

## Academy of Medicine, Singapore clinical guideline on the use of sedation by non-anaesthesiologists during gastrointestinal endoscopy in the hospital setting

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### ABSTRACT

**Introduction:** In Singapore, non-anaesthesiologists generally administer sedation during gastrointestinal endoscopy. The drugs used for sedation in hospital endoscopy centres now include propofol in addition to benzodiazepines and opiates. The requirements for peri-procedural monitoring and discharge protocols have also evolved. There is a need to develop an evidence-based clinical guideline on the safe and effective use of sedation by non-anaesthesiologists during gastrointestinal endoscopy in the hospital setting.

**Methods:** The Academy of Medicine, Singapore appointed an expert workgroup comprising 18 gastroenterologists, general surgeons and anaesthesiologists to develop guidelines on the use of sedation during gastrointestinal endoscopy. The workgroup formulated clinical questions related to different aspects of endoscopic sedation, conducted a relevant literature search, adopted Grading of Recommendations, Assessment, Development and Evaluation (GRADE) methodology and developed recommendations by consensus using a modified Delphi process.

**Results:** The workgroup made 16 recommendations encompassing 7 areas: (1) purpose of sedation, benefits and disadvantages of sedation during gastrointestinal endoscopy; (2) pre-procedural assessment, preparation and consent taking for sedation; (3) Efficacy and safety of drugs used in sedation; (4) the role of anaesthesiologist-administered sedation during gastrointestinal endoscopy; (5) performance of sedation; (6) post-sedation care and discharge after sedation; and (7) training in sedation for gastrointestinal endoscopy for non-anaesthesiologists.

**Conclusion:** These recommendations serve to guide clinical practice during sedation for gastrointestinal endoscopy by non-anaesthesiologists in the hospital setting.

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## CLINICAL IMPACT

### What is New

- This is the first Academy of Medicine, Singapore evidence-based guideline on the use of sedation during gastrointestinal endoscopy by non-anaesthesiologists, developed using Grading of Recommendations, Assessment, Development and Evaluation (GRADE) methodology.
- The guideline addresses the use of propofol for sedation by non-anaesthesiologists in the hospital setting.
- It highlights the importance of structured training for the safe and effective use of sedation.

### Clinical Implications

- This guideline will enhance the safety and quality of sedation during gastrointestinal endoscopy by non-anaesthesiologists in the hospital setting.

## INTRODUCTION

The practice of gastrointestinal (GI) endoscopy over the last 3 decades has seen both a rise in volume of routine procedures, and an increase in the breadth and complexity of procedures. Routine endoscopies have increased due to a growth in population size, and also due to the introduction of guidelines for the routine surveillance of malignant and pre-malignant lesions of the colon and the upper GI tract. There has also been a surge in the number of new complex endoscopic procedures. These more complex procedures last longer and may require patients to be well sedated. The expectations of patient populations have also changed. While gastroscopy and colonoscopy began as unsedated procedures, some patients now expect to be well sedated for routine diagnostic gastroscopy and colonoscopy.

The practice of GI endoscopy and sedation varies between different countries. In Singapore, both gastroenterologists and surgeons perform GI endoscopy. Endoscopic procedures are performed in either standalone ambulatory centres or endoscopy suites located within hospital premises. Internationally, the proportion of patients undergoing endoscopy who are sedated by endoscopists and by anaesthesiologists have increased. In the US, about 50% of patients are now sedated by anaesthesiologists.<sup>1</sup> Currently in Singapore, endoscopic sedation is often administered by the endoscopist because of considerations such as the established track record of safety and convenience,

anaesthesiology manpower constraints and additional costs associated with anaesthesiologist-administered sedation. Patients are assessed before endoscopy and those needing anaesthesiologist-administered sedation will receive that level of care. For the others, the endoscopist has been safely delivering sedation. The drugs used for sedation during GI endoscopy in hospital endoscopy centres now include propofol—in addition to benzodiazepines and opiates—unlike standalone ambulatory centres, which do not use propofol without anaesthesiologist support. The requirements for peri-procedural monitoring and discharge protocols have evolved. There is a need to develop an evidence-based clinical guideline on the safe and effective use of sedation by non-anaesthesiologists during GI endoscopy in Singapore in the hospital setting. While a guideline on the use of sedation by non-anaesthesiologists for medical and dental clinics, standalone ambulatory surgical centres and standalone endoscopy suites in Singapore has been published by the Ministry of Health (last updated in July 2021),<sup>2</sup> it does not address the issues pertinent to the hospital setting. This guideline bears no reference to the guideline for standalone endoscopy suites.<sup>2</sup> It focuses specifically on the use of sedation by non-anaesthesiologists for all GI endoscopy procedures performed within the hospital setting in adult patients. There is an extensive body of evidence for the safety and efficacy of various drugs in GI endoscopy sedation. There is also a difference between hospital-based practice and non-hospital-based practice.

## METHODS

The Academy of Medicine, Singapore (AMS) appointed an expert workgroup led by 2 co-chairs to develop a guideline on the use of sedation during GI endoscopy. (See Supplementary Materials for Appendix 1 in online version of this article.) The group comprising 9 gastroenterologists, 7 general surgeons and 2 anaesthesiologists who were fellows of AMS, involved both public and private sector stakeholders. The workgroup was divided into sections to examine clinical questions (CQ) for different aspects of endoscopic sedation (Table 1). Literature search specific to each CQ was performed by the individual sections. Table S1 (Appendix 2 in online Supplementary Materials) provides literature search terms. PubMed database was searched for original articles, meta-analyses and guidelines related to the practice of GI endoscopy and sedation use, focusing on the efficacy and safety of different types of sedation (benzodiazepines, opiates and propofol), personnel administering the sedation, as well as sedation monitoring. Meta-analyses

and randomised trials were prioritised over observational studies. The references of guidelines previously published by academic societies were also reviewed for additional relevant literature. The search period was up to 31 March 2021. Each section generated an initial set of statements. Grading of Recommendations, Assessment, Development and Evaluation (GRADE) methodology was used to evaluate the quality of evidence and assess the strength of recommendations (Table 2).<sup>3</sup> These statements were collated and edited by the co-chairmen before circulation to the entire workgroup for the first round of voting, comments and modification.

