Non-anesthesiologist administration of propofol for gastrointestinal endoscopy: European Society of Gastrointestinal Endoscopy, European Society of Gastroenterology and Endoscopy Nurses and Associates Guideline – Updated June 2015

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This Guideline is an official statement of the European Society of Gastrointestinal Endoscopy (ESGE) and the European Society of Gastroenterology and Endoscopy Nurses and Associates (ESGENA). It addresses the administration of propofol by non-anesthesiologists for gastrointestinal (GI) endoscopy.

Main Recommendations
1 We recommend that the type of endoscopic procedure and the patient’s American Society of Anesthesiologists (ASA) physical status, age, body mass index, Mallampati’s classification, and risk factors for obstructive sleep apnea (OSA) be assessed before each procedure with non-anesthesiologist administration of propofol (NAAP) (strong recommendation, moderate quality evidence).
2 We suggest primary involvement of an anesthesiologist in patients of ASA class ≥3, with a Mallampati’s class ≥3 or other conditions that put them at risk of airway obstruction (e.g. pharyngolaryngeal tumors), in patients who chronically receive significant amounts of narcotic analgesics, or in cases where a long-lasting procedure is anticipated (weak recommendation, low quality evidence).
3 We suggest consideration of capnographic monitoring during NAAP in specific situations including high risk patients, intended deep sedation, and long procedures (weak recommendation, high quality evidence).
4 We suggest propofol monotherapy except in particular situations (weak recommendation, high quality evidence).
5 We recommend administering propofol through intermittent bolus infusion or perfusor systems, including target-controlled infusion (TCI), and consideration of patient-controlled sedation (PCS) in particular situations (strong recommendation, high quality evidence).
6 We suggest that patients listen to self-selected music during upper and lower GI endoscopy procedures (weak recommendation, moderate quality evidence).
7 We do not suggest using pharyngeal anesthesia during propofol sedation for upper GI endoscopy (weak recommendation, moderate quality evidence).
8 We suggest using the post-anesthetic discharge scoring system (PADSS) to determine when patient recovery is sufficient to allow discharge (weak recommendation, low quality evidence).
9 Minimum discharge criteria should be fulfilled before discharging a patient. We recommend that patients who have received combined regimens, and all patients of ASA class >2, should upon discharge be accompanied by a responsible person and refrain for 24 hours from driving, drinking alcohol, operating heavy machinery, or engaging in legally binding decisions. Advice should be provided verbally and in written form to the patient, including a 24-hour contact phone number (strong recommendation, low quality evidence).
10 For patients of ASA classes 1–2 who have received low dose propofol monotherapy, a 6-hour limit is suggested (weak recommendation, low quality evidence).

Abbreviations
ACLS advanced cardiovascular life support
ASA American Society of Anesthesiologists
BIS bispectral index
BLS basic life support
BMI body mass index
CAPS computer-assisted personalized sedation
CORI Clinical Outcomes Research Initiative
CPAP continuous positive airway pressure
EEG electroencephalogram
**1 Introduction**

A strong interest in the use of propofol for sedation during gastrointestinal (GI) endoscopy has been demonstrated in all European countries where nationwide surveys have examined sedation regimens used for GI endoscopy [1–5]; in several countries there has been a tendency for propofol sedation to replace “traditional sedation” based on the administration of benzodiazepines either alone or combined with opioids. The Guideline on non-anesthesiologist administration of propofol (NAAP) for GI endoscopy published in 2010 by the European Society of Gastrointestinal Endoscopy (ESGE), European Society of Gastroenterology and Endoscopy Nurses and Associates (ESGENA), and the European Society of Anaesthesiology (ESA) aimed to provide a qualified basis for GI endoscopists and endoscopy nurses to provide propofol sedation [6]. New evidence that has become available since then is discussed in the present update and new recommendations are issued. The Guidelines cover the care provided to any patient undergoing GI endoscopy. They are not designed to be rigid and cannot replace clinical judgment; furthermore, their implementation may be subject to domestic regulations or local policy and they should only be used with the agreement of the relevant domestic regulatory authority or local policy maker.

**2 Methods**

The previous version of the Guideline, issued in 2010, was endorsed by three societies, namely the ESGE, the ESGENA, and the ESA; the latter has since retracted its endorsement following long internal discussions [7]. Therefore, this update of the Guideline on NAAP was commissioned and funded by the ESGE and the ESGENA only.

Methods similar to those used in the previous Guideline were employed [8]. A literature search of PubMed/MEDLINE, and searches using the Cochrane Library, EMBASE, and the internet were performed to identify publications since December 2009 on this topic. The search focused on fully published prospective studies, particularly randomized controlled trials (RCTs) and meta-analyses. Retrospective analyses and pilot studies were also included if they addressed topics not covered in the prospective studies.
With regard to adverse events, propofol may cause hypventilation, hypotension, and bradycardia relatively frequently, but severe adverse events are extremely rare [16]. Therefore, the parameters “hypoxemia” and “hypotension” are most often used as surrogate markers of clinical complications; these were used for comparing propofol with traditional sedation in RCTs that were reviewed in three meta-analyses (Table 1) [10, 15, 17]. No significant differences between propofol-based and traditional sedation were detected for hypoxemia or hypotension in these meta-analyses, with the exception that there were fewer cardiopulmonary complications with propofol sedation during colonoscopy versus traditional sedation [17].

New information since 2010

For unselected procedures and patients, three studies were found:

- A meta-analysis of 22 RCTs that compared propofol monotherapy versus traditional sedation (1798 patients) for GI endoscopy has been added to Table 1; it found shorter recovery and discharge periods, higher post-anesthesia recovery scores, better sedation, and greater patient cooperation with propofol monotherapy compared with traditional sedation, with no increase in cardiopulmonary complications [18]. The healthcare category of the provider of propofol sedation was not mentioned.

