Effect of early tracheostomy on resource utilization and clinical outcomes in critically ill patients: meta-analysis of randomized controlled trials

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Editor’s key points
- It is unclear whether early tracheostomy in acutely ill, ventilator-dependent patients reduces costs and complications.
- Small trials are unlikely to reliably estimate relative benefits and risks of tracheostomy.
- This study identifies a clear benefit of reduced duration of sedation.
- A policy of early tracheostomy will however increase the number of procedures being undertaken.

Background. Early tracheostomy may decrease the duration of mechanical ventilation, sedation exposure, and intensive care stay, possibly resulting in improved clinical outcomes, but the evidence is conflicting.

Methods. Systematic review and meta-analysis of randomized trials in patients allocated to tracheostomy within 10 days of start of mechanical ventilation was compared with placement of tracheostomy after 10 days if still required. Medline, EMBASE, the Cochrane Controlled Clinical Trials Register, and Google Scholar were searched for eligible trials. The co-primary outcomes were mortality within 60 days, and duration of mechanical ventilation, sedation, and intensive care unit stay. Secondary outcomes were the number of tracheostomy procedures performed, and incidence of ventilator-associated pneumonia (VAP). Outcomes are described as relative risk or weighted mean difference with 95% confidence intervals.

Results. Of note, 4482 publications were identified and 14 trials enrolling 2406 patients were included. Tracheostomy within 10 days was not associated with any difference in mortality [risk ratio (RR): 0.93 (0.83–1.05)]. There were no differences in duration of mechanical ventilation [20.19 days (21.13–0.75)], intensive care stay [20.83 days (22.05–0.40)], or incidence of VAP. However, duration of sedation was reduced in the early tracheostomy groups [22.78 days (23.68 to 21.88)]. More tracheostomies were performed in patients randomly assigned to receive early tracheostomy [RR: 2.53 (1.18–5.40)].

Conclusion. We found no evidence that early (within 10 days) tracheostomy reduced mortality, duration of mechanical ventilation, intensive care stay, or VAP. Early tracheostomy leads to more procedures and a shorter duration of sedation.

Keywords: complications; early medical intervention; survival; tracheostomy; ventilator-associated pneumonia

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Tracheostomy is commonly performed in critically ill patients with the objective of increasing comfort and shortening the duration of sedation, mechanical ventilation, and intensive care stay.1 However, the evidence to confirm this benefit is unclear.2

The alternative is prolonged tracheal intubation which carries the risk of respiratory tract injury and other complications including ventilator-associated pneumonia (VAP) and sinusitis.3 4 Tracheostomy is associated with procedure-related complications, including bleeding, hypoxia, oesophageal rupture, tracheal stenosis, tracheal granulomas, and death.5 8 There has been a significant increase in the utilization of tracheostomies especially since the introduction of bedside percutaneous tracheostomy in the mid-1980s.9 11 It has been estimated that up to one-third of patients who undergo mechanical ventilation in the intensive care unit (ICU) will undergo tracheostomy.10 11

As the percutaneous technique has become widely available, the earlier use of tracheostomy has become commonplace.10 11

Consequently, there is ongoing debate about the benefits of early tracheostomy. The objective of this study was to summarize the available evidence through a systematic review and meta-analysis. Specifically, we wished to confirm the effects of tracheostomy within 10 days on critical care resource utilization and short-term mortality compared with late tracheostomy or prolonged intubation.

Methods

Search strategy

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses recommendations for this meta-analysis.
Two authors (P.R. and T.S.) independently performed the electronic searches.

