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Review Article

REVIEW ARTICLE

Impact of capnography on patient safety in high- and low-income settings: a scoping review

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Abstract

Background: Capnography is universally accepted as an essential patient safety monitor in high-income countries (HICs) yet is often unavailable in low and middle-income countries (LMICs). Increasing capnography availability has been proposed as one of many potential approaches to improving perioperative outcomes in LMICs. This scoping review summarises the existing literature on the effect of capnography on patient outcomes to help prioritise interventions and guide expansion of capnography in LMICs.

Methods: We searched MEDLINE and EMBASE databases for articles published between 1980 and March 2019. Studies that assessed the impact of capnography on morbidity, mortality, or the use of airway interventions both inside and outside the operating room were included.

Results: The search resulted in 7445 unique papers, and 31 were included for analysis. Retrospective and non-randomised data suggest capnography use may improve outcomes in the operating room, ICU, and emergency department, and during resuscitation. Prospective data on capnography use for procedural sedation suggest earlier detection of hypoventilation and a reduction in haemoglobin desaturation events. No randomised studies exist that assess the impact of capnography on patient outcomes.

Conclusion: Despite widespread endorsement of capnography as a mandatory perioperative monitor, rigorous data demonstrating its impact on patient outcomes are limited, especially in LMICs. The association between capnography use and a reduction in serious airway complications suggests that closing the capnography gap in LMICs may represent a significant opportunity to improve patient safety. Additional data are needed to quantify the global capnography gap and better understand the barriers to capnography scale-up in LMICs.

Keywords: airway safety; anaesthesia outcomes; capnography; global health; low-middle income countries (LMICs); patient safety; perioperative morbidity and mortality; scoping review

Editor's key points

- Capnography is frequently unavailable in low- and middle-income countries (LMICs). The authors conducted a scoping review to summarise the evidence regarding the impact of capnography on morbidity and mortality.
- Although randomised studies are limited, existing data suggest an association between the use of capnography and a reduction in serious airway complications. Evidence is limited from LMICs.

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- Improving access to capnography in LMICs may represent a significant opportunity to improve patient safety worldwide. Additional data are needed to quantify the global capnography gap.

Despite increasing levels of baseline patient risk,[1] perioperative morbidity and mortality have progressively declined over the past five decades in high-income countries (HICs).[2] In the USA, anaesthesia-related mortality has reduced from 1 in 1560 anaesthetics in the 1950s to less than 1 in 100 000.[1,3,4] Improvements in patient safety over the past half-century have not been universal, and alarmingly high rates of perioperative morbidity and mortality remain in many low- and middle-income countries (LMICs).[1] Perioperative mortality rates (POMRs) have been reported as high as 1 in 504 in Malawi, 1 in 482 in Zimbabwe, and 1 in 133 in Togo.[5] Children in some LMICs have a POMR up to 100 times greater than those in HICs.[6]

There are many factors contributing to disparities in POMR between countries of different levels of economic development. Lack of access to patient safety monitoring devices has been identified as a likely key contributor.[7] In 2010, it was estimated that 77 700 operating rooms worldwide lacked access to pulse oximetry.[8] This recognition led to the creation of the World Federation of Societies of Anesthesiologists (WFSA) Global Oximetry Project and the Lifebox initiative to expand pulse oximetry availability in resource-constrained settings. Like pulse oximetry, capnography is considered an essential anaesthesia safety monitor in HICs.[9,10] Both are relatively simple, portable, and can be battery operated. The size of the capnography gap in LMICs is uncertain, although it is likely wider than the pulse oximetry gap.[11]

Capnography is used in a variety of hospital settings for multiple purposes: in operating rooms (ORs) for both general anaesthesia and deep procedural sedation, in PACUs for monitoring respiratory depression and airway patency, and in ICUs and emergency departments (EDs) for intubation confirmation and ventilation monitoring. For intubated patients, capnography is the fastest monitor for identifying oesophageal intubation.[12] If oesophageal intubation occurs and remains unrecognised, it is associated with a high risk of brain damage and death.[13,14] Capnography can also be useful for diagnosing airway circuit disconnection, tracheal tube dislodgement and obstruction, and circulatory, respiratory, and metabolic conditions such as circulatory hypoperfusion and cardiac arrest, pulmonary, embolism, and bronchospasm.[13,15] Detection of tracheal tube obstruction or dislodgement may be especially relevant in low-resource settings. Lack of heated or humidified circuits may substantially increase the risk of tracheal tube obstruction from inspissated secretions, and workforce shortages often result in high patient to provider ratios and therefore a potentially increased role for automated monitoring and safety alarms. For non-intubated patients, capnography can be a useful tool to monitor airway patency and ventilatory status, especially in sedated patients.

Recently, capnography has received renewed attention in the anaesthesia and critical care literature.[16] It was included by the WHO and WFSA International Standards for a Safe Practice of anaesthesia as an '*essential*' (i.e. mandatory) safety monitoring device.[17] Increasing capnography availability in LMICs has been highlighted as a potential priority for improving safe anaesthesia practice globally.[18].

In order to describe the impact of capnography on patient safety and the potential impact of increasing access to capnography in LMICs, we conducted a scoping review to summarise the existing types of evidence, identify gaps in research, and contribute to the discussion regarding the prioritisation of expanding capnography availability in LMICs. Scoping reviews provide a descriptive overview of the available data without critically appraising individual studies or synthesising evidence from different studies.

Methods

Study design

Our preliminary literature search yielded papers with heterogeneous study methodologies and outcomes which precluded systematic analysis. Therefore, a scoping review methodology was deemed most appropriate and used during the protocol stage to allow inclusion of different study designs and to illustrate gaps in the current knowledge base.[19] Consequently, no Prospective Register of Systematic Reviews (PROSPERO) protocol was registered. We followed previously published guidelines for conducting a scoping review.[20–23].

Search strategy and data sources

Using a Patient, Intervention, Comparison, Outcome and Time (PICOT) framework, this review aims to answer the following question: 'What impact has end-tidal carbon dioxide monitoring had on the morbidity and mortality of adult and paediatric patients being intubated in both in and out-of-hospital settings in high and low-income settings, and patients undergoing procedural sedation?'

For the purposes of the literature search, the research question was broken down into two themes (Appendices 1 and 2). The first encompassed all terms related to the measurement of exhaled carbon dioxide. The second encompassed mortality and all causes of morbidity as a result of adverse respiratory and cardiovascular events assumed to be associated with the absence of carbon dioxide monitoring. These were broadly categorised as airway and tracheal tube complications (e.g. oesophageal intubation), common or severe cardiorespiratory events (e.g. desaturation, cardiac arrest), and permanent neurological insult (e.g. hypoxic brain injury).

