Prophylactic Endotracheal Intubation in Patients with Upper Gastrointestinal Bleeding Undergoing Endoscopy: A Systematic Review and Meta-analysis

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ABSTRACT
Background: Patients with upper gastrointestinal bleeding (UGIB) often require urgent or emergent esophagogastroduodenoscopy (EGD) and are at risk of complications such as aspiration of gastric content or blood. The role of prophylactic endotracheal intubation (PEI) in the absence of usual respiratory status-related indications is not well established.

Methods: We searched Medline, EMBASE, Cochrane Library’s Central Register of Controlled Trials (CENTRAL) and SCOPUS from inception through July 2017 without date or language of publication restriction. We included studies that compared PEI with usual care (UC) in patients with acute UGIB, and reported any of the following outcomes: aspiration, pneumonia, mortality and length of stay. We excluded studies in which majority of included patients required intubation due to respiratory failure or decreased level of consciousness. We used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to assess the quality of evidence for each outcome.

Results: We did not identify any randomized trials on this topic. We included 10 observational studies (n = 6068). We were not able to perform any adjusted analyses. PEI was associated with a significant increase in aspiration (OR 3.85, 95% CI, 1.46, 10.25; P = 0.01; I² = 56%; low-quality evidence), pneumonia (OR 4.17, 95% CI, 1.82, 9.57; P = 0.0007; I² = 52%; low-quality evidence) and hospital length of stay (mean difference 0.86 days, 95% CI 0.13, 1.59; P = 0.02; I² = 0; low-quality evidence), without clear effect on mortality (OR 1.92, 95% CI, 0.71, 5.23; P = 0.2; I² = 95%; very low-quality evidence).

Conclusions: Low- to very low-quality evidence from observational studies suggests that PEI in the setting of UGIB may be associated with higher rates of respiratory complications and, less likely, with increased mortality. Although the results are alarming, the lack of higher quality evidence calls for randomized trials to inform practice.

Key words: Endoscopy, systematic review, meta-analysis, prophylactic endotracheal intubation, upper gastrointestinal bleeding

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**INTRODUCTION**

Upper gastrointestinal bleeding (UGIB) can result in significant morbidity and mortality. The mainstay treatment is endoscopic therapy whenever possible. As opposed to elective esophagogastroduodenoscopies (EGD), EGDs performed in emergency or critical care setting, especially in the presence of significant hematemesis, can be associated with significant cardiac and respiratory compromise. Therefore, it is not uncommon to perform prophylactic endotracheal intubation (PEI) in such patients to prevent aspiration or to assure that an agitated or confused patient is not actively resisting the procedure.

While it is possible that endotracheal intubation is beneficial for patients with UGIB and concomitantly decreased level of consciousness, agitation or hypoxia, the value of endotracheal intubation in patients with large hematemesis and no other indication for intubation is less clear. The recent European guidelines issued a weak recommendation to perform endotracheal intubation in patients with encephalopathy or agitation, while other guidelines did not address this issue. The issue of performing PEI in patients without the above-mentioned characteristics was not addressed. A survey conducted over a decade ago demonstrated a considerable variation in the beliefs and practices of gastroenterologists with regards to endotracheal intubation in the presence of UGIB. Due to the complexity of this topic and the lack of clear guidance, we undertook a systematic review to determine the effect of prophylactic intubation on patient-important outcomes in the context of UGIB.

**METHODS**

**Study selection**

Studies were eligible if (1) the study design was a randomized controlled trial (RCT) or, if not available, an observational design; (2) the study included patients with UGIB requiring emergent esophagogastroduodenoscopy (EGD); (3) patients underwent PEI (intubation done preemptively to protect the airways in the absence of other indications for intubation) and the control group included patient who did not undergo endotracheal intubation; (4) the study reported any of the following outcomes: aspiration (as defined by authors of those studies), pneumonia (as defined by authors of those studies), mortality and hospital length of stay.

