeneity: Not applicable
Test for overall effect: Z = 4.69 (P < 0.00001)
1.2.2 Colonoscopy
Ferreira 2016 3 1.3778 18.7% 3.00 [0.30, 5.70] 2016
Tiankanon 2020 0.9 2.3277 10.7% 0.90 [-3.66, 5.46] 2020
Albuquerque 2021 -1.61 0.7036 26.5% -1.61 [-2.99, -0.23] 2021
Subtotal (95% CI) 55.9% 0.59 [-2.75, 3.92]
Heterogeneity: Tau² = 6.50; Chi² = 9.30, df = 2 (P = 0.010); I² = 78%
Test for overall effect: Z = 0.34 (P = 0.73)
1.2.3 EUS
Facciorusso 2020 -3 1.6723 15.7% -3.00 [-6.28, 0.28] 2020
Subtotal (95% CI) 15.7% -3.00 [-6.28, 0.28]
Heterogeneity: Not applicable
Test for overall effect: Z = 1.79 (P = 0.07)
Total (95% CI) 100.0% -0.94 [-2.79, 0.91]
Heterogeneity: Tau² = 2.85; Chi² = 15.64, df = 4 (P = 0.004); I² = 74%
Test for overall effect: Z = 1.00 (P = 0.32)
Test for subgroup differences: Chi² = 3.16, df = 2 (P = 0.21), I² = 36.7%
-10
-5
0
5
10
Favours NAAP
Favours Anesthesia

Table 2.3.7s Certainty of evidence

The risk of bias assessment for each study can be found in **Table 2.3.4s**. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to indirectness (heterogeneity), inconsistency, and imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to very low.

Fig. 2.3.4s Rate of major AEs in NAAP

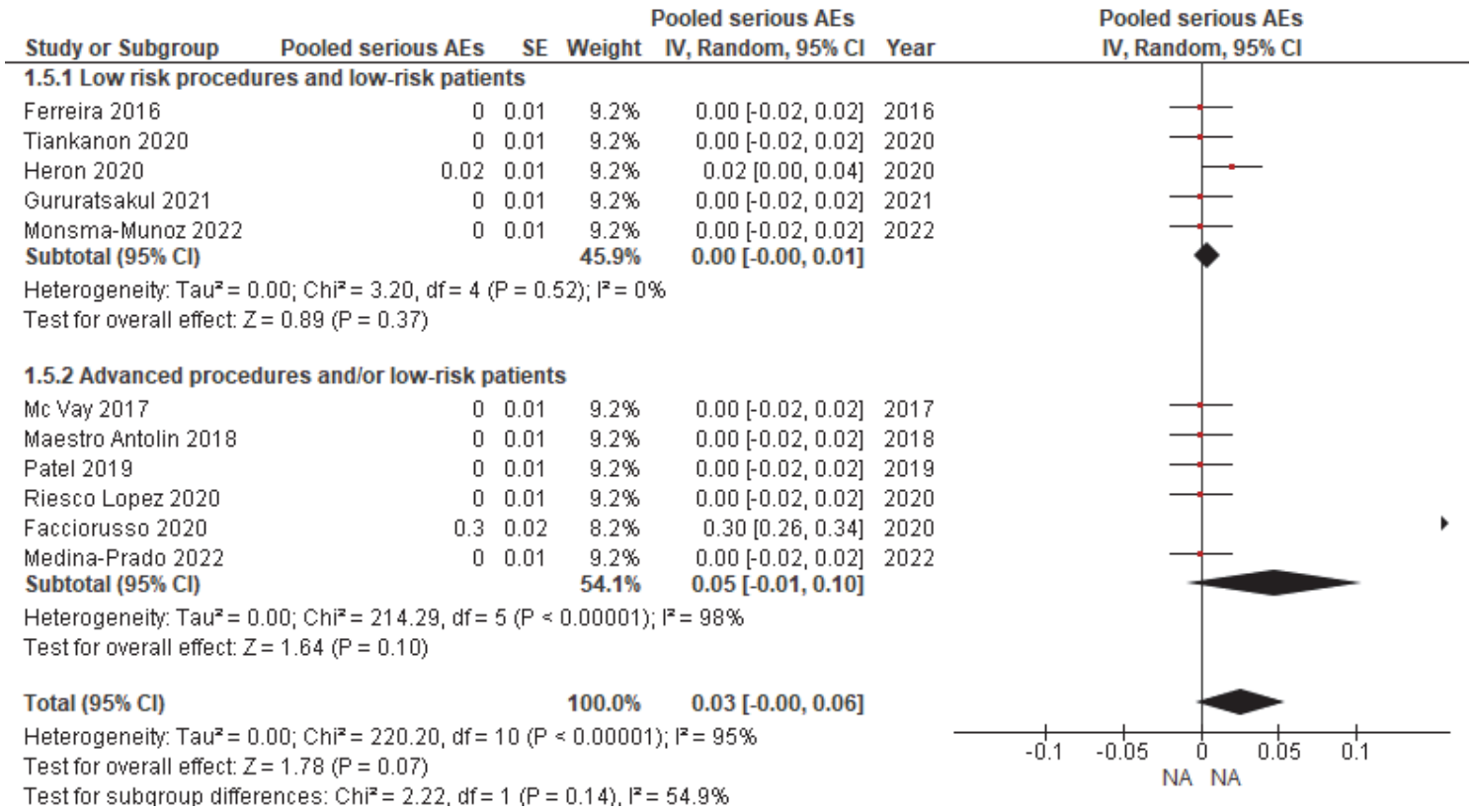


Fig. 2.3.5s Rate of non-major AEs in NAAP

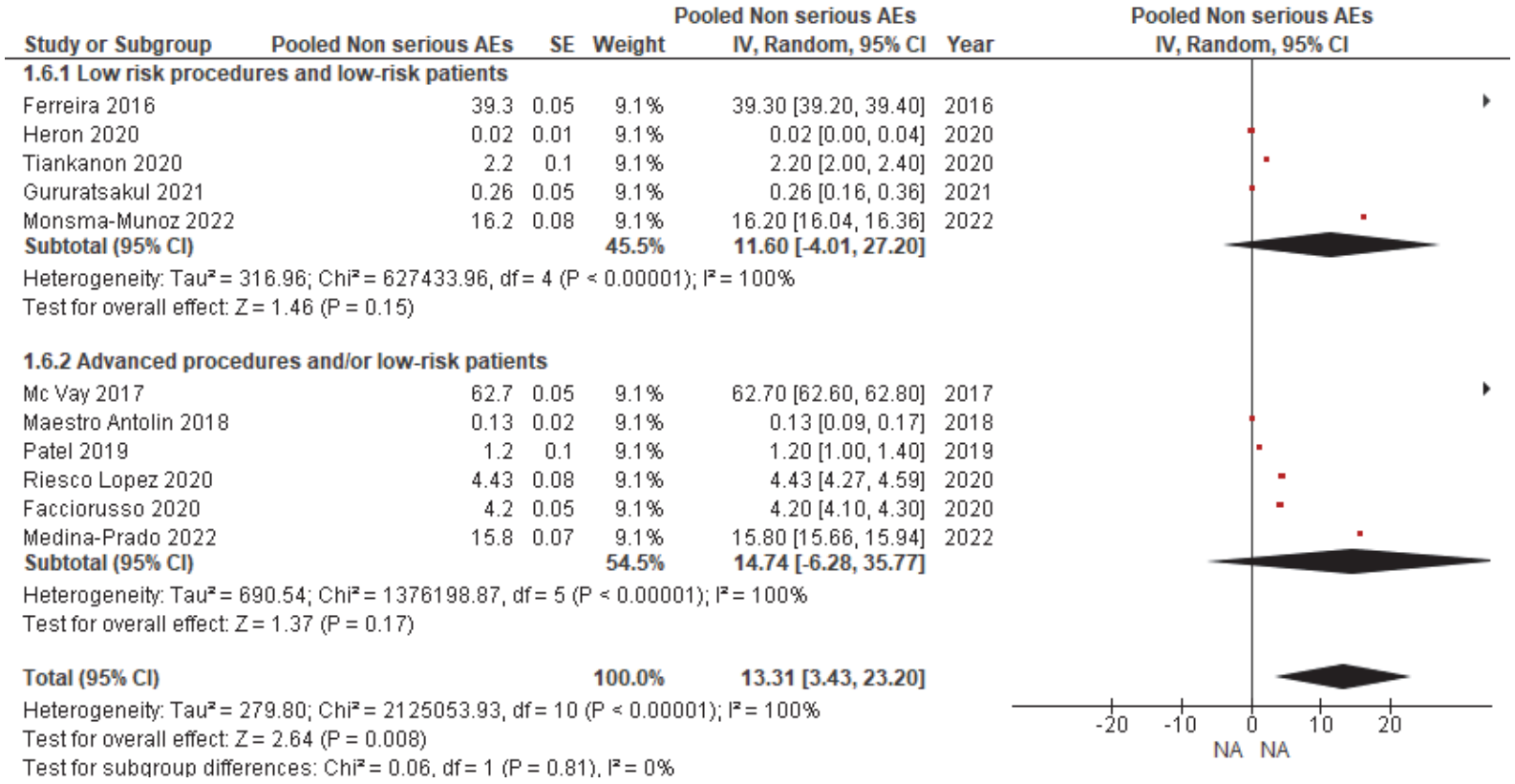


Fig. 2.3.6s Rate of non-major respiratory AEs in NAAP

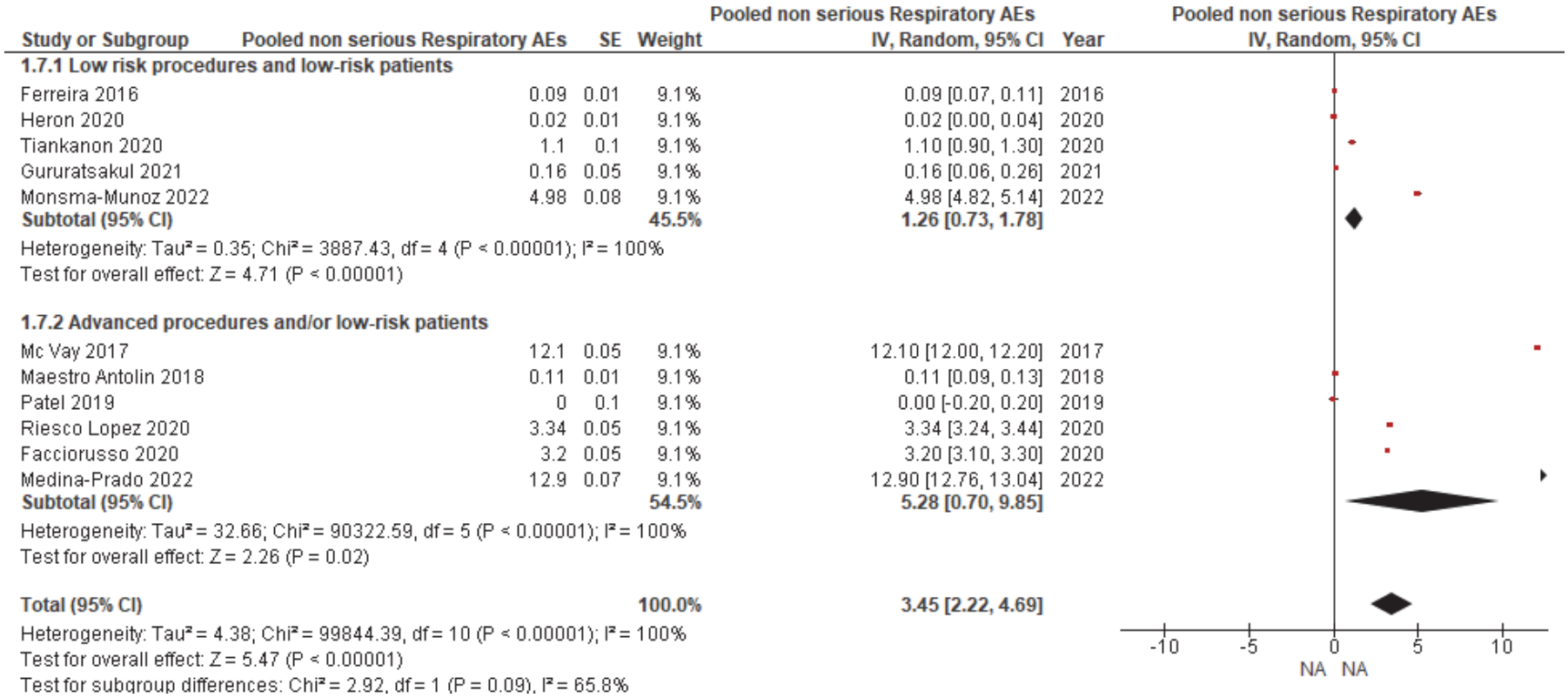


Fig. 2.3.7s Rate of non-major cardiovascular AEs in NAAP

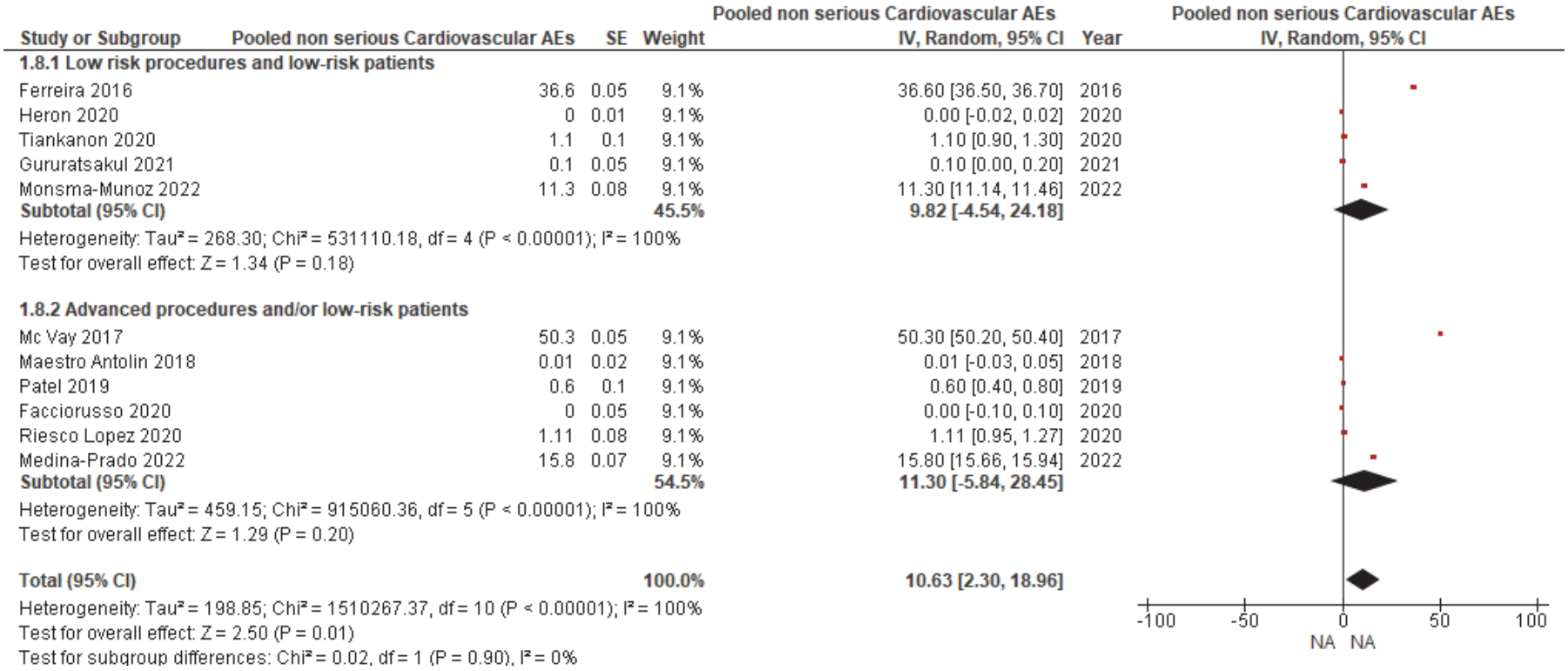


Fig. 2.3.8s Comparison of the rate of major AEs between NAAP vs. AP in non-advanced and advanced GI endoscopic procedures

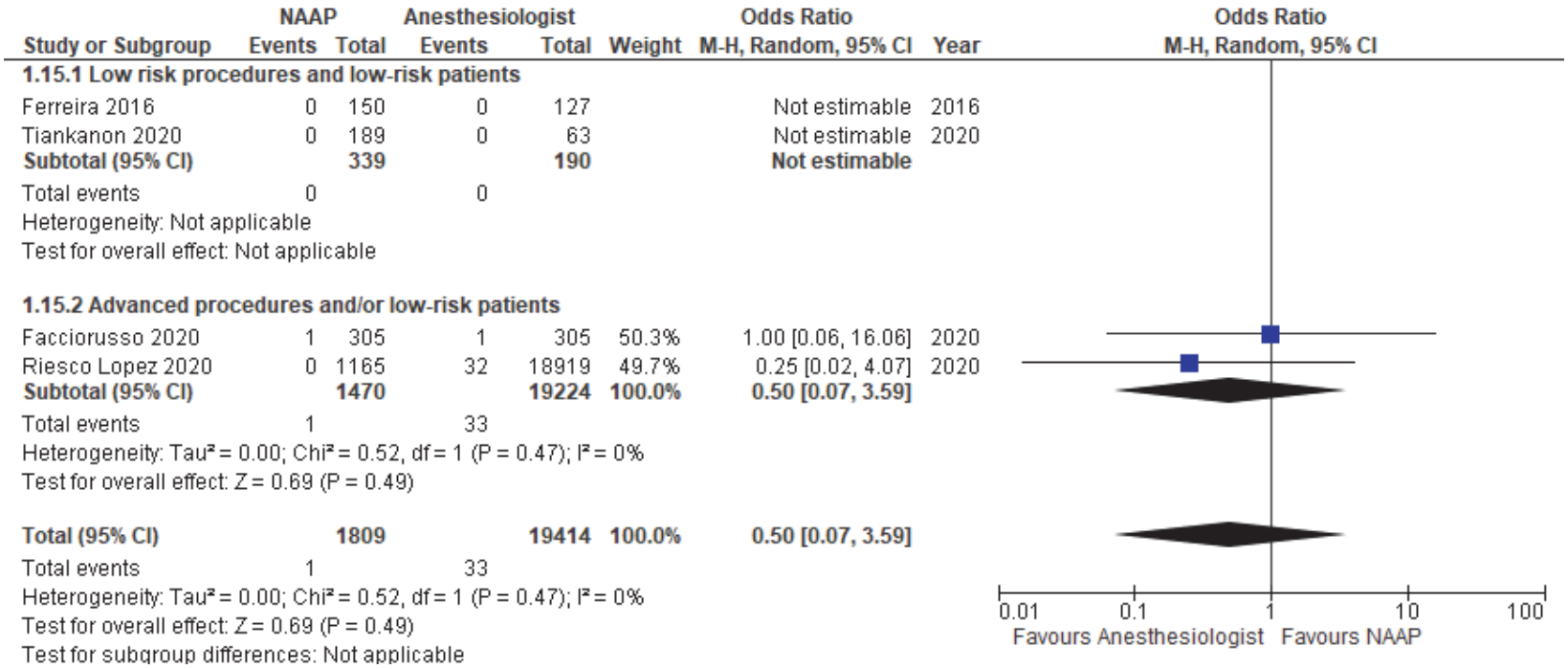


Fig. 2.3.9s Comparison of the rate of non-major AEs between NAAP vs. AP in non-advanced and advanced GI endoscopic procedures

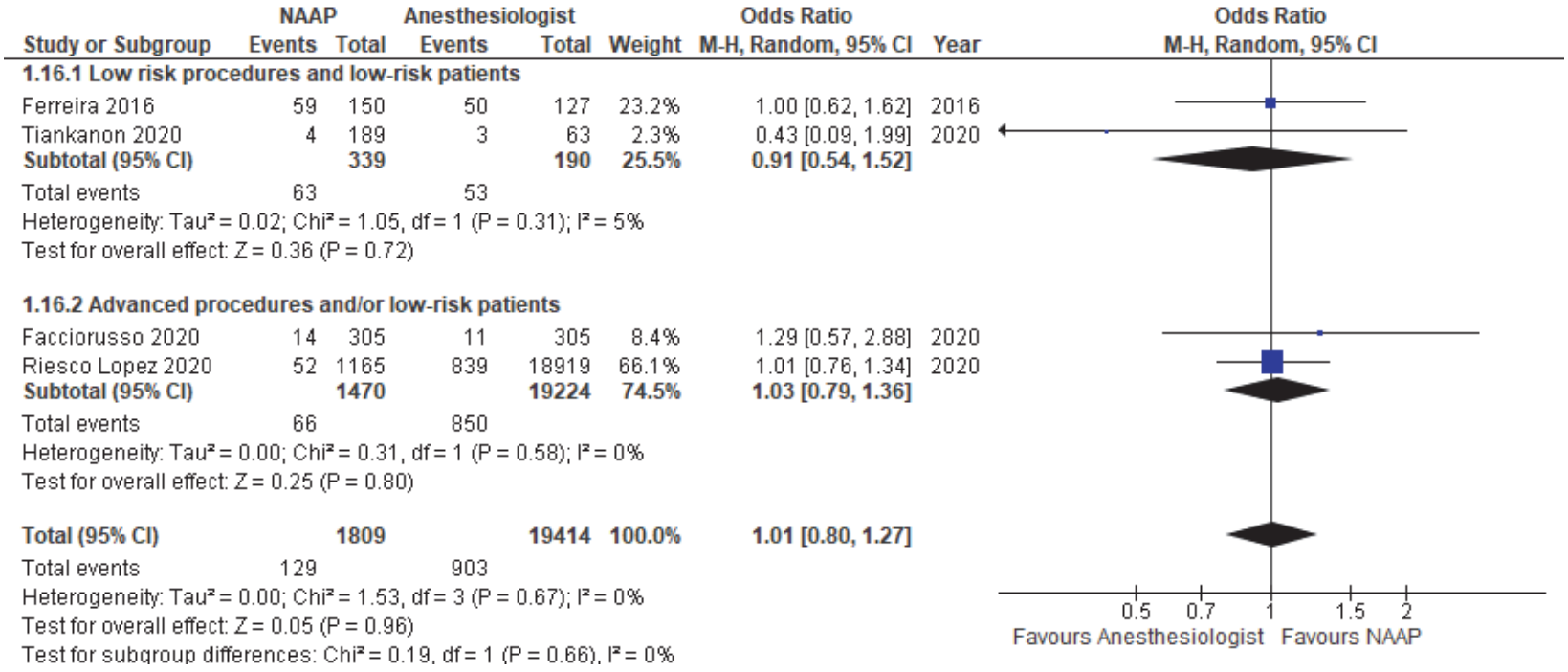


Fig. 2.3.10s Comparison of the rate of non-major respiratory AEs between NAAP vs. AP in non-advanced and advanced GI endoscopic procedures

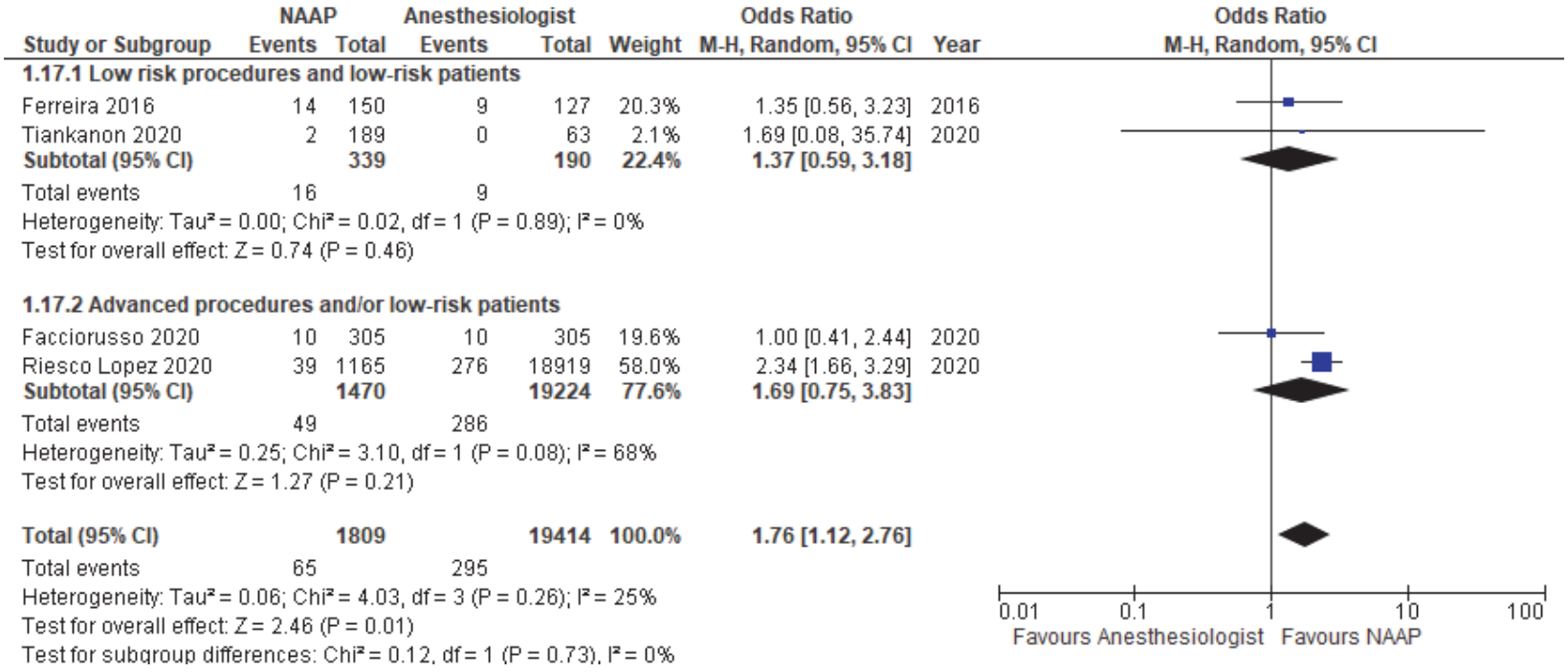


Fig. 2.3.11s Comparison of the rate of non-major cardiovascular AEs between NAAP vs. AP in non-advanced and advanced GI endoscopic procedures

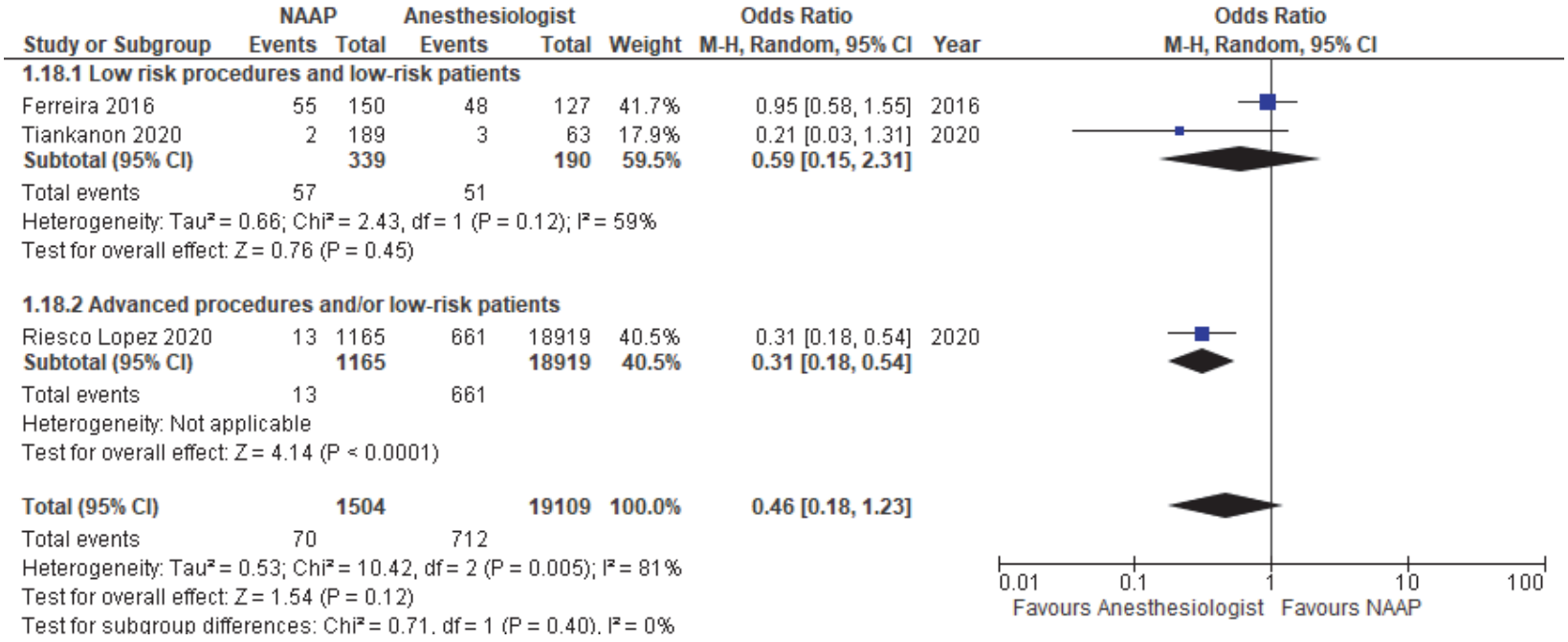


Fig. 2.3.12s Comparison of endoscopy complications: NAAP vs. AP

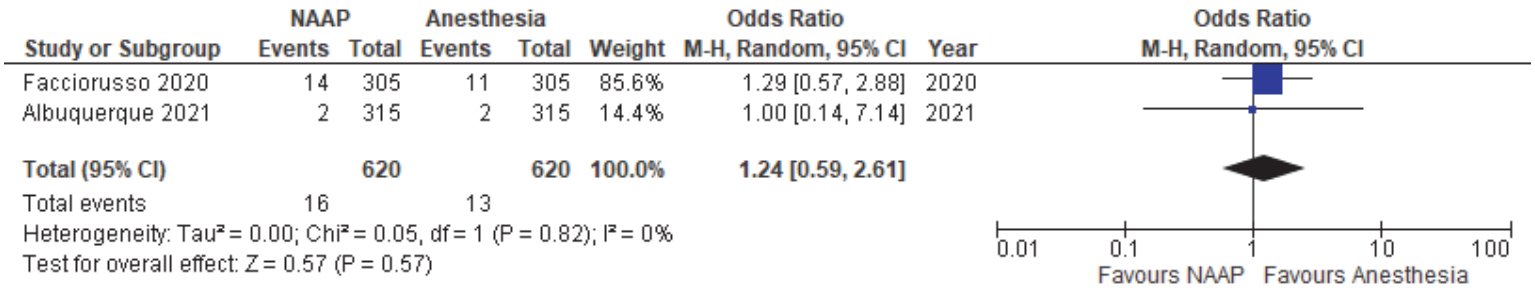


Table 2.3.8s: Risk of bias assessment for studies

Study	Selection (max 4 stars)	Comparability (max 2 stars)	Outcomes (max 3 stars)	Quality (Total 9/9)
de Paulo, 2015	**	*	**	**Fair**
Jensen, 2015	**	*	**	**Fair**
Ooi, 2015	***	*	**	**Good**
Jensen, 2016	***	*	**	**Good**
Buxbaum, 2017	***	*	**	**Good**
Albouquerque 2021	***	*	**	**Good**
McVay 2017	**	*	**	**Fair**
Maestro 2018	**	*	**	**Fair**
Patel 2019	*	*	**	**Poor**
Facciorusso 2020	***	*	**	**Good**
Heron 2020	***	*	**	**Good**
Riesco Lopez 2020	***	*	**	**Good**
Tiankanon 2020	***	*	**	**Good**
Gururatsakul 2021	***	*	**	**Good**
Medina-Prado 2022	***	*	**	**Good**

Monsma-Munoz 2022	***	*	**	**Good**

Table 2.3.9s Certainty of evidence

The risk of bias assessment for each study is available in Table 2.3.8. Overall, the included studies were deemed to be of good quality. However, the certainty of evidence regarding this PICO question was downgraded because the evidence primarily relied on non-RCTs and exhibited significant inconsistency (high heterogeneity). As a result, the quality of evidence was rated as very low,

Fig. 2.3.13s. Effect of CAPS vs. standard sedation on sedation success rate

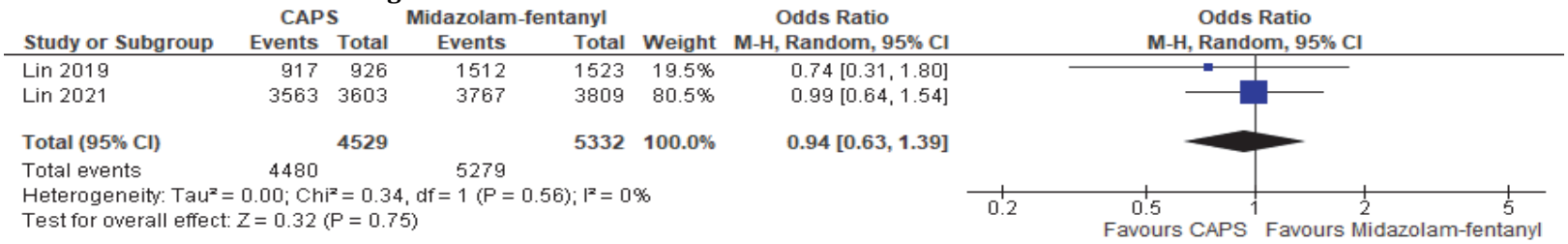


Table 2.3.10s Certainty of evidence

The risk of bias assessment for each study is available in **Table 2.3.4s**. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded because the evidence was based only on two non-randomized trials, inconsistency, and imprecision (broad CI crosses 1.0). Thus, the quality of evidence was downgraded to very low.

Fig. 2.3.14s. Effect of CAPS vs standard sedation regarding recovery time

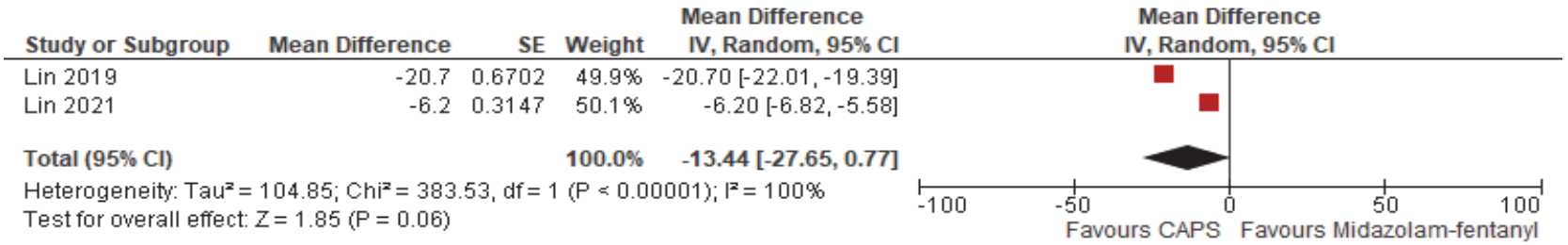
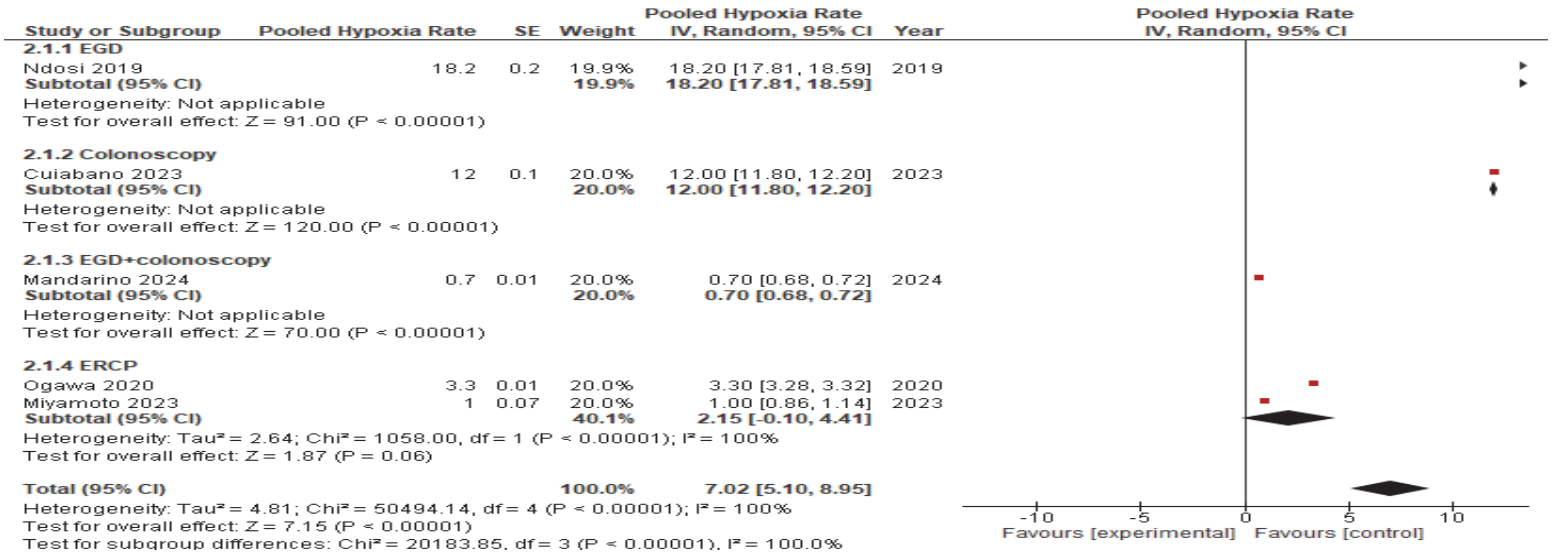


Table 2.3.11s Certainty of evidence

The risk of bias assessment for each study is available in **Table 2.3.4s**. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded because the evidence was based only on two non-randomized trials, inconsistency, and imprecision. Thus, the quality of evidence was downgraded to very low

Fig. 2.3.15s. Rate of hypoxia (Sa02<90%) in TCI NAAP and bolus infusion NAAP per endoscopy



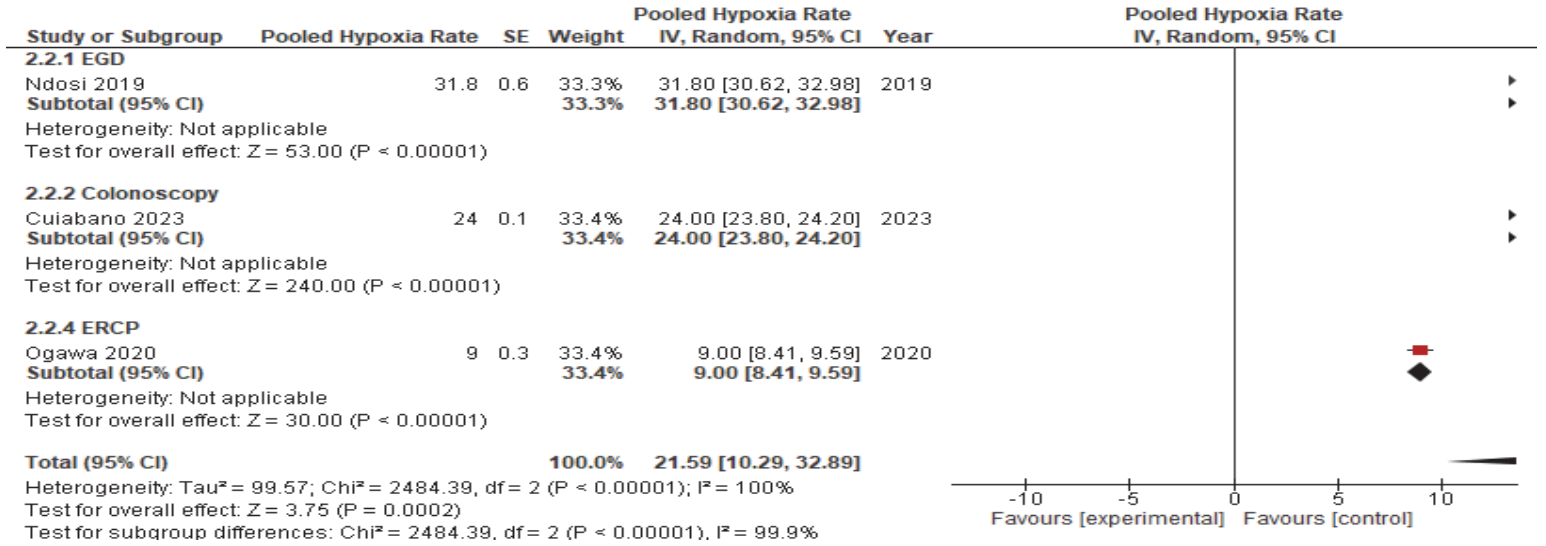
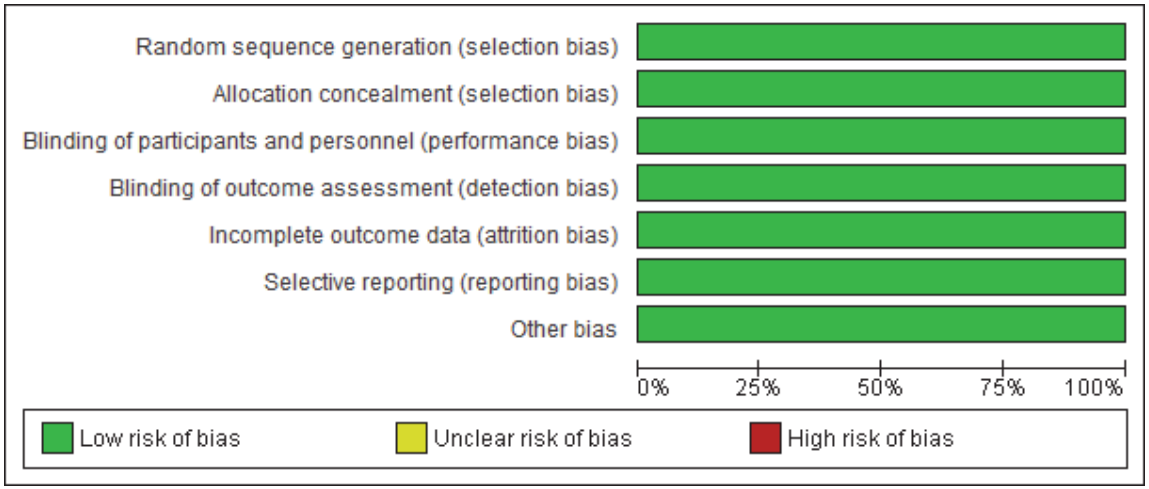
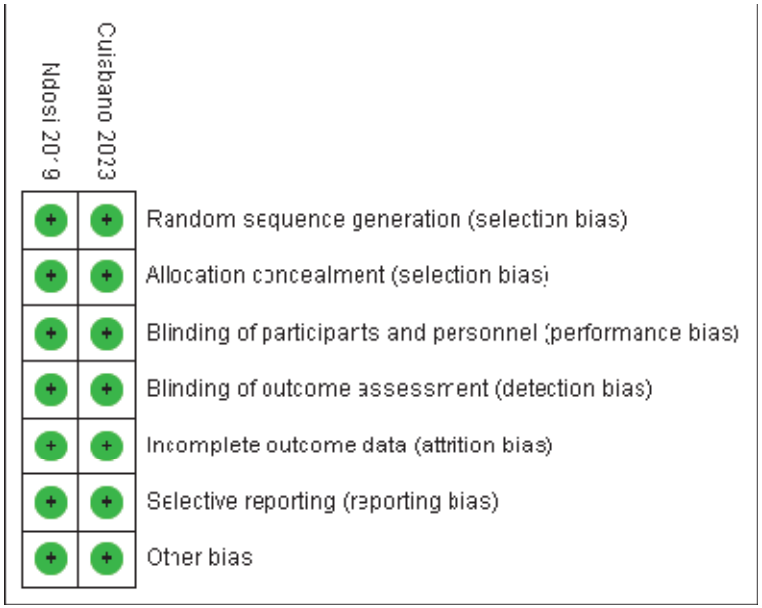