We searched MEDLINE and EMBASE databases with a publication range from 1980 until March 1, 2019. A preliminary literature review identified target articles that were deemed essential for inclusion in the final search results. Key terms were identified through an iterative process involving review of target articles and consultation with members of the WFSA equipment committee. Our search terms included a combination of Medical Subject Headings (MeSH) and keywords (Appendices 1 and 2) for papers in English only. Articles were imported into a reference manager, and duplicates were removed. Two reviewers independently screened titles and abstracts (MN, WB) to identify potential articles for inclusion. If any were included by only one reviewer, then they were retained for further analysis. The full texts of all identified articles were screened by three reviewers (EW, MN, WB) to confirm eligibility for inclusion. Disagreements were resolved through discussion with additional reviewers (ML, TL, AWG, MSL). Reference lists from included papers were also searched.

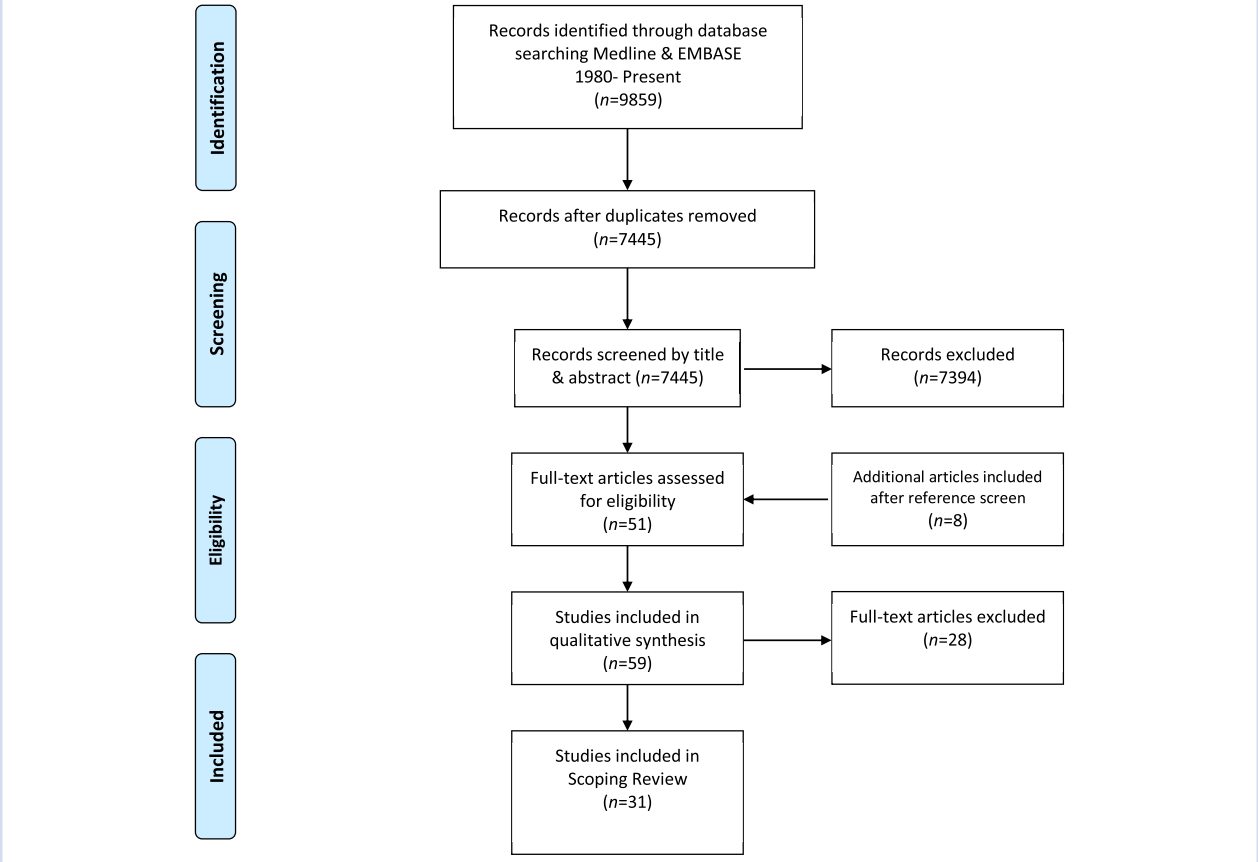

Fig. 1. Prisma diagram.

A grey literature search was conducted to identify additional studies.

Inclusion criteria

Studies were included if they evaluated the impact of end-tidal carbon dioxide monitoring on morbidity or mortality, for adult and paediatric patients in both in and out-of-hospital settings in high- and low-income countries since the introduction of capnography in the early 1980s. Studies with any comparator were included. Morbidity included common and severe cardiorespiratory and neurological outcomes, and are detailed in Appendices 1 and 2. Henceforth, for consistency the term 'capnography' will be used to refer to any form of end-tidal carbon dioxide monitoring (continuous digital and waveform representation of carbon dioxide).

Prospective studies on capnography for procedural sedation protocolised that certain interventions (i.e. early procedure termination, airway interventions such as bag-mask ventilation and oxygen supplementation) must be implemented if monitoring indicated potential imminent patient harm. Therefore, these studies would not be expected to report a high incidence of morbidity and mortality. For the purpose of this review, we included these interventions as surrogates for potential morbidity and mortality averted.

Exclusion criteria

Tracheal intubation studies were excluded if they did not evaluate the impact of capnography on mortality and morbidity. Sedation papers were excluded if they used changes in vital signs as their *only* outcome (i.e. desaturation) without reporting on resultant changes in airway management or harmful patient sequelae. Studies were excluded if they were published before 1980, as this preceded the routine clinical use of capnography. Animal studies, non-English language studies, and studies investigating the experimental effectiveness of capnography were also excluded.

Data extraction

Data were sorted using the following categories: author, journal, year, study design, article summary, clinical variables measured, outcomes, clinical context of the study, study size, and country of origin. Owing to the heterogeneity of studies included and variation in reported outcomes, standardised data forms were not used.

Data synthesis

Studies were synthesised according to whether they used tracheal intubation or procedural sedation, their clinical

Table 1 Characteristics of included tracheal intubation studies by hospital setting. ED, emergency department; HICs, high-income countries; ROSC, return of spontaneous circulation; CI, confidence interval.

