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COMPARISON OF EARLY VERSUS LATE TRACHEOSTOMY IN PATIENTS WITH PROLONGED MECHANICAL VENTILATION ON MORTALITY AND COMPLICATIONS : A SYSTEMATIC REVIEW OF RANDOMIZED CONTROLLED TRIALS AND PRIMARY STUDIES

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ABSTRACT

Introduction: Prolonged invasive mechanical ventilation is a major determinant of morbidity, mortality, and resource consumption in the ICU. Tracheostomy is performed to facilitate ventilator weaning, reduce sedation requirements, and decrease laryngotracheal injury; however, its optimal

timing remains debated. This study compares the effects of early tracheostomy (ET) and late tracheostomy (LT) on mortality and complications.

Methods: Systematic review conducted in accordance with PRISMA 2020. Included designs: RCTs, cohort, case-control, cross-sectional, and observational studies; systematic reviews were excluded from the characteristics table but used as comparators. Risk of bias: RoB 2 and NOS. Certainty of evidence: GRADE. Structured narrative and semi-quantitative synthesis.

Results: Twenty-three primary studies (>33,000 patients; 12 RCTs, 11 observational) were included. ET did not reduce 30-day mortality (TracMan: 30.8% vs 31.5%; ARR 0.7%; 95% CI -5.4 to 6.7). ET consistently improved process outcomes: shorter sedation duration (MD -2.78 days; 95% CI -3.68 to -1.88), increased ventilator-free days (+2.12 days; 95% CI 0.94-3.30), shorter duration of mechanical ventilation (-2.77 days; 95% CI -5.10 to -0.44), and shorter ICU length of stay (-6.36 days; 95% CI -9.84 to -2.88). VAP incidence decreased in high-risk subpopulations (OR 0.60-0.86). Procedural complications did not differ (5.5% vs 7.8%). The proportion of patients who underwent tracheostomy was markedly higher with ET (91.9% vs 44.9%; OR 16.1).

Discussion: The discordance between randomized and observational evidence is explained by immortal time bias and confounding by indication. Failure of clinical prediction of the need for prolonged ventilation is the principal determinant of why ET fails to demonstrate a mortality benefit. Bayesian analysis indicates a 99% posterior probability of benefit for short-term mortality, suggesting that "no benefit" conclusions based on frequentist testing may be overly conservative. In neurological and severe trauma populations, the benefit-risk balance shifts in favour of ET.

Conclusion: ET confers no mortality benefit in the general ICU population, but consistently improves sedation duration, ventilator-free days, duration of ventilation, and ICU length of stay without an increase in complications. An ET strategy should be applied selectively in patients with a high probability of requiring ventilation >14 days—particularly severe brain injury, severe stroke, high cervical spinal cord injury, and severe trauma—rather than as a universal policy.

Keywords: early tracheostomy; late tracheostomy; prolonged mechanical ventilation; mortality; ventilator-associated pneumonia; intensive care; systematic review

INTRODUCTION

Background

Invasive mechanical ventilation is the most frequently performed life-support intervention in the intensive care unit. Approximately one-third to one-half of patients admitted to the ICU require ventilatory support, and a proportion of them experience weaning failure and consequently require prolonged support. Prolonged translaryngeal intubation gives rise to a number of interrelated pathophysiological consequences: laryngeal and tracheal mucosal injury due to cuff pressure and endotracheal tube friction, high sedation requirements to maintain tube tolerance, impaired clearance of bronchial secretions, microbial colonisation of the endotracheal tube biofilm, and impediments to early mobilisation and rehabilitation. This cascade of consequences in turn prolongs the duration of ventilation, increases the risk of nosocomial infection, and raises the burden of care costs.^{24,25,43}

Tracheostomy was introduced as a solution to interrupt this cascade. Theoretically, tracheostomy reduces anatomical dead space and airway resistance, improves respiratory mechanics, allows a drastic reduction in sedation requirements, facilitates bronchial hygiene and oral nutrition, and permits earlier mobilisation and verbal communication. Collectively, these benefits are expected to accelerate ventilator weaning and reduce mortality. However, tracheostomy is not a risk-free intervention: the procedure carries risks of bleeding, pneumothorax, posterior tracheal wall injury, stomal infection, and cannula dislodgement, as well as late complications such as tracheal stenosis and tracheoinnominate fistula.^{24,40,41,42}

The central question that has not yet been satisfactorily answered is when tracheostomy should be performed. If the benefits of tracheostomy are cumulative over time, early performance should maximise those benefits. Conversely, if most patients who appear to require prolonged ventilation can in fact be extubated within one to two weeks, an early strategy will expose a large number of patients to unnecessary procedural risk. This debate has persisted since the 2005 meta-

analysis by Griffiths et al., which reported a reduction in the duration of ventilation of 8.5 days and in ICU length of stay of 15.3 days in the early group, with no difference in mortality or pneumonia.²⁴

Since then, several large randomized controlled trials have been published, including the trial by Terragni et al. in 419 Italian ICU patients, the trial by Trouillet et al. in 216 patients after cardiac surgery, the TracMan trial in 909 patients in the United Kingdom, the SETPOINT and SETPOINT2 trials in patients with severe stroke, and the TTCOV19 trial in patients with COVID-19. Successively, these trials failed to demonstrate a mortality advantage for the early strategy, although some reported improvements in secondary outcomes such as sedation duration and patient comfort. On the other hand, large-scale observational evidence in populations with traumatic brain injury, multiple trauma, spinal cord injury, and COVID-19 has consistently reported a large and significant advantage of early tracheostomy, creating a methodological discordance that requires systematic explanation.^{3,4,8,10,11,14,21,34,36}

In the Indonesian context, this question has particular practical relevance. Limited ICU capacity, a low ratio of intensive care beds to population, ventilator shortages during surge periods, and the cost burden of intensive care make every ventilator day and every ICU day a high-value resource. If early tracheostomy proves to significantly shorten the duration of ventilation and ICU length of stay without increasing mortality or complications, its implications for the efficiency of the national health-care system would be substantial. The experience of the COVID-19 pandemic in Spain demonstrated that optimising tracheostomy timing can increase ICU availability without increasing mortality.¹⁶

Therefore, a comprehensive systematic review is required that not only summarises randomized evidence but also integrates observational evidence across populations, explicitly maps the sources of heterogeneity, and simultaneously evaluates more than ten outcome domains. Such a review is presented in this manuscript.¹⁻⁴⁴

Research Questions

- Does early tracheostomy reduce short-term and long-term mortality compared with late tracheostomy in patients receiving prolonged mechanical ventilation?
- Does early tracheostomy reduce the incidence of ventilator-associated pneumonia and other infectious complications?
- How does tracheostomy timing affect the duration of mechanical ventilation, ventilator-free days, ICU length of stay, hospital length of stay, and sedation duration?
- What is the profile of procedural and laryngotracheal complications with each strategy?
- How does tracheostomy timing affect long-term functional outcomes and quality of life?
- To what extent does an early tracheostomy strategy result in overtreatment owing to clinicians' inaccurate prediction of the need for prolonged ventilation?

Research Objectives

General Objective

To systematically analyse the comparative effectiveness and safety of early tracheostomy versus late tracheostomy in patients receiving prolonged invasive mechanical ventilation, with emphasis on mortality and complication outcomes.¹⁻²³

Specific Objectives

- To assess the effect of tracheostomy timing on ICU mortality, 28–30-day mortality, 60–90-day mortality, and long-term mortality.
- To assess the effect of tracheostomy timing on the incidence of ventilator-associated pneumonia and nosocomial pneumonia.
- To quantify differences in the duration of mechanical ventilation, ventilator-free days, ICU length of stay, and hospital length of stay.
- To quantify differences in the duration and intensity of sedation, as well as the occurrence of delirium and unplanned extubation.
- To evaluate the incidence of tracheostomy procedure-related complications and long-term laryngotracheal complications.

- To evaluate long-term functional outcomes, health-related quality of life, and neurological outcomes.
- To assess the proportion of patients who actually underwent tracheostomy under each strategy as an indicator of overtreatment.
- To assess the risk of bias, heterogeneity, and certainty of evidence across the entire available literature.

Significance of the Study

Theoretical Significance

This study contributes to the pathophysiological understanding of the relationship between the duration of translaryngeal intubation, sedation burden, airway injury, and clinical outcomes. The cross-design synthesis also makes a methodological contribution by explicitly mapping how immortal time bias and confounding by indication can generate effect estimates in opposite directions between observational studies and randomized controlled trials addressing an identical clinical question.¹⁻²³

Practical Significance

For intensivists, surgeons, anaesthesiologists, and related specialists, this review provides an evidence base for individualised decision-making on tracheostomy timing according to population characteristics. For hospital management and policymakers, it provides quantitative estimates of potential savings in ventilator days and ICU days. For researchers, it identifies evidence gaps that should be addressed by future randomized controlled trials, particularly in subpopulations with predictable ventilation requirements.^{16,31}

Research Hypotheses

The null hypothesis (H0) states that there is no significant difference between early tracheostomy and late tracheostomy in mortality and complications among patients receiving prolonged mechanical ventilation. The alternative hypothesis (H1) states that early tracheostomy is associated with significant improvement in at least some clinical outcomes. Specifically, the working hypotheses tested are as follows.

- H1a: Early tracheostomy does not significantly reduce short-term mortality in the general ICU population (the null hypothesis is accepted for this domain).
- H1b: Early tracheostomy significantly reduces the duration of mechanical ventilation and ICU length of stay.
- H1c: Early tracheostomy significantly reduces sedation duration.
- H1d: Early tracheostomy reduces the incidence of ventilator-associated pneumonia in high-risk subpopulations (neurological and trauma).
- H1e: Early tracheostomy does not significantly increase procedural complications or laryngotracheal stenosis.
- H1f: An early tracheostomy strategy significantly increases the proportion of patients undergoing tracheostomy compared with a late tracheostomy strategy.

Research Gap

Several systematic reviews and meta-analyses have been published on this topic, yet each has unresolved limitations. First, most syntheses are restricted to randomized controlled trials, so that the number of available studies ranges from five to twenty-one, with inadequate statistical power; the trial sequential analysis in the review by Villemure-Poliquin et al. explicitly concluded that the primary mortality analysis was most likely underpowered. Second, the operational definition of "early" varies widely from less than 48 hours to less than 14 days, so that pooling of effects produces unresolved clinical heterogeneity. Third, existing syntheses tend to separate neurological from non-neurological populations without comparing them within a single analytical framework. Fourth, the outcomes analysed are generally limited to four or five domains, so that important outcomes such as weaning success, diaphragmatic function, six-month functional outcome, quality of life, and the proportion of overtreatment are rarely discussed in an integrated manner.²⁴⁻³⁹

The fifth and most substantial gap is the absence of a synthesis that systematically confronts observational evidence with randomized evidence while providing a methodological explanation for their discordance. The correspondence by Hoshino et al. on the CENTER-TBI

study highlighted that immortal time bias is inherent to observational studies of tracheostomy timing, because patients in the late tracheostomy group by definition cannot die before the procedure is performed. Without explicit mapping of this bias, clinicians risk interpreting observational effect sizes as causal effects.^{14,34}

Novelty

This systematic review offers several novel elements. First, it integrates 23 primary studies across designs — 12 randomized controlled trials and 11 prospective or retrospective observational studies — encompassing more than 33,000 patients across a broad spectrum of populations: general medical ICU, surgical ICU, post-cardiac surgery, adult and paediatric traumatic brain injury, severe stroke, multiple trauma, burns, and COVID-19. Second, it analyses 15 outcome domains simultaneously, far exceeding the four to five domains typically analysed in previous syntheses. Third, it applies dual risk-of-bias assessment with RoB 2 for randomized trials and the Newcastle–Ottawa Scale for observational studies within a single integrated table.¹⁻²³

Fourth, this review explicitly positions Bayesian evidence as a comparator to frequentist conclusions, thereby allowing a more informative probabilistic interpretation for clinical decision-making. Fifth, it presents an analysis stratified by timing threshold — less than 4 days, 4–7 days, 8–10 days, and 11–14 days — to identify whether an optimal time window exists, an approach previously undertaken only separately in COVID-19 populations. Sixth, this review is written in a formal medical-scientific register and places its findings within the Indonesian health-care context, so that it can be directly utilised in specialist training and in the development of national clinical practice guidelines.^{16,33,39}

METHODS

Study Design and Protocol

This study is a comprehensive systematic review of randomized controlled trials and other primary studies. Its conduct and reporting followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guideline, comprising a 27-item checklist covering the title, structured abstract, rationale, objectives, eligibility criteria, information sources, search

strategy, selection process, data extraction process, list of variables, risk-of-bias assessment, effect measures, synthesis methods, reporting bias assessment, certainty-of-evidence assessment, and reporting of results, discussion, and other information. The study protocol was developed a priori before data extraction, including definitions of the population, intervention, comparator, outcomes, and study design (PICOS), the complete search strategy, and plans for subgroup and sensitivity analyses.²⁴⁻³²