Table 2.3.12s: Risk of bias assessment for studies



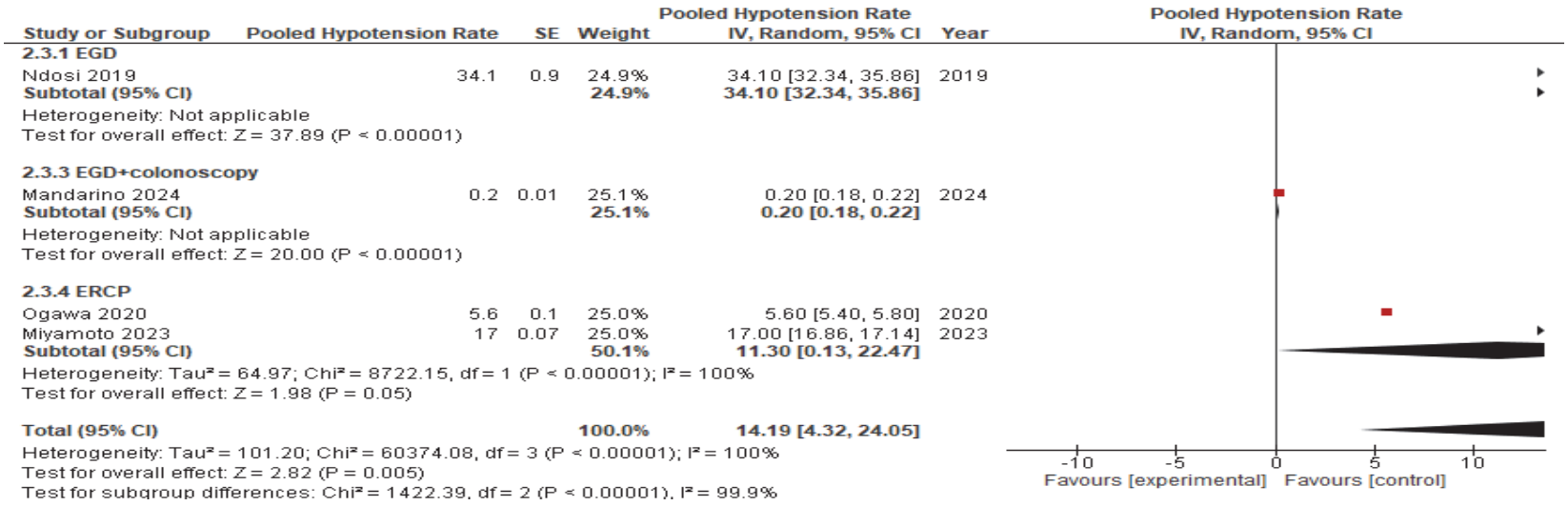


Study	Selection (max 4 stars)	Comparability (max 2 stars)	Outcomes (max 3 stars)	Quality (Total 9/9)
Ogawa 2020	**	*	**	**Fair**
Miyamoto 2023	***	*	**	**Good**
Mandarino 2024	***	*	**	**Good**

Table 2.3.13s Certainty of evidence

The risk of bias assessment for each study is available in **Table 2.3.12s**. Overall, the included studies were considered of good quality. The certainty of evidence in this PICO question was downgraded because the evidence was based only on two randomized trials and there was inconsistency. Thus, the quality of evidence was downgraded to very low.

Fig. 2.3.16s. Rate of hypotension (< 90/60mmHg or fall >20%) in TCI NAAP and bolus infusion NAAP per endoscopy



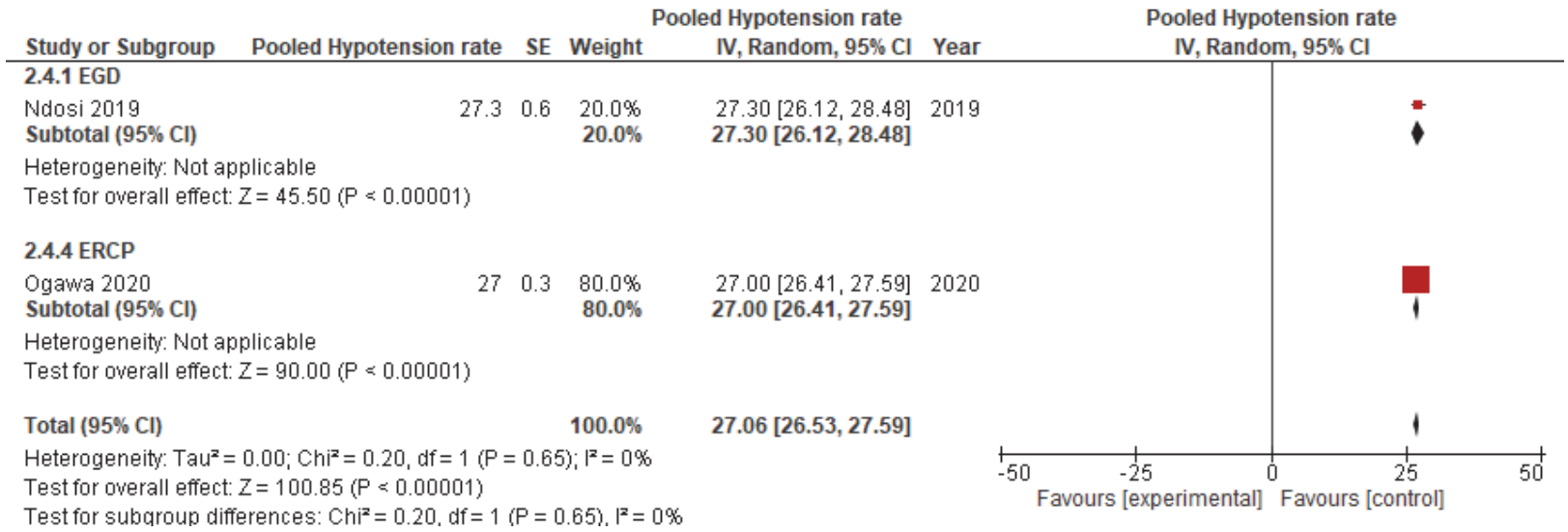


Fig. 2.3.17s Comparison of hypoxia in TCI NAAP vs bolus infusion NAAP

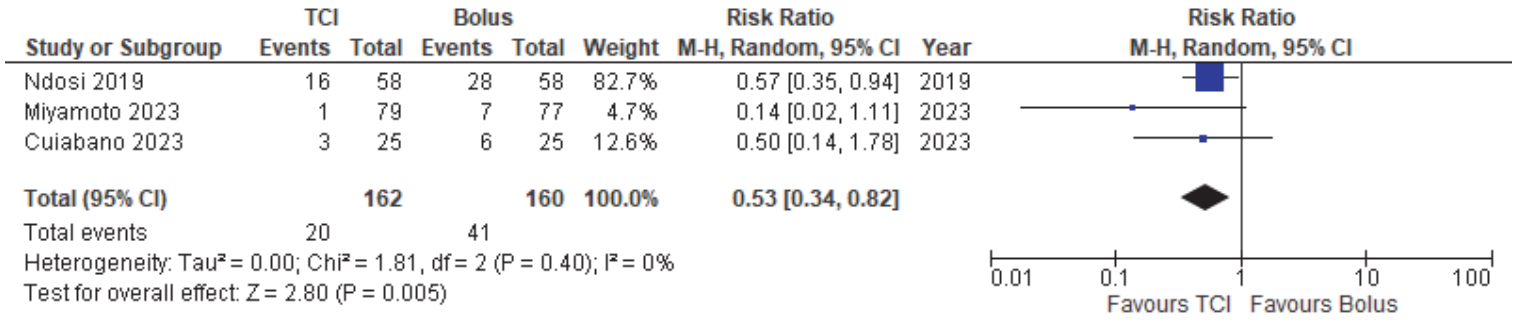


Fig. 2.3.18s Comparison of hypotension in TCI NAAP vs bolus infusion NAAP

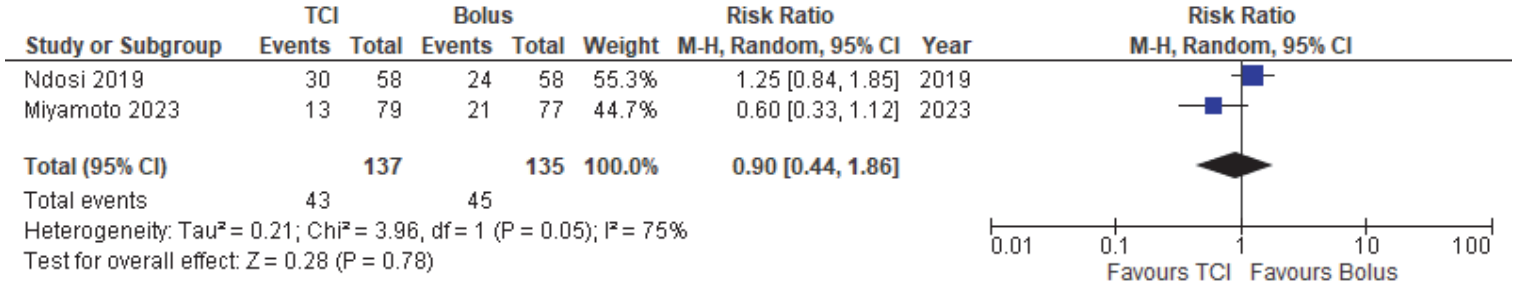


Table 2.3.14 Certainty of evidence

The risk of bias assessment for each study is available in **Table 2.3.12**. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded because the evidence was based only on one randomized trial and inconsistency, so the quality of evidence was downgraded to very low

Table 2.3.15s Certainty of evidence

Q3 NAAP compared to Anesthesia for Q32
Bibliography: TF2 for Q32. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Anesthesia	With Q3 NAAP		Risk with Anesthesia	Risk difference with Q3 NAAP
Procedure length (min)											
0 (4 non-randomised studies)	serious[a]	serious[b]	serious[c]	serious[a,b,c]	all plausible residual confounding would reduce the demonstrated effect	⨁◯◯◯ Very low[a,b,c]	0	0	-	0	MD **3.41 lower** (8 lower to 1.18 higher)

CI: confidence interval; **MD:** mean difference

Explanations

a. No RCTs

b. Inconsistent outcomes

c. Variable endoscopists

NAAP compared to Anesthesia for Q32
Bibliography: . TF2 for Q32. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Anesthesia	With NAAP		Risk with Anesthesia	Risk difference with NAAP
Pooled Severe AEs - Overall											

NAAP compared to Anesthesia for Q32
Bibliography: . TF2 for Q32. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment									Summary of findings		
2 (11 non-randomised studies)	not serious	serious[a]	not serious	not serious	none	⊕◯◯◯ Very low[a]	-/0	-/2	**Pooled severe AEs 0.03** (0.00 to 0.06)	-/0	**-- per 1.000** (from -- to --)
Pooled Mild AEs - Overall											
0 (11 non-randomised studies)	not serious	serious[a]	not serious	not serious	none	⊕◯◯◯ Very low[a]	-/0	-/0	**Pooled Mild AEs 13.29** (3.41 to 23.18)	-/0	**-- per 1.000** (from -- to --)
AEs											
21223 (4 non-randomised studies)	not serious	serious[a]	not serious	not serious	none	⊕◯◯◯ Very low[a]	907/19414 (4.7%)	82/1809 (4.5%)	**OR 0.49** (0.12 to 1.92)	907/19414 (4.7%)	**23 fewer per 1.000** (from 41 fewer to 39 more)

CI: confidence interval; **OR:** odds ratio

Explanations

a. High heterogeneity

Q5 Computer-controlled personalized sedation (CAPS) compared to placebo for Q5
Bibliography: TF2 for Q5. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With placebo	With Q5 Computer-controlled personalized sedation (CAPS)	Relative effect (95% CI)	Risk with placebo	Risk difference with Q5 Computer-controlled personalized sedation (CAPS)
Success rate											
9861 (2 non-randomised studies)	serious[a]	serious[b]	serious[c]	serious[d]	All plausible residual confounding would reduce the demonstrated effect	⊕◯◯◯ Very low[a,b,c,d]	5279/5332 (99.0%)	4480/4529 (98.9%)	**OR 0.94** (0.63 to 1.39)	5279/5332 (99.0%)	**1 fewer per 1.000** (from 6 fewer to 3 more)
Recovery time (min)											
0 (2 non-randomised studies)	serious[a]	serious[b]	serious[c]	serious[d]	All plausible residual confounding would reduce the demonstrated effect	⊕◯◯◯ Very low[a,b,c,d]	0	0	-	0	MD **13.44 lower** (27.65 lower to 0.77 higher)

TCI compared to placebo for Q32
Bibliography: TF2 for Q32. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With placebo	With TCI		Risk with placebo	Risk difference with TCI
TCI Pooled Hypoxia rate (SaO2<90%)											
0 (5 non-randomised studies)	not serious	serious[a]	not serious	not serious	none	⨁◯◯◯ Very low[a]	-/0	-/0	**Pooled Hypoxia Rate 7.02** (5.10 to 8.95)	-/0	**-- per 1.000** (from -- to --)
Bolus Pooled Hypoxia rate (SaO2<90%)											
0 (3 non-randomised studies)	not serious	serious[a]	not serious	not serious	none	⨁◯◯◯ Very low[a]	-/0	-/0	**Pooled Hypoxia Rate 21.59** (10.29 to 32.89)	-/0	**-- per 1.000** (from -- to --)
TCI Pooled Hypotension rate (<90/60mmHg or fall>20%)%)											
0 (4 non-randomised studies)	not serious	serious[a]	not serious	not serious	none	⨁◯◯◯ Very low[a]	-/0	-/0	**Pooled Hypotension Rate 14.19** (4.32 to 24.05)	-/0	**-- per 1.000** (from -- to --)
Bolus Pooled Hypotension rate (<90/60mmHg or fall>20%)%)											
0 (2 non-randomised studies)	not serious	serious[a]	not serious	not serious	none	⨁◯◯◯ Very low[a]	-/0	-/0	**Pooled Hypotension rate 27.06** (26.53 to 27.59)	-/0	**-- per 1.000** (from -- to --)

Q2.4: Pharmacological sedation

Clinical Question 2.4.1: What is the optimal regimen for patients scheduled to undergo GI endoscopy with mild-moderate sedation?

Table 2.4.1s. PICOs

PICO question no.	Population	Intervention	Comparator	Outcome
1	Patients scheduled to undergo GI endoscopy with mild to moderate sedation	Administration of a single drug	Administration of a drug combination	Procedure outcomes (completeness of procedure), patient safety, and satisfaction.

BIBLIOGRAPHIC SEARCH

Bibliographic search strategies were performed in **PubMed and Cochrane** from 01.01.2019 to 31.07.2024 using the following search strategies:

d. PubMed- Search [August 2th 2024 and January 20th 2025]

(("conscious Sedation"[MeSH Terms] AND "gastrointestinal endoscopy": 135 studies
(("conscious Sedation"[MeSH Terms] AND "Drug therapy" AND "gastrointestinal endoscopy": 4 studies
(("Endoscopy, Gastrointestinal"[Mesh]) AND "Propofol"[Mesh]): 213 studies
("Endoscopy, Gastrointestinal"[Mesh]) AND "Etomidate"[Mesh]: 10 studies
("Endoscopy, Gastrointestinal"[Mesh]) AND "Remifentanil date"[Mesh]: 8 studies
("Endoscopy, Gastrointestinal"[Mesh]) AND "Alfentanil"[Mesh]: 13 studies
("Ketamine"[Mesh]) AND "Endoscopy, Gastrointestinal"[Mesh]: 22 studies
("Endoscopy, Gastrointestinal"[Mesh]) AND "Fentanyl"[Mesh]: 50 studies
("Endoscopy, Gastrointestinal"[Mesh]) AND "Meperidine (pethidine)"[Mesh]: 2 studies
("Endoscopy, Gastrointestinal"[Mesh]) AND "Midazolam"[Mesh]: 56 studies
("Endoscopy, Gastrointestinal"[Mesh]) AND "Dexmedetomidine"[Mesh]: 15 studies
Remimazolam AND gastrointestinal endoscopy: 66 studies
("Nitrous Oxide"[Mesh]) AND "Endoscopy, Gastrointestinal"[Mesh]: 3 studies
("Esketamine" [Supplementary Concept]) AND "Endoscopy, Gastrointestinal"[Mesh]: 12 studies
("Conscious Sedation"[Mesh]) AND "Endosonography"[Mesh]: 1 study
("Endosonography"[Mesh]) AND "Propofol"[Mesh]: 3 studies
("Etomidate"[Mesh]) AND "Endosonography"[Mesh]: 2 studies

("Endosonography"[Mesh]) AND "Remifentanil"[Mesh]: 2 studies
("Endosonography"[Mesh]) AND "Fentanyl"[Mesh]: 2 studies
("Endosonography"[Mesh]) AND "Meperidine"[Mesh]:0
("Endosonography"[Mesh]) AND "Midazolam"[Mesh]:0
("Endosonography"[Mesh]) AND "Dexmedetomidine"[Mesh]: 1 study
Remimazolam AND endosonography: 1 study
("Nitrous Oxide"[Mesh]) AND "Endosonography"[Mesh]:0
("Esketamine" [Supplementary Concept]) AND "Endosonography"[Mesh]:0
Ciprofol AND EUS: 0

Results: 245 studies

Cochrane Central Register of Controlled Trials (CENTRAL)- Search [DATE] EXAMPLE (2019-2024)

#1	("conscious sedation") (Word variations have been searched)	207
#2	("Gastrointestinal Endoscopy") (Word variations have been searched)	**1423**
#3	("Propofol") (Word variations have been searched)	**1266**
#4	("Etomidate") (Word variations have been searched)	**57**
#5	("Remifentanil") (Word variations have been searched)	**420**
#6	("Alfentanil") (Word variations have been searched)	**43**
#7	("Ketamine") (Word variations have been searched)	**1026**
#8	("Fentanyl") (Word variations have been searched)	**1050**
#9	("Meperidine") (Word variations have been searched)	**63**
#10	("Midazolam") (Word variations have been searched)	**589**

#11	("Dexmedetomidine") (Word variations have been searched)	**1436**
#12	("Nitrous Oxide") (Word variations have been searched)	**126**
#13	("Endosonography") (Word variations have been searched)	**135**
#14	**#1 AND #2**	**35**
#15	#2 AND #3	**103**
#15	#2 AND #4	**8**
#17	#2 AND #5	**5**
#18	#2 AND #6	**8**
#19	#2 AND #7	**14**
#20	#2 AND #8	**28**
#21	#2 AND #9	**1**
#22	#2 AND #10	**21**
#23	#2 AND #11	**10**
#24	#2 AND #12	**1**
#25	#13 AND #3	**2**
#26	#13 AND #4	**0**

Endoscopy | DOI 10.1055/a-2898-6540 |

#27	#13 AND #5	**3**
#28	#13 AND #6	**2**
#29	#13 AND #7	**0**
#30	#13 AND #8	**3**
#31	#13 AND #9	**0**
#32	#13 AND #10	**0**
#33	#13 AND #11	**1**
#34	13 AND #12	**0**
#35	#drug combination	**8377**
#36	#2 AND #35	**23**

Results: All 514 studies, after removing duplication: 191 studies

e. Results of the bibliographic searches

Results Total 245+ 269=514 studies

After removing duplicates (n=323), 195 articles were found. 82 studies (21 meta-analyses) were considered potentially relevant and acquired in full text.

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Table 2.4.2s: Evidence: Characteristics of the included studies

Propofol vs. midazolam

Study (Author, year)	Country	Study design	No. of sites (no. of subjects)	Age (y)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm	Follow-up
Dae Bum Kim et al 2020	Korea	RCT	1 (n=267)	Mean 57.7y-60.9y	52%	Propofol	Bolus midazolam/meperidine And Titrated midazolam/meperidine	Procedure time 39.5m Induction time: 4.6m Recovery time: 11.5m Discharge time: 20.6 Patient satisfaction: 9.9 Cecal intubation time: 4.6m Propofol was superior to midazolam/meperidine	59.4m and 58.1m 6.3m and 7.6 m 29.5m and 29.2 m 34.9m and 34.7m 9.6 and 9.6 6.1m and 5.2 No difference in withdrawal time	Until Recovery And discharge
Jeong-Ju Yoo et al 2019	Korea	RCT Cirrhotic patients gastroscopy	1 (n=60)	52.6y	80	Midazolam +propofol	Midazolam Or Propofol	Higher physician satisfaction Similar safety in all 3 groups without increased risk of cognitive impairment	Time recovery was longest in the midazolam group Patients' awakening and memory were highest in the propofol group	2 hours after the procedure
Gurunathan U et al. 2020	Australia	RCT	2 (n=406)	56y	51%	Midazolam +propofol	Saline +propofol	not show evidence of any significant differences in recovery in the cognitive domain of the Postop QRS, overall quality of recovery as measured by the Postop QRS, or emergence and hospital discharge times		Until day 3 after the procedure
Alam L et al. 2021	Pakistan	Prospective study Upper endoscopy	1 (n=500)	50	60	Cirrhotic patients Midazolam +propofol	Non cirrhotic patients Midazolam +propofol	No difference between sedation safety and the rate of complications Modified Aldrete score at 10 minutes 9.5±0.5 min <0.001)		

								0.8% had grade 2 encephalopathy	9.8±0.4	
Dossa F et al 2020	Canada	Systemic review Meta analysis Colonoscopy	9 studies (n=1427)			Propofol	Midazolam	There were no significant differences in cardiorespiratory outcomes (hypotension, hypoxia, bradycardia)	Patient satisfaction was high in both groups	
Thomopson et al 2019	Australia	RCT	2 (n=200)	54 y and 47.5y	46	Midazolam +propofol Or Midazolam +propfol +fentanly	Midazolam +fentanyl	The use of propofol in GI endoscopy allows for less exposure to midazolam and fentanyl, and is associated with improved cognition at the time of discharge.	Postprocedure detection test scores were significantly impaired in the Midazolam fentanyl group	Until discharge

Remimazolam

Study (Author, year)	Country	Study design	No. of sites (no. of subjects)	Age (y)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm	Follow-up
Ahmer Wania 2024	Pakistan	Systematic review and meta-analysis Elderly	7 trials RCT 1466 subjects	>60		remimazolam	Propofol	lower risk of bradycardia, hypoxemia, and pain on injection site. No difference in other parameters	lower time to loss of consciousness. Greater sedation success after the first dose	
Pimgel 2025		Meta-analysis	64 RCTs (54 GI endosc)			Remimazolam	Propofol ciprofol	similar sedation success rate and with higher patient satisfaction compared to the active comparators lower risk of respiratory complications compared to propofol lower risk of cardiovascular complications compared to propofol	Remimazolam had a similar risk for respiratory complications compared to ciprofol similar CV risk compared to ciprofol	
Zhou, 2025		Metaanalysis	42 RCTs (34 GI)			Remimazolam	Propofol/ciprofol	The rate of respiratory adverse events was statistically lower for remimazolam and ciprofol For cardiovascular safety, remimazolam was superior to propofol and ciprofol	Propofol had the shortest (non-significant) sedation induction time no statistically significant mean difference regarding sedation recovery time was detected among the three drugs	
Xu C et al, 2022	China	RCT Gastroscopy	1 (n=914)	52y	46%	Remimazolam+ alfentanil	Propofol+ Alfentanil	Lower decrease in heart rate and blood pressure Slightly longer awaking time Higher patient satisfaction Remimazolam combined with alfentanil can provide safe and effective sedation for patients undergoing	More significant decrease in respiratory rate, PETCO2, and IPI More respiratory depression and hypotension	Until 24 hours after the procedure

								painless gastroscopy		
Rex D et al 2020	USA	RCT colonoscopy	3 (n=77)	62.5y	55.8%	Remimazolam in high-risk colonosocpy	Midazolam Or placebo	Process success in 87.1% No difference in adverse events	0% in placebo and 13.3% in midazolam	
Shi W et al 2022	China	RCT Gastroscopy	1 (n=161)	42y And 45y	48%	Remimazolam+ alfentanil	Propofol + alfentanil	Procedure success rate: 97.53% Lower incidence of injection pain, hypertension, respiratory depression and dizziness	97.50% likely to be drowsy, and their work efficiency was reduced the day after leaving the hospital	Day after discharge
Chen SH et al. 2020.	China	RCT Phase III Gastroscopy	17 (n=384)	40.78y and 41.69y	38%	Remimazolam	Propofol	Success rate of sedation: 97.34% Incidence of hypotension: 13.04% Respiarotry depression: 1.09% Advers events: 39.15% Longer time to adequate sedation Shorter time to fully alert	100% 42.86% 6.88% 60.32%	Until recovery
Liu X et al 2021	China	RCT Colonoscopy	1 (n=232)	69y	48%	Remimazolam Efficacy and safety	Etomidate/ Propofol	Success rate: 96.52% No difference in hypoxia, respiratory depression Non-inferiority in efficacy	100% Lower onset time Higher time to fully alert, ready for discharge and hospital discharge	Until recovery
Wei A et al. 2023	China	RCT Gastroscopy	8 (n=304)	44 vs 46 vs 47	48%	remimazolam	Propofol (P) Or Propofol +remimazolam (P+R)	Incidence of Hypotension: 12.6% Body movement: 26.1% Endoscopist satisfaction 3.53±0.84 Adverse events: 61.3%	P=56.7%, P+R=31.3% P=10.3%, P+R=12.5% P= 3.87±0.44 P+R=3.95±0.22 P=96.8%, P+R=42.7%	Until recovery
Yuan Ruimei et al 2023	China	RCT Gastroscopy	1 (n=140)	18-65y	47%	Remimazolam +propofol	Saline +propofol	Propofol induced injection: 13% Lower consumption of propofol: 117.4 ± 21.02 Shorter recovery time: 4.39 ± 3.28 Greater patient	51% 151.6 ± 28.57 6.12 ± 2.36	Until recovery

								satisfaction: 83%	66%	
Hu B et al 2022	China	RCT Elderly patient Gastroscopy	1 (n=346)	>65y	40	Remimazolam + sufentanil	Propofol + sufentanil	Respiratory depression: 9.8% Hypotension: 32.4% Infection pain: 12.1% No difference in rate of sedation success, time to discharge, Patients' and Endoscopist satisfaction:	17.9% 50.9% 12.1%	Until discharge
Cao Y et al 2022	China	RCT Cirrhotic patients Gastroscopy	1 (n=148)	18-65	58	Remimazolam + sufentanil	Propofol + sufentanil	Endoscopist Satisfaction rate: 90.5% Respiratory depression: 2.7% Time to sedation: 88.3±10.7 satisfactory level of sedation with a good safety profile.	 77% 17.6% 62.7±10.1	Until discharge
Tan Y et al 2022	China	RCT Elderly patients Gastroscopy	1 (n=99)	66y	62%	Remimazolam 0.1mg/kg (R1) Or 0.2mg/kg (R2)	Propofol	R2: Worsened cognitive functions (immediate recall and short delay recall) Longer sedation time: R2: 12.09min R1: 8.27 min Recovery time: R2: 6.85 R1: 3.82 Hypotension: R2: 21.2% R1: 3% The addition of 0.1 mg/kg RT as an adjunct to opiate sedation for upper gastrointestinal endoscopy not only achieves more stable perioperative hemodynamics but also achieves acceptable neuropsychiatric functions in elderly patients	 8.21 min 4.33 min 48.5%	Until recovery
Yao Yusheng et	China	RCT	1 (n=132)	49y	48%	Remimazolam	Propofol	Discharge time: 24 min	21 min	Until

al 2022		Colonoscopy						Injection pain: 17% Hypotension: 20% Bradycardia: 6% remimazolam provides a noninferior discharge time. Furthermore, remimazolam is associated with less injection pain, lower risks of hypotension and bradycardia, and improved patient satisfaction.	49% 47% 20%	discharge
Guo J et al 2022	China	RCT Elderly	1 (n=77)	>65	60	Remimazolam + alfentanil	Propofol +alfentanil	Success rate of sedation:100%: The time to LOC: 20.7 ± 6.1 Injection pain: 0/39 Hemodynamic events: 6/39 Respiratory depression: 2/39 Compared with propofol, RT can be safely and effectively used for gastrointestinal endoscopy sedation in elderly patients, and the incidence of sedation-related adverse reactions, especially haemodynamic events and respiratory depression, is lower	100% 13.2 ± 5.2s 5/38 17/38 9/38	Until discharge
Xiao et al 2022	China	RCT Gastroscopy				Remimazolam-propofol-sufentanil	propofol-sufentanil	The dosage of propofol 38±9 mg anesthesia time (8.4±1.6 min) awakening time (2.9±0.8 min) discharge time (6.7±3.1 min) In clinical practice, the remimazolam-propofol-sufentanil sedative scheme has more advantages than	115±15 mg 14.5±3.3 8.7±1.9 12.4±3.6	Until discharge

								the propofol-sufentanil sedative scheme		
Zhu H et al 2024	China	RCT gastroscopy	5 (n=1833)	40y	40%	Remimazolam 0.15mg/kg Or 0.2mg/kg	Propofol 1.5mg/kg	Sedation success rate: 0.15mg/kg: 88.5% 0.2mg/kg: 98.7% Lower adverse events: 31.7% 28.4%	99.4% 43%	Until recovery
Chen H et al 2024	China	RCT Elderly	1 (n=60)	65-95	33%	Remimazolam + Flumezanil	Propofol	Recovery time: 2.6 ± 1.6 min	10.8 ± 3.0 min	Until recovery
Zhang Q et al 2024	China	RCT Elderly	1 (n=120)	60-75	40	Remimazolam	Etomidate +propofol	Induction time: 1.5min Respiratory adverse events 5% The safety and efficacy of remimazolam besylate are not inferior to those of etomidate combined with propofol	1.15min 18%	Until 24 hours after the procedure
Choe JW et al 2024	Korea	RCT EUS	8 (n=400)	57	49	Remimazolam	Propofol	cardiorespiratory adverse events: 8.5% non-significant: Oxygen desaturation: 1% Respiratory depression: 0.5% Hypotension: 2.5% Tachycardia: 4.5% Shorter induction time Comparable awaking and recovery time Lower injection site pain Remimazolam was superior to propofol in terms of safety and efficacy during EUS examinations	16% 3.5% 1.5% 5.5% 5.5%	Until recovery
Barbosa E et al 2024	Brazil	Systematic review and meta-analysis	15 trials RCT 4516			Remimazolam plus analgesia	Propofol plus analgesia	Lower sedation success rate Longer induction time	no difference in the patient and endoscopist	

			subjects					Lower rates of Respiratory depression Hypotension Hypertension requiring treatment Bradycardia	satisfaction	
Chen D et al 2024	China	RCT Elderly Gastroscopy	1 (n=240)	71y	53	Remimazolam	Propfol	more stable circulatory functions lower incidence of pain on injection: 3.3% hypotension: 15.6% advers events: 21.3% remimazolam was as effective as propofol, but was safer with a lower incidence of adverse events.	19.5% 39% 62.7%	Until recovery
Sun Q et al 2024	China	RCT Colonoscopy	1 (n=123)	52y	51	0.2 mg/kg remimazolam (group A) Or 0.25 mg/kg remimazolam (group B)	0.2 mg/kg Propofol	The successful rate of induction: 100% and 100% no significant difference in the sedation completion rate adverse events group A: 27% group B:36.8% This study revealed that remimazolam is a safe and effective medication for colonoscopy sedation, the security of remimazolam is better than propofol, and the sedative effect with the initial dose of 0.25 mg/kg of remimazolam is optimal	100% 71%	Until discharge
Zhang L et al 2022	China	Meta analysis	3 RCTs N=528			remimazolam	midazolam	Higher procedure success (OR=9.78) lower need for rescue medication (OR=0.09) reduced incidence of hypotension OR=0.39 adverse events (OR=0.36 Remimazolam demonstrated better efficacy and safety for the sedation of gastrointestinal		

								endoscopy compared to midazolam		
Zhang K et al. 2023	China	RCT	1 (n=261)	45	53%	remimazolam + esketamine	propofol + esketamine	No difference in mild hypoxemia 14.2% Lower severe hypoexmia 4.2% Longer time to LoC:53 sec Shorter time to recovery: 48min No significant difference in adverse events	11.5% 9.2% 50 sec 55.5min	Until recovery
Liu F et al. 2023	China	RCT Elderly Gastrointestinal endoscopy	2 (n=216)	67.6y 60-80 y	47%	Remimazolam	Propofol	moderate hypoxemia: 2.8% lower incidence of hypotension: 2.8% increased supplemental doses during sedation	17.4% 12.8% No difference in mild hypoxemia Or severe hypoxemia	Until recovery
Li Fang-Zhuo et al 2024	China	Meta analysis Older patients	7 trials n=1445			Remimazolam Safety and efficacy	Propofol	Reduced risk for hypotension (relative risk, RR=0.44) respiratory depression (RR = 0.46 injection pain (RR = 0.12 bradycardia (RR = 0.37 and time to discharge Remimazolam appears to be safer than propofol for gastroenteroscopy in older adults		
Terres M et al 2024	Brazil	Meta analysis Elderly patients	7 RCTs	1499 patients		remimazolam	propofol	significantly lower risk of adverse events, including hypoxemia, respiratory depression, hypotension, bradycardia, and injection pain, compared to propofol		
Li D et al. 2024	China	RCT	1 (n=166)	52 and 54	50	Remimazolam +alfentanil effectiveness and safety	Propofol +alfentanil	Systolic blood pressure (SBP) is higher at anaesthsia induction, 3 min, and at the end of the procedure lower incidence of		Until recovery

								hypoxemia: 9 (10.8%) hypotension: 10 (12%) drug injection pain 0 Bradycardia: 2 (2.4%) shorter awakening time and higher operator satisfaction	26 (31.3%) 25 (30.1%) 7 (8.4%) 1 (1.2%)	
Li Wei et al 2023	China	RCT Colonoscopy	1 (n=150)	35-65	59	remimazolam besylate + lidocain +estkamine	Propofol + lidocain +estkamine	No difference procedure success: 93.3% Higher patients satisfaction Remimazolam besylate has a similar efficacy to propofol when combined with subanesthetic doses of esketamine during outpatient colonoscopy	98.6% Higher fatigue level Higher endoscopist satisfaction No difference in Colonosocpy time Discharge time	Until recovery

Ciprofol Vs. Propofol

Study (Author, year)	Country	Study design	No. of sites (no. of subjects)	Age (y)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm	Follow-up
Zhong Jing et al 2023	China	RCT Endoscopy Advanced	1 (n=207)	>18y	53%	Ciprofol 6mg/kg/h Ciprofol 8mg/kg/h	Propofol	Success rate of sedation 100% And 100% Longer induction time Drug-related AEs- 84.1% and 76.8%	Success rate of sedation 100% Drug-related AEs 79.7	Recovery and discharged
Gao, SH et al 2024	China	RCT colonoscopy	1 (n=164)	54	40%	Ciprofol	Propofol	No difference in success rate: 96.3% Total dose: 40mg Time of sedation: 63.4±12.3min Recovery time: 9min Injection pain: 0 Respiratory depression: 2.4% Hypotension: 65.9% Patients' satisfaction: 10 Endoscopist satisfaction: 10	97.6% 185mg 54.8±10.1 8min 40.2% 13.4% 80.5% 9 10	Until discharge
Liao Jinsong et al 2023	China	RCT Gastroscopy	1 (n=368)	45y	44	Ciprofol +sufentanil	Propofol + sufentanil	Lower incidence of severe swallowing dysfunction Higher blood pressure Lower Heart rate Higher SpO2 hypoxemia: 7.6% Lower hypotension: 12.4% Lower injection pain: 3.2%	Shorter recovery time Longer unit stagy time 16.9% 21.3% 46.4%	Until recovery
Teng Yi et al 2021	China	RCT Phase IIa and IIb	9 (n=158)	Mean 39-48y	44	Ciprofol 0.4mg/kg Ciprofol 0.5mg/kg	Propofol	Success rate: 100%, 100% Mean recovery time: 6.1 and 5.1min Time to discharge: 11.8 and 11.2 min Side effects: 16.1% and 21.9% Ciprofol 0.4-0.5 mg/kg induced equivalent sedation/anesthesia and had a similar safety profile to propofol 2.0 mg/kg	100% 4.3min 10.6min 25.8%	Until discharge
Zhang J et al 2023	China	RCT Bidirectional endoscopy	N=185			Ciprofol + Alfentanil	Propofol + Alfentanil	Cardiopulmonary adverse events: 34.4% Ciprofol can significantly decrease respiratory depression	60.9%	
Chen L et al 2023	China	RCT	1 (n=149)	18-80	42	ciprofol 0.2mg/kg, ciprofol 0.3mg/kg, and ciprofol 0.4	Propofol	In all doses time to fall asleep was significantly shortened With lower nausea, vomiting, and injection pain		Until recovery

						mg/kg				
Zhou R et al 2024	China	RCT	1 (n=360)	48	47.8	Remimazolam Or ciprofol	Propofol	No difference in dreaming incidence Ciprofol 48% Remimazolam 41.6% Hypotension: Ciprofol: 18% Remimazolam: 10%	33.3% 26.6%	Until recovery

Propofol+ dexmedetomidine

Study (Author, year)	Country	Study design	No. of sites (no. of subjects)	Age (y)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm	Follow-up
Keiichi Ashikari et al, 2021	Japan ESD	RCTs	1 (n=66)	48-88y	80%	Dexmedetomidine plus propofol	Propofol	Restlessness incidence: 3% Satisfaction score endoscopist: 89 Maintenance dose of propofol: 2mg/kg/h Number of rescue propofol injections: 1 bradycardia: 30.3%	Restlessness incidence: 27.3% Satisfaction score endoscopist: 50 Maintenance dose of propofol: 5mg/kg/h Number of rescue propofol injections: 6 bradycardia 3%	
Chen H et al 2023	China	RCT	1 (n=90)	54	33	Dex 0.5 μg/kg And Dex 1.0 μg/kg + propofol	Propofol	Propofol EC50 (μg/mL): DEX0.5: 2.51 DEX1.0: 2.10 Injection site pain: DEX0.5: 1/29 DEX1.0: 0/30 Recovery time: DEX0.5: 9.3min DEX1.0: 11.6min Dexmedetomidine reduced the EC_{50} of propofol by TCI. A 0.5-1 μg/kg dose of dexmedetomidine caused a decrease in HR without bradycardia. The decrease in dosage of propofol with increasing doses of dexmedetomidine caused a more stable MAP	3.77 6/24 18.1min	Until discharge
Edokpolo L et al 2019	USA	RCT colonoscopy	1 (n=101)	57 and 56y	36%	Dexmedetomidine +propofol	Placebo + propofol	Ready for discharge by 30min: 51% Lower Propofol consumption: 140 μg · kg-1 · min-1 For anesthesia in ambulatory colonoscopy, combining low-dose dexmedetomidine with propofol delayed discharge readiness and	88% 180 μg · kg-1 · min-1	Until discharge

								provoked hypotension compared to propofol alone		
Zhao L et al 2022	China EUS	RCT	1 (n=200)	57	53	propofol-dexmedetomidine	propofol-remifentanil	Higher endoscopist satisfaction Higher body movement Longer induction time	No difference in patients' satisfaction	Until recovery
Liu W et al 2021	China	Meta analysis	7 studies 477 patients			Dexmedetomidine	Propofol	no significant differences in the risks of hypotension, nausea, and vomiting lower risk of hypoxia (RR = 0.26, 95% CI = 0.11-0.63) and higher risk of bradycardia (RR = 3.01	no significant differences in the induction time and recovery time	