We searched the following databases: Cochrane Central Register of Clinical Trials (CENTRAL) (The Cochrane Library 2013, Issue 13); MEDLINE (January 1950 to February 2014); EMBASE (January 1980 to February 2014); CINAHL (1982 to February 2014); the NHS Trusts Clinical Trials Register and Current Controlled Trials (www.controlled-trials.com); LILACS; KoreaMed; MEDICARIB; INDMD; PANTELEIMON; Ingenta; ISI Web of Knowledge and the National Trials Register to identify all relevant randomized controlled trials available for review using the strategy detailed in Supplementary material, Appendix S1. We searched the bibliographies of reports of randomized trials and any identified reviews. Ongoing clinical trials were identified from the clinicaltrials.gov website, and additional studies of interest were found through Internet searches on Google Scholar and hand searches of bibliographies. We identified relevant studies initially by title then by abstract and finally by full text. All studies in human beings that were published in full text, abstract, or poster form were eligible for inclusion, with no restrictions on publication date, language, or status. The authors resolved any discrepancies by discussion, if necessary.

Selection criteria
We included randomized clinical trials conducted in adult critically ill patients expected to require prolonged mechanical ventilation of between 24 h and 21 consecutive days, for more than 6 h per day. We included trials where one of the groups received early tracheostomy, this must be carried out within 10 days of mechanical ventilation; the alternative is prolonged tracheal intubation with the potential for a tracheostomy to be placed after 10 days.

Unmasked quality assessment on the selected published studies (not abstract reports) was carried out by two investigators, (T.S., P.R.) on composite aspects of study quality. To draw conclusions about the overall risk of bias for an outcome it was necessary to evaluate the trials for major sources of bias, also defined as domains (random sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and other sources of bias).

Data extraction
Data extracted for each eligible study included: author; year of publication; number of subjects; timing of tracheostomy; number of procedures performed in each group; primary and other study outcomes; commercial support; mortality within 60 days; mortality at the longest reported follow-up; incidence of VAP; incidence of complications of procedure (where reported).

If sufficient studies were identified we constructed funnel plots (trial effect vs standard error) to assess for possible publication bias, expressed by asymmetry. In the case of asymmetry we chose to apply the Arcsine–Thompson test, as proposed by Rücker and colleagues. In case of publication bias, we have repeated the analysis by removing the affected trial from the analysis.

Data collection and evaluation
Two authors (P.R., T.S.) independently extracted data (as far as possible) on the basis of an intention-to-treat analysis and entered all data independently into Review Manager (RevMan 5.3.1) after checking for differences.

We used the Mantel–Haenszel model to calculate pooled risk ratios (RRs) and 95% confidence intervals (CIs) with random effects model or fixed-effect model depending on the presence or absence of statistical heterogeneity, respectively. Heterogeneity across studies was measured by $I^2$ statistics examining the percentage of heterogeneity because of variation between studies (0% suggest no heterogeneity; a value between 0 and 25% suggests very low heterogeneity; a value between 25 and 50% suggests low heterogeneity; a value between 50 and 75% suggests moderate heterogeneity; a value of >75% suggests high heterogeneity). When $I^2$ was >50% we applied the random effects model as described before. The mean difference for continuous data was analysed using the inverse variance method.

Outcome measures
The co-primary outcomes were short-term mortality within 60 days, duration of mechanical ventilation, duration of sedation, and duration of intensive care stay. Secondary outcomes were the number of tracheostomy procedures performed, ventilator-associated pneumonia and mortality at longest follow-up.

Results
We identified 4482 potential studies in the initial electronic search. No additional studies were identified after screening of reference lists of potentially eligible studies and previously published systematic reviews (Fig. 1). We included 14 published trials conducted between 1976 and 2011 and including 2406 patients. A detailed description of each trial included can be found in Table 1. Combining the data from the studies showed no significant difference in the relative risk of short-term (up to 60-days) mortality between the groups: 356/1180 (30.2%) deaths in the early tracheostomy vs 391/1226 (31.9%) deaths in the prolonged intubation group, RR: 0.93 (95% CI 0.83, 1.05; $I^2=12\%$) (Fig. 2).

