
Evidence Brief: Capnography for Moderate Sedation in Non-Anesthesia Settings

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PREFACE

The VA Evidence Synthesis Program (ESP) was established in 2007 to provide timely and accurate syntheses of targeted healthcare topics of importance to clinicians, managers, and policymakers as they work to improve the health and healthcare of Veterans. These reports help:

- Develop clinical policies informed by evidence;
- Implement effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures; and
- Set the direction for future research to address gaps in clinical knowledge.

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Comments on this evidence report are welcome and can be sent to Nicole Floyd, Deputy Director, ESP Coordinating Center at Nicole.Floyd@va.gov.

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EXECUTIVE SUMMARY

Key Findings

- 8 studies (4 RCTs, 3 prospective observational, 1 retrospective observational) evaluated capnography versus routine monitoring for patients undergoing colonoscopy, esophagogastroduodenoscopy (EGD), endoscopic retrograde cholangiopancreatography (ERCP), endoscopic ultrasonography (EUS), minor oral surgery, flexible bronchoscopy, and transesophageal echocardiography (TEE).
- Adverse events rarely occurred and were similar between capnography and routine monitoring groups. One RCT reported 1 patient received a reversal agent for persistent hypoxemia after EGD and 2 patients had colonoscopies terminated early, all in the capnography group; another RCT reported no deaths occurred during ERCP or EUS in either group; and a prospective observational study reported no hospitalizations, use of reversal agents, or other serious adverse events during colonoscopy.
- Capnography during colonoscopy was associated with reduced risk of severe hypoxemia (SpO₂ <85%) (absolute risk difference [ARD]: -13%) but not hypoxemia (SpO₂ <90%) compared to routine monitoring. Capnography during ERCP and EUS was associated with reduced risk of hypoxemia (ARD: -26%) and severe hypoxemia (ARD: -16%) compared to routine monitoring. Capnography during flexible bronchoscopy was also associated with decreased risk of hypoxemia (ARD of -17%) and severe hypoxemia (ARD of -15%) compared to routine monitoring. Capnography had no impact on hypoxemia outcomes for any other procedures.
- False alarm rates were 13% and 45% in 2 studies.
- Capnography was consistently more costly than routine monitoring due to the need for additional equipment.

Background

The ESP Coordinating Center (ESP CC) is responding to a request for a rapid review on capnography for moderate sedation from the VA National Gastroenterology Program Office and the GI Field Advisory Committee. Findings from this evidence brief will be used to inform the development of a Moderate Sedation Directive by the VA National Anesthesia Service.

Methods

To identify studies, we searched MEDLINE, CINAHL and Cochrane Central Register of Controlled Trials (CENTRAL). We used prespecified criteria for study selection, data abstraction, and rating internal validity and strength of the evidence. See our PROSPERO protocol for our full methods (Registration # CRD42020168385).

Guidelines from professional societies disagree on the incremental value of adding capnography to routine monitoring during moderate sedation. Moderate sedation is a drug-induced (typically by an opioid and a benzodiazepine) depression of consciousness during which patients respond to verbal commands, either alone or accompanied by light touch, and have adequate spontaneous breathing without medical intervention. Moderate sedation is routinely used for common outpatient procedures performed by non-anesthesiologists. Capnography is a method of measuring CO₂ levels during exhaled breaths and can be used to detect hypoventilation, an earlier indicator of respiratory compromise than other indicators such as low oxygen levels

detected by pulse oximetry. However, it is unclear whether detection of hypoventilation during moderate sedation via capnography has a clinically meaningful effect on patient outcomes, and whether there are any unintended negative effects of capnography (such as false alarms that may distract the clinician during a procedure).

We conducted a rapid evidence review evaluating studies that compare capnography to routine monitoring for procedures under moderate sedation. We identified 8 studies (4 RCTs, 3 prospective observational, and 1 retrospective observational). Both GI procedures (colonoscopy, esophagogastroduodenoscopy [EGD], endoscopic retrograde cholangiopancreatography [ERCP], endoscopic ultrasonography [EUS], and other endoscopic procedures) and non-GI procedures (minor oral surgery, flexible bronchoscopy, transesophageal echocardiography [TEE]) were represented in the literature.

Five studies (2 RCTs, 2 prospective observational, and 1 retrospective observational) evaluated capnography versus routine monitoring for GI procedures. Severe hypoxemia ($\text{SpO}_2 < 85\%$) was lower in the capnography group than routine monitoring group (5% vs 18%) during colonoscopy; however, there was no difference in severe hypoxemia between monitoring groups during EGD. There was no difference in hypoxemia ($\text{SpO}_2 < 90\%$) between capnography and routine monitoring for either EGD or colonoscopy. Those monitored by capnography for ERCP or EUS had a decreased risk of hypoxemia ($\text{SpO}_2 < 90\%$) (46% vs 69%), severe hypoxemia (15% vs 31%), apnea (41% vs 63%), and need for oxygen supplementation (52% vs 67%), but no difference in abnormal ventilation compared to routine monitoring. Complications (eg, abnormal vital signs and need for reversal agents) were rare but overall similar between capnography and routine monitoring groups. False alarms occurred in 13% of patients undergoing ERCP and EUS, and patients and nurses reported more discomfort with colonoscopy during capnography than during routine monitoring. The total cost of implementing capnography was variable depending on type of procedure, setting, and types of costs authors reported but was consistently higher for capnography than routine monitoring. In terms of subgroup differences, capnography was more beneficial at reducing hypoxemia during ERCP versus EUS procedures, and for obese patients versus non-obese patients. Overall, we have low confidence in these studies' findings because of limitations in study design and execution – such as lack of outcome assessor blinding and greater loss of data in the capnography group – and because there was an inconsistent effect of capnography across studies.

Three studies (2 RCTs and 1 prospective observational study) examined capnography for non-GI procedures, including minor oral surgery, flexible bronchoscopy, and TEE. For minor oral surgery, there was no difference between capnography and routine monitoring on hypoxemia outcomes; but for bronchoscopy, capnography was associated with a reduced risk of hypoxemia (29% vs 46%) and severe hypoxemia (17% vs 32%), as well as shorter duration of hypoxemia (average of 20.4 vs 41.7 seconds) compared to routine monitoring. For TEE, respiratory depression developed in 45% of patients monitored by capnography, but no data comparing capnography to routine monitoring is available. Similar to GI procedures, complications in non-GI procedures were rare and generally similar between capnography and non-capnography groups. False apnea alarms occurred in 45% of bronchoscopy procedures. No studies reported subgroup differences between capnography and routine monitoring groups, nor did they report costs or other downstream outcomes. Overall, we have low confidence in these findings due to similar study limitations as were seen in the GI studies, as well as an inconsistent effect of capnography across studies.

