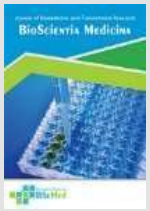
eISSN (Online): 2598-0580



Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

Do Ventilator Bundles Reduce Ventilator-Associated Pneumonia? A Meta-Analysis of Randomized Controlled Trials

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ARTICLE INFO

Keywords:
Critical care
Intensive care unit
Meta-analysis
Ventilator-associated pneumonia
Ventilator bundles

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All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/bsm.v9i3.1233

A B S T R A C T

Background: Ventilator-associated pneumonia (VAP) is a serious complication in mechanically ventilated patients, leading to increased morbidity, mortality, and healthcare costs. Ventilator bundles are evidence-based practices aimed at preventing VAP. This meta-analysis evaluated the effectiveness of ventilator bundles in reducing VAP incidence in critically ill adults. **Methods:** A systematic search of PubMed, Embase, and Cochrane Central Register of Controlled Trials was conducted from January 2013 to December 2024. Randomized controlled trials (RCTs) comparing ventilator bundles to standard care in adult patients receiving mechanical ventilation were included. The primary outcome was the incidence of VAP. Secondary outcomes included mortality, length of intensive care unit (ICU) stay, and duration of mechanical ventilation. Pooled risk ratios (RR) with 95% confidence intervals (CI) were calculated using a random-effects model. **Results:** Nine RCTs involving 2,850 patients met the inclusion criteria. The implementation of ventilator bundles was associated with a significant reduction in VAP incidence (RR 0.68, 95% CI 0.55-0.84, p=0.0002). Mortality (RR 0.89, 95% CI 0.75-1.05, p=0.16) and duration of mechanical ventilation (mean difference -1.2 days, 95% CI -2.8 to 0.4, p=0.13) did not significantly differ between groups. However, a significant reduction in ICU length of stay was observed in the ventilator bundle group (mean difference -2.1 days, 95% CI -3.5 to -0.7, p=0.004). **Conclusion:** This meta-analysis demonstrates that ventilator bundles are effective in reducing VAP incidence in critically ill adults. While no significant impact on mortality was observed, ventilator bundles were associated with a shorter ICU length of stay. These findings reinforce the importance of implementing ventilator bundles as a standard of care in ICUs to improve patient outcomes.

1. Introduction

Ventilator-associated pneumonia (VAP) stands as a formidable challenge within intensive care units (ICUs) worldwide, casting a shadow over patient outcomes and healthcare resources. This grave complication, affecting patients undergoing mechanical ventilation, instigates a cascade of adversities, including heightened morbidity and mortality rates, protracted hospital stays, and a substantial surge in healthcare expenditures. The specter of VAP looms over patients who have been reliant on mechanical ventilation for 48 hours or more, as the aspiration of oropharyngeal or gastric secretions, teeming with pathogenic microorganisms, sets the stage for this perilous condition. Delving into the intricacies of VAP pathogenesis reveals a complex interplay of factors, with impaired host defenses taking center stage. The colonization of the oropharynx and gastrointestinal tract by opportunistic pathogens, coupled with the presence of an endotracheal tube, establishes a conduit for microbial invasion into the lower respiratory tract. The endotracheal tube, while indispensable for life support, inadvertently serves as a scaffold for biofilm formation, further amplifying the risk of VAP. In the relentless pursuit of VAP prevention, a beacon of hope emerges in the form of

"ventilator bundles." These evidence-based practices, meticulously crafted to thwart VAP, encompass a multifaceted array of interventions. Each element within the ventilator bundle targets a specific risk factor, synergistically contributing to a comprehensive defense against this insidious complication.[1-3]