Early tracheostomy was not associated with any significant difference in duration of intensive care stay, duration of mechanical ventilation or incidence of VAP (Figs 3–5). We found that the duration of sedation was significantly shorter in the early tracheostomy group (5 studies, 1425 patients, –2.78 days 95% CI: –3.68, –1.88) (Fig. 6). There was no difference in the long-term outcome, which was assessed at the longest reported time by the studies (14 studies, 2281 patients RR: 0.95 95% CI: 0.87, 1.03 $I^2=0\%$) (Fig. 7). Where data were available, we analysed the number of those patients randomized to an early tracheostomy treatment arm and those who received this allocated treatment. The tracheostomy utilization was significantly higher in the
Funnel plot analysis suggested significant publication bias in the primary outcome in one of the trials. However, upon closer examination of the results as suggested by Sterne and colleagues, we determined this was due to methodological flaws in the Bosel trial, rather than publication bias.

When examining the secondary outcomes, funnel plot analysis suggested reporting bias in duration of mechanical ventilation, duration of intensive care stay and incidence of VAP. In all cases the Rumbak trial proved to be the source of publication bias and when we removed it from the analysis, the statistical heterogeneity decreased sufficiently to allow us to use the fixed-effect model. We believe this trial is indeed affected by publication bias, as we have identified several registered studies from the same period, which have never been published in full.

**Discussion**

The principal finding of this analysis was that tracheostomy within 10 days of onset of mechanical ventilation had no effect on short-term mortality, duration of mechanical ventilation, or duration of intensive care stay. Early tracheostomy was associated with a reduction in duration of sedation. Secondary outcomes were also similar in the two groups without significant differences in long-term mortality and rate of VAP. Significantly more tracheostomy procedures were carried out in the early tracheostomy cohort.

There were 14 studies with more than 2400 participants eligible for inclusion in this meta-analysis. One study was identified by our funnel plot assessment as a potential source of publication bias, and this had been directly sponsored by industry. We identified several registered randomized clinical trials from the same period, which had not been completed or published in full, supporting this suggestion. Most of the included trials were small, single centre and vulnerable to bias. Due to the nature of the intervention appropriate blinding is impossible and this creates a risk of bias even in the large multicentre trials.

We found that short-term (up to 60 days) and long-term (up to 2 yr) mortality was not significantly different between the two groups. The funnel plot suggested publication bias caused by the Bosel study, however even when this was included in the analysis, we found the result was robust across the studies without significant heterogeneity between the trials (Figs 1 and 2). All deaths in the Bosel study were attributed to the progression of the neurological sequelae in both groups and the authors have concluded that the timing of tracheostomy is unlikely to have influenced outcome.

Although there was some heterogeneity among trial results with respect to mortality, all trials included critically ill patients where various pathophysiological disturbances led to a common pathway of prolonged respiratory failure. Consequently, we believe that there is a good biological rationale to perform a broad meta-analysis, which also considerably increases the generalizability and usefulness of the review.

Based on the results, it is difficult to explain how the timing of an intervention aimed at reduction of potential long-term complications of intensive care would be able to directly influence mortality.

It has been postulated that early tracheostomy may reduce ICU resource utilization, namely length of mechanical ventilation and facilitate earlier discharge to the word or in the USA, to long-term care facility, hence reducing length of ICU and acute hospital stay.

Perhaps surprisingly, we could not find this effect in our meta-analysis. The duration of mechanical ventilation was identical in the two groups as was length of ICU stay.