There were limitations to our rapid review methods as well as limitations of primary studies. First reviewer inclusion of articles and extraction of data with second reviewer checking may have resulted in missing eligible studies or data, although we attempted to reduce this risk by establishing explicit inclusion criteria for studies and developing and using a piloted data abstraction tool. Most primary studies excluded those at highest risk of respiratory event (ASA category IV or V); therefore, findings from our review reflect lower-risk patients. The quality of the available literature was also mixed.

To weigh the added value of capnography monitoring during moderate sedation against potential trade-offs, more studies are needed that evaluate the role of timing and frequency of provider-delivered interventions to address respiratory distress on hypoxemia and clinical outcomes. More studies are also needed on downstream effects of implementing capnography (such as impact on wait times resulting from added procedural time or need for additional staffing or equipment that reduces the number of procedures that can be completed each day) as well as procedures not evaluated in any studies, such as tissue biopsies and cardiac procedures other than TEE.

Overall, the evidence does not support an effect of capnography on clinical outcomes compared to routine monitoring, for any procedure type. However, capnography may improve intermediate outcomes such as risk of hypoxemia and severe hypoxemia during ERCP, EUS, bronchoscopy, and severe hypoxemia for colonoscopy compared to routine monitoring. Capnography does not reduce hypoxemia, severe hypoxemia, or adverse events in other procedures including TEE, minor oral procedures, or EGD.

EVIDENCE BRIEF

INTRODUCTION

PURPOSE

The ESP Coordinating Center (ESP CC) developed this evidence brief on capnography for moderate sedation in response to a request from the VA National Gastroenterology Program Office and the GI Field Advisory Committee. Findings from this evidence brief will be used to inform the development of a Moderate Sedation Directive by the VA National Anesthesia Service.

BACKGROUND

Professional society guidelines disagree on the incremental value of adding capnography to routine monitoring during moderate sedation, which is defined by the American Society of Anesthesiologists (ASA) as a drug-induced depression of consciousness during which patients respond purposefully to verbal commands, either alone or accompanied by light tactile stimulation, have adequate spontaneous ventilation, and do not require interventions to maintain a patent airway.¹ Moderate sedation is routinely used for common outpatient procedures performed by gastroenterologists (eg, colonoscopy, esophagogastroduodenoscopy [EGD]), pulmonologists (eg, bronchoscopy), cardiologists (eg, transesophageal echocardiograms, cardiac ablation), interventional radiologists (eg, tissue biopsy), dentists, and others. Achieving moderate sedation typically involves use of a benzodiazepine for sedation (such as midazolam) and an opioid (such as fentanyl or meperidine) for pain control. Use of these medications can unintentionally lead to over-sedation including inadvertent deep sedation,^{2,3} which is defined as state in which patients cannot be easily aroused, may have inadequate spontaneous ventilation, and may require assistance in maintaining a patent airway.¹ Capnography refers to the measurement and graphic display of a patient's exhaled carbon dioxide, which correlates with ventilation (taking breaths). Capnography enables earlier detection of hypoventilation than other signs such as low oxygen levels and has been credited with reducing the overall mortality rate associated with general anesthesia, in which capnography monitoring is currently considered the standard of care.⁴

In 2011, the ASA recommended capnography monitoring during moderate and deep sedation based on a consensus document initiated by ASA Committee on Standards and Practice Parameters.⁵ Most recently, the 2018 ASA guideline on moderate procedural sedation recommends, “Continual monitoring of ventilatory function with capnography to supplement standard monitoring by observation and pulse oximetry.”⁶ In contrast, the 2018 American Society for Gastrointestinal Endoscopy guideline for sedation and anesthesia states that “integrating capnography into patient monitoring protocols for endoscopic procedures with moderate sedation has not been shown to improve patient safety” but recommends considering capnography for *deep* sedation.⁷

The controversy surrounding the need for capnography monitoring during moderate procedural sedation stems from differing views on the clinical significance of identifying hypoventilation earlier with capnography compared to routine monitoring, defined as a combination of oxygen measurements (pulse oximetry), heart rate and electrocardiogram tracking, serial blood pressure

measurements, and visual assessment for pauses in breathing (apnea) or abnormal breathing.⁶ Abnormalities in any of these measures may indicate evolving respiratory disturbances, which can lead to hypoxemia (low oxygen levels) and in turn lead to serious adverse events such as cardiac arrest. Transient hypoxemia is thought to be common during endoscopic procedures⁸ but has been difficult to track due to inconsistent definitions of oxygen desaturation and what changes are clinically meaningful.⁹ Similarly, adverse event (AE) rates in procedural sedation are challenging to quantify due to different AE definitions and reporting standards.⁹ In a retrospective evaluation of 324,737 endoscopy cases using opioids and benzodiazepines for sedation, rate of cardiopulmonary deaths was 8 per 100,000 (28 patients in the study).¹⁰ Recognition of respiratory disturbances during a procedure prompts the performing clinician or team member to intervene in ways including waking the patient via verbal or tactile stimulus, repositioning the patient, starting supplemental oxygen, or administering a sedation reversal agent. Members of non-anesthesia specialty groups such as gastroenterology acknowledge the potential benefits of capnography in terms of earlier detection of ventilation abnormalities but cite the overall safety of moderate procedural sedation¹¹⁻¹³ and question whether the added value of capnography justifies potential trade-offs in procedural costs and false alarms.¹⁴ Concern also exists that capnography monitoring via nasal cannula (the most common method) can interfere with certain procedures, such as EGD and bronchoscopy, and provide unreliable readings.^{15,16} On the other hand, proponents of capnography monitoring argue that it is a proven way to prevent procedural complications and should be employed regardless of how infrequently serious complications occur.¹⁷ Proponents of capnography monitoring also point to limitations of oxygen measurements via pulse oximetry, which can be falsely reassuring when patients are receiving supplemental oxygen.¹⁸

It is important to note that capnography monitoring in and of itself does not impact patient outcomes. Rather, the potential benefits of capnography are due to interventions taken in response to abnormal capnography findings that otherwise would not have been detected or detected too late with routine monitoring. Thus, the ideal study to determine the added value of capnography in moderate procedural sedation would compare not just rates of hypoxemia detection with and without capnography, but how often patients required interventions to correct respiratory disturbances and how often adverse events such as cardiac arrest occurred. The ideal study would also capture unintended negative consequences of capnography monitoring such as change in procedural costs, false alarms and other distractions for the clinician performing the procedure, and downstream impacts on patient access (*ie*, longer wait times that could result from added procedural time or need for additional staffing or equipment that could reduce the number of procedures that can be completed each day).