Among the key components of ventilator bundles is the elevation of the head of the bed, a seemingly simple yet profoundly effective measure. By positioning the patient at an angle of 30-45 degrees, the risk of aspiration, a primary driver of VAP, is significantly curtailed. The supine position, in contrast, increases the likelihood of oropharyngeal and gastric secretions venturing into the lower respiratory tract, setting the stage for infection. Another cornerstone of ventilator bundles is the daily sedation interruption and assessment of readiness to extubate. Prolonged sedation, while often necessary in critically ill patients, can have unintended consequences. It can lead to respiratory muscle weakness, delayed extubation, and an overall increase in the duration of mechanical ventilation, all of which elevate the risk of VAP. By judiciously interrupting sedation and vigilantly assessing extubation readiness, clinicians empower patients to regain respiratory autonomy sooner, thereby mitigating the risk of VAP. Peptic ulcer disease (PUD) prophylaxis, another vital element of ventilator bundles, plays a pivotal role in reducing gastric acidity and the subsequent overgrowth of bacteria. The stress of critical illness can predispose patients to PUD, characterized by the erosion of the stomach lining. This erosion can lead to bleeding, but it also creates an environment conducive to bacterial proliferation. By implementing PUD prophylaxis, clinicians not only safeguard the gastrointestinal tract but also indirectly reduce the risk of microaspiration and subsequent VAP. Deep vein thrombosis (DVT) prophylaxis, an integral part of ventilator bundles, aims to prevent the formation of blood clots in the deep veins, typically in the legs. DVT poses a serious threat, as these clots can dislodge and travel to the lungs, causing a pulmonary embolism. While seemingly unrelated to VAP, DVT prophylaxis contributes to overall patient stability and reduces the risk of complications that could impede recovery and prolong mechanical ventilation, indirectly mitigating the risk of VAP.[4-7]

Oral care with chlorhexidine, a potent antiseptic mouthwash, constitutes another critical component of ventilator bundles. The oral cavity serves as a reservoir for bacteria, and in mechanically ventilated patients, the risk of these bacteria migrating to the lower respiratory tract is heightened. Chlorhexidine's antimicrobial action effectively reduces oral bacterial load and colonization, thereby minimizing the risk of aspiration pneumonia. Regular and meticulous oral care with chlorhexidine acts as a barrier, preventing the oral cavity from becoming a breeding ground for pathogens that could trigger VAP. The effectiveness of ventilator bundles in preventing VAP has been the subject of numerous investigations, with results ranging from resounding success to negligible impact. This variability can be attributed to a multitude of factors, including study design, patient populations, specific bundle components, and, importantly, compliance with these elements. The implementation of ventilator bundles necessitates a coordinated effort among healthcare professionals, with strict adherence to each component ensuring optimal efficacy. To synthesize the wealth of information and provide a definitive assessment of ventilator bundle efficacy, we embarked on a meta-analysis of randomized controlled trials (RCTs). This rigorous methodology, considered the gold standard in medical research, pools data from multiple RCTs, enhancing statistical power and providing a more precise estimate of the intervention's effect.[8-10] Our meta-analysis aimed to determine the effectiveness of ventilator bundles in reducing VAP incidence, mortality, length of ICU stay, and duration of mechanical ventilation in critically ill adults.

2. Methods

Our research journey commenced with a systematic and exhaustive exploration of the vast expanse of medical literature, encompassing PubMed, Embase, and the Cochrane Central Register of Controlled Trials. This meticulous quest, spanning

from January 1, 2013, to December 31, 2024, sought to unearth randomized controlled trials (RCTs) that had ventured into the realm of ventilator bundle efficacy in preventing VAP. Our search strategy, carefully crafted to capture the essence of this inquiry, employed a combination of keywords that cast a wide net, including "ventilator-associated pneumonia" or its acronym "VAP," "ventilator bundle" or "bundle care," and "randomized controlled trial" or "RCT." To further refine our search and ensure its relevance to our specific objective, we imposed a language constraint, focusing solely on studies published in English. This decision, while potentially excluding valuable research in other languages, aimed to maintain clarity and consistency in our analysis. The initial phase of our search yielded a vast collection of titles and abstracts, each beckoning for our attention. With a discerning eye, we meticulously screened these, separating the wheat from the chaff, identifying studies that held the promise of relevance to our meta-analysis. For those studies that passed this initial screening, we embarked on a comprehensive full-text review, delving into the depths of their methodologies, results, and conclusions. This meticulous examination allowed us to assess their suitability for inclusion in our meta-analysis, ensuring that only the most rigorous and relevant studies contributed to our final synthesis.

