# Timing of Tracheostomy in Pediatric Patients: A Systematic Review and Meta-Analysis

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**Objectives:** Tracheostomy is a very common clinical intervention in critically ill adult patients. The indications for tracheostomy procedures in pediatric patients with complex conditions have increased dramatically in recent years, but there are currently no guidelines on the optimal timing of tracheostomy in pediatric patients undergoing prolonged ventilation.

**Data Sources:** We performed a systematic search of the existing literature in MEDLINE via PubMed and Embase databases and the Cochrane Library to identify clinical trials, observational studies, and cohort studies that compare early and late tracheostomy in children. The date of the last search was August 27, 2018. Included articles were subjected to manual searching.

**Study Selection:** Studies in mechanically ventilated children that compared early with late tracheostomy were included.

**Data Extraction:** Data were extracted into a spreadsheet and copied into Review Manager 5.3 (The Cochrane Collaboration, Copenhagen, Denmark).

**Data Synthesis:** Data were meta-analyzed using an inverse variance, random effects model. Continuous outcomes were calculated as mean differences with 95% CIs, and dichotomous outcomes were calculated as Mantel-Haenszel risk ratios with 95% CIs. We included eight studies (10 study arms). These studies were all retrospective cohort studies. Early tracheostomy was associated with significant reductions in mortality, days on mechanical ventilation, and length of intensive care and total hospital stay, although the lack of randomized, controlled trials limits the validity of these findings. Although variance was imputed for some studies, these conclusions did not change after removing these studies from the analysis.

**Conclusions:** In children on mechanical ventilation, early tracheostomy may improve important medical outcomes. However, our data demonstrate the urgent need for high-quality, randomized controlled trials in the pediatric population. (*Crit Care Med* 2019; XX:00–00)

**Key Words:** critical care; early tracheostomy; late tracheostomy; pediatric; ventilation

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Tracheostomy is a frequent clinical procedure performed in critically ill adult patients. It is especially advantageous in improving patient comfort, speech, and oral intake, compared with endotracheal intubation. Tracheostomy has also been found to reduce the risk of laryngeal injury, which is a sequela of prolonged endotracheal intubation in up to 83% of cases (1). Although the rate of tracheostomy in critically ill adult patients ranges from 10% to 24% (2), it is performed in less than 2% of children at a relatively much later time during the hospital stay (3, 4). Tracheostomy is technically challenging in the pediatric age group, with a potential for a higher risk of mortality and associated complications compared with the adult population. Nevertheless, it is becoming a more frequent practice in pediatric populations with complex medical conditions or chronic disease (5, 6). Therefore, determination of the optimal timing of tracheostomy with ongoing care becomes a critical factor in reducing associated risks in children, especially those with comorbidities.

Although the optimal timing for early tracheostomy in adult patients is considered to be 1–2 weeks following mechanical ventilation (MV), currently, there are no guidelines as to the optimal timing of tracheostomy for children under endotracheal intubation in PICUs. Previous studies have reported a large variation in tracheostomy placement ranging from 4.3 to 90 days after prolonged ventilation in the pediatric population. In a large retrospective study in the United States involving 82 PICUs, on average 6.6% of pediatric admissions received tracheostomy, with high variability in the timing of tracheostomy, ranging from 4.3 to 30.4 days across the units (7). In another study where the frequency of tracheostomy placement was 2% of all pediatric admissions across 29 PICUs in the United Kingdom, the timing was reported to be anywhere from 14 to 90 days after initiation of MV, mostly determined on an individual basis (3).

There are inconsistencies in the literature regarding the advantages of early and late tracheostomy in patients requiring prolonged ventilation. Although several meta-analyses in adult populations have concluded that there are no differences in outcomes due to the timing of tracheostomy placement (8–11), more recent meta-analyses report that earlier tracheostomy is associated with improved outcomes such as shorter ICU stays, less sedation, lower mortality rates and a shorter duration of ventilation (12–16).

Currently, there is limited clinical evidence to guide the optimal timing of tracheostomy in critically ill children who need prolonged MV. In addition, inconsistencies in the literature regarding the benefits of early versus late tracheostomy in this pediatric population warrants an appraisal of the extant published literature. We have therefore carried out a systematic review of the literature, along with a meta-analysis, in order to provide some insight into the role of the timing of tracheostomy in pediatric populations requiring MV.

## MATERIALS AND METHODS

### PICOTS and Study Registration

The Population, Intervention, Control, Outcomes, Timing, Setting (PICOTS) for this study was: In children requiring prolonged mechanical ventilation (P), does early tracheostomy (I), compared with later tracheostomy (C), improve the frequency of mortality or hospital-acquired pneumonia, days on mechanical ventilation, total ICU stay or total hospital stay (O), over the entire period of hospitalization (T) in an in-patient setting (S)?

This study was designed and developed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols guidelines (**Supplemental File 1**, Supplemental Digital Content 1, http://links.lww.com/CCM/F156) (17). The protocol for this review was registered in International Prospective Register of Systematic Reviews (PROSPERO) 2019 (registration number CRD42019124293).

### Selection Criteria

Studies were included if they were done in a pediatric population (< 18 yr) on prolonged MV, they compared early tracheostomy with late tracheostomy (as defined by the study authors), and they included at least one of the nominated outcomes. Studies without a control, as well as abstracts, case reports, or case series, or studies that did not provide the necessary clinical outcome data were excluded.