The formal consensus procedure used the modified Delphi technique. The first round of voting was conducted electronically. For each statement, members were asked to vote on whether to “accept completely”, “accept with some reservations”, “accept with major reservations”, “reject with some reservations” or “reject completely”. The statements were modified based on the comments received. The modified statements were discussed and voted on in a second round of voting during an in-person meeting on 10 April 2021 at the Academy of Medicine, Singapore. The voting process with contributions of content and voting results were documented. A statement was accepted if 80% or more of the group voted to “accept completely” or “accept with some reservations”. The explanatory text for each statement was drafted by the workgroup members of the section responsible for the specific CQ. The 2 co-chairs compiled and edited the full manuscript, which was then circulated to all workgroup members for vetting. The completed guideline was formally circulated by email for review by the governing Council of AMS and it was endorsed by the AMS Council without further amendment. Feedback through email was sought from Ministry of Health, Singapore and minor amendments were made to the manuscript explanatory text to provide greater clarity of its purpose and applicability. The statements are summarised in Table 3.

## RESULTS

### *CQ1: Purpose of sedation, benefits and disadvantages of sedation during GI endoscopy*

**Statement 1: Sedation should be offered to every patient undergoing endoscopy. Specific informed consent should be taken for procedural sedation after the risks and benefits have been discussed with the patient.**

Quality of evidence: Moderate

Strength of recommendation: Strong

Agreement: 94.4%

Table 1. Clinical questions

|    |                                                                                                    |
|----|----------------------------------------------------------------------------------------------------|
| 1. | Purpose of sedation, benefits and disadvantages of sedation during gastrointestinal (GI) endoscopy |
| 2. | Pre-procedural assessment, preparation and consent-taking for sedation                             |
| 3. | Efficacy and safety of drugs used in GI endoscopy sedation                                         |
| 4. | The role of anaesthesiologist-administered sedation during GI endoscopy                            |
| 5. | Intraprocedure monitoring of sedated patient                                                       |
| 6. | Post-sedation care and discharge after sedation                                                    |
| 7. | Training in sedation for GI endoscopy for non-anaesthesiologist                                    |

Table 2. Grading of Recommendations Assessment, Development and Evaluation (GRADE)

| Quality of evidence                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> <li>• <b>High:</b> Consistent evidence from well-performed randomised, controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk.</li> <li>• <b>Moderate:</b> Evidence from randomised, controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other research design. Further research (if performed) is likely to have an impact on our confidence in the estimate of benefit and risk and may change the estimate.</li> <li>• <b>Low:</b> Evidence from observational studies, unsystematic clinical experience, or from randomised, controlled trials with serious flaws. Any estimate of effect is uncertain.</li> </ul> |
| Strength of recommendation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| <ul style="list-style-type: none"> <li>• <b>Strong recommendation:</b> When it is very certain that benefits outweigh risks and burdens (such as difficulties of therapy and costs), or vice versa.</li> <li>• <b>Weak recommendation:</b> When risks and burdens appear to be finely balanced, or when there is appreciable uncertainty about the magnitude of benefits and risks.</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                          |

Procedural sedation, besides the direct benefit of reducing procedural discomfort,<sup>4</sup> has also been shown to reduce patient anxiety and results in greater willingness to repeat the procedure.<sup>5</sup> From the perspective of the endoscopist, there is also evidence of sedation improving endoscopy quality. For example, a recent single-centre review of outpatient colonoscopies demonstrated sedation to be associated with improved caecal intubation rates and adenoma detection rates.<sup>6</sup>

An important part of patient autonomy involves ensuring that patients give consent to procedural sedation. This allows the patient to make voluntary decision on their medical care after having understood the attendant benefits and risks of sedation. Consent for procedural moderate sedation should be taken by an individual familiar with the sedation process. Procedural sedation may be administered by a non-anaesthesiologist or an anaesthesiologist. When medically relevant or when practicable, this option will be discussed with the patient.

