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Research Article

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Cuffed versus uncuffed endotracheal tubes in pediatrics: a meta-analysis

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Abstract: Background: Cuffed and uncuffed endotracheal tubes are commonly used for pediatric patients in surgery and emergency situations. It is still controversial which approach should be adopted. The purpose of the study was to compare the application of cuffed and uncuffed endotracheal tubes in pediatric patients.

Methods: We searched PubMed, Web of Science and Cochrane Library for clinical trials, which compared the two applications in children. The study characteristics and clinical data were summarized by two independent reviewers. Meta-analysis of the data was done using Revman 5.3 software.

Results: 6 studies with 4141 cases were included in this meta-analysis. The pooling analysis showed that more patients need tube changes in uncuffed than cuffed tubes (OR: 0.07, 95% CI: 0.05-0.10, $P < 0.00001$). However, there were no differences on intubation duration, reintubation occurrence, accidental extubation rate, croup occurrence and racemic epinephrine use during the intubation process. Also we didn't find any differences on laryngospasm and stridor occurrence after extubation.

Conclusions: Our study demonstrated that uncuffed endotracheal tubes increased the need for tube changes. Other incidences or complications between the two groups had no differences. Cuffed tubes may be an optimal option for pediatric patients. But more trials are needed in the future.

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1 Introduction

Endotracheal tubes are widely used in pediatric patients in emergency department and surgical operations [1]. In clinical practice, uncuffed tracheal tubes are preferred in children for the fear that the cuff would make airway mucosal injury, tissue edema and fibrosis, leading a life-threatening result [2]. Cuffed tracheal tubes emerge for its unique role in avoiding air leakage and safety use during treatment [3]. However, there are still no clear preference for the selection of them in these sufferers. Although a meta-analysis with 4 included studies was undertaken in 2015 [4], those items analyzed in the previous pooling analysis was relatively limited. Also, new studies are being done in recent years. This encourages a new pooling of the current evidences. Thus, a new meta-analysis is done in the study to demonstrate this issue.

2 Materials and Methods

2.1 Search strategy

This meta-analysis was conducted according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) standards [5,6]. Institutional review board approval then was not needed for this study. A thorough search was done in PubMed, Cochrane Library and Web of Science for the potential studies which compared cuffed and uncuffed endotracheal tubes in children, from the inception to November, 2017, without restriction of languages and article types.

2.2 Inclusion and exclusion criteria

The study selection was done by two independent reviewers. Studies meeting the following criteria were included: (1) randomized controlled trials, prospective or retrospective studies; (2) endotracheal tubes were applied in children or pediatric patients without any restriction of disease types; (3) outcomes were compared between cuffed and uncuffed groups. The exclusion criteria were: (1) case reports, editorials, letters, basic studies and reviews; (2) articles that lack the original data.

2.3 Data extraction

Data in the included studies were extracted and summarized independently by two authors. Any disagreement was resolved by consensus-based discussion among all the authors and determined by the corresponding author. The study outcomes extracted were classified into peri- and post-procedural outcomes. Peri-intubation outcomes were tube change, duration of intubation, accidental extubation and reintubation. Post-procedural results included racemic epinephrine, croup, laryngospasm and stridor.

2.4 Quality assessment

The quality of observational studies was assessed using the Newcastle-Ottawa Quality Assessment Scale [7], which consists of three factors: patient selection, comparability of the study groups, and assessment of outcome. A score of 0–9 was allocated to each study. Studies that achieved six or more stars were considered to be of high quality. The quality assessment of randomized controlled trial was done according to the Cochrane risk of bias tool [8].

2.5 Statistical analysis

Meta-analyses were conducted using Review Manager 5.3. The weighted mean difference (WMD) and odds ratio (OR) were used to compare continuous and dichotomous variables, respectively. All results were reported with 95% confidence intervals (CIs). Statistical heterogeneity between trials in this analysis was assessed using the I^2 values and χ^2 statistics with p value < 0.1, which is significant being set at $I^2 > 50\%$ according to the Cochrane Reviewer's Handbook. Random effects and fix effects models were used for the meta-analysis. The risk of publication bias was planned to be assessed using funnel plot. All statistical tests were two-sided.