Reference	Study design	Time frame	Sample size	Country	Methods	Summary
Operating room						
Tinker and colleagues[24]	Closed claims analysis	1974–1988	1175 adult claims	USA	Analysis by expert panel of a closed claims database for theoretical preventability of cases through the use of safety monitoring devices.	Applied together, pulse oximetry and capnography could have prevented 93% of preventable mishaps.
Wang and Hägerdal[25]	Closed claims analysis	1979–1989	120 adult claims	Sweden	Retrospective review of all complications reported to the head of department in a single Swedish hospital over 11 years.	80% of cases were deemed avoidable. The use of pulse oximetry, capnography, or both could possibly have prevented 18% of all complications, excluding dental injury.
Morray and colleagues[26]	Closed claims analysis	1985–1991	2262 adult and 238 paediatric claims	USA	Authors used a standardised approach to analyse cases from the ASA closed claims database and assess if patient safety monitors could have prevented adverse outcomes.	Pulse oximetry, capnographym, or both were considered preventative in 89% of paediatric and 91% of adult claims for inadequate ventilation Of the paediatric claims, 50% were for death and 35% for brain damage *vs* 35% and 11% respectively in adults.
Williamson and colleagues[27]	Closed claims analysis	1987	2000 adult claims	Australia	The first 2000 incidents reported to the Australian Incident Monitoring Study were analysed specifically for the actual or theoretical role of capnography in preventing the incident.	In a theoretical analysis of 1256 general anaesthesia incidents, capnograph used on its own would have detected 55% of these incidents, had they been allowed to evolve to a point where capnography could have detected the abnormality.
Caplan and colleagues[28]	Closed claims analysis	1961–1994	3791 adult and paediatric claims	USA	Analysis by expert panel of a closed claims database for theoretical preventability of cases owing to gas delivery equipment issues.	Gas delivery equipment issues accounted for 72 claims (2%). 25 adverse events could have been preventable had capnography been used.
Bhananker and colleagues[29]	Closed claims analysis	1990–2002	1952 adult claims	USA	Analysis by expert panel of a closed claims database for theoretical preventability through the use of additional patient safety monitoring.	Five claims were thought to be preventable by capnography and 1 claim preventable with the use of both capnography and pulse oximetry.
Cheney and colleagues[30]	Closed Claims analysis	1975–2000	6894 adult claims	USA	Analysed adverse outcomes from a closed claims database. Documented trends in the proportion of total claims for death or brain damage, and the proportion of these claims as a result of respiratory and cardiovascular events.	Use of pulse oximetry and capnography was associated with a decrease in the proportion of claims for respiratory events and an increased proportion of claims for cardiovascular events that led to death or brain damage.

Continued

Table 1 Continued

Reference	Study design	Time frame	Sample size	Country	Methods	Summary
Charuluxananan and colleagues[31]	Closed claims analysis	2003–2004	1996 adult claims	Thailand	Reviewers analysed adverse respiratory events, cardiac arrests, and deaths within 24 h of surgery across 51 Thai hospitals. Unintended anaesthesia incidents over 6 months were reported anonymously and voluntarily.	Oesophageal intubation represented 5.3% of 2537 critical incidents. Capnography *first* detected 4.3% of all critical incidents.
Cook and colleagues[32]	Prospective	2009–2010	309 adverse airway events	UK	Reports of major airway management complications during anaesthesia (death, brain damage, emergency surgical airway, unanticipated intensive care unit admission) were collected from all NHS hospitals over 1 yr. An expert panel assessed inclusion criteria, outcome, airway management and likely contributing factors.	In total, there were 38 deaths attributable to an airway event: 16 during anaesthesia, 18 on ICU, and 4 in the ED. Reviewers judged that the use of capnography (and its appropriate interpretation) during tracheal obstruction, tube misplacement, and in recovery would have led to earlier identification and changes in clinical management. There were 3 anaesthesia-related cases of oesophageal intubation, including. Two deaths, in which optimal interpretation of capnography might have altered the outcome.
Honardar and colleagues[14]	Closed claims analysis/ retrospective case series	1970–2013	45 adult claims	USA	Analysed trends in delayed detection of oesophageal intubation from 1970–2013. Retrospective case series analysed 45 malpractice claims specifically for delayed detection of oesophageal intubation from the Anaesthesia Closed Claims Project. All cases reviewed occurred from 1995 onwards, after the ASA mandated end-tidal carbon dioxide detection to confirm intubation.	Delayed detection of oesophageal intubation declined as a proportion of anaesthesia malpractice claims from 3% to 8% of claims per year before 1990 to 1–2% per year from 1990 onwards, corresponding with the widespread uptake of capnography in HIC. The most common factors contributing to delayed detection were not using, ignoring, or misinterpreting end-tidal carbon dioxide readings. Misdiagnosis occurred in 33% of cases. Nearly all oesophageal intubations with delayed detection resulted in patient death or severe brain damage.

Continued

Table 1 Continued

Reference	Study design	Time frame	Sample size	Country	Methods	Summary
Jooste and colleagues[11]	Prospective	2017	1400 adult cases	Malawi	Capnography units were donated along accompanied by an education course. Providers were asked to record each case in which a capnograph was used and to record adverse events.	Forty-four oesophageal intubations and 81 breathing circuit disconnections were detected by capnography over 6 months. Twenty-eight (90%) of anaesthesia providers reported that the use of capnography had saved at least 57 lives during the 6 month period of capnography use.
Intensive care unit						
Jaber and colleagues[33]	Prospective	2010	244 adults patients	France	All intubations performed during two consecutive phases (a 6 month quality control phase followed by a 6 month intervention phase using an ICU intubation bundle management protocol) were evaluated. One of the 10 bundle components was capnography. The primary endpoint was incidence of life-threatening complications occurring within 60 min after intubation.	Intubations in the intervention group were associated with significant decreases in both life-threatening complications (21 *vs* 34%, $P=0.03$) and other complications (9 *vs* 21%, $P=0.01$) compared with the control group. Three oesophageal intubations led to severe hypoxaemia, all in the control group (i.e. without capnography). Four oesophageal intubations in the intervention group were detected by capnography, with none developing severe hypoxaemia, but 2 resulted in haemodynamic collapse. The remaining cases of oesophageal intubation were detected clinically.
Cook and colleagues[34]	Prospective	2009–2010	309 adverse airway events	UK	Reports of major airway management complications during anaesthesia (death, brain damage, emergency surgical airway, unanticipated intensive care unit admission) were collected from all National Health Service hospitals over 1 yr. An expert panel assessed inclusion criteria, outcome, airway management and likely contributing factors.	The failure to use capnography likely contributed to 17 cases of death or brain damage in the ICU, including 4 oesophageal intubations and 14 inadvertent tube displacements. These accounted for 82% of events leading to death or brain damage.
Emergency department						
Bhat and colleagues[35]	Retrospective	2009–2011	169 adult patients	USA	An observational study of patients intubated in the ED. Investigated the impact of	Capnography was used in 5.9% of cases. There was no significant difference in mortality and