The choice of a systematic review design without pooled quantitative meta-analysis for all domains was based on methodological considerations. Clinical heterogeneity across studies was very high, particularly in the definition of the early tracheostomy timing threshold, which ranged from 48 hours to 14 days; in population characteristics, which encompassed medical, surgical, neurological, trauma, and infectious disease ICUs; and in non-uniform outcome definitions such as ventilator-associated pneumonia. Pooling effects under such heterogeneity risks producing mean estimates that are not representative of any population. Therefore, the synthesis was conducted in a structured narrative and semi-quantitative manner, presenting effect estimates from each study with confidence intervals, accompanied by comparison with pooled estimates reported in previous meta-analyses.^{25,26,27,29,30,31,32}

Eligibility Criteria (PICOS)

Table 1. PICOS framework and study eligibility criteria

Component	Description
Population (P)	Adult and paediatric patients receiving invasive mechanical ventilation via an endotracheal tube in the intensive care unit who were anticipated or proven to require prolonged ventilation. Includes medical ICU, surgical ICU, trauma ICU, neurological/neurosurgical ICU, post-cardiac surgery, burn, and COVID-19 patients.
Intervention (I)	Early tracheostomy (ET), i.e., percutaneous dilatational or open surgical tracheostomy performed at an early timing threshold according to each

Component	Description
	study's definition (ranging from ≤ 48 hours to ≤ 14 days from intubation or ICU admission).
Comparison (C)	Late tracheostomy (LT) or prolonged translaryngeal intubation, i.e., tracheostomy performed at a later timing threshold (generally ≥ 10 to ≥ 15 days) if still indicated, or a conventional weaning and extubation strategy.
Outcome (O)	Primary outcomes: mortality (ICU, 28–30 days, 60–90 days, long-term) and complications (procedural and laryngotracheal). Secondary outcomes: VAP, duration of mechanical ventilation, ventilator-free days, ICU length of stay, hospital length of stay, sedation duration, weaning success, functional outcome, quality of life, unplanned extubation, diaphragmatic function, and the proportion of patients undergoing tracheostomy.
Study design (S)	Included: randomized controlled trials (RCTs), cohort studies (prospective and retrospective), case-control studies, cross-sectional studies, and other observational studies. Systematic reviews and meta-analyses were NOT included in the study characteristics table but were used as comparators in the outcome analyses and discussion.

ICU = intensive care unit; VAP = ventilator-associated pneumonia; RCT = randomized controlled trial.

Inclusion Criteria

- Studies directly comparing early tracheostomy with late tracheostomy or prolonged intubation.
- Randomized controlled trial, cohort, case-control, cross-sectional, observational, prospective, or retrospective study design.
- Reporting at least one relevant outcome quantitatively.
- Patient population receiving invasive mechanical ventilation.

- Full text accessible and published in a peer-reviewed journal.

Exclusion Criteria

- Systematic reviews, meta-analyses, narrative reviews, editorials, letters to the editor, and commentaries (excluded from the study characteristics table but still reviewed for the discussion).
- Case reports and case series without a comparison group.
- Studies comparing tracheostomy techniques (percutaneous versus surgical, or ultrasound-guided versus bronchoscopy-guided) without comparing timing.
- Animal studies, in vitro studies, and modelling studies.
- Studies that did not stratify outcomes by tracheostomy timing.
- Research protocols without outcome data.

Search Strategy

Keywords used in this study based on PICO:

PICO Element	Keyword 1	Keyword 2	Keyword 3
P (Population)	Prolonged mechanical ventilation	ICU patients	Critically ill
I (Intervention)	Early tracheostomy	Percutaneous dilational tracheostomy	Early vs late tracheostomy
C (Comparison)	Late tracheostomy	Prolonged translaryngeal intubation	Standard weaning
O (Outcome)	Mortality	Ventilator-associated pneumonia	ICU length of stay

The Boolean MeSH keywords inputted on databases for this research are: (*"Prolonged mechanical ventilation" OR "ICU patients" OR "Critically ill"*) AND (*"Early tracheostomy" OR*

"Percutaneous dilational tracheostomy" OR "Early vs late tracheostomy") AND ("Late tracheostomy" OR "Prolonged translaryngeal intubation" OR "Standard weaning") AND ("Mortality" OR "Ventilator-associated pneumonia" OR "ICU length of stay")

Study Selection Process

Study selection was conducted in three stages. The first stage was deduplication of records using reference management software. The second stage was title and abstract screening by two independent reviewers using a standardised screening form. The third stage was full-text review of all records passing the second stage, with documentation of the reason for exclusion for each ineligible article. Disagreements between reviewers were resolved through discussion; if consensus was not reached, a third reviewer acted as arbiter. Inter-reviewer agreement was calculated using Cohen's kappa statistic.²⁴⁻³²

Data Extraction

Data extraction was performed using a standardised form piloted on five initial studies. Extracted variables included study identifiers (first author, year of publication, country, journal), study design, number of centres, data collection period, population characteristics (age, sex, severity scores such as APACHE II, SAPS II, SOFA, GCS, ISS), number of subjects in each group, operational definitions of early and late tracheostomy, tracheostomy technique, proportion of patients who actually underwent the procedure, primary and secondary outcomes with effect measures and confidence intervals, duration of follow-up, and funding sources. Data reported as median and interquartile range were converted to mean and standard deviation using the Wan method when required for narrative comparison.¹⁻²³

Article Search Strategy

Database	Keywords	Hits
Pubmed	<i>("Prolonged mechanical ventilation" OR "ICU patients" OR "Critically ill") AND ("Early tracheostomy" OR "Percutaneous dilational tracheostomy" OR "Early vs late tracheostomy") AND ("Late tracheostomy" OR "Prolonged translaryngeal intubation" OR "Standard weaning") AND ("Mortality" OR "Ventilator-associated pneumonia" OR "ICU length of stay")</i>	69
Google Scholar	<i>("Prolonged mechanical ventilation" OR "ICU patients" OR "Critically ill") AND ("Early tracheostomy" OR "Percutaneous dilational tracheostomy" OR "Early vs late tracheostomy") AND ("Late tracheostomy" OR "Prolonged translaryngeal intubation" OR "Standard weaning") AND ("Mortality" OR "Ventilator-associated pneumonia" OR "ICU length of stay")</i>	2,710
Semantic Scholar	<i>("Prolonged mechanical ventilation" OR "ICU patients" OR "Critically ill") AND ("Early tracheostomy" OR "Percutaneous dilational tracheostomy" OR "Early vs late tracheostomy") AND ("Late tracheostomy" OR "Prolonged translaryngeal intubation" OR "Standard weaning") AND ("Mortality" OR "Ventilator-associated pneumonia" OR "ICU length of stay")</i>	5
Science-direct	<i>("Prolonged mechanical ventilation" OR "ICU patients" OR "Critically ill") AND ("Early tracheostomy") AND ("Late tracheostomy") AND ("Mortality" OR "Ventilator-associated pneumonia" OR "ICU length of stay")</i>	183
Cochrane	<i>("Prolonged mechanical ventilation" OR "ICU patients" OR "Critically ill") AND ("Early tracheostomy" OR "Percutaneous dilational tracheostomy" OR "Early vs late tracheostomy") AND ("Late tracheostomy" OR "Prolonged translaryngeal intubation" OR "Standard weaning") AND ("Mortality" OR "Ventilator-associated pneumonia" OR "ICU length of stay")</i>	3

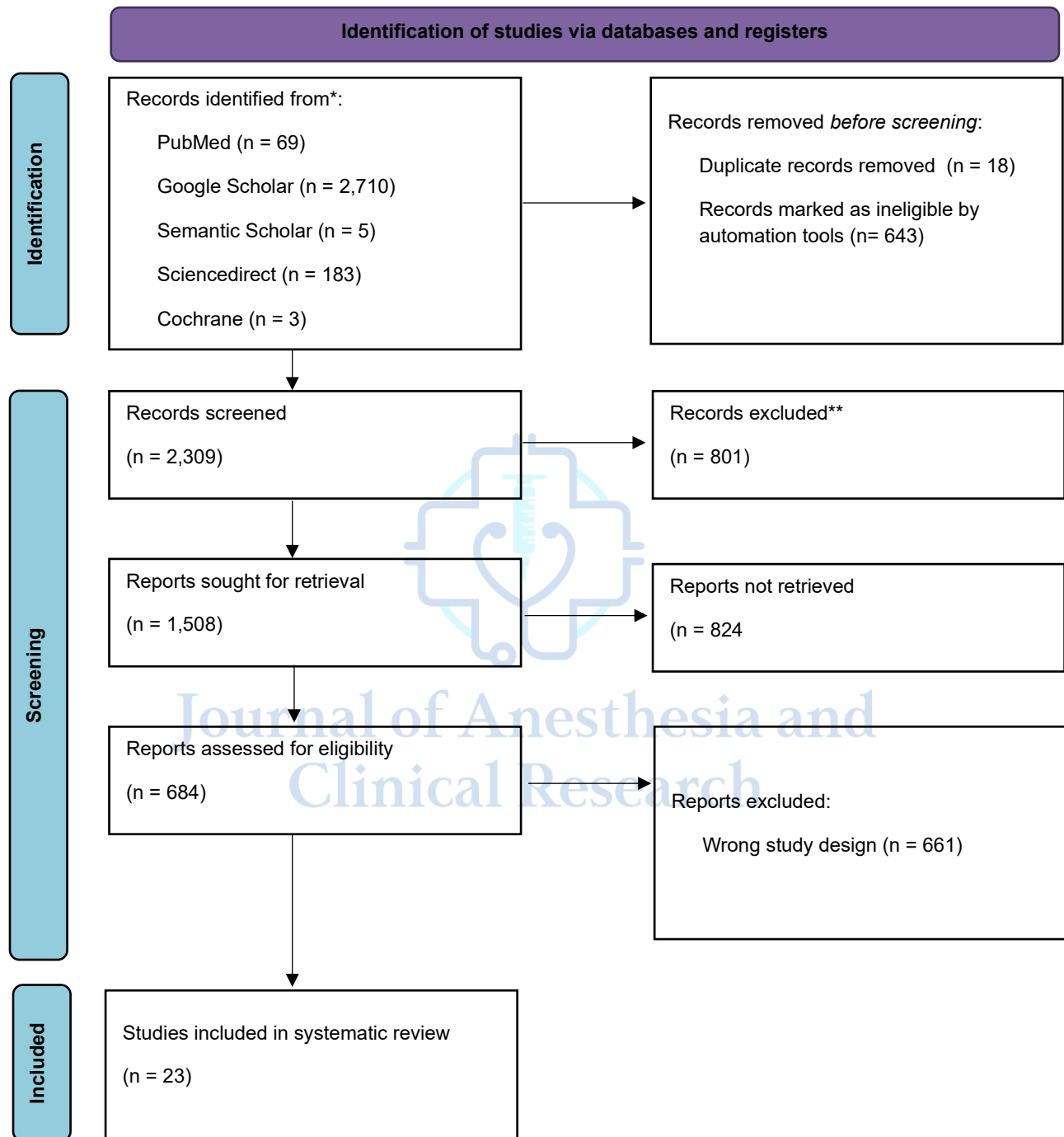


Figure 1. Search Flow Diagram

Risk-of-Bias Assessment

Risk of bias in randomized controlled trials was assessed using the Cochrane Risk of Bias 2 (RoB 2) tool, which covers five domains: bias arising from the randomization process (D1), bias due to deviations from intended interventions (D2), bias due to missing outcome data (D3), bias in measurement of the outcome (D4), and bias in selection of the reported result (D5). Each domain was rated as low (L), some concerns / unclear (U), or high (H), and the overall judgement was determined according to the RoB 2 algorithm. Notably, all randomized controlled trials on this topic were open-label because blinding of a surgical intervention is practically impossible; consequently, domain D2 systematically raised concerns for subjective outcomes, although not for hard outcomes such as mortality.¹⁻¹²

Risk of bias in observational studies was assessed using the Newcastle–Ottawa Scale (NOS), which covers three domains, namely cohort selection (maximum 4 stars), cohort comparability (maximum 2 stars), and outcome assessment (maximum 3 stars), with a maximum total score of 9 stars. Studies scoring 7–9 were categorised as good quality, 4–6 as fair, and 0–3 as poor. An additional assessment was performed for the presence of immortal time bias, i.e., bias arising because patients in the late tracheostomy group must by definition survive until the time of the procedure, so that the period between cohort entry and tracheostomy becomes an "immortal" period that artificially favours the late group.^{13-23,34}

Table 2. Risk-of-bias assessment of randomized controlled trials using the Cochrane RoB 2 tool

Study (Year)	D1	D2	D3	D4	D5	Overall
Rumbak et al. (2004)	U	H	L	H	U	High
Blot et al. (2008)	L	H	L	U	U	Some concerns
Terragni et al. (2010)	L	H	L	L	L	Some concerns
Trouillet et al. (2011)	L	H	L	L	L	Some concerns

Study (Year)	D1	D2	D3	D4	D5	Overall
Koch et al. (2012)	U	H	U	U	U	High
Zheng et al. (2012)	U	H	L	U	U	High
Bösel et al. (2013, SETPOINT)	L	H	L	L	L	Some concerns
Young et al. (2013, TracMan)	L	H	L	L	L	Some concerns
Diaz-Prieto et al. (2014)	L	H	L	U	L	Some concerns
Bösel et al. (2022, SETPOINT2)	L	L	L	L	L	Low
Eeg-Olofsson et al. (2022, TTCOV19)	L	H	L	L	L	Some concerns
Elsayed et al. (2022)	U	H	U	U	U	High

D1 = randomization process; D2 = deviations from intended interventions; D3 = missing outcome data; D4 = measurement of the outcome; D5 = selection of the reported result. L (green) = low risk; U (yellow) = some concerns/unclear; H (orange) = high risk. Domain D2 was rated high in most trials owing to the open-label design and high crossover rates, particularly in the late tracheostomy arm.