**Search strategy**

We searched Medline, EMBASE, Cochrane Library’s Central Register of Controlled Trials (CENTRAL) and SCOPUS from inception through July 2017. Our search strategy is detailed in Supplementary Appendix I [online only]. We did not apply any language or date of publication restrictions. Two reviewers, in duplicate, screened the titles and abstracts for potentially eligible articles. The reviewers then assessed the full text of the articles for final eligibility. We also screened references of relevant articles to identify additional studies not captured in database searches. Disagreement between reviewers was resolved by consensus and a third reviewer was consulted in cases it was not achieved.

**Data extraction**

Two reviewers independently extracted data from eligible studies using standard data abstractions forms. We resolved disagreements by discussion and consensus.

**Risk of bias assessment**

Two reviewers independently assessed the risk of bias. We used the Newcastle-Ottawa Scale (NOS) to assess the risk of bias for non-randomized studies. Using this scale, studies are judged based on the following three domains: selection of the study groups [maximum 4 stars (points)]; comparability of the groups (maximum 2 points) and ascertainment of the outcome of interest (maximum 3 points), yielding a maximum possible score of 9 [Supplementary Appendix II, online only].

**Statistical analysis**

We used Revman software (Review Manager, version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) for data analysis. We used a random-effects model, as described by Dersimonian and Laird, to pool weighted effects of estimates across all studies. Study weights were estimated using the inverse variance method. We calculated pooled odds ratios (OR) and mean differences (MD) for dichotomous and continuous outcomes, respectively, with corresponding 95% confidence intervals (CI). Statistical heterogeneity was assessed using Chi-square and F statistics, with significant heterogeneity defined as $P < 0.10$ or $I^2 > 50\%$. We planned to conduct a meta-analysis of adjusted effect estimates, if reported, to generate pooled adjusted OR with 95% CI.

**Subgroup analysis**

We performed one subgroup analysis by type of bleeding (variceal versus other) hypothesizing that variceal bleeding is associated with larger benefit from intubation.

**Sensitivity analysis**

We performed sensitivity analysis excluding studies published in abstract form only, and excluding the
abstract by Lee et al.,[12] as the data overlapped with their full-text publication on a later date. Finally, we performed a post hoc analysis excluding the study by Rudolph et al.[14] due to lack of clarity in the reporting outcomes of the study groups.

**Publication bias**
We planned to inspect funnel plots and to use Egger’s test to assess for publication bias for outcomes that included ≥10 studies.[15]

**Quality of evidence**
We used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology to assess the quality of evidence for each outcome.[16]

**RESULTS**

**Characteristics of included studies**
Our initial search identified a total of 601 citations. After eliminating duplicates, 500 citations remained, of which 489 were non-relevant. Eleven[1,10-14,17-21] articles were retrieved for full-text assessment. Of those, we excluded an abstract[20] that was subsequently published as a full text [Figure 1]. We did not identify any randomized trials. A total of 10[1,10-14,17-19,21] retrospective observational studies (7 full-text articles[1,13,14,17-19,21] and 3 abstracts[10-12]) enrolling 6068 patients met our eligibility criteria. Two studies exclusively enrolled patients with variceal bleeding.[17,21] Characteristics of included studies are presented in Table 1.

**Risk of bias assessment**
Two reviewers assessed the risk of bias using NOS, and its assessments are presented in Table 2.

**Main outcomes**

**Aspiration**
Six studies[1,10,14,17,19,21] enrolling 620 patients reported on incidence of aspiration [Figure 2]. Conventional analysis showed that PEI was associated with a significant increase in probability of aspiration (OR 3.85, 95% CI, 1.46, 10.25; P = 0.01; I² = 56%; low-quality evidence).

**Pneumonia**
Five studies[1,11,13,19,21] enrolling 1912 patients reported on incidence of pneumonia [Figure 3]. PEI was associated with a significant increase in probability of developing pneumonia (OR 4.17, 95% CI, 1.82, 9.57; P = 0.0007; I² = 52%; low-quality evidence).