Table 3. Summary of statements

|                                                                                                    | Statements                                                                                                                                                                                                                | Quality of evidence | Strength of recommendation | Final vote |
|----------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|----------------------------|------------|
| Purpose of sedation, benefits and disadvantages of sedation during gastrointestinal (GI) endoscopy |                                                                                                                                                                                                                           |                     |                            |            |
| Pre-procedural assessment, preparation and consent-taking for sedation                             |                                                                                                                                                                                                                           |                     |                            |            |
| 1                                                                                                  | Sedation should be offered to every patient undergoing endoscopy. Specific informed consent should be taken for procedural sedation after the risks and benefits have been discussed with the patient.                    | Moderate            | Strong                     | 94.4%      |
| 2                                                                                                  | Unsedated endoscopy is possible in selected patients. We recommend that where unsedated endoscopy is planned, options should be discussed ahead should the patient not be able to tolerate an unsedated procedure.        | Moderate            | Strong                     | 100%       |
| 3                                                                                                  | Patients undergoing sedation should be assessed medically for risks of sedation.                                                                                                                                          | Low                 | Strong                     | 100%       |
| Efficacy and safety of drugs used in GI endoscopy sedation                                         |                                                                                                                                                                                                                           |                     |                            |            |
| 4                                                                                                  | A benzodiazepine alone or in combination with an opioid is an option for sedation for patients undergoing diagnostic and therapeutic gastrointestinal endoscopy.                                                          | High                | Strong                     | 100%       |
| 5                                                                                                  | Propofol alone or in combination with a benzodiazepine or opioid is an option for sedation for patients undergoing diagnostic and therapeutic gastrointestinal endoscopy.                                                 | High                | Strong                     | 100%       |
| The role of anaesthesiologist-administered sedation during GI endoscopy                            |                                                                                                                                                                                                                           |                     |                            |            |
| 6                                                                                                  | Propofol sedation for gastrointestinal endoscopy can be safely and effectively administered by trained non-anaesthesiologists.                                                                                            | High                | <b>Weak</b>                | 94.4%      |
| 7                                                                                                  | We recommend anaesthesiologist-administered sedation in patients with a high-risk profile.                                                                                                                                | Low                 | Strong                     | 100%       |
| Intraprocedure monitoring of sedated patient                                                       |                                                                                                                                                                                                                           |                     |                            |            |
| 8                                                                                                  | A dedicated and trained assistant for sedation monitoring should be available during the procedure.                                                                                                                       | Low                 | Strong                     | 94.4%      |
| 9                                                                                                  | An individual trained in airway management and resuscitation should be on-site or immediately available.                                                                                                                  | Low                 | Strong                     | 100%       |
| 10                                                                                                 | Continuous oximetry monitoring is recommended for gastrointestinal endoscopy monitoring.                                                                                                                                  | Low                 | Strong                     | 100%       |
| Post-sedation care and discharge after sedation                                                    |                                                                                                                                                                                                                           |                     |                            |            |
| 11                                                                                                 | We recommend that the patient's clinical parameters should be monitored after endoscopy by trained staff until fit for discharge.                                                                                         | Low                 | Strong                     | 100%       |
| 12                                                                                                 | We recommend the usage of a discharge scoring system, e.g. Post-Anaesthetic Discharge Scoring System (PADSS) or Modified Aldrete Score, to assess if patient has recovered sufficiently post-sedation to allow discharge. | Low                 | Strong                     | 100%       |
| 13                                                                                                 | We recommend that patients who have received sedation should be told what is safe for them to do.                                                                                                                         | Low                 | Strong                     | 100%       |
| Training in sedation for GI endoscopy for non-anaesthesiologist                                    |                                                                                                                                                                                                                           |                     |                            |            |
| 14                                                                                                 | The person providing sedation should attend a sedation course.                                                                                                                                                            | Low                 | Strong                     | 100%       |
| 15                                                                                                 | Training in sedation should be structured. There should be assessment of competencies prior to the independent administration of sedation.                                                                                | Low                 | Strong                     | 100%       |
| 16                                                                                                 | Non-anaesthesiologists using propofol for sedation should have additional training with respect to propofol. They should have training for resuscitation with emphasis on airway management.                              | Low                 | Strong                     | 88.9%      |

The components of appropriate informed consent for procedural sedation include the following:

1. Specific informed consent must be obtained prior to procedural sedation. Ideally, this should be in documented consent, and not just oral or implied consent.
2. The sedation consent is either taken personally by the sedationist, or another healthcare provider in the context of team-based practice. There should be appropriate training and education of all healthcare providers taking sedation consent.
3. Informed consent should be carried out by trained and competent staff in a manner and language the patient can understand. If there are language difficulties, interpreters must be used.
4. The identity of the individual providing the information to the patient and family is to be documented in the medical records.
5. The purpose, risks, benefits and alternatives relating to procedural sedation are to be discussed with the patient, or with those who make decisions for the patient such as his or her family.
6. The patient may withdraw or modify his or her consent at any time.
7. The clinician must ensure that the patient understands the information given regarding sedation consent.
8. Major complications and risks of procedural sedation should be communicated to the patient.

**Statement 2: Unsedated endoscopy is possible in selected patients. We recommend that where unsedated endoscopy is planned, options should be discussed ahead should the patient not be able to tolerate an unsedated procedure.**

Quality of evidence: Moderate

Strength of recommendation: Strong

Agreement: 100%

Sedation during endoscopy may improve rate of complete endoscopies, the quality of endoscopic examination and outcomes of therapeutic endoscopy.<sup>4,6</sup> However, there are instances where sedation is not required or is not desired by the patient. These include procedures that are relatively short and less stimulating, e.g. flexible sigmoidoscopy<sup>7</sup> or water-insufflation colonoscopy.<sup>8,9</sup> Patients in whom sedation poses an increased risk, such as patients with severe obstructive sleep apnoea, may also choose to undergo endoscopy unsedated. In patients where unsedated endoscopy has been planned, it is reasonable to discuss options

should the patient not be able to tolerate the procedure unsedated. These options include the administration of sedation by the endoscopist (for which pre-procedure assessment should be performed and consent taken), or cancellation and rescheduling of the procedure with anaesthesiologist support where appropriate.

### ***CQ2: Pre-procedural assessment, preparation and consent taking for sedation***

**Statement 3: Patients undergoing sedation should be assessed medically for risks of sedation.**

Quality of evidence: Low

Strength of recommendation: Strong

Agreement: 100%

Pre-procedure assessment should be done to determine whether an anaesthesiologist should be involved during the sedation for the endoscopy.<sup>10-12</sup> This includes taking history and reviewing the medical records, performing a focused physical examination, and reviewing available investigations (Table 4 provides an example of such a schema).