Table 3. Risk-of-bias assessment of observational studies using the Newcastle–Ottawa Scale

Study (Year)	Selection (max 4)	Comparability (max 2)	Outcome (max 3)	Total	Quality	Immortal time bias
McLaughlin et al. (2019)	4	2	3	9	Good	Present (mitigated by propensity matching)
Robba et al. (2020, CENTER-TBI)	4	2	3	9	Good	Present (acknowledged by authors)
Breik et al. (2020)	3	1	3	7	Good	Present
Hernández et al. (2021)	4	2	3	9	Good	Mitigated (failure-free days)
Polok et al. (2021, COVIP)	4	2	3	9	Good	Mitigated (landmark analysis)
Vuu et al. (2022)	3	2	3	8	Good	Present (strong)
Tekin et al. (2024)	3	1	2	6	Fair	Present
Accetta et al. (2025)	3	2	3	8	Good	Present
Kamath et al. (2025)	3	2	2	7	Good	Present (strong)

Study (Year)	Selection (max 4)	Comparability (max 2)	Outcome (max 3)	Total	Quality	Immortal time bias
Kovačević et al. (2025)	3	2	3	8	Good	Present (strong)
Katsura et al. (2026)	4	2	3	9	Good	Mitigated (mixed-effects)

Score 7–9 = good quality; 4–6 = fair; 0–3 = poor. The last column shows the additional assessment of immortal time bias, which is not covered by the standard NOS instrument.

Effect Measures and Synthesis Methods

For dichotomous outcomes, effect measures were expressed as risk ratio (RR), odds ratio (OR), or hazard ratio (HR) with 95% confidence intervals. For continuous outcomes, effect measures were expressed as mean difference (MD) or weighted mean difference (WMD) with 95% confidence intervals. Effect estimates were presented per study and then compared with pooled estimates reported in relevant previous meta-analyses. Statistical heterogeneity in the comparator meta-analyses was assessed using the I-squared statistic with interpretation thresholds of 0–40% (might not be important), 30–60% (moderate heterogeneity), 50–90% (substantial heterogeneity), and 75–100% (considerable heterogeneity).²⁵⁻³²

Subgroup analyses were planned according to the early tracheostomy timing threshold (less than 4 days, 4–7 days, 8–10 days, and 11–14 days), population (neurological versus non-neurological; trauma versus non-trauma; COVID-19 versus non-COVID-19), study design (randomized controlled trial versus observational), and risk of bias (low versus high). Sensitivity analyses were performed by excluding studies at high risk of bias and studies with crossover rates exceeding 50%.^{27,29,31,39}

Certainty-of-Evidence Assessment

The certainty of evidence for each outcome was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach, which

considers five factors that lower certainty, namely risk of bias, inconsistency, indirectness, imprecision, and publication bias, as well as three factors that raise certainty for observational studies, namely a large magnitude of effect, a dose–response gradient, and residual confounding acting in the direction opposite to the observed effect. Evidence from randomized controlled trials started at high certainty, whereas observational evidence started at low certainty.^{31,43}

Ethical Considerations

This study is a synthesis of published secondary data and therefore did not require approval from a research ethics committee or informed consent from subjects. All included studies had obtained ethical approval from their respective institutions as reported in the original publications. There are no financial or non-financial conflicts of interest to declare. The existence of all references used was verified through the Consensus academic search engine, and all are accessible online.¹⁻⁴⁴

RESULTS

Characteristics of Included Studies

The included studies were published between 2004 and 2026 and originated from the United States, the United Kingdom, France, Italy, Germany, Spain, Sweden, Poland and a European network, China, Egypt, India, Brazil, Bosnia and Herzegovina, Türkiye, and Japan. Sample sizes ranged from 60 patients in the SETPOINT pilot trial to 22,156 patients in the national registry analysis by Katsura et al. The operational definition of early tracheostomy varied widely, from less than 48 hours in the trial by Rumbak et al. to 14 days or less in the studies by McLaughlin et al. and Breik et al. Definitions of late tracheostomy ranged from more than 5 days to more than 21 days. The predominant technique was percutaneous dilatational tracheostomy, although several studies permitted open surgical technique according to centre policy.¹⁻²³

Population characteristics also varied substantially. Nine studies examined general or mixed ICU populations, six studies examined neurological populations (severe stroke and traumatic brain injury), four studies examined trauma and burn populations, and six studies examined COVID-19 populations. One study examined a paediatric population with severe

traumatic brain injury. Reported severity scores included APACHE II, SAPS II, SOFA, the Glasgow Coma Scale, and the Injury Severity Score. Table 4 presents the complete characteristics of all primary studies in accordance with international reporting conventions.¹⁻²³

Table 4 Characteristics of included primary studies (randomized controlled trials and observational studies)

Author (Year)	Country	Design	Population / Setting	N (ET/LT)	ET definition	LT definition	Primary outcome
Rumbak et al. (2004)	USA	RCT	Medical ICU; projected ventilation >14 days	120 (60/60)	≤48 h after intubation	Day 14–16	Mortality, pneumonia, ICU and ventilation days
Blot et al. (2008)	France	RCT (multicentre, 25 ICUs)	Unselected severely ill ICU patients expected MV >7 days	123 (61/62)	≤4 days	Prolonged intubation	28-day mortality
Terragni et al. (2010)	Italy	RCT (12 ICUs)	Adult ICU, SAPS II 35–65, SOFA ≥5, no lung infection	419 (209/210)	Day 6–8 of intubation	Day 13–15 of intubation	Incidence of ventilator-associated pneumonia
Trouillet et al. (2011)	France	RCT (single centre)	Adults requiring MV ≥4 days after cardiac surgery	216 (109/107)	Immediate percutaneous tracheotomy	Prolonged intubation; tracheotomy at day 15	Ventilator-free days within 60 days

Author (Year)	Country	Design	Population / Setting	N (ET/LT)	ET definition	LT definition	Primary outcome
Koch et al. (2012)	Germany	RCT	Critically ill, predominantly surgical ICU patients	100 (50/50)	≤4 days (median 2.8 days)	≥6 days (median 8.1 days)	Mortality, VAP, ventilation and hospitalization time
Zheng et al. (2012)	China	RCT (surgical ICU)	Adults anticipated to require prolonged MV	119 (58/61)	Day 3 of mechanical ventilation	Day 15 of mechanical ventilation	Ventilator-free days at day 28
Bösel et al. (2013) — SETPOINT	Germany	RCT (pilot, single centre)	Severe ischaemic/haemorrhagic stroke, estimated MV ≥2 weeks	60 (30/30)	Day 1–3 from intubation	Day 7–14 from intubation	ICU length of stay
Young et al. (2013) — TracMan	UK	RCT (72 critical care units)	Adults ventilated <4 days, predicted ≥7 further days of MV	909 (455/454)	≤4 days of critical care admission	≥10 days if still indicated	30-day all-cause mortality
Diaz-Prieto et al. (2014)	Spain	RCT (single centre)	Consecutive ICU patients	489 (245/244)	Before day 8 of MV	From day 14 if still indicated	90-day mortality; MV,

Author (Year)	Country	Design	Population / Setting	N (ET/LT)	ET definition	LT definition	Primary outcome
			requiring ≥ 7 days of MV				sedation and ICU days
Bösel et al. (2022) — SETPOINT2	Germany / USA	RCT (26 centres, PROBE)	Severe acute ischaemic or haemorrhagic stroke on invasive MV	382 (188/194)	≤ 5 days of intubation	Standard weaning; tracheostomy from day 10	mRS 0–4 vs 5–6 at 6 months
Eeg-Olofsson et al. (2022) — TTCOV19	Sweden	RCT (multicentre, single-blinded)	SARS-CoV-2 infected patients requiring intubation and MV	150 (72/78)	≤ 7 days after intubation	≥ 10 days after intubation	Total number of mechanical ventilation days
Elsayed et al. (2022)	Egypt	RCT (prospective, blinded allocation)	Mechanically ventilated stroke patients	60 (30/30)	≤ 4 days of ICU stay	> 14 days	Diaphragmatic excursion and thickening fraction
McLaughlin et al. (2019)	USA	Retrospective cohort, propensity	Children < 15 y with severe TBI, ventilated > 48 h	242 matched (121/121)	≤ 14 days	≥ 15 days	Length of stay and in-hospital

Author (Year)	Country	Design	Population / Setting	N (ET/LT)	ET definition	LT definition	Primary outcome
		-matched (NTDB)					complications
Robba et al. (2020) — CENTER-TBI	Europe (multinational)	Prospective longitudinal observational cohort	TBI patients with ICU stay ≥ 72 h; 433 tracheostomised	1,358 (tracheostomy 433)	≤ 7 days from admission	> 7 days from admission	Extended Glasgow Outcome Score at 6 months
Breik et al. (2020)	UK	Prospective observational cohort	COVID-19 patients requiring MV in a tertiary ICU	164 (100 tracheostomy / 64 none)	≤ 14 days from intubation	> 14 days from intubation	30-day survival
Hernández et al. (2021)	Spain	Retrospective propensity-matched cohort (15 ICUs)	COVID-19 pneumonia patients undergoing tracheostomy	682 tracheostomised of 1,939	≤ 7 / 8–10 / 11–14 days strata	> 7 / > 10 / > 14 days strata	Ventilator-free and ICU bed-free days at 28 and 60 days
Polok et al. (2021) — COVIP	Europe (16 countries, 152 centres)	Prospective observational cohort	Patients ≥ 70 y with COVID-19 on invasive MV	1,740 (tracheostomy 461)	≤ 10 days since intubation	> 10 days since intubation	3-month mortality

Author (Year)	Country	Design	Population / Setting	N (ET/LT)	ET definition	LT definition	Primary outcome
Vuu et al. (2022)	USA	Retrospective cohort (multi-hospital system)	COVID-19 patients intubated or tracheostomised	5,911 analysed	<10 days	>10 days	Inpatient mortality
Tekin et al. (2024)	Türkiye	Prospective cohort	Unselected critically ill ICU patients with prolonged intubation	87 (33/54)	≤14 days of intubation	≥15 days of intubation	Mortality, MV need, complications
Accetta et al. (2025)	Brazil	Retrospective cohort	COVID-19 patients undergoing tracheostomy for respiratory failure	356	≤21 days of MV	>21 days of MV	In-hospital mortality and its predictors
Kamath et al. (2025)	India	Retrospective cohort	Trauma ICU patients undergoing temporary tracheostomy	383	≤7 days of MV	>7 days of MV	MV duration, ICU LOS, VAP

Author (Year)	Country	Design	Population / Setting	N (ET/LT)	ET definition	LT definition	Primary outcome
Kovačević et al. (2025)	Bosnia and Herzegovina	Retrospective observational cohort	COVID-19–associated ARDS in a low-resource ICU	711 (89 tracheotomy / 622 intubation only)	Median 10 days (IQR 6–15)	Intubation only / later	In-hospital mortality; ventilator-free days
Katsura et al. (2026)	USA	Retrospective cohort (ACS TQIP, 417 hospitals)	Adults 20–89 y with severe TBI (AIS 3–5, GCS 3–8) on MV	22,156	≤7 days after injury	>7 days after injury	Withdrawal of life-sustaining treatment after tracheostomy

ET = early tracheostomy; LT = late tracheostomy; MV = mechanical ventilation; ICU = intensive care unit; VAP = ventilator-associated pneumonia; TBI = traumatic brain injury; ARDS = acute respiratory distress syndrome; NTDB = National Trauma Data Bank; TQIP = Trauma Quality Improvement Program; mRS = modified Rankin Scale; SAPS = Simplified Acute Physiology Score; SOFA = Sequential Organ Failure Assessment; AIS = Abbreviated Injury Scale; GCS = Glasgow Coma Scale; PROBE = prospective randomized open blinded endpoint.