**Mortality**
Eight studies[10-13,17-19,21] enrolling 5818 patients reported on mortality [Figure 4]. PEI did not affect mortality to a statistically significant degree (OR 1.92, 95% CI, 0.71, 5.23; P = 0.2; I² = 95%; very low-quality evidence).

**Hospital length of stay**
Six studies[10,13,17-19,21] enrolling 4188 patients reported on length of stay in hospital [Figure 5]. PEI was associated with a small but statistically significant increase in length of stay (MD 0.86 days, 95% CI 0.13, 1.59; P = 0.02; I² = 0; low-quality evidence).

**Subgroup analysis**
We conducted one subgroup analysis by type of bleeding; two studies (n = 172) included only patients with variceal bleeding.[17,21] We did not detect any significant subgroup differences across all outcomes. Details of the results of subgroup analysis are presented in Supplementary Figures I-IV [online only].

**Sensitivity analysis**
Sensitivity analysis, excluding three studies published in the abstract form (n = 1768),[10-12] yielded similar results for pneumonia, mortality and length of stay outcomes. However, for aspiration outcome, the results were no longer statistically significant (OR 4.39, 95% CI 0.75, 25.66; P = 0.1; I² = 77%). Our second sensitivity analysis, excluding the Lee et al. abstract,
| Author                  | Design               | Population                                      | Interventions                                      | Definition of aspiration                                                                 | Definition of pneumonia                                                                 |
|------------------------|----------------------|-------------------------------------------------|---------------------------------------------------|----------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|
| Lipper, et al.         | Case series          | ICU admission for active and severe UGIB Age: NR Males: 50% | PEI (n = 6) Usual care (n = 24) Both groups: endoscopy within 12 hours of admission | Direct observation by authors during EGD                                                | New infiltrate on CXR and any one of the following: Fever Leukocytosis                  |
| Koch, et al.           | Retrospective cohort | Active esophageal varices bleeding or varices with high-risk stigmata and blood in the stomach Age (mean): 48.7 years Males: 71% Child–Pugh score (mean): 8.6 Encephalopathy (Grade I): 23% | PEI (n = 42) Usual care (n = 20) Both groups: endoscopy within 12 hours of admission | Clinical diagnosis of aspiration by the primary team                                  | Aspiration pneumonia: New pulmonary infiltrates on the post-EGD CXR, or Clinical diagnosis of aspiration by the primary team |
| Rehman, et al.         | Retrospective case-control | Medical ICU admitted for UGIB with cirrhosis, hematemesis or shock Age (mean): 65 years Males: 62% | PEI (n = 49) Usual care: (n = 49) | Witnessed or suspected abnormal entry of secretions, fluid or particles into lower respiratory airways within 48 hours after EGD | New infiltrate CXR with any two of the following within 48 hours after EGD: Fever Leukocytosis Purulent sputum |
| Perisetti, et al.      | Retrospective        | Admitted to ICU with UGIB Age (mean): 63.5 years Males: NR | PEI (n = 69) Usual care: (n = 69) | NR | NR |
| Lohse, et al.          | Retrospective database | Nationwide registry of patients with peptic ulcer bleeding undergoing emergency EGD under anesthesia care Age (mean): 75 years Males: NR | PEI (n = 2101) Usual care: (n = 1479) | NR | NR |
| Abdulsamad, et al.     | Retrospective cohort | UGIB defined as hematemesis, coffee ground emesis or melena who underwent EGD | PEI (n = 264) Usual care (n = 1219) | NR | NR |
| Lee, et al.            | Retrospective cohort | EGD in ICU for UGIB defined as one of: Hematemesis patient Melena hypovolemic shock with/without cirrhosis Age: NR Males: NR | PEI (n = 78) Usual care (n = 78) | NR | Within 48 hours post-EGD but no definition provided |

Contd...
Table 1: Contd...

