REVIEW ARTICLE

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; $P = 0.01$; $I^2 = 56\%$; low-quality evidence), pneumonia (OR 4.17, 95% CI, 1.82, 9.57; $P = 0.0007$; $I^2 = 52\%$; low-quality evidence) and hospital length of stay (mean difference 0.86 days, 95% CI 0.13, 1.59; $P = 0.02$; $I^2 = 0$; low-quality evidence), without clear effect on mortality (OR 1.92, 95% CI, 0.71, 5.23; $P = 0.2$; $I^2 = 95\%$; 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.[1] Therefore, it is not uncommon to perform prophylactic endotracheal intubation (PEI) in such patients to prevent aspiration or to assure that a 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,[2] while other guidelines did not address this issue.[3-5] 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 believes and practices of gastroenterologists with regards to endotracheal intubation in the presence of UGIB.[6] 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.[7] 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,[8] 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 I^2 statistics,[9] 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,[10-12] and excluding the

abstract by Lee *et al.*,[12] as the data overlapped with their full-text publication on a later date. [13] 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.

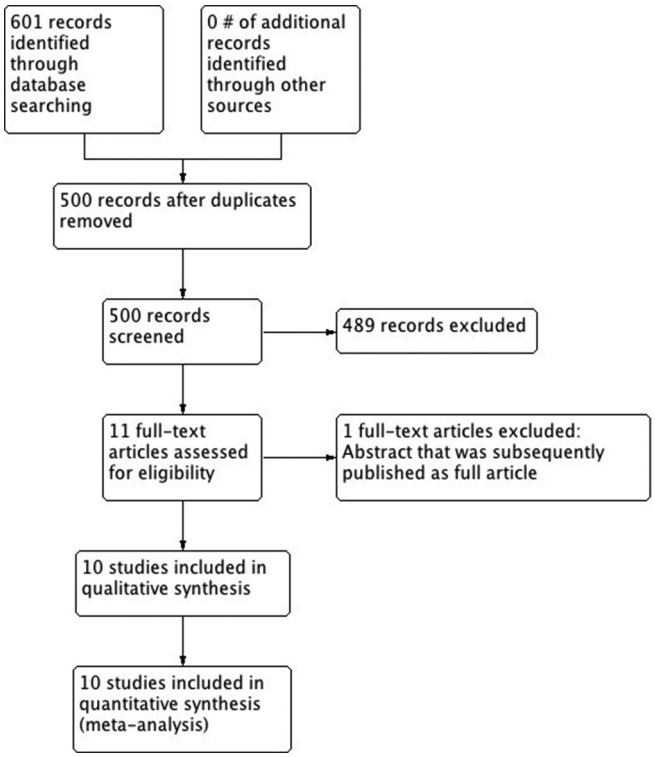

Figure 1: Study flow diagram

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; $P = 0.01$; $I^2 = 56\%$; 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; $P = 0.0007$; $I^2 = 52\%$; 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; $P = 0.2$; $I^2 = 95\%$; 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; $P = 0.02$; $I^2 = 0$; 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; $P = 0.1$; $I^2 = 77\%$). Our second sensitivity analysis, excluding the Lee *et al*. abstract,