Lidocaine +propofol

Study (Author, year)	Country	Study design	No. of sites (no. of subjects)	Age (y)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm	Follow-up
Hu Song et al 2022	China	RCT Gastroscopy Elderly	1 (n=140)	>65	59%	IV lidocaine + propofol	Saline + propofol	Lower propofol dose needed 107.32±21.39 mg Lower Incidence of hypoxia 12.9% Emergency airway management 2.9% Duration of gastroscopy 4.51±0.90 Consciousness recovery time 1.86±0.86 Postoperative pain	127.03±28.24 mg 27.1% 17.1% 5.22±1.04 2.76±1.65	Until recovery
Liu Haoran et al 2020 (included in the meta-analysis)	USA	RCT Gastroscopy	1 (n=48)	46.8y and 45y	43%	Lidocaine + propofol + sufentanil	Propofol + sufentanil	Induction ED50 propofol dose: 1.69 mg/kg	2.01 mg/kg	Until discharge
Nongnuang K et al 2022	Thailand	RCT Colonoscopy	1 (n=68)	63y	50%	IV lidocaine +propofol	Saline +propofol	Significantly reduced propofol dose: 151.76±50.78mg	242.06±50.86	Until discharge
Chen M et al	China	RCT	1 (n=79)	>65	44	IV lidocaine	Saline	total amounts of propofol: no difference		Until

2020 (included in the meta-analysis)		Elderly Colonoscopy				+propofol	+propofol	the required supplemental propofol 51.5 ± 38.6 mg) Average frequencies of boluses of supplemental propofol given after induction: 1.4 ± 0.9 The addition of intravenous lidocaine to propofol-based sedation resulted in a remarkable reduction of supplemental propofol in the elderly during colonoscopy	69.9 ± 39.2mg 2.1 ± 1.1	recovery
Li M et al 2022 (included in the meta-analysis)	China	RCT Elderly Colonoscopy	1 (n=87)	69y	63%	Iv lidocaine +propofol	Propofol	Total propofol consumption: 100.30 ± 25.29 mg Time to loss of consciousness: 40s No difference in number of airway modifications; incidence of sedation-related events; endoscopists' and patients' satisfaction scores; memory level of the procedure; and adverse events within 24 h postoperatively.	115.58 ± 27.52 mg 55s	Until 24 hours after the procedure
Barbosa E et al 2025	Brazil	Systematic review Meta analysis	8 RCTs 520 patients			IV lidocain +propofol	Propofol	significantly lower propofol dose shortened awakening time reduced post-procedural pain scores increased patient satisfaction score	no significant difference in procedure time or adverse events	

Etomidate

Study (Author, year)	Country	Study design	No. of sites (no. of subjects)	Age (y)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm	Follow-up
Yanpeng Liu et al 2023	China	RCT Gastroscopy Hypertensive elderly patients	1 (n=328)	66y	45%	Etomidate +propofol	Propofol (P) only Or etomidate (E) only	Hypoxia: 13.6% Hypotension: 0 Injection pain: 6.4% Endoscopist satisfaction: 9.88±0.59 Patients' satisfaction: 9.84±0.53	P:33.6%, E:14.8% P: 16.4%, E:0 P:31.8%, E:2.7% P: 8.69±1.21 E: 7.91±2.81 P: 7.10±1.39 E: 9.02±1.30	Until recovery

Hao L et al. 2020	China	RCT Gastroscopy	1 (n=300)	50y	53	Etomidate 10ml (PE1) or 5 ml (PE2) + propofol	Propofol	Awakening time: PE1: 196.97±143.01sec PE2: 109.30±76.63 sec PE1 group had a higher incidence of muscle spasm, body movement, choking, and deglutition	107.11±73.14 Higher incidence of hypoxemia and injection pain	Until discharge
Chen L et al 2019	China	Systematic review Meta analysis	15 RCTs 2973 patients			Propofol and etomidate	Propofol alone Or Etomidate Alone	possibly increased recovery time risk for myoclonus (OR=3.07) beneficial effect on mean arterial pressure (MAP) after anesthesia SPO2 after anesthesia apnea or hypoxemia injection pain and body movement fewer side effects on circulation and respiration in patients undergoing gastroscopy	etomidate alone had a higher risk of myoclonus	

Ketamine

Study (Author, year)	Country	Study design	No. of sites (no. of subjects)	Age (y)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm	Follow-up
Tian L et al 2020	China	RCT	1 (n=200)	45.7y And 43.4 y	58	Ketamine +propofol	Propofol	-Cognitive function: more severe impairment in one-card learning propofol dose: 142.9±22 -better 5 minutes MAP less likely to suffer from complications respiratory depression: 7.3% hypotension: 10.5% Although adding ketamine to propofol for sedation in colonoscopy provided fewer complications, such as respiratory depression and hypotension, it also causes more impairment in cognitive functions.	 189.7±27.9 18% 24%	Until recovery

Esketamine

Study (Author, year)	Country	Study design	No. of sites (no. of subjects)	Age (y)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm	Follow-up
Zhan Y et al 2022	China	RCT	1 (n=260)	Mean 44y	47%	PK1 group (propofol + esketamine 0.05 mg/kg), PK2 group (propofol + esketamine 0.1 mg/kg), and PK3 group (propofol + esketamine 0.2 mg/kg)	propofol + saline	Propofol consumption: PK1:10.56 PK2:10.14 PK3: 9.57 Induction time: PK1: 64.83 ± 13.543s PK2: 62.23 ± 15.197s PK3: 61.35 ± 14.470s The combination of 0.2 mg/kg esketamine and propofol was effective and safe in painless gastrointestinal endoscopy, as evidenced by less propofol consumption per minute, shorter induction time, and lower incidence of cough and body movement relative to propofol alone	11.78 68.52 ± 18.394s	Until recovery
Zheng et al 2023	China	RCT Obesity Gastroscopy	1 (n=104)	41y	63	propofol+esketamine 0.25 mg/kg	propofol+saline	Propofol consumption was 201.3±16.6 mg Induction time: 17.8±1.9 s awakening times: 4.8±1.3 min Hemodynamic parameters were more stable Lower side effects And higher satisfaction scores The combination of propofol and esketamine (0.25 mg/kg) improves the safety and reduces the incidence of adverse events in patients with obesity during painless gastroscopy	274.4±22.6 mg 25.4±2.3 6.2±1.1 min	Until discharge
Yang H et al 2022	China	RCT Elderly	1 (n=90)	65-89y	34%	K0.25 group (0.25 mg/kg esketamine); and SK0.5 group (0.5 mg/kg esketamine) + Propofol	Propofol	The median effective concentration (EC_{50}) SK0.25: 2.45 (1.85-3.05) SK0.5: 1.71 (1.15-2.27) μg/mL Mean arterial pressure percentage change: SK0.25: 15.2 SK0.5: 10.1 Recovery time: SK0.25: 7.8 [5.3–15.0] min SK0.5: 7.0 [5.0–12.0] Combination medication of propofol with esketamine reduced the propofol EC_{50} during gastrointestinal endoscopy in elderly patients compared with administration of propofol without esketamine. Increasing doses of SK with propofol	3.69 (2.59-4.78) μg/mL -19.7 10.3 [7.0–15.0] min	Until recovery

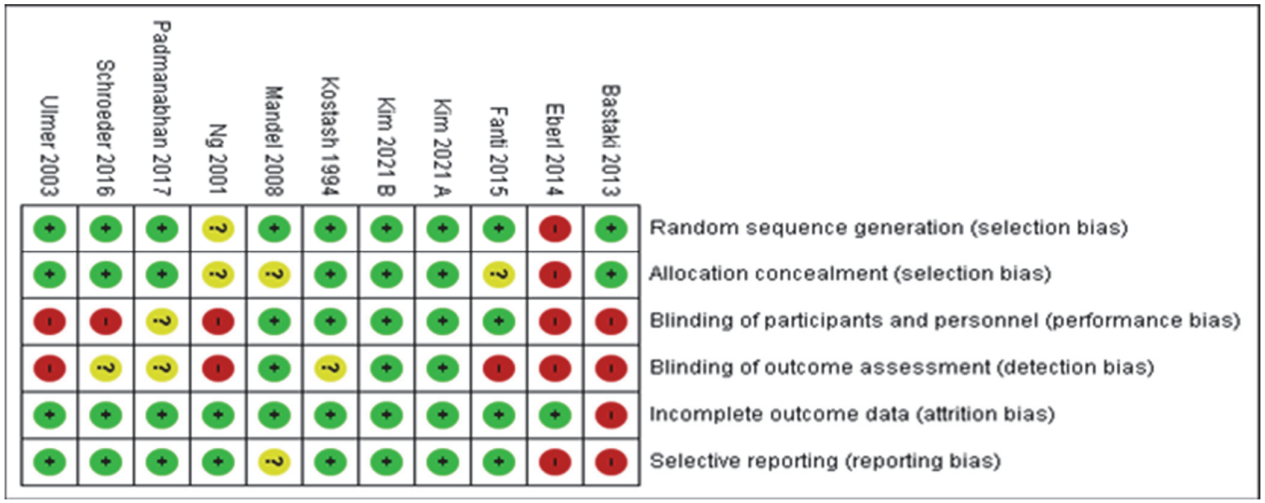
								are less likely to produce hypotension with a shorter recovery time		
Song N et al 2023	China	RCT bidirectional endoscopy	3 (n=660)	48 (36-57)	46.2	Esketamine +propofol +sufentanil	Saline +propofol +sufentanil	composite outcome of desaturation and hypotension: 8.2% Total dose of propofol: 130(110 to160) Administration of low-dose esketamine resulted in an approximately 61% reduction in the incidence of desaturation and hypotension, accompanied by decreased propofol requirements.	21% 200(160 to225)	Until recovery
Lian X et al 2023	China	Systematic review and meta-analysis	18 studies 1962 patient			Esketaine +propofol	Propofol	Reduction of the recovery time lower propofol dosage fewer complications Higher risk of visual disturbance		

Alfentanil Sufentanil

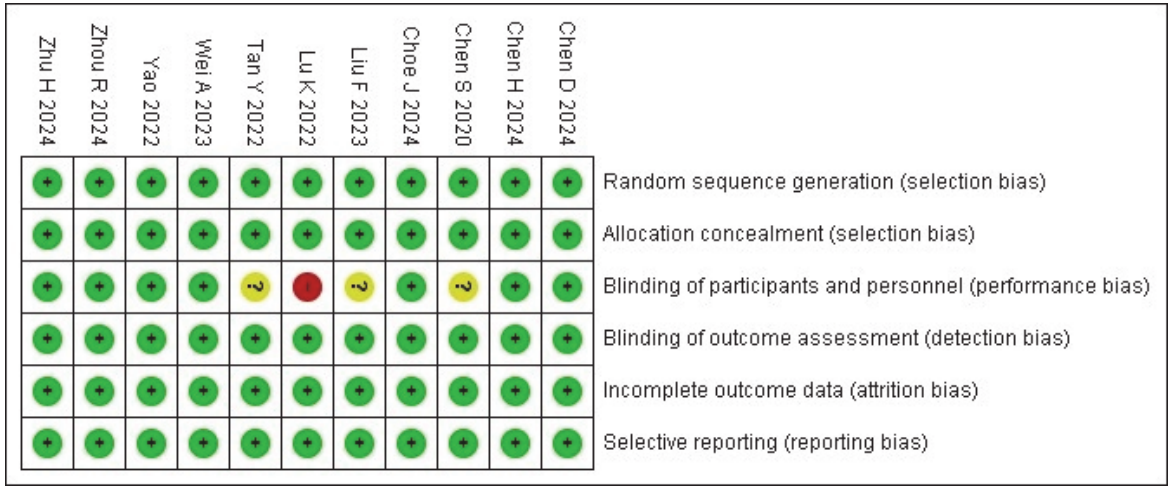
Study (Author, year)	Country	Study design	No. of sites (no. of subjects)	Age (y)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm	Follow-up
Basbosa EC, 2024	Brazil	Meta-analysis	15 trials (4516 subjects)			S-A opioids + remimazolam	S-A Opioids +Propofol	significantly lower rates of respiratory, hypotension, and hypotension requiring treatment	significantly higher sedation success rate slightly shorter induction time	
Yang H et al 2023	China	Meta-analysis	13 RCT 1762 patients			Alfentanil +propofol Efficacy and safety	Propofol	More stable mean arterial pressure, heart rate, and oxygen saturation lower propofol dose lower awakening time lower incidence of nausea and vomiting lower incidence of body movement, hypotension, respiratory depression, and cough		
Cheng X, 2025	China	Meta-analysis	17 RCTs 1450 pts			S-A Opioids + Ciprofol	S-A Opioids +Propofol	Lower incidence of hypotension, bradycardia, respiratory depression, and injection pain in the ciprofol group		
Tulin Akarsu Ayazoglu et al 2021	Turkey	RCT	1 (n=99)	48y	60%	Intranasal 0.5 µg kg Intranasal 0.25 µg kg + propofol	Intranasal 0.9% NACL +Midazolam +propofol	Longer time to spontaneous eye opening and recovery time Better Pain control and endoscopist satisfaction	Higher propofol consumption Higher hypoxemia incidence	Until recovery

Table 2.4.3s: Risk of bias assessment for studies

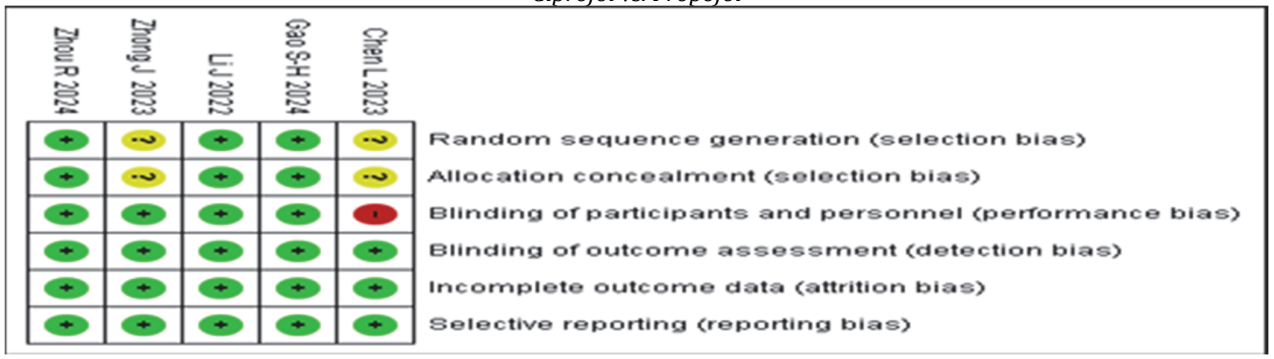
Midazolam±opoioid vs propofol



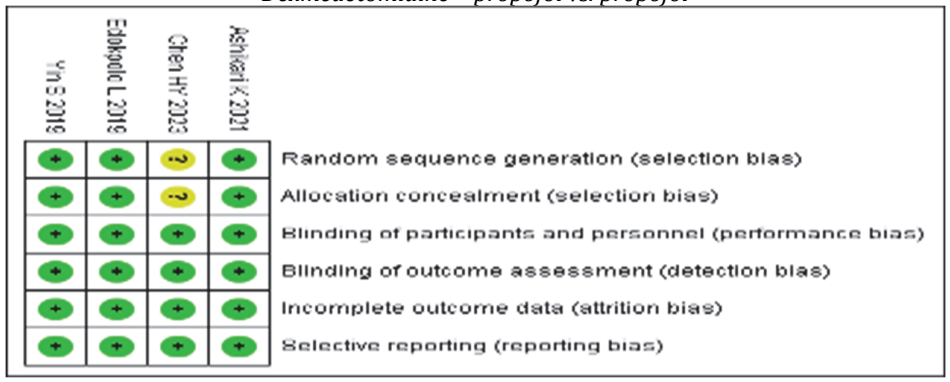
Remimazolam vs. propofol



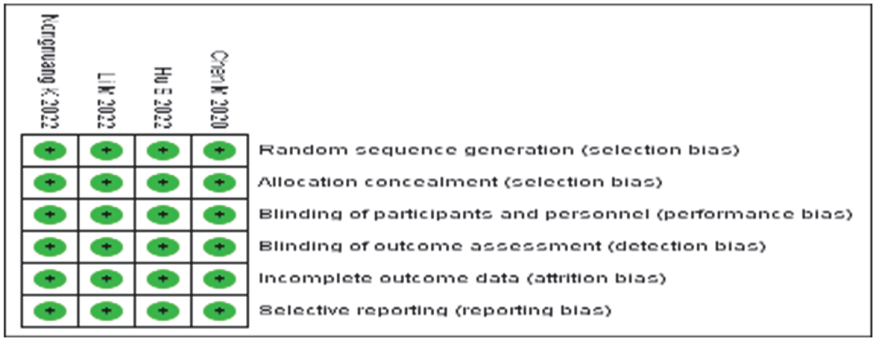
Ciprofol vs. Propofol



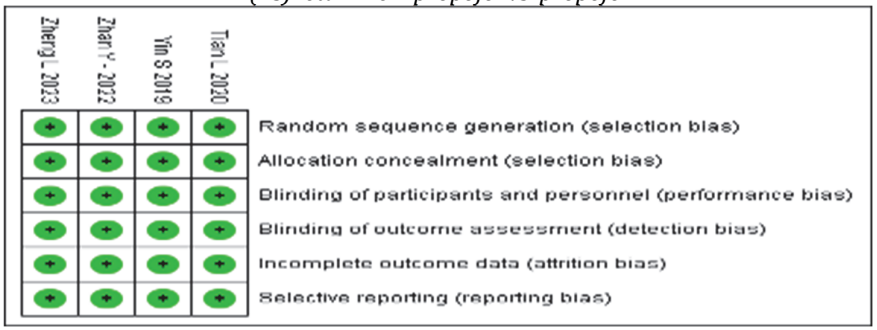
Dexmedetomidine + propofol vs. propofol



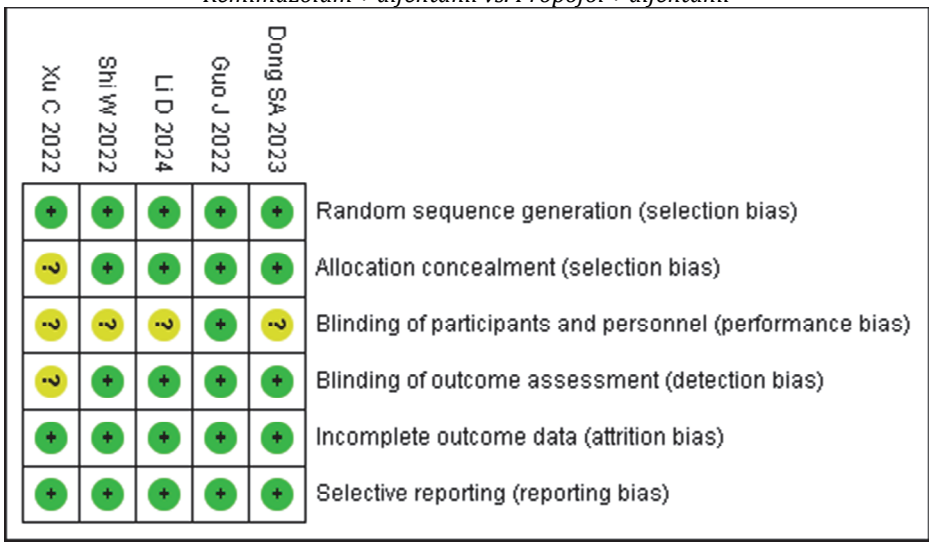
Lidocaine + propofol vs. propofol



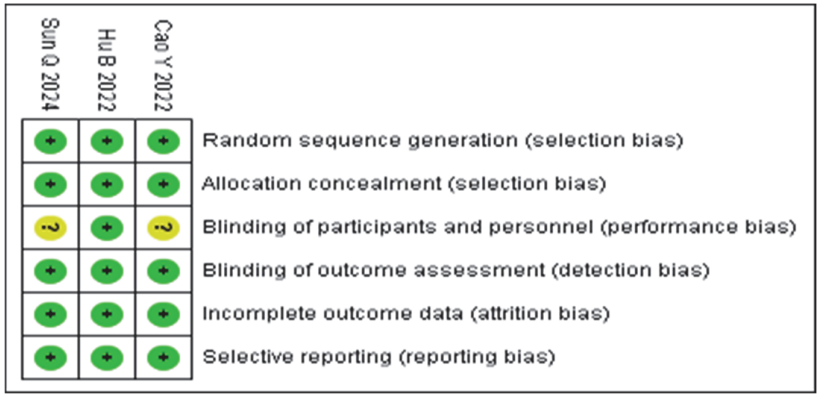
(Es)ketamine + propofol vs. propofol



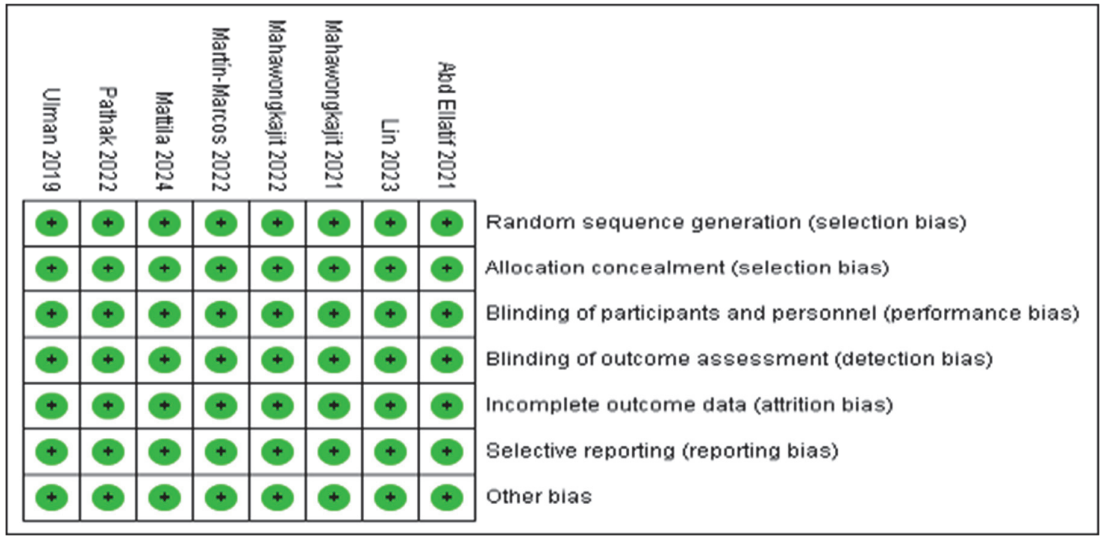
Remimazolam + alfentanil vs. Propofol + alfentanil



Remimazolam + sufentanil vs. Propofol + sufentanil



Xylocaine throat topical anesthetic



Antispasmodics

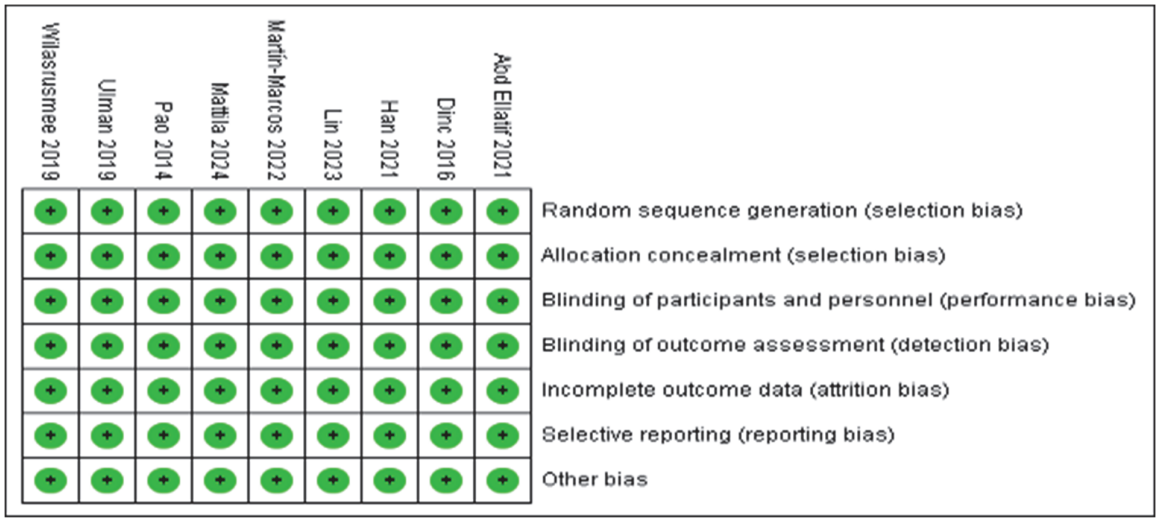


Fig. 2.4.1s. Comparison of total cardiorespiratory adverse events (overall, hypotension, hypoxia, bradycardia) between midazolam±opioid vs propofol

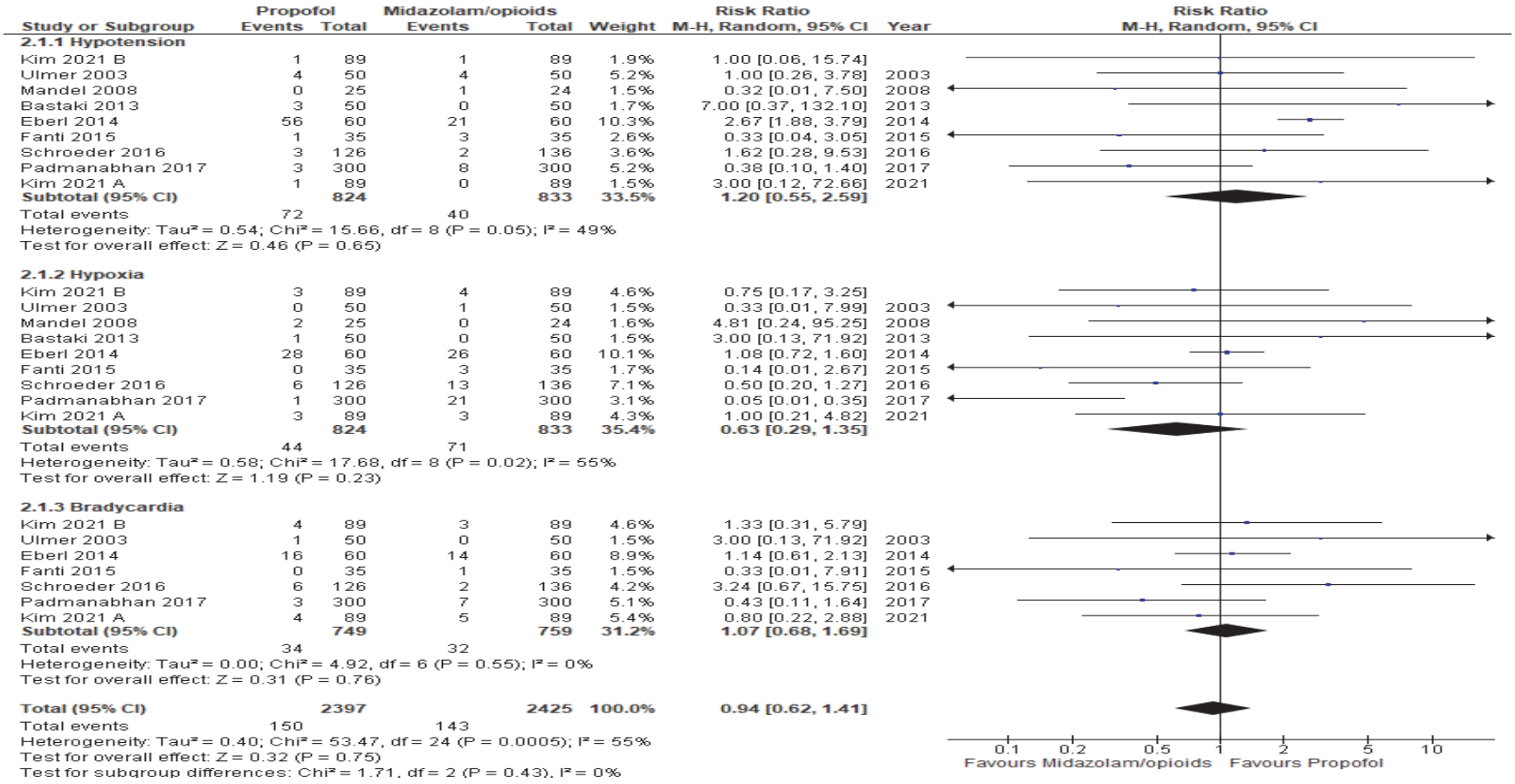


Table 2.4.4s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3s. Overall, the included studies were considered of good quality, despite concerns about the lack of blinding in many of them. The certainty of evidence for all clinical outcomes was downgraded due to indirectness (variability in sedative doses administered, outcome definitions, discharge policies, and no report on insufflation technique, air vs. CO2 vs. water), while including only studies on colonoscopy raises doubts about the generalizability of the results for procedural sedation overall. Further downgrading was applied for the main outcome, i.e., adverse events due to high inconsistency (high heterogeneity) and imprecision (broad CI crosses 1.0), resulting in a very low overall certainty of evidence and a conditional recommendation was proposed.

Fig. 2.4.2s. Comparison of patient reported satisfaction between midazolam±opioid vs propofol

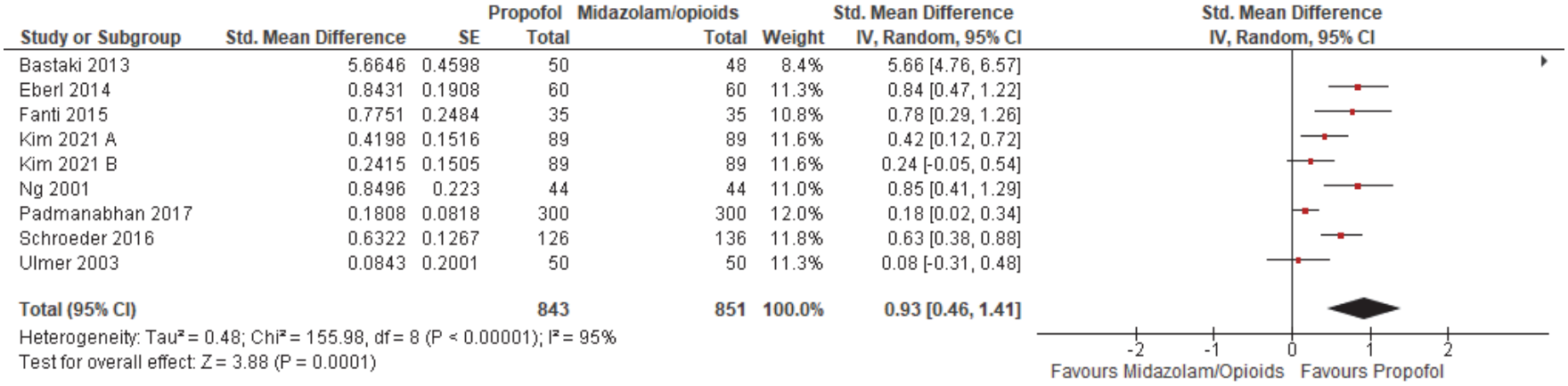


Table 2.4.5s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3s. Overall, the included studies were considered of good quality, despite concerns about the lack of blinding in many of them. The certainty of evidence for all clinical outcomes was downgraded due to indirectness (variability in sedative doses administered, outcome definitions, discharge policies, and no report on insufflation technique, air vs. CO2 vs. water), while including only studies on colonoscopy raises doubts about the generalizability of the results for procedural sedation overall. A very low overall certainty of evidence, and a conditional recommendation was proposed.

Fig. 2.4.3s. Comparison of procedural and discharge/recovery time between midazolam±opioid vs propofol

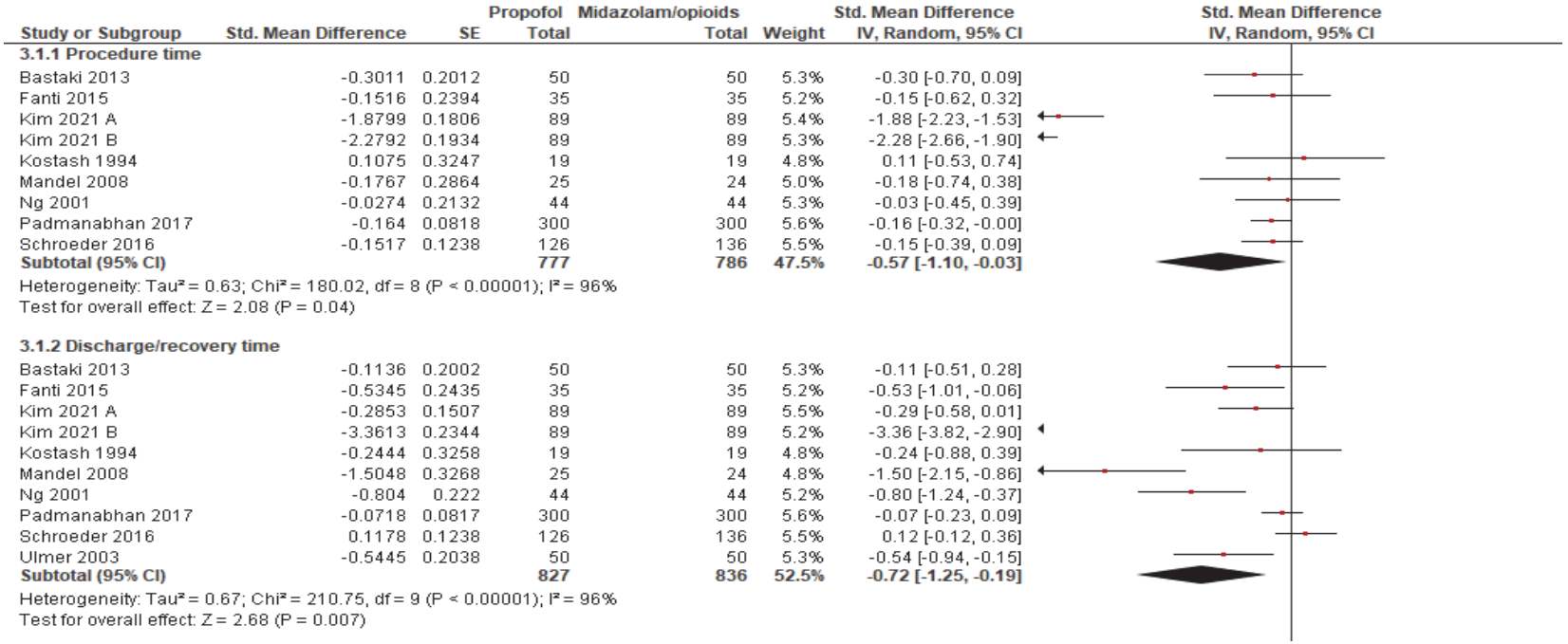


Table 2.4.6s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3s. Overall, the included studies were considered of good quality, despite concerns about the lack of blinding in many of them. The certainty of evidence for all clinical outcomes was downgraded due to indirectness (variability in sedative doses administered, outcome definitions, discharge policies, and no report on insufflation technique, air vs. CO2 vs. water), while including only studies on colonoscopy raises doubts about the generalizability of the results for procedural sedation overall. A very low overall certainty of evidence, and a conditional recommendation was proposed.

Table 2.4.4s. GRADE for between midazolam±opoioid vs propofol

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With placebo	With Patient Satisfaction	Relative effect (95% CI)	Risk with placebo	Risk difference with Patient Satisfaction
Patient Satisfaction											
1694 (9 RCTs)	Serious	serious[a]	serious[b]	not serious	none	⊕◯◯◯ Very low[a,b]	851	843	-	-	SMD **0.93 higher** (0.46 higher to 1.41 higher)
Overall cardiorespiratory events											
4822 (9 RCTs)	Serious	serious[a]	serious[b]	serious[c]	none	⊕◯◯◯ Very low[a,b,c]	143/2425 (5.9%)	150/2397 (6.3%)	**RR 0.94** (0.62 to 1.41)	143/2425 (5.9%)	**4 fewer per 1.000** (from 22 fewer to 24 more)
Procedure time											
3226 (10 RCTs)	Serious	serious[a]	serious[b]	not serious	none	⊕◯◯◯ Very low[a,b]	1622	1604	-	-	SMD **0.65 lower** (1 lower to 0.29 lower)

Fig. 2.4.4s. Effect of remimazolam vs. propofol regarding sedation induction time

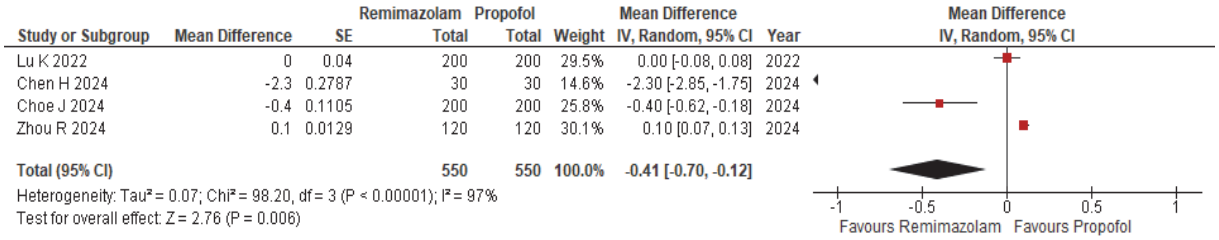


Table 2.4.7s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3s. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to inconsistency (high heterogeneity), so the quality of evidence was downgraded to low, and a conditional recommendation was proposed.

Fig. 2.4.5s. Effect of remimazolam vs. propofol regarding procedural time

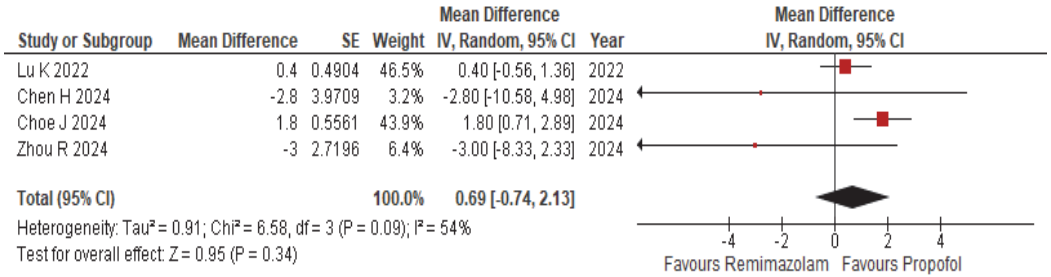


Table 2.4.8s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3s. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to inconsistency (high heterogeneity) and imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to low, and a conditional recommendation was proposed.

Fig. 2.4.6s. Effect of remimazolam vs. propofol regarding sedation success

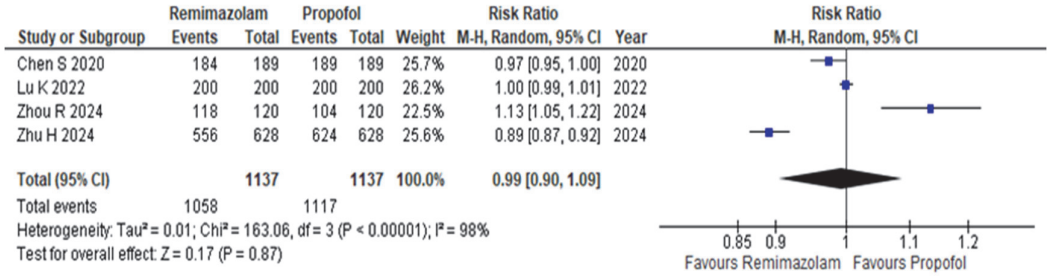


Table 2.4.9s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3s. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to inconsistency (high heterogeneity) and imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to low, and a conditional recommendation was proposed.