- Two prospective, multicenter, non-comparative, surveys from Germany that globally involved >200 000 patients found a low incidence of propofol-related complications: one survey analyzed endoscopist-administered propofol sedation and reported major adverse events (mask ventilation and laryngospasm) in 0.016% of patients [19]; in the other study, NAAP was used for sedation in >90% of cases, it reported clinically relevant sedation-related complications (defined as respiratory insufficiency that required mechanical ventilation and/or caused hospitalization or prolongation of hospital stay) in 0.042% of patients and sedation-related death in 0.003% (not 0.00042% and 0.00003% as miscalculated by the authors) [20]. For advanced endoscopic procedures, three meta-analyses were found:

  - A meta-analysis of 26 prospective observational trials that compared propofol sedation administered by a non-anesthesia provider versus an anesthesia provider in >5000 advanced endoscopic procedures (EUS, ERCP, and deep small-intestinal enteroscopy) [21]. NAAP was associated with similar safety but lower patient and endoscopist satisfaction compared with anesthesia provider–administered propofol sedation.

- Two meta-analyses compared propofol versus traditional sedation, either for advanced endoscopic procedures in general (9 RCTs, 969 patients) [22] or for ERCP alone (6 RCTs, 663 patients) [23]. Propofol was administered by a non-anesthesiologist in 7 of the 9 RCTs including advanced procedures and 3 of the 6 RCTs on ERCP. Both studies found that propofol sedation was associated with a shorter recovery time and a similar incidence of cardiopulmonary adverse events; additionally the largest study found that propofol was associated with a better sedation and amnesia level. The duration of ERCP was similar with propofol versus traditional sedation.

Cost-effectiveness of endoscopist-directed versus anesthesiologist-provided propofol administration was analyzed in the setting of colonoscopy for colorectal cancer screening [24]. If it is assumed that a single nurse would administer propofol and assist the endoscopist with ancillary tasks such as polypectomy, NAAP would be associated with savings over a 10-year period of $3.2 billion in the USA and €0.8 billion in France [25]. Anesthesiologist involvement adds 20% and 285% to the cost of a colonoscopy in the USA and in France, respectively [24, 26]. Quality indicators were analyzed in six studies:

- For ERCP, compared with historical controls who had received traditional sedation administered by the endoscopist, patients who received propofol sedation administered by an anesthesiologist had similar rates of deep duct cannulation [27].

- For colonoscopy, five studies were found:

  - In a prospective multicenter study, the adenoma detection rate was not independently associated with the drug used for sedation (midazolam versus propofol) [28]. In another multicenter study, compared with no sedation, sedation (using any drug) was associated with a higher cecal intubation rate but no difference in the adenoma detection rate [29].

  - With respect to colonoscopy-related perforations, three retrospective studies that included 2536, 6371, and 1144900 colonoscopies found no association between pro-

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Table 1  Meta-analyses of randomized controlled trials that reported the safety of propofol† versus traditional agents‡ for sedation during endoscopy.

<table>
<thead>
<tr>
<th>First author, year</th>
<th>n</th>
<th>Procedure</th>
<th>Hypoxemia, % (95%CI)</th>
<th>Hypotension, % (95%CI)</th>
<th>Odds ratio for complications, % (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qadeer, 2005 [17]</td>
<td>1161</td>
<td>EGD, colonoscopy, ERCP, EUS</td>
<td>8.8 (NA)</td>
<td>9.9 (NA)</td>
<td>2.8 (NA)</td>
</tr>
<tr>
<td>McQuaid, 2008 [10]</td>
<td>3918</td>
<td>EGD, colonoscopy</td>
<td>11 (7 - 16)</td>
<td>18 (12 - 26); 6 (4 - 7)†</td>
<td>5 (2 - 10)</td>
</tr>
<tr>
<td>Singh, 2008 [15]</td>
<td>1181*</td>
<td>Colonoscopy</td>
<td>5.4 (NA)</td>
<td>6.9 (NA)</td>
<td>12.5 (NA)</td>
</tr>
<tr>
<td>Wang, 2013 [18]</td>
<td>1798</td>
<td>EGD, colonoscopy, ERCP, EUS</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

CI, confidence interval; EGD, esophagogastroduodenoscopy; ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasound; NA, not available.

† Propofol was used as a single agent or combined with other drugs
‡ Traditional agents consisted of a benzodiazepine plus an opioid in most trials
§ Proportions stated separately for midazolam alone (18%) or midazolam given with a narcotic (6%)

- The outcome “hypotension” was analyzed in 321 patients
4 Training in NAAP

Statement 2010: Specific knowledge and skills are necessary for endoscopists and nursing staff using NAAP to ensure patient comfort and safety; none of the NAAP reports published to date used self-training to achieve competency in this technique. NAAP performed by endoscopists and endoscopy nurses should not take place without appropriate training, and self-training in NAAP is strongly discouraged. (Evidence level 2++, Recommendation grade A.) GI endoscopists and registered nurses are adequate candidates for NAAP training courses. Previous experience in intensive care medicine is desirable for the physician who is responsible for NAAP. We recommend that training courses for NAAP include a theoretical and a practical part, each part being followed by an examination to document successful training. NAAP training courses should teach techniques of basic life support (BLS) to all participants and advanced cardiovascular life support (ACLS) to caregivers who will practice in locations where an ACLS provider is not immediately available. (Evidence level 4, Recommendation grade D.) The first human cases of NAAP performed by a caregiver require particular attention because complications are more frequent during this period. We recommend that the first human cases of NAAP performed by an individual be supervised by an anesthesiologist or another person with previous experience of >300 NAAP cases (Evidence level 2−, Recommendation grade D). There was discussion in the audience, with some participants recommending preceptorship during the first cases of NAAP without defining “first cases,” and others preferring to state a number of cases (evidence only available for n ≥ 100 NAAP procedures). (Evidence level 4, Recommendation grade D).

Statement 2015: GI endoscopists and registered nurses are adequate candidates for NAAP training courses. Previous experience in intensive care medicine or in anesthesia is desirable for the physician who is responsible for NAAP (strong recommendation, low quality evidence). The European curriculum for sedation training in GI endoscopy details all aspects of training for non-anesthesiologists who desire to provide NAAP.