Table 1: Characteristics of included studies

Author	Design	Population	Interventions	Definition of aspiration	Definition of pneumonia
Lipper,[1] USA (*n* = 30)	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,[17] USA (*n* = 62)	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,[19] USA (*n* = 98)	Retrospective case-control	Medical ICU admitted for UGIB with cirrhosis, hematemesis or shock. Age (median): 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,[10] (Abstract) USA (*n* = 138)	Retrospective	Admitted to ICU with UGIB Age (mean): 63.5 years Males: NR	PEI (*n* = 69) Usual care: (*n* = 69)	NR	NR
Lohse,[18] Denmark (*n* = 3580)	Retrospective database	Nationwide registry of patients with peptic ulcer bleeding undergoing emergency EGD under anesthesia care. Age (mean): 75 years Males: 54%	PEI (*n* = 2101) Usual care: (*n* = 1479)	NR	NR
Abdulsamad,[11] (Abstract) USA (*n* = 1474)	Retrospective cohort	UGIB defined as hematemesis, coffee ground emesis or melena who underwent EGD	PEI (*n* = 264) Usual care (*n* = 1219)	NR	NR
Lee,[12] (Abstract) USA (*n* = 156)	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,[13] USA (*n* = 200)	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,[21] USA (*n* = 110)	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 the following findings within 48 hours after EGD: Fever (temperature >100.8°F) Leukocytosis (WBC >10,000/mm^3) Purulent sputum
Rudolph,[14] USA (*n* = 220)	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*.[1]	✵✵✵✵	✵	✵✵✵
Rudolph *et al*.[14]	✵✵✵	✵	✵✵
Koch *et al*.[17]	✵✵✵✵	✵✵	✵✵✵
Rehman *et al*.[19]	✵✵✵✵	✵✵	✵✵✵
Perisetti *et al*.[10]	✵✵✵	✵	✵✵
Lohse *et al*.[18]	✵✵✵✵	✵✵	✵✵✵
Abdulsamad *et al*.[11]	✵✵✵	✵	✵✵✵
Lee *et al*.[12]	✵✵✵✵	✵	✵✵✵
Hayat *et al*.[13]	✵✵✵✵	✵✵	✵✵✵
Tang *et al*.[21]	✵✵✵✵	✵✵	✵✵✵

did not significantly alter the effect on mortality (OR 2.3, 95% CI 0.79, 6.99; P = 0.12; I^2 = 96). We present the details of sensitivity analyses in Supplementary Figures V-X [online only].

Publication bias

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.

DISCUSSION

In this systematic review, we identified 10 observational studies (6068 patients) that reported the effect of

