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Prevalence of peri-intubation major adverse events among critically ill patients: A systematic review and meta analysis

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ABSTRACT

Background: Peri-intubation major adverse events (MAEs) are potentially preventable and associated with poor patient outcomes. Critically ill patients intubated in Emergency Departments, Intensive Care Units or medical wards are at particularly high risk for MAEs. Understanding the prevalence and risk factors for MAEs can help physicians anticipate and prepare for the physiologically difficult airway.
Methods: We searched PubMed, Scopus, and Embase for prospective and retrospective observational studies and randomized control trials (RCTs) reporting peri-intubation MAEs in intubations occurring outside the operating room (OR) or post-anesthesia care unit (PACU). Our primary outcome was any peri-intubation MAE, defined as any hypoxia, hypotension/cardiovascular collapse, or cardiac arrest. Esophageal intubation and failure to achieve first-pass success were not considered MAEs. Secondary outcomes were prevalence of hypoxia, cardiac arrest, and cardiovascular collapse. We performed random-effects meta-analysis to identify the prevalence of each outcome and moderator analyses and meta-regressions to identify risk factors. We assessed studies' quality using the Cochrane Risk of Bias 2 tool and the Newcastle-Ottawa Scale.
Results: We included 44 articles and 34,357 intubations. Peri-intubation MAEs were identified in 30.5% of intubations (95% CI 25–37%). MAEs were more common in the intensive care unit (ICU; 41%, 95% CI 33–49%) than the Emergency Department (ED; 17%, 95% CI 12–24%). Intubation for hemodynamic instability was associated with higher rates of MAEs, while intubation for airway protection was associated with lower rates of MAEs. Fifteen percent (15%, 95% CI 11.5–19%) of intubations were complicated by hypoxia, 2% (95% CI 1–3.5%) by cardiac arrest, and 18% (95% CI 13–23%) by cardiovascular collapse.
Conclusions: Almost one in three patients intubated outside the OR and PACU experience a peri-intubation MAE. Patients intubated in the ICU and those with pre-existing hemodynamic compromise are at highest risk. Resuscitation should be considered an integral part of all intubations, particularly in high-risk patients.

1. Introduction

The importance of planning for and preempting peri-intubation adverse events is a core tenant of emergency and critical care medicine, summarized in the popular mantra “resuscitate before you intubate” and the concept of “resuscitation sequence intubation.” Unlike the operating room, intubation in the Emergency Department (ED), intensive care unit (ICU), or medical wards is most often prompted by an acute hemodynamic, respiratory, or neurologic decompensation [1,2]. Patients requiring emergency intubation have been described as having “physiologically difficult airways,” as their pre-intubation physiologic derangements significantly increase their risk for peri-intubation adverse events [3,4]. Through the suppression of sympathomimetic and respiratory drives, neuromuscular blockade (NMB), and a rapid transition from negative- to non-physiologic positive-pressure ventilation, intubation has the potential to cause rapid cardiovascular or respiratory decline, particularly among patients with pre-existing hypoxia, hypotension, or acidosis [3]. Peri-intubation hypoxia and hypotension have

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been associated with higher rates of in-hospital mortality [5-8]. Physicians taking care of these critically ill patients are walking a thin line: lack of adequate preparation can be devastating, while excessive delay of a necessary intubation may contribute to respiratory acidosis and risk of aspiration and set the stage for hemodynamic collapse.

A clear understanding of the prevalence of various peri-intubation events and their risk factors is an essential component of the emergency and critical care medicine mental airway toolkit, and sets the foundation for effective and efficient pre-, peri- and post-intubation resuscitation and care. In 2011, the Fourth National Audit Project of the Royal College of Anaesthetists and the Difficult Airway Society found that 25% of major airway complications within the hospital setting occur in the ED or ICU [9]. They identified repeated instances of failure to identify high-risk patients and to plan for, recognize, and rapidly respond to adverse events, and identified these breakdowns in care as major contributors to avoidable complications and deaths.

In this systematic review and meta-analysis, we aim to evaluate the available evidence regarding peri-intubation major adverse events (MAE)—specifically, hypoxia, cardiovascular collapse, and cardiac arrest—quantify their prevalence, and identify relevant demographic and clinical factors and interventions most likely to increase or reduce patients' risk.

2. Methods

2.1. Search and selection criteria

We queried PubMED, Scopus, and Embase databases on October 6, 20 and again on September 4, 2022. The search terms were ((adverse AND events) OR (hypoxemia) OR (hypoxia) OR (desaturation) OR (hypotension) OR (cardiac AND arrest) OR ((hemodynamic OR cardiovascular) AND (collapse))) AND ((endotracheal AND intubation) OR (emergency AND airway AND management) OR (peri-intubation)). We included original studies (retrospective and prospective observational studies and randomized control trials) conducted among adult patients (≥18 years old) undergoing endotracheal intubation in the ED, ICU, or medical wards that reported any MAE within 30 min of endotracheal intubation. We included only articles published in English language. Studies were excluded if they did not establish clear criteria for MAE prior to data analysis, if they reported intubations or events occurring in the operating room (OR), procedural suites, or post-anesthesia care unit (PACU), events considered to be related to general anesthesia, or if the studies focused on out-of-hospital intubations.

We excluded conference publications, isolated abstracts, case reports, and other systemic reviews and meta-analyses. We excluded post-hoc or subgroup analyses of larger studies, even they met our inclusion criteria, to prevent the inclusion of duplicate data. For studies using the same database or hospital cohorts with overlapping inclusion criteria and years of data collection, we selected those with more patients, more granular reporting of adverse events, or those that reported on more recent data. We screened cited studies for potential inclusion but did not contact authors for additional data or information.

Two authors independently screened each abstract for inclusion; any disagreements were resolved by a third senior author. This process was repeated for full text screening. Two investigators had to agree that each study should proceed to the next step before it could do so. All screening was conducted through Covidence (Veritas Health Innovation, Melbourne AU). This study was conducted in accordance with the PRISMA (Preferred Reporting Items for Systemic Reviews and Meta-Analyses) 2020 statement [10], and it was registered with PROSPERO (CRD42022342134).

2.2. Outcomes of interest

Our primary outcome of interest was the prevalence of composite peri-intubation MAE, as it was defined by the authors of included studies. We selected this outcome to provide clinicians the most complete "birds-eye" view of patient risk at the time of intubation. "Peri-intubation" was defined as an event occurring after administration of sedating medications for intubation and up to 30 min following intubation. We specifically examined rates of peri-intubation cardiovascular collapse (indicated by hypotension with a systolic blood pressure (SBP) < 90 mmHg, mean arterial pressure (MAP) < 65 mmHg, requirement for new or increased vasopressors or bolus of intravenous fluids (IVF) to maintain SBP or MAP above the desired range, or as defined by study authors), hypoxia (indicated by pulse oximetry < 90% or as defined by study authors), and cardiac arrest. We separately examined the prevalence of peri-intubation hypoxia, cardiac arrest, and cardiovascular collapse as our secondary outcomes. We did not consider failure of first-pass intubation success or esophageal intubation to be a MAE.

2.3. Quality assessment

Two authors assessed the quality of each study; any disagreements were resolved *via* discussion between the two authors or by a third senior author. We reported the final results from the consensus of the involved investigators. All studies were screened using either the Cochrane Risk of Bias 2 tool [11] or the Newcastle-Ottawa scale [12] The Cochrane Risk of Bias 2 tool assesses randomized control trials (RCTs) for potential bias in patient randomization, protocol deviations, measurement and reporting of outcomes, and treatment of missing data. If any single domain is rated as having any risk of bias, the overall study is rated as having risk of bias. The Newcastle-Ottawa scale assesses observational studies based on selection of cohort, comparability of groups, and quality of outcomes. Using the Newcastle-Ottawa scale, we rated studies' quality as high (rated as ≥7 on a scale from 0 to 9), moderate (4–6), or low (≤3). We assessed for heterogeneity using the I^2 statistic and the Cochrane Q statistic.

2.4. Data extraction

Data from each study was extracted independently by two authors into a standardized Microsoft Excel spreadsheet (MicrosoftCorp, Redmond WA), and subsequently compared for consistency. Discrepancies were resolved by a third senior author. All reported data reflects the consensus of the investigators who performed data collection. We collected data regarding patient age and body mass index (BMI), location of intubation (ED, ICU, or medical floor), reason for intubation, clinical status at the time of intubation (reflected by patient vital signs and pre-intubation vasopressor use), mode of preoxygenation and induction medications used, and peri-intubation MAEs.

2.5. Statistical analysis

We reported categorical variables as percentages and continuous variables as mean (standard deviation [SD]). Continuous variables reported in individual studies as median (interquartile range [IQR]) were converted to mean (SD) [13]. The prevalence of MAE was reported as percentage and 95% Confidence Interval (CI). Primary and secondary outcomes across our pooled patient population were estimated using random-effects models. Studies reporting two similar outcomes were eligible for meta-analysis. Included studies were assumed to be a random sample from a universe of potential studies [14-18]. The "true" prevalence of MAE can be expected to fall anywhere within the confidence interval reported here [14,16,18-26]. We used multivariable meta-regressions to evaluate the association between continuous and categorical variables and rates of primary and secondary outcomes. Variables for the multivariable meta-regression were selected *a priori*. They included patients' demographics and clinical data.

Heterogeneity was assessed using the Cochrane Q statistic and the I^2 statistic. The Q statistic tests against the null hypothesis that all studies in the analysis share a common effect size. If all studies shared the same true effect size, the expected value of Q would be equal to the degrees of freedom (the number of studies minus 1). The I^2 statistic provides an estimate of the percentage of observed variance that is reflective of true variance in effect size rather than sampling error. We calculated tau (the standard deviation of true effect size between included studies) and tau-squared (the variance of true effect size in included studies) to further characterize heterogeneity. This allowed us to calculate prediction intervals to generalize our findings to a broader population. Prediction intervals suggest a range in which the true effect size in 95% of all comparable populations could be expected to fall. We calculated prediction intervals assuming true effect sizes were normally distributed.

We performed moderator analyses with categorical variables and studies' characteristics to identify possible sources of heterogeneity within our sample and to compare between subgroups. Categorical moderator variables were defined *a priori* and included study design (RCT, observational prospective, or observational retrospective), clinical setting (ED, ICU, or mixed settings), and the World Health Organization (WHO) region of the country in which the study was conducted.

We performed sensitivity analysis to assess the impact of each included study on the overall effect size, and ensure no single study had an outsized impact on our findings. Sensitivity analysis was performed using a "one-study removed" random-effects meta-analysis, in which each individual study was systemically removed, and a random-effects meta-analysis was performed on the remainder of the studies. We did not perform any assessment for publication bias, such as a funnel plot: these assessments provide information about potential missing studies that could affect the demonstrated efficacy of interventions, and as our study estimated the prevalence of MAEs, rather than comparing interventions to prevent them, they were not applicable.

All random-effects meta-analysis, sensitivity and moderator analyses and multivariable meta-regressions were performed with the software Comprehensive Meta-Analysis Version 4 (www.meta-analysis.com, Englewood, NJ).

3. Results

3.1. Study selection

We screened 5,371 abstracts and subsequently reviewed 171 articles and included 44 in our analysis (Fig. 1). Twelve studies met all inclusion criteria but were excluded from analysis due to high likelihood of dual enrollment of patients with another included study (Supp Table 1). Nine included studies were RCTs [27-35]; the rest were observational, 19 prospective [2,5,36-55] and 16 retrospective [7,56-67] (Table 1). Seventeen studies examined intubations in the ED, 23 in the ICU, and 4 in a mix of settings. Half of the included studies were from the Americas.

3.2. Study quality

We determined one RCT included in this analysis to have some concern for bias using the Cochrane Risk of Bias tool [31]; we judged the remainder to be of low risk for bias (Table 1). Details regarding study quality assessment by domain are provided in Supplemental Table 2. We judged the majority of the included observational studies to be of high quality using the Newcastle Ottawa Scale, and no studies were judged to be of low quality.