SCOPE

The aim of this rapid systematic review is to evaluate evidence on the benefits and harms of capnography monitoring during moderate sedation and whether these vary by patient characteristics, procedure types, or settings.

KEY QUESTIONS

Key Question 1: What are the benefits and harms of capnography monitoring during moderate sedation?

Key Question 2: Do these benefits and harms vary by patient characteristics, procedure types, or settings?

ELIGIBILITY CRITERIA

The ESP included studies that met the following criteria:

- **P**opulation: Adults undergoing procedures with moderate sedation (eg, opioid and benzodiazepine medication) by non-anesthesia providers
- **I**ntervention: Routine monitoring (cardiac rate and electrocardiographic rhythm, blood pressure, oxygenation using pulse oximetry, and respiratory frequency and adequacy of ventilation) with capnography
- **C**omparator: Routine monitoring (cardiac rate and electrocardiographic rhythm, blood pressure, oxygenation using pulse oximetry, and respiratory frequency and adequacy of ventilation) without capnography
- **O**utcomes: Detection of signs and symptoms of respiratory depression, adverse event rates including morbidity and mortality, unplanned interventions or post-procedure ICU or hospital admission, false alarms and other unintended consequences, access to procedural services, cost
- **T**iming: Any
- **S**etting: Any setting where moderate sedation is used by non-anesthesia providers
- **S**tudy design: Using a best evidence approach, we will prioritize evidence from systematic reviews and multisite comparative studies that adequately controlled for potential patient-, provider-, and system-level confounding factors. Inferior study designs (eg, single-site, inadequate control for confounding, noncomparative) will only be accepted to fill gaps in higher-level evidence.

METHODS

SEARCHES AND STUDY SELECTION

To identify articles relevant to the key questions, our research librarian searched Ovid MEDLINE, CINAHL, Cochrane Central Register of Controlled Trials (CENTRAL), and Cochrane Database of Systematic Reviews (CDSR), using terms for *moderate sedation* and *capnography* from database inception to January 2020 (see Supplemental Materials for complete search strategies). Additional citations were identified from hand-searching reference lists and consultation with content experts. We limited the search to published and indexed articles involving human subjects available in the English language.

Study selection was based on the eligibility criteria described above. We included studies where moderate sedation was induced through a benzodiazepine and an opioid. We excluded studies of propofol, thiopental, methohexital, ketamine, and etomidate. Although these medications can be used to induce moderate sedation, within the VHA setting anesthetic agents can only be administered by an anesthesiologist, nurse anesthetist, or other licensed independent practitioner with training to rescue a patient from general anesthesia.¹⁹ Titles, abstracts, and full-text articles were reviewed by 1 investigator and checked by another. All disagreements were resolved by consensus.

We also contacted manufacturers of capnography devices (Medtronic Inc, Phillips Healthcare, and Welch Allyn Inc) requesting unpublished data on studies that met our inclusion criteria.

QUALITY ASSESSMENT AND DATA EXTRACTION

We used predefined criteria to rate the internal validity of all studies. We used Cochrane's Risk of Bias 2 (ROB 2) tool to rate randomized controlled trials (RCTs) and the Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I) tool to rate non-randomized, controlled studies.^{20,21} We abstracted data from all studies and results for each included outcome. All data abstraction and internal validity ratings were first completed by 1 reviewer and then checked by another. All disagreements were resolved by consensus.

STRENGTH OF EVIDENCE ASSESSMENT

We informally graded the strength of the evidence based on the AHRQ Methods Guide for Comparative Effectiveness Reviews.²² This approach incorporates 4 key domains: risk of bias (includes study design and aggregate quality), consistency, directness, and precision of the evidence. Strength of evidence is graded for each key outcome measure and ratings range from high to insufficient, reflecting our confidence that the evidence reflects the true effect.

SYNTHESIS OF DATA

Due to limited data or heterogeneity, we synthesized the evidence qualitatively.

A draft version of this report was reviewed by peer reviewers as well as clinical leadership (see supplemental materials for disposition of peer review comments). The complete description of our full methods can be found on the PROSPERO international prospective register of

systematic reviews (<http://www.crd.york.ac.uk/PROSPERO/>; registration number CRD42020168385).

RESULTS

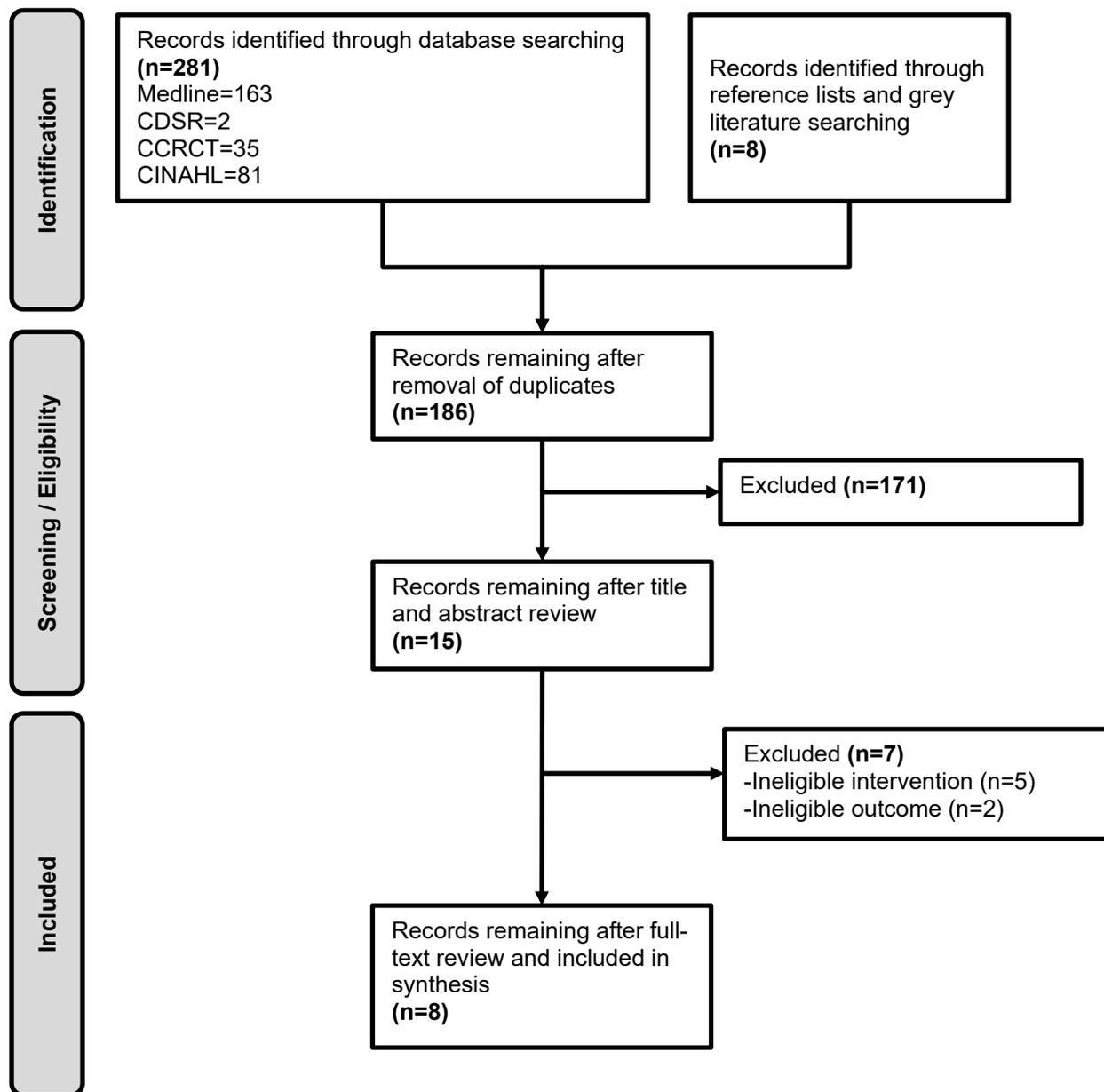
The literature flow diagram (Figure 1) summarizes the results of the search and study selection processes. Among 186 potentially relevant citations, 8 published studies^{4,15,23-28} (4 RCTs²³⁻²⁶ and 4 controlled observational studies^{4,15,27,28}) met our inclusion criteria. We did not receive any unpublished data from manufacturers of capnography devices.