### Search Strategy and Inclusion of Articles

The search terms used for the systematic search consisted of Medical Subject Headings (MeSH) and free keyword terms including "tracheostomy," "early vs late," "children" and "ventilation" with Boolean operators relevant to each database (for the representative PubMed strategy, see online **Supplemental File 2**, Supplemental Digital Content 2, http://links.lww.com/CCM/F157).

Using these search terms, we undertook systematic searches of Medline, Embase, and the Cochrane Library databases. In addition, we performed a citation analysis process on the retrieved articles using SCOPUS citation analysis software. Any relevant citations identified from the Scopus analysis software were exported to EndNote to identify any citations not found in the database searches. The search was limited to studies published in English, after a search without restrictions did not reveal any further studies. The date of our last search was August 17, 2018. Two review authors independently screened the retrieved articles at the title and abstract level, followed by full-text screening for potentially eligible studies. In addition, the references from previous reviews, as well as eligible articles were screened for other relevant literature.

We intended to restrict our analysis to randomized clinical trials (RCTs). However, no RCTs were returned in our study. We therefore included retrospective case-control and cohort studies that reported a sufficient number of patients for analysis.

### Data Extraction and Quality Assessment

We extracted data from the included studies including first author and year of publication, country, study population characteristics (age, number of patients), type of tracheostomy, rate and timing of tracheostomy, length of time on MV, duration of PICU and total hospital stay, mortality and frequency of hospital-acquired pneumonia (HAP).

Two review authors independently assessed the methodological quality of each included study using the National Institutes of Health (NIH) study quality assessment tools (18). This tool measures study quality in terms of study aims, comparability between cohorts, timing of exposure, study size calculations, and control for major covariates. Any disagreements were resolved by mutual agreement and through discussions with a third review author, and the consensus assessment was recorded.

### Statistical Analysis

Data from dichotomous outcomes (mortality, rate of hospital-acquired pneumonia) were meta-analyzed in Review Manager 5.3 (The Cochrane Collaboration, Copenhagen, Denmark) as Mantel-Haenszel risk ratios (RRs) with 95% CIs using a random effects model. Data from continuous outcomes (days on MV, length of hospital stay, length of PICU stay, or neonatal ICU [NICU] stay) were meta-analyzed in Review Manager 5.3 as mean differences (MDs) with 95% CIs using an inverse variance random effects model. Random effects models were chosen because the differences in effect sizes between studies were expected to occur not just as a consequence of chance, but because of underlying differences in the patient populations (age and gender of children, underlying cause of ventilation, etc.).

If continuous data were presented as means and SEs, SDs were obtained by multiplying the SE by the square root of the number in the study arm. If continuous data were presented as means and 95% CIs, SDs were obtained using the Review Manager 5.3 calculator.

Where SDs were missing, and they could not be calculated from other data, they were imputed by taking the median SD from other included studies reporting the same outcome and same group. Sensitivity analysis was conducted to determine if this imputation changes the conclusions of the analysis.

We were intending to undertake subgroup analysis by the gender of the patients, as well as underlying cause of tracheostomy. However, due to the small study sizes and the need for imputed SDs, we were unable to undertake these analyses.

Heterogeneity was defined by Tau$^2$, chi-square, and $I^2$. Heterogeneity as defined by $I^2$ was considered to be minor if 0% to 40%, moderate if 30% to 60%, substantial if 50% to 90% and considerable if 75% to 100%. The percent heterogeneity was interpreted in the context of the magnitude of the effect size and the strength of evidence surrounding the heterogeneity (19).

## RESULTS

### Search Results

After database searching, 978 records were identified. In addition, 20 further records were identified from other sources (**Fig. 1**). After removal of duplicates, 842 records remained. These were subjected to inclusion or exclusion at the title and abstract level. At this stage, 776 records were excluded. We obtained full texts of the remaining 57 records. Of these, 49