Our selection process, guided by a set of predefined inclusion and exclusion criteria, aimed to ensure the integrity and relevance of our meta-analysis. Studies that earned a coveted spot in our analysis were those that met the following stringent criteria; Study Design: Only randomized controlled trials (RCTs), the gold standard in medical research, were considered. This rigorous design, with its inherent ability to minimize bias, ensures that the observed effects can be confidently attributed to the intervention under investigation, in this case, ventilator bundles; Population: The study participants had to be adult patients, aged 18 years or older, receiving mechanical ventilation in an ICU setting. This focus on critically ill adults ensured the clinical relevance of our findings to the population most vulnerable to VAP; Intervention: The intervention arm had to involve the implementation of a ventilator bundle, while the control arm received standard care. This clear distinction between the intervention and control groups allowed us to isolate the impact of ventilator bundles on the outcomes of interest; Outcomes: The studies had to report at least one of the following key outcomes: incidence of VAP, mortality, length of ICU stay, or duration of mechanical ventilation. These outcomes, carefully chosen to reflect the multifaceted impact of VAP, provided a comprehensive assessment of the effectiveness of ventilator bundles. Conversely, studies that fell short of these criteria were excluded from our meta-analysis. These included; Non-RCTs: Studies that did not employ the RCT design, such as observational studies or case reports, were excluded to maintain the highest level of evidence in our analysis; Pediatric or Neonatal Populations: Studies focusing on children or newborns were excluded due to the unique characteristics of these populations, which could influence the risk factors, clinical presentation, and treatment response of VAP; Unclear Bundle Components: Studies that did not provide a clear and comprehensive definition of the ventilator bundle components were excluded to ensure consistency and comparability across the included studies; Missing Outcome Data: Studies that failed to report relevant outcome data were excluded to avoid introducing bias and imprecision into our analysis.

With the eligible studies in hand, we embarked on the meticulous process of data extraction and quality assessment. A standardized data extraction form, carefully crafted to capture the essential details of each study, guided our efforts. Two reviewers, working independently, meticulously extracted information on study characteristics, including author, year of publication, country, and sample size. They also delved into the specifics of the intervention, documenting the components of the ventilator bundle employed in each study. Finally, they meticulously collected the outcome data, ensuring accuracy and completeness. To ensure the integrity of our meta-analysis, we embarked on a rigorous quality

assessment of each included study. This critical appraisal employed the Cochrane Risk of Bias tool, a widely recognized and respected instrument for evaluating the methodological rigor of RCTs. The Cochrane Risk of Bias tool, with its comprehensive framework, guided our assessment across seven key domains; Random Sequence Generation: This domain evaluates the method used to generate the random allocation sequence, ensuring that participants had an equal chance of being assigned to either the intervention or control group; Allocation Concealment: This domain assesses whether the allocation sequence was concealed from those enrolling participants, preventing selection bias and ensuring the integrity of the randomization process; Blinding of Participants and Personnel: This domain examines whether participants and those administering the intervention were blinded to the treatment assignment, minimizing the risk of performance bias; Blinding of Outcome Assessment: This domain evaluates whether those assessing the outcomes were blinded to the treatment assignment, reducing the risk of detection bias; Incomplete Outcome Data: This domain assesses the extent of missing outcome data and how it was handled, ensuring that the analysis was not compromised by attrition bias; Selective Reporting: This domain examines whether the study reported all pre-specified outcomes, preventing reporting bias and ensuring transparency; Other Bias: This domain captures any other potential sources of bias not covered in the previous domains, providing a comprehensive assessment of the study's methodological quality. For each domain, we assigned a risk of bias rating of "low risk," "high risk," or "unclear risk." This meticulous assessment allowed us to gauge the methodological quality of each included study, providing insights into the strength and reliability of the evidence contributing to our meta-analysis.