3 Results

3.1 Description of the study selection

The study flow of this meta-analysis was displayed in Figure 1. The initial electronic search in PubMed, Cochrane Library and Web of Science from inception to November, 2017 yielded 2179 articles. After removal of the duplicates, 1293 articles were further analyzed. A following thorough review of the titles and abstracts excluded 1260 studies. We then evaluated the full-texts of the remaining studies, with a final inclusion of 6 records. The study characteristics were shown in Table 1. There were 4141 cases in total, with 2078 in cuffed and 2063 in uncuffed group. There were 2 randomized controlled trials [9,10] and 4 cohort studies [11-14] in the pooling analysis. 3 studies came from USA, 2 were undertaken in Switzerland, and 1 was from Turkey. 3 of them gave the precise study period, 1 only give the investigation duration, and this information was not applicable in 2 studies. Other information, including gender, age, weight, endotracheal pathway, peri-intubation, post-extubation variables and quality assessment were shown in detail in Table 1.

3.2 Outcome of interest

We collected and summarized the data into two sections: peri- and post-procedural. For parameters during procedure, we found that more patients in uncuffed group need tube changes than cuffed group (OR: 0.05, 95% CI: 0.03-0.07; $P < 0.00001$) (Figure 2). But the duration of intubation (Supplemental Figure 1), the incidence of accidental extubation (Supplemental Figure 2), tube reintubation (Supplemental Figure 3) and racemic epinephrine use (Supplemental Figure 4) were not significantly different between the two groups (Table 2). For post-extubation events, we collected data of the incidence of croup (Supplemental Figure 5), stridor (Supplemental Figure 6) and laryngospasm (Supplemental Figure 7). And we didn't find any differences of them between uncuffed and cuffed groups in pooling results (Table 3).

Table 1: The study characteristics of the included studies. RCT, randomized controlled trial; NA, not applicable;

					No.		Gender	
Study	Year	Region	Design	period	Cuffed	Uncuffed	Cuffed	Uncuffed
Ozden [9]	2016	Turkey	RCT	2010.06- 2011.06	40	40	7	12
Sathyamoorthy [11]	2015	USA	cohort	2011.05-2012.06	29	195	NA	NA
Weiss [10]	2009	Switzerland	RCT	NA	1197	1049	66.9%	65.00%
Newth [12]	2004	Switzerland	cohort	1 year	438	422	NA	NA
Khine [13]	1997	USA	cohort	NA	251	237	NA	NA
Deakers [14]	1994	USA	cohort	1988.07-1989.02	123	120	77	64