3.3. Summary of studies

Our analysis included data from 34,357 intubations, 21,677 of which were performed in the ED, 11,080 in the ICU, and 1,601 elsewhere, most often the medical wards or step-down units. Our patient population was 46% female, with a mean age of 59 (Table 2). Less than half of the included studies reported pre-intubation SBP [2,5,7,30,32,35,48,50,51,55,61-64,66,67], HR [2,7,30,35,51,55,61-64,66,67], IVF [2,5,47,66], or vasopressors [2,5,32-34,38,48,49,51,53,55,56,59,60,63,65-67]. Among studies reporting this data, mean SBP was 131 mmHg and mean HR was 106 bpm; one third of patients received IVF prior to intubation, and 11% vasopressors (Supp Table 3). Preoxygenation techniques were reported in 21 studies [2,5,27,28,30,33-35,38,45,48,49,51,54,55,58,60,62,64,66,67]; low-flow oxygen—including nasal cannula (NC) and non-rebreather mask (NRB)—was the most frequently reported form of preoxygenation (3,565 patients), followed by non-invasive ventilation (NIV)—including bi-level positive airway pressure (BiPAP), continuous positive airway pressure (CPAP), and bag-valve mask (BVM) ventilation—and high-flow nasal cannula (HFNC). All but 5 studies reported reasons for intubation [41-44,54]. Respiratory failure was the most reported impetus for intubation (23%), followed by airway protection (19%; Table 2).

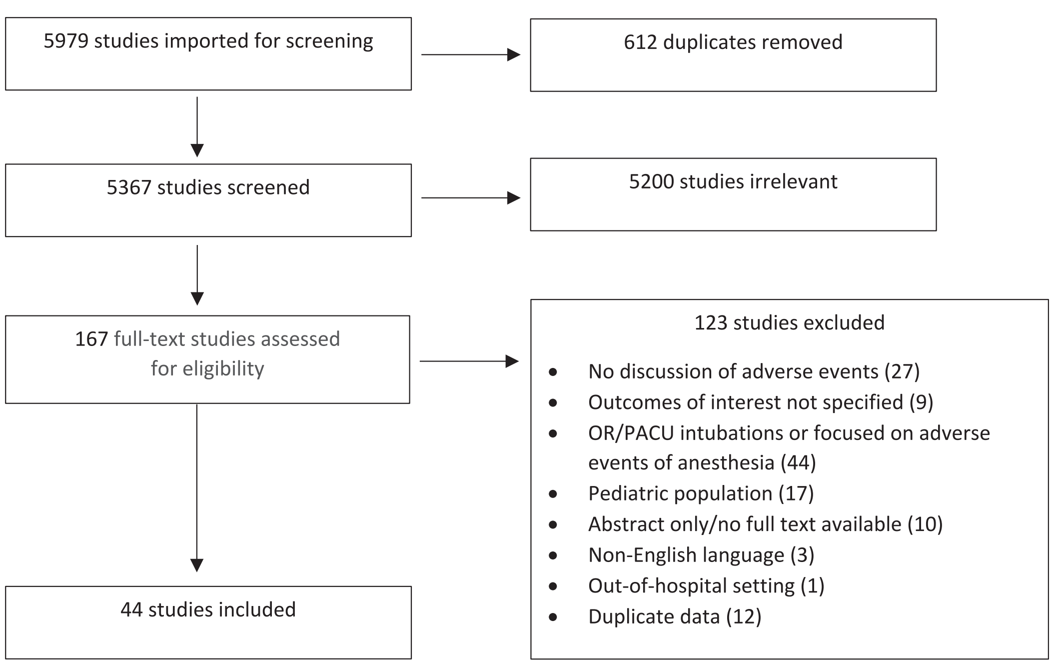


Fig. 1. Flow diagram for study selection[a].

3.4. Primary outcome: peri-intubation major adverse events

All 44 studies were included in our primary analysis. Thirty-one percent of patients included in our meta-analysis experienced a peri-intubation MAE (95% CI 25–37%; Fig. 2a). Our analysis reported a Q-statistic, of 5906 with 43 degrees of freedom and $p < 0.001$. Using a criterion alpha of 0.1, these findings reject the null hypothesis that the true effect size is the same across all included studies. I^2 was 99%, suggesting that no >1% of observed variance was due to sampling error. Tau-squared was 0.820 in logic units, and tau was 0.906 in logic units; from this calculation, we estimated that the prediction interval is 6.5–73.6%.

MAEs were less common ($p = 0.001$) among studies examining ED intubations (17%, 95% CI 12–24%), when compared to those examining ICU intubations (41%, 95% CI 33–49%) and intubations across multiple settings (41%, 24–61%; Table 3a). There was no significant difference in MAE rates when studies were compared across World Health Organization (WHO) regions, or by study type.

Our meta-regression (Table 3b) suggested a direct proportional correlation between rates of peri-intubation MAE in studies with the percentage of patients undergoing intubation for hemodynamic instability (Correlation Coefficient [Corr. Coeff.] 1.9, 95% CI 0.2–3.5, $p = 0.03$). Percentage of patients undergoing induction with propofol (Corr. Coeff. 3.4, 95% CI 0.2–6.7, $p = 0.04$) or with succinylcholine (Corr. Coeff. 4.5, 95% CI 1.9–7.0, $p = 0.01$) were positively correlated with prevalence of MAE, while percentage of patients intubated for airway protection (Corr. Coeff. −1.5, 95% CI −2.7 – −0.3, $p = 0.02$) was negatively correlated with the prevalence of peri-intubation MAE.

Our sensitivity analysis using random effects meta-analysis with one-study removed identified a consistent MAE rate of 30.5% (95% CI 22–38%), (Fig. 2b). This suggests that no single study disproportionately impacted the meta-analysis' overall effect size.

3.5. Secondary outcomes: hypoxia, cardiac arrest, and cardiovascular collapse

Our analysis of the prevalence of peri-intubation hypoxia was based on 28 studies. Hypoxia was identified in 15% of patients following intubation (95% CI 11.5–19%; Fig. 3a). This analysis was associated with a Q statistic of 1202 with 27 degrees of freedom and $p < 0.001$, rejecting the null hypothesis that the true effect size is the same across all included studies. I^2 was 98%. Tau-squared was 0.578 in logic units, and tau was 0.760 in logic units. We estimated that the prediction interval is 3.4–46.1%. Sensitivity analysis did not identify any individual study

Table 1
Characteristics of included studies.

Study (Year, Author)	Country	WHO Region	Setting	Study Type	Quality Rating[a]
1996 Khan [36]	Pakistan	EMR	ICU	Obs. Prospective	8
2006 Baillard [27]	France	EUR	ICU	RCT	Low Concern
2006 Simpson [37]	Scotland	EUR	ED	Obs. Prospective	6
2008 Griesdale [38]	Canada	AMR	MIxed	Obs. Prospective	8
2011 Mayo [39]	USA	AMR	ICU	Obs. Prospective	4
2012 Green [56]	Canada	AMR	ED	Obs. Retrospective	9
2013 Heffner [7]	USA	AMR	ED	Obs. Retrospective	8
2013 Imamura [40]	Japan	WPR	ED	Obs. Prospective	9
2013 Sakles [57]	USA	AMR	ED	Obs. Retrospective	7
2014 Roux [41]	France	EUR	ED	Obs. Prospective	5
2015 Mosier (a) [42]	USA	AMR	ICU	Obs. Prospective	5
2015 Mosier (b) [58]	USA	AMR	ICU	Obs. Retrospective	8
2015 Smith [43]	USA	AMR	ED	Obs. Prospective	8
2015 Trivedi [59]	USA	AMR	ICU	Obs. Retrospective	8
2016 Bodily [44]	USA	AMR	ED	Obs. Prospective	5
2016 Cham [60]	Hong Kong	WPR	Mixed	Obs. Retrospective	5
2016 Jaber [28]	France	EUR	ICU	RCT	Low Concern
2016 Janz [29]	USA	AMR	ICU	RCT	Low Concern
2016 Ono [61]	Japan	WPR	ED	Obs. Retrospective	9
2016 Sakles [45]	USA	AMR	ED	Obs. Prospective	8
2017 April [46]	USA	AMR	ED	Obs. Prospective	8
2017 Smischney [62]	USA	AMR	ICU	Obs. Retrospective	7
2017 Van Berkel [63]	USA	AMR	ICU	Obs. Retrospective	9
2018 Baek [64]	Korea	WPR	MIxed	Obs. Retrospective	8
2018 Corl [47]	USA	AMR	ICU	Obs. Prospective	4
2018 De Jong [48]	France	EUR	ICU	Obs. Prospective	7
2018 Driver [30]	USA	AMR	ED	RCT	Low Concern
2018 Grensemann [31]	Germany	EUR	ICU	RCT	Some Concern
2018 Janz [32]	USA	AMR	Mixed	RCT	Low Concern
2019 Casey [33]	USA	AMR	ICU	RCT	Low Concern
2019 Frat [34]	France	EUR	ICU	RCT	Low Concern
2019 Smischney [55]	USA	AMR	ICU	Obs. Prospective	8
2020 Amalric [49]	France	EUR	ICU	Obs. Prospective	5
2020 Chanthawatthanarak [50]	Thailand	SEAR	ED	Obs. Prospective	8
2020 de Alencar [51]	Brazil	AMR	ED	Obs. Prospective	9
2020 Mohr [65]	International	Other	ED	Obs. Retrospective	9
2020 Nong [35]	China	WPR	ICU	RCT	Low Concern
2020 Smischney [5]	USA	AMR	ICU	Obs. Prospective	8
2021 Mbanjumucyo [52]	Rwanda	AFR	ED	Obs. Prospective	8
2021 Russotto [2]	International	Other	Mixed	Obs. Prospective	5
2021 Walimanna Gamage [53]	Sri Lanka	SEAR	ICU	Obs. Prospective	5
2021 Zhang [54]	China	WPR	ICU	Obs. Prospective	8
2022 Ergün [66]	Turkey	EUR	ICU	Obs. Retrospective	7
2022 Yang [67]	Taiwan	WPR	ED	Obs. Retrospective	7

Abbreviations: USA, United States of America; WHO, World Health Organization; EMR, Eastern Mediterranean Region; AMR, Region of the Americas; EUR, European Region; WPR, Western Pacific Region; SEAR, South-East Asian Region; AFR, African Region; ICU, intensive care unit; ED, Emergency Department; Obs., Observational; RCT, Randomized Control Trial.

[a] The quality of observational studies was assessed using the Newcastle Ottawa Scale (1–9). The quality of randomized control trials was assessed using the Cochrane Risk of Bias 2 tool.

Table 2
Patient characteristics and rates of relevant peri-intubation MAEs reported by included studies.