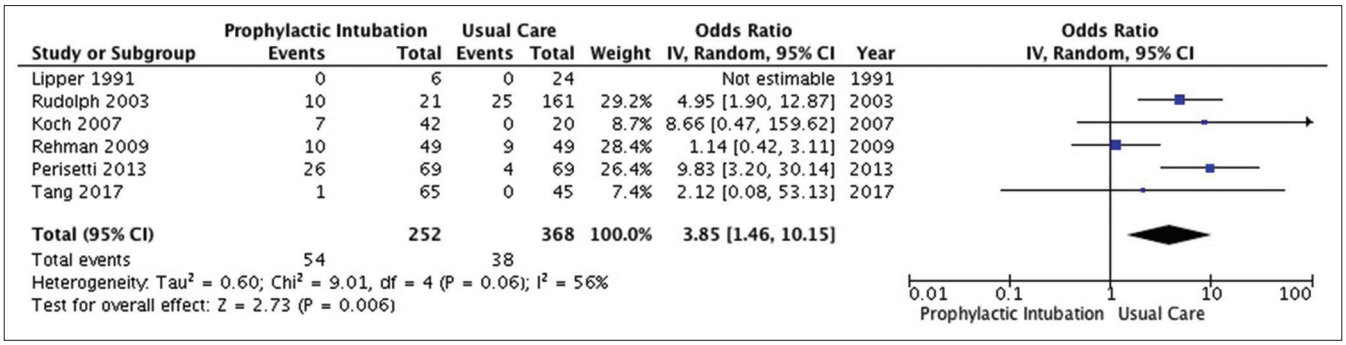

Figure 2: Aspiration outcome

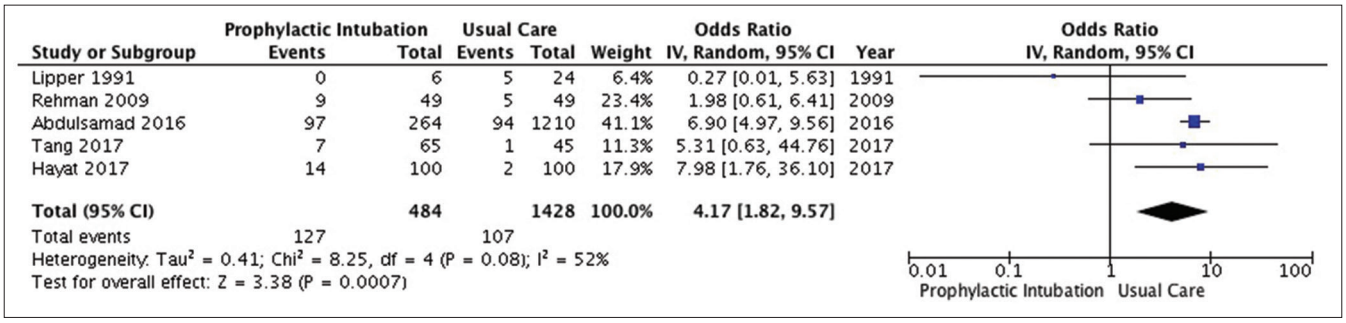

Figure 3: Pneumonia outcome

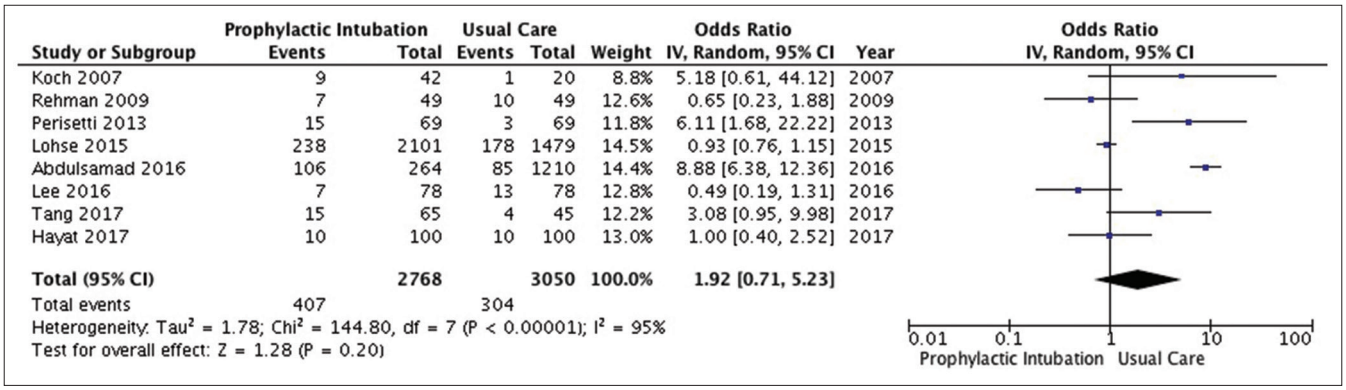

Figure 4: Mortality outcome

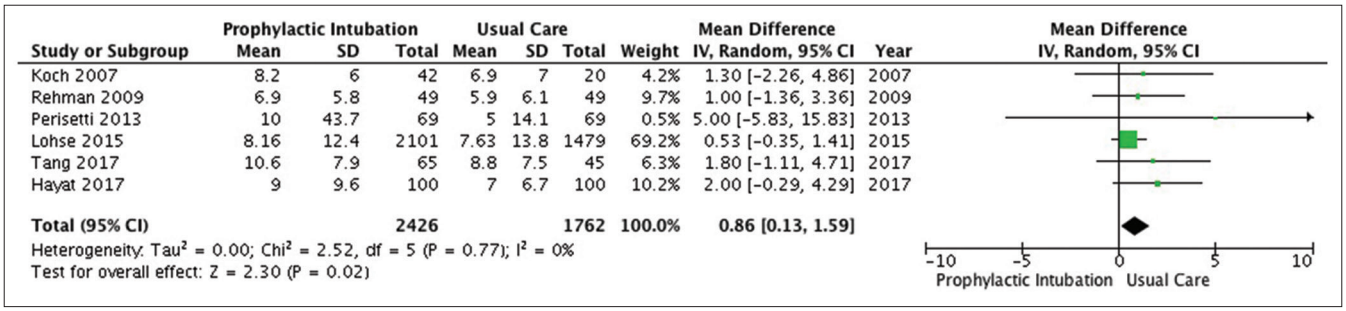

Figure 5: Hospital length of stay outcome

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[a]	Very serious[b]	Not serious	Not serious[c]	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)	⊕◯◯◯ Very Low	Critical
Pneumonia												
5	Observational studies	Serious[a]	Serious[d]	Not serious	Not serious[e]	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)	⊕⊕◯◯ Low	Critical
Aspiration												
6	Observational studies	Serious[a]	Serious[f]	Not serious	Not serious[g]	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)	⊕⊕◯◯ Low	Critical
Hospital length of stay (days)												
6	Observational studies	Serious[a]	Not serious	Not serious	Not serious[h]	None	2426	1762	-	MD 0.86 days more (0.13 more to 1.59 more)	⊕◯◯◯ Very Low	Important