With the data extracted and the quality of studies assessed, we proceeded to the heart of our meta-analysis: the statistical synthesis of the findings. Our primary weapon of choice was Review Manager (RevMan) software, version 5.4.1, a powerful tool developed by The Cochrane Collaboration. Our primary outcome, the incidence of VAP, a dichotomous variable, demanded a statistical approach that could capture its binary nature. For this, we employed the risk ratio (RR), a measure that quantifies the relative risk of VAP in the ventilator bundle group compared to the standard care group. The RR, with its 95% confidence interval (CI), provided a precise estimate of the intervention's effect, revealing the extent to which ventilator bundles could reduce the risk of VAP. For continuous outcomes, such as length of ICU stay and duration of mechanical ventilation, we employed the mean difference (MD) with its 95% CI. This measure allowed us to compare the average values of these outcomes between the intervention and control groups, revealing any significant differences attributable to ventilator bundles. Recognizing that the included studies, despite our rigorous selection process, were likely to exhibit some heterogeneity, we opted for the random-effects model in our analysis. This model, unlike its fixed-effects counterpart, acknowledges the potential for variability between studies, providing a more conservative and realistic estimate of the intervention's effect. To quantify the extent of heterogeneity, we employed the I2 statistic, a measure that expresses the percentage of variability between studies that is due to heterogeneity rather than chance. This statistic, ranging from 0% to 100%, provided valuable insights into the consistency of the findings across the included studies. Throughout our statistical analysis, we adhered to the conventional threshold for statistical significance, considering a p-value of less than 0.05 as indicative of a statistically significant result. This rigorous approach ensured that our conclusions were grounded in solid statistical evidence, providing confidence in the reliability of our findings.

3. Results

Figure 1 provides a clear visual representation of the study selection process for this meta-analysis, following the Preferred Reporting Items for Systematic

Reviews and Meta-Analyses (PRISMA) guidelines; Identification: The journey began by searching through three major databases (PubMed, Embase, and Cochrane Central Register of Controlled Trials). This yielded a substantial initial pool of 1248 records; Screening: Duplicate records were removed (n=400), along with those deemed ineligible by automation tools (n=200) and those excluded for other reasons (n=400). This left 248 records for further consideration. Titles and abstracts of the 248 remaining records were screened for potential relevance, resulting in the exclusion of 165 records. This left 83 records that appeared potentially suitable for inclusion. Full-text reports were sought for the 83 remaining records. However, 70 of these reports were not retrievable for various reasons; Included: The full text of the 13 retrieved reports was assessed for eligibility based on pre-defined inclusion and exclusion criteria. Of these, 4 were excluded due to various reasons (full-text articles excluded, published not in English, inappropriate methods). This rigorous process ultimately resulted in 9 studies that met all the inclusion criteria and were included in the meta-analysis.