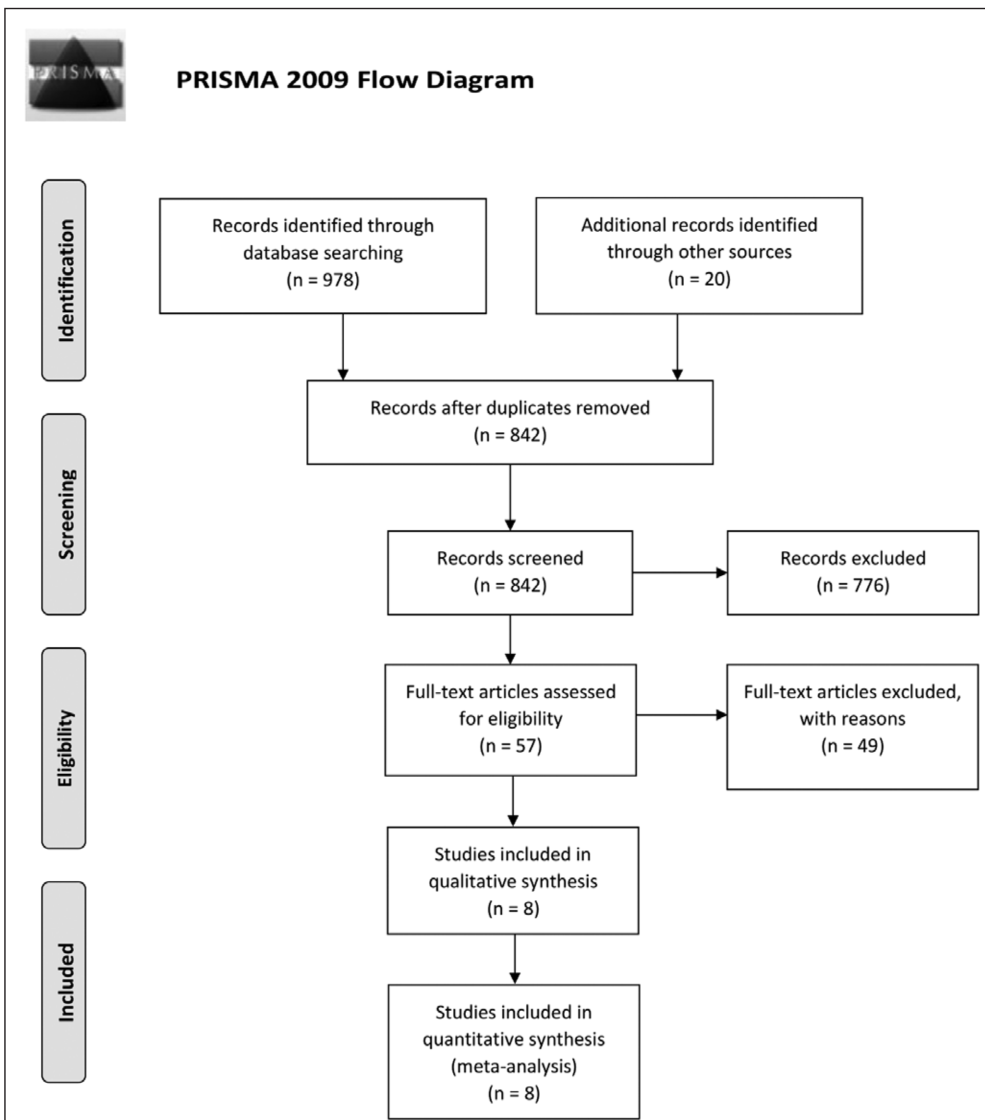


**Figure 1.** Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow chart. From a total of 842 unique citations, 776 were excluded at the title and abstract level. The 57 remaining records were screened as full texts. Of these, 49 were excluded. The remaining eight studies were included in both the qualitative and quantitative synthesis.

records were excluded, mainly due to lack of the necessary clinical outcome data. After inclusion and exclusion, eight studies (20–27) were included in the review, and of these, all are included in the meta-analysis.

## Study Characteristics

The characteristics of the included studies are given in **Supplemental Table 1** (Supplemental Digital Content 3, http://links.lww.com/CCM/F158) and **Supplemental Table 2** (Supplemental Digital Content 4, http://links.lww.com/CCM/F159). The studies range from 17 to 129 patients. Six studies examined early versus late tracheostomy in children (Supplemental Table 1, Supplemental Digital Content 3, http://links.lww.com/CCM/F158), and two studies examined early versus late tracheostomy in neonates (Supplemental Table 2, Supplemental Digital Content 4, http://links.lww.com/CCM/F159). The study authors defined early tracheostomy in children as fewer than 3 days, up to fewer than 14 days post-MV. The studies in neonates, however, defined early tracheostomy as between 45 postmenstrual weeks up to 12 weeks after birth. Cheng et al (28) provided data on the same population of children, with three different definitions of "early" and "late" tracheostomy. In order to be comparable with the other study in neonates, we included the data defining early tracheostomy as 12 weeks or fewer post-birth.

## Study Quality

The quality of the included studies is given in **Supplemental Table 3** (Supplemental Digital Content 5, http://links.lww.com/CCM/F160). The quality of the studies, as measured by the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (18), was universally good. Although none of the studies used blinded outcome assessors, and potential confounders were not always accounted for statistically, the majority of the criteria for a rating of "good" were met.

## Mortality

Four studies reported on mortality in children given a tracheostomy 7–14 days after MV ("early" tracheostomy). There were no data from the two studies defining early tracheostomy as fewer than 7 days (**Fig. 2**). Out of a total population of 274 patients, 130 were given an early tracheostomy and 144 were given a late tracheostomy. The risk of mortality in patients given early tracheostomy versus late tracheostomy was 0.75 (95% CI, 0.47–1.19; $p = 0.22$). There was no heterogeneity in this analysis.

In the two studies defining early tracheostomy by age, one study reported no mortality (Cheng et al [26]), whereas the other study in 127 children revealed a statistically significant association between early tracheostomy and a reduction in mortality (RR, 0.46; 95% CI, 0.22–0.95; $p = 0.04$).

## Days on Mechanical Ventilation

Data on the duration of MV were available for six study arms (**Fig. 3*A***). Information on the variance around the means was imputed for four of these study arms. We undertook a subgroup meta-analysis of the data by the definition of "early" tracheostomy, 7 days or fewer, or 8–14 days post-MV. In this scenario, we found a large and statistically significant difference in the duration of MV between studies defining early tracheostomy as 7 days or fewer post-MV, as opposed to those defining early tracheostomy of 8–14 days post-MV. Whereas the reduction in days on MV was small and not statistically significant in the latter group (MD, –6.18 d; 95% CI, –12.67 to 0.31; $p = 0.06$), the reduction in days on MV in the group defining early tracheostomy as 7 days or fewer post-MV was associated with a reduction of 19.40 days on MV (95% CI, –24.93 to –13.87; $p < 0.00001$). When the studies with imputed data were removed, the magnitude of the effect in children given a tracheostomy 7 days or fewer post-MV remained similar (MD, –20.83 d; 95% CI, –26.01 to –15.64; $p < 0.00001$).