The 8 included studies examined different types of procedures, including colonoscopy, esophagogastroduodenoscopy (EGD), complex GI procedures such as endoscopic retrograde cholangiopancreatography (ERCP), endoscopic ultrasonography (EUS), upper endoscopy with expandable metal stent placement, photodynamic therapy, and therapeutic push enteroscopy, transesophageal echocardiography (TEE), minor oral surgery, and flexible bronchoscopy. Most studies were conducted in an outpatient procedure unit, but settings also included a dental clinic, an emergency department, and a hospital. Sample size ranged from 49 to 5,466. Study follow-up periods were not reported but can be assumed to have ended after each procedure.

Detailed study-level data abstraction and quality assessment appear in the Supplementary Materials. The most relevant findings for each of these studies appear below, organized into 2 main categories: 1) GI procedures (colonoscopy, EGD, ERCP, EUS, and other complex GI procedures) and 2) other procedures (TEE, oral surgery, and flexible bronchoscopy).

LITERATURE FLOW

Figure 1: Literature Flowchart



GI PROCEDURES

Overview

Five studies (2 RCTs,^{25,26} 2 prospective observational,^{15,27} and 1 retrospective observational)⁴ evaluated capnography versus routine monitoring for GI procedures including colonoscopy,^{15,25} EGD,²⁵ ERCP,^{26,27} EUS,^{26,27} upper endoscopy with expandable metal stent placement,²⁷ photodynamic therapy,²⁷ and therapeutic push enteroscopy.²⁷ One study included a mix of procedures performed in an adult endoscopy suite but does not provide procedure details.⁴ Selected findings from these 5 studies are presented in Table 1.

Study design and limitations

Two RCTs^{25,26} (total n=805) evaluated the effect of capnography versus routine monitoring on hypoxemia and risk of adverse events for patients undergoing EGD, colonoscopy, ERCP, or EUS. In both RCTs, patients were randomized to either an open or blinded capnography group, with the endoscopy team blinded to assignment throughout the procedure. In both studies, an independent observer monitored capnography and alerted the endoscopist of any respiratory abnormalities in the open capnography group, but only alerted the endoscopist of apnea >30 seconds in the blinded group. The main limitations of the RCT²⁵ examining EGD and colonoscopy were that baseline systolic blood pressure was higher in the EGD capnography blinded group versus open group, more patients' data were excluded from the capnography group than the routine monitoring group (8 vs 1 patient), and outcome assessors were aware of what group patients were assigned to. The main limitation of the RCT²⁶ examining ERCP and EUS was that outcome assessors were aware of what group patients were assigned to.

Two prospective observational studies^{15,27} (total n=1,015) provide data on additional outcomes and GI procedures not covered by these RCTs, including 1 hospital's experience implementing capnography for all colonoscopy procedures. The first prospective observational study¹⁵ compared safety, patient satisfaction, and costs of colonoscopy procedures before and after hospital-wide implementation of capnography monitoring. Because data was collected from the 2 groups at different times, there is risk that other factors besides the implementation of capnography (such as hospital-wide quality improvement initiatives or secular trends) could have affected the results. The second prospective observational study²⁷ compared capnography versus routine monitoring on hypoxemia outcomes for patients undergoing ERCP, EUS, and other complex procedures. In this study, the endoscopist was blinded to the capnography device and did not receive any information from the independent observer during the procedure, meaning they did not have the opportunity to act on the data collected by capnography. Additional limitations of the study were that outcome assessors were aware of what group patients were in, and there was no information on the number of patients who were approached for or were otherwise eligible for the study compared to the number who enrolled.

One additional retrospective observational study⁴ (n=5,446) evaluated sedation-related complications in a large series of patients undergoing endoscopic procedures either monitored by capnography or routine monitoring. However, because authors provided limited information on patient characteristics, types of procedures, sedation used, and reason why capnography was used in some procedures but not others, little meaningful information can be drawn from the study.

Hypoxemia outcomes

In the RCT²⁵ of EGD and colonoscopies, there was no difference between open and blinded capnography groups on hypoxemia (risk of hypoxemia [SpO₂<90%] during EGD: 50% open vs 54% blinded; risk of hypoxemia during colonoscopy: 52% open vs 54% blinded). However, the risk of severe hypoxemia (SpO₂<85%) during colonoscopy was lower in the open capnography group (5% vs 18%). In the RCT²⁶ of ERCP and EUS, the open capnography group had a decreased risk of hypoxemia (46% vs 69%), severe hypoxemia (15% vs 31%), apnea (flat line or no respiratory rate ≥15 s) (41% vs 63%), and need for oxygen supplementation (52% vs 67%), but no difference in abnormal ventilation (flat line for ≥5 seconds but <15 seconds, >75% reduction in amplitude of respiratory waves for ≥5 seconds) compared to the blinded group. Of

patients receiving oxygen supplementation due to hypoxemia in this study, more people in the blinded arm than the open capnography arm had recurrent hypoxemia (38% vs 18%). In a prospective observational study²⁷ of ERCP, EUS, and other complex GI procedures, 54 episodes of apnea (no respiratory activity ≥ 30 seconds) and disordered respiration (45-second interval that contained ≥ 30 seconds of apneic activity) were detected in 49 patients, only 50% of which were caught by pulse oximetry, 5% of which were caught by hypercapnea, and none of which were caught by visual assessment.