Continued

Table 1 Continued

Reference	Study design	Time frame	Sample size	Country	Methods	Summary
					instituting early post-intubation interventions (such as quantitative capnography, arterial blood gas sampling, obtaining a chest X-ray) on outcomes of mortality, ventilator-associated pneumonia (VAP), ventilator days, and ICU stay.	ventilator associated pneumonia rates between groups.
Resuscitation						
Phelan and colleagues[36]	Retrospective	2000–2009	75 777 adult patients	USA	A registry of in-hospital cardiac arrests and resuscitation was analysed to calculate the rate of appropriate documentation of tracheal intubation confirmation, defined as the use of capnography or an oesophageal detector device (ODD). Logistic regression was used to determine if a relationship existed between appropriate documentation of intubation confirmation and ROSC or survival to hospital discharge	Confirmation of tracheal intubation by capnography or ODD was documented in 43 034 (56.8%) cases. Patients in whom tracheal intubation was confirmed with capnography or ODD were more likely to have ROSC (adjusted OR=1.229; 95% CI, 1.179–1.282) and to survive to hospital discharge (adjusted OR=1.093; 95% CI, 1.033–1.157).
Chen and colleagues[37]	Retrospective	2005–2012	53 adult patients*	Taiwan	Cases of out-of-hospital cardiac arrest were identified from the Taiwan National Health Insurance claims database. Patients with documented capnography monitoring were selected and matched 1:20 with patients who did not receive capnography. A logistic regression model was applied to compare the OR for sustained ROSC in the matched cohorts.	Patients who received capnography during out of hospital cardiac arrest had a higher probability (OR=2.38; 95% CI, 1.28–4.42) of sustained ROSC. Authors noted that overall use of capnography remained low, despite strong recommendations for its use. (*53 patients with capnography matched with 1060 without capnography).

Table 2 Characteristics of included sedation studies. ED, emergency department.; OR, operating room.

#	Title	Authors	Journal	Year	Design	Sample size	Hospital setting	Country	Findings
1	Does end-tidal carbon dioxide monitoring detect respiratory events prior to current sedation monitoring practices?	Burton and colleagues[38]	*Academic Emergency Medicine*	2006	Prospective	60 adults	ED	USA	Detected many clinically significant acute respiratory events before standard monitoring. The majority of acute respiratory events were preceded by capnography abnormalities before changes in pulse oximetry or observed hypoventilation occurred.
2	Emergency department procedural sedation and analgesia: A Canadian Community Effectiveness and Safety Study (ACCESS).	Mensour and colleagues[39]	*Canadian Journal of Emergency Medicine*	2006	Prospective	160 adult and paediatric patients	ED	Canada	Capnometry recording did not appear to alter patient outcomes, although the data are incomplete.
3	Capnography and depth of sedation during propofol sedation in children.	Anderson and colleagues[40]	*Annals of Emergency Medicine*	2007	Prospective	125 adults	ED	USA	Detected most airway and respiratory events leading to interventions before clinical examination or pulse oximetry.
4	A comparative evaluation of capnometry *vs* pulse oximetry during procedural sedation and analgesia on room air.	Sivilotti and colleagues[41]	*Canadian Journal of Emergency Medicine*	2010	Prospective, RCT	63 adults	ED	Canada	In context of no routine use of supplemental oxygen, desaturations detectable by pulse oximetry usually occurred before overt changes in capnometry.
5	Does end-tidal CO_2 monitoring during emergency department procedural sedation and analgesia with propofol decrease the incidence of hypoxic events? A randomized, controlled trial	Deitch and colleagues[42]	*Annals of Emergency Medicine*	2010	Prospective, RCT	132 adults	ED	USA	Reduced hypoxia and provided advance warning for all hypoxic events. Capnography evidence of respiratory depression occurred before the onset of hypoxia. More physician interventions to improve respiration with capnography.
6	A randomized controlled trial of capnography during sedation in a pediatric emergency setting.	Langhan and colleagues[43]	*American Journal of Emergency Medicine*	2015	Prospective, RCT	154 children	ED	USA	Fewer but more timely interventions for hypoventilation and fewer episodes of hypoventilation and desaturation with capnography use. Delayed interventions not timed concurrently with hypoventilation were significantly associated with higher odds of an oxygen desaturation.
7	End-tidal capnometry during emergency department	Campbell and colleagues[44]	*World Journal of Emergency Medicine*	2016	Prospective, RCT	986 adults	ED	Canada	Did not change any clinically significant outcomes. Increased

Continued

Table 2 Continued

#	Title	Authors	Journal	Year	Design	Sample size	Hospital setting	Country	Findings
	procedural sedation and analgesia: a randomized, controlled study								incidence of airway repositioning manoeuvres and hypotension with capnography use.
8	Microstream capnography improves patient monitoring during moderate sedation: a randomized, controlled trial.	Lightdale and colleagues[45]	*Pediatrics*	2006	Prospective, RCT	163 children	OR	USA	Reduced desaturations and allowed earlier detection of respiratory compromise, prompting intervention to minimise hypoxaemia. However, there was no change in airway interventions and its use cannot be directly linked to improved patient safety.
9	Capnographic monitoring of respiratory activity improves safety of sedation for endoscopic cholangiopancreatography and ultrasonography.	Qadeer and colleagues[46]	*Gastroenterology*	2009	Prospective	247 adults	OR	USA	Reduced the frequency and severity of hypoxaemia, and apnoea. However, its use had no effect on airway interventions.
10	Capnographic monitoring reduces the incidence of arterial oxygen desaturation and hypoxemia during propofol sedation for colonoscopy: a randomized, controlled study (ColoCap Study).	Beitz and colleagues[47]	*American Journal of Gastroenterology*	2012	Prospective, RCT	760 adults	OR	Germany	Significant reduction in the incidence of oxygen desaturation. Reduced need for bag-mask ventilation, though statistically insignificant.
11	The role of capnography in endoscopy patients undergoing nurse-administered propofol sedation: a randomized study	Slagelse and colleagues[48]	*Scandinavian Journal of Gastroenterology*	2013	Prospective, RCT	540 patients	OR	Denmark	Reduced the frequency and duration of hypoxia and detected inadequate ventilation before changes in pulse oximetry. However, on balance capnography was deemed of little clinical benefit.
12	Sidestream capnographic monitoring reduces the incidence of arterial oxygen desaturation during propofol ambulatory anesthesia for surgical abortion.	Zongming and colleagues[49]	*Medical Science Monitor*	2014	Prospective	704 adults	OR	China	Improved early detection of hypoventilation and reduced desaturation. No difference in rates of increased oxygen supplementation or assisted ventilation.
13	Capnographic monitoring of propofol-based sedation during colonoscopy	Friedrich-Rust and colleagues[50]	*Endoscopy*	2014	Prospective, RCT	533 adults	OR	Germany	Reduced incidence of hypoxia and reduced need for airway intervention (bag-mask ventilation specified).
14	Capnography during deep sedation with propofol by	van Loon and colleagues[51]	*Anesthesia & Analgesia*	2014	Prospective, RCT	427 adults	OR	Netherlands	In context of no routine use of supplemental oxygen, no difference for mild or severe