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**Fig 1** Preferred PRISMA flow diagram detailing search strategy and identification of studies used in data synthesis.
<table>
<thead>
<tr>
<th>Study</th>
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<th>Outcomes</th>
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<tr>
<td>Barquist and colleagues</td>
<td>Prospective, randomized trial</td>
<td>Adult ventilator dependent patients admitted to a trauma centre</td>
<td>The insertion of an early tracheostomy</td>
<td>Days on mechanical ventilation, days on mechanical ventilation after tracheostomy, length of ICU stay after tracheostomy, incidence of VAP, tracheostomy complications, survival</td>
</tr>
<tr>
<td>Blot and colleagues</td>
<td>Prospective, randomized trial</td>
<td>ICU patients ventilated for less than 4 days, but expected to be ventilated more than 7 days</td>
<td>The insertion of a tracheostomy before the fourth calendar day of mechanical ventilation, referred to as ‘early’ in this study. Late tracheostomy was one placed after 14 days of mechanical ventilation</td>
<td>Mortality, rate of VAP, length of ICU stay, duration of mechanical ventilation, type of mechanical ventilation needed, weaning phases, level of sedation, complications, cost</td>
</tr>
<tr>
<td>Bosel and colleagues</td>
<td>Prospective, randomized trial</td>
<td>Patients were 18 yr and over, had a diagnosis of non-traumatic intracerebral haemorrhage, subarachnoid haemorrhage or acute ischaemic stroke and required mechanical ventilation for at least 14 days</td>
<td>The insertion of an early tracheostomy</td>
<td>Mortality, length of ICU stay, duration of mechanical ventilation, type of mechanical ventilation needed, weaning phases, level of sedation, complications, cost</td>
</tr>
<tr>
<td>Boudker and colleagues</td>
<td>Randomized, controlled trial carried out in 1 Moroccan ICU</td>
<td>A sample size of 62 head injury ICU patients with a GCS &lt; 8 on Day 5 of mechanical ventilation was available for analysis</td>
<td>Early tracheostomy vs prolonged intubation. Early tracheostomy was carried out on the fifth or sixth day. No mention of the possibility of a tracheostomy being carried out on a patient in the prolonged intubation group</td>
<td>Length of mechanical ventilation, incidence of pneumonia, mortality</td>
</tr>
<tr>
<td>Bylappa and colleagues</td>
<td>Prospective, randomized trial</td>
<td>ICU patients requiring prolonged mechanical ventilation for 10 days</td>
<td>The insertion of an early tracheostomy</td>
<td>Duration of mechanical ventilation; complications; duration of hospital stay</td>
</tr>
<tr>
<td>El-Naggar and colleagues</td>
<td>Prospective, randomized trial. Randomization occurred on Day 3. Early tracheostomy was defined as a tracheostomy inserted between Days 5 and 7 of mechanical ventilation; prolonged intubation was defined as prolonged tracheal intubation with a tracheostomy inserted between Days 8 and 15 of mechanical ventilation. Randomization occurred at Day 4 if a patient was expected to require mechanical ventilation for another 6 days</td>
<td>Adults requiring prolonged mechanical ventilation</td>
<td>The insertion of an early tracheostomy</td>
<td>The patient’s epidemiological variables; daily pulmonary functions, severity of respiratory infections, and scores of post-intubation airway lesions</td>
</tr>
<tr>
<td>Rumbak and colleagues</td>
<td>Randomized, controlled trial</td>
<td>ICU patients projected to need ventilation for &gt; 14 days</td>
<td>Early vs late tracheostomy. Early tracheostomy was carried out within 48 h of mechanical ventilation. Late tracheostomy was carried out within 14 – 16 days of mechanical ventilation</td>
<td>Mortality, rate of VAP, length of ICU stay, duration of mechanical ventilation, duration of sedation, duration of inotropic support, organisms causing pneumonia</td>
</tr>
<tr>
<td>Saboori and colleagues</td>
<td>Randomized controlled single centre trial</td>
<td>ICU patients admitted after head trauma</td>
<td>Early tracheostomy on the fourth day of ICU admission, late tracheostomy on Day 14</td>
<td>Mortality, rate of VAP, duration of mechanical ventilation, length of ICU stay</td>
</tr>
<tr>
<td>Saffle and colleagues</td>
<td>Prospective, randomized trial. Early tracheostomy was defined as a tracheostomy inserted within one working day of randomization; prolonged intubation was defined as continued tracheal intubation with a tracheostomy inserted on Day 14 if clinically indicated</td>
<td>ICU patients ventilated for less than 4 days, but expected to be ventilated more than 7 days</td>
<td>The insertion of an early tracheostomy</td>
<td>Rate of pneumonia, duration of mechanical ventilation, incidence of VAP, complications</td>
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</table>

*Continued*
We could not find any effect of a protocolized weaning process in our sensitivity analysis between the early tracheostomy and prolonged intubation groups when we grouped together only those studies where a weaning protocol was used (data not shown). Our results suggest, that in the presence of a structured approach to weaning from mechanical ventilation, the type of breathing tube is not a determinant of outcome.