5 Practice of NAAP

5.1 Pre-procedure patient selection

Statement 2010: Specific knowledge and skills are necessary for endoscopists and nursing staff using NAAP to ensure patient comfort and safety; none of the NAAP reports published to date used self-training to achieve competency in this technique. NAAP performed by endoscopists and endoscopy nurses should not take place without appropriate training, and self-training in NAAP is strongly discouraged. (Evidence level 2++, Recommendation grade A.) GI endoscopists and registered nurses are adequate candidates for NAAP training courses. Previous experience in intensive care medicine is desirable for the physician who is responsible for NAAP. We recommend that training courses for NAAP include a theoretical and a practical part, each part being followed by an examination to document successful training. NAAP training courses should teach techniques of basic life support (BLS) to all participants and advanced cardiovascular life support (ACLS) to caregivers who will practice in locations where an ACLS provider is not immediately available. (Evidence level 4, Recommendation grade D.) The first human cases of NAAP performed by a caregiver require particular attention because complications are more frequent during this period. We recommend that the first human cases of NAAP performed by an individual be supervised by an anesthesiologist or another person with previous experience of >300 NAAP cases (Evidence level 2−, Recommendation grade D). There was discussion in the audience, with some participants recommending preceptorship during the first cases of NAAP without defining “first cases,” and others preferring to state a number of cases (evidence only available for n ≥ 100 NAAP procedures). (Evidence level 4, Recommendation grade D).

Statement 2015: GI endoscopists and registered nurses are adequate candidates for NAAP training courses. Previous experience in intensive care medicine or in anesthesia is desirable for the physician who is responsible for NAAP (strong recommendation, low quality evidence). The European curriculum for sedation training in GI endoscopy details all aspects of training for non-anesthesiologists who desire to provide NAAP.

Statement 2015: We recommend that the type of endoscopic procedure and the patient’s American Society of Anesthesiologists (ASA) physical status, age, body mass index, Mallampati’s classification, and risk factors for obstructive sleep apnea (OSA) be ascertained before each NAAP procedure by reviewing patient past medical history, performing a focused physical examination, and assessing type and anticipated complexity of the endoscopic procedure. (Evidence level 4, Recommendation grade D.) In the presence of patient-related risk factors for complications, the primary involvement of an anesthesiologist during endoscopy is suggested. These factors include ASA category ≥ 3, a Mallampati’s class of 3 or other conditions at risk for airway obstruction (e.g., pharyngolaryngeal tumors), patients who chronically receive significant amounts of pain medications or in cases of anticipated long-lasting procedure. (Evidence level 4, Recommendation grade D.)
includes vital signs, heart and lung auscultation, as well as throat examination, the patient is classified according to the ASA physical status scale and Mallampati’s class [45,46]. The presence of some patient-related risk factors may trigger consideration of primary involvement of an anesthesiologist during endoscopy [47]. Such factors are, for example: a history of stridor, snoring, or OSA; patients with dysmorphic facial features or oral abnormalities, such as a small opening (<3 cm in an adult), high arched palate, or macroglossia; patients with neck or cervical spine abnormalities, tracheal deviation, or advanced rheumatoid arthritis; patients with jaw abnormalities, such as micrognathia; patients receiving significant amounts of narcotic analgesics chronically or who for other reasons may be tolerant to agents used during sedation and analgesia.

New information since 2010

Increasing ASA class was confirmed to be associated with a stepwise increase in the odds ratio of serious adverse events in the Clinical Outcomes Research Initiative (CORI) database (1,590,648 endoscopic procedures; 1,318,495 patients). Odds ratios for serious adverse events (hospital admission, surgery, cardiopulmonary resuscitation, or emergency room referral) were, using a reference value of 1 for ASA class 1, for EGD: ASA class 2, 1.54 (95% confidence interval [CI] 1.31 – 1.82); class 3, 3.90 (95%CI 3.27 – 4.64); classes 4/5, 12.02 (95%CI 9.62 – 15.01); and for colonoscopy were: ASA class 2, 0.92 (95%CI 0.85 – 1.01); class 3, 1.66 (95%CI 1.46 – 1.87); classes 4/5, 4.93 (95%CI 3.66 – 66.3) [48]. A similar trend for ERCP was not significant. The sedation type was not detailed in this study. Another prospective registry study (13,747 endoscopic procedures under propofol sedation) showed that all of the 17 severe complications that were observed occurred in patients of ASA class ≥3 [49].

Increasing age was also associated with a stepwise increase in the incidence of serious adverse events in the above-mentioned CORI study [48]. In a prospective study of EGD/colonoscopy performed in 10,000 patients, with NAAP used in 96% of the cases, sedation-related cardiorespiratory adverse events were associated with older age [50]. In two other prospective studies (one RCT) totaling 773 patients, age was an independent predictor of sedation-related adverse events during colonoscopy under propofol sedation [51, 52]. Nevertheless, various studies have suggested that NAAP may be safely performed in elderly patients for various endoscopic procedures including ERCP [53–55]. The doses of propofol administered should be adapted in the elderly: in patients older than 90 years, a dose less than half of that administered to controls provided similar sedation levels and propofol blood concentrations [56].

Body mass index (BMI) was independently associated with sedation-related complications in two series of 799 and 1016 patients undergoing advanced endoscopic procedures under propofol, as were ASA class ≥3 (two studies), age and male sex (one study each) [57, 58]. Patients were not screened for OSA in these studies (OSA is associated with high BMI [59]). In addition, for colonoscopy under propofol sedation, higher BMI was associated with sedation-related adverse events in two prospective studies (773 patients, 1 RCT) [51, 52].

OSA is an underdiagnosed entity; in some settings, 15%–48% of the patients undergoing routine endoscopic procedures are at risk of OSA [52, 60, 61]. Patients at high risk of OSA, as identified by questionnaires, as well as those with confirmed OSA present a higher risk of hypoxemia during propofol sedation for endoscopy compared with non-OSA controls (Table 2). Various questionnaires are available to screen patients for OSA [62]; the STOP-BANG questionnaire (loud Snoring, Tiredness, Observed apnea, high blood Pressure) Body mass index, Age, Neck circumference, and Gender).