Continued

Table 2 Continued

#	Title	Authors	Journal	Year	Design	Sample size	Hospital setting	Country	Findings
	non-anesthesiologists: a randomized controlled trial								hypoxia. Incidence of airway interventions (chin-lift or jaw-thrust) was significantly higher in the capnography group.
15	Capnographic monitoring of midazolam and propofol sedation during ERCP: a randomized controlled study	Klare and colleagues[52]	*Endoscopy*	2016	Prospective, RCT	242 adults	OR	Germany	Hypoxaemia incidence was not significantly lower with capnography. Capnography resulted in improved detection of apnoea and a statistically insignificant reduction in assisted ventilation.

location (OR, ICU, ED, out-of-hospital), study design, and whether they were conducted in an HIC or LMIC context.

Risk of bias assessment

Given the overall heterogeneity of studies included and the lack of randomised clinical trials, a risk of bias assessment was not conducted.

Results

The initial literature search yielded 9859 records. After removal of 2414 duplicates, 7445 titles and abstracts were screened. Eight additional papers were included for full-text review after being identified through reference review. Fifty-nine full texts were assessed for eligibility. After full-text review, 28 were excluded and 31 included for data extraction (Fig 1). A summary of all included tracheal intubation papers is presented in Table 1 and procedural sedation papers in Table 2.

Studies are categorised by whether they report on incidents during tracheal intubation in the OR (n=11), in the ED (n=1), in the ICU (n=2), and during resuscitation (n=2), or during procedural sedation in the OR endoscopy suite (n=8) and ED (n=7). Of the tracheal intubation OR studies, nine are closed claims analyses or incident reports, and two are prospective quality improvement projects (Fig 2). All 15 procedural sedation studies are prospective, and nine of these are randomised clinical trials. Of the three ICU and ED papers, two are prospective studies, and one is retrospective. Lastly, there were two retrospective studies in the resuscitation group. Only two studies were from LMICs (Fig 3).

Of the 75 procedural sedation papers identified for abstract review, 15 met our inclusion criteria. Of note, several systematic reviews exist on the impact of capnography use during procedural sedation on rates of desaturation and use of airway interventions.[53–55] Papers included in these reviews that report only desaturations or respiratory depression as endpoints and do not report on airway interventions, morbidity, or mortality were excluded.

General anaesthesia with tracheal intubation inside the OR (HICs)

Closed claims analysis

Closed claims analyses are reviews of settled or disposed of legal claims into medical practice. They comprise most of the tracheal intubation OR papers (n=9). Overall, they report a decrease in adverse respiratory events coinciding with the widespread adoption of capnography.

Cheney and colleagues[30] examined the database of the ASA Closed Claims Project between 1975 and 2000 to analyse trends in the proportion of malpractice claims for death or permanent neurological injury and the factors influencing them. The study found an overall decrease in claims for death or brain damage between 1975 and 2000 (odds ratio, 0.95 per year; 95% confidence interval [CI], 0.94–0.96; P<0.01), a trend that predated the use of capnography or pulse oximetry. Coinciding with the introduction of capnography and pulse oximetry in 1986, there was a significant reduction in the proportion of respiratory events responsible for death or permanent brain damage. Oesophageal intubation comprised 66 of 503 (13%) respiratory cases leading to death or permanent brain damage.

Honardar and colleagues[14] conducted a retrospective case series on malpractice claims specifically for delayed detection of oesophageal intubation from the anaesthesia Closed Claims

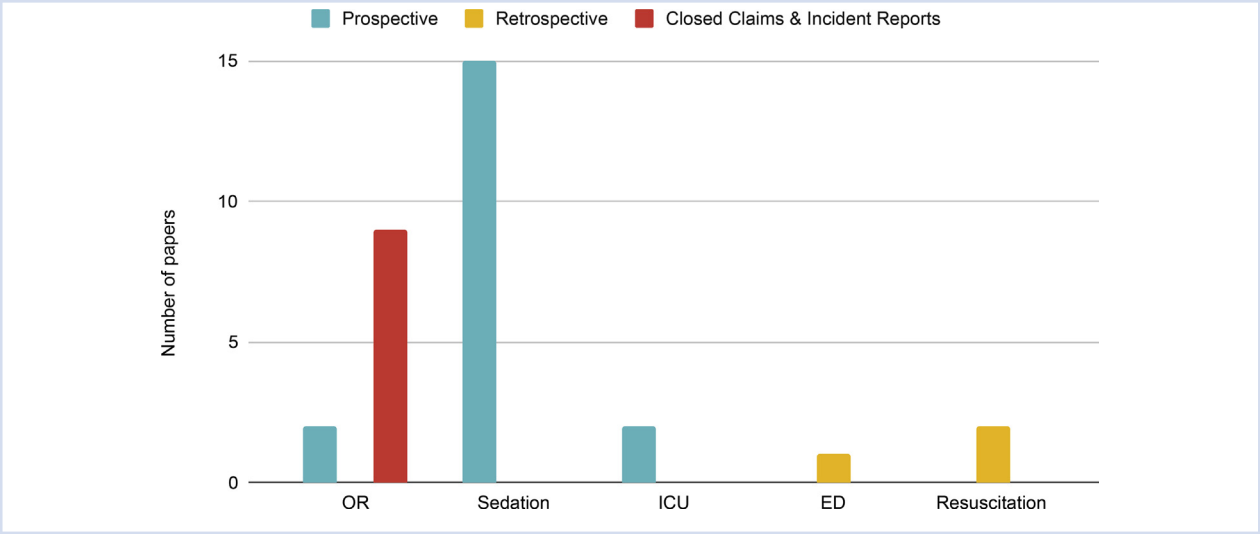

Fig. 2. Included papers by study design and hospital setting. OR, operating room; ED, emergency department.