Fig. 2.4.7s. Effect of remimazolam vs propofol regarding satisfaction

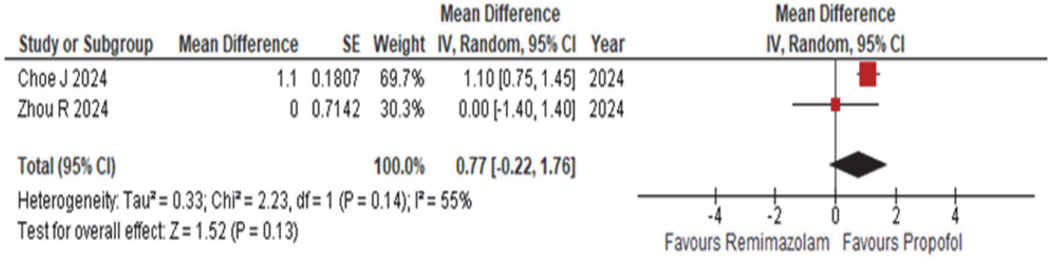


Table 2.4.10s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3s. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to inconsistency (high heterogeneity) and imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to low, and a conditional recommendation was proposed.

Fig. 2.4.8s. Effect of remimazolam vs propofol regarding the total adverse event rate

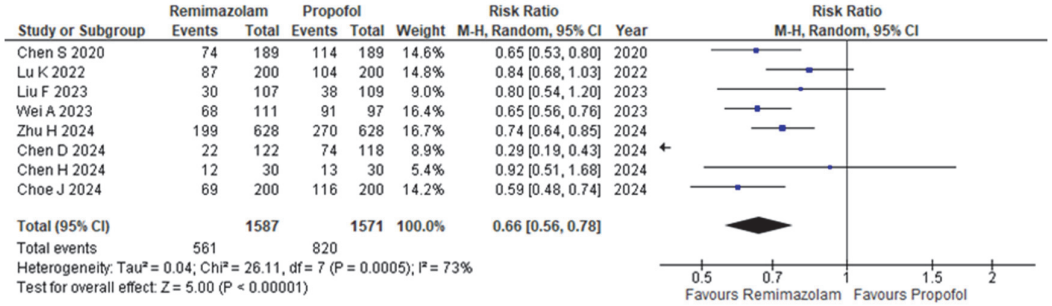


Table 2.4.11s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3s. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to inconsistency (high heterogeneity), so the quality of evidence was downgraded to low, and a conditional recommendation was proposed.

Fig. 2.4.9s. Effect of remimazolam vs. propofol regarding hypotension episodes rate

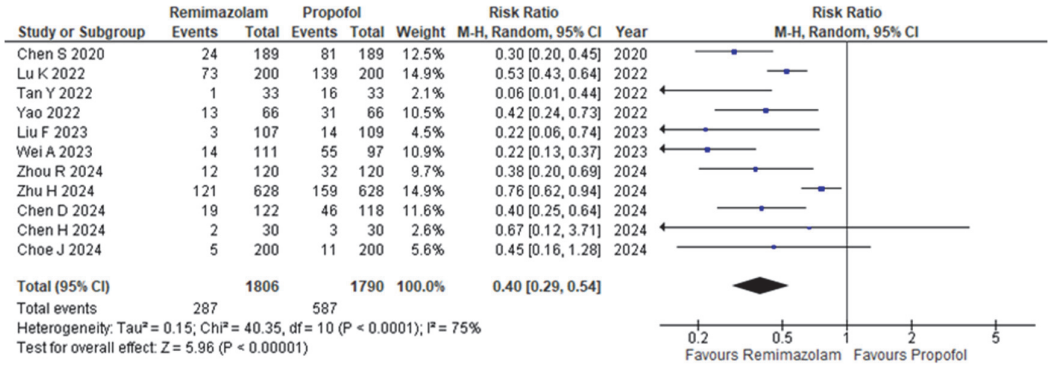


Table 2.4.12s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3s. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to inconsistency (high heterogeneity), so the quality of evidence was downgraded to low, and a conditional recommendation was proposed.

Fig. 2.4.10s. Effect of remimazolam vs propofol regarding bradycardia events rate

Table 2.4.13s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3s. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was not downgraded, so the quality of evidence was deemed high, and a conditional recommendation was proposed.

Fig. 2.4.11s. Effect of remimazolam vs. propofol regarding respiratory adverse events rate

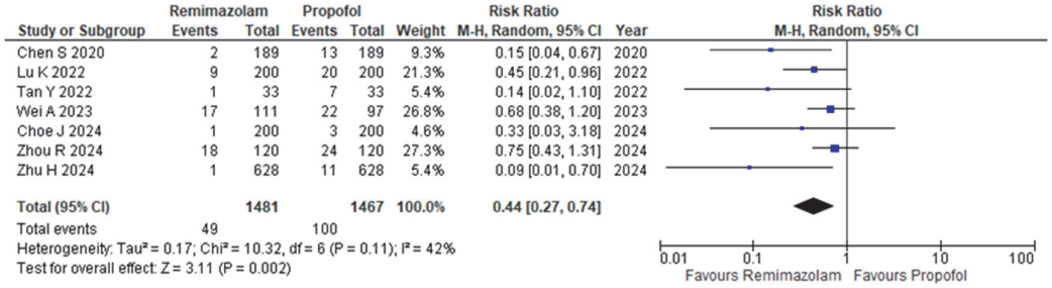


Table 2.4.14s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3s. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to inconsistency (moderate heterogeneity), so the quality of evidence was downgraded to moderate, and a conditional recommendation was proposed.

Fig. 2.4.12s. Effect of ciprofol vs. propofol regarding sedation success

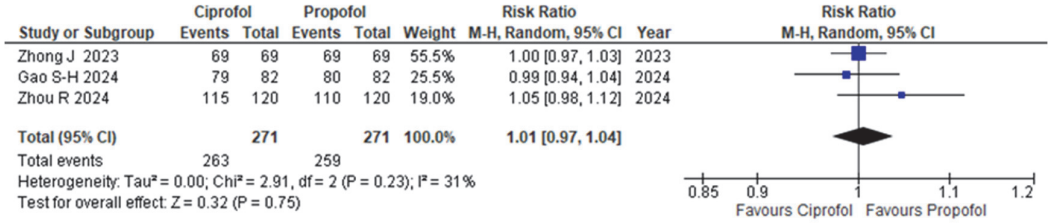


Table 2.4.15s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3s. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to inconsistency (moderate heterogeneity) and imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to low, and a conditional recommendation was proposed.

Fig. 2.4.13s. Effect of ciprofol vs propofol regarding the total adverse events rate

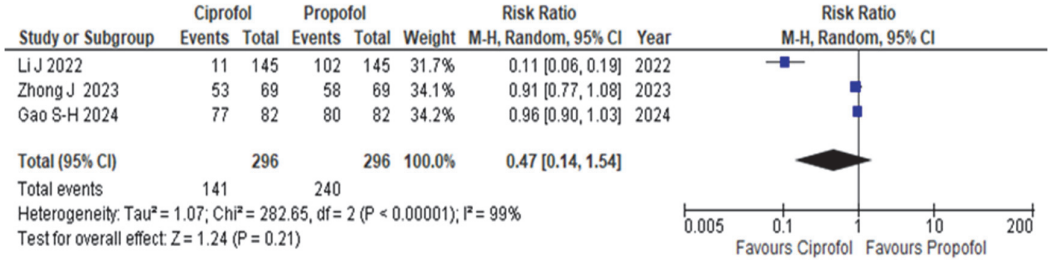


Table 2.4.16s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3s. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to inconsistency (high heterogeneity) and imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to very low, and a conditional recommendation was proposed.

Fig. 2.4.14s. Effect of ciprofol vs. propofol regarding hypotension episodes

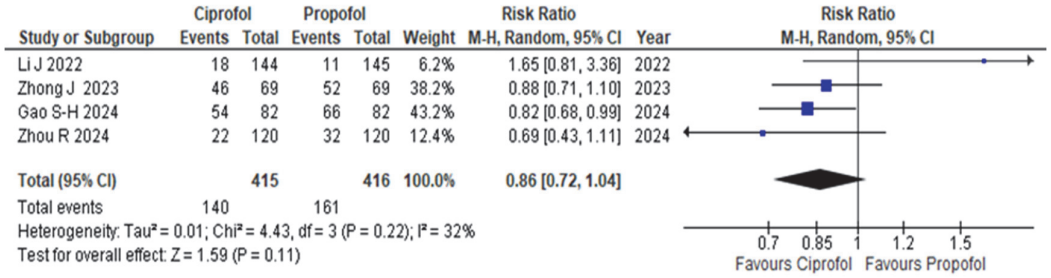


Table 2.4.17s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3s. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to inconsistency (moderate heterogeneity) and imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to low, and a conditional recommendation was proposed.

Fig. 2.4.15s. Effect of ciprofol vs. propofol regarding bradycardia rate

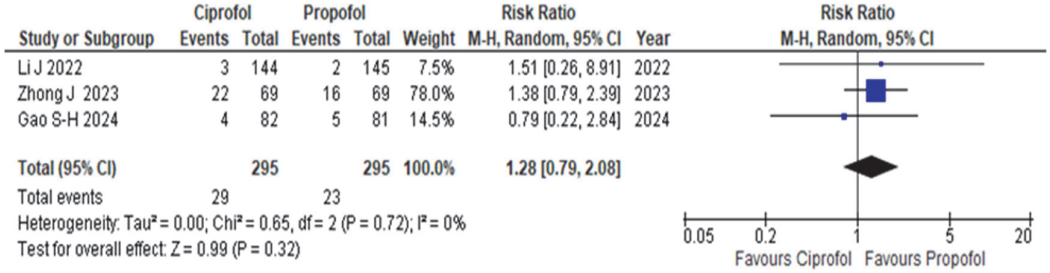


Table 2.4.18s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to moderate, and a conditional recommendation was proposed.

Fig. 2.4.16s. Effect of ciprofol vs. propofol regarding the respiratory adverse events rate

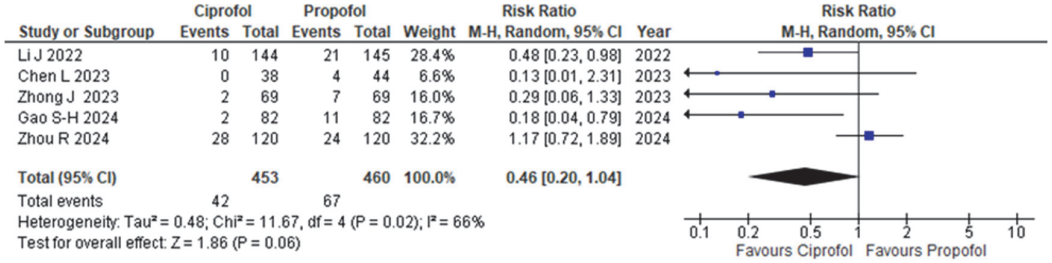


Table 2.4.19s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3s. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to inconsistency (moderate heterogeneity) and imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to low, and a conditional recommendation was proposed.

Table 2.4.7s-2.4.14s Remimazolam compared to Propofol for GI endoscopy sedation

Bibliography: Remimazolam vs. Propofol for GI endoscopy sedation. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With Propofol	With Remimazolam	Relative effect (95% CI)	Risk with Propofol	Risk difference with Remimazolam
Total adverse events											
3158 (8 RCTs)	not serious	very serious[a]	not serious[b]	not serious	none	⨁⨁◯◯ Low[a,b]	820/1571 (52.2%)	561/1587 (35.3%)	**RR 0.66** (0.56 to 0.78)	820/1571 (52.2%)	**177 fewer per 1.000** (from 230 fewer to 115 fewer)
Hypotension											
3596 (11 RCTs)	not serious	very serious[a]	not serious[b]	not serious	none	⨁⨁◯◯ Low[a,b]	587/1790 (32.8%)	287/1806 (15.9%)	**RR 0.40** (0.29 to 0.54)	587/1790 (32.8%)	**197 fewer per 1.000** (from 233 fewer to 151 fewer)
Bradycardia											
2272 (6 RCTs)	not serious	not serious	not serious[b]	not serious	none	⨁⨁⨁⨁ High[b]	90/1130 (8.0%)	40/1142 (3.5%)	**RR 0.46** (0.32 to 0.67)	90/1130 (8.0%)	**43 fewer per 1.000** (from 54 fewer to 26 fewer)
Duration induction (sec/min)											
1100 (4 RCTs)	not serious	very serious[a]	not serious[b]	not serious	none	⨁⨁◯◯ Low[a,b]	550	550	-	550	MD **0.41 lower** (0.7 lower to 0.12 lower)
Time (min)											

Table 2.4.7s-2.4.14s **Remimazolam compared to Propofol for GI endoscopy sedation**
Bibliography: Remimazolam vs. Propofol for GI endoscopy sedation. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
0 (4 RCTs)	not serious	serious[a]	not serious[b]	serious[c]	none	⨁⨁◯◯ Low[a,b,c]	0	0	-	0	MD **0.69 higher** (0.74 lower to 2.13 higher)
Success (%)											
2274 (4 RCTs)	not serious	very serious[a]	not serious[b]	serious[c]	none	⨁◯◯◯ Very low[a,b,c]	1117/1137 (98.2%)	1058/1137 (93.1%)	**RR 0.99** (0.90 to 1.09)	1117/1137 (98.2%)	**10 fewer per 1.000** (from 98 fewer to 88 more)
Respiratory AE											
2948 (7 RCTs)	not serious	serious[a]	not serious[b]	not serious	none	⨁⨁⨁◯ Moderate[a,b]	100/1467 (6.8%)	49/1481 (3.3%)	**RR 0.44** (0.27 to 0.74)	100/1467 (6.8%)	**38 fewer per 1.000** (from 50 fewer to 18 fewer)
Satisfaction											
0 (2 RCTs)	not serious	serious[a]	not serious[b]	serious[c]	none	⨁⨁◯◯ Low[a,b,c]	0	0	-	0	MD **0.77 higher** (0.22 lower to 1.76 higher)

Table 2.4.15s-2.4.19s Ciprofol compared to Propofol for GI endoscopy sedation
Bibliography: Ciprofol vs Propofol for GI endoscopy sedation. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Propofol	With Ciprofol		Risk with Propofol	Risk difference with Ciprofol
Total adverse events											
592 (3 RCTs)	not serious	very serious[a]	not serious[b]	serious[c]	none	⨁◯◯◯ Very low[a,b,c]	240/296 (81.1%)	141/296 (47.6%)	**RR 0.47** (0.14 to 1.54)	240/296 (81.1%)	**430 fewer per 1.000** (from 697 fewer to 438 more)
Hypotension											
831 (4 RCTs)	not serious	serious[a]	not serious[b]	serious[c]	none	⨁⨁◯◯ Low[a,b,c]	161/416 (38.7%)	140/415 (33.7%)	**RR 0.86** (0.72 to 1.04)	161/416 (38.7%)	**54 fewer per 1.000** (from 108 fewer to 15 more)
Bradycardia											
590 (3 RCTs)	not serious	not serious	not serious[b]	serious[c]	none	⨁⨁⨁◯ Moderate[b,c]	23/295 (7.8%)	29/295 (9.8%)	**RR 1.28** (0.79 to 2.08)	23/295 (7.8%)	**22 more per 1.000** (from 16 fewer to 84 more)
Success (%)											
542 (3 RCTs)	not serious	serious[a]	not serious[b]	serious[c]	none	⨁⨁◯◯ Low[a,b,c]	259/271 (95.6%)	263/271 (97.0%)	**RR 1.01** (0.97 to 1.04)	259/271 (95.6%)	**10 more per 1.000** (from 29 fewer to 38 more)

Table 2.4.15s-2.4.19s Ciprofol compared to Propofol for GI endoscopy sedation
Bibliography: Ciprofol vs Propofol for GI endoscopy sedation. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment									Summary of findings		
Respiratory AEs											
913 (5 RCTs)	not serious	serious[a]	not serious[b]	serious[b]	none	⨁⨁◯◯ Low[a,b,c]	67/460 (14.6%)	42/453 (9.3%)	**RR 0.46** (0.20 to 1.04)	67/460 (14.6%)	**79 fewer per 1.000** (from 117 fewer to 6 more)
Time (min)											
0 (3 RCTs)	not serious	not serious[a]	not serious[b]	serious[c]	none	⨁⨁⨁◯ Moderate[a,b,c]	0	0	-	0	MD **2.01 higher** (1.32 lower to 5.34 higher)

Fig. 2.4.17s. Effect of dexmedetomidine + propofol vs. propofol regarding hypotension episodes

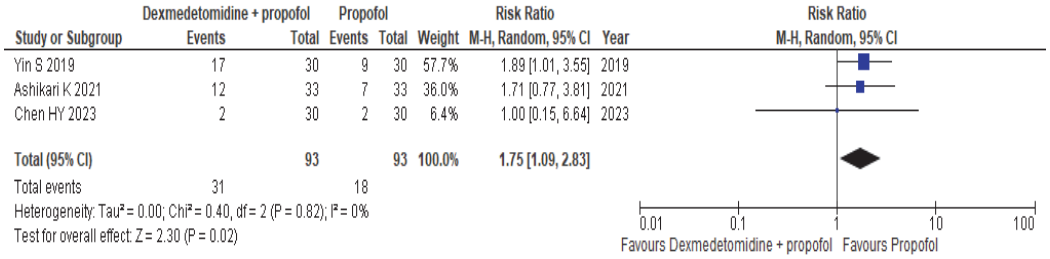


Table 2.4.20s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3s. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was not downgraded, so the quality of evidence was deemed high; however, there were only three randomized controlled trials, and a conditional recommendation was proposed.

Fig. 2.4.18s. Effect of dexmedetomidine + propofol vs. propofol regarding bradycardia

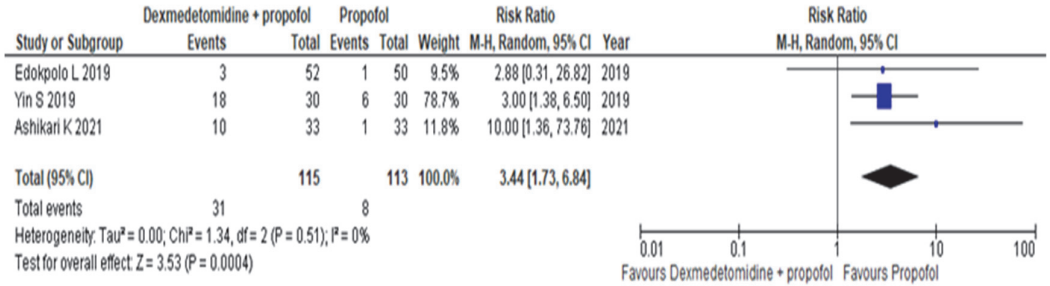


Table 2.4.21s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was not downgraded, so the quality of evidence was deemed high; however, there were only three randomized controlled trials, and a conditional recommendation was proposed.

Fig. 2.4.19s. Effect of dexmedetomidine + propofol vs. propofol regarding respiratory AEs

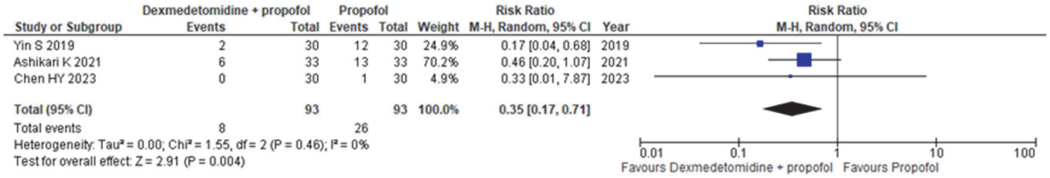


Table 2.4.22s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3s. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was not downgraded, so the quality of evidence was deemed high; however, there were only three randomized controlled trials, and a conditional recommendation was proposed.

Table 2.4.20s-2.4.22s Dexmedetomidine + propofol compared to Propofol for GI endoscopy sedation
Bibliography: Dexmedetomidine + prop vs. propofol for GI endoscopy sedation. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With Propofol	With Dexmetodine + propofol	Relative effect (95% CI)	Risk with Propofol	Risk difference with Dexmedetomidine + propofol
Hypotension											
186 (3 RCTs)	not serious	not serious	not serious	not serious	none	⊕⊕⊕⊕ High	18/93 (19.4%)	31/93 (33.3%)	**RR 1.75** (1.09 to 2.83)	18/93 (19.4%)	**145 more per 1.000** (from 17 more to 354 more)
Bradycardia											
228 (3 RCTs)	not serious	not serious	not serious	not serious	none	⊕⊕⊕⊕ High	8/113 (7.1%)	31/115 (27.0%)	**RR 3.44** (1.73 to 6.84)	8/113 (7.1%)	**173 more per 1.000** (from 52 more to 413 more)

Table 2.4.20s-2.4.22s Dexmedetomidine + propofol compared to Propofol for GI endoscopy sedation
Bibliography: Dexmedetomidine + prop vs. propofol for GI endoscopy sedation. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment									Summary of findings		
Respiratory AEs											
186 (3 RCTs)	not serious	not serious	not serious	not serious	none	⊕⊕⊕⊕ High	26/93 (28.0%)	8/93 (8.6%)	**RR 0.35** (0.17 to 0.71)	26/93 (28.0%)	**182 fewer per 1.000** (from 232 fewer to 81 fewer)

Fig. 2.4.20s. Effect of lidocaine + propofol vs. propofol regarding respiratory AEs

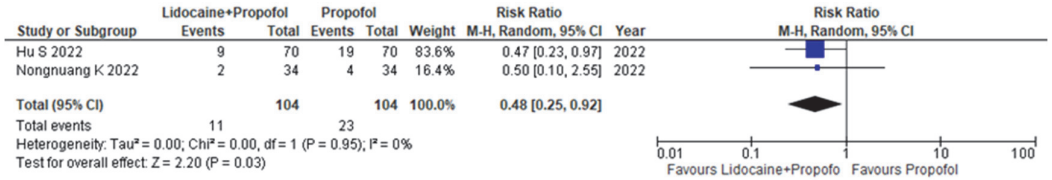


Table 2.4.23s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3s. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was not downgraded, so the quality of evidence was deemed high; however, there were only two randomized controlled trials, and a conditional recommendation was proposed.

Respiratory AE compared to placebo for GI endoscopy sedation
Bibliography: Lidocaine + propofol vs. propofol for GI endoscopy sedation. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With placebo	With Respiratory AE	Relative effect (95% CI)	Risk with placebo	Risk difference with Respiratory AE
Respiratory AE											
208 (2 RCTs)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	23/104 (22.1%)	11/104 (10.6%)	**RR 0.48** (0.25 to 0.92)	23/104 (22.1%)	**115 fewer per 1.000** (from 166 fewer to 18 fewer)

Fig. 2.4.21s. Effect of esketamine + propofol vs. propofol regarding hypotension episodes

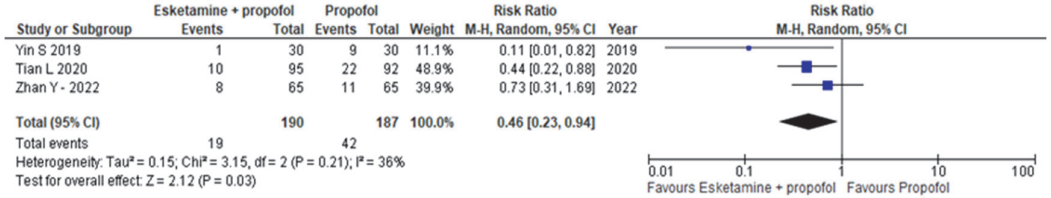


Table 2.4.24s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3s. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to inconsistency (moderate heterogeneity), so the quality of evidence was downgraded to low, and a conditional recommendation was proposed.

Fig. 2.4.22s. Effect of esketamine + propofol vs. propofol regarding bradycardia episodes

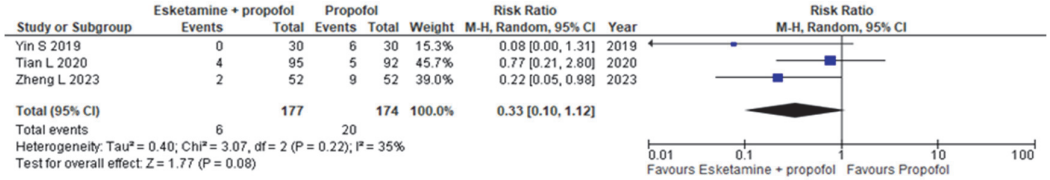


Table 2.4.25s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3s. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to inconsistency (moderate heterogeneity) and imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to low, and a conditional recommendation was proposed.

Fig. 2.4.23s. Effect of esketamine + propofol vs. propofol regarding respiratory AEs

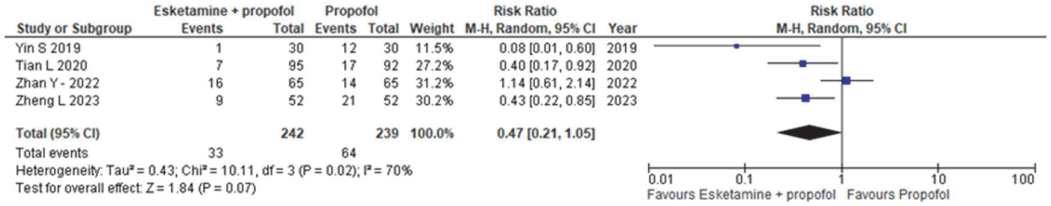


Table 2.4.26s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3s. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to inconsistency (serious heterogeneity) and imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to very low, and a conditional recommendation was proposed.

Table 2.4.24s-2.4.26s (Es)ketamine + propofol compared to Propofol for GI endoscopy sedation

Bibliography: 03_(Es)ketamine + propofol vs. propofol for GI endoscopy sedation. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With Propofol	With (Es)ketamine + propofol	Relative effect (95% CI)	Risk with Propofol	Risk difference with (Es)ketamine + propofol
Hypotension											
377 (3 RCTs)	not serious	serious[a]	not serious	not serious	none	⨁⨁⨁◯ Moderate[a]	42/187 (22.5%)	19/190 (10.0%)	**RR 0.46** (0.23 to 0.94)	42/187 (22.5%)	**121 fewer per 1.000** (from 173 fewer to 13 fewer)
Bradycardia											

Table 2.4.24s-2.4.26s **(Es)ketamine + propofol compared to Propofol for GI endoscopy sedation**

Bibliography: 03_(Es)ketamine + propofol vs. propofol for GI endoscopy sedation. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment								Summary of findings		
351 (3 RCTs)	not serious	serious[a]	not serious	serious[b]	none	⊕⊕◯◯ Low[a,b]	20/174 (11.5%)	6/177 (3.4%)	**RR 0.33** (0.10 to 1.12)	20/174 (11.5%)	**77 fewer per 1.000** (from 103 fewer to 14 more)
Respiratory AE											
481 (4 RCTs)	not serious	very serious[a]	not serious	serious[b]	none	⊕◯◯◯ Very low[a,b]	64/239 (26.8%)	33/242 (13.6%)	**RR 0.47** (0.21 to 1.05)	64/239 (26.8%)	**142 fewer per 1.000** (from 212 fewer to 13 more)

Q2.4.4: Is there any role of xylocaine throat spray use for patients undergoing GI procedures under sedation?

Table 2.4.4.1s. PICOs

PICO question no.	Population	Intervention	Comparator	Outcome
1.	Patients undergoing GI endoscopy without sedation	Xylocaine throat spray	No local anesthetic	Procedure outcomes (completeness of procedure), patient safety, and satisfaction
2.	Patients undergoing GI endoscopy without sedation	Local anesthetic throat spray	No local anesthetic	Procedure outcomes (completeness of procedure), patient safety, and satisfaction
3.	Patients undergoing GI endoscopy under sedation	Xylocaine throat spray	Minimal-moderate sedation	Procedure outcomes (completeness of procedure), patient safety, and satisfaction
4.	Patients undergoing GI endoscopy under sedation	Local anesthetic throat spray	Minimal-moderate sedation	Procedure outcomes (completeness of procedure), patient safety, and satisfaction

BIBLIOGRAPHIC SEARCH

Bibliographic search strategies were performed in **PubMed and Cochrane**, from 2019 to 2024, using the following search strategies:

a. PubMed- Search (August 19th 2024, and January 2025)

- ((xylocaine[MeSH Terms]) OR (xylocaine)) AND ((gastrointestinal endoscopy[MeSH Terms]) OR (gastrointestinal endoscopy)): 47 studies

- ((local anesthetics[MeSH Terms]) OR (local anesthetics)) AND ((gastrointestinal endoscopy[MeSH Terms]) OR (gastrointestinal endoscopy)): 40 studies

- ((throat spray[MeSH Terms]) OR (throat spray)) AND ((gastrointestinal endoscopy[MeSH Terms]) OR (gastrointestinal endoscopy)): 5 studies

Results: 92 studies

b. Cochrane Central Register of Controlled Trials (CENTRAL)- (August 19th 2024)

#1	("xylocaine") (Word variations have been searched)	162
#2	("local anesthetics") (Word variations have been searched)	3632
#3	("throat spray") (Word variations have been searched)	189
#4	("gastrointestinal endoscopy") (Word variations have been searched)	2498
#5	#1 AND #4	**3**
#6	#2 AND #4	**11**
#7	#3 AND #4	**4**

Results: 18 studies

c. <u>Results of the bibliographic searches</u>

Results Total: 92 + 18 = 110 studies

After removing duplicates (n=34), 76 articles were found. Nineteen studies were considered potentially relevant and acquired in full text.

<u>Excluded studies (8)</u>

- Lu Q et al. Intestinal topical lidocaine spray improves the efficacy and safety of endoscopic sigmoid polypectomy. Eur J Gastroenterol Hepatol. 2023 Aug 1;35(8):822-828. (Lidocaine not used as local anesthetic).

- Dai P et al. Lidocaine spray anesthesia with a disposable laryngeal anesthetic tube for gastroscopy. Asian J Surg. 2023 Jun;46(6):2550-2551. (Case report).

- Tsaousi G et al. Unsedated Outpatient Percutaneous Endoscopic Gastrostomy in Stroke Patients: Is It Feasible and Safe? Surg Laparosc Endosc Percutan Tech. 2019 Oct;29(5):383-388. (No comparison group, focused rather on PEG tube placement feasibility).

- Flores-González JC et al. Topical Pharyngeal Lidocaine Reduces Respiratory Adverse Events During Upper Gastrointestinal Endoscopies Under Ketamine Sedation in Children. Paediatr Drugs. 2019 Feb;21(1):25-31. (Pediatric population).

- Sidhu R et al. British Society of Gastroenterology guidelines on sedation in gastrointestinal endoscopy. Gut. 2024 Jan 5;73(2):219-245. (Guidelines).

- Saraiva S et al. Efficacy and safety of lidocaine versus ropivacaine for local anesthesia in patients with head and neck cancer undergoing percutaneous endoscopic gastrostomy (peg): a prospective, randomized, double blind study. Gastrointestinal Endoscopy. 89. ab480-ab481. 10.1016/j.gie.2019.03.781. (Local anesthetic for PEG).

- Unsedated upper gastrointestinal endoscopy: does topical pharyngeal anesthesia make it more tolerable? I Ferchichi, M Sabbah, D Trad, A Ouakaa, N Bibani, H Elloumi, D Gargouri, United European Gastroenterology Journal, 2019, 7(8), 816. (Abstract)

- The effect of lidocaine spray to decrease propofol dosage IRCT20200526047573N1 https://trialsearch.who.int/Trial2.aspx?TrialID=IRCT20200526047573N1, 2020 | added to CENTRAL: 30 November 2020 | 2020 Issue 11 ICTRP. (Registered protocol for trial, there is no publication)

Included studies (11 studies)

Meta-analyses (2)

- Hung KC et al. Impact of intravenous and topical lidocaine on clinical outcomes in patients receiving propofol for gastrointestinal endoscopic procedures: a meta- analysis of randomised controlled trials. Br J Anaesth. 2022 Apr;128(4):644-654.

- Watanabe J et al. Lidocaine spray versus viscous lidocaine solution for pharyngeal local anesthesia in upper gastrointestinal endoscopy: Systematic review and meta- analysis. Dig Endosc. 2021 May;33(4):538-548.

RCTs (8)

- Mattila N et al. Topical pharyngeal anesthesia with articaine for gastroscopy: a double-blinded, randomized cross-over study in healthy volunteers. Scand J Gastroenterol. 2024 Jun;59(6):755-760.

- Lin X et al. Application of topical pharyngeal anesthesia to reduce adverse reactions during painless gastroscopy: A prospective randomized study. Technol Health Care. 2023;31(4):1245-1251.

- Pathak B et al. Redefining the Role of Ketamine for Topicalisation and its Comparison with the Legend Lignocaine for Oesophagogastroduodenoscopies: A Randomised Clinical Study. Journal of Clinical and Diagnostic Research. 2022 Jul, Vol-16(7): UC64-UC68

- Mahawongkajit P et al. Comparative effectiveness of lidocaine sprays between sitting and supine position for patients undergoing upper gastrointestinal endoscopy: a prospective randomized controlled trial. Surg Endosc. 2022 Jul;36(7):5067-5075.

- Martín-Marcos I et al. Evaluation of pharyngeal lidocaine anesthesia for esophago-gastroduodenoscopy: Double-blind randomized control trial. Dig Endosc. 2022 May;34(4):808-815.

- Mahawongkajit P et al. Comparison of Lidocaine Spray and Lidocaine Ice Popsicle in Patients Undergoing Unsedated Esophagogastroduodenoscopy: A Single Center Prospective Randomized Controlled Trial. Clin Exp Gastroenterol. 2021 May 25;14:209-216.

- Abd Ellatif S et al. Effect of palatable lidocaine gel versus dexmedetomidine on gag reflex during propofol-based sedation for patients undergoing elective upper gastrointestinal endoscopy: a randomized controlled study. Research and Opinion in Anesthesia and Intensive Care. Research and Opinion in Anesthesia & Intensive Care 8:13–22 © 2021, 2356-9115

- Ullman DA et al. Relation of viscous lidocaine combined with propofol deep sedation during elective upper gastrointestinal endoscopy to discharge. Proc (Bayl Univ Med Cent). 2019 Jul 30;32(4):505-509.

Cohort studies (1)

- Chen JM et al. The effectiveness of electro-acupuncture combined with dyclonine hydrochloride in relieving the side effects of gastroscopy: a controlled trial. Ann Palliat Med. 2021 Mar;10(3):2958-2970.

Table 2.4.4.2s: Evidence: Characteristics of the included studies.

Study (Author, year)	Country	Study design	No. of sites (no. of subjects)	Age (y)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm	Follow-up
Ullman, 2019	USA	RCT	1 (93)	18-75	39.8	Lidocaine 2% + Propofol IV	Placebo + Propofol IV	No significant difference with respect to recovery time (p 0.23), Propofol consumption (p 0.55), endoscopist satisfaction (p 0.23), and patient discomfort (p 0.37)		
Abd Ellatif, 2021	Egypt	RCT	1 (120)	18-60	52.5	Lidocaine gel + Propofol IV	Propofol IV	Significant decrease in incidence of gag reflex (p 0.002), Propofol consumption (p < 0.001), patient and endoscopist (p < 0.001) satisfaction, and recovery time (p < 0.001)		
Mahawongkajit, 2021	Thailand	RCT	1 (204)	> 20	52.0	Lidocaine ice popsicle	Lidocaine spray	Significant increase in endoscopist (p 0.0022) and patient (p 0.0039) satisfaction with the popsicle. Significant decrease in gag reflex (p 0.0016), discomfort (p= 0.0012), and pain (p 0.0015) with the popsicle.		
Martín-Marcos, 2022	Spain	RCT	1 (539)	18-70	40.8	Lidocaine + Propofol IV	Placebo + Propofol IV	Significant increase in well-tolerated + difficult intubation procedures (OR 2.13, p 0.007). Significant decrease in poorly tolerated procedures (OR 3.31, p 0.001). Significant decrease of Propofol use (p 0.001), per procedure coughing (p 0.001). Significant increase in endoscopist and patient satisfaction (p < 0.001).		48 hours

Pathak, 2022	India	RCT	1 (70)	18-60	47.1	Lidocaine 2% viscous gargles	Ketamine gargles	No significant difference in sore throat (p 0.2), coughing, and change of voice (p > 0.995).	24 hours
Mahawongkajit, 2022	Thailand	RCT	1 (304)	> 20	51.3	Lidocaine spray sitting position	Lidocaine spray supine position	Significantly decreased gagging (p 0.0003) and pain (0.0059) in the supine position. Significantly easier esophageal instrumentation in the supine position (p 0.0042). No significant difference in patient (p 0.0844) and endoscopist (p 0.0734) satisfaction.	
Lin, 2023	China	RCT	1 (300)	20-80	46.7	Lidocaine 2% + Propofol IV	Propofol IV	Significant decrease of HR, MAP, and SPO2 in the control group (p < 0.05). Significant decrease of Propofol use (p < 0.014) and adverse events in the Lidocaine group (p < 0.05).	
Mattila, 2024	Finland	RCT	1 (9)	37+/-5.7	44.4	Articane + conscious sedation	Placebo + conscious sedation	Significantly less discomfort during esophageal intubation (p 0.035). Significantly higher patient satisfaction (p 0.011).	

Fig. 2.4.4.1s. Effect of local anesthetic throat spray on mean propofol consumption

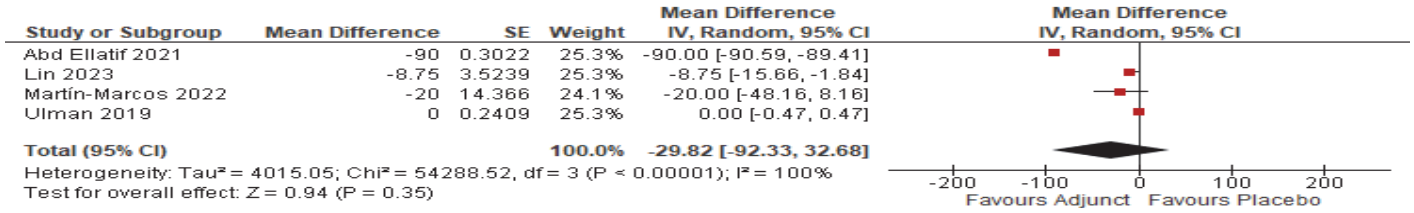


Table 2.4.4.3s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3s. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to inconsistency (moderate heterogeneity), imprecision, and indirectness, so the quality of evidence was downgraded to very low.

Fig. 2.4.4.2s Effect of local anesthetic throat spray on endoscopist satisfaction

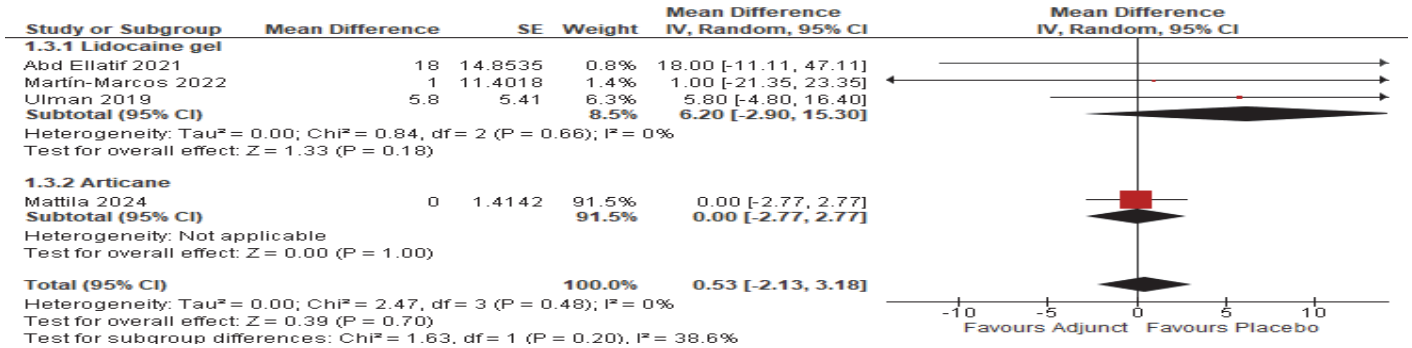


Table 2.4.4.4s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to inconsistency (moderate heterogeneity), imprecision, and indirectness, so the quality of evidence was downgraded to very low.