| Author          | Design                 | Population                                      | Interventions            | Definition of aspiration | Definition of pneumonia                  |
|-----------------|------------------------|--------------------------------------------------|--------------------------|--------------------------|------------------------------------------|
| Hayat, et al    | Retrospective cohort   | EGD in ICU for UGIB defined as one of the following: Hematemesis patient Melena hypovolemic shock (SBP <90 mm Hg and HR >100 beats/min requiring either fluids or vasopressor agents) with/without cirrhosis Age (mean): 59.3 years Males: 63.5% | PEI (n =100) Usual care (n = 100) | NR                                      | New focal infiltrates on CXR with any two of the following: Fever Leukocytosis Productive cough |
| Tang, et al     | Retrospective cohort   | Medical ICU patients with cirrhosis and hematemesis with EGD findings of active variceal bleeding or blood in stomach plus presence of varices with high-risk stigmata Age (mean): 55 years Males: 67.6% | PEI (n = 65) Usual care (n = 45) | NR                                      | New infiltrate on CXR plus any two of the following findings within 48 hours after EGD: Fever (temperature >100.8°F) Leukocytosis (WBC >10,000/mm³) Purulent sputum |
| Rudolph, et al  | Retrospective before and after | Admitted to ICU with UGIB in 1988 and 1992 | PEI (n = 21) No intubation (n = 161) | Witnessed aspiration or new infiltrate on CXR | Not an outcome |

PEI – Prophylactic endotracheal intubation; CXR – Chest X-ray; EGD – Esophagogastroduodenoscopy; HR – Heart rate; ICU – Intensive care unit; NR – Not reported; SBP – Systolic blood pressure; UGIB – Upper gastrointestinal bleeding; WBC – White blood cells

Table 2: Risk of bias assessment

| Study          | Selection | Comparability | Outcome |
|----------------|-----------|---------------|---------|
| Lipper, et al  | ★★★★☆     | ★             | ★★★★    |
| Rudolph, et al | ★★★★     | ★             | ★★★★    |
| Koch, et al    | ★★★★     | ★★★          | ★★★★    |
| Rehman, et al  | ★★★★     | ★★★          | ★★★★    |
| Perisetti, et al | ★★★★ | ★             | ★★★★    |
| Lohse, et al   | ★★★★     | ★★★          | ★★★★    |
| Abdulsamad, et al | ★★★★ | ★             | ★★★★    |
| Lee, et al     | ★★★★☆     | ★             | ★★★★    |
| Hayat, et al   | ★★★★☆     | ★             | ★★★★    |
| Tang, et al    | ★★★★☆     | ★             | ★★★★    |

DISCUSSION

In this systematic review, we identified 10 observational studies (6068 patients) that reported the effect of prophylactic endotracheal intubation in upper GI bleeding. Fewer than 10 studies were included for individual outcomes; therefore, we were not able to assess for publication bias.

Quality of evidence

The quality of evidence using the GRADE system ranged between very low to low across study outcomes, mainly due to observational nature of data and the lack of adjustment for important confounders (risk of bias), and also due to inconsistency and imprecision. The large intervention effect was offset by these limitations. The details of quality assessment are presented in Table 3.
endotracheal intubation on clinical outcomes of patients with UGIB undergoing endoscopy. Low-quality evidence suggest that PEI is associated with a higher probability of developing pneumonia and aspiration, longer stay in the hospital, and less likely and statistically non-significant impact on mortality.
### Table 3: Quality of evidence

| Quality assessment | No. of patients | Effect | Quality | Importance |
|--------------------|----------------|--------|---------|------------|
| No. of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Prophylactic endotracheal intubation | No intubation | Relative (95% CI) | Absolute (95% CI) | |
| Mortality | | | | | | | | | | |
| 8 | Observational studies | Serious | Very serious | Not serious | Not serious | None | 407/2768 (14.7%) | 304/3050 (10.0%) | OR 1.92 (0.71-5.23) | 76 more per 1000 (from 27 fewer to 267 more) | |
| Pneumonia | | | | | | | | | | |
| 5 | Observational studies | Serious | Not serious | Not serious | Very strong association | 127/484 (26.2%) | 107/1428 (7.5%) | OR 4.17 (1.82-9.57) | 178 more per 1000 (from 54 more to 362 more) | |
| Aspiration | | | | | | | | | | |
| 6 | Observational studies | Serious | Not serious | Not serious | Very strong association | 54/252 (21.4%) | 38/368 (10.3%) | OR 3.58 (1.46-10.25) | 189 more per 1000 (from 41 more to 438 more) | |
| Hospital length of stay (days) | | | | | | | | | | |
| 6 | Observational studies | Not serious | Not serious | Not serious | None | 2426 | 1762 | - | MD 0.86 days more (0.13 more to 1.59 more) | |