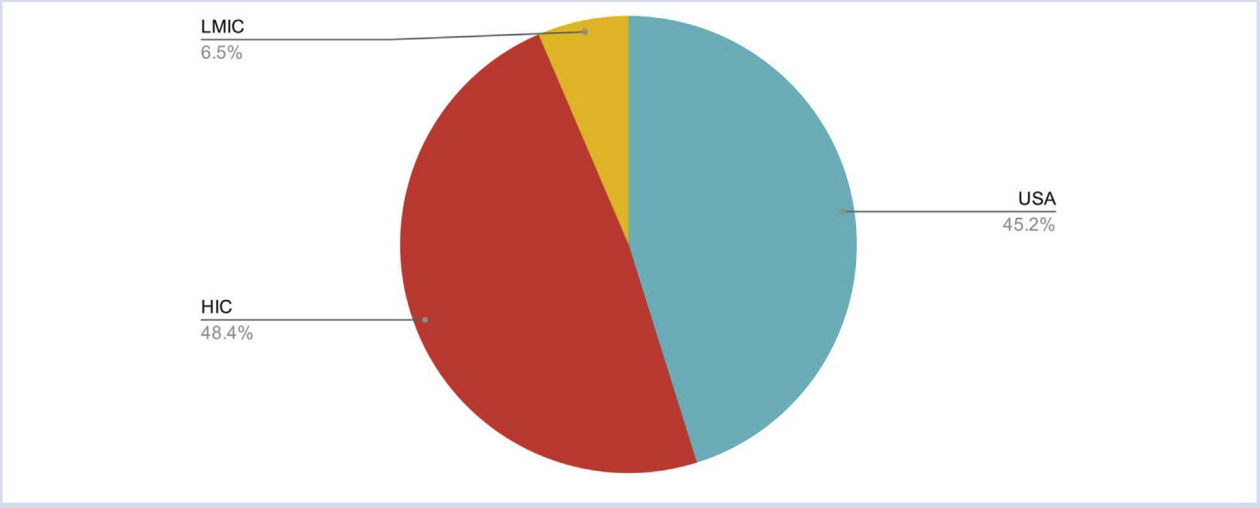

Fig. 3. Included papers by country income classification. LMIC, low- and middle-income country; HIC, high-income country.

Project Database. Only claims occurring after the widespread adoption of capnography were included. Forty-three of the 45 cases (96%) of oesophageal intubation with delayed detection resulted in patient death or severe brain damage. Twenty-two (49%) occurred in the OR in other anaesthesia locations, nine (20%) in the ICU, and four (9%) in the PACU. Not using, ignoring, or misinterpreting capnography contributed to almost three-quarters of the 45 claims.[14] Of the 29 oesophageal intubations by an anaesthesiologist, four were not diagnosed until autopsy.

Morray and colleagues[26] compared paediatric and adult subsets of ASA closed claims between 1985 and 1991. Compared with adults, paediatric cases had a higher mortality rate, a higher rate of severe brain damage, and a higher proportion of claims attributed to respiratory events, especially inadequate ventilation (20% of paediatric *vs* 9% of adult cases). Reviewers of these closed claims concluded that, had capnography, pulse oximetry, or both been available, 89% of claims related to inadequate ventilation could have been prevented.

In 1989, Tinker and colleagues[24] reviewed 1097 anaesthesia-related closed claims cases that occurred between 1962 and 1987, before the widespread availability of both pulse oximetry and capnography, to evaluate whether cases could have been prevented through the use of either or both of capnography or pulse oximetry, had they been available at the time. Cases were identified as potentially preventable using factors such as whether other monitoring devices were used, the type of critical incident, the presence of premonitory clinical signs, complications, and eventual outcome. Subsequently, the ability of capnography and pulse oximetry to prevent the outcome was

assessed subjectively, based on the reviewer's understanding of the sequence of events that preceded the critical incident and the probable cause of injury.

Of 1097 cases, 346 (31.5%) were thought preventable by the use of pulse oximetry, capnography, or both. Sixty percent of all claims were for death or brain damage. Clinical signs of deterioration such as cyanosis, bradycardia, and hypotension were noted at least once in 88% of cases considered preventable, compared with 31% of cases thought unpreventable.[24] Overall, the reviewers stated that application of either or both of capnography and pulse oximetry would have prevented a combined total of 322 injuries or deaths, or 93% of all preventable cases. A total of 24 cases (7%) were deemed preventable by other monitors such as automated blood pressure devices. The reviewers determined that the most useful preventative monitors — if used, interpreted, and acted upon properly — were pulse oximetry and capnography. Because of concerns that reviewer variability might render the study unreliable, a reliability study was subsequently performed by *Caplan and colleagues[56] that demonstrated that independent anaesthesiologist reviewers exhibited significant inter-rater reliability in the analysis of closed claims ($P<0.001$).

Incident reporting

The Australian Incident Monitoring Study (AIMS) involved the voluntary and anonymous reporting of any unintended incident which reduced or could have reduced patient safety. The first 2000 incidents reported to the study were analysed in 1993 specifically with respect to the impact of capnography on these events.[27] The incidents were divided into 'actual incidents' ($n=1256$) and 'theoretical incidents' ($n=744$). 'Theoretical incidents' were defined as those that would have been theoretically detectable had capnography been used on its own, and had the incident been allowed to progress to a point where capnography would detect the physiological abnormality. Of the 1256 'actual incidents' reported during general anaesthesia, 604 were 'human detected' and 652 'monitor detected'. Pulse oximetry was important in more of the monitor-detected incidents than capnography. Of the monitor-detected incidents, the capnograph detected 153 (24%) before pulse oximetry or other monitors. The figure would have been nearly 30% if a correctly checked and calibrated capnograph (i.e. intact gas sampling line, correct connection to the breathing circuit) had always been used.

There were 27 oesophageal intubations amongst the general anaesthesia incidents, and all were detected when capnography was properly used. Pulse oximetry detected 8 of 27 oesophageal intubations; in each of these the capnograph was incorrectly or not being used.