Fig. 2.4.4.3s Effect of local anesthetic throat spray on patient satisfaction

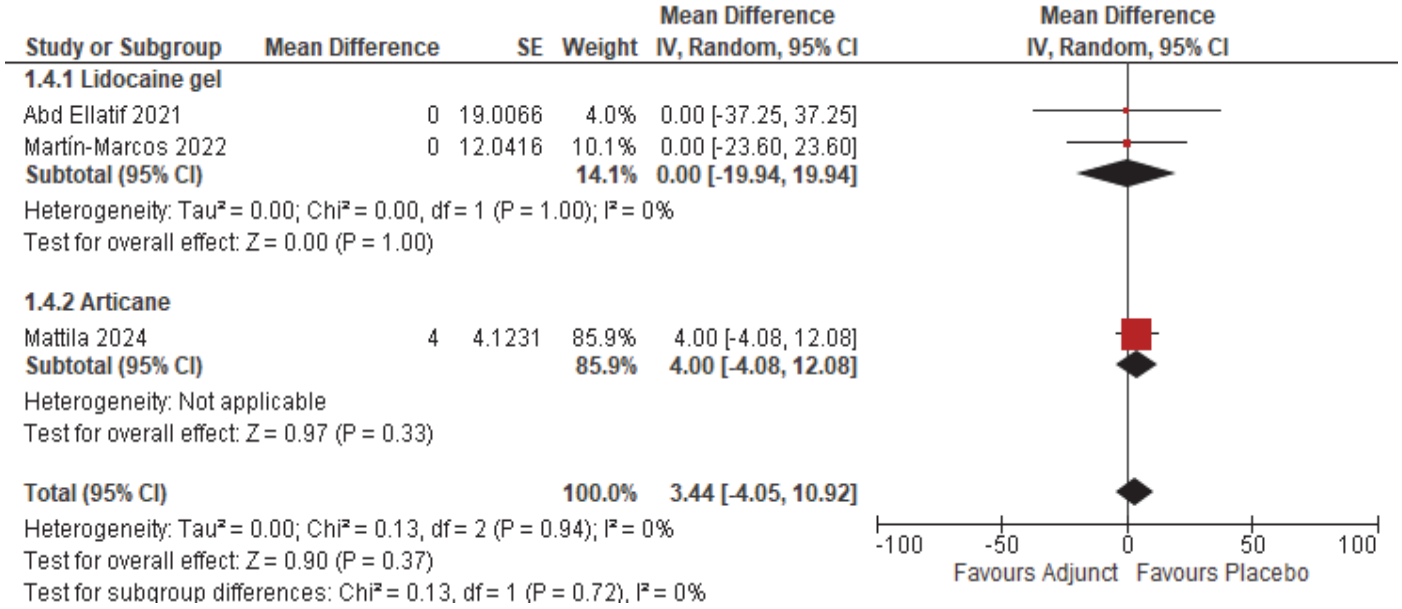


Table 2.4.4.5s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3s. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to inconsistency (moderate heterogeneity), imprecision, and indirectness, so the quality of evidence was downgraded to very low

Fig. 2.4.4.4s. Effect of local anesthetic throat spray on discomfort/tolerance

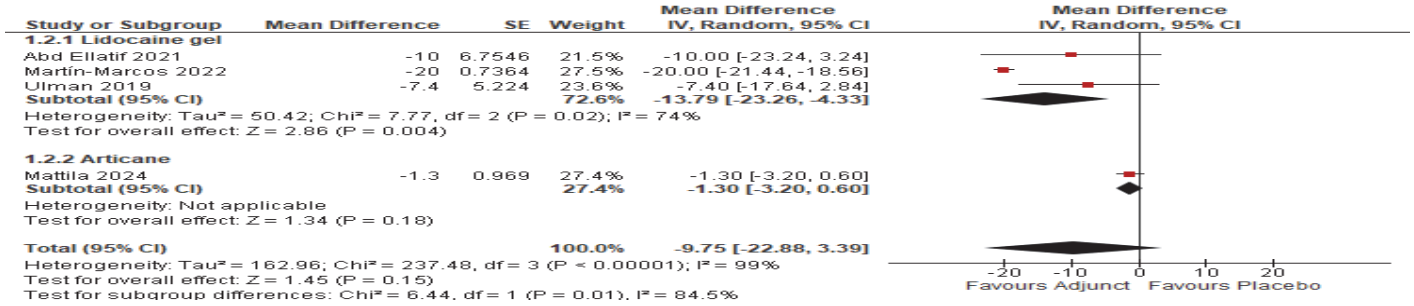


Table 2.4.4.6s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to inconsistency (moderate heterogeneity), imprecision, and indirectness, so the quality of evidence was downgraded to very low.

Fig. 2.4.4.5s. Effect of local anesthetic throat spray on coughing

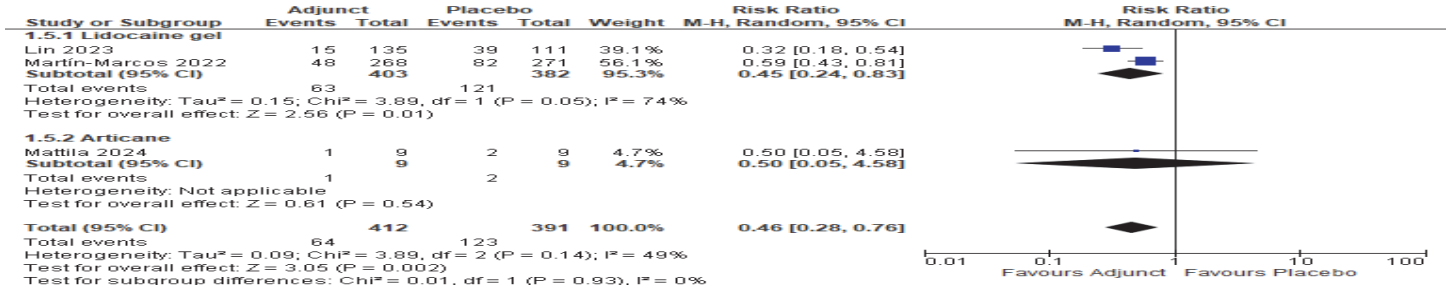


Table 2.4.4.7s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3s. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to inconsistency (moderate heterogeneity), imprecision, and indirectness, so the quality of evidence was downgraded to very low.

Table 2.4.4.3s – 2.4.4.7s Q4.1 Adjunct compared to placebo for Q4
Bibliography: TF2 for Q4. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With placebo	With Q4.1 Adjunct		Risk with placebo	Risk difference with Q4.1 Adjunct
Propofol consumption (mg)											
0 (4 RCTs)	not serious	serious	serious	serious	none	⨁◯◯◯ Very low	0	0	-	0	MD **29.82 lower** (92.33 lower to 32.68 higher)
Poor tolerance/discomfort											
0 (4 RCTs)	not serious	serious	serious	serious	none	⨁◯◯◯ Very low	0	0	-	0	MD **9.75 lower** (22.88 lower to 3.39 higher)
Endoscopist satisfaction											
0 (4 RCTs)	not serious	not serious	serious	serious	none	⨁⨁◯◯ Low	0	0	-	0	MD **0.53 higher** (2.13 lower to 3.18 higher)
Patient satisfaction											
0 (3 RCTs)	not serious	serious	serious	serious	none	⨁◯◯◯ Very low	0	0	-	0	MD **3.44 higher** (4.05 lower to 10.92 higher)
Coughing											
803 (3 RCTs)	not serious	serious	serious	serious	none	⨁◯◯◯ Very low	123/391 (31.5%)	64/412 (15.5%)	**RR 0.46** (0.28 to 0.76)	123/391 (31.5%)	**170 fewer per 1.000** (from 226 fewer to 75 fewer)

Q2.4.5: Is there any role of Hyoscine-n-butylbromide (Buscopan) /antispasmodics administration for patients undergoing GI procedures under sedation?

Table 2.4.5.1s. PICOs

PICO question no.	Population	Intervention	Comparator	Outcome
1.	Patients undergoing GI endoscopy under sedation	With Buscopan	Without Buscopan	Procedure outcomes (completeness of procedure), patient safety, and satisfaction
2.	Patients undergoing GI endoscopy under sedation	With antispasmodics	Without antispasmodics	Procedure outcomes (completeness of procedure), patient safety, and satisfaction

BIBLIOGRAPHIC SEARCH

Bibliographic search strategies were performed in **PubMed and Cochrane**, from 2019 to 2024 using the following search strategies:

a. PubMed- Search (August 22th 2024)

- ((Buscopan[MeSH Terms]) OR (Buscopan)) AND ((gastrointestinal endoscopy[MeSH Terms]) OR (gastrointestinal endoscopy)): 12 studies

- ((antispasmodics[MeSH Terms]) OR (antispasmodics)) AND ((gastrointestinal endoscopy[MeSH Terms]) OR (gastrointestinal endoscopy)): 28 studies

- ((Parasympatholytics[MeSH Terms]) OR (Parasympatholytics)) AND ((gastrointestinal endoscopy[MeSH Terms]) OR (gastrointestinal endoscopy)): 10 studies

The use of conscious sedation, deep sedation and anesthesia as Mesh terms did not change the outcome of this research.

Results: 50 studies

b. Cochrane Central Register of Controlled Trials (CENTRAL)- (August 22th 2024)

#1	("Buscopan") (Word variations have been searched)	37

#2	("antispasmodics") (Word variations have been searched)	36
#3	("parasympatholytics") (Word variations have been searched)	28
#4	("gastrointestinal endoscopy") (Word variations have been searched)	2498
#5	#1 AND #4	**0**
#6	#2 AND #4	**3**
#7	#3 AND #4	**0**

Results: 3 studies

c. **Results of the bibliographic searches**

Results Total: 50 + 3 = 53 studies

After removing duplicates (n=16), 37 articles were found. Thirteen studies were considered potentially relevant and acquired in full text.

Given the very limited data available, the research was extended to 5 years prior to 2019. This allowed the inclusion of 2 supplemental RCTs.

Excluded studies (9 studies)

- Scarpellini E et al. The Use of Peppermint Oil in Gastroenterology. Curr Pharm Des. 2023;29(8):576-583 (Not focused on endoscopy).

- Sekiguchi M et al. Detection rates of colorectal neoplasia during colonoscopies and their associated factors in the SCREESCO study. J Gastroenterol Hepatol. 2022 Nov;37(11):2120-2130 (Lesion detection).

- Kim SY et al. Assessment of Cimetropium Bromide Use for the Detection of Gastric Neoplasms During Esophagogastroduodenoscopy. JAMA Netw Open. 2022 Mar 1;5(3):e223827 (Lesion detection).

- Jung H et al. Effectiveness of oral phloroglucinol as a premedication for unsedated esophagogastroduodenoscopy: A prospective, double-blinded, placebo-controlled, randomized trial. PLoS One. 2021 Aug 4;16(8):e0255016 (Unsedated patients).

- Meng F et al. Antiperistaltic effect and safety of l-menthol oral solution on gastric mucosa for upper gastrointestinal endoscopy in Chinese patients: Phase III, multicenter, randomized, double-blind, placebo-controlled study. Dig Endosc. 2021 Nov;33(7):1110-1119. (Unsedated patients).

- Suzuki H et al. A Prospective Study of Factors Associated with Abdominal Pain in Patients during Unsedated Colonoscopy Using a Magnifying Endoscope. Intern Med. 2020;59(15):1795-1801 (Unsedated patients).

- Inoue K et al. Effects of L-Menthol and Carbon Dioxide on the Adenoma Detection Rate during Colonoscopy: L-Menthol and Carbon Dioxide on Colonoscopy. Digestion. 2020;101(3):323-331 (Unsedated patients).

- Omata F et al. Noneffectiveness of scopolamine for facilitating detection of upper gastrointestinal neoplasia during screening esophagogastroduodenoscopy: propensity score-matched study. Endoscopy. 2020 Jul;52(7):556-562 (Lesion detection).

- Chen CW et al. Factors associated with polyp detection during colonoscopy: A retrospective observational study. Kaohsiung J Med Sci. 2019 Sep;35(9):572-577 (Lesion detection).

Included studies (6 studies)

Meta-analyses (1)

- Aziz M et al. The anti-spasmodic effect of peppermint oil during colonoscopy: a systematic review and meta-analysis. Minerva Gastroenterol Dietol. 2020 Jun;66(2):164-171.

RCTs (4)

- Wilasrusmee C et al. Effect of alverine citrate plus simethicone in colonoscopy: a randomized controlled trial. Sci Rep. 2024 May 27;14(1):12035.

- Han JY et al. Oral IBGard™ Before Colonoscopy: A Single-Center Double-Blinded, Randomized, Placebo- Controlled Trial. Dig Dis Sci. 2021 May;66(5):1611-1619. - Peppermint oil formulation to inhibit smooth muscle contractions

- Dinc B et al. The efficacy of intravenous hyoscine-N-butylbromide during colonoscopy: a prospective, randomized, double-blind, placebo-controlled study. Acta Gastroenterol Belg. 2016 Apr-Jun;79(2):179-85.

- Pao YY et al. The hemodynamic effect of an intravenous antispasmodic on propofol requirements during colonoscopy: A randomized clinical trial. Acta Anaesthesiol Taiwan. 2014 Mar;52(1):13-6.

Cohort studies (1)

- Ullmann O et al. Provider-reported use of butylscopolamine in gastrointestinal endoscopy in Germany. Endosc Int Open. 2024 Jan 5;12(1):E36-E42.

Table 2.4.5.2s: Evidence: Characteristics of the included studies

Study (Author, year)	Country	Study design	No. of sites (no. of subjects)	Age (y)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm	Follow-up
Pao, 2014	Taiwan	RCT	1 (116)	18-75	50.9	Buscopan IV (colonoscopy)	Normal saline IV (colonoscopy)	No significant difference with regards to Propofol concentration to induce LOC (p 0.261), total Propofol dosage required (p 0.698), total procedure time (p 0.835), and technical difficulty (0.243). Significantly higher heart rate (p < 0.001)		
Dinc, 2016	Turkey	RCT	1 (121)	18-80	53.7	Buscopan IV (colonoscopy)	Normal saline IV (colonoscopy)	No significant difference with regards to Propofol doses (p 0.092), pain (p 0.944), total procedure time (p 0.415) Significantly higher heart rate (p < 0.001).		
Han 2021	USA	RCT	NA	18-80	NA	IBGard oral administration peppermint oil formulation (colonoscopy)	Normal saline IV (colonoscopy)	No significant difference o significant difference in baseline characteristics or dose-timing distribution between IBGard™ and placebo groups no difference in ADR (IBGard™ = 47.8%, placebo = 43.1%, p = 0.51), intubation spasm score (1.23 vs 1.2, p = 0.9), withdrawal spasm score (1.3 vs 1.23, p = 0.72), or polypectomy spasm score (0.52 vs 0.46, p = 0.69). Significantly higher heart rate (p <		

0.001).

LOC: loss of consciousness

Fig. 2.4.5.1s Effect of Hyoscine-n-butylbromide (Buscopan) on total propofol dose

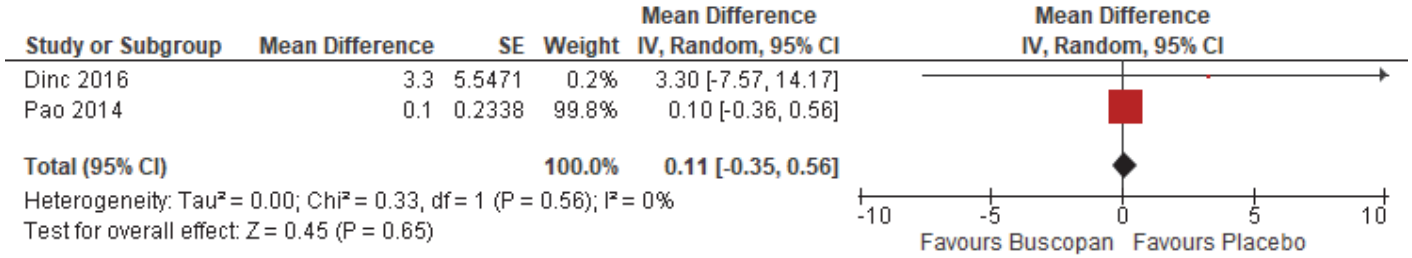


Table 2.4.5.3 Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to inconsistency (moderate heterogeneity), indirectness, and imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to very low.

Fig. 2.4.5.2s. Effect of Hyoscine-n-butylbromide (Buscopan) on total procedure time

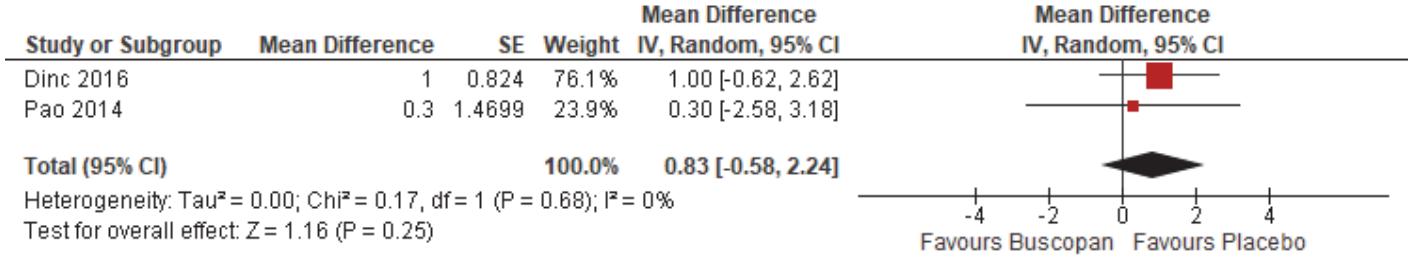


Table 2.4.5.4s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3s. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to inconsistency (moderate heterogeneity), indirectness, and imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to very low.

Table 2.4.5.3s – 2.4.5.4s 4.2 Buscopan compared to placebo for Q4

Bibliography: TF2 for Q4. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With placebo	With Q4.2 Buscopan	Relative effect (95% CI)	Risk with placebo	Risk difference with Q4.2 Buscopan
Total propofol dosage											
0 (2 RCTs)	not serious	serious[a]	serious[b]	serious[c]	none	⨁◯◯◯ Very low[a,b,c]	0	0	-	0	MD **0.11 higher** (0.35 lower to 0.56 higher)
Total procedure time											
0 (2 RCTs)	not serious	serious[a]	serious[b]	serious[c]	none	⨁◯◯◯ Very low[a,b,c]	0	0	-	0	MD **0.83 higher** (0.58 lower to 2.24 higher)

Fig. 2.4.5.3s. Effect of various antispasmodics on caecal intubation time

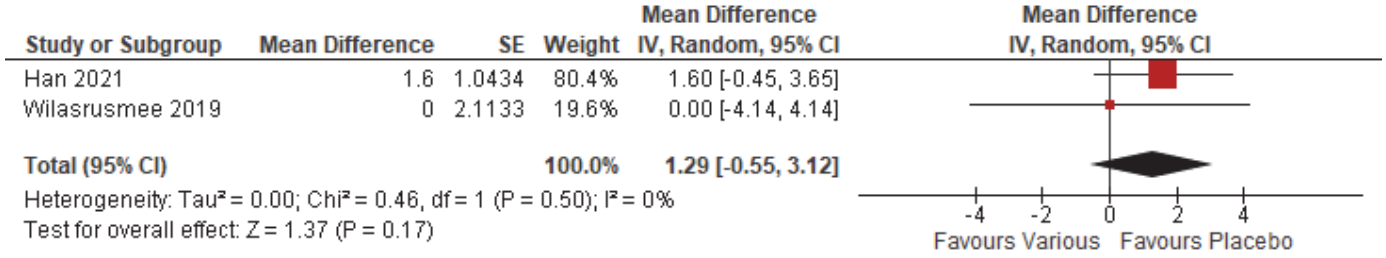


Table 2.4.5.5s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3s. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to inconsistency (moderate heterogeneity), indirectness, and imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to very low.

Fig. 2.4.5.4s. Effect of various antispasmodics on technical difficulty

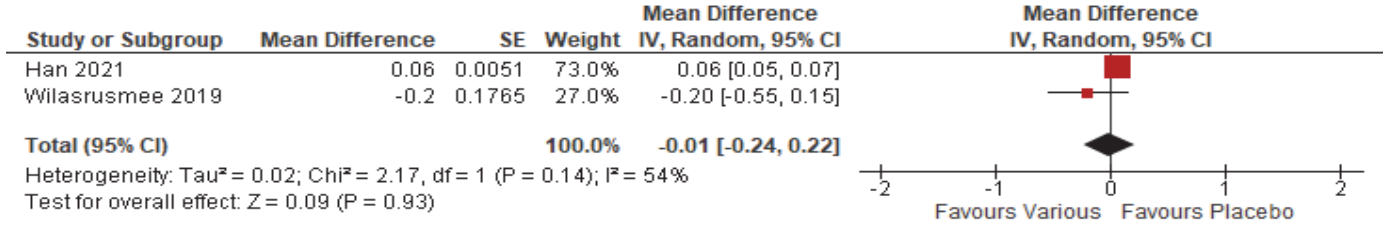


Table 2.4.5.6s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3s. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to inconsistency (moderate heterogeneity), indirectness, and imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to very low.

Fig. 2.4.5.5s Effect of various antispasmodics on pain

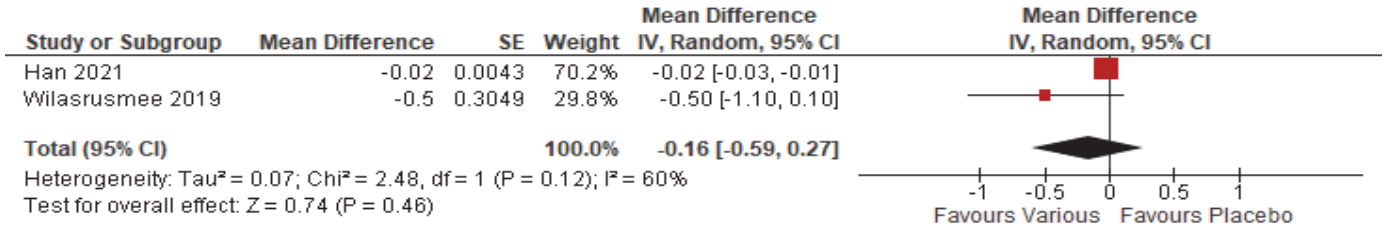


Table 2.4.5.7s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3s. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to inconsistency (moderate heterogeneity), indirectness, and imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to very low.

Fig. 2.4.5.6s. Effect of Hyoscine-n-butylbromide (Buscopan) on heart rate

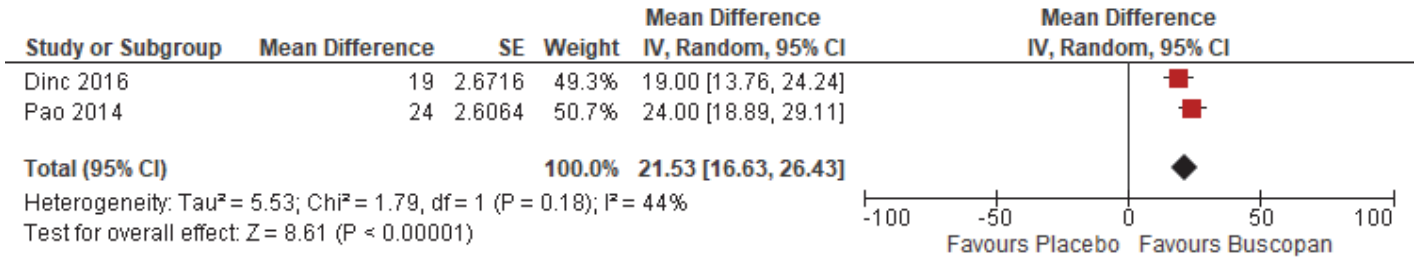


Table 2.4.5.8s Certainty of evidence

The risk of bias assessment for each study can be found in Table 2.4.3s. Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to inconsistency (moderate heterogeneity), indirectness, and imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to very low.

Table 2.4.5.5s – 2.4.5.8s Q4.2 Various antispasmodics compared to placebo for Q4
Bibliography: TF2 for Q4. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With placebo	With Q4.2, Various antispasmodics	Relative effect (95% CI)	Risk with placebo	Risk difference with Q4.2: Various antispasmodics
Total cecal intubation time											
0 (2 RCTs)	not serious	serious[a]	serious[b]	serious[c]	none	⊕◯◯◯ Very low[a,b,c]	0	0	-	0	MD **1.29 higher** (0.55 lower to 3.12 higher)
Technical difficulty											
0 (2 RCTs)	not serious	serious[a]	serious[b]	serious[c]	none	⊕◯◯◯ Very low[a,b,c]	0	0	-	0	MD **0.01 lower** (0.24 lower to 0.22 higher)
Pain											
0 (2 RCTs)	not serious	serious[a]	serious[b]	serious[c]	none	⊕◯◯◯ Very low[a,b,c]	0	0	-	0	MD **0.16 lower** (0.59 lower to 0.27 higher)
Heart rate											
0 (2 RCTs)	not serious	serious[a]	serious[b]	serious[c]	none	⊕◯◯◯ Very low[a,b,c]	0	0	-	0	MD **21.53 higher** (16.63 higher to 26.43 higher)

Q2.5: Non-pharmacological adjuncts to sedation procedures

Table 2.5.1s. PICOs

PICO	Population	Intervention	Comparator	Outcome
1	Patients scheduled for GI endoscopy	Hypnosis + sedation	sedation	Procedure outcomes, safety, and satisfaction
2	Patients scheduled for GI endoscopy	Acupuncture + sedation	sedation	Procedure outcomes, safety, and satisfaction
3	Patients scheduled for GI endoscopy	VR + sedation	sedation	Procedure outcomes, safety, and satisfaction
4	Patients scheduled for GI endoscopy	Auditory distraction/music + sedation	sedation	Procedure outcomes, safety, and satisfaction
8.	Patients scheduled for GI endoscopy	Sedation + auditory distraction/music	Sedation	Procedure outcomes, safety, and satisfaction, dosage of sedation, cost-effectiveness

BIBLIOGRAPHIC SEARCH

Bibliographic search strategies were performed in **PubMed** and **Cochrane** from 2019 to 2024 using the following search strategies:

a. PubMed- Search (July 3rd 2024)

- (("hypnosis"[MeSH Terms] OR "hypnosis"[All Fields]) AND (“gastrointestinal endoscopy"[MeSH Terms] OR "gastrointestinal endoscopy"[All Fields]): 3 studies
- (("acupuncture"[MeSH Terms] OR "acupuncture"[All Fields]) AND (“gastrointestinal endoscopy"[MeSH Terms] OR "gastrointestinal endoscopy"[All Fields]): 33 studies
- (("virtual reality"[MeSH Terms] OR "virtual reality"[All Fields]) AND (“gastrointestinal endoscopy"[MeSH Terms] OR "gastrointestinal endoscopy"[All Fields]): 46 studies
- (("auditory distraction"[All Fields] OR "music"[MeSH Terms] OR "music"[All Fields]) AND (“gastrointestinal endoscopy"[MeSH Terms] OR "gastrointestinal endoscopy"[All Fields]): 13 studies

Results: 95 studies

b. Cochrane Central Register of Controlled Trials (CENTRAL)- Search 2019-2024

#1	("hypnosis") (Word variations have been searched)	544
#2	("acupuncture") (Word variations have been searched)	6571
#3	("virtual reality") (Word variations have been searched)	4863
#4	("auditory distraction") (Word variations have been searched)	86
#5	("music") (Word variations have been searched)	3622
#6	("gastrointestinal endoscopy") (Word variations have been searched)	1430
#7	("sedation") (Word variations have been searched)	10179
#8	#1 AND #6	**1**
#9	#2 AND #6	**6**
#10	#3 AND #6	**24**
#11	#4 AND #6	**0**
#12	#5 AND #6	**14**

Results: 45 studies

Results of the bibliographic searches

Results Total 95 + 45 = 140 studies

After removing duplicates (n=9), 131 articles were found. 40 studies were considered potentially relevant and acquired in full text.

Excluded studies (16 studies)

- Blokzijl et al. Eur J Gastroenterol Hepatol 2019; 31: 334-339. (survey)
- Nguyen et al. Clin Gastroenterol Hepatol 2019; 17: 2455-2462. (VR non-interventional)
- Bay Muntnich et al. Gastrointest Endosc 2020; 91: AB52 (conference abstract + pediatric population)
- Bay et al. Dig Endosc 2020; 32: 189-190 (pediatric population)
- Palanica et al. J Pediatr Gastroenterol Nutr 2020; 70: 341-343. (pre-endoscopy training)
- Sogabe et al. BMC Gastroenterol 2020; 20: 122. (pre-endoscopy)
- Beacham et al. Dig Liver Dis 2021; 53: 669-671. (retrospective quality improvement analysis)
- Friedlander et al. J Allergy Clin Immunol Pract 2021; 9: 3494-3496. (VR non-interventional)
- Tran et al. Front Pediatr 2021; 9: 719626. (pediatric population)
- Sogabe et al. J Med Invest 2022; 69: 8-18. (pre-endoscopy)
- Yu et al. Trials 2022; 23(1): 364. (protocol paper)
- Aksu. Gastroenterol Nurs 2023; 46: 428-435. (pre-endoscopy)
- Shamali et al. Expert Rev Gastroenterol Hepatol 2023; 17: 1149-1157. (review)
- Siripongsaporn & Chirapongsathorn. Gastroenterology 2023; 164: S-942 (conference abstract)
- Sue-Chue-Lam et al. BMJ Open Gastro 2023; 10: e001129. (review)
- Siripongsaporn et al. JGH Open 2024; 8: e13046. (pre-endoscopy training)

Included studies (24 studies)

5 meta-analyses

- Roelandt P, Tziatzios G, Leebeeck N, Triantafyllou K. Non-pharmacological techniques complementary to sedation administration decrease pain and anxiety during gastrointestinal endoscopic procedures: a meta-analysis. Ann Gastroenterol. 2025;38(6):1-11. doi: 10.20524/aog.2025.1000. Epub 2025 Sep 25.
- Ahmed JF, Ashrafian H, Darzi A, Baena FR, Patel N. The effect of music and distraction on pain and anxiety during colonoscopy: a systematic review and meta-analysis. Therap Adv Gastroenterol. 2025 Oct 2;18:17562848251378236. doi: 10.1177/17562848251378236.
- Sorkpor et al. The Effect of Music Listening on Pain in Adults Undergoing Colonoscopy: A Systematic Review and Meta-Analysis. J Perianesth Nurs 2021; 36: 573-580.

- Gao et al. Acupuncture to improve patient discomfort during upper gastrointestinal endoscopy: systematic review and meta-analysis. Front Med (Lausanne) 2022; 9: 865035.
- Yang et al. Sedative-sparing effect of acupuncture in gastrointestinal endoscopy: systematic review and meta-analysis. Front Med (Lausanne) 2023; 10: 1189429.

19 RCTs

- Ko et al. Effects of easy listening music intervention on satisfaction, anxiety, and pain in patients undergoing colonoscopy: a pilot randomized controlled trial. Clin Interv Aging 2019; 14: 977-986.
- Li et al. Using Yoga Nidra Recordings for Pain Management in Patients Undergoing Colonoscopy. Pain Manag Nurs 2019; 20: 39-46.
- Çelebi et al. The effect of music therapy during colonoscopy on pain, anxiety and patient comfort: A randomized controlled trial. Complement Ther Clin Pract 2020; 38: 101084.
- Eberl et al. Effect of electroacupuncture on sedation requirements during colonoscopy: a prospective placebo-controlled randomised trial. Acupunct Med 2020; 38: 131-139.
- Pedersen et al. Music and pain during endorectal ultrasonography examination: A prospective questionnaire study and literature review. Radiography (Lond) 2020; 26: e164-e169.
- Spagnuolo et al. Effects of listening to music in digestive endoscopy: A prospective intervention study led by nursing. J Adv Nurs 2020; 76: 2993-3002.
- Chen et al. Effects of transcutaneous electrical acupuncture point stimulation on peripheral capillary oxygen saturation in elderly patients undergoing colonoscopy with sedation: a prospective randomized controlled trial. Acupunct Med 2021; 39: 292-298.
- Joan Gan at. Smartphone-controlled patch electro-acupuncture versus conventional pain relief during colonoscopy: a randomized controlled trial. ANZ J Surg 2021; 91: E375-E381.
- Karaveli Çakır & Evirgen. The Effect of Virtual Reality on Pain and Anxiety During Colonoscopy: A Randomized Controlled Trial. Turk J Gastroenterol 2021; 32: 451-457.
- Boonreunya et al. Virtual reality distraction during upper gastrointestinal endoscopy: a randomized controlled trial. J Gastroenterol Hepatol 2022; 37: 855-860.
- Brix & Pedersen. Effect of music intervention in colonoscopy-naive adults: a randomised controlled trial. Br J Nurs 2022; 31: 526-532.
- Chen et al. Suppression effect and safety of acupuncture on colonic spasm during colonoscopy: a randomized controlled trial. J Gastrointest Oncol 2022; 13: 1169-1177.
- Liu et al. Implementation of virtual reality technology to decrease patients' pain and nervousness during colonoscopies: a prospective randomised controlled single-blinded trial. Clin Med (Lond) 2022; 22: 237-240.

- Sun et al. Effects of light music played by piano intervention on satisfaction, anxiety, and pain in patients undergoing colonoscopy: A randomized controlled trial. Medicine (Baltimore) 2022; 101: e32339.
- Cakir & Evirgen. Three Distraction Methods for Pain Reduction During Colonoscopy: A Randomized Controlled Trial Evaluating the Effects on Pain and Anxiety. J Perianesth Nurs 2023; 38: e1-e7.
- Dogan Yilmaz & Ünlüsoy Dinçer. The effects of virtual reality glasses on vital signs and anxiety in patients undergoing colonoscopy: a randomized controlled trial. Gastroenterol Nurs 2023; 46: 318-328.
- Donghia et al. Effect of music therapy in patients undergoing endoscopy: pilot study of anxiety, pain, and cardiopulmonary parameters. Br J Surg 2023; 110: 1013-1014.
- Yin et al. Effect of electroacupuncture on discomfort during gastroscopy: A randomised controlled trial. Complement Ther Med 2023; 73: 102936.
- Chuah et al. Transcutaneous electric nerve stimulation of acupuncture points improves tolerance in adults undergoing diagnostic upper gastrointestinal endoscopy: a single-center, double-blinded, randomized controlled trial. Surg Endosc 2024; 38(6): 3279-3287.
- Shamali et al. Virtual Reality intervention to improve quality of care during Colonoscopy: A hybrid type 1 randomized controlled trial. Gastrointest Endosc 2024 Jun 6:S0016-5107(24)03260-7. doi: 10.1016/j.gie.2024.05.023.

1 cohort study

- Chen et al. The effectiveness of electro-acupuncture combined with dyclonine hydrochloride in relieving the side effects of gastroscopy: a controlled trial. Ann Palliat Med 2021; 10: 2958-2970.

Table 2.5.2s: Evidence related to non-pharmacological techniques such as virtual reality (VR) and/or auditory distractions/music as alternatives or adjuncts to sedation administration for GI endoscopic procedures: Characteristics of the included studies.

Study (Author, year)	Country	Study design	No. of sites (no. of studies)	Findings
Roelandt, 2025	NA	Systematic review and meta-analysis	12 RCTs	• Non-pharmacological techniques resulted overall in significantly lower pain [MD] -1.02, 95% confidence interval [CI] -1.64 to -0.41; I^2 =64%) and anxiety (MD -1.07, 95%CI -1.75 to -0.39; I^2 =20%), with higher satisfaction (MD 1.67, 95%CI 0.50-2.84; I^2 =94%). • Performance and detection bias in the majority of the studies, and a high level of heterogeneity. • This effect consistent for virtual reality (3 RCTs, n=241) and music (10 RCTs, n=1270): MD -1.05, 95%CI -1.74 to -0.37; I^2 =0%, and MD -1.00, 95%CI -1.80 to -0.20; I^2 =73%, respectively.
Ahmed JF, 2025	NA	Systematic review and meta-analysis	11 RCTs	• Music resulted in a significant reduction in pain (95% CI 0.69-2.31, p < 0.05) and anxiety (95% CI 0.86-6.27). • Distraction (virtual reality) resulted in a significant reduction of pain (95% CI 0.79-2.39) and anxiety (95% CI 3.64-11.35). • High heterogeneity in both pain and anxiety studies (I^2 >90%)

VIRTUAL REALITY

Study (Author, year)	Country	Study design	No. of sites (no. of subjects)	Age (y)	Male sex (%)	Intervention	Comparator	Outcome in intervention arm	Outcome in comparator arm	Follow-up
Karaveli Cakir, 2021	Turkey	RCT	1 (n=120)	> 18	65.0	VR glasses	Routine care colonoscopy	Pain VAS 2.76 Anxiety 39.73	Pain VAS 3.76 Anxiety 46.70	-
Boonreunya, 2022	Thailand	RCT	1 (n=96)	> 18	61.5	VR distraction	Routine care OGD	No difference in pain VAS, patient or endoscopist satisfaction		-

Liu, 2022	China	RCT	1 (n=117)	20-75	59.8	VR glasses	Sedation-free colonoscopy	Pain VAS 5 Heart rate 5 min after insertion 67 bpm Complete satisfaction 21.4%	Pain VAS 7 Heart rate 5 min after insertion 78 bpm Complete satisfaction 7.7%	-
Cakir, 2023	Turkey	RCT	1 (n=120)	> 18	58.3	VR glasses	Routine care colonoscopy	Pain VAS 3.20 Satisfaction VAS 9.26	Pain VAS 4.10 Satisfaction VAS 7.53	-
Shamali, 2024	Denmark	RCT	1 (n=47)	≥ 18	42.6	VR glasses	Routine care colonoscopy	Pain VAS 2.3 Discomfort 1.6 Midazolam 0.87 Satisfaction 9.7	Pain VAS 4.0 Discomfort 2.8 Midazolam 1.54 Satisfaction 8.7	-
Dogan Yilmaz, 2023	Turkey	RCT	1 (n=44)	18-79	68.2	VR glasses	Routine care colonoscopy without sedation	Pain VAS 1.71	Pain VAS 3.57	

MUSIC

Study (Author, year)	Country	Study design	No. of sites (no. of subjects)	Age (y)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm	Follow-up
Ko, 2019	Hong Kong	RCT	1 (n=80)	>45	51.2	Easy listening to popular Chinese songs	Routine care colonoscopy	Procedural satisfaction 8.57 Satisfaction with pain management 8.28	Procedural satisfaction 7.83 Satisfaction with pain management 7.35	
Li, 2019	China	RCT	1 (n=144)	>18	53.5	Music (Mozart) or yoga nidra recording	Routine care colonoscopy	Pain VAS 5.0 (music or yoga nidra) Satisfaction 10.0 (music or yoga nidra)	Pain VAS 7.0 Satisfaction 7.0	
Celebi, 2020	Turkey	RCT	1 (n=112)	>18	50	Ajam Ashiran maqam (low and relaxing instrumental music)	Routine care colonoscopy	Pain VAS 1.5 Anxiety STAI-S 42.00 Heart rate 77 bpm Blood pressure 105/70	Pain VAS 4.0 Anxiety STAI-S 48.50 Heart rate 90 bpm Blood pressure 130/80	
Pedersen, 2020	Denmark	RCT	1 (n=126)	?	64.3	Music	Routine care rectal EUS	Pain VAS 1.95	Pain VAS 2.30	

Spagnuolo, 2020	Italy	RCT	1 (n=147)	>18	53.8	Music + moderate sedation	Moderate sedation endoscopy	Pain 2 Satisfied 90% Willing to repeat 60%	Pain 4 Satisfied 70% Willing to repeat 51%	
Spagnuolo, 2020	Italy	RCT	1 (n=64)	>18	42.2	Music + deep sedation	Deep sedation endoscopy	Pain 0 Satisfied 33% Willing to repeat 89%	Pain 2 Satisfied 15% Willing to repeat 51%	
Brix, 2022	Denmark	RCT	1 (n=337)	>18	52.5	Niels Eje's composition (instrumental acoustic music with integrated sounds of nature)	Routine care colonoscopy	No differences in pain intensity, duration of the colonoscopy, consumption of alfentanil and midazolam, vital signs, patient satisfaction and CIR.		
Sun, 2022	China	RCT	1 (n=216)	?	51.9	Popular piano pieces with soft melody, moderate rhythm and no lyrics	Routine care colonoscopy	Pain 13.71 Anxiety 30.18 Satisfaction 86.17	Pain 20.60 Anxiety 33.20 Satisfaction 68.46	-
Cakir, 2023	Turkey	RCT	1 (n=120)	> 18	58.3	Music	Routine care colonoscopy	Pain VAS 2.76 Satisfaction VAS 9.73	Pain VAS 4.10 Satisfaction VAS 7.53	-
Donghia, 2023	Italy	RCT	1 (n=62)	?	?	Preferred music Spotify app	Routine care colonoscopy	Reduction in pain and anxiety (STAI-Y)		

TASK FORCE 3. Requirements for safe sedation administration

Leader: Vicente Lorenzo-Zúñiga

Members: Vicente Lorenzo-Zúñiga, Naim Abu Freha, Arianna Parella

CLINICAL QUESTION:

Q3.1: Who should monitor the sedated patient?

Clinical Question: Who should monitor the sedated patient according to the intended level of sedation?

The TF reviewed the evidence of the clinical question 2.3 of TF 2. They felt that the topic was fully covered, including their task

Q3.2: Equipment required for monitoring patients undergoing GI endoscopy under sedation

Clinical Question: What is the minimum required equipment for monitoring the sedated patient? (ECG, BP, Oxygen saturation, capnography, etc.)

The TF focused on capnography and BIS monitoring and on high flow oxygen supplementation since new evidence has accumulated on these topics

Endoscopy | DOI 10.1055/a-2898-6540 |

Table 3.2s PICOs

PICO question no.	Population	Intervention	Comparator	Outcome
1	Patients undergoing GI procedures under moderate sedation or no sedation	With Capnography	Without capnography monitoring	Safety of procedure
2	Patients undergoing GI procedures under deep sedation	With Bispectral Index monitoring	Without Bispectral Index monitoring	Safety of procedure
	Patients undergoing GI procedures under deep sedation	High-flow oxygen supplementation	Without high-flow oxygen supplementation	Safety of procedure

Q3.2.1 Capnography Monitoring

Clinical Question: Should all sedated patients undergoing GI endoscopy be monitored with capnography to minimize the risks of sedation-related adverse events?