The proportion of people who had obstructive sleep apnea – a potential driver of hypoxemia during moderate sedation – was reported in 3 studies. In the RCT²⁵ of EGD and colonoscopies, those with sleep apnea were excluded from enrollment. In the RCT²⁶ of ERCP and EUS, the percentages of people with sleep apnea were similar between open and blinded capnography groups (11.3% vs 13%). Finally, in the prospective observational study²⁷ of ERCP, EUS, and other complex GI procedures, the number of people with sleep apnea was not reported but one can infer they were included as a history of sleep apnea was found to be associated with increased propensity to desaturation.

Adverse events and interventions to address respiratory distress

Complications (*eg*, abnormal vital signs and need for reversal agents) were rare but overall similar between capnography and routine monitoring groups in these studies. In the RCT²⁵ of EGD and colonoscopies, 1 patient in the EGD open capnography group received naloxone after their procedure due to persistent hypoxemia, and 2 patients in the colonoscopy open capnography group had their procedure terminated early (no other details provided). Similar rates of hypotension and bradycardia were seen in both capnography and routine monitoring groups for both procedure types. In the RCT²⁶ of ERCP and EUS, there were no deaths in either capnography or routine monitoring groups. False alarms (defined as a flat line of respiratory activity for at least 50 seconds without an associated decrease in oxygen saturations or normal chest excursions) occurred in 35 out of 263 (13%) patients in this study. Authors hypothesized these false alarms were caused by diminution of air stream because of narrow oropharyngeal inlet or blockage of the connecting tube with moisture.

In a prospective observational study¹⁵ of colonoscopies, sedation events (defined as any of the following: oxygen saturation $< 90\%$ or leading to an intervention; problematic changes in heart rate or blood pressure; any hemodynamic or respiratory condition that interrupted procedure; use of any reversal agent; hospitalization) were similar before and after implementation of capnography (8.2% vs 11.2%), and no patients were hospitalized or required reversal agents in either group. However, patients and nurses reported more discomfort with the colonoscopy procedure after capnography implementation (1.71 vs 1.00 for patients and 1.82 vs 1.33 for nurses on PROSAS survey) than before. In a retrospective observational study⁴ of endoscopic procedures, 14 (out of 4,846) procedures without capnography encountered an over-sedation complication that required either assisted bag-mask ventilation or reversal agents while 0 (out of 600) procedures with capnography resulted in an over-sedation complication, although the difference between groups was not statistically significant.

These studies report when patients required reversal agents or bag mask ventilation but do not report how often lesser interventions such as patient stimulation or repositioning occurred. The

studies thereby leave gaps in our full understanding of the practical implications of adding capnography monitoring, such as staffing needs.

Costs and other system-level outcomes

The total cost of implementing capnography was variable depending on the type of procedure and setting, as well as what types of costs authors reported. Authors reported both fixed costs (*eg*, costs of procuring and maintaining hardware and software for procedure rooms) as well as variable costs (*eg*, costs of single-use capnograph lines and cannulas). Implementing capnography for colonoscopies in a single hospital was estimated to cost an additional \$40,000 to upgrade procedure rooms and provide cannulas for patients.¹⁵ Capnography was more expensive than routine monitoring for endoscopic procedures in an adult endoscopic unit⁴ (costs were approximately \$2,100-\$12,900 for capnography vs \$725-\$3,075 for pulse oximetry). Finally, the addition of capnography was associated with additional costs for ERCP, EUS, and other complex procedures in another hospital (*ie*, a one-time software activation fee [\$150], an in-line dehumidifying module that is changed weekly [\$23]) and a disposable nasal cannula used for each patient [\$4].²⁷

Studies reported^{25,26} that procedure times were generally similar between capnography and routine monitoring groups (EGD lasted 5.6 minutes in both groups; colonoscopy lasted 17.3 in capnography group vs 17.5 minutes in routine group; ERCP/EUS lasted 34.4 in capnography group vs 37.2 minutes in routine group), indicating that capnography does not add time to procedures. Studies did not report any other implementation-related outcomes (such as costs and time required to train staff and any differential staffing requirements during procedures) or any other downstream, system-level outcomes such as wait times.

Differences by subgroups

One RCT²⁶ found that capnography monitoring was more beneficial at reducing hypoxemia during ERCP versus EUS procedures, and for obese patients versus non-obese patients. RCTs^{25,26} also reported that certain patient characteristics (older age, female sex, lower baseline oxygen saturation, higher BMI, higher baseline diastolic blood pressure) were associated with hypoxemia across monitoring groups. One RCT²⁵ also found that higher doses of fentanyl were associated with severe hypoxemia across monitoring groups. One prospective observational study²⁷ additionally found that patient comorbidities (ischemic heart disease, pack-year smoking history) were associated with apnea and disordered respiration across monitoring groups. A final retrospective observational study⁴ found that those who experienced sedation-related complications (all of whom were routinely monitored) had some common patient and procedural characteristics (longer duration of procedure, older age, and medical comorbidities such as previous stroke or COPD), although these weren't compared to those who did not experience sedation-related complications.

Strength of evidence

We have low confidence in these studies' findings given that outcome assessors and sometimes providers were aware of what group patients were assigned to, more people were excluded from analyses due to data loss in capnography compared to routine monitoring groups, and there was not a consistent effect of capnography seen across studies.

Table 1. Selected findings of studies of capnography versus routine monitoring for GI procedures