Because capnography was not used in 46% of the 1256 general anaesthesia cases, a 'theoretical assessment' of the potential value of capnography was performed. It concluded that the majority (55%) of these incidents would have been detected and averted had capnography been used.[27]

Wang and colleagues[25] retrospectively analysed 120 anaesthetic events that had potential medico-legal consequences in Sweden between 1979 and 1989. Cases were included if they were self-reported by the anaesthesiologist or a patient lodged a formal complaint. There was a total of 120 events reported from 262 850 anaesthetics. Eighty percent were considered avoidable. The authors concluded that 18% of non-dental damage adverse events could have been avoided with the use of capnography, oximetry or both.[25]

General anaesthesia with tracheal intubation inside the OR (LMICs)

Prospective

A 2017 study in Malawi estimated the capnography gap, and assessed the feasibility of capnography implementation and whether capnography use could improve early recognition of critical airway incidents.[11] This is one of only two included studies from an LMIC, and the only one from Africa. At baseline, only one capnograph was available nationally in 31 ORs, representing a 97% capnography gap. None were available for the eight ICU beds surveyed. During the 6 month trial, capnography devices were distributed to 32 non-physician anaesthesia providers along with a capnography education package. The impact of the interventions on morbidity and mortality was estimated by collecting provider case-log books and through surveys. Overall, 77% of the 32 providers reported detection of a combined 44 oesophageal intubations. Meanwhile 81 circuit disconnections were detected over 1418 total cases. A post-study questionnaire indicated that 28 (90%) anaesthesia providers reported that they believed that the use of capnography had saved lives. The study estimated that at least 57 lives had been saved during the 6 month study period.

General anaesthesia with tracheal intubation outside the OR

Intensive care units

In the UK's Fourth National Audit Project (NAP4) an expert panel examined all major complications of airway management (inclusion criteria being death, brain damage, emergency surgical airway, unanticipated ICU admission, and prolonged ICU stay) that were collected from all NHS hospitals between September 2008 and August 2009. Every month representatives from every NHS hospital prospectively reported the total number of cases and any major airway events to the study's coordinators.[32 34] An expert panel reviewed inclusion criteria, outcomes, and airway management in each case to determine preventability. A total of 184 cases met inclusion criteria. Overall, 133 (72%) of these major airway events were from complications during anaesthesia, 36 (20%) from the ICU and 15 (8%) from the ED. The use of capnography was universal in ORs.[32] Outside the OR, delayed recognition and failed rescue owing to either lack of or failure to accurately interpret capnography was cited as a contributing factor.[34]

In a smaller prospective, multicentre study across three medical–surgical ICUs in France in 2009, Jaber and colleagues[33] recorded all intubations performed during two consecutive phases (a 6 month quality control phase followed by a 6 month intervention phase involving the implementation of an ICU intubation bundle management protocol). The intubation management bundle protocol included capnography and preoxygenation with noninvasive positive pressure ventilation, the presence of two operators, rapid sequence induction, cricoid pressure, lung protective ventilation, fluid loading, preparation and early administration of sedation, and vasopressor use, if indicated. Capnography was never used in the control arm (0/121) and in 56% (69/123) of intubations in the intervention arm. It was not used in the intervention arm either for logistical reasons or because of provider oversight. Separate analysis of capnography utilisation showed that there were 12 oesophageal intubations (six in each group). Three oesophageal intubations led to severe hypoxaemia, all in the control group (i.e. without capnography). Four of the

oesophageal intubations in the intervention group were detected by capnography, with none developing severe hypoxaemia, but two resulted in haemodynamic collapse. The remaining cases of oesophageal intubation were detected clinically. The authors concluded that the paper was underpowered to statistically demonstrate capnography's effect on outcomes.

Capnography in resuscitation

Phelan and colleagues[36] retrospectively analysed data from the American Heart Association's Get With the Guidelines-Resuscitation (GWTG-R) project, a prospective observational registry of in-hospital cardiac arrest and resuscitation between 2000 and 2009. The aim was to determine the rate of documentation of confirmed tracheal intubation and determine whether outcomes were associated with documentation rate. Appropriate tracheal intubation confirmation included either end-tidal carbon dioxide detection or an oesophageal detection device (ODD; i.e. a manual suction device that attaches directly to a tracheal tube and can help distinguish between tracheal and oesophageal intubation based on the ability to hold negative pressure (oesophageal intubation) or not (tracheal intubation)). Overall, 75 777 intubations during in-hospital cardiac arrest in 507 Canadian and USA hospitals were recorded between 2000 and 2009. Confirmation of tracheal intubation was documented 82.5% of the time, either by auscultation alone (25.7% of arrests) or by capnography/ODD (56.8% of arrests). Patients in whom tracheal intubation was confirmed by capnography or ODD were more likely to have return of spontaneous circulation (ROSC) (adjusted odds ratio=1.23; 95% CI, 1.179–1.28) and to survive to hospital discharge (adjusted odds ratio=1.1; 95% CI, 1.033–1.157). Auscultation alone demonstrated no effect.[36]

Chen and colleagues[37] analysed 5041 out-of-hospital cardiac arrests. Fifty-three had end-tidal carbon dioxide monitoring, and each of these patients was matched with 20 controls (1060) who did not receive end-tidal carbon dioxide monitoring. The odds of achieving sustained ROSC in the group with end-tidal carbon dioxide monitoring was significantly increased compared with those with no monitoring (odds ratio=2.38; 95% CI, 1.28–4.42). The paper did not examine whether the potential benefit of capnography was through impact on airway management, cardiopulmonary resuscitation (CPR) quality, identifying return of ROSC or other potential aspects of advanced cardiac life support (ACLS).[58,59]

Procedural sedation inside and outside the OR

A total of 15 sedation papers were included (Table 2). Ten papers reported a reduction in the frequency and severity of hypoxic episodes and earlier detection of hypoventilation and apnoea with capnography use.[38,40,42,43,45-50] Two papers reported no improvement in detection of hypoxic episodes with the use of capnography.[41,51] These were the only two studies that did not protocolise the use of supplemental oxygen for all sedated patients. Four studies showed increased or more timely use of airway repositioning manoeuvres with capnography, such as chin-lift and jaw thrust.[40,43,45,51] Six studies showed a reduced need for assisted ventilation (i.e. bag-mask ventilation), though these occurrences were rare.[42,46–48,50,52] Six of the studies concluded that the addition of capnography to standard monitoring did not improve clinically significant outcomes.[39,44–46,48,49]

These findings can be compared with the conclusions made by the most comprehensive systematic review, which noted that addition of capnography to visual assessment and pulse oximetry was associated with a statistically significant reduction in mild and severe desaturations and in the use of assisted ventilation.[53] It suggested that earlier detection may reduce the use of clinical interventions, which theoretically prevent adverse outcomes. However, no conclusion could be made on whether capnography affected morbidity or mortality.