The duration of sedation was significantly shorter in the early tracheostomy.

Less sedative use was a uniform finding among all studies, which reported this outcome, however, the heterogeneity between the trials was again statistically significant. This is a concern and our data should be interpreted with caution. It could partly be explained by the different sedation protocols and pharmacological agents used in the various trials. Only two of the trials described the use of a protocol driven sedation and analgesia regime and the others only refer to guidelines for sedative use. It is important to emphasize that there is a gulf between perceived and actual sedation practices in ventilated patients, with only a fraction of evidence-based recommendations currently used in the majority of ICUs. It has been shown that nurse-led protocol driven sedation, analgesia and delirium management can significantly reduce the

### Table 1 Continued

<table>
<thead>
<tr>
<th>Description</th>
<th>Participants</th>
<th>Interventions</th>
<th>Outcomes</th>
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</thead>
<tbody>
<tr>
<td>Sugerman and colleagues (1997)</td>
<td>Adult patients who were hospitalized within 24 h of acute burns injury, requiring on-going mechanical ventilation</td>
<td>The insertion of an early tracheostomy</td>
<td>Mortality, duration of mechanical ventilation, length of stay</td>
</tr>
<tr>
<td>Methods</td>
<td>Multicentre, prospective, randomized trial. Patients were anticipated that they would require mechanical ventilation for at least 7 days. Early tracheostomy was defined as a tracheostomy inserted between Days 3 and 5; prolonged intubation was defined as a tracheostomy inserted, if clinically relevant, after 10–14 days</td>
<td>Multi-centre, prospective, randomised controlled trial</td>
<td></td>
</tr>
<tr>
<td>Participants</td>
<td>Head trauma, non-head trauma, and critically ill non-trauma patients requiring prolonged mechanical ventilation</td>
<td>The insertion of an early tracheostomy</td>
<td>Mortality, length of stay on the ICU, incidence of VAP, evidence of short- or long-term pharyngeal, laryngeal, or tracheal injury.</td>
</tr>
<tr>
<td>Terragni and colleagues (2010)</td>
<td>Patients requiring prolonged mechanical ventilation</td>
<td>Early tracheostomy vs late tracheostomy. Early tracheostomy was defined as one carried out within 6–8 days of mechanical ventilation. A late tracheostomy occurred after 15 days of mechanical ventilation</td>
<td>The primary outcome was the incidence of VAP. The secondary outcomes were Day 28: number of ventilator-free days, number of ICU-free days, mortality</td>
</tr>
<tr>
<td>Methods</td>
<td>Randomised controlled trial performed in 12 Italian ICUs</td>
<td>Number of days alive and breathing without ventilatory support. Secondary end points: number of ventilator-free Days at 28 and 90 days (based on data through 28 and 90 days); 28-, 60-, and 90-day mortality rates; duration of mechanical ventilation and length of ICU and hospital stay, sedation-free days at Day 28, the number of tracheal prosthesis-free days at Day 60; frequencies of unscheduled extubations, decannulations and reintubations or recannulations; 7-, 14-, 21-, and 28-day sequential organ function assessment scores in the ICU; duration of vasopressor and renal replacement therapy, rate of VAP</td>
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<tr>
<td>Trouillet and colleagues (2011)</td>
<td>Patients who still required mechanical ventilation 4 days after operation after cardiac surgery</td>
<td>Immediate tracheostomy (early tracheostomy group) vs prolonged mechanical ventilation with a possibility of a tracheostomy after Day 15 of randomization</td>
<td>Number of days alive and breathing without ventilatory support. Secondary end points: number of ventilator-free Days at 28 and 90 days (based on data through 28 and 90 days); 28-, 60-, and 90-day mortality rates; duration of mechanical ventilation and length of ICU and hospital stay, sedation-free days at Day 28, the number of tracheal prosthesis-free days at Day 60; frequencies of unscheduled extubations, decannulations and reintubations or recannulations; 7-, 14-, 21-, and 28-day sequential organ function assessment scores in the ICU; duration of vasopressor and renal replacement therapy, rate of VAP</td>