Author year Study design Size	Population & intervention	Hypoxemia outcomes	Unplanned interventions	Adverse events (eg, false alarms, etc)	Relevant subgroup analyses
Mehta 2016 ²⁵ RCT n= 542 Fair quality	Population: Patients undergoing esophago-gastroduodenoscopy (EGD) or colonoscopy Intervention: Open arm (capnography & routine monitoring with an independent observer who would alert endoscopist of any respiratory abnormalities) vs blinded arm (same intervention but observer would only alert endoscopist when apnea lasted >30 seconds)	EGD <ul style="list-style-type: none"> No difference in rates of hypoxemia (SpO₂<90% for ≥10 s): 50% cap vs 54% reg No difference in severe hypoxemia (SpO₂<85% any duration): 19% vs 17% No difference in disordered respirations (>75% reduction from the baseline waveform) No difference in apnea/pseudo apnea (flat line or no respiratory rate ≥5 s) No difference in hypoventilation (respiratory rate ≤8 breaths/min) Colonoscopy <ul style="list-style-type: none"> No difference in rates of hypoxemia between groups (52% vs 54%), disordered respiration, apnea, pseudo apnea, or hypoventilation Fewer people in open capnography group experienced severe hypoxemia than routine monitoring group (5% vs 18%) 	1 subject in the EGD open capnography group received naloxone-reversal agent post procedurally due to persistent hypoxemia.	EGD <ul style="list-style-type: none"> Similar rates of hypotension & bradycardia in both groups Neither group had any procedures terminated early Colonoscopy <ul style="list-style-type: none"> Similar rates of hypotension & bradycardia in both groups 2/231 people in open capnography had procedure terminated early 	NR
Qadeer 2009 ²⁶ RCT n= 263 Good quality	Population: Adult inpatients/outpatients undergoing ERCP or EUS Intervention: Open arm (capnography & routine monitoring with an independent	Fewer people in capnography arm than routine monitoring arm experienced: <ul style="list-style-type: none"> Any hypoxemia (SpO₂<90% for ≥15 s): 46% vs 69%. Severe hypoxemia (SpO₂<85% any duration): 15% vs 31%. 	NR	<ul style="list-style-type: none"> False alarms: in 35 (13%) procedures, capnography erroneously displayed flat line for >50 seconds No other adverse events 	Capnography more beneficial at reducing occurrence of hypoxemia for ERCP compared with EUS and in obese patients compared

Author year Study design Size	Population & intervention	Hypoxemia outcomes	Unplanned interventions	Adverse events (eg, false alarms, etc)	Relevant subgroup analyses
	observer who would alert endoscopist of any respiratory abnormalities) vs blinded arm (same intervention but observer would only alert endoscopist when apnea lasted >30 seconds)	<ul style="list-style-type: none"> Apnea (flat line or no respiratory activity ≥ 15 s): 41% vs 63% No difference between groups in abnormal ventilation (flat line for ≥ 5 seconds but <15 seconds, >75% reduction in amplitude of respiratory waves for ≥ 5 seconds): 77% vs 82%		occurred in either group	with nonobese patients.
Barnett 2016 ¹⁵ Prospective case-control n= 966 Fair quality	Population: Adult patients undergoing colonoscopy Intervention: Before and after hospital-wide capnography implementation	Sedation events (oxygen saturation <90% or leading to an intervention; problematic changes in heart rate or blood pressure; any hemodynamic or respiratory condition that interrupted procedure; use of any reversal agent; hospitalization) were similar in both cohorts (8.2% pre-cap vs 11.2% post-cap)	No reversal agents needed and no hospitalizations in either group	Patients and nurses reported more discomfort with colonoscopy procedure after capnography implementation (1.71 vs 1.00 for patients and 1.82 vs 1.33 for nurses on PROSAS survey)	NR
Vargo 2002 ²⁷ Prospective observational study n= 49 Fair quality	Population: Hospitalized pts undergoing ERCP, EUS, upper endoscopy with expandable metal stent placement, photodynamic therapy, or therapeutic push enteroscopy Intervention: All pts monitored by capnography and routine monitoring	Episodes of apnea (no respiratory activity ≥ 30 s) and disordered respiration (45 s interval that contained ≥ 30 s of apneic activity) (ADR) detected by capnography = 54. ADR detected by pulse oximetry (50% of time), hypercapnea (5.5% of time), and visual assessment (0% of time).	NR	NR	NR
Koniaris 2003 ⁴ Retrospective	Population: Adult patients (n=5,466) who underwent	NR	NR	14 (out of 4,846) procedures without capnography encountered an	NR

Author year Study design Size	Population & intervention	Hypoxemia outcomes	Unplanned interventions	Adverse events (eg, false alarms, etc)	Relevant subgroup analyses
n= 5,446 Poor quality	endoscopic procedures Intervention: Capnography & routine monitoring vs routing monitoring			over-sedation complication that required either assisted bag-mask ventilation or reversal agents. Zero (out of 600) procedures with capnography encountered an over-sedation complication. No statistical difference between 2 groups.	

OTHER PROCEDURES

Overview

Three studies (2 RCTs and 1 prospective observational study) examined capnography for non-GI procedures, including minor oral surgery,²³ flexible bronchoscopy,²⁴ and TEE.²⁸

Study design and limitations

One RCT²³ (n=190) compared capnography to routine monitoring for patients undergoing minor oral surgery on hypoxemia outcomes. A major limitation of this study is that patients and providers were aware of their group assignment by the time of the surgery. An additional limitation was that more people in the capnography group than routine monitoring group were removed from analysis because of missing data (6 vs 2 people). A second RCT²⁴ (n=185) compared capnography to routine monitoring for patients undergoing flexible bronchoscopy on hypoxemia outcomes, false alarms, and risk of adverse events. Similar to the previous RCT, providers were aware of group assignment before the procedure. In addition, 21 total patients were excluded from analysis due to protocol deviations or incomplete data on vital signs (although rates of missing data were similar between capnography and routine monitoring groups). A third prospective observational study²⁸ (n=200) of patients undergoing transesophageal echocardiography (TEE) provides data on how many patients experienced respiratory depression as measured by capnography as well as overall rates of sedation reversal agents or advanced airway procedures. However, because all providers were blinded to the capnography monitor during the procedures and no comparative analyses were conducted afterwards, no comparative data is available on the effect of capnography compared to routine monitoring.

Hypoxemia outcomes

In the RCT²³ of minor oral surgeries, there was no difference between capnography and routine monitoring on any hypoxemia outcomes (including any hypoxemia [$\text{SpO}_2 \leq 94\%$], moderate hypoxemia [SpO_2 90-92%] or severe hypoxemia [$\text{SpO}_2 < 90\%$]). In the RCT²⁴ of flexible bronchoscopy, capnography was associated with reduced risk of hypoxemia ($\text{SpO}_2 < 90\%$) (29% vs 46%) and severe hypoxemia ($\text{SpO}_2 < 85\%$) (17% vs 32%), as well as reduced duration of hypoxemia (average of 20.4 vs 41.7 seconds) compared to routine monitoring. In the prospective observational study²⁸ of TEE, respiratory depression (defined as ETCO_2 level of greater ≥ 50 mm Hg at any time during the procedure, an ETCO_2 change from baseline greater than 10 mm Hg, or a loss of ETCO_2 waveform ≥ 15 seconds) developed in 45% of patients monitored by capnography. This study's abstract states that capnography identified respiratory depression earlier than pulse oximetry but does not provide data to support this statement.

The proportion of people who had obstructive sleep apnea was reported in 2 studies. In the RCT²⁴ of flexible bronchoscopy, those with severe sleep apnea were excluded. In the prospective observational study²⁸ of TEE, 15% of participants had obstructive sleep apnea and 7.5% used a CPAP or BiPAP machine.