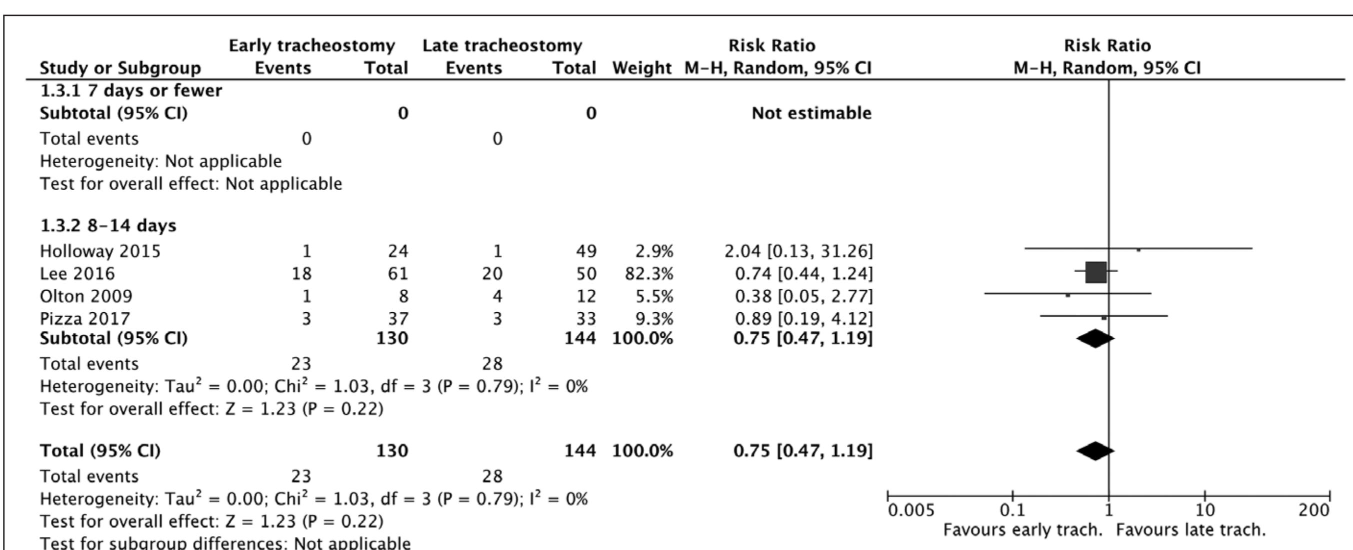


**Figure 2.** Subgroup meta-analysis of studies comparing mortality in children receiving early versus late tracheostomy by definition of early tracheostomy. Data are given as risk ratios with 95% CIs. *df* = degrees of freedom, M-H = Mantel-Haenszel.