Table 2

<table>
<thead>
<tr>
<th>First author, year</th>
<th>Study design</th>
<th>n</th>
<th>Procedure</th>
<th>Sedation provider</th>
<th>Diagnostic criteria for OSA</th>
<th>Hypoxemia OSA–</th>
<th>Hypoxemia OSA+</th>
<th>Hypotension OSA–</th>
<th>Hypotension OSA+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mehta, 2014 [52]</td>
<td>Prospective</td>
<td>243</td>
<td>EGD/ colonoscopy</td>
<td>Anesthesiologist or certified registered nurse anesthetist</td>
<td>STOP-BANG ≥3</td>
<td>14/125</td>
<td>20/118</td>
<td>13/125</td>
<td>7/118</td>
</tr>
<tr>
<td>Deng, 2012 [60]</td>
<td>Prospective</td>
<td>210</td>
<td>Colonoscopy</td>
<td>Anesthesiologist</td>
<td>STOP ≥2</td>
<td>3/178</td>
<td>10/32</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Corso, 2012 [139]</td>
<td>Prospective</td>
<td>272</td>
<td>EGD/ colonoscopy/ ERCP</td>
<td>NA</td>
<td>STOP-BANG ≥3</td>
<td>2/131</td>
<td>21/141</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Friedrich-Rust, 2014 [51]</td>
<td>Randomized controlled trial</td>
<td>533</td>
<td>EGD/ colonoscopy</td>
<td>NAAP or anesthesiologist</td>
<td>Clinical history</td>
<td>120/513</td>
<td>13/20</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Coté, 2010 [140]</td>
<td>Prospective</td>
<td>231</td>
<td>ERCP/EUS</td>
<td>Anesthesiologist</td>
<td>STOP-BANG ≥3</td>
<td>4/131</td>
<td>12/100</td>
<td>22/131</td>
<td>14/100</td>
</tr>
<tr>
<td>Subtotal (EGD/ colonoscopy)</td>
<td></td>
<td>231</td>
<td></td>
<td></td>
<td></td>
<td>18/358</td>
<td>34/207</td>
<td>15/180</td>
<td>15/175</td>
</tr>
<tr>
<td>Total (all procedures)</td>
<td></td>
<td>24/620</td>
<td></td>
<td></td>
<td></td>
<td>67/448</td>
<td>37/311</td>
<td>29/275</td>
<td></td>
</tr>
</tbody>
</table>

EGD, esophagogastrroduodenoscopy; ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasonography; NAAP, non-anesthesiologist administration of propofol; NA, not available; n.s., not significant; STOP, STOP score (loud Snoring, Tiredness, Observed apnea, high blood Pressure); STOP-BANG, STOP-BANG score (loud Snoring, Tiredness, Observed apnea, high blood Pressure-Body mass index, Age, Neck circumference, and Gender).

* Using polysomnography, portable monitoring, or on clinical grounds given their history and positive response to the use of a continuous positive airway pressure (CPAP) machine

1 P<0.001

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Neck circumference, and Gender) is a list of eight questions that is easy to fill and interpret and that has been validated in both unselected and obese patients [63, 64]. It provides a high negative predictive value for the diagnosis of moderate (90%) and severe (100%) OSA [63], and it is the most frequently used tool to screen for OSA before endoscopy. In an RCT that included 533 patients [51], OSA was an independent predictor of hypoxemia during colonoscopy under propofol sedation, together with older age, BMI, and total dose of propofol.

In cirrhotic patients, a meta-analysis of five RCTs that compared propofol versus midazolam for upper GI endoscopy found similar safety for both regimens; propofol sedation was associated with a shorter deterioration of psychometric scores than midazolam [65]. However, most studies included patients with Child A and B cirrhosis only. Propofol was administered by a non-anesthesiologist in three of the five RCTs.

Risk classification of patients before NAAP may be performed using a combination of review of a patient's past medical history, questionnaires (e.g. the STOP-BANG questionnaire), and a focused physical examination.

Patients of ASA classes 3 and 4 are included in NAAP studies with increasing frequency, even for advanced endoscopic procedures, as shown in the latest meta-analysis of NAAP (ASA class 3–4 patients accounted for 29% of the patients included in the studies that detailed ASA category; 257 of 896 patients) [21]. No impact on patient safety has been detected. Sedation-related deaths are however most frequently reported in these categories of patients [20].

5.2 Performance of sedation
5.2.1 Personnel

Statement 2015: No new recommendation could be made about the necessity of continuous patient monitoring by a person dedicated to NAAP.

Background
Various guidelines have recommended that NAAP be performed by a person who has NAAP as his/her sole task [Evidence level 1+]. It is recommended that patients be continuously monitored by a person dedicated to NAAP. (Recommendation grade A).

Statement 2010: In the vast majority of NAAP studies, propofol was administered by a person who had patient sedation as his/her sole task (Evidence level 1+). It is recommended that patients be continuously monitored by a person dedicated to NAAP. (Recommendation grade A).

New information since 2010
A study of prospectively collected adverse events that included 13 747 endoscopic procedures under NAAP has been reported [49]; it is a retrospective comparison of two 2-year periods, each with similar numbers of endoscopies, one with a person dedicated to NAAP in all of the cases and the other without someone dedicated to NAAP for “most endoscopic procedures.” Sedation-related circulatory complications tended to be less frequent during the period with a person dedicated to NAAP compared with the other period but no significant differences were observed. The study found that all of the 17 severe complications occurred in patients of ASA class ≥3 but, because of its limitations, this study does not allow the conclusion to be drawn that both approaches are equally safe.

Three surveys reporting that NAAP is commonly practiced with no staff member dedicated exclusively to sedation during NAAP were identified:

▶ In a survey of gastroenterologists practicing in Switzerland, 67% of the 158 survey respondents who were regularly using NAAP stated that a single assistant was present during EGD and colonoscopy [3]. The overall complication rate was comparable with that reported in other large studies (morbidity and mortality rates of 0.14% and 0.0018%, respectively). Of the gastroenterologists performing NAAP, 61% had either undergone formal training in anaesthesiology or a 6-month training period in an intensive care unit during their training in internal medicine.