### ***CQ3: Efficacy and safety of drugs used in GI endoscopy sedation***

**Statement 4: A benzodiazepine alone or in combination with an opioid is an option for sedation for patients undergoing diagnostic and therapeutic gastrointestinal endoscopy.**

Quality of evidence: High

Strength of recommendation: Strong

Agreement: 100%

Adequate comfort improves the safety and quality of digestive endoscopy.<sup>6,13,14</sup> Nearly all gastroscopies in the US and Australia are done with sedation and greater than 98% of the colonoscopies done in the US, Australia and Canada involve the use of sedation.<sup>15</sup> Although sedation practices vary from country to country, among the drugs used most commonly for GI endoscopy are opioids and benzodiazepines.

A benzodiazepine is typically used to minimise anxiety and to provide sedation during digestive endoscopy.<sup>12</sup> Its amnesic property helps in persuading patients for repeat procedures when indicated. An opioid, on the other hand, provides both sedative and analgesic effects and improves the quality of endoscopy. The combination of a benzodiazepine and opioid has been accepted and adopted by endoscopists worldwide as a regimen for

Table 4. Pre-procedure assessment for sedation

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1. History                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| a. Significant past medical history such as cardiopulmonary disorders                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| b. Stridor, snoring or obstructive sleep apnoea                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| c. Adverse reaction to sedation or anaesthesia                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| d. Current medications and allergies                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| e. Alcohol use                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| f. American Society of Anesthesiologists (ASA) physical status classification                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| i. ASA I, ASA II patients and some ASA III patients are appropriate candidates for administration of sedation by an endoscopist.                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| ii. The assistance of an anaesthesiologist should be considered for some ASA III and all ASA IV, V patients.                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| 2. Physical examination                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| a. Vital signs and weight                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| b. Auscultation of heart and lungs                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| c. Baseline level of consciousness                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| d. Assessment of airway                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| • The airway evaluation is designed to identify patients with anatomy that may make emergency tracheal intubation during resuscitation more difficult. This includes patients with obesity, short thick neck, cervical spine disease, decreased hyoid-mental distance, decreased thyromental distance, short inter-incisor distance and structural abnormalities of the mouth, jaw and oral cavity, and higher Mallampati score. Anaesthesiologist referral and support may need to be considered in patients with such airway abnormalities undergoing sedation. |
| 3. Investigation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| a. Blood test: not routinely indicated                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| b. Electrocardiogram: not routinely indicated                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| c. Chest X-ray: not routinely indicated                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |

providing moderate sedation for routine GI endoscopy.<sup>16,17</sup> Although this approach carries a small risk of adverse events including hypotension, hypoxia, cardiac arrhythmia and apnoea, these risks have largely been mitigated with active pre-procedure case selection, intraprocedure and post-procedure monitoring.<sup>18</sup> The overall cost-benefit effect after risk balancing is in favour of such sedation regime in both inpatient and outpatient settings provided there are no added risk factors for sedation related adverse events.

**Statement 5: Propofol alone or in combination with a benzodiazepine or opioid is an option for sedation for patients undergoing diagnostic and therapeutic gastrointestinal endoscopy.**

Quality of evidence: High

Strength of recommendation: Strong

Agreement: 100%

#### *Efficacy and safety of propofol*

Propofol sedation is efficacious and has advantages over benzodiazepines and other sedatives for GI endoscopy, in terms of peri-procedural amnesia effect, faster recovery profile, patient satisfaction and endoscopist satisfaction. Propofol is more effective and safer than benzodiazepine in diagnostic and therapeutic endoscopy in patients with certain comorbidities such as liver cirrhosis.<sup>19</sup> Propofol sedation is efficacious

and is equivalent to benzodiazepines for GI endoscopy in terms of peri-procedural haemodynamic changes and oxygenation. There is abundant medical literature in the form of randomised control trials<sup>19-63</sup> as well as meta-analyses/systematic reviews<sup>5,64-72</sup> comparing the use of propofol with benzodiazepines during GI endoscopy. Most studies were published from the year 2000 onwards with the majority concentrated in the last 10 years. The studies originated from centres with different healthcare systems from across the world, involving both adult and paediatric endoscopic procedures. The studies included diagnostic gastroscopy and colonoscopy, balloon-assisted enteroscopy, endoscopic ultrasound (EUS), and therapeutic procedures such as oesophageal band ligation, endoscopic mucosal resection and endoscopic retrograde cholangiopancreatography (ERCP). The studies assessed metrics related to patient cardiorespiratory parameters (oxygen saturation, heart rate and blood pressure) and related adverse events (hypoxaemia, bradycardia, hypotension and necessity of airway intervention), technical performance of endoscopy (e.g. caecal intubation and time to completion), recovery time, patient's satisfaction and endoscopist's satisfaction. A significant finding was that propofol was associated with faster recovery time after endoscopy. There was also improved patient satisfaction and endoscopist satisfaction with the use propofol. Meta-analyses noted that propofol sedation produced deeper sedation than traditional agents.<sup>5,64-72</sup> However, there

was no difference in complications in respect to cardiorespiratory parameters, with the exception of 1 meta-analysis noting a higher incidence of hypotension in propofol sedation.<sup>64</sup> One meta-analysis noted lower cardiorespiratory complications (blood pressure, oxygen saturation and heart rate) in the group sedated with propofol for colonoscopy but there were no differences in complications for other endoscopic procedures.<sup>69</sup> Propofol was also associated with a significantly faster recovery time. Both patients' and endoscopists' satisfaction was better with propofol than traditional agents. The confidence intervals in the meta-analyses were not wide.