BIBLIOGRAPHIC SEARCH

a) Bibliographic search strategies were performed in **PubMed** and **Cochrane**, from June 2024 to March 2025, using the following search strategies:

h. PubMed- Search June 15th 2025

Search: gastrointestinal endoscopy AND capnography Sort by: Most Recent

("endoscopy, gastrointestinal"[MeSH Terms] OR ("endoscopy"[All Fields] AND "gastrointestinal"[All Fields]) OR "gastrointestinal endoscopy"[All Fields] OR ("gastrointestinal"[All Fields] AND "endoscopy"[All Fields])) AND ("capnography"[MeSH Terms] OR "capnography"[All Fields] OR "capnographies"[All Fields])

Translations

gastrointestinal endoscopy: "endoscopy, gastrointestinal"[MeSH Terms] OR ("endoscopy"[All Fields] AND "gastrointestinal"[All Fields]) OR "gastrointestinal endoscopy"[All Fields] OR ("gastrointestinal"[All Fields] AND "endoscopy"[All Fields])

capnography: "capnography"[MeSH Terms] OR "capnography"[All Fields] OR "capnographies"[All Fields]

Results: 74 studies

i. Cochrane Central Register of Controlled Trials (CENTRAL)- Search June 15th 2024

#1	("gastrointestinal endoscopy") (Word variations have been searched)	2117
#2	("capnography") (Word variations have been searched)	823
#3	#1 AND #2	**11**

Results: 11 studies

Results Total 74 + 11 = 85 studies

35 studies were considered potentially relevant and acquired in full text. After removing duplicates (n=16), 19 articles were found. 9 studies were considered relevant.

Included studies

2 Meta-analyses (Saunders et al 2017 was excluded because it included the same GI studies as the one included (1)

3 RCTs (2-4)

5 Non-RCTs (5-9)

Table 3.2.1.1s: Evidence related to monitoring patients with capnography: Characteristics of the included studies.

Author, year	Country	Study design	No. of subjects	Age (y)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm	Follow-up
Kim, 2018	Korea	Systematic review and meta-analysis Nine studies derived from eight RCTs Gastro, colon, EUS, ERCP, and other interventional procedures. 5 studies on propofol and others used fentanyl, midazolam, meperidine, or ketamine, or a combo	3088: 1 pediatric ASA1-2:3 ASA1-3: 5 ASA 1-4:1	///	///	Capnography 1,542	Standard monitoring 1,546	Capnography significantly reduced the incidence of hypoxemia (OR 0.61, 95% CI 0.49–0.77), and the analysis showed that the addition of capnography to standard monitoring has a benefit in reducing the incidence of severe hypoxemia (OR 0.53, 95% CI 0.35–0.81)	The incidence of apnea was comparable between the two groups (OR 0.74, 95% CI 0.39–1.43 The provision of supplemental oxygen was comparable in the two groups (OR 0.74, 95% CI 0.52–1.03). The incidences of bradycardia (OR 1.18, 95% CI 0.84–1.65) and hypotension (OR 0.92, 95% CI 0.68–1.25) did not differ significantly between the two groups There were no significant differences in early procedure termination (OR 4.96, 95% CI 0.24–104.39)	
Peveling-Oberhag 2020	GE	RCT, PEG Propofol				73 ASA2: 77 ASA3: 23	74 ASA2: 72 ASA3: 28	(Mild OD + SOD) (6+13)=19/74 On average, CA was able to detect imminent mild and severe hypoxemia 83 and 99 s before standard monitoring. Standard monitoring represented an independent risk factor for hypoxemia and severe hypoxemia.	(12+31)43/74 Standard monitoring represented an independent risk factor for hypoxemia and severe hypoxemia	
Wang 2023	Chi	RCT, EGD, Col Mild obesity ASA 1-2 propofol				112	113	Mild OD + SOD (9+6)=15/112	(18+16)=32/113	
Takimoto 2025	JAP	ERCP/EUS No propofol				125 ASA3: 1.6%	125 ASA3: 4%	Hypoxemia=SpO2 to <90% 33	37	
Bisschops 2021	Bel	Bronchoscopy 16.5% Gastro, colon, EUS				1044 858 gastr	1092 929 gastr	Mild Oxygen desaturation + severe OD 49/1044 The absolute difference	103/1092	////

		ASA 1-3 ~99% Non-propofol and propofol sedation			between baseline and capnography was −6.4 events per 100 procedures [95% confidence interval (CI), −4.1 to −8.7; $P \leq 0.0001$]. The 55% reduction in adverse events surpassed the 20% improvement in patient safety set as the goal of this quality improvement. After multivariate regression, the adjusted odds ratio for events after implementation of capnography was 0.46 (95% CI, 0.32–0.66).		
Baytas 2023	tur	Before-after All propofol-based ALL GI ASA1-2~95%	880	730	Mild + Sever OD 20/880 A significant reduction was observed for mild oxygen desaturation, with a resulting odds ratio of 0.25 (95% CI 0.14 to 0.46). ASA I patients had the highest difference in combined incidence of any oxygen desaturation of 5.85% in the pre-capnography group and 0.64% in the post-capnography group.	51/730	////
Barnett 2016	US	Before after Colonoscopy with moderate sedation (no propofol) ASA1-2 ~95%	501	465	OD 25/501 No serious adverse events were seen, and minor sedation-related adverse events occurred with similar frequency in both groups (8.2% pre-EtCO2 vs. 11.2% EtCO2, P =0.115).	11/465	////
Corbett 2022	UK	Before after Did not report separately Endoscopy 42.5% Cardiology 48%	339/735 endoscopy	262/666 endoscopy	Resp AE 84 Cardiac AE 2	Resp AE 116 Cardiac AE 27	

		Bronchoscopy 9.5%					
Valbuena 2025	Spain	Prospective cohort ASA1-IV Mixed drugs are given at the discretion of the anesthetist	608	538	Moderate + SOD 40	54	

Fig. 3.2.1.1s Effect of capnography on oxygen desaturation

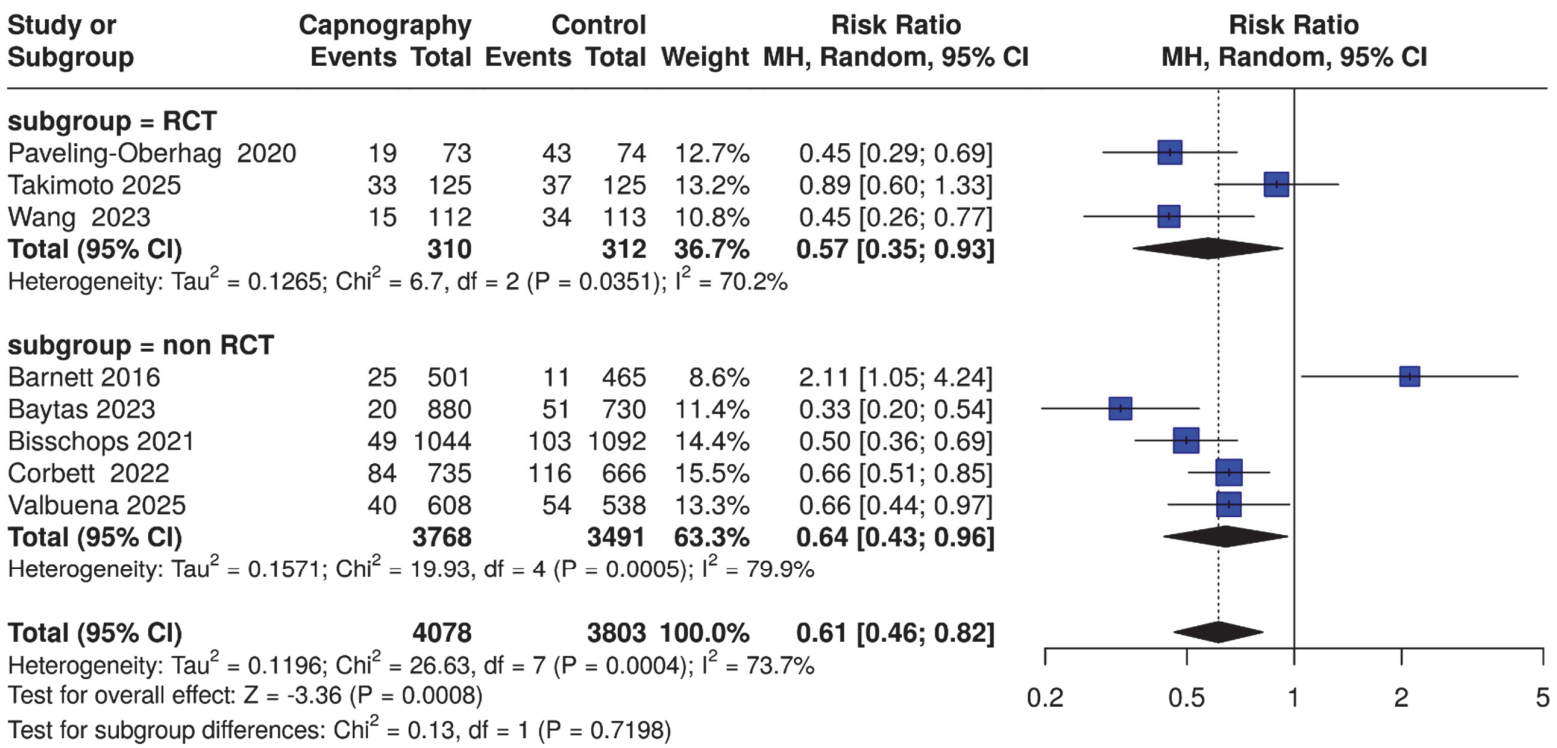


Fig. 3.2.1.2s Effect of capnography on oxygen desaturation

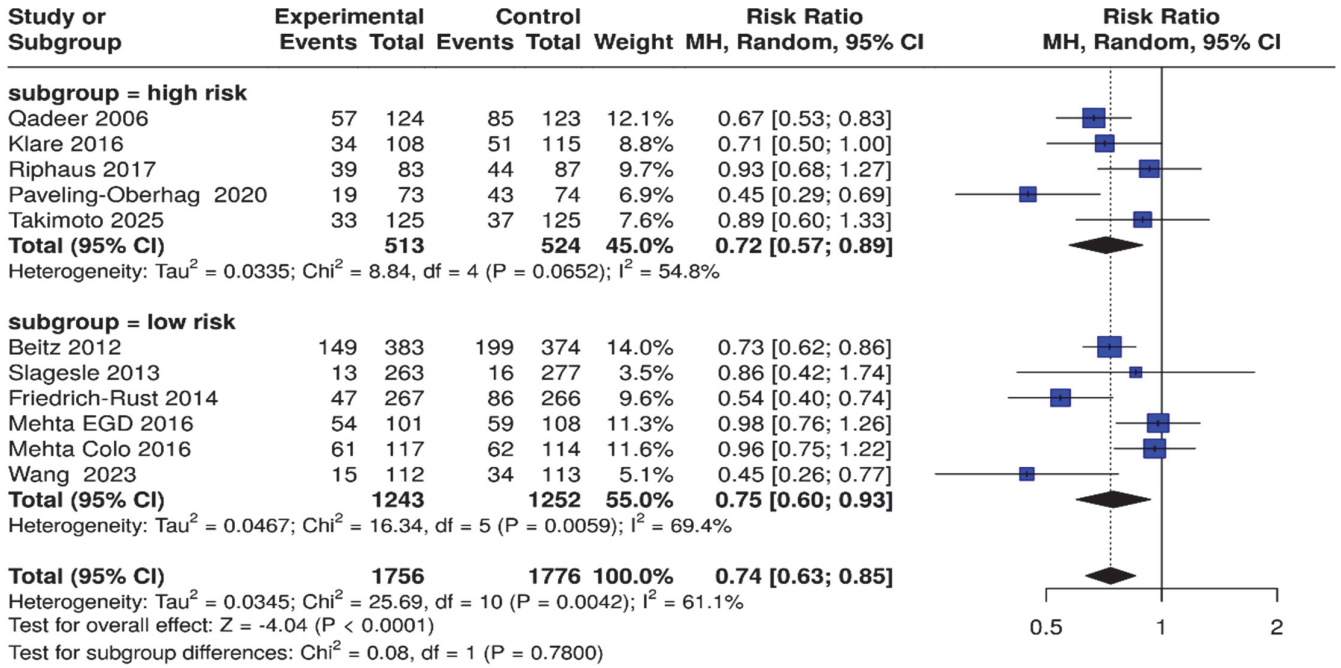


Fig. 3.2.1.3s Effect of capnography on oxygen desaturation according to type of sedation

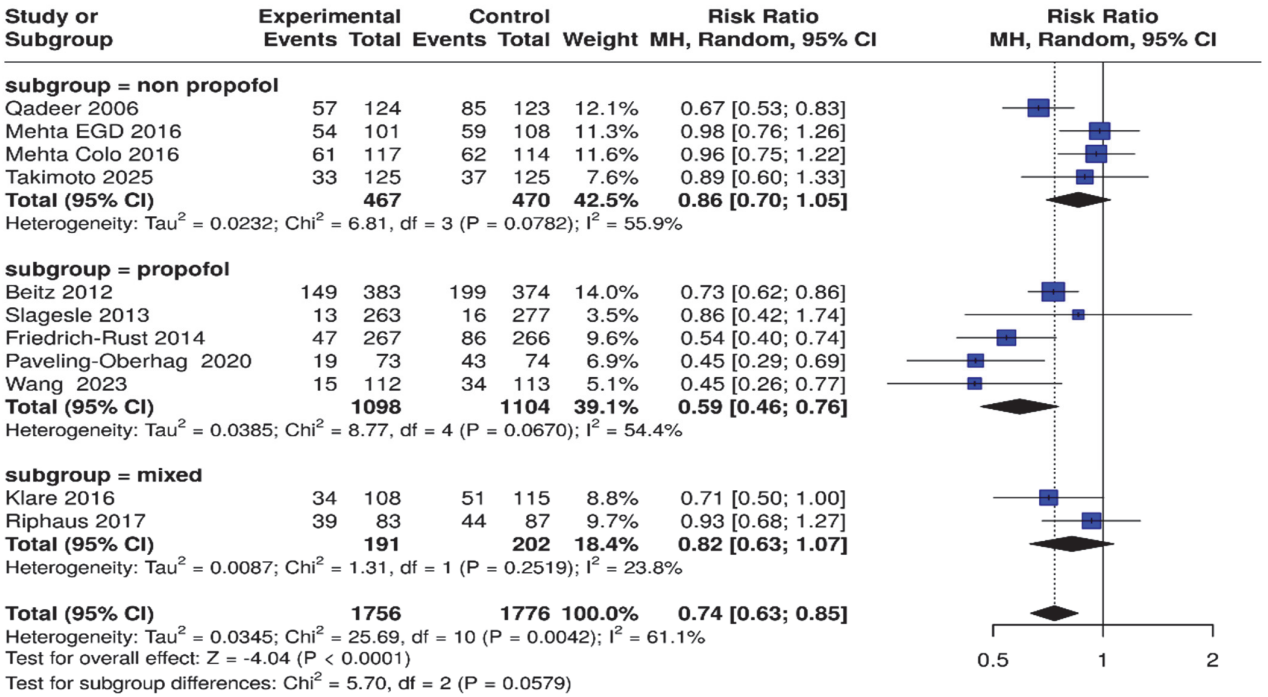
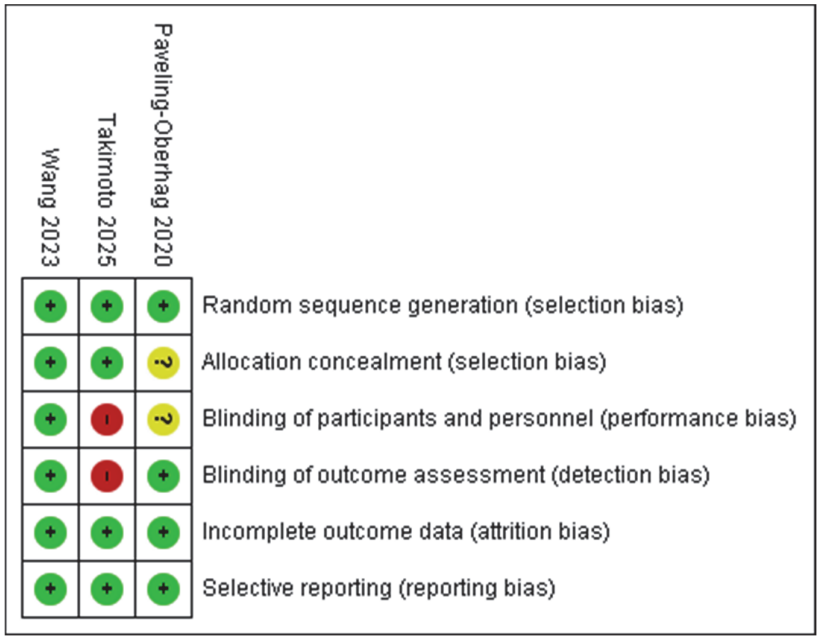


Table 3.2.1.2s: Risk of bias assessment for studies related to monitoring patients with capnography (RCTs and cohort studies)



Study	Selection (max 4 stars)	Comparability (max 2 stars)	Outcomes (max 3 stars)	Quality (Total 9/9)
Barnett 2016	***	*	**	**Good**
Baytas 2023	***	*	**	**Good**
Bisschops 2021	***	*	**	**Good**
Corbett 2022	***	*	**	**Good**
Valbuena 2025	***	*	**	**Good**

Table 3.2.1.3s Certainty of evidence for studies related to monitoring patients with capnography

The risk of bias assessment for each study can be found in **Table 3.2.1.2s**. Overall, the included studies were considered of high quality. The certainty of evidence was downgraded due to indirectness (heterogeneity in the endoscopic expertise) and inconsistency regarding the benefits for hypoxia. Due to the absence of evidence regarding major adverse events and propofol dose reduction, as well as the inconsistent effects on other secondary outcomes, we further downgraded the certainty of evidence to very low.

Table 3.2.1.4s: GRADE assessment for studies related to monitoring patients with capnography

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With placebo	With Table 1.2 Evidence in sedation by non-anesthesiologists	Relative effect (95% CI)	Risk with placebo	Risk difference with Table 1.2 Evidence in sedation by non-anesthesiologists
Oxygen desaturation											
7881 (8 Studies)	not serious	serious[a]	serious	not serious	none	⊕⊕◯◯ Low[a]	449/3803 (11.8%)	285/4078 (6.3%)	**RR 0.61** (0.46 to 0.82)		
Mild Oxygen desaturation											
3532 (11 studies)	not serious	serious[a]	serious	not serious	none	⊕⊕◯◯ Low[a]	716/1776 (40.4%)	521/1756 (29.6%)	**RR 0.74** (0.63 to 0.85)		
Severe Oxygen desaturation											
2572 (8 studies)	not serious	serious[a]	serious	not serious	none	⊕⊕◯◯ Low[a]	205/1287 (15.5%)	110/1285 (8.5%)	**RR 0.54** (0.40 to 0.73)		

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio. Explanations a. High heterogeneity

Q3.2.2 Bispectral Index (BIS) Monitoring

Clinical Question: Should all sedated patients undergoing GI endoscopy be monitored with bispectral index (BIS) to minimize the risks of sedation-related adverse events?

BIBLIOGRAPHIC SEARCH

a) Bibliographic search strategies were performed in **PubMed** and **Cochrane** from June 2024 to March 2025 using the following search strategies:

a. PubMed - Search June 15th 2025

Search: gastrointestinal endoscopy AND bispectral index Sort by: Most Recent

("endoscopy, gastrointestinal"[MeSH Terms] OR ("endoscopy"[All Fields] AND "gastrointestinal"[All Fields]) OR "gastrointestinal endoscopy"[All Fields] OR ("gastrointestinal"[All Fields] AND "endoscopy"[All Fields])) AND ("bispectral"[All Fields] AND ("abstracting and indexing"[MeSH Terms] OR ("abstracting"[All Fields] AND "indexing"[All Fields]) OR "abstracting and indexing"[All Fields] OR "index"[All Fields] OR "indexed"[All Fields] OR "indexes"[All Fields] OR "indexing"[All Fields] OR "indexation"[All Fields] OR "indexations"[All Fields] OR "indexe"[All Fields] OR "indexer"[All Fields] OR "indexers"[All Fields] OR "indexs"[All Fields]))

Translations

gastrointestinal endoscopy: "endoscopy, gastrointestinal"[MeSH Terms] OR ("endoscopy"[All Fields] AND "gastrointestinal"[All Fields]) OR "gastrointestinal endoscopy"[All Fields] OR ("gastrointestinal"[All Fields] AND "endoscopy"[All Fields])

index: "abstracting and indexing"[MeSH Terms] OR ("abstracting"[All Fields] AND "indexing"[All Fields]) OR "abstracting and indexing"[All Fields] OR "index"[All Fields] OR "indexed"[All Fields] OR "indexes"[All Fields] OR "indexing"[All Fields] OR "indexation"[All Fields] OR "indexations"[All Fields] OR "indexe"[All Fields] OR "indexer"[All Fields] OR "indexers"[All Fields] OR "indexs"[All Fields]

Results: 58 studies

b. Cochrane Central Register of Controlled Trials (CENTRAL)- Search June 15th 2024

#1	("gastrointestinal endoscopy") (Word variations have been searched)	2117
#2	("bispectral index ") (Word variations have been searched)	3516

#3	#1 AND #2	**13**

Results: 13 studies

Results Total 58 + 13 = 71 studies

28 studies were considered potentially relevant and acquired in full text. After removing duplicates (n= 10), 11 articles were found. 7studies were considered relevant.

Included studies

2 Meta-analyses (1,2)

4 RCTs (2-5)

1 non-RCTs (6)

Table 3.2.2.1s: Evidence related to monitoring the patient with BIS monitoring: Characteristics of the included studies.

Author, year	Country	Study design	No. of subjects	Age (y)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm	Follow-up
Zang 2019	China	Meta-analysis and trial of 12 RCTs, 13 sets of data, 1 bronch, 1EBUS diagnosis or therapy, GI endoscopy 6 Propofol 6 Mixed 1 midaz + remofentalil	1372			BIS monitoring	clinical signs	Intraprocedural hypoxia (defined as SpO_2 lower than the pooled relative risk (RR) was 0.76 (95% CI=0.62 to 0.94, P=0.009). TSA did not confirm the results of the meta-analysis Pooled analysis revealed no superiority of BIS in reducing the development of abnormal blood pressure during endoscopy compared with clinical signs (RR=0.883, 95% CI=0.525 to 1.485, P=0.639) no difference on the mean heart rates (P=0.201, pooled WMD=-2.237 beats per minute (BPM), 95% CI=-5.668 to 1.194 BPM) The average time to recovery: no significant difference (pooled WMD=-0.87 minutes, 95% CI=-1.86 to 0.11 min) Bis monitoring was not useful for determining sedation depth, in reducing the dosage of sedatives compared with clinical observation (pooled SMD=-0.134, 95% CI=-0.469 to 0.202, P=0.434).		
Park, 2016	Korea	Meta- 11 RCTs 12 sets of data	1039			BIS n,526	Non-BIS n, 513	total propofol consumption (the pooled standardized mean difference [SMD]: -0.15, 95 % confidence interval [CI]: -0.28 to -0.01) was significantly lower in	Recovery time (the pooled SMD: -0.04 [95 % CI -0.46 to 0.38, P = 0.85]), procedure time (the pooled SMD: 0.13 [95 % CI -0.03 to 0.29, P = 0.11]), adverse events, and satisfaction-related outcomes were	

		Propofol					the BIS group desaturation rate (BIS group [41/371, 11.05 %] vs. non-BIS group [49/364, 13.46 %]: OR 0.79; 95 % CI 0.51–1.24)	not significantly superior in the BIS	
González-Mendibil 2024	Spain	**RCT** Colonoscopy Propofol Asa 1 20% ASA 2 60% ASA 3 20%			BIS 90	Non-BIS 90	SpO2< 90%, **p=0.0269** <60 s: 21 (23.33) vs. 24 (26.67) >60 s: 2 (2.22) vs.13 (14.44)	**No difference**: Hypotension, Bradycardia, vomiting/retching, number of complications, pharmacological intervention, pts satisfaction	
Sargin, 2019	Türkiye	**RCT** ASA I-III to undergo planned colonoscopy,	18 - 70 yrs		BIS	Non-BIS	Total propofol dose (mg), median [IQR] 100 [100-140] vs 150 [100-200], p< 0.001 MOAA/S on arrival at PACU, Median [IQR] 3 [3-4] vs. 4 [3-4] , p =0.001 MMSE = mini-mental state examination test; TDT = Trieger dot test; CDT = clock drawing test were significantly better in BIS group	No difference for pts satisfaction	
Heo, 2015	Korea	**RCT** Colonoscopy ASA 1-3			BIS 141	MOAA/S group 139		The mean total propofol dose administered **in the BIS group was higher than that in the MOAA/S group**, independently of the endoscopists' experience level (36.9 ± 29.6 and 11.3 ± 20.7, respectively; $p < 0.001$).	
Lin, 2020	Taiwan	**RCT** ERCP AND EUS	63,4 - 64,1	51,2 (%)	TCI+BIS, 99	TCI, 100	The mean propofol infusion rate was lower in the group assigned to TCI with BIS monitoring (4.76 (1.84) vs. 5.44 (2.12), P = 0.016).	Use of the nasal airway to assist ventilation, management of hypertension, hypotension, bradycardia, hypoxia, and recovery times did not differ significantly between the two study groups.	**Follow-up**

		ASA 1-3						Final target blood concentration was lower in the TCI with BIS 1.54 (0.64) vs. 1.76 (0.68), P = 0.02) Levels of endoscopist satisfaction were significantly higher when patients were assigned to BIS monitoring
Okamoto, 2022	Japan	Retrospective study EUS Sedated with propofol	725	64.9	51.7	BIS	without BIS	median dose (159.2 mg vs. 167.5 mg; *p*=0.015) Especially for patients 75 years of age or older, the use of the BIS monitor might limit body movements and the reduction in HR that can occur during EUS examinations

Fig. 3.2.2.1s Effect of BIS on total propofol dose

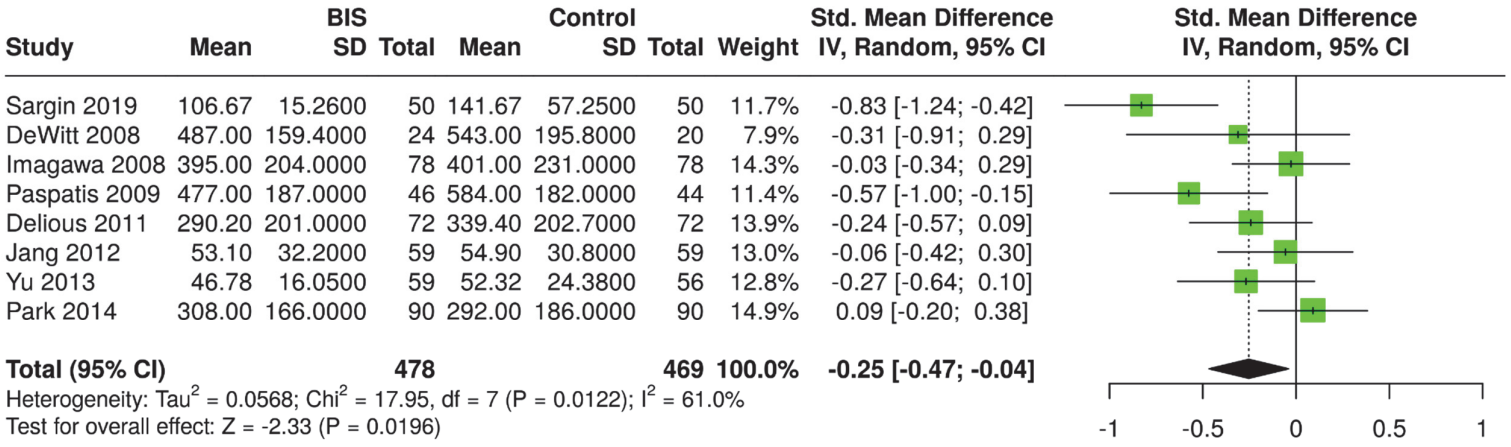


Fig. 3.2.2.2s Effect of BIS on mean propofol dose

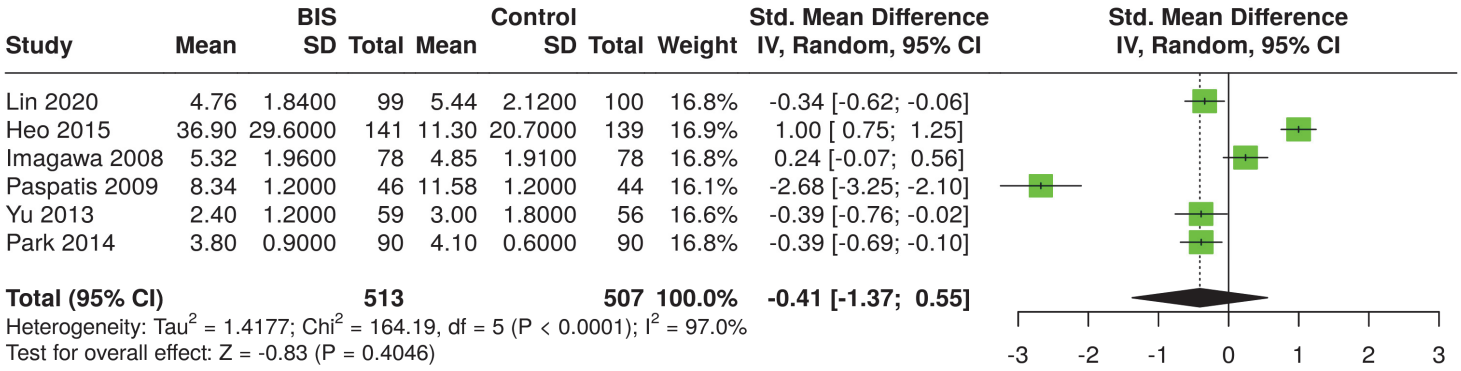
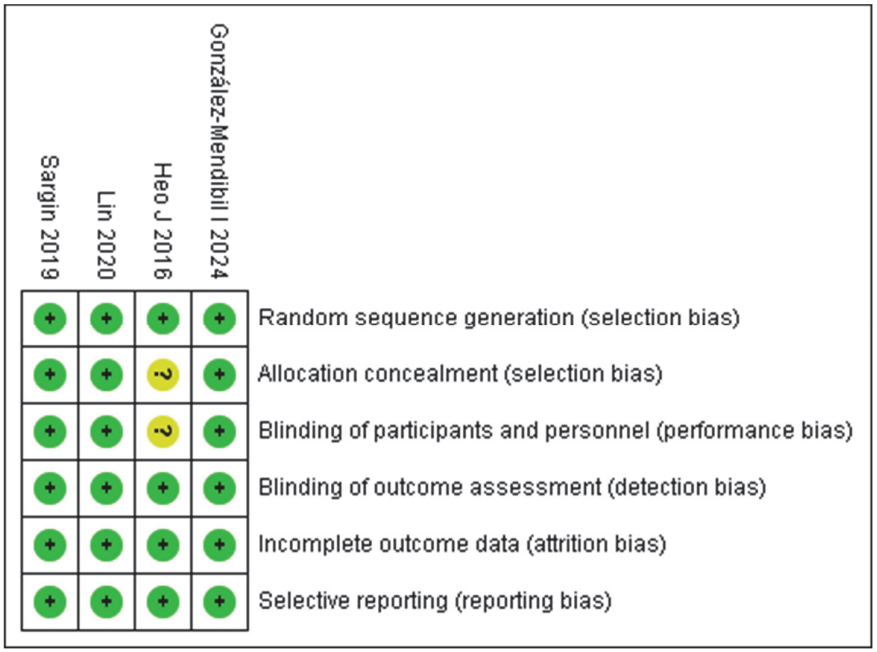


Table 3.2.2.2s: Risk of bias assessment for studies related to monitoring the patient with BIS monitoring (RCTs and cohort studies)



Study	Selection (max 4 stars)	Comparability (max 2 stars)	Outcomes (max 3 stars)	Quality (Total 9/9)
Okamoto 2024	***	*	**	**Good**

Table 3.2.2.3s Certainty of evidence related to monitoring the patient with BIS monitoring

The risk of bias assessment for each study can be found in **Table 3.2.2.2s**. Overall, the included studies were considered at high quality. The certainty of evidence for the outcome total propofol dose was downgraded due to inconsistency (moderate heterogeneity), so the quality of evidence was downgraded to moderate, and a conditional recommendation was proposed. For the outcome of mean propofol dose, further downgrading was applied due to imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to very low, and a conditional recommendation was proposed.

Table 3.2.2.4s: GRADE assessment for studies related to monitoring the patient with BIS monitoring

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With placebo	With Table 1.2		Risk with placebo	Risk difference with Table 1.2
Total propofol dose											
0 (4 RCTs)	not serious	serious[a]	not serious	not serious	none	⨁⨁⨁◯ Moderate[a]	0	0	-	0	MD **0.25 l**ower (-0.47 lower to 0.04 higher)
Mean propofol dose											
0 (4 RCTs)	not serious	serious[a]	serious[b]	serious[c]	none	⨁◯◯◯ Very low[a,b,c]	0	0	-	0	MD **0.46 lower** (11.37 lower to 0.55 higher)

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio

Explanations

a. High heterogeneity

b. No comparable populations

c. Wide Cis

Q3.2.3 High-flow oxygen (or air?) supplementation

Clinical Question: Should all sedated patients undergoing GI endoscopy receive oxygen supplementation via high-flow nasal canula (HFNC) to minimize the risk of hypoxemia?

BIBLIOGRAPHIC SEARCH

a) Bibliographic search strategies were performed in **PubMed** and **Cochrane** from June 2024 to March 2025 using the following search strategies***:***

a. PubMed - Search June 15th 2025

Search: **gastrointestinal endoscopy AND high-flow oxygen** Sort by: **Most Recent**

("endoscopy, gastrointestinal"[MeSH Terms] OR ("endoscopy"[All Fields] AND "gastrointestinal"[All Fields]) OR "gastrointestinal endoscopy"[All Fields] OR ("gastrointestinal"[All Fields] AND "endoscopy"[All Fields])) AND ("high-flow"[All Fields] AND ("cell respiration"[MeSH Terms] OR ("cell"[All Fields] AND "respiration"[All Fields]) OR "cell respiration"[All Fields] OR "oxygenation"[All Fields] OR "oxygen"[Supplementary Concept] OR "oxygen"[All Fields] OR "oxygen"[MeSH Terms] OR "oxygen s"[All Fields] OR "oxygenate"[All Fields] OR "oxygenated"[All Fields] OR "oxygenates"[All Fields] OR "oxygenating"[All Fields] OR "oxygenations"[All Fields] OR "oxygenative"[All Fields] OR "oxygenator s"[All Fields] OR "oxygenators"[MeSH Terms] OR "oxygenators"[All Fields] OR "oxygenator"[All Fields] OR "oxygene"[All Fields] OR "oxygenic"[All Fields] OR "oxygenous"[All Fields] OR "oxygens"[All Fields]))

Translations

gastrointestinal endoscopy: "endoscopy, gastrointestinal"[MeSH Terms] OR ("endoscopy"[All Fields] AND "gastrointestinal"[All Fields]) OR "gastrointestinal endoscopy"[All Fields] OR ("gastrointestinal"[All Fields] AND "endoscopy"[All Fields])

oxygen: "cell respiration"[MeSH Terms] OR ("cell"[All Fields] AND "respiration"[All Fields]) OR "cell respiration"[All Fields] OR "oxygenation"[All Fields] OR "oxygen"[Supplementary Concept] OR "oxygen"[All Fields] OR "oxygen"[MeSH Terms] OR "oxygen's"[All Fields] OR "oxygenate"[All Fields] OR "oxygenated"[All Fields] OR "oxygenates"[All Fields] OR "oxygenating"[All Fields] OR "oxygenations"[All Fields] OR "oxygenative"[All Fields] OR "oxygenator's"[All Fields] OR "oxygenators"[MeSH Terms] OR "oxygenators"[All Fields] OR "oxygenator"[All Fields] OR "oxygene"[All Fields] OR "oxygenic"[All Fields] OR "oxygenous"[All Fields] OR "oxygens"[All Fields]

Results: 48 studies

b. Cochrane Central Register of Controlled Trials (CENTRAL) - Search June 15th 2024

#1	("gastrointestinal endoscopy") (Word variations have been searched)	2117

#2	("high-flow oxygen") (Word variations have been searched)	2701
#3	#1 AND #2	**21**

Results: 21 studies

Results Total 48 + 21 = 69 studies

26 studies were considered potentially relevant and acquired in full text. After removing duplicates (n= 8), 16 articles were found. 3 studies were considered relevant.

Included studies

3 Meta-analyses (1,2, 3)

Table 3.2.3.1s: Evidence related to oxygen supplementation via high-flow nasal cannula (HFNC) .*Characteristics of the included studies.*

Author, year	Country	Study design	No. of subjects	Age (y)	Male sex (%)	Intervention	Comparator	Outcome in intervention arm	Outcome in the comparator arm	Follow-up
Doubleris 2022	Greece	5 RCTs 1 colono, 1 ERCP, 1 mixed, two gastro	n=2656, 1299			High-flow nasal canula	Standard NC 1357	significant reduction of RR for hypoxemia (*RR* = 0.18, CI95%: 0.05–0.61), The overall risk of endoscopy interruption was lower (*RR*:0.12, CI95%: 0.02–0.64)	data on airway manipulations – jaw thrust, nasal airway tube insertion, intubation, and ventilation optimization via bag-mask or FiO2 increase – did not provide a significant RR reduction in the HFNC subgroup	
Zang 2022	China	7 RCTs Gastro, ERCP, and 1 colono	2998			High-flow nasal canula	Standard NC	significant reduction in hypoxemia incidence (OR 0.24, 95% CI 0.09 to 0.64) and airway intervention requirements (OR 0.15, 95% CI 0.03		

		and 1 mixed					to 0.69). In subgroup analysis, low-risk of hypoxemia subjects were associated with a significant reduction in hypoxemia incidence (OR 0.02, 95% CI 0.00 to 0.07) and airway intervention requirements (OR 0.02, 95% CI 0.01 to 0.04).	In high-risk of hypoxemia subjects, there were no significant differences between the two oxygen administration techniques in both primary (OR 0.81, 95% CI 0.36 to 1.78) and secondary outcomes (OR 0.85, 95% CI).
Wei, 2024	China	12 RCTs gastro and ERCP	3,726		High-flow nasal canula	Standard NC	HFNC reduced the incidence of hypoxemia: OR= 0.39, 95% CI: 0.29–0.53, MD = 4.07, (5% CI: 3.14–5.01 significantly lower risk of hypoxemia for gastroscopy (OR = 0.46, 95% CI: 0.23–0.93) and ERCP (OR =0.38, 95% CI: 0.27–0.53). significant reduction in the adoption of airway interventions (OR = 0.16, 95% CI: 0.05–0.53)	incidence of hypercapnia: MD = −0.21, 95%CI: −0.49–0.07; OR = 1.43, 95% CI: 0.95–2.15. Procedure time: the difference was not statistically significant

Table 3.2.3.2s Certainty of evidence related to oxygen supplementation via high-flow nasal cannula (HFNC).
Overall, the included studies were considered of high quality. The certainty of evidence in this PICO question was downgraded due to heterogeneity, indirectness, and inconsistency to very low for all the meta-analyses.

Q3.3: Sedation-analgesia reversal agents

Clinical Question: Should sedation-analgesia reversal agents be restricted to the management of sedation-analgesia adverse events only?

Table 3.3.1s PICOs

PICO question no.	Population	Intervention	Comparator	Outcome
1	Patients undergoing GI endoscopy under sedation	use of reversal agents to manage adverse events only	use of reversal agents for all Patients routinely	safety measures (hypoxemia, hypotension, respiration depression etc.)

BIBLIOGRAPHIC SEARCH

a) Bibliographic search strategies were performed in **PubMed** and **Cochrane** from June 2024 to March 2025 using the following search strategies*:*

a. PubMed - Search June 15th 2025

Search: gastrointestinal endoscopy AND sedation AND reversal Sort by: Computed Author

("endoscopy, gastrointestinal"[MeSH Terms] OR ("endoscopy"[All Fields] AND "gastrointestinal"[All Fields]) OR "gastrointestinal endoscopy"[All Fields] OR ("gastrointestinal"[All Fields] AND "endoscopy"[All Fields])) AND ("sedate"[All Fields] OR "sedated"[All Fields] OR "sedating"[All Fields] OR "sedation"[All Fields] OR "sedations"[All Fields]) AND ("reversal"[All Fields] OR "reversals"[All Fields] OR "reverse"[All Fields] OR "reversed"[All Fields] OR "reversely"[All Fields] OR "reverses"[All Fields] OR "reversibilities"[All Fields] OR "reversibility"[All Fields] OR "reversible"[All Fields] OR "reversing"[All Fields] OR "reversion"[All Fields] OR "reversions"[All Fields])

Translations

gastrointestinal endoscopy: "endoscopy, gastrointestinal"[MeSH Terms] OR ("endoscopy"[All Fields] AND "gastrointestinal"[All Fields]) OR "gastrointestinal endoscopy"[All Fields] OR ("gastrointestinal"[All Fields] AND "endoscopy"[All Fields])

sedation: "sedate"[All Fields] OR "sedated"[All Fields] OR "sedating"[All Fields] OR "sedation"[All Fields] OR "sedations"[All Fields]

reversal: "reversal"[All Fields] OR "reversals"[All Fields] OR "reverse"[All Fields] OR "reversed"[All Fields] OR "reversely"[All Fields] OR "reverses"[All Fields] OR "reversibilities"[All Fields] OR "reversibility"[All Fields] OR "reversible"[All Fields] OR "reversing"[All Fields] OR "reversion"[All Fields] OR "reversions"[All Fields]

Results: 64 studies

b. Cochrane Central Register of Controlled Trials (CENTRAL)- Search June 15th 2024

#1	("gastrointestinal endoscopy") (Word variations have been searched)	2117
#2	("high-flow oxygen") (Word variations have been searched)	27507
#3	("reversal") (Word variations have been searched)	5837
#4	#1 AND #2 AND #3	**13**

Results: 13 studies

Results Total 64 + 13 = 77 studies

26 studies were considered potentially relevant and acquired in full text. After removing duplicates (n= 8), 16 articles were found. 3 studies were considered relevant.