Short-Term Mortality (ICU, 28–30 Days)

Short-term mortality was the primary outcome in the majority of included randomized controlled trials. The TracMan trial, the largest trial, reported 30-day all-cause mortality of 30.8% (95% CI 26.7–35.2) in the early tracheostomy group compared with 31.5% (95% CI 27.3–35.9) in the late tracheostomy group, with a statistically non-significant absolute risk reduction of 0.7% (95% CI –5.4 to 6.7). The trial by Terragni et al. reported a hazard ratio for death of 0.80 (95% CI

0.56–1.15) over 28 days post-randomization, likewise without statistical significance. The trial by Trouillet et al. in a post-cardiac surgery population reported 28-day mortality of 16% versus 21%, with no significant difference.^{3,4,8}

Two small trials reported a striking mortality advantage in the early group. The trial by Rumbak et al. reported mortality of 31.7% versus 61.7%, and the SETPOINT pilot trial reported ICU mortality of 10% versus 47%. Both trials had small sample sizes (120 and 60 patients, respectively) and were judged to be at high risk of bias or to raise some concerns, so their effect estimates were most likely influenced by small-study effects. Large trials specifically designed to test mortality consistently failed to replicate these findings.^{1,7,8}

Table 5. Short-term mortality (ICU, 28–30 days) in randomized controlled trials and observational studies

Study (Year)	n	Early tracheostomy	Late tracheostomy	Effect estimate (95% CI)	p
Rumbak et al. (2004)	120	31.7%	61.7%	Absolute difference –30.0%	<0.05
Blot et al. (2008)	123	No difference	No difference	No difference in any endpoint	NS
Terragni et al. (2010)	419	—	—	HR 0.80 (0.56–1.15)	NS
Trouillet et al. (2011)	216	16%	21%	Absolute difference –5.0%	NS
Koch et al. (2012)	100	No difference	No difference	No significant reduction	NS
Zheng et al. (2012)	119	—	—	Comparable 60-day cumulative incidence	0.949

Study (Year)	n	Early tracheostomy	Late tracheostomy	Effect estimate (95% CI)	p
Bösel et al. (2013)	60	10% (3/30)	47% (14/30)	Absolute difference −37.0%	<0.01
Young et al. (2013)	909	30.8% (26.7–35.2)	31.5% (27.3–35.9)	ARR 0.7% (−5.4 to 6.7)	NS
Diaz-Prieto et al. (2014)	489	25.7% (90 days)	29.9% (90 days)	Absolute difference −4.2%	NS
Eeg-Olofsson et al. (2022)	150	—	—	Overall ICU mortality 32.7%; no difference	NS
Elsayed et al. (2022)	60	—	—	Comparable 28-day mortality	0.612
Polok et al. (2021)	461	—	—	HR 0.96 (0.70–1.33)	NS
Vuu et al. (2022)	5,911	44.7%	33.1%	aOR 0.73 (0.52–1.01) vs 0.44 (0.34–0.58)	<0.05
Accetta et al. (2025)	356	—	—	Tracheostomy timing not a predictor of mortality	NS
Kovačević et al. (2025)	711	—	—	HR for tracheotomy 0.16 (0.11–0.23)	<0.001

NS = not statistically significant; HR = hazard ratio; ARR = absolute risk reduction; aOR = adjusted odds ratio. Effect estimates are presented as reported in the original publications.

By way of comparison, meta-analyses of randomized controlled trials have consistently produced pooled estimates approaching but not crossing the conventional threshold of significance. Siempos et al. reported an OR of 0.80 (95% CI 0.59–1.09; p=0.16) from 13 trials

with 2,434 patients. Villemure-Poliquin et al. reported an RR of 0.91 (95% CI 0.82–1.01; I² 18%) from nine trials with 2,457 patients, accompanied by a trial sequential analysis showing that the analysis was underpowered. Han et al. reported an RR of 0.86 (95% CI 0.73–1.00; p=0.06) from 21 trials. Huang et al. reported an RR of 0.91 (95% CI 0.81–1.03), Wang et al. an RR of 0.86 (95% CI 0.65–1.13), Szakmany et al. an RR of 0.93 (95% CI 0.83–1.05), Griffiths et al. an RR of 0.79 (95% CI 0.45–1.39), and Liu et al. an RR of 0.84 (95% CI 0.67–1.04). The uniform direction of effect across eight independent syntheses, with upper confidence limits repeatedly touching or nearly touching unity, is a pattern statistically consistent with a small protective effect that remains undetected owing to limited power.^{24,25,26,27,28,29,31,32}

Long-Term Mortality

Long-term mortality was reported in several studies with adequate follow-up. The TracMan trial reported two-year mortality of 51.0% (95% CI 46.4–55.6) in the early group compared with 53.7% (95% CI 49.1–58.3) in the late group (p=0.74). The trial by Trouillet et al., with a median follow-up of 873 days, reported comparable survival between groups. In contrast, the SETPOINT pilot trial reported six-month mortality of 27% versus 60% (p=0.02) in a severe stroke population, although this finding was not replicated in the larger SETPOINT2 trial.^{4,7,8,10}

Table 6. Long-term mortality (60 days to 2 years)

Study (Year)	n	Early tracheostomy	Late tracheostomy	Effect estimate (95% CI)	p
Young et al. (2013) — 2 years	909	51.0% (46.4–55.6)	53.7% (49.1–58.3)	Absolute difference –2.7%	0.74
Bösel et al. (2013) — 6 months	60	27% (8/30)	60% (18/30)	Absolute difference –33.0%	0.02
Trouillet et al. (2011) — median 873 days	216	Comparable	Comparable	No difference in survival	NS

Study (Year)	n	Early tracheostomy	Late tracheostomy	Effect estimate (95% CI)	p
Zheng et al. (2012) — 60 days	119	—	—	Comparable cumulative incidence	0.949
Polok et al. (2021) — 3 months	461	—	—	HR 0.96 (0.70–1.33); landmark HR 0.78 (0.57–1.06)	NS
Robba et al. (2020) — 6 months	433	20.6%	15.0%	Poor neurological outcome OR 1.69 (1.07–2.67) for LT	0.018
Siempos et al. (2015) — 1 year (MA)	1,529	—	—	RR 0.93 (0.85–1.02)	0.14
Hosokawa et al. (2015) — long-term (MA)	2,689	—	—	OR 0.83 (0.69–0.99)	0.04
Huang et al. (2014) — long-term (MA)	2,072	—	—	RR 0.90 (0.76–1.08)	0.27
Wang et al. (2011) — long-term (MA)	1,044	—	—	RR 0.84 (0.68–1.04)	NS

MA = meta-analysis (presented as a comparator, not included in the study characteristics table).

LT = late tracheostomy.

The only synthesis reporting a significant reduction in long-term mortality was that of Hosokawa et al., with an OR of 0.83 (95% CI 0.69–0.99; $p=0.04$) from 12 trials with 2,689 patients.

This finding should be interpreted with caution because the upper confidence limit lies very close to unity and the synthesis pooled three a priori distinct timing-threshold categories. Conversely, CENTER-TBI data showed the opposite pattern in crude mortality (20.6% in the early versus 15.0% in the late group) but worse neurological outcomes in the late group, a paradox that, according to the correspondence by Hoshino et al., is best explained by immortal time bias.^{14,30,34}

Ventilator-Associated Pneumonia and Nosocomial Pneumonia

Ventilator-associated pneumonia is the outcome most frequently invoked as a pathophysiological justification for early tracheostomy, because tracheostomy is thought to reduce microaspiration of oropharyngeal secretions and eliminate the endotracheal tube biofilm. The trial by Terragni et al., specifically designed for this outcome, reported an incidence of 14% (95% CI 10–19) versus 21% (95% CI 15–26), $p=0.07$, with a hazard ratio of 0.66 (95% CI 0.42–1.04) — a direction of effect clearly favouring the early strategy but not crossing the conventional threshold of significance. The smaller trials by Zheng et al. and Koch et al. reported significant reductions.^{3,5,6}

Table 7. Incidence of ventilator-associated pneumonia and nosocomial pneumonia

Study (Year)	n	Early tracheostomy	Late tracheostomy	Effect estimate (95% CI)	p
Rumbak et al. (2004)	120	5%	25%	Absolute difference –20.0%	<0.05
Terragni et al. (2010)	419	14% (10–19)	21% (15–26)	HR 0.66 (0.42–1.04)	0.07
Trouillet et al. (2011)	216	Comparable	Comparable	No significant difference	NS
Koch et al. (2012)	100	38%	64%	Absolute difference –26.0%	<0.05

Study (Year)	n	Early tracheostomy	Late tracheostomy	Effect estimate (95% CI)	p
Zheng et al. (2012)	119	29.3% (17/58)	49.2% (30/61)	Absolute difference –19.9%	<0.05
Eeg-Olofsson et al. (2022)	150	Comparable	Comparable	No difference in infectious complications	NS
McLaughlin et al. (2019)	242	24%	41%	Absolute difference –17.0%	<0.05
Robba et al. (2020)	433	27.2%	39.7%	Absolute difference –12.5%	0.010
Kamath et al. (2025)	383	15.9%	47.4%	Absolute difference –31.5%	<0.05
Siempos et al. (2015) — MA	1,599	—	—	OR 0.60 (0.41–0.90)	0.01
Han et al. (2024) — MA	21 RCT	—	—	RR 0.86 (0.74–1.01)	0.06
Griffiths et al. (2005) — MA	406	—	—	RR 0.90 (0.66–1.21)	NS
Wang et al. (2011) — MA	1,044	—	—	RR 0.94 (0.77–1.15)	NS
Huang et al. (2014) — MA	2,072	—	—	RR 0.88 (0.71–1.10)	0.27

Study (Year)	n	Early tracheostomy	Late tracheostomy	Effect estimate (95% CI)	p
Foran et al. (2022) — MA (spinal cord injury)	2,043	—	—	RR 0.86 (0.75–0.98)	0.02
de Franca et al. (2020) — MA (traumatic brain injury)	7 studies	—	—	Risk difference 0.78 (0.70–0.88)	<0.05

MA = comparator meta-analysis. The operational definition of VAP was not uniform across studies; some used clinical-radiological criteria and others used quantitative microbiological confirmation.

There is a clear divergence between syntheses restricted to general ICU populations and those focusing on high-risk populations. In general ICU populations, pooled estimates ranged from RR 0.86 to 0.94 with confidence intervals crossing unity. In contrast, in spinal cord injury and traumatic brain injury populations, the reduction in pneumonia risk was significant, with an RR of 0.86 (95% CI 0.75–0.98) and a risk difference of 0.78 (95% CI 0.70–0.88). This pattern indicates effect modification by baseline risk: in populations with a high incidence of VAP due to impaired protective airway reflexes, the absolute benefit of early tracheostomy becomes larger and more readily detectable.^{24,25,26,27,32,35,36}

Duration of Mechanical Ventilation

The duration of mechanical ventilation is one of the domains with the most consistent evidence favouring the early strategy. The recent meta-analysis by Han et al. of 21 randomized controlled trials reported a significant reduction of 2.77 days (95% CI –5.10 to –0.44; $p=0.02$). This estimate is more conservative than that of the early meta-analysis by Griffiths et al., which

reported a reduction of 8.5 days (95% CI −15.3 to −1.7), a difference reflecting the inclusion of large trials with smaller effects in the more recent synthesis.^{24,32}

Table 8. Duration of mechanical ventilation

Study (Year)	n	Early tracheostomy	Late tracheostomy	Effect estimate (95% CI)	p
Rumbak et al. (2004)	120	7.6 ± 2.0 days	17.4 ± 5.3 days	Difference −9.8 days	<0.05
Koch et al. (2012)	100	367.5 hours (±15.3 days)	507.5 hours (±21.1 days)	Difference −140 hours (−5.8 days)	<0.05
Eeg-Olofsson et al. (2022) — ITT	150	—	—	MD −1.5 days (−5.7 to 2.8)	0.5
Eeg-Olofsson et al. (2022) — per protocol	61	—	—	MD −8.0 days (−13.8 to −2.27)	0.0064
Elsayed et al. (2022)	60	Shorter	Longer	Significant reduction in ventilator days	<0.01
Breik et al. (2020)	100	—	—	MD −6.0 days (−9.0 to −3.1)	<0.0001
McLaughlin et al. (2019)	242	14 days (9–19)	25 days (19–35)	Difference −11 days	<0.05
Kamath et al. (2025)	383	13 days (11–14)	31 days (27–33)	Difference −18 days	<0.05
Han et al. (2024) — MA	21 RCT	—	—	MD −2.77 days (−5.10 to −0.44)	0.02

Study (Year)	n	Early tracheostomy	Late tracheostomy	Effect estimate (95% CI)	p
Griffiths et al. (2005) — MA	406	—	—	WMD −8.5 days (−15.3 to −1.7)	<0.05
Szakmany et al. (2015) — MA	2,406	—	—	MD −0.19 days (−1.13 to 0.75)	NS
Huang et al. (2014) — MA	2,072	—	—	WMD −2.91 days (−7.21 to 1.40)	0.19
Ji et al. (2022) — MA (COVID-19)	2,098	—	—	MD −9.08 days (−10.91 to −7.26)	<0.01
de Franca et al. (2020) — MA (TBI)	7 studies	—	—	MD −4.15 days (−6.30 to −1.99)	<0.05
Mubashir et al. (2021) — MA (SCI)	1,220	—	—	MD −18.30 days (−24.33 to −12.28)	0.001
Coffin et al. (2025) — MA (cervical SCI)	210	—	—	MD −5.3 days (−6.33 to −4.28); I ² 0%	<0.05

ITT = intention to treat; MD = mean difference; WMD = weighted mean difference; TBI = traumatic brain injury; SCI = spinal cord injury. Note the magnitude of effect in observational studies and special populations, which far exceeds the estimates from randomized controlled trials in general ICU populations.