In the 45 randomised control trials, propofol was compared with other sedation agents such as midazolam, fentanyl and etomidate.<sup>19-63</sup> Propofol was either given as monotherapy or in combination with one of these agents. Salient findings are as listed: propofol results in faster recovery time; propofol gives better quality upper GI endoscopy; propofol used in cirrhotic patients results in much less issues with hepatic encephalopathy post-sedation;<sup>19,23</sup> the adverse events were similar whether propofol was used or added to traditional agents; and etomidate is a promising alternative to propofol.

#### *Propofol monotherapy versus combination therapy*

Monotherapy propofol sedation has a low sedation-related complication rate. A recent large (n=368,206) multicentre German study recorded a 0.01% rate for major complication, where propofol monosedation had the lowest rate (odds ratio 0.75) compared with midazolam (reference) and combinations (odds ratio 1.0–1.5).<sup>73</sup> In a randomised controlled trial of 150 elderly patients 80 years or older presenting for routine ERCP, propofol as a single sedation agent was superior to midazolam and pethidine in terms of patient cooperation, recovery times and recovery score; with comparable intraprocedural desaturation.<sup>74</sup> In contrast, a randomised controlled trial (n=135) comparing propofol versus propofol and midazolam for colonoscopy sedation by non-anaesthesiologists showed that drug synergy in the combination group improved patient satisfaction rates but prolonged recovery time.<sup>39</sup> A dose-ranging study with propofol and increasing doses of fentanyl (up to 1µg/kg) in elderly colonoscopy patients (n=90) demonstrated that propofol dose can be reduced with combination therapy without significant difference in anaesthesia associated adverse events.<sup>75</sup> Similarly, safe and effective sedation for colonoscopy (n=121) with low-dose propofol together with dexmedetomidine or intranasal sufentanil or pethidine, can be achieved in different regimens.<sup>76</sup> Combination sedation regimens with preprocedural oral

midazolam 7.5mg and propofol showed a propofol-sparing effect with less procedural anxiety and intraprocedural desaturation versus propofol monotherapy.<sup>77</sup> Large observational studies have demonstrated that propofol monotherapy has lower complication rates. However, several randomised controlled trials have shown that combination sedation can also be safely and effectively administered. Therefore, the evidence to support propofol monotherapy over propofol combination therapy is conflicting and the recommendation is weak. The experience of the endoscopist/sedationist utilising different regimens would be an important consideration for the use of combination therapy, vis-à-vis propofol with midazolam, dexmedetomidine, fentanyl, pethidine or other anxiolytic or analgesic agents.

#### **Statement 6: Propofol sedation for gastrointestinal endoscopy can be safely and effectively administered by trained non-anaesthesiologists.**

Quality of evidence: High

Strength of recommendation: Weak

Agreement: 94.4%

On the question of the safety of non-anaesthesiologist-administered propofol for sedation during endoscopy, 2 areas were investigated, namely comparison of non-anaesthesiologist-administered versus anaesthesiologist-administered propofol for sedation in endoscopy and comparison of non-anaesthesiologist-administered propofol versus benzodiazepine. Three meta-analyses showed that the incidence of complications such as hypoxia and requirements for airway intervention during endoscopy were similar in both the non-anaesthesiologist-administered and anaesthesiologist-administered propofol groups.<sup>78-80</sup> Bradycardia was more common in the non-anaesthesiologist group. The non-anaesthesiologist group administered lower doses of propofol.

In the 2 randomised control trials directly comparing non-anaesthesiologist-administered versus anaesthesiologist-administered propofol, restricted to low-risk patients (American Society of Anesthesiologists [ASA] I–II), there were no differences between the 2 groups in complication rates (hypoxaemia, airway intervention, hypotension and bradycardia), technical success of endoscopy, as well as patient and endoscopist satisfaction.<sup>81,82</sup> In 3 large case series, 2 studies showed anaesthesiologist-administered sedation resulted in higher rates of serious adverse effects events and did not provide a safety benefit over non-anaesthesiologist-directed sedation, as well as higher rate of colonoscopy complications.<sup>83,84</sup> The third and smallest case series

concluded equal effectiveness of both non-anaesthesiologist-administered propofol and anaesthesiologist-administered propofol.<sup>85</sup> A small single-centre study by Goudra et al. showed that “the frequencies of most adverse events were significantly higher in patients anaesthetised with propofol”.<sup>86</sup> This study compared adverse events when patients were sedated with propofol by anaesthesiologists or anaesthesiology nurses compared with non-propofol-based sedation by endoscopists. These conclusions have to be taken in the context of the limitations of case series studies where inherent bias may be present. In the randomised control trials comparing non-anaesthesiologist-administered sedation using propofol compared with benzodiazepine-based regimes, there was uniformity and concordance; there was no difference in safety and complication rates between the 2 groups.<sup>39,45,87-89</sup>

These studies comprising meta-analyses, randomised control trials and non-randomised studies point to safety of non-anaesthesiologist-administered propofol for sedation in endoscopy, in particular when compared to anaesthesiologist-administered propofol sedation, and compared to non-propofol, benzodiazepine-based regimens. We note that propofol was associated with a shorter recovery time, although it has a narrow therapeutic range and no reversal agent, with a tendency for progression from moderate to deep sedation.