▶ In a prospective multicenter survey from Germany that involved 191 142 patients, NAAP was used in approximately 90% of patients and no additional person was present for NAAP “in a majority of cases” (no more information was available) [20]. Complications were defined as respiratory insufficiency that required mechanical ventilation and/or caused hospitalization or prolongation of hospital stay. Overall, the endoscopy-related complication rate was 0.22% (n = 424) and the sedation-related complication rate was 0.042% (n = 82). A limitation of this study is that hypoxemic events requiring bag and mask ventilation were not registered. Sedation-related death occurred in six patients (0.003%), all of them classified as ASA 3 before endoscopy, and occurred in the presence of an additional person trained for NAAP.

▶ Finally, an international survey showed that NAAP was used by 30% of 48 gastroenterologists and that one-third of them did not have a person dedicated solely to propofol administration [4].

An online survey performed after extended discussion and provision of the relevant literature to all of the authors of this Guideline found that half of all authors supported a modification of the staff requirements for NAAP in well-defined conditions while the other half wanted to keep the 2010 recommendation unchanged. The ESGE/ESGENA NAAP task force emphasizes that patient safety was the highest priority when elaborating this Guideline.

Statement 2010: There is no evidence that quick availability of a life support team is required for propofol administration. We do not recommend compulsory availability of a life support team if propofol is administered in the presence of a person trained in ACLS. (Evidence level 2+; Recommendation grade C).

Background
No study has analyzed if availability of a life support team modifies any aspect of NAAP.

New information since 2010
None.

5.2.2 Patient preparation and monitoring

Statement 2010: Intravenous access is required for sedation in GI endoscopy and should be maintained using a catheter, not a winged steel needle, until full patient recovery. (Evidence level 4, Recommendation grade D.)

Dumonceau Jean-Marc et al. NAAP: ESGE-ESGENA Guideline 2015... Endoscopy 2015; 47: 1175–1189
Background
Reliable intravenous access is required for the duration of NAAP; Teflon cannulas are as easy to insert as winged steel needles and provide more reliable intravenous access [70].

New information since 2010
None.

Statement 2010: Continuous supplemental oxygen is indicated during NAAP for endoscopy. (Evidence level 1+, Recommendation grade B.)

Background
Administration of oxygen is widely recommended because RCTs have shown that oxygen desaturation is frequent during endoscopy if the patient breathes room air and that this may be prevented by supplemental oxygen administration during endoscopy under traditional sedation [71 – 78]. However, the potential benefit of routine prophylactic oxygen supplementation in terms of decreased cardiopulmonary complications is unclear [79].

New information since 2010
Regular use of supplemental oxygen during sedated endoscopy, using propofol or other drugs, was reported by 39%, 35%, 20% – 41%, and 58% – 78% of respondents to nationwide surveys in Italy, Germany, Greece, and Switzerland, respectively [3].

Statement 2010: Patient monitoring is recommended in all patients using continuous pulse oximetry and automated noninvasive blood pressure measurement (at baseline and then at 3–5-minute intervals) during both NAAP and the recovery period; continuous electrocardiography is recommended in selected patients with a history of cardiac and/or pulmonary disease. Baseline, minimum and maximum heart rate/blood pressure, as well as baseline and minimum oxygen blood saturation should be recorded. (Evidence level 2++, Recommendation grade B.)

Statement 2015: No changes (strong recommendation, moderate quality evidence).

Background
Most studies that have established the safety of NAAP have used patient monitoring as stated above [16]. Although their clinical utility has not been demonstrated, the equipment is widely available, inexpensive, and easy to use. Hypoxemia, but not hypoventilation, can be detected early with pulse oximetry. As hypotension is a frequent side effect of propofol that requires intervention, blood pressure monitoring seems to be useful. Monitoring of these parameters has become standard practice for NAAP [80, 81].

New information since 2010
Pulse oximetry monitoring during sedated endoscopy, using propofol or other drugs, was reported by ≥90% of respondents to nationwide surveys in Italy, Germany, Greece, and Switzerland [3]. The Swiss survey detailed figures for NAAP: pulse oximetry and blood pressure monitoring were used by 100% and 66% of respondents, respectively [3].

Statement 2015: No changes (weak recommendation, moderate quality evidence).

Statement 2010: Visual assessment of respiratory activity during anticipated long endoscopy procedures is not a reliable method of detecting apnea. During NAAP, capnographic monitoring of respiratory activity may reduce episodes of hypoxemia during long endoscopic procedures or when visual assessment of patient breathing is impaired, but no clinical impact has been demonstrated. Therefore, capnography cannot be recommended as standard. (Evidence level 1+, Recommendation grade B.)

Statement 2015: We suggest consideration of capnographic monitoring during NAAP in specific situations including high risk patients, intended deep sedation, and long procedures (weak recommendation, high quality evidence).

Background
Detection of hypoventilation and apnea using visual inspection of respiratory activity is unreliable [82]. The lag times from start of apnea to capnographic findings and to hypoxemia are about 5 seconds and another 10–20 seconds [83], so that capnography provides an “early warning” window for interventions aimed at improving ventilation. Two RCTs reported that hypoxemia was more frequently and more reliably detected if capnography was available [84, 85] but no difference in clinical outcome was found whether or not capnography was used. Both RCTs used traditional sedation, for either advanced endoscopy procedures in adults [84], or EGD/colonoscopy in children [85]. False-positive results (flat capnography line) were observed in one of these studies in a significant proportion of patients [84].