Adverse events and interventions to address respiratory distress

Similar to GI procedures, complications in non-GI procedures were rare and generally similar between capnography and non-capnography groups. In the RCT²⁴ of flexible bronchoscopy, there were similar rates of adverse events (hypotension and bradycardia) in both capnography and routine monitoring groups. False apnea alarms (flat line > 10 seconds determined to be false after physical assessment) occurred in 45% of these procedures. Of note, bronchoscopy is often performed by inserting a tube through the nose, which can interfere with capnography reading which is also measured through the nose. False alarms in this study were caused by continuous suction with bronchoscope, oral suction with suction catheter, or disconnection or obstruction of sample line, and authors noted the suction may have prevented the capnography device from sampling expired air. The prospective observational study²⁸ of TEE concluded that blinding providers to capnography data and not giving patients a subsequent intervention to address respiratory depression “was not harmful” but did not provide any data to support this.

The RCT²³ of minor oral surgeries reported that more people in the capnography group received verbal stimulation to take breaths than in the control group (54 vs 38 people), but the number of people requiring supplemental oxygen was the same (3 in each group). The RCT²⁴ of flexible bronchoscopy reported that interventions to address apnea or hypoxemia episodes were similar in capnography versus routine monitoring groups, with the most commonly received procedures being increased O_2 supply (45 vs 42 participants) and a chin-lift/jaw-thrust movement (14 vs 8). Timing of these interventions was not reported. The prospective observational study²⁸ of TEE blinded providers to capnography throughout the procedure.

Costs and other system-level outcomes

The RCT²⁴ of bronchoscopy reported procedure times were similar in capnography versus routine monitoring groups (28.3 vs 27.4 minutes), indicating the use of capnography did not increase procedure time. No studies reported on costs or any other downstream outcomes such as access.

Differences by subgroups

None of these studies reported subgroup differences in the effect of capnography versus routine monitoring. However, 1 prospective observational study²⁸ did report that those with lower baseline respiratory rates and those who received more hydromorphone were more likely to experience respiratory depression during TEE across monitoring groups.

Strength of evidence

We have low confidence in these studies' findings, as providers were made aware of which group patients were assigned to assignment before the procedure, more data was missing from capnography than routine monitoring groups, and the effects of capnography were inconsistent across procedure types.

Table 2. Selected findings of studies of capnography versus routine monitoring for non-GI procedures

Author year Study design Size	Population & intervention	Hypoxemia outcomes	Unplanned interventions	Adverse events (eg, false alarms, etc.)	Subgroup differences
Brady 2016 ²³ RCT n= 190 Fair quality	Population: Patients undergoing minor oral procedures Intervention: Capnography & routine monitoring vs routine monitoring alone	No difference between groups in the proportion of patients who experienced: <ul style="list-style-type: none"> Any hypoxemia (SpO₂ ≤94% any duration) 34% vs 39% Moderate hypoxemia (SpO₂ 90-92%) 25% vs 24% Severe hypoxemia (SpO₂ <90%) 12% vs 8% 	NR	NR	NR
Ischiwata 2018 ²⁴ RCT n= 185 Fair quality	Population: Patients undergoing sedated flexible bronchoscopy (FB) Intervention: Capnography & routine monitoring vs routine monitoring alone	Those in capnography arm had better outcomes than routine monitoring in terms of: <ul style="list-style-type: none"> Any hypoxemia (SpO₂ <90%) 29% vs 46% Duration of hypoxemia: 20.4 vs 41.7 seconds Severe hypoxemia (SpO₂ <85%) 17% vs 32% 	NR	83/185 (45%) procedures had false apnea alarms Groups were similar in terms of hypotension and bradycardia (2 vs 1) and bradycardia alone (2 vs 1)	NR

Author year Study design Size	Population & intervention	Hypoxemia outcomes	Unplanned interventions	Adverse events (eg, false alarms, etc.)	Subgroup differences
		<ul style="list-style-type: none"> Mean lowest SpO2 value: 90.5% vs 87.6% Similar rates of apnea (47% vs 44%) in both groups			
Adams 2015 ²⁸ Prospective, single-group observational n= 200 Fair quality	Population: Adults undergoing transesophageal echocardiography (TEE) Intervention: All pts received capnography & routine monitoring but providers were blinded to capnography monitor	Capnography-detected respiratory depression (ETCO2 level of greater \geq 50 mm Hg at any time during the procedure, an ETCO2 change from baseline greater than 10 mm Hg, or a loss of ETCO2 waveform \geq 15 seconds) developed/occurred in 45% of patients	NA	NA	NA

SUMMARY AND DISCUSSION

We conducted a rapid evidence review evaluating the benefits and harms of capnography monitoring for procedures involving moderate sedation with a benzodiazepine and an opioid. Previous systematic reviews on capnography for moderate sedation have either focused on a specific clinical specialty (such as emergency department²⁹) or a limited set of outcomes (such as hypoxemia, sedation-related adverse events, and patient satisfaction^{30,31}). Our review includes a broader range of specialty areas and outcomes to help health systems determine which patients and procedures might benefit from capnography monitoring, and when added value of capnography may not justify potential trade-offs.

We found 8 studies (4 RCTs and 4 observational) examining capnography for a variety of GI and non-GI procedures. In 4 of these studies^{4,24-26} on ERCP, EUS, flexible bronchoscopy, colonoscopy, and EGD, both capnography and routine monitoring were associated with low rates of adverse events such as abnormal vital signs and use of reversal agents. Across studies, no patients died²⁶ or were hospitalized.¹⁵ Otherwise, we found no data indicating that capnography provides a clinical benefit to patients. In terms of system outcomes, 3 studies²⁴⁻²⁶ found that procedure times were similar when capnography or routine monitoring were used, but no other implementation-related outcomes (such as training time or staffing requirements for procedures) were reported. Three studies found capnography added costs to systems, although the total amount was variable depending on what aspects of capnography were included in their calculations.^{4,15,27} Our findings are consistent with a 2017 Cochrane review²⁹ which found “a lack of convincing evidence that the addition of capnography to standard monitoring in ED PSA [procedural sedation and anesthesia] reduces the rate of clinically significant adverse events.”