Study	Demographics				Reason for Intubation					Complications			
Year, Author	Total Patients	Female N (%)	Age Mean (SD)	BMI Mean (SD)	Resp Failure N (%)	Airway Protection N (%)	CV Instability N (%)	Cardiac Arrest N (%)	Other N (%)	CV Instability N (%)	Hypoxia N (%)	Cardiac Arrest N (%)	Any MAE N (%)
1996 Khan [36]	126	NR	47 (18)	NR	0 (0%)	0 (0%)	0 (0%)	0 (0%)	126 (100%)	6 (5%)	NR	NR	6 (5%)
2006 Baillard [27]	53	17 (32%)	NR	NR	45 (85%)	0 (0%)	0 (0%)	0 (0%)	4 (8%)	NR	14 (26%)	NR	14 (26%)
2006 Simpson [37]	180	NR	NR	NR	0 (0%)	0 (0%)	0 (0%)	0 (0%)	180 (100%)	6 (3%)	15 (8%)	2 (1%)	23 (13%)
2008 Griesdale [38]	136	51 (38%)	58 (18)	26 (7)	89 (65%)	25 (18%)	11 (8%)	0 (0%)	11 (8%)	13 (10%)	26 (19%)	61 (45%)	100 (74%)
2011 Mayo [39]	128	NR	NR	NR	34 (27%)	29 (23%)	0 (0%)	0 (0%)	65 (51%)	20 (16%)	NR	1 (1%)	21 (16%)
2012 Green [56]	218	85 (39%)	57 (21)	NR	45 (21%)	14 (6%)	0 (0%)	0 (0%)	135 (62%)	96 (44%)	NR	NR	96 (44%)
2013 Heffner [7]	410	147 (36%)	49 (19)	NR	80 (20%)	294 (72%)	0 (0%)	0 (0%)	36 (9%)	NR	NR	17 (4%)	17 (4%)
2013 Imamura [40]	3178	1253 (39%)	65 (19)	NR	570 (18%)	971 (31%)	271 (9%)	1174 (37%)	192 (6%)	46 (1%)	5 (0%)	4 (0%)	55 (2%)
2013 Sakles [57]	1828	635 (35%)	NR	NR	312 (17%)	1143 (63%)	26 (1%)	200 (11%)	147 (8%)	5 (0%)	309 (17%)	3 (0%)	317 (17%)
2014 Roux [41]	1007	NR	NR	NR	NR	NR	NR	NR	NR	NR	87 (9%)	NR	87 (9%)
2015 Mosier (a) [42]	861	376 (44%)	NR	NR	NR	NR	NR	NR	NR	71 (8%)	189 (22%)	4 (0%)	264 (31%)
2015 Mosier (b) [58]	235	96 (41%)	NR	NR	183 (78%)	37 (16%)	12 (5%)	0 (0%)	3 (1%)	70 (30%)	66 (28%)	NR	136 (58%)
2015 Smith [43]	141	NR	NR	NR	NR	NR	NR	NR	NR	2 (1%)	7 (5%)	0 (0%)	9 (6%)
2015 Trivedi [59]	140	63 (45%)	62 (15)	NR	108 (77%)	91 (65%)	0 (0%)	0 (0%)	0 (0%)	55 (39%)	NR	NR	55 (39%)
2016 Bodily [44]	166	45 (27%)	NR	NR	NR	NR	NR	NR	NR	NR	59 (36%)	NR	59 (36%)
2016 Cham [60]	325	108 (33%)	67 (16)	NR	186 (57%)	42 (13%)	24 (7%)	33 (10%)	40 (12%)	69 (21%)	NR	4 (1%)	73 (22%)
2016 Jaber [28]	49	11 (22%)	62 (3)	24 (3)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	49 (100%)	13 (27%)	6 (12%)	0 (0%)	19 (39%)
2016 Janz [29]	150	59 (39%)	NR	NR	85 (57%)	39 (26%)	0 (0%)	0 (0%)	26 (18%)	15 (10%)	30 (20%)	2 (1%)	47 (31%)
2016 Ono [61]	123	38 (31%)	56 (10)	NR	76 (62%)	0 (0%)	0 (0%)	0 (0%)	47 (38%)	7 (6%)	NR	5 (4%)	12 (10%)
2016 Sakles [45]	127	37 (29%)	NR	NR	1 (1%)	117 (92%)	0 (0%)	0 (0%)	9 (7%)	13 (10%)	NR	NR	13 (10%)
2017 April [46]	259	NR	NR	NR	12 (5%)	31 (12%)	10 (4%)	14 (5%)	8 (3%)	13 (5%)	36 (14%)	10 (16%)	59 (23%)
2017 Smischney [62]	420	176 (42%)	NR	NR	282 (67%)	173 (41%)	166 (40%)	18 (4%)	103 (25%)	NR	74 (18%)	NR	74 (18%)
2017 Van Berkel [63]	384	184 (48%)	NR	NR	340 (89%)	35 (9%)	5 (1%)	0 (0%)	4 (1%)	244 (64%)	NR	NR	244 (64%)
2018 Baek [64]	958	337 (35%)	63 (6)	NR	658 (69%)	138 (14%)	128 (13%)	0 (0%)	4 (0%)	181 (19%)	24 (3%)	NR	205 (21%)
2018 Corl [47]	275	143 (52%)	NR	NR	0 (0%)	44 (16%)	199 (72%)	16 (6%)	5 (2%)	33 (12%)	NR	3 (1%)	36 (13%)
2018 De Jong [48]	1847	655 (35%)	NR	NR	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1847 (100%)	1026 (55%)	NR	49 (3%)	1075 (58%)
2018 Driver [30]	757	230 (30%)	NR	NR	39 (5%)	406 (54%)	48 (6%)	55 (7%)	708 (94%)	97 (13%)	NR	55 (7%)	152 (20%)
2018 Grensemann [31]	53	24 (45%)	NR	NR	0 (0%)	0 (0%)	0 (0%)	0 (0%)	53 (100%)	9 (17%)	9 (17%)	NR	18 (34%)
2018 Janz [32]	262	97,937%)	NR	NR	224 (85%)	99 (38%)	28 (11%)	0 (0%)	34 (13%)	58 (22%)	60 (23%)	7 (3%)	125 (48%)
2019 Casey [33]	401	175 (44%)	NR	NR	327 (82%)	150 (37%)	0 (0%)	0 (0%)	34 (8%)	25 (6%)	85 (21%)	6 (1%)	116 (29%)
2019 Frat [34]	313	101 (32%)	NR	NR	186 (59%)	13 (4%)	66 (21%)	0 (0%)	12 (4%)	156 (50%)	80 (26%)	6 (2%)	242 (77%)
2019 Smischney [55]	269	124 (46%)	NR	NR	169 (63%)	109 (41%)	0 (0%)	6 (2%)	42 (16%)	141 (52%)	NR	NR	141 (52%)
2020 Amalric [49]	202	76 (38%)	66 (5)	26 (2)	122 (60%)	0 (0%)	24 (12%)	4 (2%)	44 (22%)	35 (17%)	NR	2 (1%)	37 (18%)
2020 Chanthawatthanarak [50]	267	100 (37%)	67 (15)	NR	173 (65%)	51 (19%)	29 (11%)	0 (0%)	14 (5%)	16 (6%)	2 (1%)	4 (1%)	22 (8%)
2020 de Alencar [51]	112	51 (46%)	NR	NR	0 (0%)	2 (2%)	110 (98%)	0 (0%)	0 (0%)	106 (95%)	NR	2 (1%)	108 (96%)
2020 Mohr [65]	12,722	8450 (66%)	NR	NR	0 (0%)	0 (0%)	531 (4%)	0 (0%)	12,191 (96%)	2051 (16%)	966 (8%)	NR	3017 (24%)
2020 Nong [35]	106	31 (29%)	NR	NR	102 (96%)	0 (0%)	0 (0%)	0 (0%)	4 (4%)	37 (35%)	24 (23%)	NR	61 (58%)
2020 Smischney [5]	1033	431 (42%)	62 (15)	30 (9)	751 (73%)	888 (86%)	189 (18%)	41 (4%)	187 (18%)	189 (18%)	216 (21%)	NR	405 (39%)
2021 Mbanjumucyo [52]	198	52 (26%)	36 (8)	NR	NR	146 (74%)	NR	13 (7%)	4 (2%)	20 (10%)	45 (23%)	7 (4%)	65 (33%)
2021 Russotto [2]	2964	1107 (37%)	62 (7)	26 (2)	1685 (57%)	902 (30%)	277 (9%)	NR	96 (3%)	1172 (40%)	272 (9%)	93 (3%)	1537 (52%)
2021 Walimanna Gamage [53]	150	63 (42%)	NR	NR	0 (0%)	0 (0%)	0 (0%)	0 (0%)	129 (86%)	69 (46%)	75 (50%)	4 (3%)	148 (98%)
2021 Zhang [54]	315	103 (33%)	32 (11)	37 (11)	NR	NR	NR	NR	NR	154 (49%)	79 (25%)	10 (7%)	243 (77%)
2022 Ergün [66]	141	39 (28%)	73 (5)	26 (1)	141 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	NR	141 (100%)	0 (0%)	141 (100%)
2022 Yang [67]	368	127 (35%)	NR	NR	211 (57%)	88 (24%)	NR	0 (0%)	68 (28%)	NR	NR	92 (25%)	92 (25%)

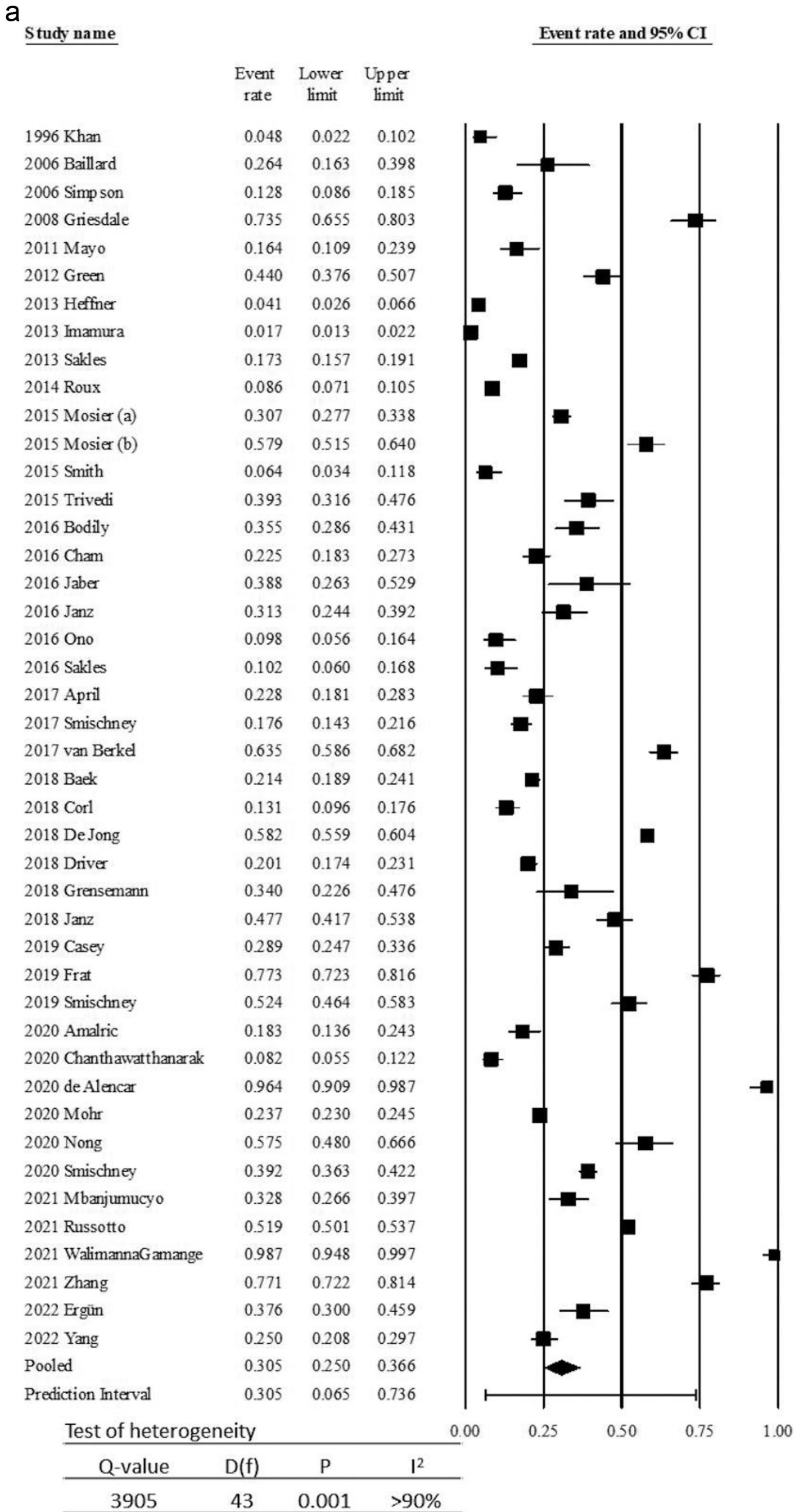


Fig. 2. a. Prevalence of peri-intubation major adverse events in patients undergoing intubation outside of the post-anesthesia care unit or operating room. b. Sensitivity analysis for prevalence of peri-intubation major adverse events, performed using random-effects meta-analysis with one-study-removed.

b

Name of Removed Study	Point	Lower limit	Upper limit
1996 Khan	0.314	0.258	0.377
2006 Baillard	0.306	0.250	0.368
2006 Simpson	0.310	0.254	0.373
2008 Griesdale	0.296	0.242	0.356
2011 Mayo	0.309	0.253	0.371
2012 Green	0.302	0.247	0.364
2013 Heffner	0.316	0.260	0.378
2013 Imamura	0.321	0.267	0.380
2013 Sakles	0.309	0.252	0.372
2014 Roux	0.313	0.257	0.374
2015 Mosier (a)	0.305	0.248	0.368
2015 Mosier (b)	0.299	0.244	0.360
2015 Smith	0.313	0.257	0.376
2015 Trivedi	0.303	0.247	0.365
2016 Bodily	0.304	0.248	0.366
2016 Cham	0.307	0.251	0.370
2016 Jaber	0.303	0.248	0.365
2016 Janz	0.305	0.249	0.367
2016 Ono	0.311	0.255	0.374
2016 Sakles	0.311	0.255	0.374
2017 April	0.307	0.251	0.369
2017 Smischney	0.309	0.252	0.371
2017 van Berkel	0.298	0.243	0.358
2018 Baek	0.308	0.251	0.371
2018 Corl	0.310	0.254	0.373
2018 De Jong	0.299	0.245	0.358
2018 Driver	0.308	0.251	0.371
2018 Grensemann	0.304	0.249	0.366
2018 Janz	0.301	0.246	0.363
2019 Casey	0.305	0.249	0.368
2019 Frat	0.294	0.241	0.354
2019 Smischney	0.300	0.245	0.362
2020 Amalric	0.308	0.252	0.371
2020 Chanthawatthanarak	0.313	0.256	0.375
2020 de Alencar	0.289	0.236	0.349
2020 Mohr	0.308	0.246	0.378
2020 Nong	0.299	0.244	0.361
2020 Smischney	0.303	0.246	0.367
2021 Mbanjumucyo	0.304	0.249	0.367
2021 Russotto	0.300	0.245	0.362
2021 WalimannaGamange	0.289	0.236	0.348
2021 Zhang	0.294	0.241	0.354
2022 Ergün	0.303	0.248	0.365
2022 Yang	0.306	0.250	0.369
Pooled	0.305	0.250	0.366
Prediction Interval	0.305	0.065	0.736