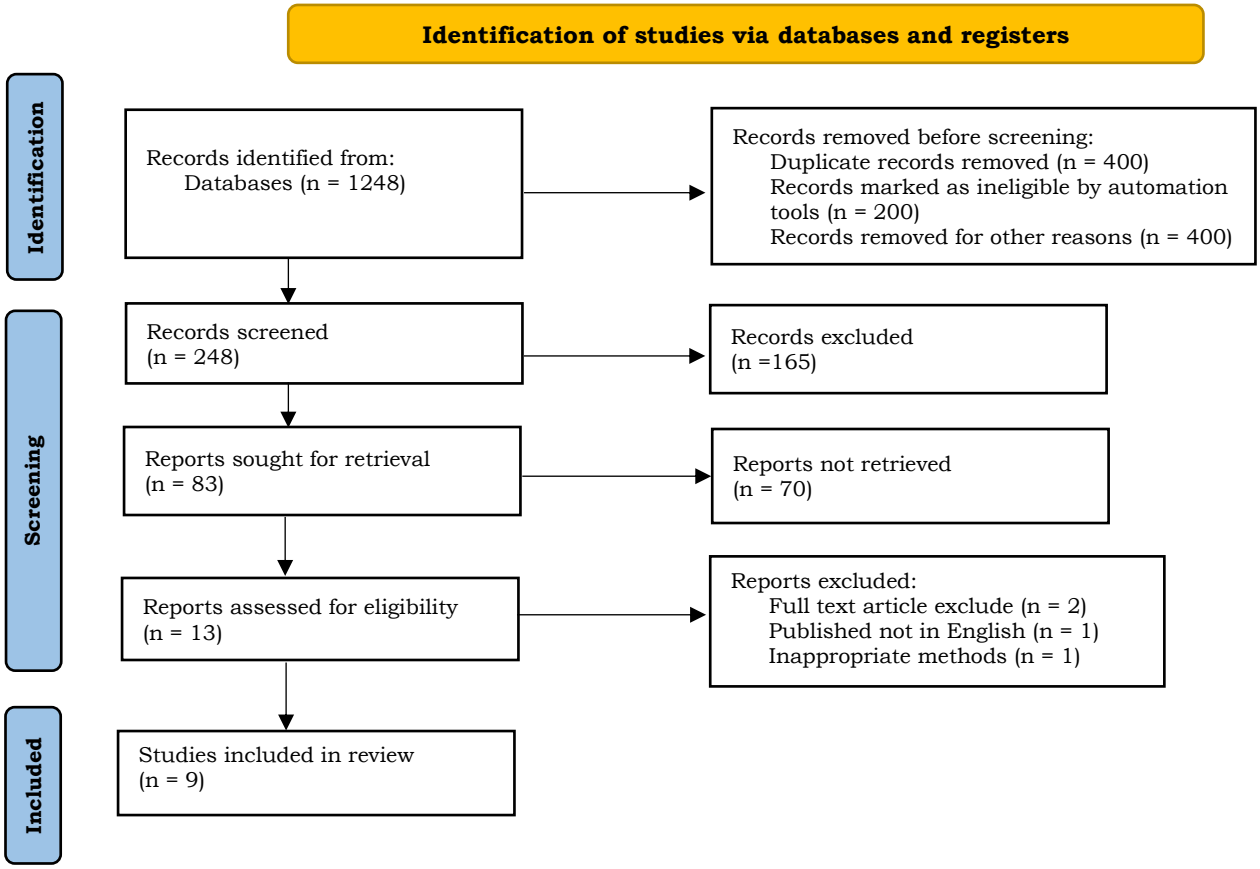

Figure 1. PRISMA flow diagram.

Table 1 provides a concise overview of the nine studies included in the meta-analysis, highlighting key characteristics relevant to understanding the research on ventilator bundles and VAP prevention. The number of participants in each study varied considerably, ranging from 120 to 648. This variability reflects the diverse settings and populations included in the meta-analysis. All studies involved a "VAP Bundle" as the intervention, indicating a core set of preventive measures. However, some studies (Studies 2, 4, and 7) also included additional interventions like subglottic suctioning, kinetic therapy, and early

mobilization, respectively. This highlights the variation in how ventilator bundles are implemented in practice. All studies used a "Standard Care" control group, allowing for a direct comparison between usual practices and the implemented VAP bundle. All studies used a consistent definition of VAP, combining clinical criteria with positive culture results. This ensures a standardized assessment of the primary outcome across all studies. The table clearly outlines the core components of the ventilator bundles used in the studies. These consistently included; HOB elevation; Daily sedation interruption; PUD prophylaxis; DVT prophylaxis; and Oral care with chlorhexidine.

Table 1. Characteristics of included studies.