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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SUPPLEMENTARY

APPENDIX I

Database(s): Embase 1974 to 2017 July 07, OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

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
Description:

ID	Search	Hits
#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

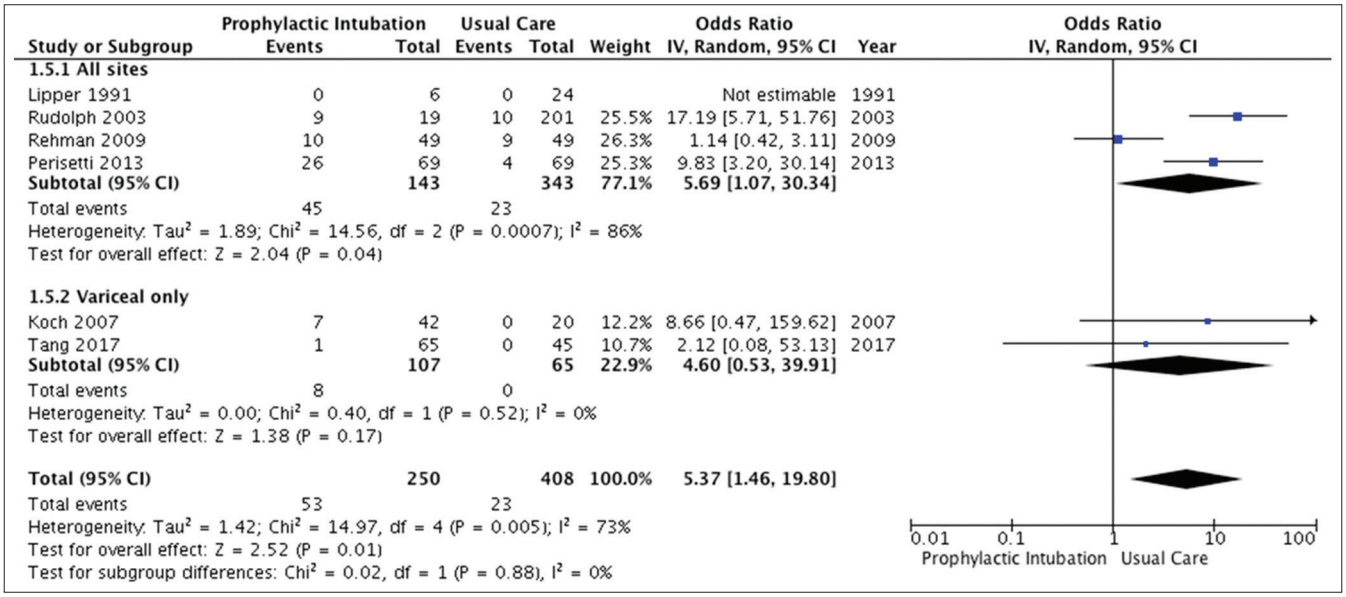
1) Comparability of cohorts on the basis of the design or analysis
   a) Study controls for _____ (select the most important factor) ☐
   b) Study controls for any additional factor ☐ (This criteria could be modified to indicate specific control for a second important factor.)