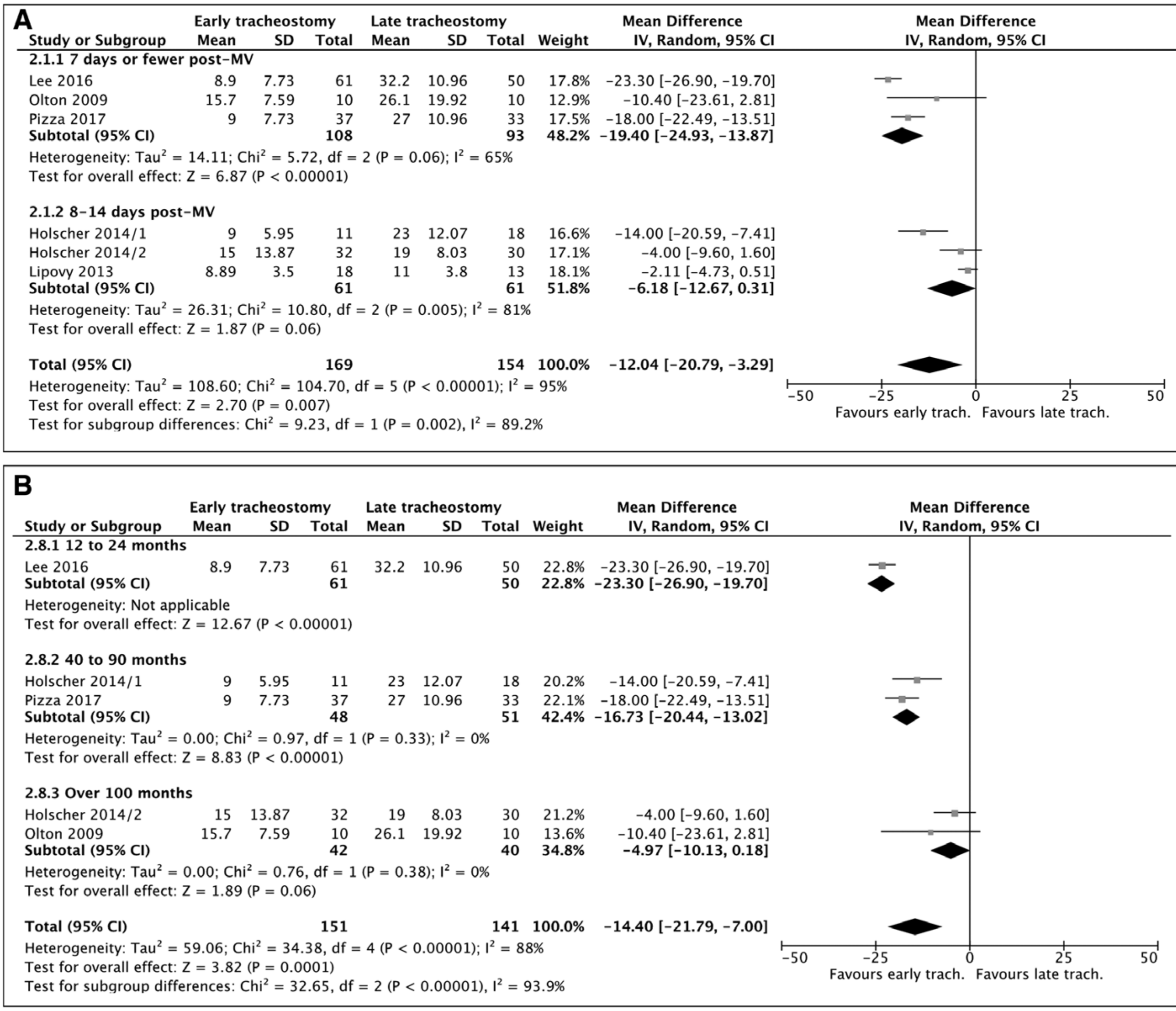


**Figure 3.** Meta-analysis of studies comparing days on mechanical ventilation (MV) in children given early versus late tracheostomy by definition of early tracheostomy and by age at tracheostomy. **A**, Subgroup meta-analysis of studies comparing days on MV in children given early versus late tracheostomy by definition of early tracheostomy. **B**, Subgroup meta-analysis of studies comparing days on MV in children given early versus late tracheostomy by age at tracheostomy. Data are given as mean differences with 95% CIs. *df* = degrees of freedom.

In order to determine if the age of the children at the time of tracheostomy had an impact on the length of MV, we undertook a subgroup meta-analysis by age (**Fig. 3*B***). We found an inverse association between increasing age of the children and the magnitude of the reduction in days on MV. Whereas children 12 to 24 months old were associated with a reduction in days on MV of 23.30 days (95% CI, –26.90 to –19.70; $p < 0.00001$), this reduced to fewer than 5 days in children over 100 months old at tracheostomy (MD, –4.97 d; 95% CI, –10.13 to 0.18; $p = 0.06$). The differences between subgroups was also highly significant (test for subgroup differences: $p < 0.00001$).

In the two studies comparing neonatal age at tracheostomy, rather than days post-MV, one study showed no significant differences (Cheng et al [26]), whereas the other study showed a large and significant difference (MD, –17.50 d; 95% CI, –20.82 to –14.18; $p < 0.00001$).

## Length of PICU or NICU Stay

Five studies (six study arms) included data on the length of stay in intensive care (**Fig. 4**). SDs were imputed for three studies. Overall, early tracheostomy was associated with a significantly reduced length of PICU or NICU stay (MD, –10.10 d; 95% CI, –18.58 to –1.6; $p = 0.02$). Heterogeneity was very high (93%) but driven entirely by Lee et al (21). There were no significant differences in the length of PICU stay in the studies defining early tracheostomy as 7 days or fewer post-MV compared with those defining early tracheostomy as 8–14 days post-MV (test for subgroup differences: $p = 0.92$). There were also no differences in length of PICU stay when the data were subgrouped by the age at tracheostomy. When the studies with imputed values were removed, the association remained (MD, –10.35 d; 95% CI, –14.77 to –5.93; $p < 0.00001$). Heterogeneity was reduced to zero. Neither of the studies in neonates reported on NICU stay.

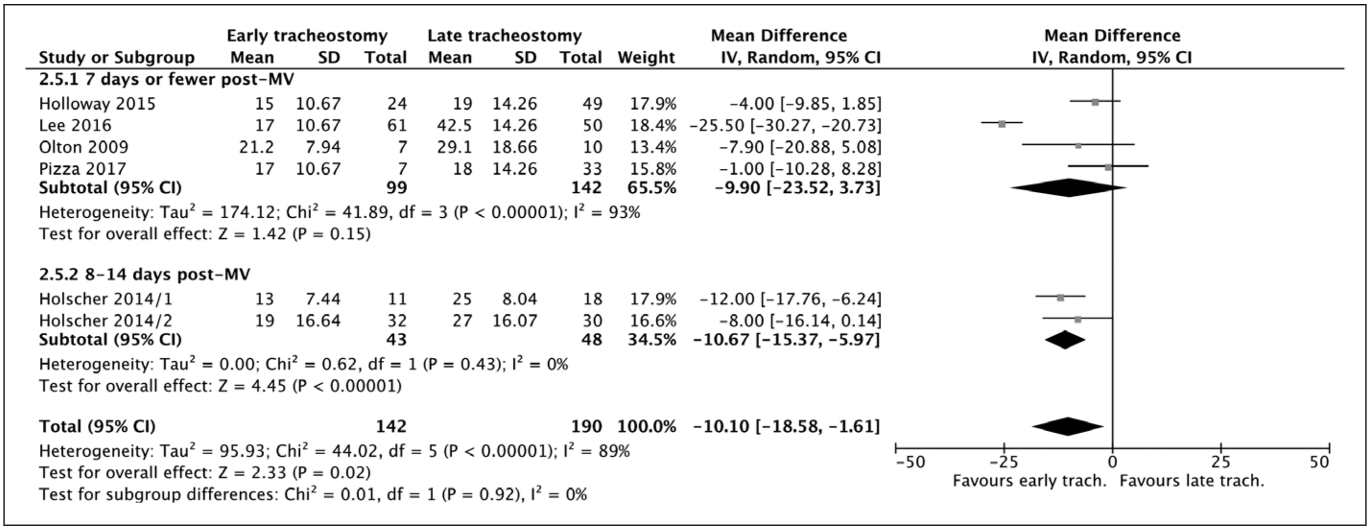


**Figure 4.** Subgroup meta-analysis of studies comparing length of PICU stay in children given early versus late tracheostomy by definition of early tracheostomy. Data are given as mean differences with 95% CIs. *df* = degrees of freedom, MV = mechanical ventilation.