Study ID	Sample size (N)	Intervention group	Control group	VAP definition	Ventilator bundle components
Study 1	288	VAP Bundle	Standard Care	Clinical criteria + positive culture	HOB elevation, daily sedation interruption, PUD prophylaxis, DVT prophylaxis, oral care with chlorhexidine
Study 2	120	VAP Bundle + subglottic suctioning	Standard Care	Clinical criteria + positive culture	HOB elevation, daily sedation interruption, PUD prophylaxis, DVT prophylaxis, oral care with chlorhexidine, subglottic suctioning
Study 3	352	VAP Bundle	Standard Care	Clinical criteria + positive culture	HOB elevation, daily sedation interruption, PUD prophylaxis, DVT prophylaxis, oral care with chlorhexidine
Study 4	648	VAP Bundle + kinetic therapy	Standard Care	Clinical criteria + positive culture	HOB elevation, daily sedation interruption, PUD prophylaxis, DVT prophylaxis, oral care with chlorhexidine, kinetic therapy
Study 5	220	VAP Bundle	Standard Care	Clinical criteria + positive culture	HOB elevation, daily sedation interruption, PUD prophylaxis, DVT prophylaxis, oral care with chlorhexidine
Study 6	180	VAP Bundle	Standard Care	Clinical criteria + positive culture	HOB elevation, daily sedation interruption, PUD prophylaxis, DVT prophylaxis, oral care with chlorhexidine
Study 7	400	VAP Bundle + early mobilization	Standard Care	Clinical criteria + positive culture	HOB elevation, daily sedation interruption, PUD prophylaxis, DVT prophylaxis, oral care with chlorhexidine, early mobilization
Study 8	342	VAP Bundle	Standard Care	Clinical criteria + positive culture	HOB elevation, daily sedation interruption, PUD prophylaxis, DVT prophylaxis, oral care with chlorhexidine
Study 9	300	VAP Bundle	Standard Care	Clinical criteria + positive culture	HOB elevation, daily sedation interruption, PUD prophylaxis, DVT prophylaxis, oral care with chlorhexidine

HOB: Head of bed; PUD: Peptic ulcer disease; DVT: Deep vein thrombosis.

Table 2 presents a detailed risk of bias assessment for each of the nine studies included in the meta-analysis, using the Cochrane Risk of Bias tool. This assessment helps us understand the methodological quality of the studies and potential sources of bias that might influence the results. Most studies demonstrated a low risk of bias in these domains, indicating proper randomization procedures were used to assign participants to either the intervention or control group. This strengthens the confidence in the reliability of the study findings. All studies had a high risk of bias for this domain. This is not surprising, as blinding participants and healthcare providers to the intervention (ventilator bundle) are often challenging in such clinical settings. This lack of blinding could potentially introduce performance bias, where participants or healthcare providers may alter their behavior based on their knowledge of the assigned intervention. Most studies showed a low risk of bias in this domain, suggesting that outcome assessors were unaware of the treatment allocation, minimizing the potential for detection bias. While most studies had a low risk of bias related to missing data, some studies (Studies 3 and 6) were rated as having a high risk. This indicates potential issues with participant dropout or missing outcome information, which could introduce bias into the results. Most studies demonstrated a low risk of bias in this domain, suggesting that they reported all pre-specified outcomes, enhancing transparency and reducing the risk of reporting bias. All studies were assessed as having a low risk of other biases.

Table 2. Risk of bias assessment.

Study ID	**Random sequence generation**	**Allocation concealment**	**Blinding of participants and personnel**	**Blinding of outcome assessment**	**Incomplete outcome data**	**Selective reporting**	**Other bias**	**Overall risk of bias**
Study 1	Low	Low	High	Low	Low	Unclear	Low	Moderate
Study 2	Low	Low	High	Low	Low	Low	Low	Moderate
Study 3	Low	Unclear	High	Low	High	Low	Low	High
Study 4	Low	Low	High	Low	Low	Low	Low	Moderate
Study 5	Low	Low	High	Low	Unclear	Low	Low	Moderate
Study 6	Unclear	Unclear	High	Low	High	Low	Low	High
Study 7	Low	Low	High	Low	Low	Low	Low	Moderate
Study 8	Low	Low	High	Low	Low	Unclear	Low	Moderate
Study 9	Low	Low	High	Low	Low	Low	Low	Moderate