While studies suggested there are no clinical or system-level benefits of capnography, capnography can reduce the occurrence of hypoxemia for certain types of procedures. Two RCTs^{24,26} of ERCP, EUS, and bronchoscopy indicated capnography is associated with a lower risk of hypoxemia and severe hypoxemia than routine monitoring. In addition, another RCT²⁵ found capnography is associated with lower risk of severe hypoxemia but no difference in hypoxemia when compared to routine monitoring. Otherwise, there were no effects of capnography compared to routine monitoring on hypoxemia for any other procedure. Harms of capnography included high rates of false alarms (13% and 45% depending on the procedure)^{24,26} and more procedural discomfort as reported by patients and nurses.¹⁵ Our findings are consistent with 2 recent reviews^{30,31} which found that capnography may reduce risk of hypoxemia. One of these reviews³⁰ found that capnography did not lead to additional harms related to assisted ventilation, patient satisfaction, recovery time, or the quality and duration of sedation, but did not consider false alarms to be a harm, and did not include the prospective observational study¹⁵ indicating patients experienced more discomfort with capnography than routine monitoring. The high rates of false alarms in these studies align with clinicians’ anecdotal accounts of their experiences using capnography monitoring^{14,32} – specifically, that false alarms have the potential to lead to “needless disruption, prolongation, or abandonment of procedures that the sedation was intended to facilitate.”^{14,32} Tellingly, the ASA revised its Standards for Basic Monitoring in 2005³³ to mandate that pulse oximeter and capnography not be turned off, indicating that many proceduralists find capnography alarms to be more harmful than helpful.

Subgroup analyses from a single RCT²⁶ indicated that capnography was more beneficial at reducing hypoxemia events during ERCP versus EUS procedures, and for obese patients versus

non-obese patients. Other studies reported that certain patient and sedation characteristics were associated with increased risk of hypoxemia^{25,26} (*ie*, lower baseline oxygen saturation, female sex, higher BMI, older age) and severe hypoxemia²⁵ or respiratory depression²⁵ (*ie*, higher doses of fentanyl or hydromorphone) across monitoring groups. Comorbidities such as ischemic heart disease and pack-year smoking history were also associated with apnea and disordered respiration²⁷ across monitoring groups. Consistent with standard practice,⁶ these findings suggest that clinicians should consider patient, procedure, and sedation characteristics when determining a monitoring plan, as some patients may be at higher risk of respiratory distress and other adverse outcomes than others undergoing the same procedure.

LIMITATIONS

There are limitations to both our rapid review methods and methodological limitations of our included primary studies.

In terms of rapid review methods, one reviewer assessed articles for inclusion and abstracted data with second reviewer checking. This could have resulted in missing eligible studies or data, although we made attempts to reduce this risk by establishing explicit inclusion criteria for studies and developing and using a piloted data abstraction tool.

In terms of primary study limitations, most studies excluded those at highest risk of respiratory event (ASA category IV or V). In practice, those with ASA IV/V or other comorbidities that put them at higher risk would be referred to an anesthesiologist rather than undergo moderate sedation performed by a non-anesthesiologist.¹⁵ Findings from our review therefore reflect lower-risk patients and should not be universally applied to all patients undergoing these procedures. An additional limitation is that the quality of the available literature supporting capnography for moderate sedation is mixed. Potential issues that could have biased results across studies include the fact that in general, more patients from capnography groups than routine monitoring groups were excluded due to data loss. This could have potentially biased results in favor of capnography, if patients whose data were lost were sicker or otherwise had more complications than those whose data were retained. Lack of outcome assessor and provider blinding also could have also biased results, depending on how assessors and providers felt about capnography.

GAPS AND FUTURE RESEARCH

More studies are needed that evaluate the full scope of outcomes when capnography monitoring is added to moderate procedural sedation, including the specific actions providers take when alerted to hypoventilation via capnography. Despite a reduction in hypoxemia, delivery of earlier or more frequent interventions to address respiratory distress could also have downsides – such as patient discomfort when taking deep breaths – so studies should include an evaluation of patients' experiences during the procedure as well as their clinical outcomes. These questions could be addressed by a carefully documented, single-arm prospective observational study rather than an RCT. For example, researchers could conduct a study in which an observer documents how often and when capnography alarms occur during a certain procedure, what actions (if any) were taken to address the alarm, providers' self-reported impressions of the alarms (whether they felt distracted or not), and patients' self-reported impressions of the procedure (level of

discomfort), in addition to recording hypoxemia outcomes, unplanned interventions, adverse events, and any other relevant, post-procedure clinical outcomes.

In addition, more studies are needed on the effects of capnography on downstream health system outcomes (eg, costs of training/staffing, wait times). While capnography adds costs to systems due to the use of additional equipment, studies did not report costs of any additional training of providers or staffing of procedures. Measurement of the downstream effects of capnography – such as longer wait times for a procedure due to limited access to equipment or staff – could indicate whether there are any other downsides of the use of capnography on patients' access to these procedures. Given the large volume of procedures performed under moderate sedation at the VA each year (for example, 300,000 colonoscopies are performed under VA care every year),³⁴ even a small increase in wait times could have a large impact on the number of Veterans who receive these procedures in a timely way. This is an especially important outcome for colonoscopy, given the importance of early screening and detection of colorectal cancer on patient outcomes.

Finally, studies are needed on other types of routine procedures such as those completed by interventional radiology (such as tissue biopsies) and cardiac procedures other than TEE. We identified no studies examining these types of procedures.

CONCLUSIONS

Overall, the evidence does not support an effect of capnography on clinical outcomes compared to routine monitoring, for any procedure type. However, capnography may improve intermediate outcomes such as risk of hypoxemia and severe hypoxemia during ERCP, EUS, bronchoscopy, and severe hypoxemia for colonoscopy compared to routine monitoring. Capnography is not associated with any difference in hypoxemia, severe hypoxemia, or adverse events in other types of procedures including TEE, minor oral procedures, or EGD. More detailed information is needed on how the timing of provider-delivered interventions affects hypoxemia, how the use of capnography affects downstream system outcomes such as wait times, as well as on the use of capnography for interventional radiology and cardiac procedures other than TEE.

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In designing the study questions and methodology at the outset of this report, the ESP consulted with technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicting opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodologic approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts.

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Operational Partners

Operational partners are system-level stakeholders who have requested the report to inform decision-making. They recommend Technical Expert Panel (TEP) participants; assure VA relevance; help develop and approve final project scope and timeframe for completion; provide feedback on draft report; and provide consultation on strategies for dissemination of the report to field and relevant groups.

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To ensure robust, scientifically relevant work, the TEP guides topic refinement; provides input on key questions and eligibility criteria, advising on substantive issues or possibly overlooked areas of research; assures VA relevance; and provides feedback on work in progress. TEP members are listed below:

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The Coordinating Center sought input from external peer reviewers to review the draft report and provide feedback on the objectives, scope, methods used, perception of bias, and omitted evidence. Peer reviewers must disclose any relevant financial or non-financial conflicts of interest. Because of their unique clinical or content expertise, individuals with potential conflicts may be retained. The Coordinating Center and the ESP Center work to balance, manage, or mitigate any potential nonfinancial conflicts of interest identified.

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