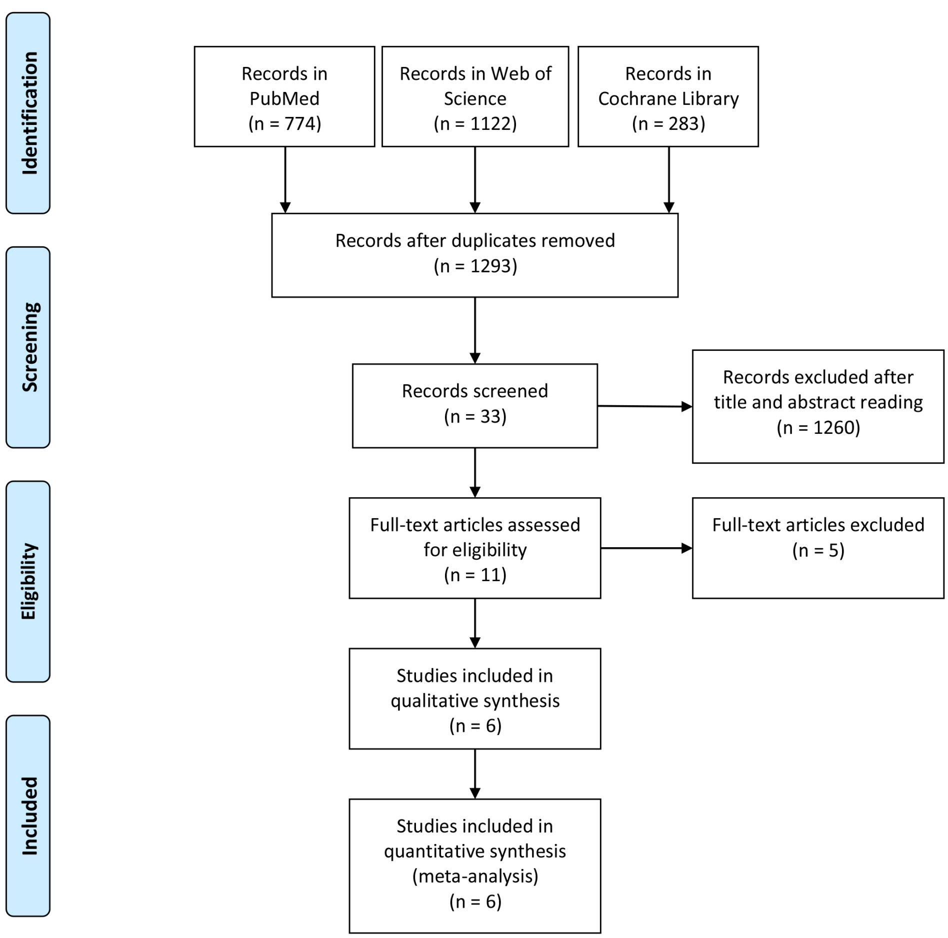
Table 1 continued

	Age		Weight		Oral/Nasal		Peri-intubation	Post-extubation	Quality
Study	Cuffed	Uncuffed	Cuffed	Uncuffed	Cuffed	Uncuffed			
Ozden [9]	14.2 ± 8.6	10.2 ± 8.9	10 ± 3.3	8 ± 3.2	NA	NA	duration of intubation, surgery time, anesthesia time, reintubation, O2 desaturation, difficulties with intubation	stridor, laryngospasm, croup, coughing, retching, vomiting, blood on tubes, blood at aspiration	RCT
Sathyamoorthy [11]	NA	NA	NA	NA	NA	NA	NA	stridor	7
Weiss [10]	1.84	1.85	11.4 ± 4.7	11.2 ± 4.6	1142/55	961/88	patients need tube changes, duration of intubation, accidental extubation, reintubation	stridor, laryngospasm	RCT
Newth [12]	NA	NA	NA	NA	NA	NA	duration of intubation, racemic epinephrine use	NA	5
Khine [13]	3.3 ± 2.4	2.9 ± 2.2	15.1 ± 7.4	14.3 ± 7.7	NA	NA	patients need tube changes, patients need >2 FGF, duration of intubation, reintubation, racemic epinephrine use	croup	7
Deakers [14]	8.08 ± 0.59	2.53 ± 0.35	NA	NA	114/9	112/8	duration of intubation, accidental extubation, air leak present at extubation, PRISM score, reintubation	stridor	7

Table 2: The meta-analysis results of peri-procedure parameters.

			Study heterogeneity			
Peri-intubation	**OR/WMD (95% CI)**	**P**	**df**	**χ^2**	**P-Q test**	**I^2**
tube change	0.05 (0.03, 0.07)	<0.00001	1	0.08	0.77	0
duration of intubation	0.02 (-0.13, 0.09)	0.58	3	10.41	0.02	71
accidental extubation	0.93 (0.45, 1.95)	0.86	1	1.02	0.31	2
reintubation	0.77 (0.20, 2.93)	0.7	3	0.69	0.41	0

PRISMA 2009 Flow Diagram



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For more information, visit www.prisma-statement.org.

Figure 1: The study flow of the meta-analysis.

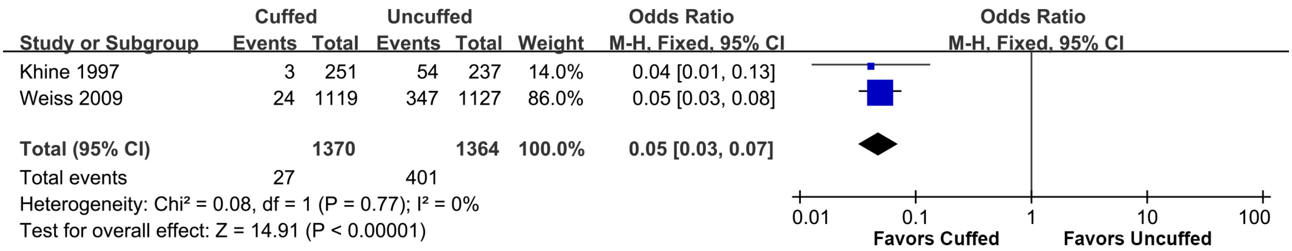

Figure 2: The meta-analysis of tube changes between cuffed and uncuffed groups.

Table 3: The meta-analysis results of post-extubation parameters.