New information since 2010
In its 2011 revision of the “Standards for basic anesthetic monitoring,” the ASA states “During moderate [italics added] or deep sedation the adequacy of ventilation shall be evaluated by continual observation of qualitative clinical signs and monitoring for the presence of exhaled carbon dioxide unless precluded or invalidated by the nature of the patient, procedure or equipment” [86]. The American Society for Gastrointestinal Endoscopy, the American Gastroenterological Association, and the American College of Gastroenterology answered that “There are insufficient data to demonstrate that improved clinical outcomes or care quality derive from the use of capnography in adults undergoing targeted moderate sedation for upper endoscopy and colonoscopy” [87]. Reluctance toward generalized use of carbon dioxide monitoring was also motivated by costs. Three recent RCTs have compared standard monitoring with versus without capnography during GI endoscopy procedures under propofol sedation in a total of 1833 patients [51, 88, 89]. Sedation was provided by non-anesthesiologists in two RCTs [88, 89], and by anesthesiologists or non-anesthesiologists in one [51]. The RCTs included patients who underwent colonoscopy (2 studies) or unselected endoscopy procedures (1 study). All RCTs found a lower incidence of oxygen desaturation with capnography versus without, and the difference reached statistical significance in two RCTs [51, 88]. The drawbacks of capnography include cost and false alarms that may lead to unnecessary procedure interruption, delay, or termination.

Statement 2010: Electroencephalogram (EEG)-based monitoring may be used during NAAP to target a sedation level; it may help to reduce propofol consumption during complex endoscopic procedures with targeted deep sedation. No clinical impact of EEG-based monitoring has been demonstrated (Evidence level 1+), and no specific recommendation is made due to the paucity of data.
Background
The BIS is an EEG-derived parameter that has been used during NAAP to achieve a target sedation level. The use of the BIS compared with clinical parameters during propofol sedation for endoscopy had been assessed by four RCTs [90–93]. Two of these found no difference in propofol consumption or recovery time for colonoscopy and gastric endoscopic submucosal dissection [92, 93]; the other two found lower propofol doses were used and recovery times were shorter for ERCP in the BIS-monitored group [90, 91]. No side effect had been attributed to the use of BIS.

New information since 2010
An RCT that included 144 patients undergoing ERCP showed no difference in cardiopulmonary complications, numbers of hypoxemic events, mean propofol doses, and quality of sedation whether or not BIS monitoring was used [94]. Recovery times after the procedure were shorter with BIS but the clinical benefit for daily practice was limited (mean duration from end of endoscopy until leaving the procedure room was 5.9 minutes versus 7.5 minutes, with versus without BIS, respectively). Three RCTs that included patients undergoing ERCP (n = 59) [95], colonoscopy (n = 115) [96], and gastric ESD (n = 180) [97] found no clinically significant advantage associated with the use of BIS monitoring.

5.2.3 Level of sedation

Statement 2010: Simple endoscopic procedures can be performed with moderate sedation, maintaining a high degree of patient satisfaction. Prolonged or complex procedures (e.g. EUS and ERCP) are frequently performed under deep sedation. (Evidence level 1++, Recommendation grade A.)

Statement 2015: We do not recommend using the bispectral index (BIS) during NAAP (strong recommendation, high quality evidence).

Background
The level of sedation can be assessed using different scales; an example is given in Table 3 [47, 98, 99]. The targeted levels of sedation are usually moderate for EGD/colonoscopy and deep for advanced procedures, such as EUS-guided fine needle aspiration (EUS-FNA) and ERCP.

New information since 2010
In a retrospective study of 486 ERCP procedures performed under targeted moderate sedation using midazolam and an opioid, the procedure could not be completed in 14% of the cases because of patient intolerance [100]. Independent predictors of failed ERCP under moderate sedation included substance abuse and higher difficulty of intervention as assessed on a standardized 3-point scale [101].

5.2.4 Protocols of propofol-based sedation

5.2.4.1 Propofol alone or combined with other drugs

Statement 2010: Combining propofol with an additional drug (benzodiazepine/opioid/ketamine) allows the dose of propofol administered to be decreased without reproducible effect on recovery time; there is no clear evidence that combining propofol with another drug leads to a decrease in adverse effects (Evidence level 1+). No recommendation is made about combination of propofol with other drugs.

Statement 2015: We suggest propofol monotherapy except in particular situations (weak recommendation, high quality evidence).

Background
Seven RCTs had compared sedation with propofol administered alone or combined with various drugs. No consistent difference had been found between the two regimens, except that a lower dose of propofol was administered if it was combined with traditional sedative agents.

New information since 2010
A meta-analysis of 9 RCTs (1505 patients) that compared propofol monotherapy versus propofol combined with traditional sedative agents found no significant differences between the groups in terms of complications (hypoxemia, hypotension, arrhythmias, and apnea) and of amnesia; the total dose of propofol was lower if propofol was combined with traditional sedative agents [102].

Propofol monotherapy presents the advantage of allowing more rapid patient recovery as the half-life of propofol is shorter than that of all other drugs used for sedation [103, 104]. However, in some individual situations, low dose midazolam premedication might be beneficial to facilitate intravenous line placement and to reduce the need for propofol [105]. Such situations include patients with a high anxiety potential, long-lasting procedures in patients with a known important need for sedatives, and patients with limited left ventricular function or with previous pronounced hypotension following propofol administration [106].

5.2.4.2 Propofol administration techniques

Statement 2010: Intermittent bolus administration of propofol is the current standard administration technique for NAAP. Data about propofol administration using perfusor systems during endoscopy are accumulating and show that these systems are as effective and safe as the standard technique. Patient-controlled sedation (PCS) is a valid administration technique but it is not applicable in a significant minority of patients. (Evidence level 1+.)

Table 3  Stages of sedation modified according to the American Society of Anesthesiologists [47].

<table>
<thead>
<tr>
<th>Minimal (anxiolysis)</th>
<th>Moderate</th>
<th>Deep</th>
<th>Anesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reaction being addressed</td>
<td>Patient reaction is adequate to verbal commands</td>
<td>Somnolence, reaction to louder commands, if needed with additional tactile stimulation</td>
<td>Somnolence, hard to wake, targeted reaction to repeated tactile stimulation and pain stimulus</td>
</tr>
<tr>
<td>Spontaneous breathing Not influenced</td>
<td>Adequate</td>
<td>Respiratory function mildly restricted</td>
<td>Inadequate, orotracheal intubation or larynx mask necessary</td>
</tr>
</tbody>
</table>
Statement 2015: We recommend administering propofol through intermittent bolus infusion or perfusor systems, including target-controlled infusion (TCI), and considering patient-controlled sedation (PCS) in particular situations (strong recommendation, high quality evidence).