The striking difference between the intention-to-treat and per-protocol analyses in the TTCOV19 trial merits particular attention. In the intention-to-treat analysis, the difference in

duration of ventilation was only -1.5 days (95% CI -5.7 to 2.8 ; $p=0.5$), whereas in the per-protocol analysis the difference reached -8.0 days (95% CI -13.8 to -2.27 ; $p=0.0064$). The overall correlation between tracheostomy timing and the number of mechanical ventilation days was significant, with a Spearman correlation coefficient of 0.39 ($p<0.0001$). This pattern indicates that the dilution of effect in the intention-to-treat analysis was due to the high proportion of patients who did not receive the intervention as allocated, rather than to the absence of a biological effect.¹¹

Ventilator-Free Days

Ventilator-free days are a composite outcome integrating survival and liberation from the ventilator and are therefore methodologically more robust against bias arising from competing death. The trial by Zheng et al. reported 9.57 ± 5.64 days in the early group compared with 7.38 ± 6.17 days in the late group ($p<0.05$). The propensity-matched cohort by Hernández et al. in a COVID-19 population showed a consistent gradient across three timing-threshold strata, with the difference remaining significant in each stratum.^{6,16}

Table 9. Ventilator-free days and days free of ventilation at day 28

Study (Year)	n	Early tracheostomy	Late tracheostomy	Effect estimate (95% CI)	p
Trouillet et al. (2011) — 60 days	216	30.4 ± 22.4 days	28.3 ± 23.7 days	Difference 2.1 days (-4.1 to 8.3)	NS
Zheng et al. (2012) — 28 days	119	9.57 ± 5.64 days	7.38 ± 6.17 days	Difference $+2.19$ days	<0.05
Hernández et al. (2021) — ≤ 7 vs >7 days	116	9 days (0–15)	3 days (0–7)	Difference 4.5 days (2.3–6.7)	<0.05

Study (Year)	n	Early tracheostomy	Late tracheostomy	Effect estimate (95% CI)	p
Hernández et al. (2021) — 8–10 vs >10 days	222	6 days (0–10)	0 days (0–6)	Difference 3.1 days (1.7–4.5)	<0.05
Hernández et al. (2021) — 11–14 vs >14 days	318	4 days (0–9)	0 days (0–2)	Difference 3.0 days (2.1–3.9)	<0.05
Kovačević et al. (2025) — alive and ventilator-free at day 28	711	—	—	SHR 2.87 (1.88–4.38)	<0.001
Hosokawa et al. (2015) — MA	2,689	—	—	WMD +2.12 days (0.94–3.30)	<0.01

SHR = subdistribution hazard ratio. Data from Hernández et al. derive from a propensity-matched cohort with three timing-threshold strata analysed separately.

Length of Stay in the Intensive Care Unit

ICU length of stay is the outcome with the most direct implications for economics and system capacity. The available pooled estimates show a direction of effect consistently favouring the early strategy, although the magnitude of effect varies widely across syntheses. Han et al. reported a reduction of 6.36 days (95% CI −9.84 to −2.88; $p=0.0003$) from 21 randomized controlled trials, whereas Szakmany et al. reported only a non-significant 0.83 days (95% CI −2.05 to 0.40). The TracMan trial and the SETPOINT pilot trial, which designated ICU length of stay as a primary or key secondary outcome, showed no difference.^{7,8,29,32}

Table 10. Intensive care unit length of stay

Study (Year)	n	Early tracheostomy	Late tracheostomy	Effect estimate (95% CI)	p
Rumbak et al. (2004)	120	4.8 ± 1.4 days	16.2 ± 3.8 days	Difference −11.4 days	<0.05
Young et al. (2013)	909	13.0 days (median)	13.1 days (median)	Difference −0.1 days	0.74
Bösel et al. (2013)	60	18 days (16–28)	17 days (13–22)	Median difference 1 day (−2 to 6)	0.38
Koch et al. (2012)	100	21.5 days	27 days	Difference −5.5 days	<0.05
Breik et al. (2020)	100	—	—	MD −6.7 days (−9.6 to −3.7)	<0.0001
McLaughlin et al. (2019)	242	19 days (14–25)	31 days (24–43)	Difference −12 days	<0.05
Kamath et al. (2025)	383	15 days (13–17)	33 days (30–36)	Difference −18 days	<0.05
Han et al. (2024) — MA	21 RCT	—	—	MD −6.36 days (−9.84 to −2.88)	0.0003
Griffiths et al. (2005) — MA	406	—	—	WMD −15.3 days (−24.6 to −6.1)	<0.05
Liu et al. (2015) — MA	11 studies	—	—	WMD −9.13 days (−17.55 to −0.70)	0.03
Hosokawa et al. (2015) — MA	2,689	—	—	WMD −5.14 days (−9.99 to −0.28)	0.04

Study (Year)	n	Early tracheostomy	Late tracheostomy	Effect estimate (95% CI)	p
Szakmany et al. (2015) — MA	2,406	—	—	MD −0.83 days (−2.05 to 0.40)	NS
Huang et al. (2014) — MA	2,072	—	—	WMD −4.41 days (−13.44 to 4.63)	0.34
Ji et al. (2022) — MA (COVID-19)	1,224	—	—	MD −9.41 days (−12.36 to −6.46)	<0.01
de Franca et al. (2020) — MA (TBI)	7 studies	—	—	MD −5.87 days (−8.74 to −3.00)	<0.05
Mubashir et al. (2021) — MA (SCI)	1,220	—	—	MD −13.0 days (−19.18 to −7.00)	0.001

Note that trials at low risk of bias (TracMan, SETPOINT) showed no difference, whereas observational studies and small trials reported differences of 5–18 days.

Hospital Length of Stay

Hospital length of stay showed a more heterogeneous pattern than ICU length of stay. The meta-analysis by Han et al. reported a non-significant difference of −3.24 days (95% CI −7.99 to 1.52; $p=0.18$), and Wang et al. even reported an opposite direction of effect with a difference of +1.45 days (95% CI −5.31 to 8.22). In contrast, observational studies and syntheses in special populations consistently reported significant reductions. The study by Tekin et al. reported that tracheostomy performed after day 14 was associated with a longer hospital length of stay.^{19,25,32,35,36}

Table 11. Hospital length of stay

Study (Year)	n	Early tracheostomy	Late tracheostomy	Effect estimate (95% CI)	p
Koch et al. (2012)	100	31.5 days	68 days	Difference -36.5 days	<0.05
Tekin et al. (2024)	87	Shorter	Longer	Tracheostomy >day 14 associated with longer stay	<0.05
McLaughlin et al. (2019)	242	26 days (19–41)	39 days (31–54)	Difference -13 days	<0.05
Robba et al. (2020)	433	38.5 days	49.4 days	Difference -10.9 days	0.003
Han et al. (2024) — MA	21 RCT	—	—	MD -3.24 days (-7.99 to 1.52)	0.18
Wang et al. (2011) — MA	1,044	—	—	WMD +1.45 days (-5.31 to 8.22)	NS
Foran et al. (2022) — MA (SCI)	423	—	—	MD -7.39 days (-11.03 to -3.74)	<0.0001
de Franca et al. (2020) — MA (TBI)	7 studies	—	—	MD -6.68 days (-8.03 to -5.32)	<0.05

Duration and Burden of Sedation

The sedation domain is the only outcome showing a significant and consistent advantage of the early strategy across all syntheses of randomized controlled trials. Szakmany et al. reported a reduction in sedation duration of 2.78 days (95% CI -3.68 to -1.88), an estimate that does not cross zero and that originates from a synthesis which otherwise concluded an absence of benefit in all other domains. Hosokawa et al. reported a reduction of 5.07 days (95% CI -10.03 to -0.10;

p<0.05). The trial by Trouillet et al. reported reduced use of intravenous sedatives, less time under deep sedation, and reduced use of haloperidol for agitation and delirium.^{4,29,30}

Table 12. Duration and burden of sedation

Study (Year)	n	Early tracheostomy	Late tracheostomy	Effect estimate (95% CI)	p
Trouillet et al. (2011)	216	Lower	Higher	Less IV sedation, deep sedation, and haloperidol	<0.05
Bösel et al. (2013)	60	Lower	Higher	Median difference 17.5 percentage points (3.3–29.2)	0.02
Zheng et al. (2012) — sedation-free days	119	20.84 ± 2.35 days	17.05 ± 2.30 days	Difference +3.79 days	<0.05
Diaz-Prieto et al. (2014)	489	11 days (2–92)	14 days (0–79)	Median difference –3 days	<0.02
Tekin et al. (2024)	87	Comparable	Comparable	No difference in sedation requirement	NS
Szakmany et al. (2015) — MA	2,406	—	—	MD –2.78 days (–3.68 to –1.88)	<0.001
Hosokawa et al. (2015) — MA	2,689	—	—	WMD –5.07 days (–10.03 to –0.10)	<0.05
Wang et al. (2011) — MA	1,044	—	—	WMD –7.09 days (–14.64 to 0.45)	NS

Study (Year)	n	Early tracheostomy	Late tracheostomy	Effect estimate (95% CI)	p
Liu et al. (2015) — MA	3 studies	—	—	All studies reported a significant reduction	<0.05

Reduction in sedation burden is an intermediate mechanism that theoretically explains the shorter duration of ventilation, reduced delirium, and earlier mobilisation.

Tracheostomy Procedure-Related Complications

The principal concern regarding an early tracheostomy strategy is the exposure of a large number of patients to procedural risk that may be unnecessary. The available data do not support the concern that the early strategy increases complications per procedure. The TracMan trial reported tracheostomy-related complications in 6.3% (95% CI 4.6–8.5) of all patients, with 5.5% in the early group and 7.8% in the late group. The SETPOINT2 trial reported tracheostomy-related serious adverse events of 5.0% (6 of 121 events) in the early group compared with 3.4% (4 of 118 events) in the standard group.^{8,10}

Table 13. Tracheostomy procedure-related complications

Study (Year)	n	Early tracheostomy	Late tracheostomy	Effect estimate (95% CI)	p
Young et al. (2013)	909	5.5%	7.8%	Overall 6.3% (4.6–8.5)	NS
Bösel et al. (2022)	382	5.0% (6/121 SAEs)	3.4% (4/118 SAEs)	Absolute difference +1.6%	NS
Eeg-Olofsson et al. (2022)	150	Comparable	Comparable	No difference in complications/adverse events	NS

Study (Year)	n	Early tracheostomy	Late tracheostomy	Effect estimate (95% CI)	p
Blot et al. (2008)	123	Comparable	Comparable	No difference in laryngeal and tracheal complications	NS
Bösel et al. (2013)	60	Comparable	Comparable	No difference in adverse effects	NS
Tekin et al. (2024)	87	—	—	Surgical technique associated with more complications (not significant)	NS
Wang et al. (2011) — MA	1,044	—	—	RR 0.94 (0.66–1.34)	NS
Villemure-Poliquin et al. (2023) — MA	2,457	—	—	No difference in complications	NS
Foran et al. (2022) — MA (SCI)	812	—	—	RR 0.64 (0.48–0.84)	0.001

SAE = serious adverse event. Note that complications are reported per patient undergoing the procedure; hence, the absolute number of complications at the population level remains higher with the early strategy owing to the greater number of procedures.

Laryngotracheal Complications and Tracheal Stenosis

One of the strongest pathophysiological arguments for early tracheostomy is the prevention of endotracheal tube-related laryngotracheal injury. The trial by Rumbak et al. reported significantly more oral and laryngeal damage in the prolonged translaryngeal intubation group.