The current product insert by the manufacturer states that propofol should be administered by “persons trained in the administration of general anaesthesia”. Published evidence shows the efficacy and safety of non-anaesthesiologist-administered propofol for endoscopy compared with anaesthesiologist-administered propofol sedation. The product insert does not take into account post-marketing extensive evidence on the safety of propofol in the real-world setting, and propofol sedation is already currently been administered by non-anaesthesiologists. It is because of this evidence that it was felt necessary to have separate guidelines for sedation in GI endoscopy to create a framework for safe practice. The resources required to enable this parity in safety and efficacy should be noted. Specifically, the availability of clinical protocols, training requirements of non-anaesthesiologists, availability of personnel trained in airway management, and the manpower onsite. In the absence of a funnel plot, we also cannot rule out publication bias from the meta-analyses.<sup>78-80</sup> Dossa et al. performed a systemic review of the recommendations from published North American and European guidelines on sedation practices for routine GI endoscopy, and found that recommendations relating to the drugs to be

used for sedation, the healthcare personnel capable of administering propofol and monitoring patients sedated with propofol, and the need for capnography when monitoring sedated patients varied.<sup>90</sup> There are controversies and limitations of available data and recommendations. We find that the level of evidence for this proposed recommendation statement moderate to high, with a weak recommendation due to possible publication bias, indirectness and the imprecision of the studies. The critical issue for endoscopic procedures is not the administration of propofol by an anaesthesiologist versus an endoscopist, but rather the monitoring of the patient to detect complications, the ability of the physician to recognise and manage the complications, and the availability of resources to manage these complications.

#### ***CQ4: The role of anaesthesiologist administered sedation during gastrointestinal endoscopy***

**Statement 7: We recommend anaesthesiologist-administered sedation in patients with a high-risk profile.**

Quality of evidence: Low

Strength of recommendation: Strong

Agreement: 100%

A high-risk profile includes critically ill and/or decompensated patients (ASA IV–V); some ASA III patients; the presence of pathological anatomical features associated with a higher risk of airway obstruction during the intervention; history of obstructive sleep apnoea; obese patients with BMI > 35 kg/m<sup>2</sup>; anticipated difficult airway; anticipated or history of intolerance to moderate sedation; patients with high risk of aspiration, prolonged or complex therapeutic endoscopic procedures requiring deep sedation; and anticipated difficulty in sedating patient.

The need for anaesthesiologist-administered sedation can be divided into patient and procedural factors. Patient factors include patients with a high-risk profile;<sup>11,91</sup> patients with anatomic or post-therapy airway variants predisposing to airway obstruction; patients with anticipated intolerance to standard sedatives, e.g. a history of alcohol or substance abuse; pregnancy; morbid obesity; neurologic or neuromuscular disorders; severe obstructive sleep apnoea; and patients who are uncooperative or delirious. The endoscopist may want to consider anaesthesiologist-administered sedation in geriatric patients and patients with BMI > 30 kg/m<sup>2</sup>.

Procedural factors include prolonged or therapeutic procedures requiring deep sedation.<sup>11</sup>

In keeping with patient autonomy, the endoscopist may also consider anaesthesiologist-administered sedation in patients who have requested for an anaesthesiologist.

***CQ5: Intraprocedure monitoring of the sedated patient***

**Statement 8: A dedicated and trained assistant for sedation monitoring should be available during the procedure.**

Quality of evidence: Low

Strength of recommendation: Strong

Agreement: 94.4%

Monitoring of a patient under sedation serves the following purposes:

1. Gauge the level of sedation reached. This allows titration of the drugs used.
2. Observe and evaluate physiologic functions and extent of changes.
4. Early detection of unintended depth of sedation.
5. Evaluate patient's responses to intervention.

It is recommended that a dedicated and trained assistant, who could be a nurse or physician, be assigned to monitor the sedated patient and should have no other major duty.<sup>92-99</sup> Such individuals would have been trained to recognise and react to abnormalities in the parameters being monitored. While the assistant may provide momentary non-technical assistance to the other staff engaged in the technical part of the endoscopy, attention on the patient must not be diverted by these tasks.

**Statement 9: An individual trained in airway management and resuscitation should be on-site or immediately available.**

Quality of evidence: Low

Strength of recommendation: Strong

Agreement: 100%

A sedated patient is at risk of hypoventilation, obstruction, apnoea or losing the airway, which leads to hypercapnia and hypoxaemia.<sup>9,21</sup> Often ventilatory support would stabilise the patient.<sup>73</sup> In the hospital setting, an emergency response team (e.g. code blue team) with personnel proficient in airway management and cardiac resuscitation should be available at all time of the day. In the absence of this team, the endoscopist and/or endoscopy nurse should be trained and competent in airway management and resuscitation. Airway management equipment must be readily available.

**Statement 10: Continuous oximetry monitoring is recommended for gastrointestinal endoscopy monitoring.**

Quality of evidence: Low

Strength of recommendation: Strong

Agreement: 100%

The use of oximetry is currently ubiquitous in clinical practice, because of its easy non-invasive application, low cost and negligible risk. Observational studies have shown the utility of oximetry when procedural sedation is administered for endoscopy.<sup>100-102</sup> Timely intervention is enhanced with the use of oximetry monitoring in endoscopy units, which in turn improves patient safety.<sup>103</sup> In contrast, Bilotta et al. monitored oximetry in 103 patients undergoing office colonoscopy. As there were no adverse outcomes noted in this small patient group, the authors suggested that oximetry monitoring may not be clinically useful in low-risk endoscopies.<sup>104</sup>

***Other monitoring devices***

The group considered the evidence for the routine use of capnography and continuous electrocardiogram for intraprocedural monitoring but decided against making statements on their use as there was variation in actual clinical practice, differences in opinion about the necessity, and we did not consider these to be crucial in all cases.