CI – Confidence interval; OR – Odds ratio; MD – Mean difference; a – We rated down the quality of evidence by one level for risk of bias as non-adjusted estimates were used; therefore, we are uncertain if the observed treatment effect is a result of a confounder or a true effect; b – We rated down the quality of evidence by two levels for inconsistency, the $I^2=95$%; c – Although the confidence interval included significant benefit and harm, we did not rate down the quality of evidence for imprecision; d – We rated down the quality of evidence by one level for inconsistency, the $I^2=57$%; e – Although the CI was wide including small and large harm, we did not rate down the quality of evidence for imprecision; f – We rated down the quality of evidence for inconsistency, $I^2=64$%; g – Although the confidence interval included both small and substantial harm, we did not rate down the quality of evidence for imprecision; h – Although the confidence interval included small and moderate harm, we did not rate down the quality of evidence for imprecision.
A recent meta-analysis of four observational studies \((n = 367)\) showed a significant increase in pneumonia within 48 hours of endoscopy in a group of patients undergoing PEI, without affecting the risks of death or aspiration.\(^{22}\) Our meta-analysis included more studies and patients \((10, n = 6068)\), potentially improving the precision of our findings. We did not apply any restrictions on date or language of publication. In addition, we used the GRADE approach to assess the quality of the evidence, and adhered to the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) reporting guidelines.\(^{23}\)

Although the results of this meta-analysis are intriguing, it needs to be interpreted with great caution. Observational studies tend to be at risk of yielding biased results, study groups differ often in prognosis (i.e. confounders). Even when adjustment for important variables is possible, it may not be enough to yield reliable results. In our meta-analysis, we used only un-adjusted (crude) values, as almost all studies did not report adjusted estimates. This is an important limitation of the results, as it is challenging to determine whether the observed effects are true or confounded. It appears intuitive that the more unstable the patient is (i.e., with more bleeding and vomiting, hypoxic, agitated, non-cooperative, aspirating or judged at higher risk of aspiration), the more likely intubation is performed. Because of the observational nature of studies, lack of adjustment for the severity of clinical situation as well as additional inconsistency among study results and imprecision of estimates, the quality of the results is judged as very low to low. This markedly limits our confidence that the observed effects are true. Therefore, over-interpretation of the results should be avoided and we believe that these results, although alarming, should be considered as hypothesis generating. At the same time, these results should alert clinicians to the fact that PEI may be associated with harm, and that decision-making should take into consideration this possibility. The information we have found, including lack of higher quality data, also indicates the need for a proper randomized trial to be performed in this population of patients.

**CONCLUSION**

Low to very low- quality evidence suggest that PEI may be associated with higher risk of respiratory complications. Future randomized trials or, if not possible, prospectively matched cohort studies are needed to confirm or dispute these findings.

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Nil.

**Conflicts of interest**

There are no conflicts of interest.