5.2.5 Non-pharmacological measures available to reduce doses of propofol

5.2.5.1 Listening to music

Statement 2010: Listening to patient-selected music during colonoscopy allows the dose of propofol administered to be decreased; we recommend this for colonoscopy. (Evidence level 1 –, Recommendation grade B.)

Statement 2015: We suggest that patients listen to self-selected music during upper and lower GI endoscopy procedures (weak recommendation, moderate quality evidence).

Background
Music has historically been used as a non-pharmacological method used for relieving patient anxiety and pain.

New information since 2010
A new meta-analysis reviewed 21 RCTs that compared patients undergoing various endoscopic examinations with versus without music (total number of patients, 2134 [115]). Of these RCTs, 15 included upper and lower GI endoscopy procedures, while six RCTs included genitourinary or pulmonary endoscopy procedures. Listening to music during endoscopy was associated with significant improvements in pain and in anxiety, a lower heart rate and arterial blood pressure, as well as higher satisfaction scores. Better results were observed for GI as compared with non-GI endoscopy procedures; for GI endoscopies, procedure duration was shorter with music, although the doses of sedoanalgesic drugs were not significantly decreased in the music group compared with the control group. However, most of the trials included in this meta-analysis used traditional sedative regimens rather than propofol.

5.2.5.2 Pharyngeal anesthesia

Statement 2010: The role of pharyngeal anesthesia during propofol sedation for upper digestive endoscopy has not been assessed. No recommendation is made.

Statement 2015: We do not suggest using pharyngeal anesthesia during propofol sedation monotherapy for upper GI endoscopy (weak recommendation, moderate quality evidence).

Background
Pharyngeal anesthesia decreases patient discomfort during upper GI endoscopy under traditional sedation [116].

New information since 2010
Two placebo-controlled RCTs examined the effect of pharyngeal lidocaine (40 mg and 50 mg) on EGD under propofol monotherapy sedation in 419 patients [117, 118]. Both RCTs found that topical pharyngeal anesthesia did not reduce the necessary dose of propofol or improve the anesthetist’s or endoscopist’s satisfaction with the procedure; one RCT found that the use of lidocaine topical pharyngeal anesthesia reduced the gag reflex and that this had no clinical consequence.
5.2.6 Precautions and management of complications

Statement 2010: Propofol is contraindicated in patients with a known allergy to soy protein. Pain at the injection site is frequent and can be prevented by lidocaine (Evidence level 1++). Hypoxemia and hypotension are the most frequent adverse effects of propofol and develop during NAAP in 5%–10% of patients. Measures to be taken in case of complications should be established in a check-list that is updated and tested at regular intervals. If a patient proves difficult to sedate adequately for the examination purpose, endoscopy termination and referral to an anesthesiologist should be considered (Evidence level 4, Recommendation grade D).

Background

Propofol is contraindicated in patients with a known allergy to soy protein. Recommendations about allergies to other components (e.g., eggs, peanuts, sulfites) vary depending on the propofol formulation.

Hypoxemia and hypotension, the most frequent adverse events with propofol, are usually defined as hemoglobin oxygen saturation <90% and systolic blood pressure <90 mmHg, respectively. Their incidence during propofol-based sedation was, in a meta-analysis, 11% (95% CI 7%–16%) and 5% (95% CI 2%–10%), respectively [10].

Treatment of hypoxemia includes discontinuing the infusion of sedative drugs, increasing oxygen administration, and maintaining airway patency. Flumazenil/naloxone may be administered if benzodiazepines/opioids have been used. If the patient does not respond adequately to these measures, endoscopy should be stopped. If hypoxemia does not reverse, an emergency call must be made according to local protocols and ACLS must be initiated.

Hypotension is treated with administration of intravenous crystalloid solution and, if needed, vasopressor catecholamines. In cases of bradycardia, atropine should be administered intravenously.

Strict aseptic conditions should be maintained during manipulation of propofol [119, 120]. Propofol may cause pain at the injection site; this may be prevented by intravenous administration of lidocaine (0.5 mg/kg) with a rubber tourniquet on the forearm [121].

New information since 2010

In a nonrandomized controlled trial that included 216 patients undergoing EGD and/or colonoscopy under propofol combined with midazolam, routine placement of a Wendl nasopharyngeal tube reduced the frequency of hypoxic events during endoscopic sedation, with 4.7% of the patients showing minor nasopharyngeal injury [122].

With respect to allergy to soy oil as a contraindication to propofol administration, evidence has appeared that refined soy oil, such as that present in propofol, could be safe for people with soy allergy because the allergenic proteins are removed during the refining process [123].

5.3 Post-sedation care

5.3.1 Surveillance during recovery

Statement 2010: A small minority of sedation-related adverse effects occur after, as opposed to during, the procedure. We recommend patient observation until discharge by a person who is aware of the adverse effects of the drugs administered. (Evidence level 2+, Recommendation grade C.)

Statement 2015: No changes (strong recommendation, low quality evidence).

New information since 2010

None.

5.3.2 Discharge

Statement 2010: Minimum discharge criteria are useful for discharging patients after sedation for digestive endoscopy. We recommend using a standardized discharge scoring form. (Evidence level 2+, Recommendation grade C.)

Statement 2015: We suggest using the post-anesthetic discharge scoring system (PADSS) to determine when patient recovery is sufficient to allow discharge (weak recommendation, low quality evidence).

New information since 2010

A prospective study compared PADSS versus clinical criteria for the determination of sufficient patient recovery to permit discharge after outpatient colonoscopy under traditional sedation [128]; use of PADSS allowed earlier discharge. During follow-up phone calls, no hospital re-admissions related to endoscopy were identified.