***CQ6: Post-sedation care and discharge after sedation***

**Statement 11: We recommend that the patient's clinical parameters should be monitored after endoscopy by trained staff until fit for discharge.**

Quality of evidence: Low

Strength of recommendation: Strong

Agreement: 100%

In general, evidence on post-sedation care and discharge after endoscopic procedures is limited. Post-sedation complications (commonly hypoxia, hypotension or stridor) may happen after completion of the procedure. This usually happens within 30 minutes from the final sedative administration or in patients who have received reversal agents during or after the procedure.<sup>105</sup> Therefore, clear documentation of the sedative administration timing and usage of reversal agents is essential. Patients who have received sedation need to be closely monitored post-procedure by trained staff who can recognise and manage any common complications early. These complications are observed to be less

frequent when patients received propofol monotherapy, compared to the combination of benzodiazepines and opioids.<sup>74</sup>

**Statement 12: We recommend the usage of a discharge scoring system, e.g. Post-Anaesthetic Discharge Scoring System (PADSS) or Modified Aldrete Score, to assess if patient has recovered sufficiently post-sedation to allow discharge.**

Quality of evidence: Low

Strength of recommendation: Strong

Agreement: 100%

There are several discharge scoring systems available. The commonly used scoring systems are Post-Anaesthetic Discharge Scoring System (PADSS) and Modified Aldrete Score, which use the combination of vital signs, functional status and symptoms to allow trained staff to objectively assess if patients can be safely discharged after receiving sedation. Usage of these scoring systems may also allow earlier discharge, with no additional adverse outcome, compared to conventional clinical assessment.<sup>106-109</sup> These scoring systems, however, do not measure a patient's psychomotor or cognitive function and do not assess one's ability to drive or to make legally binding decisions. If reversal agents such as flumazenil or naloxone are used, one would need to ensure that sufficient time be allowed for the effects of these reversal agents to wear off, to avoid the situation of apparent fulfilment of discharge criteria, only for the patient to return to a sedated state which may endanger the patient or others after the reversal agents wear off.

**Statement 13: We recommend that patients who have received sedation should be told what is safe for them to do.**

Quality of evidence: Low

Strength of recommendation: Strong

Agreement: 100%

Discharge scoring systems often focus on only the cardio-respiratory function.<sup>12,106-110</sup> Despite patients appearing clinically alert post-reversal agents, they may have prolonged impairment in their cognition and psychomotor skills. The duration of this impairment depends on the sedative agent used.<sup>111</sup> These simple discharge scoring systems often do not assess patients' psychomotor function fully, which is important to determine if the patients are able to make use of road

transport, operate heavy machinery or make legally binding decisions.

They should refrain from driving, drinking alcohol, operating heavy machinery, or engaging in legally binding decisions for a period of time, taking into account the half-life of the drug used and the patient's health profile. Advice should be provided verbally and in written form to the patient. Older studies on the recovery of psychomotor function after sedation with diazepam and midazolam showed recovery of psychomotor function to pre-sedation levels after 10 hours even when benzodiazepines were used at higher doses (midazolam 0.15mg/kg body weight [bw] or diazepam 0.45mg/kg bw).<sup>112,113</sup> Diazepam is seldom used in endoscopy now. The dose of midazolam administered also rarely exceeds 0.1mg/kg bw in current practice. Only when pethidine 75mg was used were psychomotor functions impaired for up to 12 hours.<sup>114</sup> This dose of pethidine is now seldom used during endoscopy. More recent studies have shown that patients sedated with propofol monotherapy recover psychomotor skills 2 hours post-sedation.<sup>115,116</sup> Patients in both studies had similar results on the driving simulator 2 hours after sedation. Japanese patients had similar number connection test (NCT) results before and 2 hours after propofol sedation while German patients took 1 second longer to complete the NCT. German patients who were sedated with midazolam and an opioid however scored worse on both the NCT and the driving simulator 2 hours post-sedation. American and Japanese experience suggests patients sedated with drugs with a short half-life may be safely discharged without an accompanying person,<sup>117,118</sup> and that they may drive home safely within a few hours of sedation.<sup>117</sup> Patients who have received sedation should be discharged with a responsible person and avoid operating heavy machinery, driving or signing any legally binding documents for a period. Based on current evidence on the duration of psychomotor function impairment by the drugs currently in use, patients given midazolam and fentanyl should be discharged with a responsible person and avoid these activities for up to 12 hours. Patients given propofol monotherapy could potentially avoid these activities for a shorter period. Published data would suggest it is safe for such activity to resume 2 hours after sedation.<sup>115-117</sup> However, given medico-legal considerations, it will be prudent for individual endoscopy units and endoscopists to discuss the implications of this with individual patients before sedation is given.

**CQ7: Training in sedation for GI endoscopy for non-anaesthesiologist**

**Statement 14: The person providing sedation should attend a sedation course.**

Quality of evidence: Low

Strength of recommendation: Strong

Agreement: 100%

Training and achieving competency in the use of medications, as well as in airway assessment and management is important. Drugs widely used in endoscopy sedation include benzodiazepines and opioids, such as midazolam and fentanyl, respectively.<sup>119-122</sup> Optimal sedation in endoscopy requires the proceduralist or sedationist administering sedation to be aware of the drugs' different pharmacokinetics, pharmacodynamics, route of elimination, common adverse effects and potential drug-drug interactions.<sup>121,123-125</sup> This enables the proceduralist or sedationist to choose the appropriate type, combination, and dose of sedation to administer depending on the patient profile, dosing aliquot interval, monitoring, and available and clinical setting. Adequate training in the properties of reversal agents such as flumazenil and naloxone are necessary in case these agents are required.<sup>126,127</sup> The continuum from complete consciousness to general anaesthesia does not progress in discrete and well-defined stages. As such, it is crucial that the proceduralist or sedationist who intends to administer sedation be trained in the assessment of the patient's level of sedation.<sup>128,129</sup> It is also important that the endoscopist or sedationist should be able to assess a patient's suitability for endoscopist directed sedation. This should include classifying patients' general health status using the ASA classification system<sup>15</sup> and a detailed airway evaluation including body habitus, cervical spine movement, hyoid-mental distance and oropharyngeal status (e.g. mouth opening and Mallampati classification).<sup>12</sup>