However, the systematic review by Curry and Rowan, which specifically examined laryngotracheal stenosis in seven studies with 966 patients, reported a mean incidence of 8.9% (range 0–20.8%), with 8.1% in the early group and 10.9% in the late group; in the studies at lowest risk of bias, no difference was found. The review by Liu et al. likewise reported that none of the studies reporting laryngotracheal outcomes found a significant difference.^{1,28,40}

Table 14. Laryngotracheal complications and stenosis

Study (Year)	n	Early tracheostomy	Late tracheostomy	Effect estimate (95% CI)	p
Rumbak et al. (2004)	120	Fewer	More	Significantly more oral and laryngeal damage with LT	<0.05
Blot et al. (2008)	123	Comparable	Comparable	No difference in laryngeal and tracheal complications	NS
Curry & Rowan (2020) — SR	966 (496/470)	8.1%	10.9%	Overall mean incidence 8.9% (0–20.8%)	NS
Liu et al. (2015) — MA	11 studies	—	—	None of the studies found a significant difference	NS
Putensen et al. (2014) — MA (technique)	973	—	—	Percutaneous tracheostomy reduced stomal	<0.00001

Study (Year)	n	Early tracheostomy	Late tracheostomy	Effect estimate (95% CI)	p
				infection OR 0.22 (0.11–0.41)	
Johnson-Obaseki et al. (2016) — MA (technique)	—	—	—	Lower infection rate with percutaneous technique	<0.05

SR = systematic review. The last two entries compare techniques, not timing, and are presented as context for the choice of procedural modality.

Weaning Success and ICU Discharge Rate

The trial by Zheng et al. is the only randomized controlled trial that explicitly reported weaning success and ICU discharge rates as structured secondary outcomes, with significant results in both domains. The study by Kamath et al. reported that the proportion of extubation attempts was far higher in the late tracheostomy group (43.1% versus 9.3%), which, according to the authors, was the principal mechanism of prolonged ICU stay in that group.^{6,21}

Table 15. Weaning success and ICU discharge rate

Study (Year)	n	Early tracheostomy	Late tracheostomy	Effect estimate (95% CI)	p
Zheng et al. (2012) — successful weaning	119	74.1%	55.7%	Absolute difference +18.4%	<0.05

Study (Year)	n	Early tracheostomy	Late tracheostomy	Effect estimate (95% CI)	p
Zheng et al. (2012) — ICU discharge	119	67.2%	47.5%	Absolute difference +19.7%	<0.05
Kovačević et al. (2025)	711	—	—	SHR for alive and ventilator-free 2.87 (1.88–4.38)	<0.001
Kamath et al. (2025) — extubation attempts	383	9.3%	43.1%	Repeated extubation attempts prolonged ICU stay	<0.05
Tekin et al. (2024)	87	Comparable	Comparable	No difference in weaning from the ventilator	NS
Breik et al. (2020)	164	85% (30-day survival)	42% (without tracheostomy)	RR 3.9 (2.3–6.4)	<0.0001

Long-Term Functional Outcomes and Quality of Life

The SETPOINT2 trial is the only randomized controlled trial that designated six-month functional outcome as its primary outcome. The proportion of patients without severe disability, defined as a modified Rankin Scale score of 0 to 4, was 43.5% in the early group compared with 47.1% in the standard group, with a difference of -3.6% (95% CI -14.3 to 7.2) and an adjusted odds ratio of 0.93 (95% CI 0.60 – 1.42 ; $p=0.73$). The authors emphasised that the wide confidence interval did not permit exclusion of clinically relevant benefit or harm. The trial by Trouillet et al.

reported comparable health-related quality of life and psychosocial evaluation at a median follow-up of 873 days.^{4,10}

Table 16. Long-term functional outcomes and quality of life

Study (Year)	n	Early tracheostomy	Late tracheostomy	Effect estimate (95% CI)	p
Bösel et al. (2022) — mRS 0–4 at 6 months	382	43.5%	47.1%	aOR 0.93 (0.60–1.42); difference –3.6% (–14.3 to 7.2)	0.73
Trouillet et al. (2011) — HRQoL	216	Comparable	Comparable	Comparable survival, psychosocial status, and HRQoL	NS
Bösel et al. (2013) — 6-month mortality	60	27%	60%	Absolute difference –33.0%	0.02
Robba et al. (2020) — 6-month GOSE	433	Better	Worse	OR for poor outcome with LT 1.69 (1.07– 2.67)	0.018
Katsura et al. (2026) — withdrawal of life- sustaining treatment	22,156	—	—	aOR 1.35 (1.10–1.66) in hospitals with a high propensity for ET	0.004

mRS = modified Rankin Scale; GOSE = Glasgow Outcome Scale Extended; HRQoL = health-related quality of life. The findings of Katsura et al. indicate that an institutional propensity for early tracheostomy is associated with an increased likelihood of withdrawal of life-sustaining

treatment after tracheostomy, a care pathway that should be considered when interpreting mortality outcomes.

Proportion of Patients Undergoing Tracheostomy (Overtreatment)

This domain is key to understanding why the early tracheostomy strategy failed to yield a mortality benefit in randomized controlled trials. In the TracMan trial, 91.9% of patients in the early arm actually underwent tracheostomy, compared with only 44.9% in the late arm. This means that more than half of the patients whom clinicians judged would require prolonged ventilation were in fact successfully extubated without requiring tracheostomy at all. The TracMan authors explicitly concluded that clinicians' ability to predict the need for prolonged ventilatory support is very limited.⁸

Table 17. Proportion of patients who actually underwent tracheostomy according to allocation

Study (Year)	n	Early tracheostomy	Late tracheostomy	Effect estimate (95% CI)	p
Young et al. (2013)	909	91.9% (89.0–94.1)	44.9% (40.4–49.5)	Absolute difference +47.0%	<0.001
Terragni et al. (2010)	419	69.4% (145/209)	56.7% (119/210)	Absolute difference +12.7%	<0.05
Diaz-Prieto et al. (2014)	489	68.2% (167/245)	55.3% (135/244)	Absolute difference +12.9%	<0.004
Bösel et al. (2022)	382	95.2%	67.0%	Absolute difference +28.2%	<0.001
Eeg-Olofsson et al. (2022)	150	—	—	68% overall underwent tracheotomy; 61 per protocol	—

Study (Year)	n	Early tracheostomy	Late tracheostomy	Effect estimate (95% CI)	p
Hosokawa et al. (2015) — MA	2,689	87%	53%	OR 16.1 (5.7–45.7)	<0.01
Szakmany et al. (2015) — MA	2,406	—	—	RR for number of procedures 2.53 (1.18–5.40)	<0.05

This difference in proportions indicates that the early strategy exposes approximately 13% to 47% additional patients to an invasive procedure that, under the late strategy, would never have been required.

Unplanned Extubation, Delirium, and Patient Comfort

The domain of comfort and airway safety consistently favoured the early strategy in all studies reporting it, although most were secondary outcomes without correction for multiple comparisons. The trial by Rumbak et al. reported zero accidental extubations in the early group compared with six events in the prolonged intubation group. The trial by Trouillet et al. reported fewer unscheduled extubations, lower use of haloperidol for agitation and delirium, better comfort and ease of care, and earlier resumption of oral nutrition. In the trial by Blot et al., which was neutral overall, better comfort on patients' subjective self-assessment was the only benefit identified.^{1,2,4}

Table 18. Unplanned extubation, delirium, and patient comfort

Study (Year)	n	Early tracheostomy	Late tracheostomy	Effect estimate (95% CI)	p
Rumbak et al. (2004)	120	0 events	6 events	Significantly fewer accidental extubations	<0.05

Study (Year)	n	Early tracheostomy	Late tracheostomy	Effect estimate (95% CI)	p
Trouillet et al. (2011)	216	Fewer	More	Unscheduled extubation, haloperidol, comfort, oral nutrition	<0.05
Blot et al. (2008)	123	Better	Worse	Subjective comfort was the only benefit	<0.05
Bösel et al. (2013)	60	Lower	Higher	Lower sedative requirement accompanied by better comfort	0.02

Non-Respiratory Complications and Diaphragmatic Function

Two additional domains rarely analysed in previous syntheses are immobilisation-related non-respiratory complications and diaphragmatic function. The propensity-matched study by McLaughlin et al. in children with severe traumatic brain injury reported significant reductions in venous thromboembolism (3% versus 13%) and decubitus ulcers (4% versus 13%). The trial by Elsayed et al., using diaphragmatic ultrasonography, reported significant improvement in diaphragmatic excursion and diaphragmatic thickening fraction in the early group, mechanistically linking reduced sedation and earlier recovery of spontaneous respiratory activity with the prevention of ventilator-induced diaphragmatic atrophy.^{12,13}

Table 19. Non-respiratory complications and diaphragmatic function

Study (Year)	n	Early tracheostomy	Late tracheostomy	Effect estimate (95% CI)	p
McLaughlin et al. (2019) — venous thromboembolism	242	3%	13%	Absolute difference –10.0%	<0.05
McLaughlin et al. (2019) — decubitus ulcer	242	4%	13%	Absolute difference –9.0%	<0.05
Elsayed et al. (2022) — diaphragmatic excursion	60	Significantly increased	Not increased	Improvement in DE and DTF after tracheotomy	<0.01
Trouillet et al. (2011) — oral nutrition	216	Earlier	Later	Faster resumption of oral intake	<0.05

DE = diaphragmatic excursion; DTF = diaphragmatic thickening fraction.

Subgroup Analysis by Timing Threshold

Analysis stratified by operational timing threshold shows that the magnitude and direction of effect depend on the definition used. The meta-analysis by Kim et al. in COVID-19 populations found a paradoxical pattern: at the seven-day and fourteen-day thresholds, no difference in short-term mortality was found, but at the ten-day threshold the early group actually showed higher mortality (49.7% versus 32.6%; OR 1.91; 95% CI 1.37–2.65). This finding is most likely a selection artefact, because patients with the greatest severity tended to undergo tracheostomy earlier during surge periods.³⁹

Table 20. Subgroup analysis by early tracheostomy timing threshold

ET timing threshold	Representative studies	Mortality	Duration of mechanical ventilation	ICU length of stay	Domain conclusion
≤48 hours	Rumbak (2004)	Significantly reduced (small-study bias)	Significantly reduced	Significantly reduced	Large effect but high risk of bias
≤3–4 days	TracMan, Blot, Koch, SETPOINT, Elsayed	No difference	Reduced (variable)	No difference to reduced	Process benefit without mortality benefit
≤5 days	SETPOINT2	No difference	Not reported as primary	No difference	No difference in 6-month functional outcome
6–8 days	Terragni (2010), Diaz-Prieto (2014)	No difference	Ventilator HR 0.70 (0.56–0.87)	ICU HR 0.73 (0.55–0.97)	Significant process benefit
≤7 days	TTCOV19, Robba, Kamath, Hernández	No difference	Significantly reduced (per protocol)	Significantly reduced	Clear benefit for ICU capacity
8–10 days	Hernández, Polok, Kovačević	No difference	Significantly reduced	Significantly reduced	Pragmatic window in

ET timing threshold	Representative studies	Mortality	Duration of mechanical ventilation	ICU length of stay	Domain conclusion
					overburdened systems
11–14 days	Hernández, McLaughlin, Breik, Tekin	No difference to improved	Significantly reduced	Significantly reduced	Still confers process benefit
≥15–21 days	Accetta (2025)	Not associated with mortality	Prolonged	Prolonged	No advantage in further delay

Summary of Certainty of Evidence (GRADE)

Table 21. Summary of findings and certainty of evidence according to the GRADE approach

Outcome	Direction and magnitude of effect	Factors lowering certainty	Certainty of evidence
Short-term mortality	No significant difference; pooled RR 0.86–0.93	Imprecision (serious), risk of bias (D2)	Fair
Long-term mortality	No difference; one MA reported OR 0.83	Imprecision (serious), inconsistency	Low
Ventilator-associated pneumonia	Reduced in high-risk subpopulations; OR 0.60–0.86	Inconsistency (serious), indirectness of definition	Low to moderate

Outcome	Direction and magnitude of effect	Factors lowering certainty	Certainty of evidence
Duration of mechanical ventilation	Reduced by 2.8–9.1 days	Inconsistency (serious)	Fair
Ventilator-free days	Increased by 2.1–4.5 days	Imprecision	Fair
ICU length of stay	Reduced by 5.1–15.3 days (variable)	Inconsistency (very serious)	Low
Hospital length of stay	Inconsistent	Inconsistency, imprecision	Low
Sedation duration	Reduced by 2.8–7.1 days	No serious downgrading	Moderate to high
Procedural complications	No difference; 5.5% vs 7.8%	Imprecision	Fair
Laryngotracheal stenosis	No difference; 8.1% vs 10.9%	Risk of bias, imprecision	Low
Weaning success	Significantly increased in a single study	Imprecision (serious), single-study evidence	Low
6-month functional outcome	No difference; aOR 0.93 (0.60–1.42)	Imprecision (serious)	Fair

Outcome	Direction and magnitude of effect	Factors lowering certainty	Certainty of evidence
Proportion undergoing tracheostomy	Sharply increased; OR 16.1	No downgrading	High
Comfort and delirium	Improved in all reporting studies	Risk of bias (subjective outcome, no blinding)	Low
Diaphragmatic function	Significantly improved in one trial	Imprecision, single-study evidence	Very low