</tr>
<tr>
<td>Methods</td>
<td>Prospective randomized controlled single center trial</td>
<td>Patients requiring prolonged mechanical ventilation with a possibility of a tracheostomy after Day 15 of randomization</td>
<td>Number of days alive and breathing without ventilatory support. Secondary end points: number of ventilator-free Days at 28 and 90 days (based on data through 28 and 90 days); 28-, 60-, and 90-day mortality rates; duration of mechanical ventilation and length of ICU and hospital stay, sedation-free days at Day 28, the number of tracheal prosthesis-free days at Day 60; frequencies of unscheduled extubations, decannulations and reintubations or recannulations; 7-, 14-, 21-, and 28-day sequential organ function assessment scores in the ICU; duration of vasopressor and renal replacement therapy, rate of VAP</td>
</tr>
<tr>
<td>Young and colleagues (2013)</td>
<td>ICU patients estimated to require mechanical ventilation for more than 14 days</td>
<td>Late tracheostomy was one placed within 4 days of mechanical ventilation. A late tracheostomy was one placed on Day 10 or later if still clinically relevant</td>
<td>Mortality at ICU and hospital discharge and at 1 and 2 yr, length of ICU stay, antibiotic-free days</td>
</tr>
<tr>
<td>Methods</td>
<td>Randomized controlled trial performed in 72 centres within the UK</td>
<td>The primary outcome was the incidence of VAP. The secondary outcomes were: mortality at ICU and hospital discharge and at 1 and 2 yr, length of ICU stay, antibiotic-free days</td>
<td></td>
</tr>
<tr>
<td>Participants</td>
<td>Patients requiring mechanical ventilation for more than 14 days</td>
<td>The primary outcome was the incidence of VAP. The secondary outcomes were: mortality at ICU and hospital discharge and at 1 and 2 yr, length of ICU stay, antibiotic-free days</td>
<td></td>
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<tr>
<td>Zheng and colleagues (2012)</td>
<td>ICU patients estimated to require mechanical ventilation for more than 14 days</td>
<td>Late tracheostomy was one placed within 4 days of mechanical ventilation. A late tracheostomy was one placed on Day 10 or later if still clinically relevant</td>
<td>The primary outcome was the number of ventilator-free days at Day 28 after randomization. The secondary outcomes were: sedation-free and ICU-free days, successful weaning and ICU discharge rate, incidence of VAP at Day 28, mortality at 60 days</td>
</tr>
</tbody>
</table>
unnecessary over sedation and improve patient comfort regardless of the type of breathing tube used for mechanical ventilation.\textsuperscript{31} Importantly, long-term cognitive impairment does not seem to be associated with reduction of sedative use and it is uncertain if reduced sedation is beneficial in reducing the incidence and severity of ICU delirium.\textsuperscript{31, 32} Based on our results it is impossible to ascertain if early tracheostomy is indeed the main reason for the reduction of sedative exposure, or whether other strategies could achieve the same results. We have investigated whether important complications usually associated with a worse outcome, for example VAP rates, are different between the two groups. Randomized controlled trials conducted at the beginning of the millennium and retrospective case–control studies suggested that early tracheostomy could reduce the rate of VAP.\textsuperscript{14, 33, 34} According to our analysis, the incidence of VAP was similar in the two groups, but the heterogeneity between the trials was statistically significant (Fig. 5). This heterogeneity could be
explained by the very different tools and definitions used to describe VAP across the studies. There was insufficient patient level data available to use a standardized VAP definition across the studies. It is also unclear from the published trials what, if any, evidence-based procedures were used to try to prevent VAP. It has been shown that the systematic adoption of these methods could significantly reduce the rate of VAP, regardless of the type of tube used for mechanical ventilation.35 The results were too diverse for us to be able to group the studies according to their chosen VAP definition, and consequently this result should be interpreted with caution.