**Statement 15: Training in sedation should be structured. There should be assessment of competencies prior to the independent administration of sedation.**

Quality of evidence: Low

Strength of recommendation: Strong

Agreement: 100%

Training in sedation pharmacology and recognition of the different levels of sedation can be taught in theory, often taking the form of instructional videos with quizzes at the end of these videos in the local setting. These

are required for proceduralists starting training in GI endoscopy and are valid for a defined duration, often 2 to 3 years, before a refresher course is required. Sedation training curriculums have been published by professional societies in the US (American Gastroenterological Association [AGA], American College of Gastroenterology [ACG], American Society for Gastrointestinal Endoscopy [ASGE], American Association for the Study of Liver Diseases [AASLD] and Society of Gastroenterology Nurses and Associates. [SGNA])<sup>130</sup> and in Europe (European Society of Gastrointestinal Endoscopy [ESGE] and European Society of Gastroenterology and Endoscopy Nurses and Associates [ESGENA]).<sup>131</sup> In Singapore, trainees are under direct supervision while undergoing training in GI endoscopy. There is also hands-on supervision in the actual administration of sedation. This is consistent with the training recommendations from the US<sup>129</sup> and Europe.<sup>131</sup> The ability to manage adverse events from sedation is also an important part of training. The ESGE/ESGENA curriculum recommends that all endoscopists and sedationists be trained in basic cardiac life support. In addition, those practising in facilities where an advanced cardiac life support (ACLS) provider is not immediately available should also be trained in ACLS.<sup>110,131</sup> The AGA/ACG/ASGE/AASLD/SGNA curriculum recommends that all endoscopists and sedationists be trained in ACLS or its equivalent.<sup>129</sup> The assessment of competency in the safe use of sedation in GI endoscopy may vary in different countries and healthcare systems.<sup>131-133</sup> In the Singapore context, the assessment of trainee competency is under the purview of bodies such as the Residency Advisory Committee (RAC) that oversees specialist training at the national level, and the Clinical Competencies Committees (CCC) of the respective institutions offering training in GI endoscopy.

The workgroup agrees with the recommendation from ESGE/ESGENA that ACLS training of the endoscopist or sedationist is required only in the context of facilities without a code blue team. European endoscopic sedation data after the introduction of these European training guidelines have demonstrated the safety and effectiveness.<sup>73</sup> Despite more widespread adoption of sedation during endoscopy including the use of propofol by non-anaesthesiologists, sedation-related complications have remained low.<sup>134</sup> American data from the same period showed increased adoption of anaesthesiologist-administered sedation (in up to 53% of commercially insured patients) with increased cost and utilisation of limited anaesthesiology resources even for ASA 1 and 2 patients.<sup>1,135</sup>

**Statement 16: Non-anaesthesiologists using propofol for sedation should have additional training with respect to propofol. They should have training for resuscitation with emphasis on airway management.**

Quality of evidence: Low

Strength of recommendation: Strong

Agreement: 88.9%

Data demonstrated the safety and efficacy of non-anaesthesiologist-administered propofol sedation (NAAP). NAAP requires specialised training, patient selection, and personnel dedicated to continuous physiologic monitoring.<sup>12,132</sup> The current sedation training for endoscopy trainees in Singapore focuses only on the safe and effective use of benzodiazepines and opiates. Hence, there should be additional structured training on the safe use of propofol. Unlike benzodiazepines and opiates, there are no reversal agents for propofol. Hence the ability to manage adverse events such as airway compromise from propofol is even more crucial. Training curricula have been published in the US by AGA/ACG/ASGE/AASLD/SGNA<sup>130</sup> and in Europe by ESGE/ESGENA.<sup>110,131</sup> The Korean NAAP training guideline developed by anaesthesiologists is similar to the ESGE guideline.<sup>136</sup> Propofol can be safely used by non-anaesthesiologists for endoscopic sedation after rigorous training.<sup>137</sup> As training in the use of propofol is currently not incorporated during training for GI endoscopy, a dedicated formal structured course on the use of propofol would be needed for endoscopists intending to provide NAAP if they do not have prior experience in its usage. ACLS training will also be required if propofol sedation is administered in a centre without a code blue team. The training course should involve all relevant stakeholders, and could potentially be organised under the auspices of AMS, or specific institutions or professional bodies. In current clinical practice, propofol sedation is already being administered safely by non-anaesthesiologists in the private practice setting. These doctors would have either undergone formal or informal training on the use of propofol in the past and should be allowed to continue this practice based on past track records. Individual institutions may consider the need for specific credentialling. For non-anaesthesiologists who now intend to begin providing propofol sedation, formal training would be recommended.

## CONCLUSION

This is the first AMS guideline for sedation during GI endoscopy by non-anaesthesiologists in the hospital setting, summarising the available evidence according to GRADE, and making recommendations by the modified

Delphi process. The guideline addresses pre-, peri- and post-procedural issues related to the administration of sedation during GI endoscopy, provides evidence-based appraisal of the efficacy and safety of benzodiazepines, opiates and propofol. The guideline also addresses the roles of anaesthesiologists and non-anaesthesiologists in the administration of sedation. In particular, it addresses the use of propofol by non-anaesthesiologists. It is hoped that this guideline would enhance the safety and quality of sedation during GI endoscopy by non-anaesthesiologists. At the same time, it is also important that individual hospitals track and audit adverse outcomes arising from the provision of sedation during GI endoscopy. This guideline will be revised as necessary to cover progress and changes in technology, and evidence from clinical practice.

## Disclosure

*The guideline was commissioned by the Academy of Medicine, Singapore.*

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