After extubation	OR/WMD (95% CI)	P	Study heterogeneity			
			df	χ^2	P-Qtest	I^2
racemic epinephrine	0.69 (0.39, 1.20)	0.18	1	0.2	0.65	0
croup	0.80 (0.27, 2.43)	0.7	NA	NA	NA	NA
laryngospasm	1.27 (0.86, 1.88)	0.23	1	0.04	0.84	0
stridor	1.04 (0.74, 1.45)	0.82	3	2	0.57	0

3.3 Quality Assessment, sensitivity and publication bias analysis

A description of the quality of the included trials was provided in Table 1. All the study quality were relatively high, indicating the reliability of the pooling analysis. As there were less than 5 studies in each comparison, the sensitivity analysis cannot be performed accurately. Publication bias was not assessed using funnel plot as the number of studies in each category was too small to make an appropriate inference.

4 Discussion

This meta-analysis compared the application of cuffed with uncuffed endotracheal tubes among pediatric patients. We found that more patients need tube changes in the uncuffed group than those with cuffed tubes. However, no significant differences were found between the two groups on intubation duration, reintubation occurrence, accidental extubation rate, croup occurrence and racemic epinephrine use during the intubation process. Also we didn't find any differences on laryngospasm and stridor occurrence after tube extubation.

We are fully aware of a previous meta-analysis which was done on the same topic [4]. The conclusions in the two studies were quite similar, but the parameters analyzed in that article were limited. The outcomes in the current meta-analysis were displayed as peri- and post-procedural. For parameters during procedure, tube change, duration of intubation accidental extubation, tube reintubation and racemic epinephrine use were compared. For post-extubation events, we collected data of the incidence of croup, stridor and laryngospasm. This increased the evidence level of our study. Also, a few studies have been published in recent years. Two more studies were included in this analysis, compared with the previous one.

Endotracheal intubation is a frequent procedure in pediatric emergency and surgery department. The intubation in children may be performed by staff in emergency department, intensive care unit, anesthesia and general pediatric staff [15]. Once the decision for intubation has been made, the choice should be between the cuffed or uncuffed endotracheal tubes [16]. Cuffed tubes provide a leak-proof connection between the patient's lung and the bag or ventilator without causing undue pressure to laryngeal or tracheal structures [17]. However, an uncuffed endotracheal tube usually causes air leakage or laryngeal injury. The unappropriate size of the tube might be the main cause, leading to an increased number of tube exchanges in these patients [18]. From the pooling analysis we found that patients with uncuffed endotracheal tubes had a higher incidence of tube changes. This is consistent with the previous meta-analysis by Shi et al. [4]. They demonstrated that cuffed tubes may be safely used in children. There was also no significance of post-procedural stridor. Although the conclusion was quite similar between the two studies, our study provided more subjects, indicating a reliable basis.

We then didn't reveal any significance of duration of intubation. The intubation time should be determined by the disease severity and surgery method. From this point, the option of tube types didn't affect it. Accidental extubation is a potentially life-threatening event, which leads to emergent, less-controlled endotracheal reintubation [19]. Sometimes, the unwillingness or unconsciousness of the children usually make the intubation failed. The repeated intubations increase the risk of laryngeal or tracheal injury or scarring, pulmonary injury and ventilator-related pneumonia. In this study, both accidental extubation and reintubation between cuffed and uncuffed groups shared no differences. Croup, laryngospasm and stridor are common adverse events occurring after extubation [20-22]. Reintubation is needed in serious condition of them. The pooling analysis identified no differences of them between the two groups. Racemic epinephrine is used to produce vasoconstriction which markedly decreases blood flow to capillary beds, especially in the mucosal surfaces [23]. It alleviates the airway resistance, decreasing the risk of respiratory insufficiency and extubation failure.

Also, there were some limitations in this study. First, although it is an updated meta-analysis for the previous one, the number of the included studies was relatively small. This hindered the operation of the sensitivity and publication bias analysis. Second, because of the limited information, not all the peri-intubation and postextubation incidences were recorded. More studies were needed in the future to assist a thorough comparison of cuffed and uncuffed endotracheal tubes application.

Our study demonstrated that uncuffed endotracheal tubes increased the need for tube changes. Other incidences or complications between the two groups had no differences. Cuffed tubes may be an optimal option for pediatric patients. But more trials are needed in the future.