Outcome

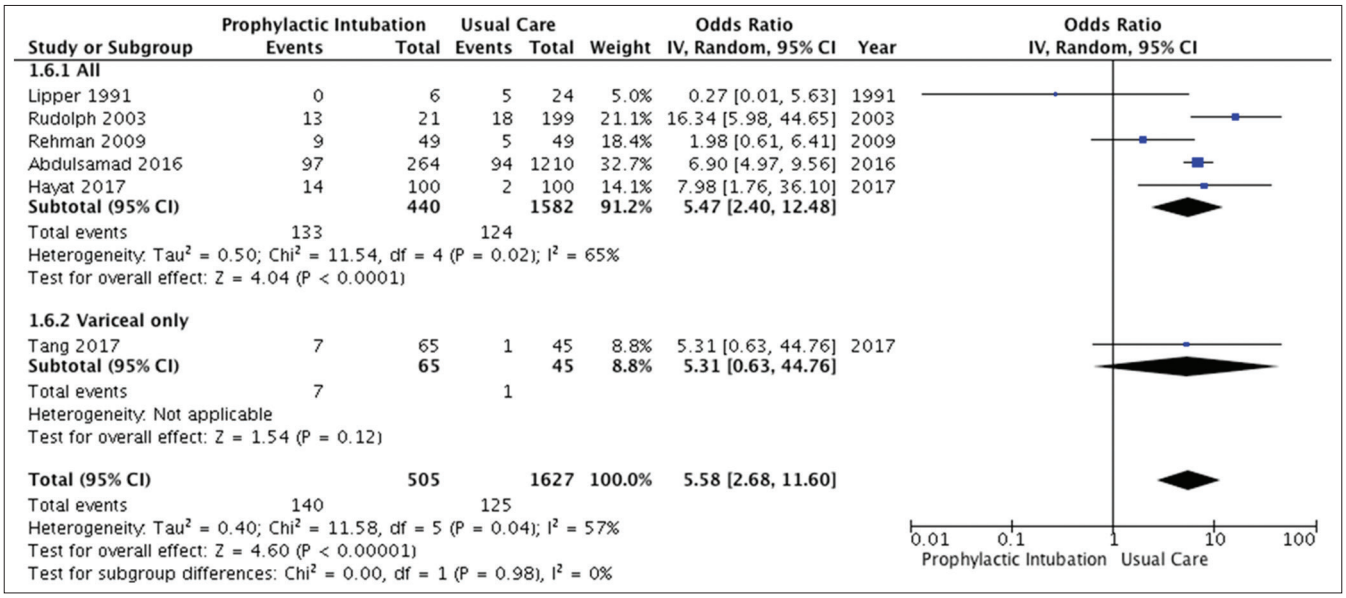
1) Assessment of outcome
   a) Independent blind assessment ☐
   b) Record linkage ☐
   c) Self report ☐
   d) No description ☐
2) Was follow-up long enough for outcomes to occur
   a) Yes (select an adequate follow up period for outcome of interest) ☐
   b) No ☐
3) Adequacy of follow up of cohorts
   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 quailty of nonrandomised studies in meta-analyses. http://www ohri ca/programs/clinical_epidemiology/oxford htm 2009 Feb 1.