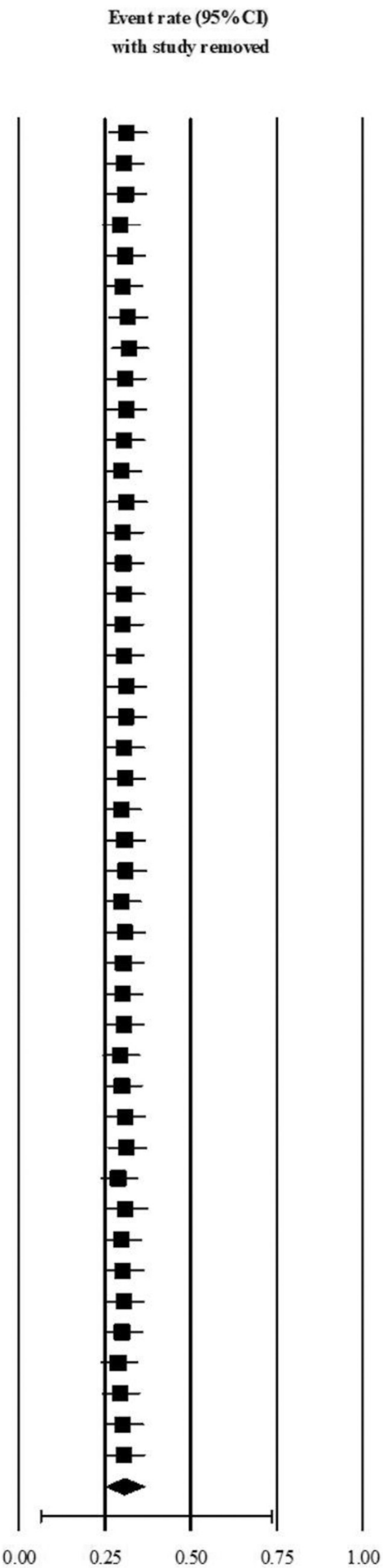


Fig. 2 (*continued*).

Table 3
Moderator analysis and meta-regression for primary outcome of any peri-intubation MAE.

A. Moderator analysis

Moderator Variables		Meta-analysis			Heterogeneity				Between group comparison
		# Studies	Outcome	95% CI	Q-value	D(f)	P	I^2	P
Study design	RCT	9	0.4	0.27–0.56	304	8	0.001	>90	0.21
	Obs prospective	19	0.26	0.19–0.34	2086	18	0.001	>90	
	Obs retrospective	16	0.32	0.23–0.42	674	15	0.001	>90	
Study settings	ED	17	0.17	0.12–0.24	853	16	0.001	>90	0.001
	ICU	23	0.41	0.33–0.49	948	22	0.001	>90	
	Mixed	4	0.41	0.24–0.61	351	3	0.001	>90	
WHO regions	AMR	22	0.32	0.23–0.42	954	21	0.001	>90	0.42
	EUR	9	0.32	0.19–0.48	729	8	0.001	>90	
	SEAR	2	0.59	0.23–0.88	81	2	0.001	>90	
	WPR	7	0.23	0.12–0.40	832	6	0.001	>90	
	Multi-national	2	0.37	0.12–0.71	864	1	0.001	>90	
	Other	2	0.14	0.04–0.43	26	1	0.001	>90	

B. Meta-Regression

	Variables	# Studies	Corr. Coeff.	95% CI	P
Demographics	Age (mean)	12	0.02	−0.06–0.10	0.86
	Female (%)		−4.20	−12.1–3.40	0.28
	BMI (kg/m^{2,} mean)		0.02	−0.14–0.18	0.82
Vital signs	Pre-intubation SBP (mmHg, mean)	13	−0.04	−0.10 to −0.01	0.14
	Pre-intubation HR (bpm, mean)		-0.01	−0.09–0.08	0.79
Reasons for intubation	Respiratory failure (%)	37	0.90	−0.01–1.80	0.05
	Airway protection (%)		−1.50	−2.70– −0.28	0.02
	CV instability (%)		1.90	0.20–3.50	0.03
Pre-Intubation Interventions	Vasopressors/Inotropes (%)	7	−0.70	−3.30–1.80	0.56
	Preoxygenation with NIV (%)		3.10	−2.40–8.50	0.27
	Preoxygenation with HFNC (%)		1.90	−2.70–6.60	0.4
Induction Medications	Propofol (%)	11	3.40	0.19–6.71	0.04
	Etomidate (%)		1.30	−0.11–2.78	0.07
	Midazolam (%)		−0.33	−2.40–1.74	0.76
NMB	Succinylcholine (%)	17	4.50	1.90–7.02	0.01
	Rocuronium (%)		1.80	−0.45–4.11	0.12

Abbreviations: RCT, randomized control trial; ED, emergency department; ICU, intensive care unit; WHO, World Health Organization; AMR, Region of the Americas; EUR, European Region; SEAR, South-East Asian Region; WPR, Western Pacific Region; BMI, body mass index; CV, cardiovascular; NIV, non-invasive ventilation; HFNC, high-flow nasal annula.

that disproportionately impacted the overall effect size of hypoxia prevalence (Fig. 3b).

Rates of hypoxia varied significantly ($p = 0.001$) by location of intubation, ranging from 8% in studies examining ED intubations (95% CI 6–12%) and those in mixed settings (95% CI 4–16%) to 24% (95% CI 18–31%) in the ICU (Table 4a). We also observed significant variation in rates of hypoxia based on WHO region; studies completed in the Western Pacific Region had the lowest rates of hypoxia (8%, 95% CI 4–17%), while those completed in the Americas had the highest (20%, 95% CI 15–24%). Hypoxia was most common in RCTs (21%, 95% CI 13–30%), and least commonly in observational prospective studies (8%, 95% CI 5–13%).

Multivariable meta-regression (Table 4b) indicated that age, and higher percentages of female patients, patients intubated for respiratory failure or receiving propofol or either succinylcholine or rocuronium were positively correlated with higher prevalence of hypoxia, while higher mean BMI and higher percentages of patients receiving midazolam were negatively correlated with higher prevalence of hypoxia.

Our analysis of peri-intubation cardiac arrest was based on 28 studies. Peri-intubation cardiac arrest occurred in 2% (95% CI 1–3.5%) of patients included in our meta-analysis (Fig. 4a). This analysis was associated with a Q statistic of 716 with 27 degrees of freedom and $p = 0.001$, and I^2 was 96%. Tau-squared was 2.006, and tau was 1.416 in logic units. We estimated that the prediction interval is 0.1–28.8%. Sensitivity analysis also did not identify any individual study that overwhelmingly affected the overall effect size for prevalence of cardiac arrest (Fig. 4b). There was no significant difference in rates of cardiac arrest based on studies' WHO region, location of intubation (ED v ICU v mixed), or study type (Table 4a).

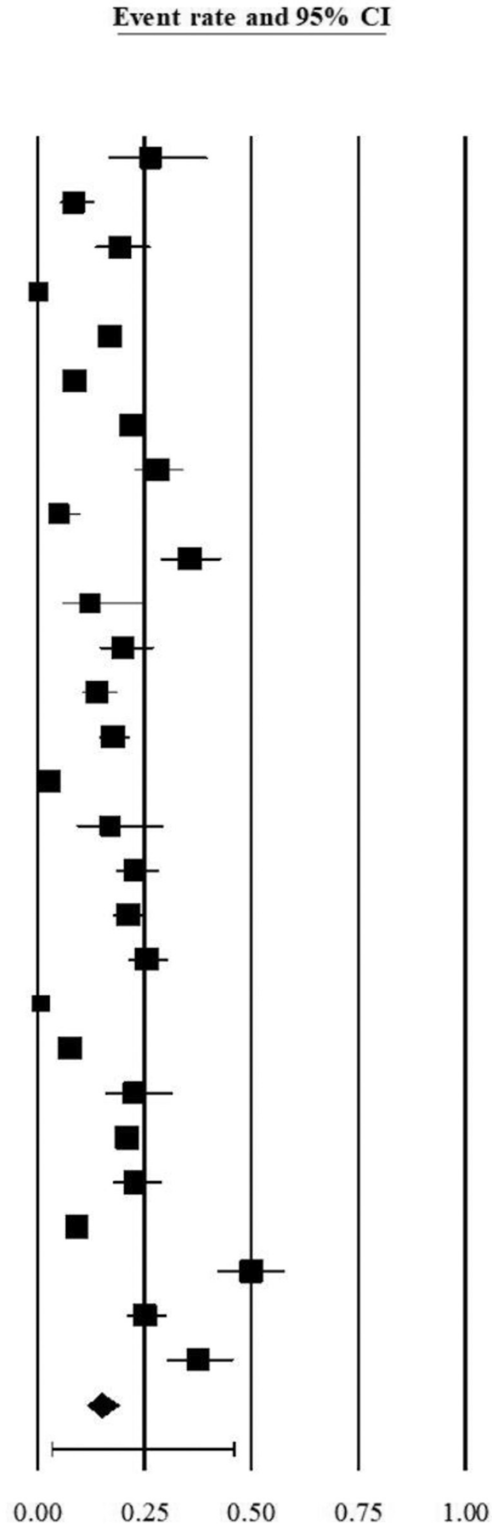
Multivariable meta-regression (Table 4b) suggested that a higher mean HR prior to intubation (Corr. Coeff. 0.13, 95% CI 0.01–0.25, $p = 0.03$) was associated with a higher prevalence of peri-intubation cardiac arrest, while a greater percentage of patients receiving etomidate during induction (Corr. Coeff. −2.7, 95% CI −5.2– −0.1, $p = 0.04$) were associated with lower prevalence of peri-intubation cardiac arrest.

Peri-intubation cardiovascular collapse was reported by 37 included studies and occurred in 18% (95% CI 13–23%) of patients included in our analysis (Supp Fig. 1a). This analysis was associated with a Q statistic, of 3453 with 36 degrees of freedom and $p = 0.001$, and I^2 was >90%. We estimated that the prediction interval is 3–63%. Sensitivity analysis did not identify any individual study that overwhelmingly affected the overall effect size for prevalence of cardiac arrest (Supp Fig. 1b). Studies reporting ED intubations had significantly lower rates of cardiovascular collapse than those reporting intubations in the ICU or mixed settings (Table 4a); there was no significant difference in rates of cardiovascular collapse based on studies' WHO region or study type.