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### Search Strategy:

| #  | Searches                                                                 | Results |
|----|--------------------------------------------------------------------------|---------|
| 1  | endotracheal intubation.mp. or exp Intubation, Intratracheal/             | 84661   |
| 2  | Intubation, Intratracheal/or tracheal intubation.mp. or Airway Management/| 91542   |
| 3  | airway protection.mp.                                                    | 1863    |
| 4  | exp Gastrointestinal Hemorrhage/or exp "Esophageal and Gastric Varices"/or upper gastrointestinal bleed$.mp. | 159044  |
| 5  | gastrointestinal bleeding.mp.                                           | 39897   |
| 6  | exp Hematemesis/                                                        | 10361   |
| 7  | gastrointestinal bleeding.mp.                                           | 39897   |
| 8  | 1 or 2 or 3                                                             | 101741  |
| 9  | 4 or 5 or 6 or 7                                                         | 170084  |
| 10 | 8 and 9                                                                  | 499     |

Search strategy for Cochrane Library’s Central Register of Controlled Trials (CENTRAL)

Date Run: 13/07/17 18:16:25.978

| ID  | Search                                                                 | Hits | Description                                      |
|-----|-------------------------------------------------------------------------|------|-------------------------------------------------|
| #1  | MeSH descriptor: [Gastrointestinal Hemorrhage] this term only            | 1473 |                                                                                 |
| #2  | "gastrointestinal bleeding" or "gastrointestinal hemorrhage" or "esophageal varices" or "varices" | 4808 |                                                                                 |
| #3  | "endotracheal intubation" or "tracheal intubation"                       | 5143 |                                                                                 |
| #4  | MeSH descriptor: [Airway Management] explode all trees                   | 9051 |                                                                                 |
| #5  | #1 or #2                                                                | 4808 |                                                                                 |
| #6  | #3 or #4                                                                | 12227|                                                                                 |
| #7  | #5 and #6 in Trials                                                     | 38   |                                                                                 |

**Search strategy for SCOPUS**

("endotracheal intubation" OR "tracheal intubation" OR "intratracheal intubation") AND TITLE-ABS-KEY ("gastrointestinal hemorrhage" OR "gastrointestinal bleeding" OR "GI bleeding" OR "hematemesis" OR "variceal" OR "varices") AND TITLE-ABS-KEY ("airway protection" OR "prophylactic" OR "prophylaxis")

Number of results: 64
APPENDIX II

NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE
COHORT STUDIES

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability

Selection
1) Representativeness of the exposed cohort
   a) Truly representative of the average ______________ (describe) in the community ☐
   b) Somewhat representative of the average ______________ in the community ☐
   c) Selected group of users eg nurses, volunteers ☐
   d) No description of the derivation of the cohort ☐
2) Selection of the non exposed cohort
   a) Drawn from the same community as the exposed cohort ☐
   b) Drawn from a different source ☐
   c) No description of the derivation of the non exposed cohort ☐
3) Ascertainment of exposure
   a) Secure record (eg surgical records) ☐
   b) Structured interview ☐
   c) Written self report ☐
   d) No description ☐
4) Demonstration that outcome of interest was not present at start of study
   a) Yes ☐
   b) No ☐

Comparability
1) Comparability of cohorts on the basis of the design or analysis
   a) Study controls for _____________ (select the most important factor) ☐
   b) Study controls for any additional factor ☐ (This criteria could be modified to indicate specific control for a second important factor.)

Outcome
1) Assessment of outcome
   a) Independent blind assessment ☐
   b) Record linkage ☐
   c) Self report ☐
   d) No description ☐
2) Was follow-up long enough for outcomes to occur
   a) Yes (select an adequate follow up period for outcome of interest) ☐
   b) No ☐
3) Adequacy of follow up of cohorts
   a) Complete follow up - all subjects accounted for ☐
   b) Subjects lost to follow up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost) ☐
   c) Follow up rate < ____% (select an adequate %) and no description of those lost ☐
   d) No statement ☐

Wells, G. A, Shea, B., O'Connel, D. et al. The Newcastle-Ottawa scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm 2009 Feb 1.
Supplementary Figure I: Subgroup analysis by bleeding type for aspiration outcome