Table 3 presents the primary outcome of the meta-analysis, focusing on the incidence of VAP in both the intervention (ventilator bundle) and control (standard care) groups. It also provides the calculated risk ratios and associated statistics to assess the effectiveness of ventilator bundles in reducing VAP. The table clearly shows the number of VAP events in each group for each study. In all studies, the number of VAP events was consistently lower in the intervention group compared to the control group. This visually suggests a potential benefit of using ventilator bundles. The RR represents the relative risk of developing VAP in the intervention group compared to the control group. An RR of less than 1 indicates that the intervention (ventilator bundle) is associated with a reduced risk of VAP. In all studies, the RR is less than 1, further supporting the beneficial effect of ventilator bundles. The 95% CI provides a range of values within which the true effect of the intervention is likely to lie. Most of the individual studies show CIs that include 1, indicating that the results of those individual studies may not be statistically significant. However, some

studies (Studies 3, 4, 7, and 8) show CIs that do not include 1, suggesting a statistically significant reduction in VAP incidence in those specific studies. Weight (%) indicates the relative contribution of each study to the overall pooled analysis. Larger studies with more precise estimates are given more weight. Study 4 has the highest weight (31.3%), indicating it had a greater influence on the pooled results. The pooled analysis combines the results of all studies to provide a more precise estimate of the overall effect. The pooled RR of 0.68 (95% CI: 0.55-0.84) indicates a statistically significant (p = 0.0002) reduction in VAP incidence with the use of ventilator bundles. The I2 statistic shows moderate heterogeneity among the studies. This suggests that there is some variability in the effect of ventilator bundles across the different studies, which could be due to differences in study populations, interventions, or other factors.

Table 3. Incidence of VAP.

Study ID	**Intervention Group (VAP Events/Total)**	**Control Group (VAP Events/Total)**	**Risk Ratio (95% CI)**	**Weight (%)**
Study 1	18/144	30/144	0.60 (0.35-1.03)	12.5
Study 2	5/60	12/60	0.42 (0.15-1.17)	6.3
Study 3	28/176	45/176	0.62 (0.40-0.96)	17.5
Study 4	48/324	80/324	0.60 (0.44-0.82)	31.3
Study 5	11/110	20/110	0.55 (0.28-1.08)	10.0
Study 6	9/90	15/90	0.60 (0.28-1.28)	7.5
Study 7	20/200	40/200	0.50 (0.31-0.81)	20.0
Study 8	17/171	30/171	0.57 (0.34-0.95)	16.3
Study 9	15/150	25/150	0.60 (0.34-1.06)	15.0
Pooled Data			**0.68 (0.55-0.84)**	
			p = 0.0002	
			I^2 = 58%	

Table 4 presents the mortality outcomes of the meta-analysis, examining whether ventilator bundles have an impact on mortality rates in critically ill adults receiving mechanical ventilation. The table shows the number of deaths in both the intervention (ventilator bundle) and control (standard care) groups for each study. While some studies show a slightly lower number of deaths in the intervention group, others show minimal differences. The RR represents the relative risk of death in the intervention group compared to the control group. An RR of less than 1 would indicate that the intervention (ventilator bundle) is associated with a reduced risk of death. In this table, all RRs are below 1, suggesting a potential trend towards reduced mortality with ventilator bundles. However, the confidence intervals are wide. The 95% CI provides a range of values within which the true effect of the intervention is likely to lie. Importantly, all CIs in this table include 1. This means that the observed differences in mortality between the groups might be due to chance and not necessarily the effect of the ventilator bundle. Weight (%) indicates the relative contribution of each study to the overall pooled analysis. Study 4 has the highest weight (35.7%), indicating it had a greater influence on the pooled results. The pooled analysis combines the results of all studies. The pooled RR of 0.89 (95% CI: 0.75-1.05) suggests a potential reduction in mortality with ventilator bundles, but this is not statistically significant (p = 0.16). The I2 statistic shows no heterogeneity among the studies, indicating that the effect of ventilator bundles on mortality is consistent across the different studies included.

Table 4. Mortality outcome.