Conflict of interest statement: Authors state no conflict of interest

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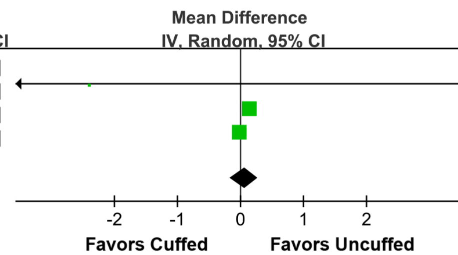
Study or Subgroup	Cuffed Mean	Cuffed SD	Cuffed Total	Uncuffed Mean	Uncuffed SD	Uncuffed Total	Weight	Mean Difference IV, Random, 95% CI
Deakers 1994	146.4	204.96	123	89.76	155.04	120	0.0%	56.64 [11.02, 102.26]
Newth 2004	43.2	103.1	438	45.6	88.9	422	0.0%	-2.40 [-15.25, 10.45]
Weiss 2009	1.79	1.33	1197	1.65	1.21	1049	50.1%	0.14 [0.03, 0.25]
Ozden 2016	0.84	0.25	40	0.86	0.24	40	49.9%	-0.02 [-0.13, 0.09]
Total (95% CI)			**1798**			**1631**	**100.0%**	**0.06 [-0.16, 0.28]**

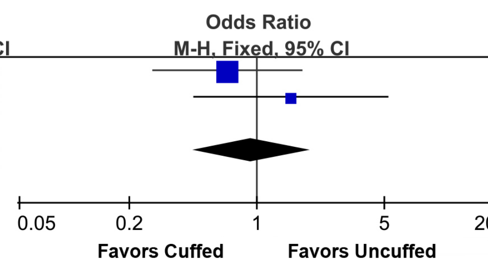
Heterogeneity: Tau² = 0.02; Chi² = 10.41, df = 3 (P = 0.02); I² = 71%
Test for overall effect: Z = 0.55 (P = 0.58)



Supplemental Figure 1: The meta-analysis of duration of intubation between cuffed and uncuffed groups.

Study or Subgroup	Cuffed Events	Cuffed Total	Uncuffed Events	Uncuffed Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Deakers 1994	8	123	11	120	71.1%	0.69 [0.27, 1.78]
Weiss 2009	7	1197	4	1049	28.9%	1.54 [0.45, 5.26]
Total (95% CI)		**1320**		**1169**	**100.0%**	**0.93 [0.45, 1.95]**
Total events	15		15			

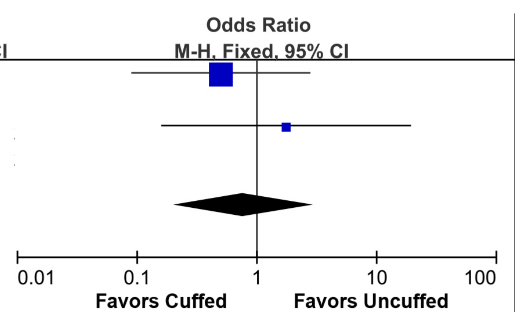
Heterogeneity: Chi² = 1.02, df = 1 (P = 0.31); I² = 2%
Test for overall effect: Z = 0.18 (P = 0.86)



Supplemental Figure 2: The meta-analysis of accidental extubation between cuffed and uncuffed groups.

Study or Subgroup	Cuffed Events	Cuffed Total	Uncuffed Events	Uncuffed Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Deakers 1994	2	93	4	95	78.4%	0.50 [0.09, 2.80]
Khine 1997	0	251	0	237		Not estimable
Weiss 2009	2	1197	1	1049	21.6%	1.75 [0.16, 19.37]
Ozden 2016	0	40	0	40		Not estimable
Total (95% CI)		**1581**		**1421**	**100.0%**	**0.77 [0.20, 2.93]**
Total events	4		5			

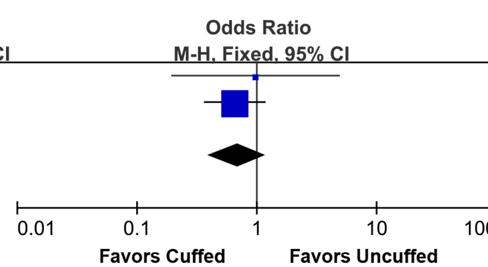
Heterogeneity: Chi² = 0.69, df = 1 (P = 0.41); I² = 0%
Test for overall effect: Z = 0.38 (P = 0.70)



Supplemental Figure 3: The meta-analysis of tube reintubation between cuffed and uncuffed groups.