Multivariable meta-regression (Table 4b) suggested that intubation for pre-existing cardiovascular instability (Corr. Coeff. 2.90, 95% CI 0.91–4.80, $p = 0.004$), and use of propofol (Corr. Coeff. 7.50, 95% CI 3.20–11.7, $p = 0.001$) or succinylcholine (Corr. Coeff. 5.60, 95% CI 1.90–9.30, $p = 0.003$) during induction were associated with a higher prevalence of peri-intubation cardiovascular collapse; older age (Corr. Coeff. 0.08, 95% CI 0.01–0.15, $p = 0.017$) and higher BMI (Corr. Coeff. 0.11, 95% CI 0.01–0.22, $p = 0.038$) were weakly associated with this outcome. Female sex (Corr. Coeff. −7.50, 95% CI −12.7– −2.20, $p = 0.006$), higher pre-intubation SBP (Corr. Coeff. −0.09, 95% CI −0.18– −0.01, $p = 0.039$), and intubation for airway protection (Corr. Coeff. −1.60, 95% CI −3.10– −0.03, $p = 0.046$) were associated with lower prevalence of peri-intubation cardiovascular collapse.

a

Study name	Event rate	Lower limit	Upper limit	Total	Relative weight
2006 Baillard	0.264	0.163	0.398	14 / 53	3.34
2006 Simpson	0.083	0.051	0.134	15 / 180	3.47
2008 Griesdale	0.191	0.134	0.266	26 / 136	3.61
2013 Imamura	0.002	0.001	0.004	5 / 3178	2.90
2013 Sakles	0.169	0.153	0.187	309 / 1828	3.88
2014 Roux	0.086	0.071	0.105	87 / 1007	3.82
2015 Mosier (a)	0.220	0.193	0.248	189 / 861	3.86
2015 Mosier (b)	0.281	0.227	0.342	66 / 235	3.77
2015 Smith	0.050	0.024	0.100	7 / 141	3.10
2016 Bodily	0.355	0.286	0.431	59 / 166	3.74
2016 Jaber	0.122	0.056	0.247	6 / 49	2.94
2016 Janz	0.200	0.144	0.272	30 / 150	3.64
2017 April	0.139	0.102	0.187	36 / 259	3.70
2017 Smischney	0.176	0.143	0.216	74 / 420	3.80
2018 Baek	0.025	0.017	0.037	24 / 958	3.64
2018 Grensemann	0.170	0.091	0.295	9 / 53	3.17
2018 Janz	0.229	0.182	0.284	60 / 262	3.76
2019 Casey	0.212	0.175	0.255	85 / 401	3.81
2019 Frat	0.256	0.210	0.307	80 / 313	3.80
2020 Chanthawatthanarak	0.007	0.002	0.029	2 / 267	2.09
2020 Mohr	0.076	0.071	0.081	966 / 12722	3.90
2020 Nong	0.226	0.157	0.316	24 / 106	3.57
2020 Smischney	0.209	0.185	0.235	216 / 1033	3.87
2021 Mbanjumucyo	0.227	0.174	0.291	45 / 198	3.72
2021 Russotto	0.092	0.082	0.103	272 / 2964	3.88
2021 WalimannaGamange	0.500	0.421	0.579	75 / 150	3.73
2021 Zhang	0.251	0.206	0.302	79 / 315	3.79
2022 Ergün	0.376	0.300	0.459	53 / 141	3.71
Pooled	0.148	0.115	0.189		
Prediction Interval	0.148	0.034	0.461		



Test of heterogeneity

Q-value	D(f)	P	I^2
1202	27	0.001	>90%

Fig. 3. a. Prevalence of peri-intubation hypoxia in patients undergoing intubation outside of the post-anesthesia care unit or operating room. b. Sensitivity analysis for prevalence of peri-intubation hypoxia, performed using random-effects meta-analysis with one-study-removed.

b

Name of Removed Study	Point	Lower limit	Upper limit
2006 Baillard	0.145	0.112	0.186
2006 Simpson	0.151	0.116	0.194
2008 Griesdale	0.146	0.113	0.188
2013 Imamura	0.167	0.131	0.211
2013 Sakles	0.146	0.111	0.191
2014 Roux	0.151	0.116	0.194
2015 Mosier (a)	0.145	0.111	0.187
2015 Mosier (b)	0.144	0.111	0.185
2015 Smith	0.153	0.118	0.196
2016 Bodily	0.143	0.110	0.183
2016 Jaber	0.149	0.115	0.191
2016 Janz	0.146	0.112	0.188
2017 April	0.148	0.114	0.191
2017 Smischney	0.147	0.113	0.189
2018 Baek	0.158	0.123	0.201
2018 Grensemann	0.147	0.113	0.189
2018 Janz	0.145	0.112	0.187
2019 Casey	0.146	0.112	0.188
2019 Frat	0.145	0.111	0.186
2020 Chanthawatthanarak	0.157	0.121	0.200
2020 Mohr	0.154	0.121	0.193
2020 Nong	0.146	0.112	0.187
2020 Smischney	0.146	0.111	0.188
2021 Mbanjumucyo	0.145	0.112	0.187
2021 Russotto	0.150	0.114	0.195
2021 WalimannaGamange	0.140	0.109	0.179
2021 Zhang	0.145	0.111	0.186
2022 Ergün	0.142	0.110	0.182
Pooled	0.148	0.115	0.189
Prediction Interval	0.148	0.034	0.461

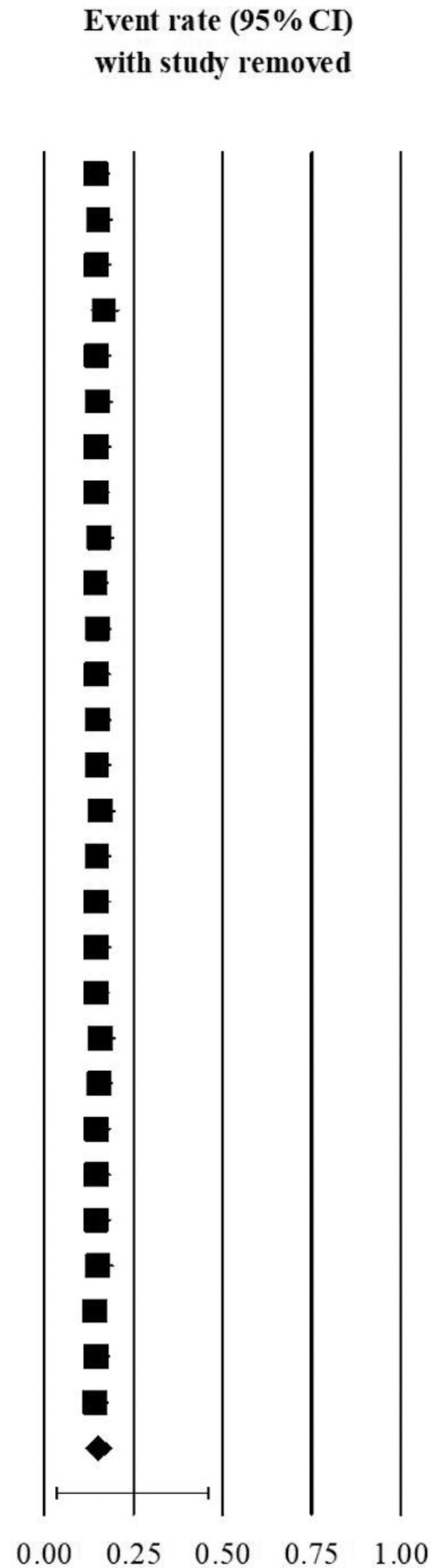


Fig. 3 (*continued*).

Table 4
Moderator analyses and meta-regressions for secondary outcomes of peri-intubation hypoxia and cardiac arrest.

A. Moderator analysis

Moderator Variables		Meta-analysis			Heterogeneity				Between group comparison
		# Studies	Outcome	95% CI	Q-value	D(f)	*P*	I^2	*P*
Outcome: Hypoxia									
Study design	Obs prospective	11	0.08	0.05–0.13	301	10	0.001	>90	0.007
	Obs retrospective	9	0.2	0.13–0.30	773	8	0.001	>90	
	RCT	8	0.21	0.13–0.32	6.8	7	0.45	0%	
Study settings	ED	10	0.08	0.06–0.12	419	9	0.001	>90	0.001
	ICU	15	0.24	0.18–0.31	91	14	0.001	84%	
	Mixed	3	0.08	0.04–0.16	58	2	0.001	>90	
WHO regions	AMR	12	0.2	0.15–0.24	72	11	0.001	85%	0.001
	EUR	7	0.18	0.12–0.25	115	6	0.001	>90	
	SEAR	2	0.19	0.08–0.38	45	1	0.001	>90	
	WPR	4	0.08	0.04–0.17	222	3	0.001	>90	
	Multi-national	2	0.08	0.04–0.17	8	1	0.001	87%	
	Other	1	0.23	0.08–0.49	NA	NA	NA	NA	
Outcome: Cardiac Arrest									
Study design	Obs prospective	14	0.02	0.008–0.046	382	13	0.001	>90	0.98
	Obs retrospective	8	0.019	0.006–0.057	225	7	0.001	>90	
	RCT	6	0.022	0.006–0.081	31	5	0.001	84%	
Study settings	ED	12	0.02	0.008–0.049	294	11	0.001	>90	0.27
	ICU	13	0.014	0.006–0.034	21	12	0.053	42%	
	Mixed	3	0.068	0.013–0.29	267	2	0.001	>90	
WHO regions	AMR	13	0.02	0.008–0.052	325	12	0.001	>90	0.99
	EUR	6	0.012	0.003–0.055	6	5	0.32	15%	
	SEAR	2	0.02	0.002–0.19	1	1	0.41	0	
	WPR	5	0.024	0.005–0.10	189	1	0.001	>90	
	Multi-national	1	0.031	0.001–0.54	NA	NA	NA	NA	
	Other	1	0.035	0.001–0.54	NA	NA	NA	NA	
Outcome: Cardiovascular Collapse									
Study design	Obs prospective	18	0.16	0.10–0.24	1622	17	0.001	>90%	0.77
	Obs retrospective	11	0.19	0.11–0.31	787	10	0.001	>90%	
	RCT	8	0.2	0.10–0.34	231	7	0.001	>90%	
Study settings	ED	13	0.09	0.05–0.14	696	12	0.001	>90%	0.002
	ICU	20	0.25	0.18–0.35	1145	19	0.001	>90%	
	Mixed	4	0.21	0.09–0.42	185	3	0.001	>90%	
WHO regions	AMR	19	0.17	0.11–0.25	986	18	0.001	>90%	0.069
	EUR	6	0.24	0.12–0.43	187	5	0.001	>90%	
	SEAR	2	0.19	0.05–0.52	72	1	0.001	>90%	
	WPR	6	0.15	0.07–0.30	533	5	0.001	>90%	
	Multi-national	2	0.26	0.08–0.61	752	1	0.001	>90%	
	Other	2	0.07	0.02–0.26	2.8	1	0.09	65%	

B. Meta-Regression

	Variables	# Studies	Corr. Coeff.	95% CI	P
Outcome: Hypoxia					
Demographics	Age (mean)	6	0.20	0.05–0.15	0.01
	Female (%)		3.90	0.31–7.61	0.03
	BMI (kg/m^2, mean)		−0.11	−0.14–−0.07	0.01
Vital signs	Pre-intubation SBP (mmHg, mean)	6	−0.09	−0.05–0.25	0.22
	Pre-intubation HR (bpm, mean)		−0.08	−0.20–0.01	0.08
Reasons for intubation	Respiratory failure (%)	22	1.10	0.02–2.11	0.046
	Airway protection (%)		−0.30	−2.03–1.40	0.7
	CV instability (%)		−2.30	−6.50–1.72	0.26
Pre-Intubation Interventions	Vasopressors/Inotropes (%)	10	0.80	−1.40–2.99	0.48
	Preoxygenation with NIV (%)	7	4.10	−0.77–8.90	0.1
	Preoxygenation with HFNC (%)		−0.04	−4.10–4.00	0.98
Induction Medications	Propofol (%)	7	9.40	1.60–17.1	0.02
	Etomidate (%)		0.70	−2.20–3.60	0.64
	Midazolam (%)		−11.7	−21.4–−2.10	0.02
Paralytics	Succinylcholine (%)	10	7.20	4.60–9.80	0.01
	Rocuronium (%)		4.40	3.10–5.70	0.01
Outcome: Cardiac Arrest					
Demographics	Age (mean)	11	−0.10	−0.33–0.08	0.24
	Female (%)		2.10	−17.4–21.7	0.83
	BMI (kg/m^2, mean)		−0.03	−0.40–0.37	0.87
Vital signs	Pre-intubation SBP (mmHg, mean)	8	−0.02	−0.07–0.02	0.33
	Pre-intubation HR (bpm, mean)		0.13	0.01–0.25	0.03
Reasons for intubation	Respiratory failure (%)	23	0.40	−1.80–2.60	0.71
	Airway protection (%)		−0.22	−3.50–3.01	0.89
	CV instability (%)		−0.10	−3.10–2.90	0.95
Pre-Intubation Interventions	Vasopressors/Inotropes (%)	13	−3.40	−8.40–1.72	0.2
	Preoxygenation with NIV (%)	7	−7.30	−18.2–3.60	0.19
	Preoxygenation with HFNC (%)		3.03	−8.26–12.3	0.6
Induction Medications	Propofol (%)	6	5.20	−2.80–13.2	0.2

Table 4 (*continued*)

B. Meta-Regression

	Variables	# Studies	Corr. Coeff.	95% CI	P
	Etomidate (%)		−2.70	−5.20–−0.13	0.04
	Midazolam (%)		−5.60	−14.2–2.90	0.2
Paralytics	Succinylcholine (%)	12	1.60	−3.10–6.40	0.5
	Rocuronium (%)		2.40	−3.20–8.10	0.4
Demographics	Age (mean)	8	0.08	0.01–0.15	0.017
	Female (%)		−7.50	−12.7–−2.20	0.006
	BMI (kg/m^{2,} mean)		0.11	0.01–0.22	0.038
Vital signs	Pre-intubation SBP (mmHg, mean)	9	−0.09	−0.18–−0.01	0.039
	Pre-intubation HR (bpm, mean)		−0.13	−0.10–0.07	0.77
Reasons for intubation	Respiratory failure (%)	33	1.20	0.00–2.30	0.05
	Airway protection (%)		−1.60	−3.10–−0.03	0.046
	CV instability (%)		2.90	0.91–4.80	0.004
Pre-Intubation Interventions	Vasopressors/Inotropes (%)	17	2.50	−0.80–5.70	0.14
	Preoxygenation with NIV (%)	7	1.20	−4.10–6.50	0.67
	Preoxygenation with HFNC (%)		1.50	−2.80–5.90	0.49
Induction Medications	Propofol (%)	10	7.50	3.20–11.7	0.001
	Etomidate (%)		1.20	−0.49–2.90	0.16
	Midazolam (%)		−0.86	−3.50–1.70	−0.52
Paralytics	Succinylcholine (%)	16	5.60	1.90–9.30	0.003
	Rocuronium (%)		−1.70	−5.90–2.40	0.41

Abbreviations: RCT, randomized control trial; ED, emergency department; ICU, intensive care unit; WHO, World Health Organization; AMR, Region of the Americas; EUR, European Region; SEAR, South-East Asian Region; WPR, Western Pacific Region; BMI, body mass index; CV, cardiovascular; NIV, non-invasive ventilation; HFNC, high-flow nasal cannula.