DISCUSSION

Summary of Main Findings

This systematic review of 23 primary studies with more than 33,000 patients yields a coherent yet layered pattern of findings. At the level of hard outcomes, namely short-term and long-term mortality, the early tracheostomy strategy did not produce a statistically significant advantage in the general ICU population. Pooled estimates from eight independent meta-analyses ranged from a risk ratio of 0.79 to 0.93, all pointing towards a protective effect but with confidence intervals crossing unity. At the level of process-of-care outcomes, by contrast, the early strategy consistently improved sedation duration, ventilator-free days, duration of mechanical ventilation, and ICU length of stay. At the level of safety, no evidence was found that the early strategy increased procedural complications or laryngotracheal stenosis.¹⁻⁴⁴

The most conceptually decisive finding is the proportion of patients who actually underwent tracheostomy. In the TracMan trial, the difference in proportions reached 47 percentage points, and in the meta-analysis by Hosokawa et al. the odds ratio reached 16.1 (95% CI 5.7–45.7). This finding shows that an early tracheostomy strategy is not merely an intervention that shifts

timing but one that substantially increases the number of invasive procedures performed in the population. Every benefit–risk assessment must take this dimension into account.^{8,30}

Failure of Clinical Prediction as the Principal Determinant

The most fundamental reason why randomized controlled trials failed to demonstrate a mortality benefit lies in clinicians' inability to predict who will require prolonged ventilation. In TracMan, clinicians judged that all 909 enrolled patients were likely to require at least seven additional days of ventilation, yet 55.1% of patients in the late arm were successfully extubated without requiring tracheostomy. When more than half of the patients identified as tracheostomy candidates turn out not to need it, any benefit that may be real in the subgroup truly requiring prolonged ventilation will be completely diluted by patients who do not require it at all.⁸

A similar phenomenon was observed in the trial by Diaz-Prieto et al., in which attending physicians agreed to the randomization protocol in only 42% of cases (205 of 489). In the per-protocol analysis of the subgroup of patients whom clinicians actually judged to be tracheostomy candidates, the early group gained more ventilator-free days, shorter sedation duration, and a shorter ICU length of stay. The authors explicitly concluded that clinicians' inaccuracy in selecting patients who will require prolonged ventilation challenges the potential benefit of early tracheostomy. An identical pattern emerged in the TTCOV19 trial, in which the difference in duration of ventilation changed from a non-significant –1.5 days in the intention-to-treat analysis to a significant –8.0 days in the per-protocol analysis.^{9,11}

The methodological implication is fundamental: the available randomized controlled trials in fact test a management strategy, not the surgical intervention itself. The conclusion that can validly be drawn is that a universal policy of performing early tracheostomy in all patients anticipated to require prolonged ventilation does not reduce mortality. This conclusion is not identical to the statement that early tracheostomy is of no benefit to patients who will certainly require prolonged ventilation. The development and validation of tools to predict the need for prolonged ventilation is therefore a methodological prerequisite for the next generation of trials.^{8,9,11,31}

Discordance between Randomized and Observational Evidence

One of the most prominent findings of this review is the magnitude of the difference in effect estimates between randomized controlled trials and observational studies. In the duration of mechanical ventilation domain, randomized controlled trials produced a pooled estimate of -2.77 days, whereas observational studies in trauma reported a difference of 18 days and a meta-analysis in spinal cord injury reported -18.30 days. This six- to seven-fold difference in magnitude cannot be explained by population differences alone.^{21,32,37}

The principal methodological explanation is immortal time bias. In observational studies, patients are grouped according to the time at which the procedure was actually performed, not according to initial allocation. Consequently, patients classified in the late tracheostomy group must survive until day 7, 10, or 14 to be included in that group; this period is "immortal" by definition. Conversely, patients in the early group are exposed to the risk of death from the first day. This bias systematically favours the late group for mortality outcomes, yet simultaneously disadvantages the late group for duration of ventilation and length of stay outcomes, because patients who survive longer automatically accumulate more ventilator days and hospital days.^{14,34}

CENTER-TBI data provide the clearest illustration of this paradox. That study reported lower six-month mortality in the late tracheostomy group (15.0% versus 20.6%), but simultaneously reported worse neurological outcomes in the same group, with an odds ratio of 1.69 (95% CI 1.07–2.67; $p=0.018$), as well as a longer length of stay (49.4 versus 38.5 days; $p=0.003$). The combination of lower mortality with worse functional outcome in the same group is a hallmark of immortal time bias operating alongside a genuine effect of prolonged exposure to ventilation. The correspondence by Hoshino et al. on that study called for sensitivity analyses using risk set matching and time-fixed analysis to quantify the magnitude of this bias.^{14,34}

The second category of bias is confounding by indication, which operates in two opposite directions depending on the context. In routine practice, patients with severe brain injury, a low GCS, and non-reactive pupils are more likely to undergo early tracheostomy because neurological recovery is not expected in the near term; this causes the early group to be populated by patients

with a worse prognosis. Conversely, in capacity-surge situations such as the COVID-19 pandemic, the most unstable patients had their tracheostomy deferred because they were deemed unfit for the procedure; this causes the late group to be populated by patients with a worse prognosis. The meta-analysis by Kim et al., which found higher mortality in the early group only at the ten-day threshold but not at the seven- or fourteen-day thresholds, is most plausibly explained by such a selection mechanism rather than by a genuine biological effect.^{14,23,39}

Bayesian Interpretation and the Limits of Frequentist Significance Testing

The Bayesian analysis performed by Quinn et al. of 19 randomized controlled trials with 3,508 patients offers a perspective that substantially alters the interpretation. Using non-informative priors, the posterior probability that early tracheostomy confers at least some benefit (risk ratio less than one) reached 99% for short-term mortality, 94% for ventilator-associated pneumonia, 97% for duration of mechanical ventilation, and 97% for ICU length of stay. The probability of a small benefit, defined as a number needed to treat of 200, reached 99% for short-term mortality.³³

The difference between Bayesian and frequentist conclusions is not a contradiction but a consequence of asking different questions. The frequentist approach asks whether the data are sufficiently extreme to reject the null hypothesis at an alpha threshold of 0.05; the Bayesian approach asks how probable it is that the effect lies in a particular direction given the available data. When eight independent syntheses consistently yield point estimates below one, with upper confidence limits repeatedly touching 1.00 to 1.05, the interpretation "no effect" becomes less accurate than the interpretation "there is most likely a small effect that cannot yet be detected with the available sample size". The trial sequential analysis in the review by Villemure-Poliquin et al. independently confirmed that the mortality analysis remains far from the required information size.^{31,33}

Pathophysiological Mechanisms of the Benefits of Early Tracheostomy

The benefits observed in the process-of-care domains have a coherent pathophysiological basis. First, tracheostomy reduces the length of the artificial airway, thereby decreasing airway

resistance and the work of breathing and enabling gradual weaning with lower pressure support. Second, tracheostomy eliminates the need for sedation to maintain endotracheal tube tolerance; the reduction in sedation burden is the only domain that is significant across all syntheses and serves as an intermediate causal pathway towards a shorter duration of ventilation. Third, tracheostomy facilitates clearance of bronchial secretions through more effective suctioning. Fourth, tracheostomy enables early mobilisation, chest physiotherapy, and rehabilitation.^{4,10,29,30}

The trial by Elsayed et al. provides direct mechanistic evidence for this pathway by demonstrating significant improvement in diaphragmatic excursion and diaphragmatic thickening fraction in the early tracheotomy group. Ventilator-induced diaphragmatic dysfunction develops rapidly during controlled ventilation with deep sedation, and earlier recovery of spontaneous respiratory activity is the most effective preventive strategy. Thus, the most likely causal chain is as follows: early tracheostomy reduces sedation, reduced sedation preserves diaphragmatic activity, preserved diaphragmatic function accelerates weaning, and accelerated weaning shortens ICU length of stay.¹²

What this chain has failed to demonstrate is translation into reduced mortality. The most plausible explanation is that the causes of death in ICU populations receiving prolonged ventilation are dominated by the severity of the underlying disease, multiple organ failure, and comorbidities, rather than by the duration of ventilation itself. Duration of ventilation is both a marker of severity and a risk factor, but its contribution to overall mortality is relatively small compared with other determinants that are unaffected by tracheostomy timing.^{8,10,31}

Ventilator-Associated Pneumonia and Effect Modification by Baseline Risk

Ventilator-associated pneumonia is the domain with the most polarised results. The meta-analysis by Siempos et al. reported a significant reduction, with an OR of 0.60 (95% CI 0.41–0.90; $p=0.01$) from 13 trials with 1,599 patients, and the authors explicitly stated that this finding may call into question the practice of delaying tracheostomy beyond the first week. In contrast, Han et al., Wang et al., Huang et al., and Szakmany et al. found no significant difference. Notably, the original version of the publication by Siempos et al. was retracted and republished because of a

data discrepancy in one included trial; the estimates cited in this review are therefore from the corrected version.^{25,26,27,29,32}

The explanation most consistent with the totality of the data is effect modification by baseline risk. In populations with a low baseline incidence of VAP, a relative risk reduction of 14% yields an absolute risk reduction too small to be detected. In populations with impaired protective airway reflexes — traumatic brain injury, severe stroke, cervical spinal cord injury — the baseline incidence of VAP ranges from 27% to 47%, so that the same relative risk reduction yields a far larger and readily detectable absolute reduction. This is reflected in the significant estimates from Foran et al. (RR 0.86; 95% CI 0.75–0.98) and de Franca et al. in these populations, as well as in the observational data of Robba et al. (27.2% versus 39.7%; $p=0.010$) and Kamath et al. (15.9% versus 47.4%).^{14,21,35,36}

Heterogeneity in VAP definitions further amplifies inconsistency. Some studies used clinical-radiological criteria based on the CPIS score, some used quantitative microbiological confirmation via bronchoalveolar lavage, and others used administrative diagnostic codes in registry databases. This indirectness of definition was one of the reasons for downgrading the certainty of evidence in the GRADE assessment.^{3,14,21,35}

Early Tracheostomy in Neurological Populations

Neurological populations have the characteristics theoretically most favourable to an early tracheostomy strategy, because the need for prolonged ventilation can be predicted with greater accuracy on the basis of the level of consciousness and loss of protective airway reflexes. The SETPOINT pilot trial in 60 patients with severe stroke reported a dramatic reduction in ICU mortality (10% versus 47%) and six-month mortality (27% versus 60%). However, the SETPOINT2 trial, designed to confirm these findings in 382 patients at 26 centres, failed to demonstrate improvement in six-month functional outcome, with an adjusted odds ratio of 0.93 (95% CI 0.60–1.42; $p=0.73$).^{7,10}

This discrepancy is a classic illustration of the limitations of small pilot trials. Nevertheless, the SETPOINT2 authors cautiously noted that the wide confidence interval around the effect

estimate did not permit exclusion of clinically relevant benefit or harm. The meta-analysis by Marra et al. in traumatic brain injury populations found that early tracheostomy reduced the risk of pneumonia, ICU length of stay, hospital length of stay, and duration of mechanical ventilation, but did not reduce mortality. The meta-analysis by de Franca et al. reported reductions in the duration of ventilation of 4.15 days, ICU length of stay of 5.87 days, and hospital length of stay of 6.68 days, with no difference in mortality.^{10,34,35}

The European Society of Intensive Care Medicine consensus on mechanical ventilation in acute brain injury noted that the GRADE ratings for all related domains were low, very low, or unavailable, so that recommendations on tracheostomy timing in this population still rest on individual clinical judgement. The study by Katsura et al. adds a dimension that warrants consideration: hospitals with a high propensity to perform early tracheostomy had a greater likelihood of withdrawal of life-sustaining treatment after tracheostomy (adjusted odds ratio 1.35; 95% CI 1.10–1.66; $p=0.004$), indicating that decisions on tracheostomy timing are closely intertwined with goals-of-care determination during periods of prognostic uncertainty.^{23,43}

Early Tracheostomy in Trauma and Spinal Cord Injury

In trauma and cervical spinal cord injury populations, observational evidence uniformly supports early tracheostomy with a substantial magnitude of effect. The meta-analysis by Foran et al. of 17 studies with 2,804 patients reported reductions in the duration of ventilation of 13.1 days, ICU length of stay of 10.20 days, and hospital length of stay of 7.39 days, together with reductions in the incidence of ventilator-associated pneumonia (RR 0.86; 95% CI 0.75–0.98) and tracheostomy-related complications (RR 0.64; 95% CI 0.48–0.84). The meta-analysis by Mubashir et al. reported reductions in ICU length of stay of 13 days and duration of ventilation of 18.30 days, with numerically lower but non-significant mortality (OR 0.56; 95% CI 0.32–1.01; $p=0.054$).^{36,37}

The pathophysiological rationale is clear: patients with high cervical spinal cord injury have respiratory muscle paralysis that is permanent or requires months to recover, so that the probability of requiring prolonged ventilation approaches certainty. In this context, the prediction

problem that underlies the failure of randomized trials in general ICU populations does not apply. The meta-analysis by Coffin et al. in patients undergoing anterior cervical decompression showed that concerns regarding contamination of the anterior surgical wound by the tracheostomy stoma were not substantiated, with an odds ratio for surgical site infection of 0.32 (95% CI 0.06–1.59; I^2 0%).^{36,37,44}