Study or Subgroup	Cuffed Events	Cuffed Total	Uncuffed Events	Uncuffed Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Khine 1997	3	123	3	120	9.8%	0.97 [0.19, 4.93]
Newth 2004	21	251	29	237	90.2%	0.65 [0.36, 1.18]
Total (95% CI)		**374**		**357**	**100.0%**	**0.69 [0.39, 1.20]**
Total events	24		32			

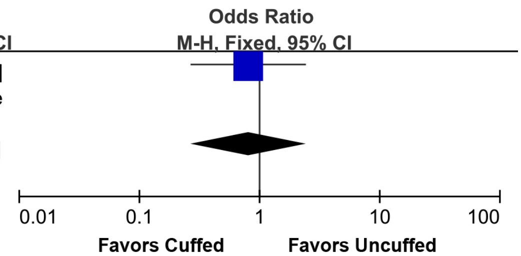
Heterogeneity: Chi² = 0.20, df = 1 (P = 0.65); I² = 0%
Test for overall effect: Z = 1.33 (P = 0.18)



Supplemental Figure 4: The meta-analysis of racemic epinephrine use between cuffed and uncuffed groups.

Study or Subgroup	Cuffed Events	Cuffed Total	Uncuffed Events	Uncuffed Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Khine 1997	6	251	7	237	100.0%	0.80 [0.27, 2.43]
Ozden 2016	0	40	0	40		Not estimable
Total (95% CI)		**291**		**277**	**100.0%**	**0.80 [0.27, 2.43]**
Total events	6		7			

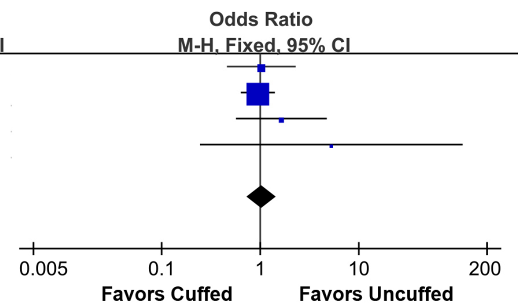
Heterogeneity: Not applicable
Test for overall effect: Z = 0.39 (P = 0.70)



Supplemental Figure 5: The meta-analysis of croup between cuffed and uncuffed groups.

Study or Subgroup	Cuffed Events	Cuffed Total	Uncuffed Events	Uncuffed Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Deakers 1994	14	93	14	95	17.6%	1.03 [0.46, 2.29]
Weiss 2009	53	1197	49	1049	74.7%	0.95 [0.64, 1.41]
Sathyamoorthy 2015	5	29	22	195	7.1%	1.64 [0.57, 4.73]
Ozden 2016	2	40	0	40	0.7%	5.26 [0.24, 113.11]
Total (95% CI)		**1359**		**1379**	**100.0%**	**1.04 [0.74, 1.45]**
Total events	74		85			

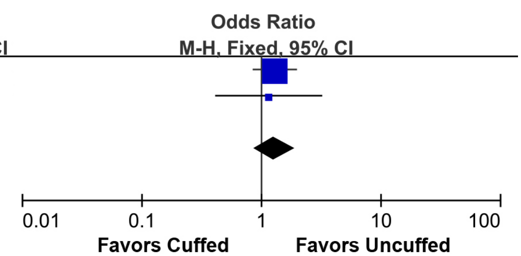
Heterogeneity: Chi² = 2.00, df = 3 (P = 0.57); I² = 0%
Test for overall effect: Z = 0.22 (P = 0.82)



Supplemental Figure 6: The meta-analysis of stridor between cuffed and uncuffed groups.

Study or Subgroup	Cuffed Events	Cuffed Total	Uncuffed Events	Uncuffed Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Weiss 2009	54	1197	37	1049	84.8%	1.29 [0.84, 1.98]
Ozden 2016	10	40	9	40	15.2%	1.15 [0.41, 3.22]
Total (95% CI)		**1237**		**1089**	**100.0%**	**1.27 [0.86, 1.88]**
Total events	64		46			

Heterogeneity: Chi² = 0.04, df = 1 (P = 0.84); I² = 0%
Test for overall effect: Z = 1.19 (P = 0.23)



Supplemental Figure 7: The meta-analysis of laryngospasm between cuffed and uncuffed groups.