Tracheostomy utilization was significantly higher in the early tracheostomy compared with the prolonged intubation group. Only 417 of the 1214 patients randomized into the prolonged intubation group eventually received tracheostomy (Fig. 8), as opposed to 1027 of the 1166 patients in the early tracheostomy group. While in the early tracheostomy group the main reason for not performing the procedure was cardio-respiratory instability, in the prolonged intubation group in the main reason for not performing the procedure was cardio-

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Early tracheostomy</th>
<th>Prolonged intubation</th>
<th>Mean difference</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Biolt et al 2008</td>
<td>12.5</td>
<td>67.5</td>
<td>61</td>
<td>13.75</td>
</tr>
<tr>
<td>Young et al 2013</td>
<td>5</td>
<td>4.44</td>
<td>455</td>
<td>7</td>
</tr>
<tr>
<td>Trouillet et al 2011</td>
<td>6.4</td>
<td>5.9</td>
<td>109</td>
<td>9.6</td>
</tr>
<tr>
<td>Bosel 2012</td>
<td>7.19</td>
<td>3.4</td>
<td>29</td>
<td>11</td>
</tr>
<tr>
<td>Zheng et al 2012</td>
<td>7.16</td>
<td>0.8</td>
<td>58</td>
<td>10.5</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>712</td>
<td></td>
<td>713</td>
<td>100.0%</td>
</tr>
<tr>
<td>Total events</td>
<td>203</td>
<td></td>
<td>246</td>
<td></td>
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</tbody>
</table>

Heterogeneity. Tau² = 0.04; Chi² = 18.20, df = 7 (P = 0.01); I² = 62%
Test for overall effect. Z = 1.12 (P = 0.26)
because there was an unintended violation of the study protocol. Despite this significant difference in the rate of procedure, the overall outcome and resource utilization was similar in both groups (Fig. 2). This suggests that patient outcomes are the same in the prolonged intubation group without the added risk of performing a surgical procedure early in their clinical course. The implications of our findings are significant: out of 100 mechanically ventilated patients on an ICU which uses an early tracheostomy policy, routinely inserting tracheostomies before Day 10 of mechanical ventilation means that 54 more patients could receive a tracheostomy without any real benefit in outcome. This excess activity could result in immediate, short- and long-term complications. Recent studies found that percutaneous dilatational tracheostomy procedures carry a 0.17–0.6% chance of fatal outcome. As this is a common procedure on ICUs on the western hemisphere, the potential of reducing harm by adopting a more conservative approach to management is considerable. While the incidence of immediate complications such as bleeding, pneumothorax or death attributed to the procedure was similar in both groups, there were only occasional reports on long-term functional outcomes in terms of incidence of tracheal stenosis, tracheomalacia, or difficulty in swallowing. Incidence rates for tracheostomy related short-term complications such as desaturation, bleeding, hypotension, and need for increased ventilator support were similar at around 17% in both groups (data not shown), hence we postulate that the unwarranted procedures could also lead to avoidable harm.

It remains possible, that early tracheostomy is associated with undetected harm or benefit in the general ICU population. We believe that our approach offers significant advantages over previously published work investigating the effects of the timing of the procedure in the critically ill.