4. Discussion

Our findings suggest that approximately 1 in 3 patients undergoing intubation in the ED, the ICU or medical wards will experience a clinically significant peri-intubation adverse event, including hypoxia, cardiovascular instability, or cardiac arrest. Fifteen percent of these patients experienced hypoxia, 18% cardiovascular instability, and 2% cardiac arrest. Our exploratory multivariable meta-regression also identified intubation for hemodynamic instability and use of propofol or succinylcholine for inductionas independent risk factors associated with a higher prevalence of peri-intubation MAEs, and specifically with higher rates of peri-intubation hypoxia and cardiovascular collapse. Intubation for airway protection was correlated with a lower prevalence of peri-intubation MAEs.

High heterogeneity was observed in this meta-analysis and across many subgroup analyses, likely due to differences in studies' clinical setting and patient selection: while many studies reported data for all-comers, others focused only on critically ill patients or those anticipated to have difficult airways, and still others on those with specific disease-entities, such as COVID-19. This resulted in a wide range of reported rates of MAEs, from 2% by Imamura et al. in 2013 to 98% by Walimanna Gamange et al. in 2021. However, this meta-analysis indicated that across a wide variety of patient populations and clinical settings similar to the included studies, the prevalence for composite MAEs would range from 22% to 38%.

The ED and ICU are the most studied (and likely most common) settings in which patients are intubated outside the OR or PACU and have significantly different rates of adverse events: 17% in the ED as opposed to 23% in the ICU. We expect this is primarily reflective of distinct patient populations (the ICU by default selects a more critically ill subset of patients) and clinical scenarios surrounding intubation: 28% of ICU patients were intubated for respiratory failure, compared to 7% of ED patients.Wwhile intubation for respiratory failure did not meet statistical significance as a risk factor for peri-intubation MAE, it was associated with an increased risk of hypoxia. Moreover, we did see a trend towards increased risk of overall MAEs in this population (Corr. Coeff. 0.9, 95% CI -0.01 to 1.8, $p = 0.05$). Furthermore, almost two-thirds of included patients intubated in the ED were intubated for "other" reasons (i.e., not respiratory failure, airway protection, hemodynamic instability, or cardiac arrest), which often included facilitation of procedures in patients who may have been otherwise relatively healthy. Seven percent of ED intubations occurred in the setting of cardiac arrest, compared to just under 1% of ICU intubations. In the absence of return of spontaneous circulation, it is likely that patients intubated for cardiac arrest woul not be counted as experiencing any peri-intubation MAEs. Regardless, the high rates of MAEs seen here should encourage all physicians to carefully consider and prepare for MAEs during and following all intubations.

In general, the risk factors identified here as contributors to various peri-intubation MAEs are common indicators of overall critical illness and risk for a variety of adverse events, most notably, intubation for pre-existing respiratory failure or hemodynamic instability. Older patients were also found to be at higher risk of peri-intubation hypoxia. Interestingly, increased BMI was associated with a lower risk of peri-intubation hypoxia, but a higher risk of peri-intubation cardiovascular collapse. Obesity has been recognized as a herald of an anatomically difficult airway and has previously been associated with increased peri-intubation complications in the ICU [48]. Of the 9 studies included in this meta-analysis that reported mean BMI, only two reported mean BMIs in the "obese" category (>30 kg/m^2). It is difficult to say what this apparent protective feature of elevated BMI with respect to hypoxia reflects—for example, increased precautions during the intubation of obese patients due to anticipated difficult airways, or a lower percentage of underweight or cachectic patients.

Induction medications – both sedatives and NMB – were also associated with rates of overall MAEs, hypoxia, and cardiac arrest. The studies investigating these agents were primarily observational; as such, it is difficult to determine if these findings reflect a true risk associated with these medications or physicians' assessment of risk prior to induction (that is, physicians may have been more likely to use certain agents in what they perceived to be higher risk intubations). We found propofol was associated with higher rates of overall MAEs and hypoxia. While propofol has not been commonly associated with higher risks of hypoxia in previous literature, it has been associated with hypotension: tThe multicenter observational INTUBE study, published in 2021 and included in this meta-analysis, identified use of propofol as the only modifiable factor associated with increased risk of peri-intubation cardiovascular instability or collapse [68]. In our analysis, use of midazolam was associated with a lower rate of peri-intubation hypoxia, and etomidate with a lower rate of peri-intubation cardiac arrest. The a

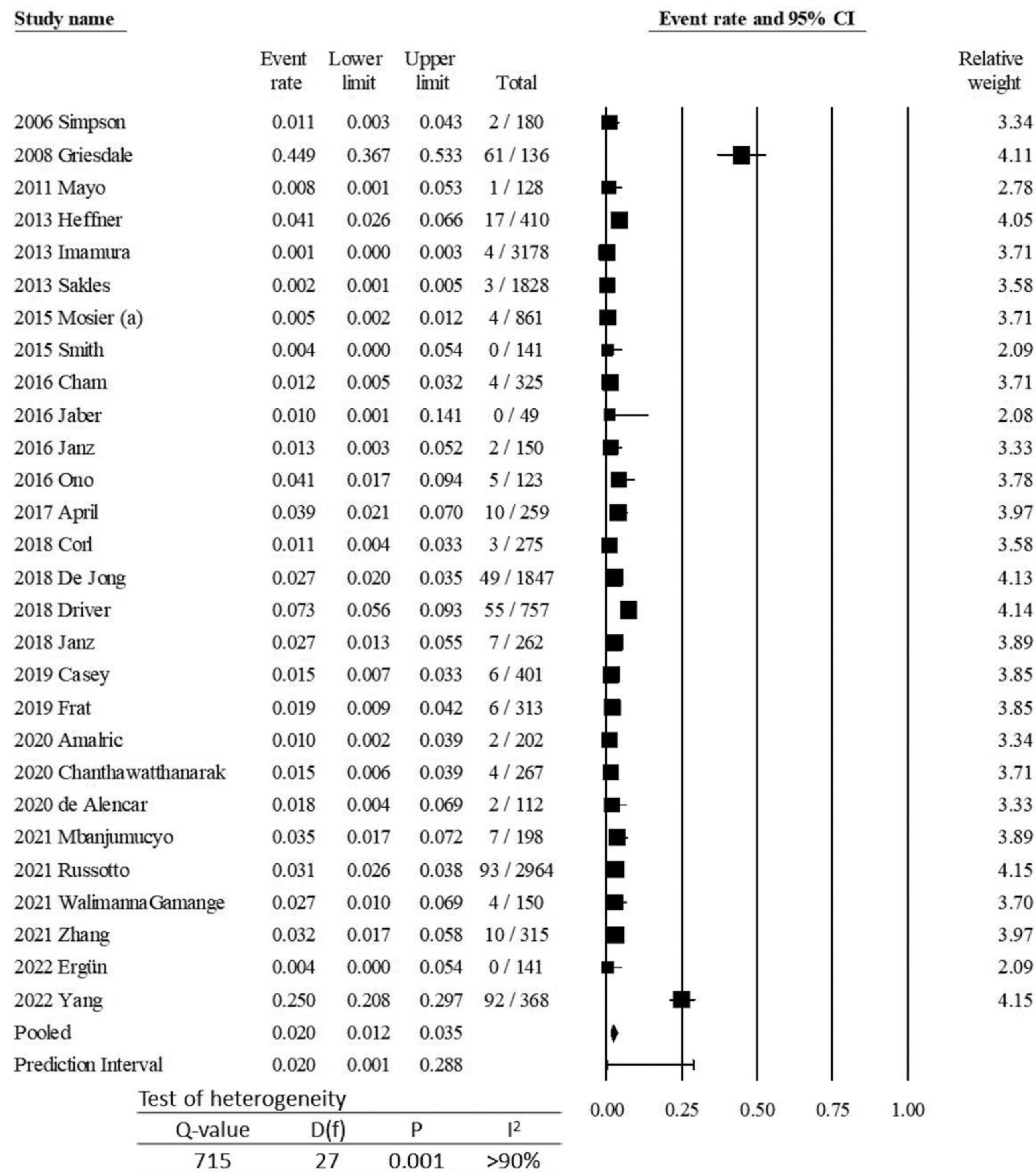


Fig. 4. a. Prevalence of peri-intubation cardiac arrest in patients undergoing intubation outside of the post-anesthesia care unit or operating room. b.Sensitivity analysis for prevalence of peri-intubation cardiac arrest, performed using random-effects meta-analysis with one-study-removed.

b

Name of Removed Study	Point	Lower limit	Upper limit
2006 Simpson	0.021	0.012	0.036
2008 Griesdale	0.018	0.011	0.029
2011 Mayo	0.021	0.012	0.036
2013 Heffner	0.020	0.011	0.035
2013 Imamura	0.023	0.013	0.039
2013 Sakles	0.022	0.013	0.039
2015 Mosier (a)	0.022	0.012	0.037
2015 Smith	0.021	0.012	0.037
2016 Cham	0.021	0.012	0.036
2016 Jaber	0.021	0.012	0.036
2016 Janz	0.021	0.012	0.036
2016 Ono	0.020	0.011	0.035
2017 April	0.020	0.011	0.035
2018 Corl	0.021	0.012	0.036
2018 De Jong	0.020	0.011	0.036
2018 Driver	0.019	0.010	0.035
2018 Janz	0.020	0.011	0.035
2019 Casey	0.021	0.012	0.036
2019 Frat	0.020	0.011	0.036
2020 Amalric	0.021	0.012	0.036
2020 Chanthawatthanarak	0.021	0.012	0.036
2020 de Alencar	0.020	0.012	0.036
2021 Mbanjumucyo	0.020	0.011	0.035
2021 Russotto	0.020	0.011	0.036
2021 WalimannaGamange	0.020	0.011	0.035
2021 Zhang	0.020	0.011	0.035
2022 Ergün	0.021	0.012	0.037
2022 Yang	0.018	0.011	0.031
Pooled	0.020	0.012	0.035
Prediction Interval	0.020	0.001	0.288

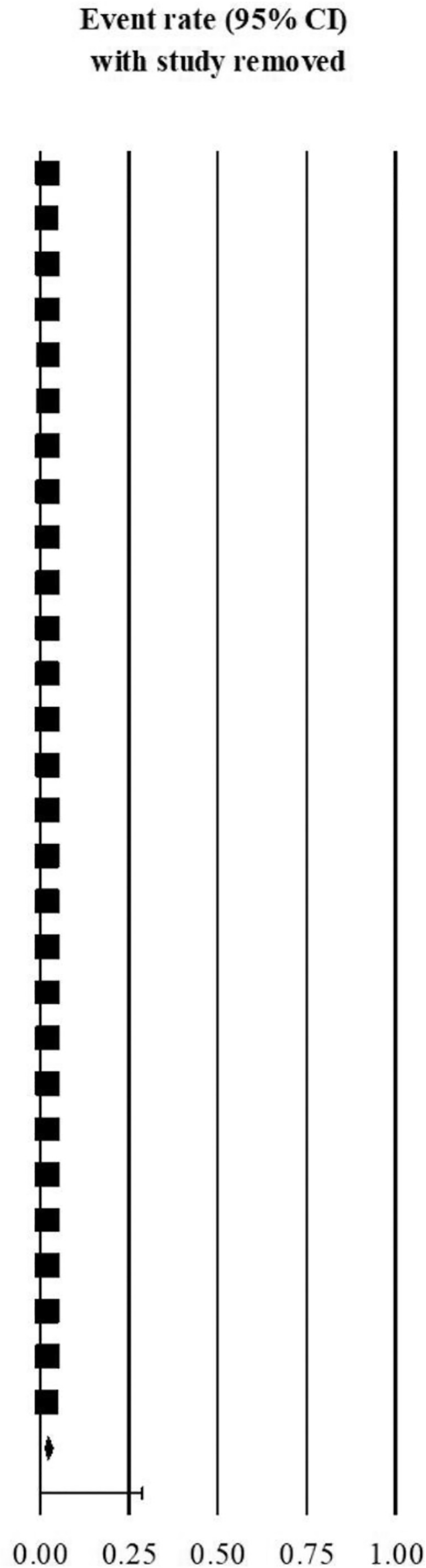


Fig. 4 (*continued*).

association between midazolam and a lower rate of hypoxia was unexpected, given the known association between benzodiazepines and respiratory depression. Etomidate is recognized as having a relatively neutral hemodynamic profile, and has been previously associated with relatively lower rates of peri-intubation hypotension in the Emergency Department [69].