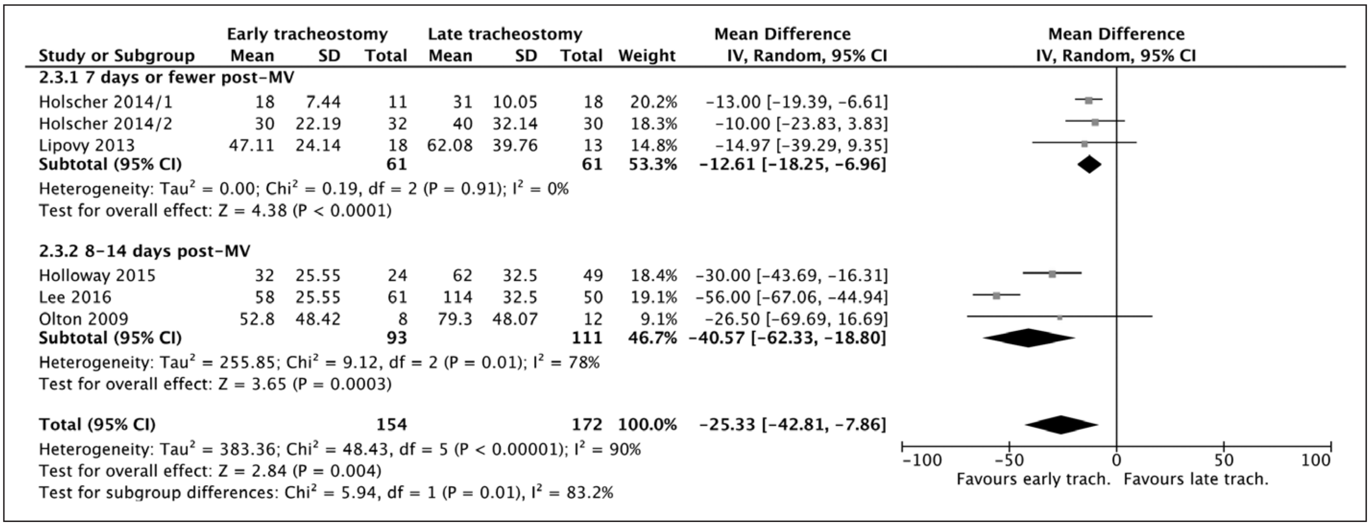


**Figure 5.** Subgroup meta-analysis of studies comparing length of hospital stay by definition of early tracheostomy. *df* = degrees of freedom, MV = mechanical ventilation.

## Length of Hospital Stay

Five studies (six study arms) included data on the total length of the hospital stay (**Fig. 5**). SDs were imputed for two studies. Overall, early tracheostomy was associated with a significant reduction in total hospital stay (MD, –25.33 d; 95% CI, –42.81 to –7.86; $p = 0.0042$). There was a large, statistically significant difference between studies defining early tracheostomy as 7 or fewer days than in studies defining early tracheostomy as 8–14 days post-MV. The number of days in hospital was reduced by 40.57 days in the latter group (95% CI, –62.33 to –18.80; $p = 0.0003$), compared with 12.61 days in the former group (95% CI, –18.25 to –6.96; $p < 0.0001$). Heterogeneity was very high in the 8–14 days post-MV group (78%) but driven entirely by Lee et al (21). When studies with imputed data were removed, the MD was reduced to –12.84 days (95% CI, –18.44 to –7.24) but remained statistically significant ($p < 0.00001$). Heterogeneity was also reduced to 0%.

Another interesting finding was the subgroup analysis by age of the children at the time of the tracheostomy (**Supplemental Fig. 1**, Supplemental Digital Content 6, http://links.lww.com/CCM/F161; **legend**, Supplemental Digital Content 10, http://links.lww.com/CCM/F165). There was an inverse association between the age of the children at tracheostomy and the reduction in the length of hospital stay. Whereas children 12 to 24 months old showed a large difference in days in hospital (MD, –43.33 d; 95% CI, –68.80 to –17.85; $p = 0.0009$), the difference was much smaller in children over 100 months old (MD, –11.54 d; 95% CI, –24.71 to 1.64; $p = 0.09$). The difference between these subgroups was also statistically significant ($p = 0.03$).

## Hospital-Acquired Pneumonia

Data on the frequency of HAP were available for four study arms (**Supplemental Fig. 2**, Supplemental Digital Content 7, http://links.lww.com/CCM/F162; legend, Supplemental

Digital Content 10, http://links.lww.com/CCM/F165). Overall, there was no significant difference in the frequency of HAP between early and late tracheostomy (RR, 0.60; 95% CI, 0.30–1.20; $p$ = 0.15). However, when subgrouped by the definition of early tracheostomy, the meta-analysis of the two studies defining "early" as 7 days or fewer post-MV were associated with a significant reduction in HAP (RR, 0.44; 95% CI, 0.24–0.83; $p$ = 0.01), whereas the meta-analysis of the two study arms defining "early" as 8–14 days post-MV was not significantly different (RR, 0.71; 95% CI, 0.26–1.97; $p$ = 0.51). Heterogeneity was moderate. Because of the small number of studies, we did not carry out a meta-analysis by age at tracheostomy.