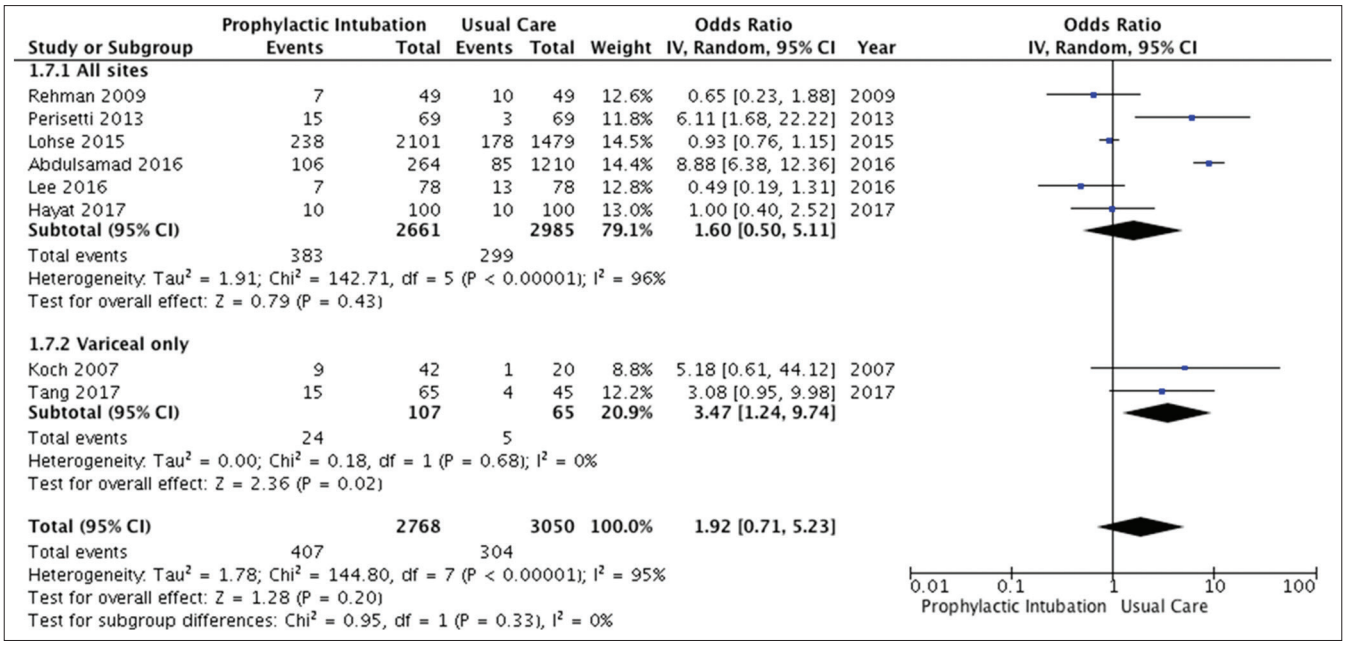
SUPPLEMENTARY FIGURES



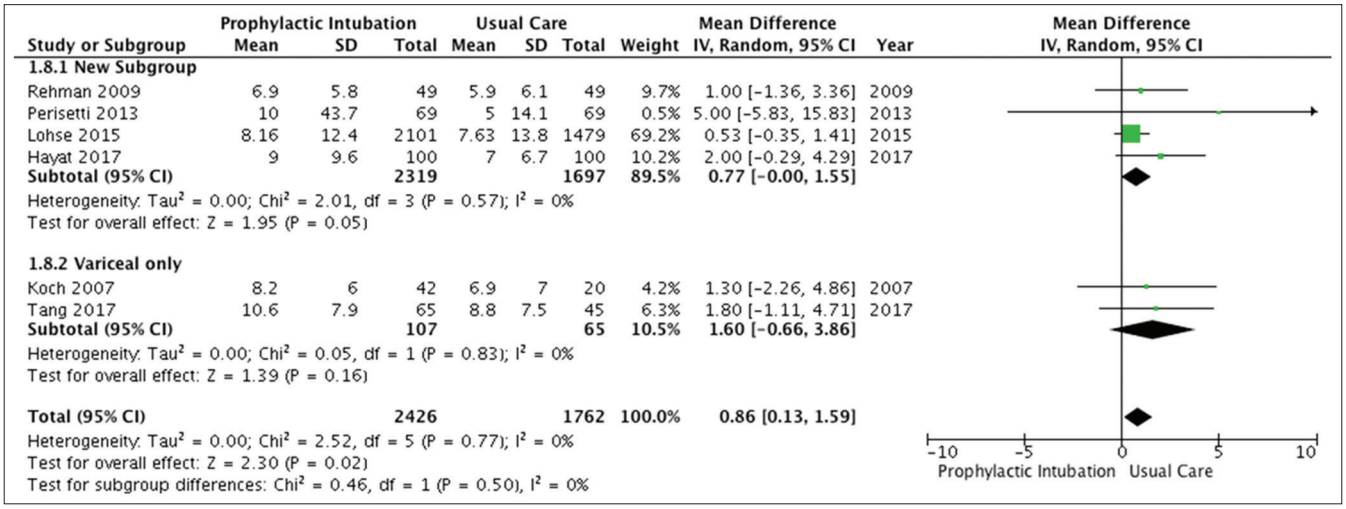
Supplementary Figure I: Subgroup analysis by bleeding type for aspiration outcome



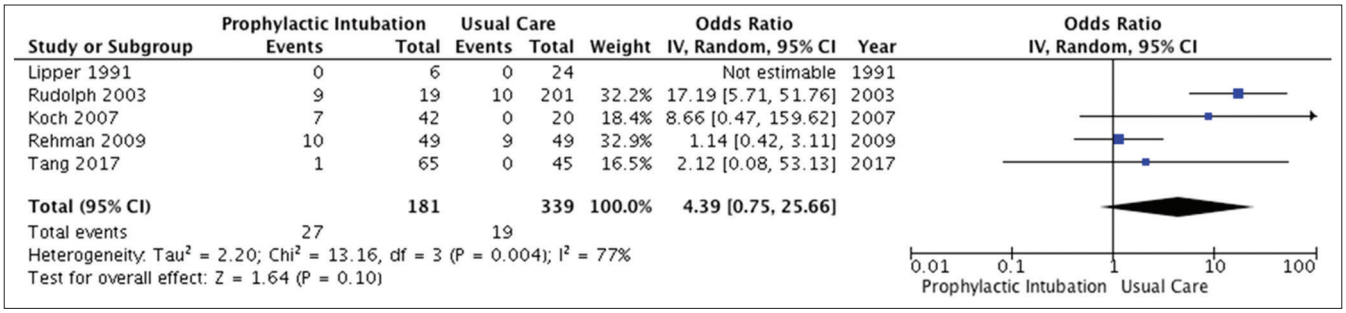
Supplementary Figure II: Subgroup analysis by bleeding type for pneumonia outcome