Administration of any NMB was associated with a higher rate of peri-intubation hypoxia, while only succinylcholine was associated with increased risk of overall MAEs. The association of NMB with hypoxia may be due to suppression of respiratory drive, especially in patients with poor respiratory reserve (such as those with obesity, restrictive lung disease, or COVID-19) or in patients who were not pre-oxygenated or were inadequately pre-oxygenated prior to induction [70,71]. Succinylcholine has previously been associated with a wider range of adverse effects than rocuronium, including hyperkalemia [72], arrhythmias, fasciculations, and malignant hyperthermia [73]. A 2019 RCT investigating success of out-of-hospital intubation using either succinylcholine or rocuronium found fewer complications (including arrhythmias and hypotension) among patients intubated with rocuronium [74]. Despite this, succinylcholine has been suggested to more reliably create optimal conditions for intubation, and as such remains recommended as first-line for intubation of patients for whom there are no known contraindications to its use [75].

4.1. Limitations

The findings presented here are limited by the lack of consensus regarding the definitions of important major adverse events, including hypoxia, hypotension, and hemodynamic instability. The included studies used a variety of different thresholds for each criterion; as such, our findings are influenced by their definitions as well as the authors' data. This lack of consensus also increased the heterogeneity of this meta-analysis. Other outcomes, such as administration of IVF boluses or vasopressors, may directly be reflective of physicians' decisions, rather than a direct measure of patient status, and thus may be influenced by individual or institutional practice patterns. Finally, the outcomes of peri-intubation hypoxia and hypotension are not in themselves necessarily patient-oriented, though prior research has drawn a clear connection between these metrics and in-hospital mortality [5-8].

Several included studies did not report a comprehensive set of pre-intubation vital signs or interventions, limiting our ability to adequately characterize patients' clinical status prior to intubation and thus their risk. Moreover, data was not reported in such a way that allowed us to perform subgroup analyses of patients with or without pre-intubation hypoxia or cardiovascular instability, who would reasonably be expected to be at high risk of these clinical outcomes in the peri-intubation period as well. This may reflect a historic focus in the airway literature on the anatomically difficult airway and physicians' technical capability in achieving "first pass success", as opposed to the more nuanced resuscitative monitoring and treatment involved in the management of the physiologically difficult airway.

4.2. Implications for future research

Our analysis highlights the prevalence of peri-intubation MAEs across intubations occurring outside the OR or PACU, particularly in the ICU. Additional research is needed to evaluate potential interventions to prevent these adverse events. Many studies did not report in detail many known risk factors for peri-intubation MAE: obesity and severe acidosis have been reported as known risk factors [76,77] for the "physiologically difficult airway" but a majority of studies did not report this information. Further studies about peri-intubation should pay attention and report the risk factors for "physiologically difficult airway" to help physicians prepare for caring of critically ill patients.

5. Conclusions

Peri-intubation adverse events occur in almost one third of all intubations in the ED, ICU or medical wards. They are more common in the ICU and among patients with pre-existing hemodynamic compromise. Physicians should evaluate all patients for the likelihood of a physiologically difficult airway prior to intubation, and plan appropriately and accordingly for potential hypoxia, hypotension, or cardiac arrest in the peri-intubation period.

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CRediT authorship contribution statement

Jessica Downing: Writing – review & editing, Writing – original draft, Validation, Supervision, Project administration, Methodology, Investigation, Data curation. **Isha Yardi:** Validation, Project administration, Data curation. **Christine Ren:** Writing – review & editing, Validation, Supervision, Project administration, Methodology, Data curation. **Stephanie Cardona:** Writing – review & editing, Validation, Supervision, Project administration, Methodology, Data curation. **Manahel Zahid:** Validation, Data curation. **Kaitlyn Tang:** Validation, Data curation. **Vera Bzhilyanskaya:** Validation, Data curation. **Priya Patel:** Validation, Data curation. **Ali Pourmand:** Methodology, Conceptualization. **Quincy K. Tran:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Project administration, Methodology, Formal analysis, Conceptualization.

Declaration of Competing Interest

The authors have no conflicts of interest to disclose.

References

[1] Hsiao YJ, Chen CY, Hung HT, et al. Comparison of the outcome of emergency endotracheal intubation in the general ward, intensive care unit and emergency department. Biom J. 2021;44(6 Suppl 1):S110–8. https://doi.org/10.1016/j.bj.2020.07.006.

[2] Russotto V, Myatra SN, Laffey JG, et al. Intubation practices and adverse Peri-intubation events in critically ill patients from 29 countries. JAMA. 2021;325(12):1164–72. https://doi.org/10.1001/jama.2021.1727.

[3] Mosier JM, Joshi R, Hypes C, Pacheco G, Valenzuela T, Sakles JC. The physiologically difficult airway. West J Emerg Med. 2015;16(7):1109–17. https://doi.org/10.5811/westjem.2015.8.27467.

[4] Sakles JC, Pacheco GS, Kovacs G, Mosier JM. The difficult airway refocused. Br J Anaesth. 2020;125(1):e18–21. https://doi.org/10.1016/j.bja.2020.04.008.

[5] Smischney NJ, Khanna AK, Brauer E, et al. Risk factors for and outcomes associated with Peri-intubation hypoxemia: a multicenter prospective cohort study. J Intensive Care Med. 2021;36(12):1466–74. https://doi.org/10.1177/0885066620962445.

[6] Heffner AC, Swords D, Kline JA, Jones AE. The frequency and significance of postintubation hypotension during emergency airway management. J Crit Care. 2012;27(4):417.e9–417.e13. https://doi.org/10.1016/j.jcrc.2011.08.011.

[7] Heffner AC, Swords DS, Neale MN, Jones AE. Incidence and factors associated with cardiac arrest complicating emergency airway management. Resuscitation. 2013;84(11):1500–4. https://doi.org/10.1016/j.resuscitation.2013.07.022.

[8] Ferrada P, Manzano-Nunez R, Lopez-Castilla V, et al. Meta-analysis of post-intubation hypotension: a Plea to consider circulation first in hypovolemic patients. Am Surg. 2019;85(2):167–72.

[9] Cook TM, Woodall N, Harper J, Benger J, Fourth National Audit Project. Major complications of airway management in the UK: results of the fourth National Audit Project of the Royal College of Anaesthetists and the difficult airway society. Part 2: intensive care and emergency departments. Br J Anaesth. 2011;106(5):632–42. https://doi.org/10.1093/bja/aer059.

[10] Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;n71. https://doi.org/10.1136/bmj.n71.

[11] Higgins JPT, Altman DG, Gotzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011;343(oct18 2):d5928. https://doi.org/10.1136/bmj.d5928.

[12] Wella G, Shea B, O'Connell D, Peterson J, Welch V, Losos TT, et al. The Newcastle-Ottawa scale (NOS) for assessing the quality of nonrandomised studies in metaanalyse; 2000. Accessed August 2, 2019. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.

[13] Luo D, Wan X, Liu J, Tong T. Optimally estimating the sample mean from the sample size, median, mid-range, and/or mid-quartile range. Stat Methods Med Res. 2018;27(6):1785–805. https://doi.org/10.1177/0962280216669183.

[14] Borenstein M. Common Mistakes in Meta-Analysis and How to Avoid Them; 2019.