Table 3.3.3.1s: Evidence related to use of sedation-analgesia reversal agents: *Characteristics of the included studies.*

Study (Author, year)	Country	Study design	No. of sites (no. of subjects)	Age (y)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm	Follow-up
Chen H et al 2024	China Elderly	RCT	1 (n=60)	65-95	33	Remimazolam + flumazenil	Propofol	Recovery time: 2.6 ± 1.6 min time to attain an OAA/S score of 3: 1.6 ± 0.9 min (Observer's Assessment of Alertness and Sedation scale) Remimazolam anesthesia combined with flumazenil antagonism causes a shorter recovery time for elderly patients undergoing gastrointestinal endoscopy compared to propofol	10.8 ± 3.0 min 9.6 ± 2.6 min	Until recovery
Lee S et al	Korea	RCT	1 (n=409)	48	47	Flumazenil	No antidote	Length of stay in recovery room: 20.10± 8.71min The time in the recovery room after flumazenil administration was significantly shortened, and the use of the drug did not increase the risk of adverse events or discomfort.	41.12± 11.37min	Until discharge
Tae C et al 2014	Korea	RCT	1 (n=4140)	57.7	55	15 patients with paradoxical reaction treated with flumazenil		1.4% paradoxical reaction Procedures were completed in 93.3% of cases (14/15)		
Hung A et al 2016	USA	Retrospective	1 42,118 upper GI endoscopies And 88,016 colonoscopies	61	39.2	Reversal agent use (n=45)	Non-use of the reversal agent (controls n=90)	Prevalence of reversal ageing use was 0.03% For events: Desaturation:64.4% Respiration changes 24.4% Hypotension 8.9% Bradycardia 6.7% Patients receiving reversal aging: older age, female, and lower body index	Prevalence of reversal agent use during moderate sedation is low, and outcomes are generally good	

Recovery time (min)

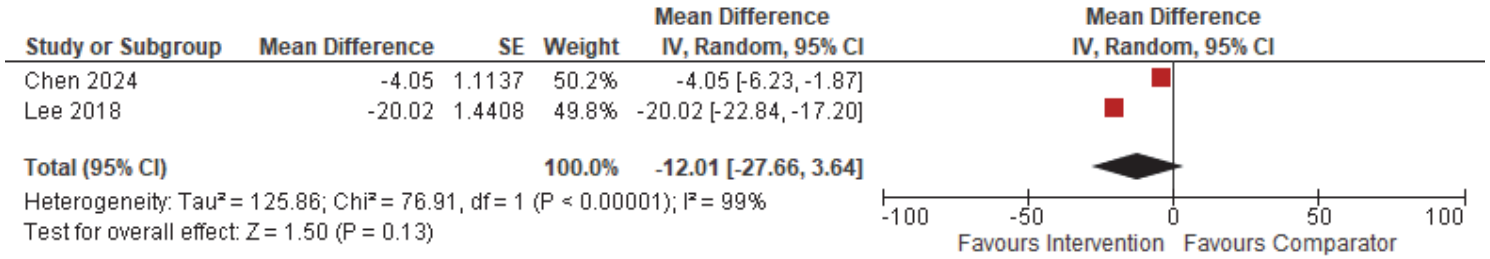


Table 3.3.3.2s: Risk of bias assessment for studies with sedation-analgesia reversal agents

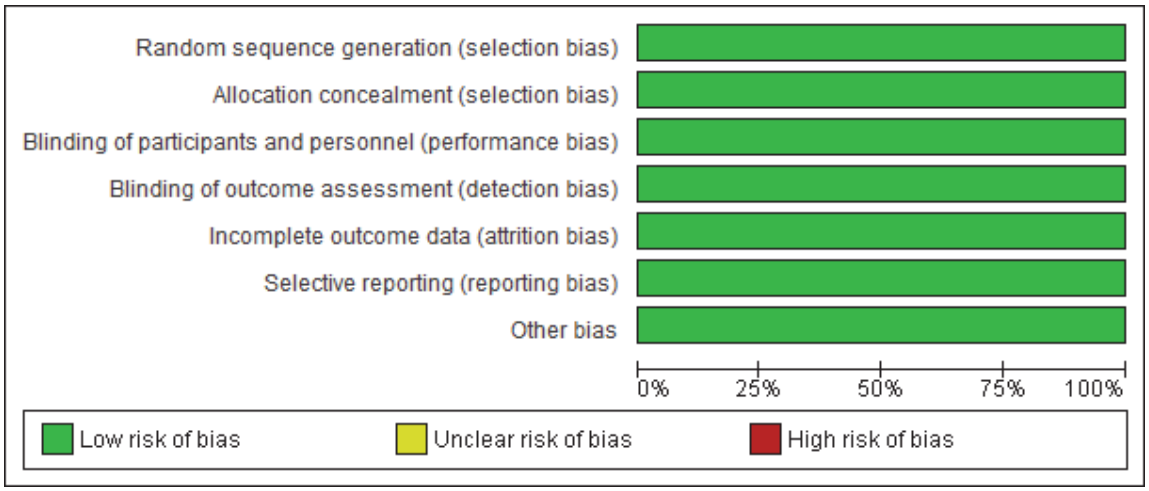


Table 3.3.3.3s Certainty of evidence related to use of sedation-analgesia reversal agents

The risk of bias assessment for each study can be found in **Table 3.3.3.3**. Overall, the included studies were considered of high quality. The certainty of evidence for this PICO was downgraded because only two RCTs were available, as well as the presence of inconsistency (high heterogeneity). Further downgrading was applied due to indirectness (different populations and examinations), imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to very low, and a conditional recommendation was proposed.

Table 3.3.3.4s: GRADE assessment for studies related to the use of sedation-analgesia reversal agents

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With placebo	With Table 3.2, Evidence related to flumazenil	Relative effect (95% CI)	Risk with placebo	Risk difference with Table 3.2 Evidence related to flumazenil
Recovery time (min)											
0 (2 RCTs)	not serious	serious[a,b]	serious[c]	serious[a]	none	⨁◯◯◯ Very low	0	0	-	0	MD **12.01 lower** (27.66 lower to 3.64 higher)

CI: confidence interval; **MD:** mean difference

Explanations a. Different regimens compared, b. c. Different regimens, outcomes, and patients

TASK FORCE 4: Safe discharge of the patient

Leader: Ulrike Beilenhoff

Members: Ulrike Beilenhoff, Bojan Kovacevic, Arianna Parrella, Stefano Pontone

CLINICAL QUESTION:

Q1. Personnel and equipment

Q4.1: Personnel and minimum equipment required for monitoring patients during the post-endoscopy period

- *Clinical Question:* According to the level of sedation administered, which personnel should be responsible for monitoring patients who undergo GI endoscopy until discharge?

Q4.2: Equipment

- *Clinical Question:* What is the minimum required equipment for monitoring the sedated patient until discharge, according to the level of sedation?

Q4.2: Discharge criteria

Q2.1 *Scoring system for safe discharge.*

- *Clinical Question: Should a validated scoring system be implemented for safe discharge?*

Q2.2 *Who signs off on discharge?*

- *Clinical Question:* Who should be responsible for signing off on discharge for patients who undergo sedated GI endoscopy?

Q2.3. *Discharge instructions*

- *Clinical Question:* Which instructions should be given to patients who underwent sedated GI endoscopy, according to the level of administered sedation?

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Table 4.1s. PICOs

PICO question no.	Population	Intervention	Comparator	Outcome
1.1	Patient is recovering following a sedated GI endoscopy	Deep sedation	Moderate sedation	Patient safety and satisfaction
2.1.	Patient recovery following a sedated GI endoscopy	A validated scoring system	Decision per-case	Patient safety and satisfaction
2.2.	Patients who underwent a sedated GI endoscopy	The health professional who administered sedation	The endoscopist who performed the procedure/other	Patient safety and satisfaction

BIBLIOGRAPHIC SEARCH

Bibliographic search strategies were performed from 2019 to 2024 using the following search strategies:

PubMed:

("endoscopy, digestive system"[MeSH Terms] OR "endoscop*" OR "EGD") AND ("Conscious Sedation"[MeSH Terms] OR "Anesthesia"[MeSH Terms] OR "Deep Sedation"[MeSH Terms] OR "Propofol"[MeSH Terms] OR "Midazolam"[MeSH Terms] OR "Anesthetics, Intravenous"[MeSH Terms] OR "Nurse Anesthetists"[MeSH Terms] OR ”NAPS” OR ”NAAP”) AND ("Continuity of Patient Care"[MeSH Terms] OR "Recovery Room"[MeSH Terms] OR "recover*"[All Fields] OR "discharg*"[All Fields] OR "postendoscopy care"[All Fields] OR "postprocedure care"[All Fields]) AND 2019/01/01:3000/12/31[Date - Publication] AND "English"[Language]

Embase:

exp digestive tract endoscopy/ or ("gastrointest* endoscop*" or ”GI endoscop*” or "EGD").mp. [mp=title, abstract, heading word, original title, keyword heading word, floating subheading word, candidate term word]

AND

exp conscious sedation/ or exp propofol/ or exp deep sedation/ or exp sedation/ or exp midazolam/ or exp anesthesia/ or exp anesthesia nursing/ or exp intravenous anesthesia/ or exp nurse anesthetist/ or ("NAPS" or "NAAP").mp. [mp=title, abstract, heading word, original title, keyword heading word, floating subheading word, candidate term word]

AND

exp patient care/ or exp recovery room/ or exp hospital discharge/ or ("recover*" or "discharg*" or "postendoscopy care" or "postprocedure care").mp. [mp=title, abstract, heading word, original title, keyword heading word, floating subheading word, candidate term word]
AND
limit to (human and english language and "remove medline records" and yr="2019 -Current")

Cochrane:
exp digestive tract endoscopy/ or ("gastrointest* endoscop*" or "GI endoscop*" or "EGD").mp. [mp=title, abstract, heading word, original title, keyword heading word, floating subheading word, candidate term word]
AND
exp conscious sedation/ or exp propofol/ or exp deep sedation/ or exp sedation/ or exp midazolam/ or exp anesthesia/ or exp anesthesia nursing/ or exp intravenous anesthesia/ or exp nurse anesthetist/ or ("NAPS" or "NAAP").mp. [mp=title, abstract, heading word, original title, keyword heading word, floating subheading word, candidate term word]
AND
exp patient care/ or exp recovery room/ or exp hospital discharge/ or ("recover*" or "discharg*" or "postendoscopy care" or "postprocedure care").mp. [mp=title, abstract, heading word, original title, keyword heading word, floating subheading word, candidate term word]
AND
limit to (human and english language and cochrane library and yr="2019 -Current")

Search results:
Medline (through PubMed): 233
Embase (through Ovid): 705
Cochrane (through Ovid): 13

Duplicates: 92
Total number of articles for screening: 859

Inclusion criteria:
Meta-analyses, RCT's, and prospective and retrospective trials on patients undergoing gastrointestinal endoscopy with sedation and focusing on:

- Requirements for the recovery area, including the type of personnel and equipment
- Discharge criteria, including scoring systems
- Discharge procedure including instructions

All published clinical guidelines concerning these topics

Full text Review:

Excluded studies

- Agrawal A, Kaushal K, Chatrasal C, Bharani A. Effect of propofol sedation during upper gastrointestinal endoscopy in cirrhotics and utility of psychometric tests, inhibitory control test and critical flicker frequency in assessment of recovery from sedation. Journal of Gastroenterology and Hepatology 2019; 34: 765. https://dx.doi.org/10.1111/jgh.14865 PT - **Conference Abstract**
- Chen HY, Wang XX, Lu YG, Tang SH, Ding T, Song JC, Chen G. Comparison of the recovery time of remimazolam besylate and propofol for gastrointestinal endoscopy sedation in elderly patients. Int J Med Sci 2024. 10.7150/ijms.93045 – **Routine use of Flumazenil**
- Conigliaro R. L. and Pigo F. and Gottin M. and Grande G. and Russo S. and Cocca S. and Marocchi M. and Lupo M. and Marsico M. and Bertani H. SAFETY OF ENDOSCOPIST-DIRECTED NURSE-ADMINISTERED SEDATION IN AN ITALIAN REFERRAL HOSPITAL: RETROSPECTIVE AUDIT ON 2 YEARS AND 19.407 PROCEDURES. Digestive and Liver Disease 2024; 56, S228https://dx.doi.org/10.1016/S1590-**Conference Abstract**
- De Castro Ferreira L.E.V.V. and De Mello Lanziotti dos Reis C.S. and Ferreira V.H.P. and Correa T.S. and Carvalho B.E. and Halfeld L.C.O. and Ferreira J.P. and De Oliveira Costa V. and Teixeira F.M. and Tonisi A.J.R. and Guimaraes L.M.P. A new discharge scale directed to patients submitted to endoscopic procedures with sedation. Digestive Endoscopy 2020; 32: 112. https://dx.doi.org/10.1111/den.13597 PT Reason: - **Conference Abstract**
- Hayakawa E, Barger J, Main W et al. Return to normal activity after colonoscopy using propofol sedation. American Surgeon 2019; 85 (4):434-437 https://dx.doi.org/10.1177/000313481908500437 PT - Reason: **Review**
- Nishizawa T, Yoshida S, Toyoshima O, et al. Risk factors for prolonged hospital stay after endoscopy. Clinical Endoscopy 2021; 54(6): 851-856. https://dx.doi.org/10.5946/ce.2020.292 Reason:**, no new information**
- Roelandt P, Haesaerts R, Missotten R, et al. Implementation of Aldrete's scoring system significantly reduces recovery time after procedural sedation by more than 20 %. Endoscopy 2021;53:S61 https://dx.doi.org/10.1055/s-0041-1724407 Reason: **Conference Abstract ➔ Full article is included**
- Smith Z, Flowers L, Samiullah S, et al. Driving after propofol sedation for routine outpatient colonoscopy and esophago-gastroduodenoscopy: a patient survey. Gastrointestinal Endoscopy 2021; 93(6): AB42 https://dx.doi.org/10.1016/j.gie.2021.03.146 Reason: **Conference Abstract**
- Shirota Y, Hirase Y, Suda T, Miyazawa M, Hodo Y, Wakabayashi T. More than half of hypoxemia cases occurred during the recovery period after completion of esophagogastroduodenoscopy with planned moderate sedation. Nat Scientific Reports 2020; 10:4312. DOI:10.1038/s41598-020-61120-0 Reason: **no dedicated person for sedation during the procedure. No staff in recovery area - detection of desaturation by alarm system only, oxygen only in case of desaturation.**
- Thirumurthi S, Hagan K.B, Tan J, Cata J, Hernandez M. A pilot study on the recovery rate in patients who receive propofol sedation during upper endoscopy (EGD). American Journal of Gastroenterology 2019; 114, S321https://dx.doi.org/10.14309/01.ajg.0000591756.65139.28 Reason: **Conference Abstract**
- Walke S.S. and Chauhan S. and Pandey V. and Jadhav R. and Chaudhari V. and Vishwanathan D. and Kolhe K. and Ingle M. AO - Walke, Swapnil Sahebrao; When to Discharge a Patient After Endoscopy: A Narrative Review.Clinical Endoscopy 2022; 55 (1) Aug 14 https://dx.doi.org/10.5946/ce.2021.110 Reason: **Review –criteria focused on endoscopic techniques, no sedation specific criteria**

Included studies

RCT

- De Benito Sanz M, de la Torre S.M., de las Heras M.A.S. et al. Randomized clinical trial to assess the mPADSS scale in recovery and home discharge after endoscopy. Revista Española de Enfermedades Digestivas.2020; 112:762-767. https://dx.doi.org/10.17235/reed.2020.6420/2019 PT - Article
- Leonard U. Edokpolo, Daniel J. Mastriano, Joanna Serafin, Jeremy C. Weedon, Maryam T. Siddiqui Dennis P. Dimaculangan. Discharge Readiness after Propofol with or without Dexmedetomidine for Colonoscopy - A Randomized Controlled Trial. Anesthesiology 2019; 131:279–86. DOI: 10.1097/ALN.0000000000002809
- 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. Eur J Anaesthesiol 2022; 39:911–917. DOI:10.1097/EJA.0000000000001715
- Riphaus A, Gstettenbauer T, Frenz MB, et al.Quality of psychomotor recovery after propofol sedation for routine endoscopy: a randomized and controlled study. Endoscopy 2006; 38: 677-683. https:// doi. org/ 10.1055/s-2006-925244.

Prospective Studies

- Allampati S, Wen S, Liu F, Kupec JT. Recovery of cognitive function after sedation with propofol for outpatient gastrointestinal endoscopy, Saudi J Gastroenterol 2019; 25:188-193. DOI:10.4103/sjg.SJG_369_18
- Borrat X, Ubre M, Risco R, Gambus PL, Pedroso A, Iglesias A, Fernandez-Esparrach G, Gines A, Balust J, Martinez Palli G.Computerized tests to evaluate recovery of cognitive function after deep sedation with propofol and remifentanil for colonoscopy. Clin Monit Comput 2019; 33:107-113. DOI:10.1007/s10877-018-0134-3
- Hao XW, Zhan YL, Li P, Zhang ST, Yan XD, Li XM, Xiang W. Recovery of driving skills after endoscopy under propofol sedation: a prospective pilot study to assess the driving skills after endoscopic sedation using driving simulation. BMC Anesthesiology 2023; 23: DOI:10.1186/s12871-023-02122-z
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- Roelandt P, Haesaerts R, Demedts I, Bisschops R. Implementation of the Aldrete score reduces recovery time after non-anesthesiologist-administered procedural sedation in gastrointestinal endoscopy. Endoscopy International Open 2022; 10:E1544-E1547. DOI:https://dx.doi.org/10.1055/a-1964-7458 PT - Article
- Thompson R, Seck V, Riordan S, Wong S. Comparison of the Effects of Midazolam/Fentanyl, Midazolam/Propofol, and Midazolam/Fentanyl/Propofol on Cognitive Function After Gastrointestinal Endoscopy. Surg Laparosc Endosc Percutan Tech 2019; 29 (6). 441-446. DOI:10.1097/SLE.0000000000000679
- Yamaguchi D, Morisaki T, Sakata Y, Mizuta Y, Nagatsuma G, Inoue S, Shimakura A, Jubashi A, Takeuchi Y, Ikeda K, Tanaka Y, Yoshioka W, Hino N, Ario K, Tsunada S, Esaki M. Usefulness of discharge standards in outpatients undergoing sedative endoscopy: a propensity score-matched study of the modified post-anesthetic discharge scoring system and the modified Aldrete score.BMC Gastroenterology 2022; 22:445. DOI:10.1186/s12876-022-02549-7

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Survey

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Audit

- Xianli Cai. Et al Discharge following sedation for endoscopic procedures:a best practice implementation project. JBI Evid Synth 2020; 18(2):348–356. DOI: 10.11124/JBISRIR-D-19-00053

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- Park H.J. and Kim B.-W. and Lee J.K. and Park Y. and Park J.M. and Bae J.Y. and Seo S.Y. and Lee J.M. and Lee J.H. and Chon H.K. and Chung J.-W. and Choi H.H. and Kim M.H. and Park D.A. and Jung J.H. and Cho J.Y. Korean Society of Gastrointestinal Endoscopy Clinical Practice Guidelines for Endoscopic Sedation. Gut and Liver 2022; 16: 341-356 .https://dx.doi.org/10.5009/gnl210530 PT - Review
- Sidhu R, Turnbull D, Haboubi H, Leeds JS, Healey C, Hebbar S, Collins P, Jones W, Peerally MF, Brogden S, Neilson LJ, Nayar M, Gath J, Foulkes G, Trudgill NJ, Penman I. British Society of Gastroenterology guidelines on sedation in gastrointestinal endoscopy. Gut 2024;73: 219–245.DOI: 10.1136/gutjnl-2023-330396
- Viazis N., Vlachogiannakos J, Apostolopoulos P. et al. Sedation during endoscopic procedures: a Hellenic Society of Gastroenterology Position Statement. Annals of Gastroenterology 2023; 36:231-243. DOI: https://dx.doi.org/10.20524/aog.2023.0789 PT - Article
- Wehrmann T, Riphaus A, et al. Updated S3 Guideline “Sedation for Gastrointestinal Endoscopy” of the German Society of Gastroenterology, Digestive and Metabolic Diseases (DGVS) June 2023 – AWMF-Register-No. 021/014. Z Gastroenterol 2023; 61: 1246–1301DOI 10.1055/a-2165-6388

Table 4.2s: Evidence: Characteristics of the included studies.

Authors, yr	Study Design	No of subjects	Age (mean, SD)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm	Follow-up
Allampati S, 2019 USA	Prospective non-randomized	169	50.76±14.06 (cases) 46.66±16.95 (controls)	0,38	Cognitive tests before and after propofol (30-45 min)	Controls	delta time 3.6s (SD 17.3 s) p=0.013	delta time −4.8s (SD 12.8s) p=0.006	no
Borrat X, 2019 Spain	Prospective observational double blind clinical study	34	median 59 (range 50-69)	0,59	Cognitive tests 10 min (T10), 40 min (T40), and 120 min (T120) after the end of sedation	Baseline	This cognitive decay is recovered in 64% patients 10 min after the stop of sedation and completely back to normal in all patients 40 min after propofol and remifentanil infusions were stopped		
De Benito Sanz M. 2020 Spain	RCT (nonblinded)	118	60(IQR 47-70)	0,593	MPADDS group: scale performed every 10 min until they reach a score equal to or greater than 9	Best care practice	10 min (10-10) Recovery was faster in the mPADSS group, who were discharged in a median of 10 min (IQR: 10-10) compared to The control group, who required a median of 15 min (IQR:11-22.5) (p = 0.002). 1 readmission	15 min (11-22.5) 3 readmissions	24-72 hrs by telephone
Hao XW 2023	Prospective	18	47 (range 25-	0,77	Driving simulation	no control group	No significant	-	no

China	observational study	58)	before and after 2h and 4h	difference at 4 hrs compared to baseline	

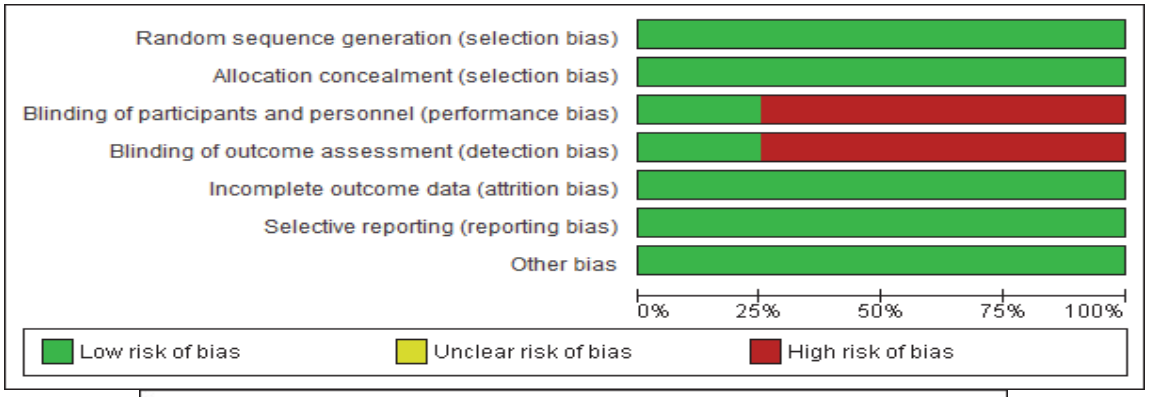
Authors	Study Design	No of subjects	Age (mean, SD)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm	Follow-up
Lois FJ, 2023 Belgium	Prospective observational study	60	55,3 (SD 12,2)	0,567	Driving simulation when PADSS was 9.	Controls (patient escorts)	Patients crossed the midline significantly more frequently than escorts (3 [2 to 4] and 2 [1 to 3] crossings, P=0.015] and speeding for a higher proportion of the distance travelled (37 ± 20 and 24 ± 17, P=0.029).		no
Chua N, 2021, Australia	Prospective observational study	73	72,5 (SD 5,5)	0,534	MoCA cognitive screening and three-minute diagnostic confusion assessment method (3D-CAM) before endoscopy and on discharge	Baseline	small but significant decline in MoCA score at discharge from a mean (SD) of 23.8 (3.6) to 22.2 (4.0), P < 0.01.		
Pozin I.E. 2023 Israel	Retrospective Cohort Study	657	63.0±15.3	54.8	Procedural Sedoanalgesia during Endoscopy	no	12.5 % desaturation in recovery time, increase of desaturation events during recovery in patients with higher ASA score and comorbidity (Ischemic heart disease, Hypertension, Diabetes), desaturation during precedure and use of Fentanyl; no major complications (e.g., Apnoe)	no	3 days after the procedure

Authors	Study Design	No of subjects	Age (mean, SD)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm	Follow-up
Roelandt P. 2023 Belgium	PROSPECTIVE INTERVENTIONAL STUDY	328	NA	NA	Implementation of the Aldrete Score	best practice before implementation	Recovery time decreased significantly to 47 ± 25 minutes (P < 0.01) with similar doses of procedural sedation (3.5 ± 1.2mg midazolam and 32 ± 19mg pethidine).	no	no
Thompson R, 2021 Australia	PROSPECTIVE COHORT STUDY	200	53.9± 14.8 / 54.9 ± 15.1 / 47.5 ±18.1	46.5	computerised neurocognitive score	3 different groups of sedation	Neurocognitive scores were significantly lower in the postprocedure test compared with baseline scores for detection, identification, and one-card learning (P<0.001). Postprocedure detection test scores were significantly impaired in the M/F group compared with the M/F/P and M/P groups. Predictors of poorer neurocognitive function were midazolam dosage >3mg (P<0.006) and fentanyl dosage >50 µg (P<0.009).		no

Authors	Study Design	No of subjects	Age (mean, SD)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm	Follow-up
Yamaguchi D, 2020 Japan	PROSPECTIVE NON-RANDOMISED TRIAL	376	64.2 ± 14.3 GROUP M / 62.8 ± 15.7 GROUP A	36.7	MPADSS	MODIFIED ALDRETE SCORE	The proportion of patients who had recovery within 60 min after endoscopy was significantly higher in group A than in group M (42.5% versus 25.0%, respectively; P < 0.01). The patient's level of consciousness should be assessed carefully when using the modified Aldrete score, especially in patients who visit the hospital alone	The mean recovery time was comparable between the two groups	telephone call 24h after discharge
Yao Y, 2022 China	PROSPECTIVE RANDOMISED TRIAL	132	49 (41-56) / 48 (39-56)	47.7	REMIMAZOLAM GROUP	PROPOFOL GROUP	discharge time 24 min. Injection pain occurred in 11 of 66 (17%) participants receiving remimazolam versus 32 of 66 (49%) participants receiving Propofol (P<0.001); hypotension occurrence was 20%	discharge time 21 min, more adverse events	no
Xianli Cai 2020 China	Audit	no patients			Implementation of 8 criteria	after implementation	improvements in 6 of 8 criteria to 100%		no

Authors	Study Design	No of subjects	Age (mean, SD)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm	Follow-up
Edokpolo L 2021 USA	RCT double-blind, randomized controlled trial	114 (57 vs. 56)	57 [52 - 61] vs. 56 [49 - 65]	56.14	propofol plus dexmedetomidine	propofol plus Placebo	delayed home-readines in patients received dexmedetomidine, 26 pt (51%) were Ready for discharge by 30 min, 82% by 40 min (mPADSS)	Only propofol for colonoscopy provided more stable hemodynamics, allowed for faster recovery from anesthesia; 44 pt (88%) receiving propofol were ready for discharge (P < 0.001). 96% by 40 Min	no
Dahlberg K, 2020 USA	Survey. International cross-sectional study	no patients					Phase II PACU = Recovery Area: 3-4 pt per nurse		
Riphaus Endoscopy 2006	RCT	100	51 men, 45 women; mean age 52 ± 12 years)	51	Propofol	Midazolam	The mean recovery time and quality of recovery were significantly better after propofol sedation (14 ± 9 min vs. 25 ± 8 min and 8.7 ±1.3 vs. 6.3 ± 1.1 points) (P < 0.01). Psychomotor and driving skills after propofol sedation were similar to the baseline results, while in the midazolam/pethidine group, patients showed significantly more lane deviations (1.1 ± 0.9 vs. 1.6 ± 0.9), time over the speed limit (0.3 ± 0.83 vs. 0.6 ±0.88), missed stoplights more often (0.05 ± 0.31 vs.0.11 ± 0.35), and had slower reaction times for unexpected Events (1.11 ± 0.46 s vs. 1.39 v 0.44 s) (P < 0.01). The time needed to complete the NCT after sedation did not differ between the two groups (32.1 ± 12.0 s vs. 33.4 ± 12.6 s for propofol; 31.5 ± 11.2 s vs. 34.6 ± 12.8 s for midazolam/pethidine).		

Table 4.3s: Risk of bias assessment for studies evaluating recovery, discharge



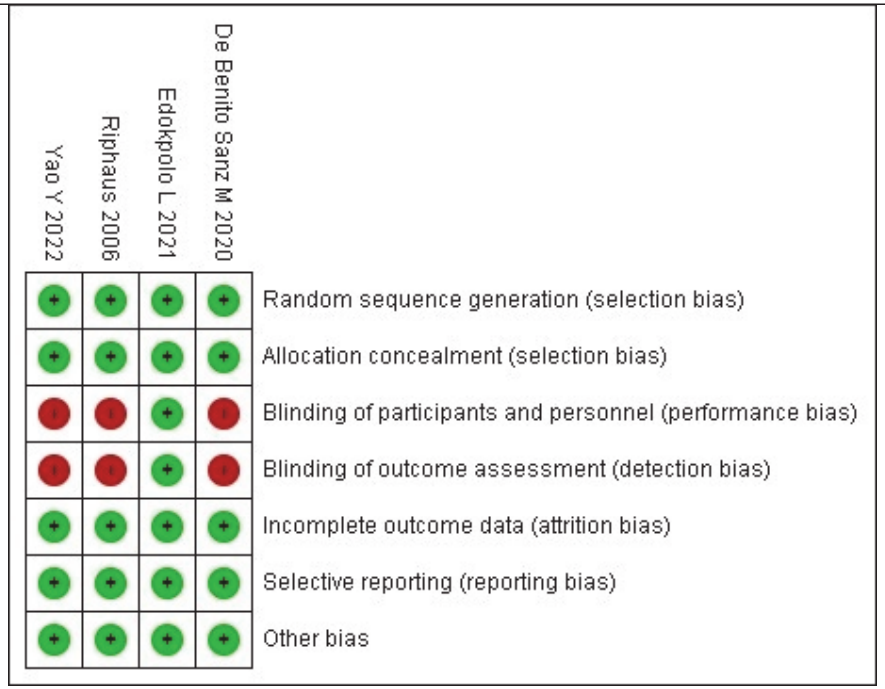


Table 4.4s: Risk of bias assessment for studies

Study	Selection (max 4 stars)	Comparability (max 2 stars)	Outcomes (max 3 stars)	Quality (Total 9/9)
Allampati S, 2019	***	**	**	**Good**
Borrat X, 2019	***	*	**	**Good**
Hao XW 2023	***	**	**	**Good**
Lois FJ, 2023	***	**	**	**Good**
Chua N, 2021	***	*	**	**Good**
Pozin I.E. 2023	**	**	**	**Fair**
Shirota Y 2020	***	**	**	**Good**
Roelandt P. 2023	***	**	**	**Good**
Thompson R, 2021	***	**	**	**Good**
Yamaguchi D, 2020	***	**	**	**Good**

Good quality: 3 or 4 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain.

Fair quality: 2 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain.

Poor quality: 0 or 1 star in selection domain OR 0 stars in comparability domain OR 0 or 1 stars in outcome/ exposure domain

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TASK FORCE 5: Special Situations

Leader: Roos Pouw

Members: Marcin Romańczyk, Emanuel Coron, Marcus Hollenbach

Q5.1: Sedation in emergency GI endoscopy

Table 5.1.1s PICOs for question 5.1

PICO question no.	Population	Intervention	Comparator	Outcome
1	Patients undergoing emergency gastrointestinal (GI) endoscopy	Under sedation	Without sedation	Procedure outcomes (e.g, completeness of procedure), Patient's safety, patient's satisfaction
2	Patients undergoing emergency gastrointestinal (GI) endoscopy	Anesthetists administer sedation	Non-anesthetist administers sedation	Procedure outcomes (e.g, completeness of procedure), Patient's safety, patient's satisfaction

BIBLIOGRAPHIC SEARCH 5.1

Bibliographic search strategy was performed in **PubMed** to 01.09.2024 using the following search strategies:

"sedation"[tiab] AND ("endoscopy"[tiab] OR "gastroscopy"[tiab]) AND "emergency"[tiab])"

Pubmed: 99 hits; after screening titles: 10; after screening abstracts: 4; 2 studies identified via references.

Results: 99 studies

After removing duplicates (n=0), 10 studies were identified based on screening title; 3 studies remained after screening abstract; 4 additional studies were added after screening references.

Included studies: 3 Prospective studies [6,7,8], 5 Retrospective studies [1-5,]

Table 5.1.2s: Characteristics of the included studies.

Study (Author, year)	Country	Study design	No. of sites (no. of subjects)	Age (y)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm
Yamaguchi 2023	Japan	Retrospective cohort study with propensity score matching between the intervention and control groups	1 site 389 subjects; For propensity score matching, 133 in both groups	I: 70.1±13.9 C: 74.8±12.3	I: 71.9% C: 61%	sedation	Non sedation	Successful hemostasis: 123 (92.5%) Mean procedure time: 17.6 ±10min Adverse events: Aspiration pneumonia: 10 (7.5%) 30-day mortality: 12 (9%)	Successful hemostasis: 123 (92.5%) Mean procedure time: 20.2 ±10.2min Adverse events: Aspiration pneumonia: 7 (5.3%) 30-day mortality: 9 (6.8%)
Park 2020	Korea	Retrospective study	6 sites I: 430 C: 870	I: 55.2±10.7 C: 55.9±11.8	I: 82.8% C: 79.7%	Sedation	No sedation	Successful hemostasis: 398 (92.6%) Mean procedure time: 12.4 ±9.5min Adverse events: Aspiration pneumonia: 10 (2.3%) 30-day mortality: 35 (8.1%)	Successful hemostasis: 791 (90.9%) Mean procedure time: 13.8 ±9.4min Adverse events: Aspiration pneumonia: 13 (1.5%) 30-day mortality: 84 (9.6%)

Park 2016	Korea	Retrospective cohort study All patients received sedation for upper GI bleeding, two groups were compared	1 site 703 examinations 539 non-variceal bleeding 164 variceal bleeding	Variceal bleeding (VB): 55 Non-variceal bleeding (NVB): 60.8	VB: 80.5 NVB: 74.3	All patients had sedation	n.a.	Successful hemostasis: VB: 164 (100%) NVB: 536 (99%) Mean procedure time: VB: 22.7±9.3 min NVB: 17.2±11.4 min Adverse events: Hypoxia: VB: 3 (1.8%) NVB: 19 (3.5%)	
Koch 2007	USA	Retrospective cohort study	1 site 69 episodes of variceal bleeding	I: 49±9 C: 48±13	I: 74% C: 65%	Intubation	Non-intubated	Aspiration pneumonia (based on x-ray): 9 (19%) Mortality: 9 (21%)	Aspiration pneumonia: 0 Mortality: 1 (5%)
Rudolph 2003	USA	Retrospective cohort study 1 period (1988) before standard intubation, compared to 1 period (1992) after more standard	1 site 1988: n=101 1992: n=119	1988: 55.5±17.7 1992: 50.3±15.3	1988: 68.3% 1992: 68.9%	Intubation more after performed in 1992	Non-intubated was standard in 1988	Adverse events: Aspiration pneumonia: 2 (1.7%) Mortality: 14 (11.8%)	Adverse events: Aspiration pneumonia: 4 (4%) Mortality: 16 (15.9%)

		intubation							
Lohse 2015	Denmark	Prospective cohort study	Nationwide study I: 2101 C: 1479	I: 74.1 (63.4-83) C: 75.9 (65.6-84)	I: 1133 (53.9%) C: 798 (54%)	Intubated	Non-intubated	30-day mortality: 277 (13.2%)	30-day mortality: 178 (12.1%)
Duch 2016	Denmark	Prospective cohort study	Nationwide study, 21 sites I: 2074 C: 982	I: 74.4 (65.2-82.9) C: 73.9 (64.5-81.)	I: 56.2% C: 53.9%	Anesthesia care	No anesthesia care	30-day mortality: 10.4%	30-day mortality: 5.6%

Fig. 5.1.1s Efficacy of hemostasis

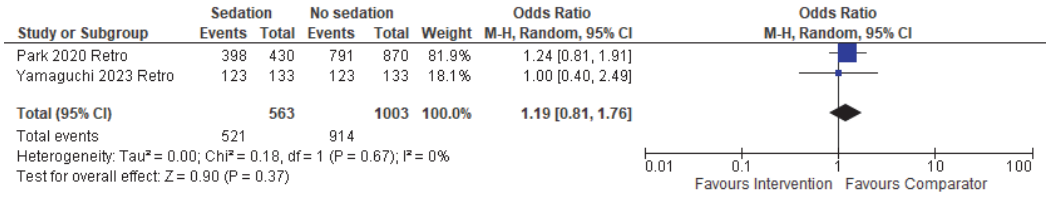

Table 5.1.3s: Risk of bias assessment for studies

Study	Selection (max 4 stars)	Comparability (max 2 stars)	Outcomes (max 3 stars)	Quality (Total 9/9)
Yamaguchi, 2023	***	*	**	**Good**
Park, 2020	***	*	**	**Good**

Table 5.1.4s Certainty of evidence

The risk of bias assessment for each study can be found in **Table 5.1.3s**. Overall, the included studies were considered of good quality. The certainty of evidence in this PICO question was downgraded because the evidence was based only on two non-randomized observational studies without RCTs. For the outcome of efficacy of hemostasis, further downgrading was applied due to indirectness (heterogeneity in the endoscopic modalities for hemostasis) and imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to very low.

Fig. 5.1.2s Mean Procedure Time during hemostasis

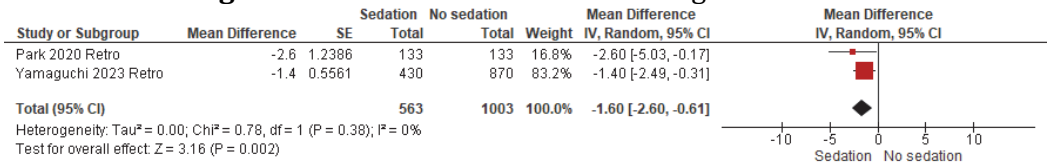

Table 5.1.5s: Risk of bias assessment for studies

Study	Selection (max 4 stars)	Comparability (max 2 stars)	Outcomes (max 3 stars)	Quality (Total 9/9)
Yamaguchi, 2023	***	*	**	**Good**
Park, 2020	***	*	**	**Good**

Table 5.1.6s Certainty of evidence

The risk of bias assessment for each study can be found in **Table 5.1.5s**. Overall, the included studies were considered of good quality. The certainty of evidence in this PICO question was downgraded because the evidence was based only on two non-randomized observational studies without RCTs. For the outcome of mean procedure time during hemostasis, further downgrading was applied due to indirectness (heterogeneity in the endoscopic modalities for hemostasis), so the quality of evidence was downgraded to very low.

fig 5.1.3s Aspiration pneumonia during hemostasis

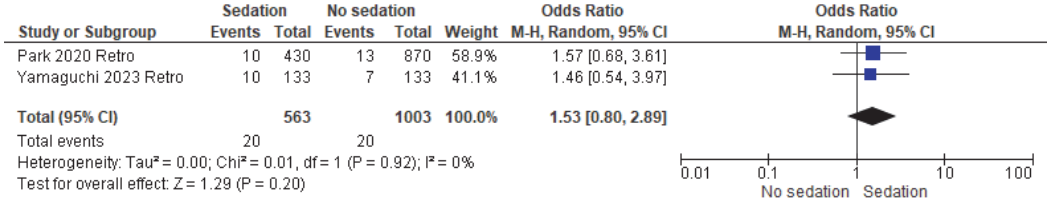

Table 5.1.7s: Risk of bias assessment for studies

Study	Selection (max 4 stars)	Comparability (max 2 stars)	Outcomes (max 3 stars)	Quality (Total 9/9)
Yamaguchi, 2023	***	*	**	**Good**
Park, 2020	***	*	**	**Good**

Table 5.1.8s Certainty of evidence

The risk of bias assessment for each study can be found in **Table 5.1.7**. Overall, the included studies were considered of good quality. The certainty of evidence in this PICO question was downgraded because the evidence was based only on two non-randomized observational studies without RCTs. For the outcome of mean procedure time during hemostasis, further downgrading was applied due to indirectness (heterogeneity in the endoscopic modalities for hemostasis) and imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to very low.