### Decannulation

Two studies reported on the rate of successful decannulation (**Supplemental Fig. 3**, Supplemental Digital Content 8, http://links.lww.com/CCM/F163; legend, Supplemental Digital Content 10, http://links.lww.com/CCM/F165). There were no significant differences between early and late tracheostomy in the rate of decannulation (RR, 1.01; 95% CI, 0.69–1.48; $p$ = 0.97). Cheng et al (26) reported on the rate of decannulation in children given tracheostomy early versus later in life. There was no significant difference in decannulation in children given tracheostomy at 12 weeks old or earlier than in children given a tracheostomy after 12 weeks old (RR, 1.37; 95% CI, 0.65–2.90; $p$ = 0.41).

### Other Outcomes

In order to determine if early tracheostomy is associated with airway complications, we undertook a meta-analysis of the two study arms reporting on this outcome (**Supplemental Fig. 4**, Supplemental Digital Content 9, http://links.lww.com/CCM/F164; legend, Supplemental Digital Content 10, http://links.lww.com/CCM/F165). There was a numerically large reduction in the risk of airway complications in children given an early tracheostomy (RR, 0.27; 95% CI, 0.07–1.06; $p$ = 0.06), but due to small sample sizes, this was not statistically significant.

We also investigated the association between early tracheostomy and long-term ventilation (Supplemental Fig. 4, Supplemental Digital Content 9, http://links.lww.com/CCM/F164; legend, Supplemental Digital Content 10, http://links.lww.com/CCM/F165). There were no significant differences in the necessity for long-term ventilation between children given early versus late tracheostomy (RR, 0.88; 95% CI, 0.63–1.24; $p$ = 0.48).

## DISCUSSION

Despite the fact that tracheostomy has occurred since the early 15th century (28), and the procedure may allow a child to leave the hospital early, the optimal timing of this life-saving procedure has remained unclear. Tracheostomy remains a rare procedure in children and has generally been carried out far later than in adult patients (3, 4). However, it does not appear that the decision to perform tracheostomy later in pediatric patients is based on evidence. Despite a recent narrative review on the subject (5), little systematic evidence is available that enables caregivers to make informed choices about tracheostomy timing in children.

In our systematic review and meta-analysis, we found that in the retrospective cohort studies, early tracheostomy was associated with a significant reduction in days on MV, mortality, reduced length of intensive care stay, and reduced length of total hospital stay. These findings are consistent with a recent meta-analysis on the timing of tracheostomy in adult patients (15). Thus, pediatric or even neonatal patients may not represent a special group with different needs.

Furthermore, our analysis of the studies by the definition of "early" tracheostomy produced some interesting insights. For example, a definition of 7 days or fewer post-MV (in contrast with a definition of 8–14 d post-MV) revealed significant differences in the association of early tracheostomy with HAP, days on MV, and length of hospital stay. In addition, our subgroup meta-analysis by age at tracheostomy revealed inverse relationships between the age of the children at the time of tracheostomy and differences in the number of days on MV, PICU stay, and length of hospital stay. It is possible that children are more robust and resilient as they age, and thus a potential advantage from early tracheostomy becomes less important and has less of an effect in older children. However, these data come from retrospective cohort studies, and thus, we cannot rule out that the differences we observed result entirely from differences in the health and clinical status of the children involved. If these data are confirmed in randomized controlled trials, they would suggest that the benefits of early tracheostomy are greatest in the youngest children and make less difference in older children.

Our analysis was hampered by several factors. First, only a small number of studies was available, and these tended to be small, and retrospective in design. We did not identify any randomized, controlled trials. This means that our results are hypothesis-generating in nature. The associations we discovered here suggest that there may be an advantage to pediatric patients in early tracheostomy, but until high-quality randomized, controlled trials are carried out, it is impossible to draw any strong conclusions on the relative advantages of early or later tracheostomy in these patients. The need for a stronger evidence is essential as it is vital to consider that, clinically, a tracheostomy carried out in patients during their first year of life can be extremely disabling and that tracheostomy can be difficult to remove in view of the fact that the dimension of the tracheostomy cannula is the same as that of the trachea, and that it is necessary to surgically remove most of two or more cartilaginous rings in order to position it correctly. Decannulation in the youngest age group can lead to tracheal collapse and the cannula entry point becomes a stenosis that is only tractable with surgery or the application of stents (29).

Many of the studies provided data as medians with interquartile ranges. This is reasonable for data that are not normally distributed. However, it is currently not possible for data in this form to be combined in a meta-analysis. We overcame this limitation by including the median value and imputing SDs. Although our sensitivity analyses showed that this imputation did not substantially change the conclusions of our study, it did limit our ability to provide accurate effect sizes for all outcomes.

There was generally a moderate degree of heterogeneity, especially in the analyses that included imputed variance. This, in combination with expected covariates between studies, such as the injury or illness underlying the need for tracheostomy, and possibly other factors, such as gender, would explain the observed heterogeneity. In circumstances where many studies are available, and no data are imputed, meta-regression would reveal the impact of underlying covariates, which would provide vital information about the efficacy of early tracheostomy in different groups of children. Unfortunately, we had insufficient data to undertake meta-regression.

## CONCLUSIONS

Given our limited current knowledge, our study show evidence that early tracheostomy may provide potential benefits in pediatric populations relying on MV albeit (the available evidence) derived from two nonstatistically significant observational studies. Further large-scale clinical controlled studies are expected to appropriately and significantly elucidate indication for early versus late tracheostomy. Among patients with an acute condition, and especially in children under 1–2 years old, tracheostomy must be considered with utmost caution and careful watchfulness using a respiratory model appropriate for the pediatric patient and disease categories, correct and adequate nursing, and an appropriate respirator weaning protocol making use of early extubation and of a noninvasive face-mask ventilation modality. Clinicians lack evidence-based guidelines when caring for these critically ill children.