In paediatric populations with severe traumatic brain injury, the propensity-matched analysis by McLaughlin et al. of 121 pairs showed reductions in ventilator days, ICU days, and hospital days, as well as reductions in pneumonia (24% versus 41%), venous thromboembolism (3% versus 13%), and decubitus ulcers (4% versus 13%). The authors also noted that extubation without tracheostomy rarely occurred after post-injury day 18, providing an empirical basis for setting a decision threshold in this population.¹³

Tracheostomy in Patients with COVID-19 and ICU Capacity Management

The COVID-19 pandemic created a unique context in which tracheostomy timing became not only a question of clinical effectiveness but also one of resource allocation. The study by Hernández et al. in 15 Spanish ICUs, using a failure-free days approach and propensity matching, showed that earlier tracheostomy consistently yielded more ventilator-free days across all timing-threshold strata, with differences of 4.5 days in the ≤ 7 -day stratum, 3.1 days in the 8–10-day stratum, and 3.0 days in the 11–14-day stratum. The authors concluded that optimising tracheostomy timing can relieve the burden on ICU capacity without increasing mortality.¹⁶

The TTCOV19 randomized controlled trial did not confirm the superiority of early tracheotomy in the intention-to-treat analysis, but found a significant reduction in the per-protocol analysis and a significant overall correlation between tracheotomy timing and the number of ventilation days. The authors recommended that the early strategy should still be considered in selected cases in which a need for ventilation exceeding 14 days cannot be excluded. The COVIP cohort study of 1,740 patients aged 70 years and older in 16 European countries found very wide variation in tracheostomy rates between countries (8.3% to 52.9%) without evidence of an effect on three-month survival.^{11,17}

Several COVID-19 observational studies reported apparently conflicting results. Vuu et al. concluded that the optimal timing was 11 days or more on the basis of lower in-hospital mortality in the late group, whereas Kovačević et al., in a resource-limited setting, reported that tracheotomy was independently associated with reduced in-hospital mortality (HR 0.16; 95% CI 0.11–0.23). This difference can be almost entirely explained by the difference in comparator groups: Vuu et al. compared early with late tracheostomy, whereas Kovačević et al. compared tracheotomised patients with patients who were intubated only. The latter comparison is highly susceptible to immortal time bias and to selection bias related to procedural eligibility.^{18,22}

Procedural Safety and Choice of Technique

Safety data do not support the concern that the early strategy increases procedural risk. The rate of tracheostomy-related complications in the TracMan trial was 6.3% overall, with an even lower figure in the early group (5.5% versus 7.8%). In SETPOINT2, tracheostomy-related serious adverse events occurred in 5.0% versus 3.4% of events, a small and non-significant difference. The systematic review by Curry and Rowan showed that the incidence of laryngotracheal stenosis did not differ significantly between the two strategies in the studies at lowest risk of bias.^{8,10,40}

The choice of technique has a greater impact on safety than timing. The meta-analysis by Putensen et al. of 14 randomized trials with 973 patients showed that percutaneous tracheostomy was performed more quickly (mean difference –13.06 minutes) and reduced stomal inflammation (OR 0.38; 95% CI 0.19–0.76) and infection (OR 0.22; 95% CI 0.11–0.41), but increased procedural technical difficulty (OR 4.58; 95% CI 2.21–9.47). Among percutaneous techniques, the multiple-dilator and single-step dilator techniques carried the lowest intraprocedural risk. The meta-analysis by Johnson-Obaseki et al. confirmed a lower infection rate and a shorter procedure time with the percutaneous technique, with no difference in mortality or bleeding.^{41,42}

The practical implication is that a decision to bring forward tracheostomy timing should be accompanied by the choice of bedside percutaneous dilatational technique performed by an experienced operator, so that the additional risk arising from the increased number of procedures can be minimised. In settings with limited operator experience or without bronchoscopic or

ultrasonographic guidance, the safety advantage of the percutaneous technique cannot be assumed automatically.^{41,42}

Implications for Health-Care System Capacity and Efficiency

Although a mortality benefit has not been demonstrated, the magnitude of effect in the process-of-care domains has economic consequences that cannot be ignored. A reduction in ICU length of stay of 6.36 days as reported by Han et al., or even the more conservative estimate of 5.14 days from Hosokawa et al., is equivalent to freeing an ICU bed for almost one additional care cycle per patient. In health-care systems with a low intensive care bed ratio and high occupancy, the cumulative effect at the population level becomes substantial.^{30,32}

However, this calculation must be adjusted for the increased number of procedures. If the early strategy increases the proportion of patients undergoing tracheostomy from 45% to 92%, as in TracMan, then for every 100 patients managed with the early strategy there are approximately 47 additional procedures. With a procedural complication rate of approximately 6%, this means approximately three additional complications per 100 patients. A comprehensive health-economic evaluation needs to weigh savings in ICU days against the cost of additional procedures, the cost of complications, and the burden of long-term tracheostomy care, including decannulation and swallowing rehabilitation.^{8,30,32}

The most economically and ethically rational approach is a risk-guided strategy: applying early tracheostomy in subpopulations with a high probability of requiring prolonged ventilation, while maintaining conventional weaning and extubation strategies in patients with a high probability of rapid recovery. This approach preserves process benefits for those who will derive them while avoiding unnecessary procedural exposure in those who do not need it.^{8,9,11,31}

Ethical Considerations and Goals-of-Care Determination

The finding by Katsura et al. regarding the association between an institutional propensity for early tracheostomy and increased withdrawal of life-sustaining treatment after tracheostomy opens an important ethical dimension. Tracheostomy in patients with severe brain injury is often performed during a period of prognostic uncertainty and evolving goals of care. A decision to

perform early tracheostomy may be perceived by patients and families as a commitment to ongoing care, and at the same time as a signal that rapid recovery is not expected.²³

Therefore, the decision on tracheostomy timing cannot be reduced to an effectiveness calculation alone. Structured goals-of-care discussions, honest prognostic communication regarding uncertainty, and respect for patients' values and preferences must precede the procedural decision. In the Indonesian context, where decision-making is often based on the extended family and strong religious considerations, this communication process requires time and a culturally adapted approach.^{23,43}

Strengths of the Review

- Broad coverage of primary studies, with 23 studies across designs and more than 33,000 patients, far exceeding previous syntheses, which were generally limited to 5 to 21 randomized controlled trials.
- Simultaneous analysis of 15 outcome domains, including rarely synthesised domains such as weaning success, diaphragmatic function, non-respiratory complications, and the proportion of overtreatment.
- Dual risk-of-bias assessment using RoB 2 and the Newcastle–Ottawa Scale, with additional assessment of immortal time bias not covered by the standard instruments.
- Verification of the existence of all references through the Consensus academic search engine with a medical-mode filter and exclusion of preprints.
- Explicit confrontation of randomized, observational, and Bayesian evidence, with a methodological explanation of the discordance among the three.

Future Research Directions

The most urgent research priority is the development and external validation of prediction models for the need for prolonged mechanical ventilation that can be applied on days 3 to 5 of care. Without such tools, every new randomized controlled trial will repeat the same dilution problem. Next-generation trials should use designs that enrich the population with high-probability

patients, for example through validated prediction scores or by restricting enrolment to populations with predictable ventilation requirements, such as high cervical spinal cord injury.^{8,9,11,31}

The second priority is standardisation of outcome definitions, particularly ventilator-associated pneumonia and tracheostomy complications, so that cross-study synthesis is no longer hampered by indirectness of definition. The third priority is the reporting of patient-centred outcomes, including the ability to communicate, time to decannulation, swallowing function, voice quality, and health-related quality of life at 6 to 12 months. The fourth priority is research in resource-limited settings, including Indonesia, where limited ventilators and ICU beds may substantially alter the benefit–risk balance compared with the high-income settings in which most of the evidence has been generated.^{16,22,31,43}

CONCLUSIONS AND RECOMMENDATIONS

Conclusions

Based on the synthesis of 23 primary studies comprising 12 randomized controlled trials and 11 observational studies with more than 33,000 patients, together with comparison against 21 systematic reviews and meta-analyses, the following conclusions can be drawn.

- Early tracheostomy does not significantly reduce short-term or long-term mortality in the general intensive care unit population. Pooled estimates from eight independent syntheses ranged from a risk ratio of 0.79 to 0.93 with confidence intervals crossing unity, and trial sequential analysis indicates that the available evidence remains underpowered to exclude a small but clinically relevant benefit (moderate certainty of evidence).^{8,24-32}
- Early tracheostomy consistently and significantly shortens sedation duration (mean difference –2.78 days; 95% CI –3.68 to –1.88), increases ventilator-free days (+2.12 days; 95% CI 0.94 to 3.30), shortens the duration of mechanical ventilation (–2.77 days; 95% CI –5.10 to –0.44), and shortens ICU length of stay (–6.36 days; 95% CI –9.84 to –2.88) (moderate certainty of evidence, high for the sedation domain).^{29,30,32}
- The reduction in the incidence of ventilator-associated pneumonia is population-dependent: significant in patients with traumatic brain injury, severe stroke, cervical spinal

cord injury, and severe trauma, but inconsistent in the general ICU population (low to moderate certainty of evidence).^{27,35,36}

- Early tracheostomy does not increase procedure-related complications (5.5% versus 7.8%) or the incidence of laryngotracheal stenosis (8.1% versus 10.9%); hence, the early strategy can be considered safe from the perspective of procedural safety per patient undergoing the procedure (moderate certainty of evidence).^{8,40}
- An early tracheostomy strategy substantially increases the number of tracheostomy procedures, with an odds ratio of 16.1 (95% CI 5.7–45.7) and a difference in proportions of up to 47 percentage points, thereby exposing a large number of patients to an invasive procedure that would never have been required under a conventional strategy (high certainty of evidence).^{8,30}
- Six-month functional outcome in patients with severe stroke does not differ between the early and standard strategies (adjusted odds ratio 0.93; 95% CI 0.60–1.42), although the wide confidence interval does not permit exclusion of clinically relevant benefit or harm.¹⁰
- The discordance between observational and randomized evidence is explained mainly by immortal time bias and confounding by indication; the effect sizes reported by observational studies cannot be interpreted as causal effects.^{14,34}
- The principal determinant of the failure of the early strategy to yield a mortality benefit is clinicians' inability to predict the need for prolonged ventilation, rather than an absence of biological effect of tracheostomy itself.^{8,9,11}

Recommendations

Recommendations for Clinical Practice

- Early tracheostomy is not recommended as a universal policy for all patients receiving mechanical ventilation. Timing decisions should be individualised according to the probability of requiring prolonged ventilation.
- Consider early tracheostomy (days 4 to 7) in patients with a high probability of requiring ventilation for more than 14 days, particularly severe traumatic brain injury with GCS 3–

8, severe stroke with loss of protective airway reflexes, high cervical spinal cord injury, and severe multiple trauma.

- Maintain conventional weaning and extubation trial strategies in patients without clear prognostic markers, given that more than half of such patients are successfully extubated without requiring tracheostomy.
- When tracheostomy is decided upon, use a bedside percutaneous dilatational technique with bronchoscopic or ultrasonographic guidance by an experienced operator to minimise complications.
- Implement daily sedation interruption protocols and early mobilisation after tracheostomy, because reduction of sedation burden is the main pathway linking early tracheostomy to improved process outcomes.
- Conduct structured goals-of-care discussions with patients and families before the tracheostomy decision, particularly in patients with severe brain injury and prognostic uncertainty.
- Perform systematic monitoring for long-term complications, including tracheal stenosis, dysphagia, and voice disorders, and plan decannulation in a structured manner.

Recommendations for Institutions and Policymakers

- Develop institutional protocols on tracheostomy criteria and timing based on risk stratification rather than on a single uniform timing threshold.
- During ICU capacity surges, consider optimisation of tracheostomy timing as one strategy to increase intensive care bed availability without compromising mortality.
- Establish percutaneous dilatational tracheostomy training programmes for intensivists and surgeons, as well as prospective complication registries at the hospital level.
- Develop post-tracheostomy care pathways that include swallowing rehabilitation, speech therapy, and structured decannulation protocols.

Recommendations for Future Research

- Develop and externally validate prediction models for the need for prolonged mechanical ventilation that can be applied on days 3 to 5 of intensive care.
- Design randomized controlled trials with population enrichment (enrichment design) that restrict inclusion to patients with a high probability of requiring prolonged ventilation.
- Standardise outcome definitions, particularly for ventilator-associated pneumonia and tracheostomy complications, in accordance with international consensus criteria.
- Report patient-centred outcomes, including time to decannulation, swallowing function, voice quality, communication ability, and health-related quality of life at 6 to 12 months.
- Conduct research in resource-limited settings, including Indonesia, taking into account limitations in ventilators, ICU beds, and the availability of experienced operators.
- Apply analyses that correct for immortal time bias, such as risk set matching, landmark analysis, or time-dependent exposure modelling, in all observational studies of tracheostomy timing.

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