Compared with the Cochrane meta-analysis of Silva and colleagues published in 2012, we have included 14 trials, 5 of which were published since the last date of the literature search of the Silva study, with the inclusion of an additional 1388 patients. Silva and colleagues only summarized four studies, including one, which had a quasi-randomized design. This meta-analysis only examined whether early vs late tracheostomy is associated with better outcomes, hence excluded a number of clinically important studies, which compared early tracheostomy with prolonged intubation. Because of the restrictive nature of their search strategy it is not surprising that Silva and colleagues found insufficient data to successfully evaluate the procedure.2

Similarly, the very recent meta-analysis by Huang and colleagues only included nine studies. Compared with their analysis we have included five more studies including the very recently concluded Bosel trial. The main findings of Huang and colleagues are very similar to ours in terms of short-term mortality, length of mechanical ventilation and length of ICU stay. Importantly, they have also noted that the Rumbak study was a source of statistical heterogeneity, but contrary to our assessment, they did not find it to be a source of publication bias.39

Our meta-analysis has wider inclusion criteria with studies representing the whole critical care spectrum, does not have language or geographic restrictions and investigates more diverse clinical outcomes including length of sedation. Our principle aim was to investigate if there is a difference between outcomes if early tracheostomy is performed as opposed to prolonged intubation with a possibility of late tracheostomy. This question more closely describes the dilemma encountered in usual critical care practice and we believe our results are generalizable over a wide range of clinical scenarios. The larger sample size enables us to present clinically important findings, which can direct clinical practice and further research.

Our meta-analysis has several limitations. First, as a meta-analysis our research is retrospective and subject to the methodological soundness of the individual studies. We have tried to keep the probability of bias to a minimum by developing a detailed protocol a priori, carrying out a thorough search for published and unpublished data, and using explicit criteria for study selection, data collection, and data analysis. As a result, we consider that our robust approach has resulted in recommendations directly applicable to clinical practice.

Secondly, our review includes trials from 1976 to 2012. There has been an enormous change in clinical practice during this period, which could account for the negative findings. However
when we grouped the trials according to their recruitment period, we did not find any significant differences in the results between trials conducted before or after the millennium (data not shown).

Thirdly, there is little guidance on the prediction of prolonged mechanical ventilation and the timing of tracheostomy insertion is based on this assessment. The clinical judgement of the attending clinician necessary to provide an estimate for the length of mechanical ventilation carries the risk of selection bias. Overall, all of the included studies have different definitions of early tracheostomy and prolonged mechanical ventilation. Consequently, we can only provide data on the safety and effectiveness of early tracheostomy on reduction of mortality compared with standard treatment.

It is clear that continued research is needed to find appropriate tools to predict the duration of mechanical ventilation on the ICU.

Future research should be aimed at standardizing the definitions of early tracheostomy and examining if it would be beneficial in certain patient groups. The safety and late complication rates of tracheostomy are poorly understood and further efforts should be directed to examine the wider socio-economic consequences of the procedure.

Conclusions
Despite hypothesized and plausible clinical benefits, our analysis suggests that early tracheostomy does not carry any mortality advantage in the heterogeneous patient population included in this work. According to our data, early tracheostomy does not help to reduce length of ICU stay or incidence of VAP. There appears to be a reduction in the duration of sedative use when performing early tracheostomy, although this is not accompanied by a reduction in duration of mechanical ventilation. Our results suggest that the use of early tracheostomy leads to unnecessarily high procedural rate with associated increased morbidity and possibly financial cost. This leads us to suggest that tracheostomy before Day 10 of mechanical ventilation should be avoided. Further research with adequately powered and methodologically sound clinical trials should address the questions if any particular subgroups of critically ill patients would benefit from the procedure and to understand the longer term effects of the intervention.

Supplementary material
Supplementary material is available at British Journal of Anaesthesia online.

Authors’ contributions
T.S.: study design, data collection, data analysis and interpretation of the results, and writing of the paper; P.R.: study design, data collection, data analysis, and writing of the first draft of the paper; A.R.W.: data analysis, interpretation of the results, and writing of the first draft of the paper; J.E.H.: study design, interpretation of the results, and writing of the paper.

Declaration of interest
None declared.

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