## REFERENCES


1. Brodsky MB, Levy MJ, Jedlanek E, et al: Laryngeal injury and upper airway symptoms after oral endotracheal intubation with mechanical ventilation during critical care: A systematic review. *Crit Care Med* 2018; 46:2010–2017
2. Groves DS, Durbin CG Jr: Tracheostomy in the critically ill: Indications, timing and techniques. *Curr Opin Crit Care* 2007; 13:90–97
3. Wood D, McShane P, Davis P: Tracheostomy in children admitted to paediatric intensive care. *Arch Dis Child* 2012; 97:866–869
4. Principi T, Morrison GC, Matsui DM, et al: Elective tracheostomy in mechanically ventilated children in Canada. *Intensive Care Med* 2008; 34:1498–1502
5. Watters KF: Tracheostomy in infants and children. *Respir Care* 2017; 62:799–825
6. Edwards JD, Houtrow AJ, Lucas AR, et al: Children and young adults who received tracheostomies or were initiated on long-term ventilation in PICUs. *Pediatr Crit Care Med* 2016; 17:e324–e334
7. Wakeham MK, Kuhn EM, Lee KJ, et al: Use of tracheostomy in the PICU among patients requiring prolonged mechanical ventilation. *Intensive Care Med* 2014; 40:863–870
8. Siempos II, Ntaidou TK, Filippidis FT, et al: Effect of early versus late or no tracheostomy on mortality and pneumonia of critically ill patients receiving mechanical ventilation: A systematic review and meta-analysis. *Lancet Respir Med* 2015; 3:150–158
9. Andriolo BN, Andriolo RB, Saconato H, et al: Early versus late tracheostomy for critically ill patients. *Cochrane Database Syst Rev* 2015; 1:CD007271
10. Gomes Silva BN, Andriolo RB, Saconato H, et al: Early versus late tracheostomy for critically ill patients. *Cochrane Database Syst Rev* 2012; (3):CD007271
11. Huang H, Li Y, Ariani F, et al: Timing of tracheostomy in critically ill patients: A meta-analysis. *PLoS One* 2014; 9:e92981
12. Khammas AH, Dawood MR: Timing of tracheostomy in intensive care unit patients. *Int Arch Otorhinolaryngol* 2018; 22:437–442
13. McCredie VA, Alali AS, Scales DC, et al: Effect of early versus late tracheostomy or prolonged intubation in critically ill patients with acute brain injury: A systematic review and meta-analysis. *Neurocrit Care* 2017; 26:14–25
14. Meng L, Wang C, Li J, et al: Early vs late tracheostomy in critically ill patients: A systematic review and meta-analysis. *Clin Respir J* 2016; 10:684–692
15. Hosokawa K, Nishimura M, Egi M, et al: Timing of tracheotomy in ICU patients: A systematic review of randomized controlled trials. *Crit Care* 2015; 19:424
16. Shan L, Zhang R, Li LD: Effect of timing of tracheotomy on clinical outcomes: An update meta-analysis including 11 trials. *Chin Med Sci J* 2013; 28:159–166
17. Moher D, Shamseer L, Clarke M, et al; PRISMA-P Group: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015; 4:1
18. National Heart, Lung, and Blood Institute (NHLBI): Study Quality Assessment Tools. Available at: https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools. Accessed February 12, 2018
19. Higgins JP, Greeen S: 9.5.2 Identifying and Measuring Heterogeneity. Available at: https://handbook-5-1.cochrane.org/chapter_9/9_5_2_identifying_and_measuring_heterogeneity.htm. Accessed March 25, 2019
20. Pizza A, Picconi E, Piastra M, et al: Early versus late tracheostomy in pediatric intensive care unit: Does it matter? A 6-year experience. *Minerva Anestesiol* 2017; 83:836–843
21. Lee JH, Koo CH, Lee SY, et al: Effect of early vs. late tracheostomy on clinical outcomes in critically ill pediatric patients. *Acta Anaesthesiol Scand* 2016; 60:1281–1288
22. Holloway AJ, Spaeder MC, Basu S: Association of timing of tracheostomy on clinical outcomes in PICU patients. *Pediatr Crit Care Med* 2015; 16:e52–e58
23. Holscher CM, Stewart CL, Peltz ED, et al: Early tracheostomy improves outcomes in severely injured children and adolescents. *J Pediatr Surg* 2014; 49:590–592
24. Lipový B, Brychta P, Rihová H, et al: Effect of timing of tracheostomy on changes in bacterial colonisation of the lower respiratory tract in burned children. *Burns* 2013; 39:255–261
25. Olton S, Hariharan S, Chen D: Outcome evaluation of patients requiring tracheostomy in an intensive care unit in Trinidad. *West Indian Med J* 2009; 58:173–178
26. Cheng J, Lioy J, Sobol S: Effect of tracheostomy timing in premature infants. *Int J Pediatr Otorhinolaryngol* 2013; 77:1873–1876
27. Goodall EW: On infectious diseases and epidemiology in the hippocratic collection: (Section of the history of medicine). *Proc R Soc Med* 1934; 27:525–534
28. Rane S, Bathula S, Thomas RL, et al: Outcomes of tracheostomy in the neonatal intensive care unit: Is there an optimal time? *J Matern Fetal Neonatal Med* 2014; 27:1257–1261
29. Zeitouni A, Manoukian J: Tracheotomy in the first year of life. *J Otolaryngol* 1993; 22:431–434