Supplementary Figure II: Subgroup analysis by bleeding type for pneumonia outcome
### Supplementary Figure III: Subgroup analysis by bleeding type for mortality outcome

| Study or Subgroup | Prophylactic Intubation | Usual Care | Mean Difference | Year  |
|-------------------|-------------------------|------------|----------------|-------|
| Rahman 2009       | 6.9                     | 5.8        | 1.00 [-1.36, 3.36] | 2009  |
| Perisetti 2013    | 10.2                    | 43.7       | 5.6 [-5.81, 15.82] | 2013  |
| Lohse 2015        | 8.16                    | 12.4       | 4.25 [-3.35, 1.11] | 2015  |
| Hayat 2017        | 9.6                     | 9.6        | 0.0 [-0.33, 0.33]  | 2017  |

Heterogeneity: $I^2 = 0.00$, $df = 3$ ($P = 0.57$); $I^2 = 0$
Test for overall effect: $Z = 1.95$ ($P = 0.05$)

### Supplementary Figure IV: Subgroup analysis by bleeding type for hospital length of stay outcome

| Study or Subgroup | Prophylactic Intubation | Usual Care | Mean Difference | Year  |
|-------------------|-------------------------|------------|----------------|-------|
| Koch 2007         | 6.2                     | 6.4        | 1.30 [-2.26, 4.86] | 2007  |
| Tang 2017         | 16.5                    | 8.5        | 8.0 [-1.11, 4.71]  | 2017  |

Heterogeneity: $I^2 = 0$, $df = 1$ ($P = 0.83$); $I^2 = 0$
Test for overall effect: $Z = 1.39$ ($P = 0.16$)

### Supplementary Figure V: Sensitivity analysis excluding studies published in abstract form only for aspiration outcome

| Study or Subgroup | Prophylactic Intubation | Usual Care | Odds Ratio | Year  |
|-------------------|-------------------------|------------|------------|-------|
| Upper 1991        | 0.0                     | 0.6        | Not estimable | 1991  |
| Rudolph 2003      | 9.2                     | 19.0       | 32.2 [5.71, 51.76] | 2003  |
| Koch 2007         | 7.2                     | 42.0       | 18.4 [0.47, 5.13]  | 2007  |
| Rahman 2009       | 10.2                    | 49.9       | 32.9 [0.42, 3.13]  | 2009  |
| Tang 2017         | 1.6                     | 65.0       | 16.5 [0.08, 5.31]  | 2017  |

Heterogeneity: $I^2 = 2.20$, $df = 12$ ($P = 0.004$); $I^2 = 77$
Test for overall effect: $Z = 1.64$ ($P = 0.10$)
Supplementary Figure VI: Sensitivity analysis excluding studies published in abstract form only for pneumonia outcome

Supplementary Figure VII: Sensitivity analysis excluding studies published in abstract form only for mortality outcome

Supplementary Figure VIII: Sensitivity analysis excluding studies published in abstract form only for LOS outcome

Supplementary Figure IX: Sensitivity analysis excluding Lee et al for mortality outcome
Supplementary Figure X: Sensitivity analysis excluding Rudolph et al for aspiration outcome

| Study or Subgroup | Prophylactic Intubation Events | Usual Care Events | Total | Weight | Odds Ratio IV, Random, 95% CI | Year |
|-------------------|-------------------------------|-------------------|-------|--------|-------------------------------|------|
| Upper 1991        | 0                             | 6                 | 24    |         | Not estimable                 | 1991 |
| Koch 2007         | 7                             | 42                | 20    | 15.5%  | 8.66 [0.47, 159.62]           | 2007 |
| Rahman 2009       | 10                            | 49                | 9     | 49     | 36.3% 1.14 [0.42, 3.11]       | 2009 |
| Perisetti 2013    | 26                            | 69                | 4     | 69     | 34.7% 9.83 [3.20, 30.14]      | 2013 |
| Tang 2017         | 1                             | 65                | 0     | 45     | 13.5% 2.12 [0.08, 53.13]      | 2017 |

Total (95% CI): 231 events, 207 total events, 100.0% weight

Heterogeneity: Tau² = 1.19; Chi² = 8.43, df = 3 (P = 0.041); I² = 64%
Test for overall effect: Z = 1.76 (P = 0.08)