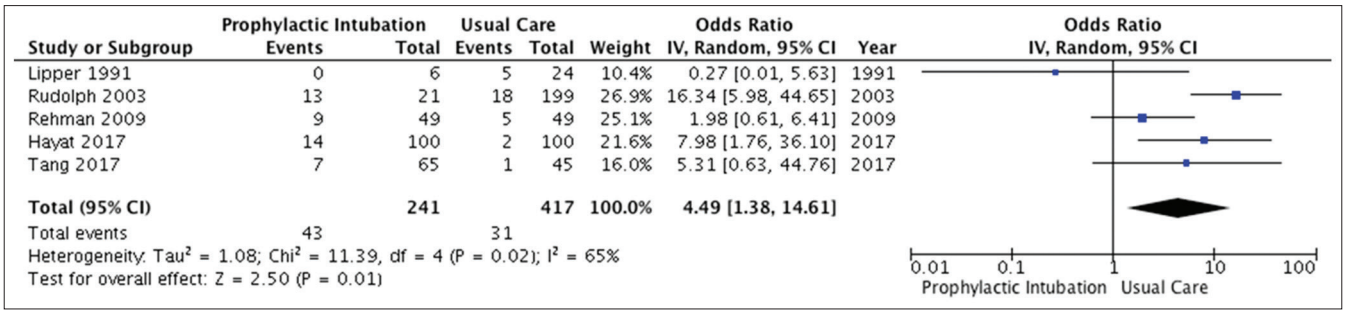
Supplementary Figure III: Subgroup analysis by bleeding type for mortality outcome



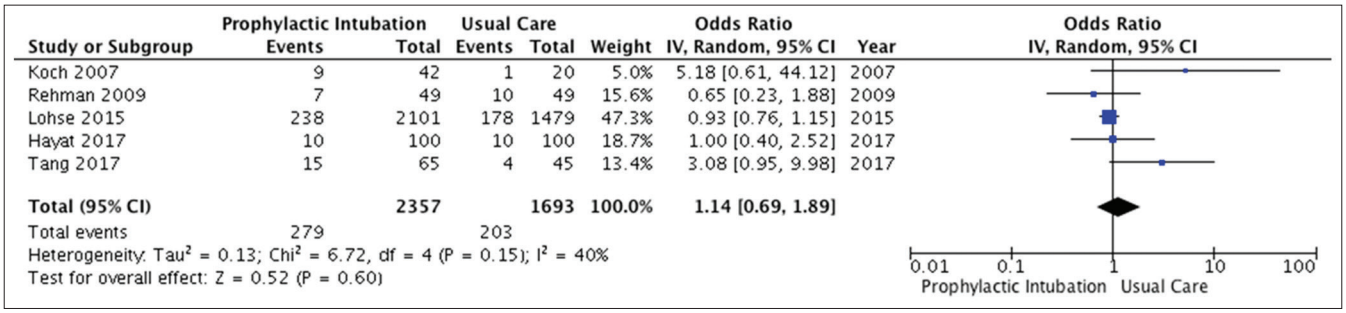
Supplementary Figure IV: Subgroup analysis by bleeding type for hospital length of stay outcome