[15] Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. A basic introduction to fixed-effect and random-effects models for meta-analysis. Res Synth Methods. 2010;1(2):97–111. https://doi.org/10.1002/jrsm.12.
[16] Borenstein M, editor. Introduction to Meta-analysis. John Wiley & Sons; 2009.
[17] Hedges LV, Vevea JL. Fixed- and random-effects models in meta-analysis. Psychol Methods. 1998;3(4):486–504. https://doi.org/10.1037/1082-989X.3.4.486.
[18] Higgins JPT, Cochrane Collaboration. Cochrane Handbook for Systematic Reviews of Interventions. 2nd ed. Wiley-Blackwell; 2020.
[19] Borenstein M. Research note: in a meta-analysis, the I index does not tell us how much the effect size varies across studies. J Physiother. 2020;66(2):135–9. https://doi.org/10.1016/j.jphys.2020.02.011.
[20] Borenstein M, Higgins JPT, Hedges LV, Rothstein HR. Basics of meta-analysis: I^2 is not an absolute measure of heterogeneity: I^2 is not an absolute measure of heterogeneity. Res Synth Methods. 2017;8(1):5–18. https://doi.org/10.1002/jrsm.1230.
[21] DerSimonian R, Laird N. Meta-analysis in clinical trials revisited. Contemp Clin Trials. 2015;45:139–45. https://doi.org/10.1016/j.cct.2015.09.002.
[22] DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials. 1986;7(3):177–88. https://doi.org/10.1016/0197-2456(86)90046-2.
[23] Higgins JPT. Commentary: heterogeneity in meta-analysis should be expected and appropriately quantified. Int J Epidemiol. 2008;37(5):1158–60. https://doi.org/10.1093/ije/dyn204.
[24] Higgins JPT, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med. 2002;21(11):1539–58. https://doi.org/10.1002/sim.1186.
[25] Higgins JPT. Measuring inconsistency in meta-analyses. BMJ. 2003;327(7414):557–60. https://doi.org/10.1136/bmj.327.7414.557.
[26] IntHout J, Ioannidis JPA, Rovers MM, Goeman JJ. Plea for routinely presenting prediction intervals in meta-analysis. BMJ Open. 2016;6(7):e010247. https://doi.org/10.1136/bmjopen-2015-010247.
[27] Baillard C, Fosse JP, Sebbane M, et al. Noninvasive ventilation improves Preoxygenation before intubation of hypoxic patients. Am J Respir Crit Care Med. 2006;174(2):171–7. https://doi.org/10.1164/rccm.200509-1507OC.
[28] Jaber S, Monnin M, Girard M, et al. Apnoeic oxygenation via high-flow nasal cannula oxygen combined with non-invasive ventilation preoxygenation for intubation in hypoxaemic patients in the intensive care unit: the single-Centre, blinded, randomised controlled OPTINIV trial. Intensive Care Med. 2016;42(12):1877–87. https://doi.org/10.1007/s00134-016-4588-9.
[29] Janz DR, Semler MW, Lentz RJ, et al. Randomized trial of video laryngoscopy for endotracheal intubation of critically ill adults*. Crit Care Med. 2016;44(11):1980–7. https://doi.org/10.1097/CCM.0000000000001841.
[30] Driver BE, Prekker ME, Klein LR, et al. Effect of use of a Bougie vs endotracheal tube and stylet on first-attempt intubation success among patients with difficult airways undergoing emergency intubation: a randomized clinical trial. JAMA. 2018;319(21):2179. https://doi.org/10.1001/jama.2018.6496.
[31] Grensemann J, Eichler L, Wang N, Jarczak D, Simon M, Kluge S. Endotracheal tube-mounted camera-assisted intubation versus conventional intubation in intensive care: a prospective, randomised trial (VivaITN). Crit Care. 2018;22(1):235. https://doi.org/10.1186/s13054-018-2152-4.
[32] Janz DR, Semler MW, Joffe AM, et al. A multicenter randomized trial of a checklist for endotracheal intubation of critically ill adults. Chest. 2018;153(4):816–24. https://doi.org/10.1016/j.chest.2017.08.1163.
[33] Casey JD, Janz DR, Russell DW, et al. Bag-mask ventilation during tracheal intubation of critically ill adults. N Engl J Med. 2019;380(9):811–21. https://doi.org/10.1056/NEJMoa1812405.
[34] Frat JP, Ricard JD, Quenot JP, et al. Non-invasive ventilation versus high-flow nasal cannula oxygen therapy with apnoeic oxygenation for preoxygenation before intubation of patients with acute hypoxaemic respiratory failure: a randomised, multicentre, open-label trial. Lancet Respir Med. 2019;7(4):303–12. https://doi.org/10.1016/S2213-2600(19)30048-7.
[35] Nong L, Liang W, Yu Y, et al. Noninvasive ventilation support during fiberoptic bronchoscopy-guided nasotracheal intubation effectively prevents severe hypoxemia. J Crit Care. 2020;56:12–7. https://doi.org/10.1016/j.jcrc.2019.10.017.
[36] Khan FH, Khan FA, Irshad R, Kamal RS. Complications of endotracheal intubation in mechanically ventilated patients in a general intensive care unit. JPMA J Pak Med Assoc. 1996;46(9):195–8.
[37] Simpson J. Rapid sequence intubation in the emergency department: 5 year trends. Emerg Med J. 2006;23(1):54–6. https://doi.org/10.1136/emj.2004.019398.
[38] Griesdale DEG, Bosma TL, Kurth T, Isac G, Chittock DR. Complications of endotracheal intubation in the critically ill. Intensive Care Med. 2008;34(10):1835–42. https://doi.org/10.1007/s00134-008-1205-6.
[39] Mayo PH, Hegde A, Eisen LA, Kory P, Doelken P. A program to improve the quality of emergency endotracheal intubation. J Intensive Care Med. 2011;26(1):50–6. https://doi.org/10.1177/0885066610384070.
[40] Imamura T, Brown CA, Ofuchi H, et al. Emergency airway management in geriatric and younger patients: analysis of a multicenter prospective observational study. Am J Emerg Med. 2013;31(1):190–6. https://doi.org/10.1016/j.ajem.2012.07.008.
[41] Roux D, Reignier J, Thiery G, et al. Acquiring procedural skills in ICUs: a prospective multicenter study*. Crit Care Med. 2014;42(4):886–95. https://doi.org/10.1097/CCM.0000000000000049.
[42] Mosier JM, Malo J, Sakles JC, et al. The impact of a comprehensive airway management training program for pulmonary and critical care medicine fellows. A three-year experience. Ann Am Thorac Soc. 2015;12(4):539–48. https://doi.org/10.1513/AnnalsATS.201501-023OC.
[43] Smith KA, High K, Collins SP, Self WH. A Preprocedural checklist improves the safety of emergency department intubation of trauma patients. Reardon R, ed. Acad Emerg Med. 2015;22(8):989–92. https://doi.org/10.1111/acem.12717.
[44] Bodily JB, Webb HR, Weiss SJ, Braude DA. Incidence and duration of continuously measured oxygen desaturation during emergency department intubation. Ann Emerg Med. 2016;67(3):389–95. https://doi.org/10.1016/j.annemergmed.2015.06.006.
[45] Sakles JC, Mosier JM, Patanwala AE, Dicken JM. Apneic oxygenation is associated with a reduction in the incidence of hypoxemia during the RSI of patients with intracranial hemorrhage in the emergency department. Intern Emerg Med. 2016;11(7):983–92. https://doi.org/10.1007/s11739-016-1396-8.
[46] April MD, Schauer SG, Brown Rd CA, et al. A 12-month descriptive analysis of emergency intubations at Brooke Army medical center: a National Emergency Airway Registry study. US Army Med Dep J. 2017;3-17:98–104.
[47] Corl KA, Dado C, Agarwal A, et al. A modified Montpellier protocol for intubating intensive care unit patients is associated with an increase in first-pass intubation success and fewer complications. J Crit Care. 2018;44:191–5. https://doi.org/10.1016/j.jcrc.2017.11.014.
[48] De Jong A, Rolle A, Molinari N, et al. Cardiac arrest and mortality related to intubation procedure in critically ill adult patients: a multicenter cohort study. Crit Care Med. 2018;46(4):532–9. https://doi.org/10.1097/CCM.0000000000002925.
[49] Amalric M, Larcher R, Brunot V, et al. Impact of Videolaryngoscopy expertise on first-attempt intubation success in critically ill patients. Crit Care Med. 2020;48(10):e889–96. https://doi.org/10.1097/CCM.0000000000004497.
[50] Chanthawatthanarak S, Tangpaisarn T, Kotruchin P, Phungoen P, Ienghong K, Apiratwaraku K. First-pass success rates of endotracheal intubation using ramped versus supine positioning in the emergency department. J Med Assoc Thai. 2020;103(6):51–7.
[51] JCG Alencar, Marques B, Marchini JFM, et al. First-attempt intubation success and complications in patients with COVID-19 undergoing emergency intubation. J Am Coll Emerg Physicians Open. 2020;1(5):699–705. https://doi.org/10.1002/emp2.12219.
[52] Mbanjumucyo G, Aluisio A, Cattermole GN. Characteristics, physiology and mortality of intubated patients in an emergency care population in sub-Saharan Africa: a prospective cohort study from Kigali, Rwanda. Emerg Med J. 2021;38(3):178–83. https://doi.org/10.1136/emermed-2019-208521.
[53] Walimanna Gamage RJK. Endotracheal intubation in critically ill patients, practices, complications and factors associated with post intubation hypotension: a study in National Hospital Sri Lanka. Sri Lankan J Anaesthesiol. 2020;28(2):101. https://doi.org/10.4038/slja.v28i2.8569.
[54] Zhang C, Ou M. Comparison of hypoxemia, intubation procedure, and complications for non-invasive ventilation against high-flow nasal cannula oxygen therapy for patients with acute hypoxemic respiratory failure: a non-randomized retrospective analysis for effectiveness and safety (NIVaHIC-aHRF). BMC Emerg Med. 2021;21(1):6. https://doi.org/10.1186/s12873-021-00402-w.
[55] Smischney NJ, Seisa MO, Cambest J, et al. The incidence of and risk factors for Postintubation hypotension in the immunocompromised critically ill adult. J Intensive Care Med. 2019;34(7):578–86. https://doi.org/10.1177/0885066617704844.
[56] Green RS, Edwards J, Sabri E, Fergusson D. Evaluation of the incidence, risk factors, and impact on patient outcomes of postintubation hemodynamic instability. CJEM. 2012;14(02):74–82. https://doi.org/10.2310/8000.2012.110548.
[57] Sakles JC, Chiu S, Mosier J, Walker C, Stolz U. The importance of first pass success when performing Orotracheal intubation in the emergency department. Reardon RF, ed. Acad Emerg Med. 2013;20(1):71–8. https://doi.org/10.1111/acem.12055.
[58] Mosier JM, Sakles JC, Whitmore SP, et al. Failed noninvasive positive-pressure ventilation is associated with an increased risk of intubation-related complications. Ann Intensive Care. 2015;5(1):4. https://doi.org/10.1186/s13613-015-0044-1.
[59] Trivedi S, Demirci O, Arteaga G, Kashyap R, Smischney NJ. Evaluation of preintubation shock index and modified shock index as predictors of postintubation hypotension and other short-term outcomes. J Crit Care. 2015;30(4):861.e1–7. https://doi.org/10.1016/j.jcrc.2015.04.013.
[60] Cham E, Wong O, Yip K. Clinical practice and risk factors for immediate complications of endotracheal intubation by intensive care unit doctors in a regional Hospital in Hong Kong. Hong Kong J Emerg Med. 2016;23(3):135–44. https://doi.org/10.1177/102490791602300302.
[61] Ono Y, Sugiyama T, Chida Y, et al. Association between off-hour presentation and endotracheal-intubation-related adverse events in trauma patients with a predicted difficult airway: a historical cohort study at a community emergency department in Japan. Scand J Trauma Resusc Emerg Med. 2016;24(1):106. https://doi.org/10.1186/s13049-016-0296-2.
[62] Smischney NJ, Seisa MO, Heise KJ, et al. Predictors of arterial desaturation during intubation: a nested case-control study of airway management—part I. J Thorac Dis. 2017;9(10):3996–4005. https://doi.org/10.21037/jtd.2017.08.138.
[63] Van Berkel MA, Exline MC, Cape KM, et al. Increased incidence of clinical hypotension with etomidate compared to ketamine for intubation in septic patients: a propensity matched analysis. J Crit Care. 2017;38:209–14. https://doi.org/10.1016/j.jcrc.2016.11.009.
[64] Baek MS, Han M, Huh JW, Lim CM, Koh Y, Hong SB. Video laryngoscopy versus direct laryngoscopy for first-attempt tracheal intubation in the general ward. Ann Intensive Care. 2018;8(1):83. https://doi.org/10.1186/s13613-018-0428-0.
[65] Mohr NM, Pape SG, Runde D, Kaji AH, Walls RM, Brown CA. Etomidate use is associated with less hypotension than ketamine for emergency department Sepsis intubations: a NEAR cohort study. Reardon R, ed. Acad Emerg Med. 2020;27(11):1140–9. https://doi.org/10.1111/acem.14070.
[66] Ergün B, Ergan B, Yakar MN, et al. Incidência e fatores de risco para hipotensão pós-intubação em pacientes críticos com COVID-19. Rev Bras Ter Intensiva. 2022;34(1). https://doi.org/10.5935/0103-507X.20220007-pt.

[67] Yang TH, Chen KF, Gao SY, Lin CC. Risk factors associated with peri-intubation cardiac arrest in the emergency department. Am J Emerg Med. 2022;58:229–34. https://doi.org/10.1016/j.ajem.2022.06.013.
[68] Russotto V, Tassistro E, Myatra SN, et al. Peri-intubation cardiovascular collapse in patients who are critically ill: insights from the INTUBE study. Am J Respir Crit Care Med. 2022;206(4):449–58. https://doi.org/10.1164/rccm.202111-2575OC.
[69] April MD, Arana A, Schauer SG, et al. Ketamine versus etomidate and Peri-intubation hypotension: a National Emergency Airway Registry Study. Acad Emerg Med. 2020;27(11):1106–15. https://doi.org/10.1111/acem.14063.
[70] Broens SJL, Boon M, Martini CH, et al. Reversal of partial neuromuscular block and the Ventilatory response to hypoxia: a randomized controlled trial in healthy volunteers. Anesthesiology. 2019;131(3):467–76. https://doi.org/10.1097/ALN.0000000000002711.
[71] Christensson E, Ebberyd A, Hårdemark Cedborg A, et al. Hypoxic ventilatory response after rocuronium-induced partial neuromuscular blockade in men with obstructive sleep apnoea. Anaesthesia. 2020;75(3):338–47. https://doi.org/10.1111/anae.14806.
[72] Martyn JAJ, Richtsfeld M. Succinylcholine-induced hyperkalemia in acquired pathologic states: etiologic factors and molecular mechanisms. Anesthesiology. 2006;104(1):158–69. https://doi.org/10.1097/00000542-200601000-00022.
[73] Larach MG, Klumpner TT, Brandom BW, et al. Succinylcholine use and Dantrolene availability for malignant hyperthermia treatment: database analyses and systematic review. Anesthesiology. 2019;130(1):41–54. https://doi.org/10.1097/ALN.0000000000002490.
[74] Guihard B, Chollet-Xémard C, Lakhnati P, et al. Effect of Rocuronium vs succinylcholine on endotracheal intubation success rate among patients undergoing out-of-hospital rapid sequence intubation: a randomized clinical trial. JAMA. 2019;322(23):2303–12. https://doi.org/10.1001/jama.2019.18254.
[75] Tran DTT, Newton EK, Mount VAH, Lee JS, Wells GA, Perry JJ. Rocuronium versus succinylcholine for rapid sequence induction intubation. Cochrane Database Syst Rev. 2015;2015(10):CD002788. https://doi.org/10.1002/14651858.CD002788.pub3.
[76] Capone J, Gluncic V, Lukic A, Candido KD. Physiologically difficult airway in the patient with severe hypotension and metabolic acidosis. Case Rep Anesthesiol. 2020;2020:8821827. https://doi.org/10.1155/2020/8821827.
[77] De Jong A, Molinari N, Pouzeratte Y, et al. Difficult intubation in obese patients: incidence, risk factors, and complications in the operating theatre and in intensive care units. Br J Anaesth. 2015;114(2):297–306. https://doi.org/10.1093/bja/aeu373.