Fig. 5.1.4s 30-day mortality after hemostasis

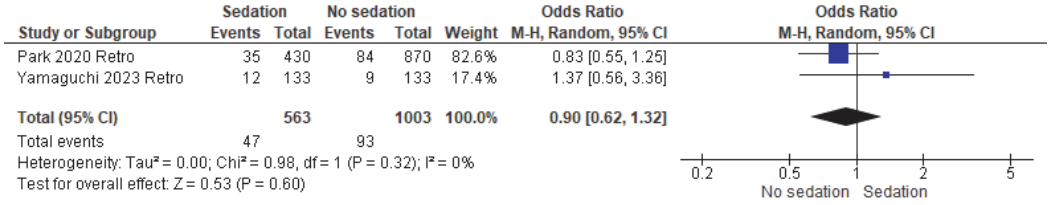

Table 5.1.9s: Risk of bias assessment for studies

Study	Selection (max 4 stars)	Comparability (max 2 stars)	Outcomes (max 3 stars)	Quality (Total 9/9)
Yamaguchi, 2023	***	*	**	**Good**
Park, 2020	***	*	**	**Good**

Table 5.1.10s Certainty of evidence

The risk of bias assessment for each study can be found in **Table 5.1.10s**. Overall, the included studies were considered of good quality. The certainty of evidence in this PICO question was downgraded because the evidence was based only on two non-randomized observational studies without RCTs. For the outcome of 30-day mortality after hemostasis, further downgrading was applied due to indirectness (heterogeneity in the endoscopic modalities for hemostasis) and imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to very low.

Fig. 5.1.5s Aspiration pneumonia with vs without intubation in GI emergencies

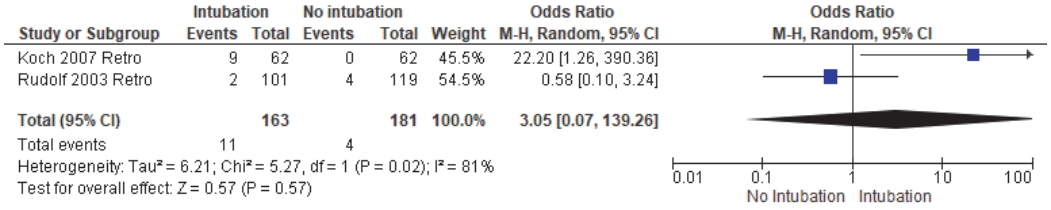

Table 5.1.11s: Risk of bias assessment for studies

Study	Selection (max 4 stars)	Comparability (max 2 stars)	Outcomes (max 3 stars)	Quality (Total 9/9)
Koch, 2007	**	*	**	**Fair**
Rudolph, 2003	**	*	**	**Fair**

Table 5.1.12s Certainty of evidence

The risk of bias assessment for each study can be found in **Table 5.1.11s**. The certainty of evidence in this PICO question was downgraded because the evidence was based only on two non-randomized observational studies of fair quality, in the absence of RCTs. For the outcome of aspiration pneumonia with vs. without intubation in GI emergencies, further downgrading was applied due to inconsistency (high heterogeneity), indirectness (heterogeneity in the endoscopic modalities for hemostasis), and imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to very low.

Fig. 5.1.6s 30-day mortality: intubation vs. no intubation in GI emergencies

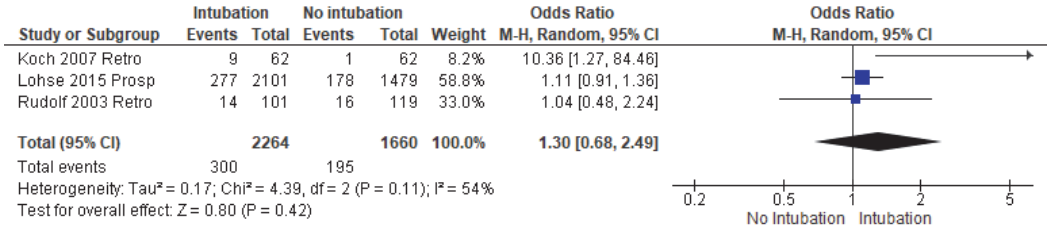

Table 5.1.13s: Risk of bias assessment for studies

Study	Selection (max 4 stars)	Comparability (max 2 stars)	Outcomes (max 3 stars)	Quality (Total 9/9)
Koch, 2007	**	*	**	**Fair**
Rudolph, 2003	**	*	**	**Fair**
Lohse, 2015	**	*	***	**Fair**
Duch, 2016	***	*	**	**Good**
Park, 2016	***	*	**	**Good**

Table 5.1.14s Certainty of evidence

The risk of bias assessment for each study can be found in **Table 5.1.13s**. The certainty of evidence in this PICO question was downgraded because the evidence was based only on non-randomized observational studies of fair quality, in the absence of RCTs. For the outcome of 30-day mortality: intubation vs. no intubation in GI emergencies, further downgrading was applied due to inconsistency (high heterogeneity), indirectness (heterogeneity in the endoscopic modalities for hemostasis), and imprecision (broad CI crosses 1.0), so the quality of evidence was downgraded to very low.

Table 5.1.15s GRADE assessment

Bibliography: TF 5 for Special Situations. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With placebo	With Table Q1		Risk with placebo	Risk difference with Table Q1
Efficacy of haemostasis											
1566 (2 non-randomised studies)	not serious	not serious	serious[a]	serious[b]	none	⨁◯◯◯ Very low[a,b]	914/1003 (91.1%)	521/563 (92.5%)	**OR 1.19** (0.81 to 1.76)	914/1003 (91.1%)	**13 more per 1,000** (from 19 fewer to 36 more)
Hemostasis with or without sedation - Mean Procedure Time											
1566 (2 non-randomised studies)	not serious	not serious	serious[a]	not serious	none	⨁◯◯◯ Very low[a]	1003	563	-	1003	MD **1.6 lower** (2.6 lower to 0.61 lower)
Hemostasis with or without sedation - Aspiration pneumonia											
1566 (2 non-randomised studies)	not serious	not serious	serious[a]	serious[b]	none	⨁◯◯◯ Very low[a,b]	20/1003 (2.0%)	20/563 (3.6%)	**OR 1.53** (0.80 to 2.89)	20/1003 (2.0%)	**10 more per 1,000** (from 4 fewer to 36 more)
Hemostasis with or without sedation - 30-day mortality											
1566 (2 non-randomised studies)	not serious	not serious	serious[a]	serious[b]	none	⨁◯◯◯ Very low[a,b]	93/1003 (9.3%)	47/563 (8.3%)	**OR 0.90** (0.62 to 1.32)	93/1003 (9.3%)	**8 fewer per 1,000** (from 33 fewer to 26 more)
Intubation vs. No intubation - Aspiration pneumonia											

Table 5.1.15s GRADE assessment

Bibliography: TF 5 for Special Situations. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
344 (2 non-randomised studies)	not serious	serious[c]	serious[a]	serious[b]	none	⨁◯◯◯ Very low[a,b,c]	4/181 (2.2%)	11/163 (6.7%)	**OR 3.05** (0.07 to 139.26)	4/181 (2.2%)	**42 more per 1,000** (from 21 fewer to 737 more)
Intubation vs. No intubation - 30-day mortality											
3924 (3 non-randomised studies)	not serious	serious[c]	serious[a]	serious[b]	none	⨁◯◯◯ Very low[a,b,c]	195/1660 (11.7%)	300/2264 (13.3%)	**OR 1.30** (0.68 to 2.49)	195/1660 (11.7%)	**30 more per 1,000** (from 34 fewer to 131 more)

CI: confidence interval; **MD:** mean difference; **OR:** odds ratio
Explanations: a. Heterogeneity in the endoscopic modalities for hemostasis, b. Broad CI crosses 1.0, c. High heterogeneity

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Q5.2: Sedation for GI procedures during pregnancy and lactation

Table 5.2.1s PICOs for clinical question 5.2

PICO question no.	Population	Intervention	Comparator	Outcome
1	Patients undergoing gastrointestinal (GI) endoscopy during pregnancy and lactation	Administration of sedation, analgesia, and anesthesia	No sedation	Procedure outcomes (e.g, Completeness of procedure
3	Patients undergoing gastrointestinal (GI) endoscopy during pregnancy and lactation	Administration of sedation, analgesia, and anesthesia	No sedation	Patient's safety
4	Patients undergoing gastrointestinal (GI) endoscopy during pregnancy and lactation	Administration of sedation, analgesia, and anesthesia	No sedation	Patient's satisfaction

BIBLIOGRAPHIC SEARCH 5. 2
Bibliographic search strategy was performed in **PubMed** to 09.09.2024 using the following search strategies:

("conscious sedation"[Title/Abstract] OR "deep sedation"[Title/Abstract] OR "Anesthesia"[Title/Abstract] OR "Analgosedation"[Title/Abstract] OR "Sedation"[Title/Abstract] OR "nitrous oxide"[Title/Abstract] OR "propofol"[Title/Abstract] OR "midazolam"[Title/Abstract] OR "remimazolam"[Title/Abstract] OR "fentanyl"[Title/Abstract] OR "remifentanyl"[Title/Abstract])
AND
("endoscopy"[Title/Abstract] OR "gastroscopy"[Title/Abstract] OR "colonoscopy"[Title/Abstract] OR "esophagogastroduodenoscopy"[Title/Abstract] OR "EUS"[Title/Abstract] OR "endoscopic ultrasound"[Title/Abstract] OR "ERCP"[Title/Abstract] OR "endoscopic retrograde cholangiopancreatography"[Title/Abstract] OR "enteroscopy"[Title/Abstract])
AND
("pregnancy"[Title/Abstract] OR "pregnant"[Title/Abstract] OR "Lactation" [Title/Abstract])

Results: 120 studies
After removing duplicates (n=0), 9 articles were considered potentially relevant and acquired in full text.
Excluded studies
1 study (refs) was excluded due to being a review article
Included studies: 8 retrospective studies[1-8]

Table 5.2.2s: Characteristics of the included studies.

Study (Author, year)	Country	Study design	No. of sites (no. of subjects)	Age (y)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm
Quan, 2006	Singapore	Retrospective case series	1 site N=4, 1 patient lost to FU	27.8 (range 23-35)	na	ERCP with sedation		3 full-term deliveries and a healthy baby	
Iyilikci, 2007	Turkey	Case report	1 site N=1					Uneventful	
Tang, 2008	USA	Retrospective cohort	1 site N=65	25.8 ±6.1	na	ERCP with sedation		89.8% had term pregnancy; the highest risk of pre-term delivery was in the 1st trimester.	
Akcakaya, 2009	Turkey	Retrospective case series	1 site N=6	28 (range 21-33)	na	ERCP with sedation		No premature birth, abortion, or intrauterine growth retardation was observed.	
Arce-Lievano, 2021	Mexico	Retrospective study	1 site N=9	?	na	ERCP with sedation		Pregnancy progression was normal in 100%	
Fine, 2014	USA	Retrospective cohort study	1 site N=22	26.4 (range 18-38)	na	ERCP with sedation		Birth records were available in 16 cases; 15 had full-term pregnancies.	
Garcia-Cano,	Spain	Retrospective	6 sites	30.6	na	ERCP with sedation		All patients had healthy babies with normal	

2012		survey	N=11				deliveries.
Kamani, 2019	Pakistan	Retrospective cohort study	1 site N=48	26.38±5.5	na	Endoscopic procedures	1 miscarriage in the second trimester (2%)

References

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Q5.3: Sedation for GI procedures in patients premedicated with mucolytic and defoaming agents

Table 5.3.1s: PICOs for Clinical Question 5.3

PICO question no.	Population	Intervention	Comparator	Outcome
1	Premedicated patients with defoaming with or without mucolytic agents undergoing upper GI endoscopy	Administration of sedation, analgesia, and anesthesia	No sedation	Patient's safety

BIBLIOGRAPHIC SEARCH 5.3

Bibliographic search strategies were performed in **PubMed, Cochrane,** from 2019 to the end of 2024 using the following search strategies:

d. PubMed- Search [DATE]

("conscious sedation"[Title/Abstract] OR "deep sedation"[Title/Abstract] OR "Anesthesia"[Title/Abstract] OR "Analgosedation"[Title/Abstract] OR "Sedation"[Title/Abstract] OR "nitrous oxide"[Title/Abstract] OR "propofol"[Title/Abstract] OR "midazolam"[Title/Abstract] OR "remimazolam"[Title/Abstract] OR "fentanyl"[Title/Abstract] OR "remifentanyl"[Title/Abstract])
AND
("upper endoscopy"[Title/Abstract] OR "gastroscopy"[Title/Abstract] OR "esophagogastroduodenoscopy"[Title/Abstract])
AND
("preparation"[Title/Abstract] OR "simethicone"[Title/Abstract] OR "dimethicone"[Title/Abstract] OR "pronase"[Title/Abstract] OR "N-acetylcysteine "[Title/Abstract])

Results: 44 studies

After removing duplicates (n=1), 43 articles were found. 2 studies were considered potentially relevant and acquired in full text[2,3]. After reviewing the references of these 2 studies, another 10 were found to be related (assessment of preparation for EGD and adverse events). 0ne study was excluded because all procedures were performed without sedation.

Included studies 2 Metaanalyses [4,5], 8 RCTs [1,8], 1 cohort study [6]

Table 5.3.2s: Characteristics of the included studies.

Study (Author, year)	Country	Study design	No. of sites (no. of subjects)	Age (y)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm	Follow-up
Burke E, Surg Res Pract. 2021	n/a	Meta-analysis	13 studies with AE assessment, 6 included in the meta-analysis for effectiveness (11086 patients for AE assessment)	53.4	4908 (44.3%)	Premedication with defoaming and mucolytic agents	No premedication	No AE	No AE	N/A
Li Y, Saudi J Gastroenterol 2019	n/a	Meta-analysis	10 studies (5750) 4 for AE assessment	42.2 – 63.8	33.3 – 69.6	Premedication with simethicone (for whole study +/- other agents)	water	RR 0.45 (0.2-1.0) I2=0%	ref	N/A
Zhang Ly, Dig Endosc 2018	China	RCT	610 (1 center, an anesthesiologist administered propofol deep sedation to all)	50.1±12.5 51.0±11.6 p=0.391	40.7%	Premedication with simethicone_pronase	No premedication	SpO2 at: Gastric cardia 99.72±0.81 Duodenal papilla 98.22±1.36 Gastric fundus 98.46±1.01 All values NS	SpO2 at: Gastric cardia 99.71±0.75 Duodenal papilla 98.27±1.26 Gastric fundus 98.55±1.00	N/A
Cao L, Clin Transl	China	RCT	496 (1 center, all sedated)	Median 43 (33, 53) - 51	49%	simethicone+/- pronase +/- postural	saline +/- postural	Adverse events: nausea, abdominal distension, vomiting,	. Adverse events: nausea, abdominal	n/a

Gastroenterol 2024				(37, 57)		change	change	hemorrhage, perforation, and asphyxia. No AE/SAE in all study groups	distension, vomiting, hemorrhage, perforation, and asphyxia. No AE/SAE in all study groups	
Mahawongkajit P, Surg Endosc 2021	Thailand	RCT	128 (1 center, 25 sedated patients)	Mean 60.21 ± 12.75 - 61.18 ± 11.54	50.78%	Simethicone/simethicone+NAC/ simethicone+NAC+ sodium bicarbonate + peppermint oil	water	No AE	No AE	n/a
Duez L, Endosc Int Open 2022	Belgium	RCT	110(46 sedation with midazolam and butyl hyoscine, 1 center)	median age 45.5 years [range: 19–84]	49.1%	simethicone	water	Side effects (mild nausea, vomiting, regurgitation) p=0.58; no SAE	Side effects (mild nausea, vomiting, regurgitation) p=0.58; no SAE	n/a
Krishnamurthy V, Endosc Int Open 2022	India	RCT	768 (762 sedation 3mg midazolam1 center)	44.18	57%	Simethicone/NAC/simethicone+NAC	water	No AE	No AE	n/a
Fuentes-Valenzuela E, Revista Española de Enfermedades Digestivas 2023	Spain	cohort	205 (1 center, all propofol sedation endoscopists directed)	52.6	49.8%	Simethicone +NAC	No prep	Median SpO2 98 % (IQR 98-100) p=0.9. 7 cases of SpO2 <90. 5 cases of symptoms after EGD, P=0.04. No delayed AE	100 % (IQR 97-100) p=0.9. 3 cases of SpO2 <90. 19 cases of symptoms after EGD, P=0.04. No delayed AE	n/a
Manfredi G, Endosc Int Open	Italy	RCT	197(all under conscious sedation, 1	55±19 - 59±16	52.3%	Simethicone +NAC	No prep	No AE	No AE	n/a

2021			center)							
Nabi Z, Indian Journal of Gastroenterology 2023	India	RCT	800 (anestesiologist administred propofol sedation all1 center)	39 (32–49)	68.75%	Simethicone/ Simethicone +NAC/NAC	water	No AE	No AE	n/a
Liu X, Surg Endosc 2018	China	RCT	7243 (6 centers, anestesiologist administred propofol sedation all,	53.5 ± 7.6 - 53.9 ± 7.6	41.2%	Pronase+NaHCO3/simethicone/ Pronase+NaHCO3 + simethicone	water	No complications related to the endoscopic operation, no adverse events that need hospitalization	No complications related to the endoscopic operation, no adverse events that need hospitalization	n/a

Fig 5.3.1s. Can patients prepared with an oral solution of defoaming with or without mucolytics undergo sedated upper gastrointestinal endoscopy (all studies)?

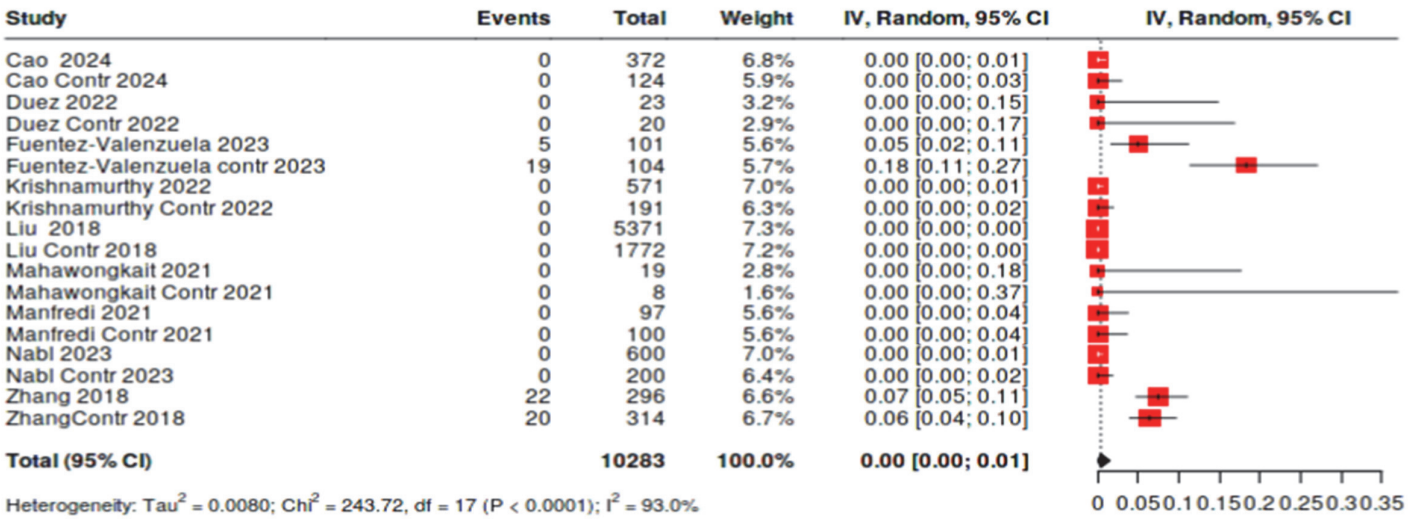

Fig 5.3.2s. Can patients prepared with an oral solution of defoaming with or without mucolytics, undergo sedated upper gastrointestinal endoscopy (only studies with nil by mouth as a comparator)?

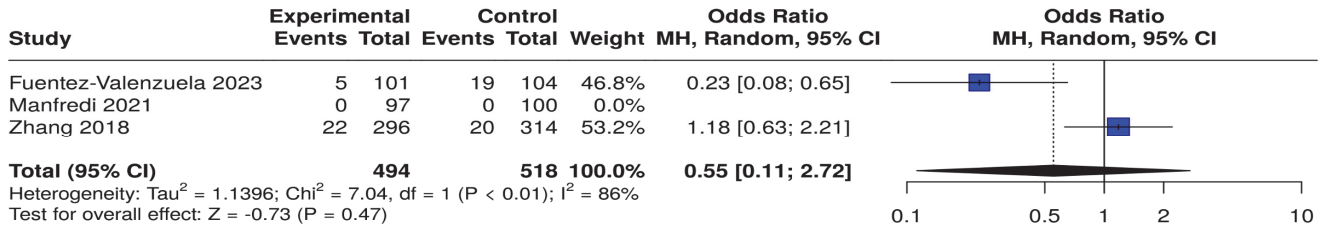

Table 5.3.3s Risk of Bias assessment

Study	Selection (max 4 stars)	Comparability (max 2 stars)	Outcomes (max 3 stars)	Quality (Total 9/9)
Fuentes-Valenzuela 2023	***	*	**	**Good**

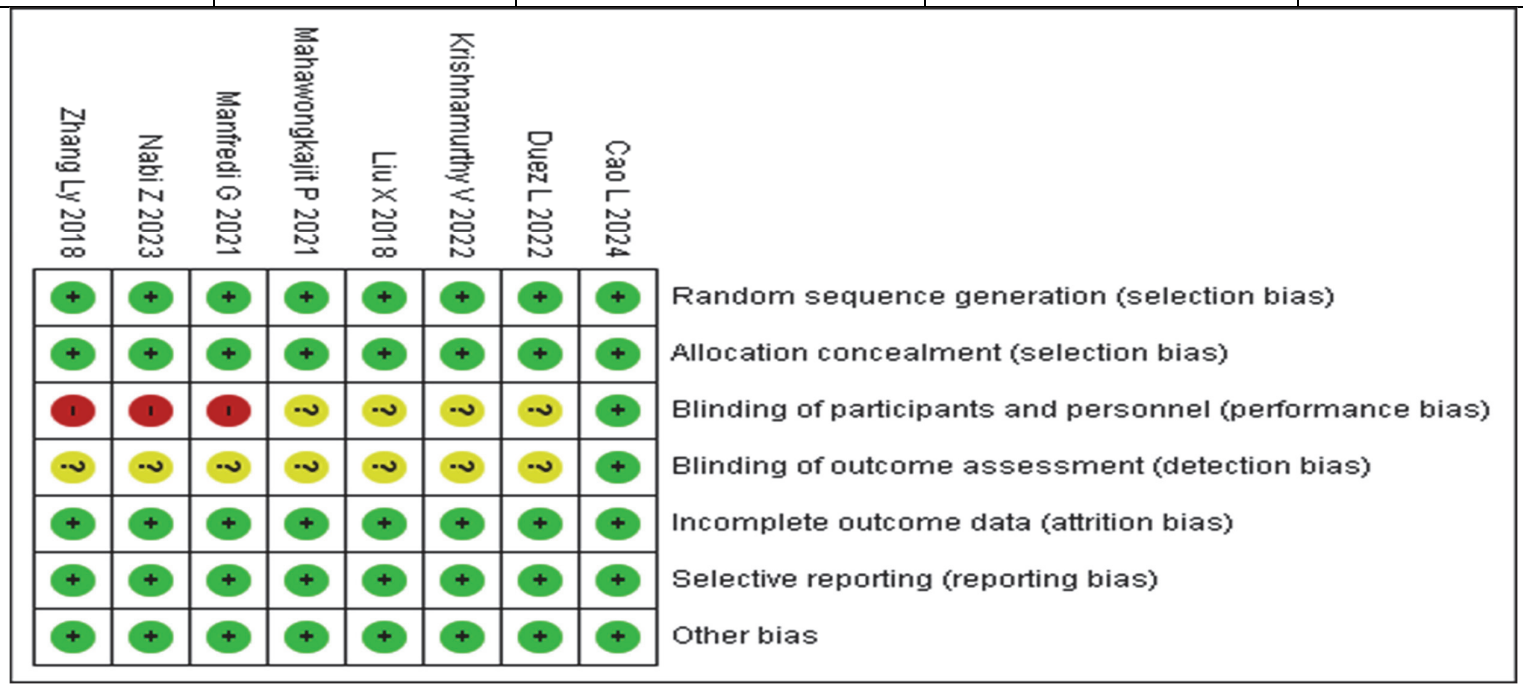

Table 5.3.4s Certainty of evidence assessment

The risk of bias assessment for each study can be found in **Table 5.3.3s**. The certainty of evidence in this PICO question was downgraded due to inconsistency (high heterogeneity), so the quality of evidence was downgraded to moderate.

Table 5.3.5s GRADE assessment for sedation administration compared to placebo for special situations

Bibliography: TF 5 for Special Situations. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With placebo	With Table 3 Q3		Risk with placebo	Risk difference with Table 3 Q3
Adverse Events											
10283 (8 randomised and one non-randomised)	not serious	serious[a]	not serious	not serious	none	⨁⨁⨁◯ Moderate[a]					0, 0-0.01

CI: confidence interval; **RR:** risk ratio

Explanations

a. Presence of significant heterogeneity in the outcome measures

References

1. Sidhu R, Turnbull D, Haboubi H, et al. British Society of Gastroenterology guidelines on sedation in gastrointestinal endoscopy. Gut 2024;73(2):219-245. (In eng). DOI: 10.1136/gutjnl-2023-330396.
2. Zhang LY, Li WY, Ji M, et al. Efficacy and safety of using premedication with simethicone/Pronase during upper gastrointestinal endoscopy examination with sedation: A single-center, prospective, single-blinded, randomized controlled trial. Digestive Endoscopy 2018;30(1):57-64. DOI: 10.1111/den.12952.
3. Cao L, Zheng F, Wang D, et al. The effect of using Premedication of simethicone/pronase with or without Postural Change on Visualization of the Mucosa before Endoscopy: A prospective, double-blinded, randomized controlled trial. Clinical and Translational Gastroenterology 2023. DOI: 10.14309/ctg.0000000000000625.
4. Burke E, Harkins P, Moriarty F, Ahmed I. Does Premedication with Mucolytic Agents Improve Mucosal Visualization during Oesophagogastroduodenoscopy: A Systematic Review and Meta-Analysis. Surgery Research and Practice 2021;2021:1-12. DOI: 10.1155/2021/1570121.
5. Li Y, Du F, Fu D. The effect of using simethicone with or without N-acetylcysteine before gastroscopy: A meta-analysis and systemic review. Saudi Journal of Gastroenterology: Wolters Kluwer Medknow Publications; 2019:218-228.
6. Fuentes-Valenzuela E, Pérez-Arenas E, de Benito Sanz M, et al. Prospective cohort study to evaluate premedication with simethicone and N-acetylcysteine for upper diagnostic gastrointestinal endoscopy. Revista Espanola de Enfermedades Digestivas 2023;115(1):10-15. DOI: 10.17235/reed.2022.8576/2022.

TASK FORCE 6: Training and quality

Leader: Theodor Voiosu

Members: Marcin Romanczyk, Theodor Voiosu

Q6.1: Training for sedation administration for GI procedures

Q6.2: Measuring quality in sedation and implementation of an improvement program for sedation in GI endoscopy

Table 6.1s PICOs

PICO question no.	Population	Intervention	Comparator	Outcome
1	Patients undergoing GI endoscopy under sedation	Measured quality parameters	Unmeasured quality parameters	Safety of the procedures
2	Patients undergoing GI endoscopy under sedation	Measured quality parameters	Unmeasured quality parameters	Outcome of the procedures
3	Patients undergoing GI endoscopy under sedation	Measured quality parameters	Unmeasured quality parameters	Patient's experience

BIBLIOGRAPHIC SEARCH

Bibliographic search strategies were performed in **PubMed** using the following search strategies:

a. **PubMed- Search [21.07.2024]**

("conscious sedation"[MeSH Terms] OR ("conscious"[All Fields] AND "sedation"[All Fields]) OR "conscious sedation"[All Fields] OR ("deep sedation"[MeSH Terms] OR ("deep"[All Fields] AND "sedation"[All Fields]) OR "deep sedation"[All Fields]) OR "conscious sedation"[MeSH Terms]) AND ("endoscopy"[Title/Abstract] OR "gastroscopy"[Title/Abstract] OR "colonoscopy"[Title/Abstract] OR "esophagogastroduodenoscopy"[Title/Abstract] OR "EUS"[Title/Abstract] OR "endoscopic ultrasound"[Title/Abstract] OR "ERCP"[Title/Abstract] OR "endoscopic retrograde

cholangiopancreatography"[Title/Abstract] OR "enteroscopy"[Title/Abstract]) AND ("quality assurance, health care"[MeSH Terms] OR "quality improvement"[MeSH Terms] OR "quality improvement"[Title/Abstract])

Results: 97 papers retrieved and reviewed (21.07.2024))

b. Results of the bibliographic searches

7 studies were considered potentially relevant and acquired in full text.

Included studies (examples)

0 Meta-analyses (refs)

2 RCTs (refs)

5 cohort studies (refs)

Table 6.2s: Characteristics of the included studies.

Study (Author, year)	Country	Study design	No. of sites (no. of subjects)	Age (y)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm	Follow-up
C Grant Anaesth Intensive Care. 2008	Australia	Cohort anesthesiologists	1 (3790, not clear how many post audit)	n/a	Na/	Audit based on electronic patietns report	Before audit	Sedation-related adverse events 6.3%	Sedation-related adverse events 2.8%	n/a
Conigliaro R, Endoscopy 2006	Italy	Cross sectional	29 (3733, 2164 sedated)	57 +/- 17.6 F 55 =/- 16.8 M	1837/3733	Specific training based on the sedation guidelines of SIED	Data before the training intervention	Compliance with guidelines – 66.4%	Compliance with sedation guidelines – 61.7%	n/a
Dietrich CG, Scand J	Germany	Observational	1	n/a	n/a	Application of	Before	Adverse event rate –	Adverse event rate –	n/a

Gastroenterol 2013		(cross-sectional)	(6435+6138)			S-3 guidelines	guidelines	NS (no exact values)	NS (no exact values)	
Branch R AANA J 2022	USG	Cross-sectional	1 (229)	53 SD 14.24 and 57 SD 14.45	39.74%	Preoxygenation of obese patients is done by a nurse before EGD	No preoxygenation	14.3% hypoxemic events p=0.003	30.8% of hypoxemic events	n/a
Sarkar S, Eur J Gastroenterol Hepatol. 2009	UK	Cross-sectional	1 (7234+5999)	59.6 and 60.4 years	n/a	NCEPOD, BSG, GRS guidelines	Before implementation	2% AE p=0.44	1.7% AE	30-day mortality (NS)
Harewood GC, Aliment Pharmacol Ther 2011	Irleand	RCT	1(206)	55.5 – 62.4	89/206	Prefilled midazolam syringes to a 6mg dose on discretion of endoscopists	Prefilled midazolam syringes to a 10 mg dose on discretion of endoscopists	No AE, lower dose	No AE, higher dose	n/a
Steenholdt Casper, Clinical Gastroenterology and Hepatology 2022;20:559–568	Denmark	RCT	1 (130)	41.9 (SD 13.3)	66 (50.7%)	NAPS (propofol) for colonoscopy in IBD patients	Midazolam + fentanyl for colonoscopy in IBD patients	Improved patient satisfaction score 60.1 (maximum possible 65) (SD 3.4)	Lower patient satisfaction score compared to NAPS – 51.2 (SD 8.4)	n/a

Table 6.3s: Risk of bias assessment for studies in **Q1**

Study	Selection (max 4 stars)	Comparability (max 2 stars)	Outcomes (max 3 stars)	Quality (Total 9/9)
C Grant, 2008	***	*	**	**Good**
Conigliaro R, 2006	***	**	**	**Good**
Dietrich CG, 2013	**	*	**	**Fair**
Branch R, 2022	**	*	**	**Fair**
Sarkar S, 2009	***	*	**	**Good**

Good quality: 3 or 4 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain.

Fair quality: 2 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain.

Poor quality: 0 or 1 star in selection domain OR 0 stars in comparability domain OR 0 or 1 stars in outcome/ exposure domain

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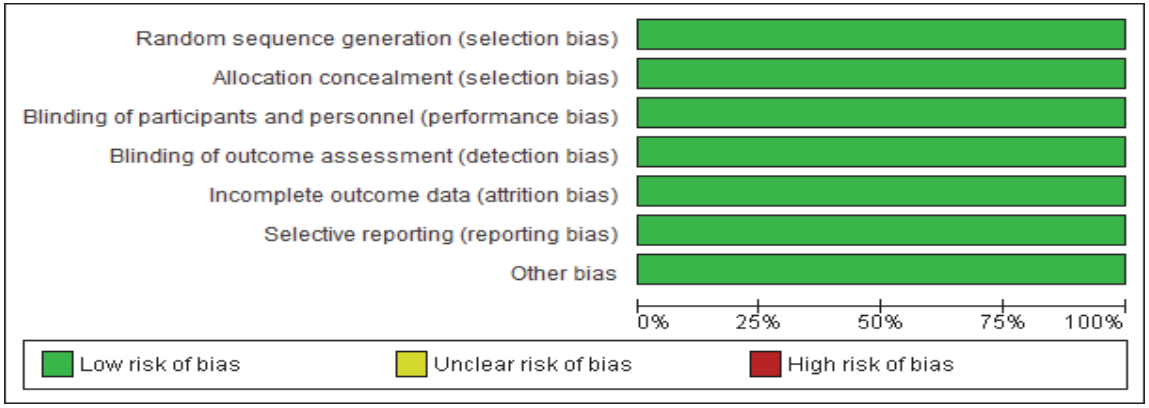
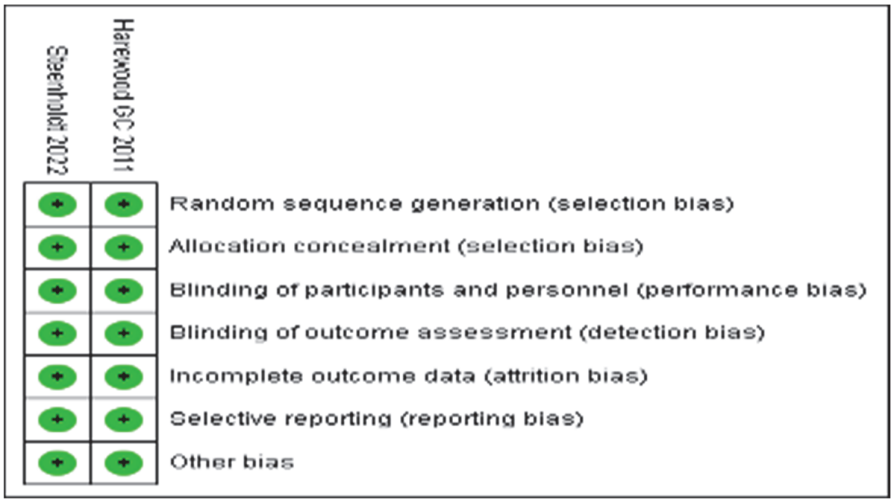
Table 6.4s: Risk of bias assessment for studies evaluating the quality of sedation administration measurements





Q6.3: Environmental impact of sedation during GI endoscopy

Table 6.5s. PICOs

PICO question no.	Population	Intervention	Comparator	Outcome
1	Patients undergoing GI endoscopy	Sedation	No sedation	Environmentally-harmful waste generated

BIBLIOGRAPHIC SEARCH

Bibliographic search strategies were performed in **PubMed** from inception to 15.07.2024 using the following search strategies:

PubMed- Search [DATE]

("conscious sedation"[Title/Abstract] OR "deep sedation"[Title/Abstract] OR "Anesthesia"[Title/Abstract] OR "Analgosedation"[Title/Abstract] OR "Sedation"[Title/Abstract] OR "nitrous oxide"[Title/Abstract] OR "propofol"[Title/Abstract] OR "midazolam"[Title/Abstract] OR "remimazolam"[Title/Abstract])

AND

("waste"[Title/Abstract] OR "pollution"[Title/Abstract] OR "sustainability"[Title/Abstract] OR "climat"[Title/Abstract] OR ("climat"[All Fields] AND "change"[Title/Abstract]) OR "green"[Title/Abstract] OR "greenhouse effect"[Title/Abstract] OR "greenhouse"[Title/Abstract] OR "carbon footprint"[Title/Abstract] OR "biodegradation"[Title/Abstract] OR "environment"[Title/Abstract] OR "environmental"[Title/Abstract])
AND

("endoscopy"[Title/Abstract] OR "gastroscopy"[Title/Abstract] OR "colonoscopy"[Title/Abstract] OR "esophagogastroduodenoscopy"[Title/Abstract] OR "EUS"[Title/Abstract] OR "endoscopic ultrasound"[Title/Abstract] OR "ERCP"[Title/Abstract] OR "endoscopic retrograde cholangiopancreatography"[Title/Abstract] OR "enteroscopy"[Title/Abstract])

Results: 75 studies

c. Results of the bibliographic searches

Excluded studies

73 studies(refs) were excluded after scanning the title/abstract due to lack of relevance to the topic of the search

Included studies (examples)

2 cohort studies (refs)

1. Gadd KJ, Wang S, Mauldon EC. Waste and cost of disposable drug and fluid products used in anaesthetist-provided sedation for gastrointestinal endoscopy. Anaesth Intensive Care. 2023 Mar;51(2):155-157.
2. Damle A, Andrew N, Kaur S, Orquiola A, Alavi K, Steele SR, Maykel J. Elimination of waste: creation of a successful Lean colonoscopy program at an academic medical center. Surg Endosc. 2016 Jul;30(7):3071-6

+ 2 additional papers identified scanning the references list

3. Nordin EJ, Dugan SM, Kusters AC, Schimek CA, Sherman KA, Ebert TJ. How an Audit-and-Feedback-Based Educational Program Contributed to a Reduction in Environmentally Harmful Waste Anesthetic Gases Among Anesthesiology Residents. J Grad Med Educ. 2024 Apr;16(2):175-181. doi: 10.4300/JGME-D-23-00402.1. Epub 2024 Apr 15. PMID: 38993317; PMCID: PMC11234298.
4. Yang L, Hubert J, Gitundu S, Brovman E, Cobey F. Carbon Footprint of Total Intravenous and Inhalation Anesthesia in the Transcatheter Aortic Valve Replacement Procedure. J Cardiothorac Vasc Anesth. 2024 Jun;38(6):1314-1321. doi: 10.1053/j.jvca.2024.02.027. Epub 2024 Feb 22. PMID: 38490897.

Table 6.6s: Characteristics of the included studies

Study (Author, year)	Country	Study design	No. of sites (no. of subjects)	Age (y)	Male sex (%)	Intervention	Comparator	Outcome in the intervention arm	Outcome in the comparator arm	Follow-up
Gadd KJ, Anaesth Intensive Care 2023	Australia	Observational	1 (57)	n/a	58%	-N/A	N/A-	Waste 4.0 (2.4–7.1 (0.66–21)) g/min (IQR range); Cost 0.48 (0.22–1.17 (0.04–3.18)) A$/min (IQR range)	N/A	n/a
Damle A, Surg Endosc 2016	USA	Cohort (staff)	1 (217)	n/a	n/a	Lean process	Previous to implementation	Sedation time (to scoping) 3.7 (SD 4.2) min	2.4 (SD1.6) min	n/a
Nordin EJ, J Grad Med Educ 2024	USA	Cohort (staff - residents)	40 residents	n/a	n/a	education program for residents	Previous to program	Fresh gas flow 1.42 l/min; 0.44; 95% CI 1.29-1.56; P<.0001;	Fresh gas flow 1.83 l/min STD 0.58 95% CI 1.67-2.02 P<.0001;	n/a
Yang L, J Cardiothorac Vasc Anesth 2024	USA	Cross-sectional	1 (604) TAVI patients	Abstract only n/a	Abstract only n/a	General anesthesia	Deep sedation	16.188 kg CO2e	1.518 kg CO2e p < 0.001	n/a

Table 6.7s: Risk of bias assessment for studies

Study	Selection (max 4 stars)	Comparability (max 2 stars)	Outcomes (max 3 stars)	Quality (Total 9/9)
Gadd KJ, 2023	**	*	**	**Fair**
Damle A, 2016	***	**	***	**Good**
Nordin EJ, 2024	***	**	***	**Good**
Yang L, J 2024	***	*	**	**Good**

Good quality: 3 or 4 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain.

Fair quality: 2 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain.

Poor quality: 0 or 1 star in selection domain OR 0 stars in comparability domain OR 0 or 1 stars in outcome/ exposure domain

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