Statement 2010: Minimum discharge criteria should be fulfilled before discharging a patient. However, psychomotor functions remain significantly impaired when standard discharge criteria are met. Upon discharge, patients should be accompanied by a responsible person and refrain from driving, operating heavy machinery, or engaging in legally binding decisions for at least 12 hours if sedation with propofol alone was administered (24 hours in cases of combined regimen). Advice should be provided verbally and in written form, including a 24-hour contact phone number. (Evidence level 1+, Recommendation grade A.)

Statement 2015: Minimum discharge criteria should be fulfilled before discharging a patient. We recommend that patients who have received combined regimens, and all patients of ASA class > 2, should upon discharge be accompanied by a responsible person and refrain for 24 hours.
from driving, drinking alcohol, operating heavy machinery, or engaging in legally binding decisions. Advice should be provided verbally and in written form to the patient, including a 24-hour contact phone number (strong recommendation, low quality evidence).

For patients of ASA classes 1 – 2 who have received low dose propofol monotherapy, a 6-hour limit is suggested (weak recommendation, low quality evidence).

Background
Psychomotor functions remain significantly impaired when standard discharge criteria are met [129]. Therefore, patients should be informed in advance of precautions to be taken after discharge; these instructions should be repeated at the time of discharge. Precautions include the presence of an escort to ensure safe return home following outpatient procedures. Advice should be provided verbally and in written form, including a 24-hour contact phone number.

Current recommendations from various professional associations to neither drive nor use public transport without an accompanying person, nor operate heavy machinery or engage in any legal decision-making for 24 hours seem too strict if propofol is used in low dose monotherapy. In a study, 92% of 400 patients who received low dose propofol for EGD wanted to drive when leaving the endoscopy unit, and all did so without incident [130].

New information since 2010
In a prospective study of 48 patients of ASA classes 1 – 3 who underwent colonoscopy under propofol monotherapy, psychomotor recovery, driving ability, and blood concentrations of propofol were within normal limits 1 hour after colonoscopy [103]. In another prospective study of 2101 patients of ASA classes 1 – 2 who underwent outpatient colonoscopy under low dose propofol monotherapy, 65% of the patients drove safely to their home or office after their colonoscopy [104]. An RCT that compared three sedation regimens for colonoscopy, namely propofol monotherapy, propofol-fentanyl, and midazolam-fentanyl, in 96 patients showed that propofol monotherapy had the least impact on post-procedure cognitive function [131].

5.4 Procedure documentation and medicolegal issues

Statement 2010: Documentation should be maintained throughout all phases of patient management, including:
– Vital signs assessed at regular intervals (oxygen saturation, heart rate, and blood pressure)
– Drugs (name, dosage), intravenous fluids (type, quantity), and oxygen (flow rate) administered
– Sedation-associated complications and their management
– Fulfillment of discharge criteria.
A minority of the audience thought that it should be recommended to record, in addition to this, the level of consciousness at regular intervals. Maintaining documentation in an electronic database may help to monitor quality and will provide a record in the event of medicolegal investigation. (Evidence level 4, Recommendation grade D.)

Statement 2015: No changes (weak recommendation, low quality evidence).

New information since 2010
None.

Statement 2010: The endoscopist bears the ultimate medicolegal responsibility to ensure proper personal training of the endoscopy staff involved in NAAP. (Evidence level 4.)

Statement 2015: No changes (low quality evidence).

New information since 2010
None.

Statement 2010: Informed consent for NAAP should be obtained from the patient or his/her legal representative according to domestic laws and regulations in a way similar to that of other endoscopy procedures. It is generally obtained during a face-to-face discussion between a physician familiar with the procedure and the patient, with information given in lay language to the patient and the opportunity for him/her to ask questions prior to the procedure. The informed consent regarding sedation issues may be incorporated into the main body of the endoscopy consent form. The procedure of informed consent should be documented. (Evidence level 4, Recommendation grade D.)

Statement 2015: We recommend that informed consent for NAAP be obtained from the patient or his/her legal representative according to domestic laws and regulations in a way similar to that for endoscopy procedures. We suggest using alternative methods for vulnerable populations such as elderly patients (weak recommendation, low quality evidence).

New information since 2010
None.

Statement 2010: The fact that the label accompanying propofol packages in many countries stipulates that “propofol should be administered only by persons trained in the administration of general anesthesia” means that, in some countries, during NAAP propofol is used “off-label.” Off-label use of drugs is common in medical practice and it has been endorsed by various associations, such as the Food and Drug Administration and the American Medical Association [133]. However, departure from label recommendations may in some courts shift to the defendant the burden of proving that the method of use accords with recognized clinical practice.

Background
A significant proportion of complications after endoscopy is related to sedation [41, 42]. In a series of 59 ERCP procedures for which malpractice was alleged, Cotton showed the importance of face-to-face communication between the endoscopist and the patient [134]. Information pertaining to sedation should be provided, including the pros and cons of sedation, with information about alternatives and about the option of unsedated endoscopy.

New information since 2010
A review of 13 studies (3 RCTs), including but not limited to endoscopy, found that patients’ recollection and understanding of the medical procedures, risks, and complications is often low, particularly among older individuals [135]. In a study from South Korea, only 56% of patients who underwent endoscopy under sedation answered that they were aware of the risks of sedatives [136]. The use of interactive multimedia and written material that are easy to read and comprehend increases patient awareness, recollection, and understanding of the consent procedure [135]. For vulnerable populations, it has been proposed that education classes be given to groups of patients with the informed consent procedure provided at the end of the class and before the scheduling of the endoscopic procedure [137].
These guidelines from ESGE and ESGENA represent a consensus of best practice based on the available evidence at the time of preparation. They may not apply in all situations and should be interpreted in the light of specific clinical situations and resource availability. Further controlled clinical studies may be needed to clarify aspects of the statements, and revision may be necessary as new data appear. Clinical consideration may justify a course of action at variance to these recommendations. ESGE guidelines are intended to be an educational device to provide information that may assist endoscopists in providing care to patients. They are not rules and should not be construed as establishing a legal standard of care or as encouraging, advocating, requiring, or discouraging any particular treatment.

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