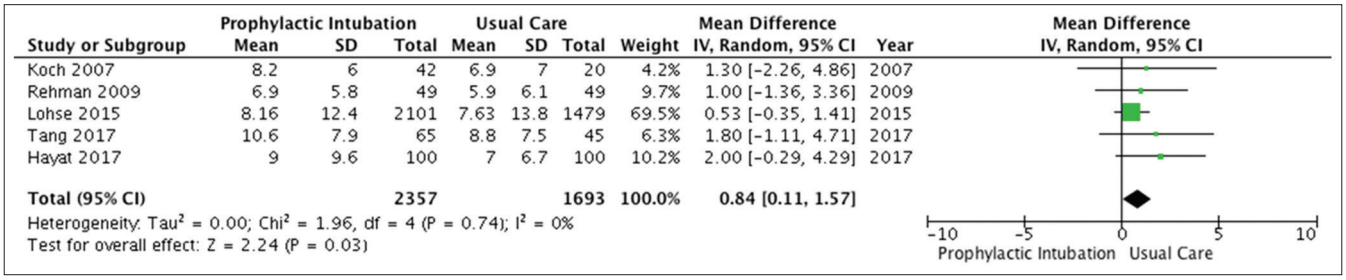
Supplementary Figure V: Sensitivity analysis excluding studies published in abstract form only for aspiration outcome



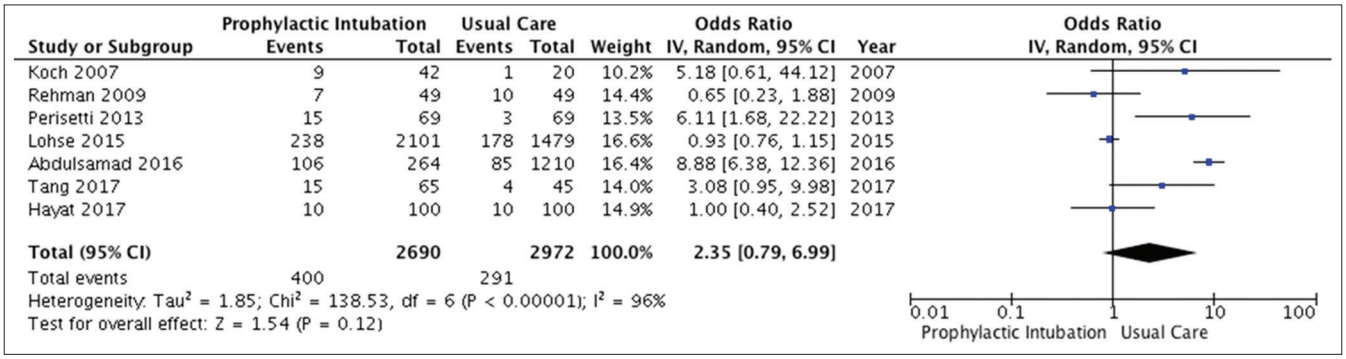
Supplementary Figure VI: Sensitivity analysis excluding studies published in abstract form only for pneumonia outcome



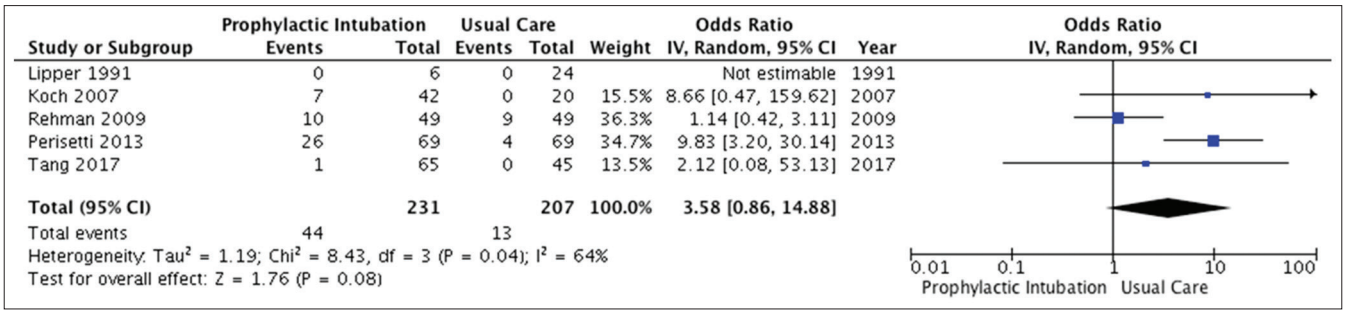
Supplementary Figure VII: Sensitivity analysis excluding studies published in abstract form only for mortality outcome



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