Discussion

This scoping review summarises existing evidence on capnography's use in airway management and its role in reducing patient morbidity and mortality, both inside and outside the operating theatre in HICs and LMICs. It includes three main findings.

First, we found a lack of high-quality evidence linking capnography use to improvements in patient morbidity and mortality. Most of the data included are retrospective and non-randomised, precluding the ability to ascribe causation. The lack of prospective studies may be attributable to the relative rarity of severe adverse events thought preventable by capnography in HICs,[53] making powering studies impractical. The limited number of prospective studies assessing capnography's effect on outcomes after tracheal intubation were underpowered to find a statistically significant difference. In addition, capnography was universally accepted as standard of care in HICs before a solid evidence base existed for its use.[60] This renders RCTs ethically difficult to conduct. Second, despite a lack of rigorous data, most of the included studies reported an association between capnography use and improved patient outcomes inside and outside the OR. The magnitude of this effect varied, likely because of differences in study design. Although there are obvious limitations of closed claims analysis, incident reporting and review of patient records, they do provide valuable information for relatively rare adverse events and for following trends over time. The third finding of this review is that limited evidence exists from LMICs on this topic.

This review reinforces claims that capnography's utility extends beyond the OR and intubation.[16] NAP4 noted that most major ICU airway events, such as tracheal tube displacement, occurred during prolonged periods of mechanical ventilation and not during intubation. Given that airway events in the ICU or ED were more likely to be out of hours, managed by doctors with less airway experience and resulted in more severe outcomes, the reports' call for mandatory capnography for all ICU and ED intubations, and for continuous monitoring of all ventilated patients in all clinical areas, seems appropriate.

At present, the penetrance of capnography in LMICs is unknown, but there is likely a large gap between HICs and LMICs.[11] Serious events such as undetected tracheal tube obstructions and circuit disconnections are likely more common in LMICs (e.g. because of malfunctioning circuit alarms, provider shortages, limited suction, and absent humidified circuits). Therefore, it is likely that capnography could play a relatively larger role in LMICs than in HICs in averting morbidity and mortality. Furthermore, a lack of access to capnography, although important, needs to be viewed as one of several issues in a broader landscape that includes workforce numbers and training, availability of essential

medicines, and infrastructure. Quantifying the capnography gap will be one piece of a larger puzzle that must be solved to improve access to safe anaesthesia worldwide.

Without strong data, how should the anaesthesia community prioritise implementation of patient safety interventions such as capnography in low-resource settings? There are many practices in HICs that are considered standard of care but are not based on high-quality evidence. Patient safety monitors are designed specifically to detect dangerous deviations from *physiological norms*, which does not necessarily guarantee an improvement in patient outcomes.[61] Therefore, a lack of conclusive data on capnography's impact on morbidity and mortality should not necessarily preclude efforts to increase its availability.

Pulse oximetry provides an instructive case study.[62] It has been widely accepted as mandatory for any surgery in HICs without substantial evidence linking its utilisation to improved perioperative outcomes. Large randomised trials showed only a reduction in hypoxia but not improved patient outcomes.[63,64] Pulse oximetry was nevertheless identified as an indispensable perioperative patient safety monitor, initially in the Harvard monitoring standards,[60] and subsequently incorporated into guidelines by national and international anaesthesia bodies and included in the WHO surgical checklist.[65,66]

Although pulse oximetry and capnography share many similarities as monitors, they also differ in several important respects. Pulse oximetry has potential utility in a broader array of healthcare settings, is simpler to use and may require less training for interpretation. At present, capnography is relatively more expensive and requires disposable components, though efforts to create low cost capnography are underway.[67] Any attempt to increase capnography availability in LMICs should carefully consider these barriers to easy adoption.[18,67]

Limitations

There are several limitations to this review. Although we followed standardised methods, it is possible that relevant studies were missed. Non-English studies were not included, which meant that some studies may have been inadvertently overlooked, especially from LMICs.

Ascribing a causal relationship between capnography use and patient outcomes is not possible with the available retrospective data and is confounded by the concomitant introduction of pulse oximetry into mainstream practice. Furthermore, other improvements in patient safety beyond these monitors have occurred with time, such as the improved safety profile of anaesthetic medications and an increased overall focus on patient safety. These patient care improvements cannot be definitively excluded as the causes of the observed trends.

There were a variety of study designs included, with their own inherent limitations. For example closed claims analysis, by their nature, are studies of litigation, which include information gathered by insurance companies for the purpose of resolving claims and not for patient safety research. Malpractice claims are biased by the presence of substandard care and severe injuries. It is impossible to know to what extent the standards of practice and injuries in the claims' cases are representative of the broader practice of anaesthesia. This methodology also assumes capnography machines were always used correctly and interpreted and responded to appropriately. Expert review of patient records estimating preventability of adverse events with the use of capnography is similarly open to bias, potentially over- or under-exaggerating capnography's utility in certain clinical scenarios and its impact on morbidity and mortality. Studies based on provider self-reporting may under-represent the incidence of important adverse events.

Finally, almost all of the included studies were from HICs, limiting their generalisability to LMICs, where capnography could be disproportionately valuable (Fig 3).[18]

Conclusions

Despite WHO and WFSA endorsement of capnography as a highly recommended perioperative monitor, rigorous data demonstrating impact on patient outcomes or quality of care are limited. As is the case for most widely accepted anaesthesia monitoring standards, we argue that a lack of evidence should not necessarily impede action. This review presents studies suggesting an association between capnography use and a reduction in airway complications associated with morbidity and mortality. Given capnography's infrequent utilisation in many parts of the world, closing the capnography gap may represent a significant opportunity to improve patient safety worldwide.

Authors' contributions

Literature search: EW, MMN, WB, SC
Title and abstract screen: MN, WB, SC
Review of full text articles for inclusion: EW, MMN, WB, AWG, MSL
First draft write-up: EW, TL, AWG, MSL
All authors participated in study design and final manuscript editing

Declarations of interests

Professor Adrian Gelb is a consultant for Haisco Pharma; Masimo Inc.

The other authors declare that they have no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2020.04.057.

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