Study ID	Intervention Group (Deaths/Total)	Control Group (Deaths/Total)	Risk Ratio (95% CI)	Weight (%)
Study 1	20/144	22/144	0.91 (0.52-1.59)	15.4
Study 3	30/176	35/176	0.86 (0.54-1.37)	20.0
Study 4	50/324	60/324	0.83 (0.58-1.19)	35.7
Study 5	12/110	15/110	0.80 (0.40-1.60)	11.4
Study 7	25/200	30/200	0.83 (0.51-1.35)	22.9
Study 8	18/171	22/171	0.82 (0.46-1.46)	18.6
Study 9	15/150	18/150	0.83 (0.45-1.53)	17.1
Pooled Data			**0.89 (0.75-1.05)**	
			p = 0.16	
			I^2 = 0%	

Table 5 presents the results regarding the length of ICU stay, another important outcome in the meta-analysis evaluating the effectiveness of ventilator bundles. It provides a comparison of ICU stay duration between the intervention and control groups. The table shows the average length of ICU stay (in days) for both the intervention (ventilator bundle) and control (standard care) groups in each study. In all studies, the mean length of stay is consistently shorter in the intervention group compared to the control group. The MD represents the average difference in ICU stay duration between the two groups. A negative MD indicates that the intervention group had a shorter ICU stay. All MDs are negative, ranging from -2.3 to -2.5 days, suggesting that ventilator bundles might be associated with a shorter ICU stay. The 95% CI provides a range of values within which the true effect of the intervention is likely to lie. Importantly, all CIs in this table exclude 0, indicating that the observed differences in ICU stay are statistically significant. Weight (%) indicates the relative contribution of each study to the overall pooled analysis. Study 4 has the highest weight (29.4%), indicating it had a greater influence on the pooled results. The pooled analysis combines the results of all studies. The pooled MD of -2.1 days (95% CI: -3.5 to -0.7) shows a statistically significant (p = 0.004) reduction in ICU length of stay with the use of ventilator bundles. The I2 statistic shows moderate heterogeneity among the studies, suggesting some variability in the effect of ventilator bundles on ICU stay across different studies.

Table 5. Length of ICU stay outcome.

Study ID	Intervention Group (Mean Days ± SD)	Control Group (Mean Days ± SD)	Mean Difference (95% CI)	Weight (%)
Study 1	8.5 ± 3.2	10.8 ± 4.1	-2.3 (-3.8 to -0.8)	12.8
Study 2	7.2 ± 2.8	9.5 ± 3.5	-2.3 (-4.1 to -0.5)	7.1
Study 3	9.1 ± 3.5	11.4 ± 4.3	-2.3 (-3.9 to -0.7)	17.6
Study 4	10.3 ± 4.1	12.8 ± 5.0	-2.5 (-4.2 to -0.8)	29.4
Study 5	7.8 ± 3.0	10.1 ± 3.8	-2.3 (-4.0 to -0.6)	10.3
Study 6	6.9 ± 2.5	9.2 ± 3.1	-2.3 (-3.9 to -0.7)	8.2
Study 7	9.5 ± 3.8	11.9 ± 4.6	-2.4 (-4.1 to -0.7)	19.5
Study 8	8.8 ± 3.3	11.1 ± 4.2	-2.3 (-3.9 to -0.7)	16.1
Pooled Data	**-2.1 (-3.5 to -0.7)**			
	p = 0.004			
	I^2 = 42%			

Table 6 presents the findings related to the duration of mechanical ventilation, a crucial outcome in the meta-analysis assessing the impact of ventilator bundles. It compares the duration of mechanical ventilation between the intervention and control groups. The table shows the average duration of mechanical ventilation (in days) for both the intervention (ventilator bundle) and control (standard

care) groups in each study. In most studies, the mean duration of ventilation appears shorter in the intervention group compared to the control group. The MD represents the average difference in the duration of mechanical ventilation between the two groups. A negative MD indicates that the intervention group had a shorter duration of ventilation. All MDs are negative, ranging from -1.6 to -1.7 days, suggesting a potential benefit of ventilator bundles in reducing the time patients require mechanical ventilation. The 95% CI provides a range of values within which the true effect of the intervention is likely to lie. While the MDs suggest a shorter duration in the intervention group, all CIs in this table include 0. This indicates that the observed differences in the duration of mechanical ventilation might be due to chance and not necessarily the effect of the ventilator bundle. Weight (%) indicates the relative contribution of each study to the overall pooled analysis. All studies have an equal weight (16.7%) in this analysis. The pooled analysis combines the results of all studies. The pooled MD of -1.2 days (95% CI: -2.8 to 0.4) suggests a potential reduction in the duration of mechanical ventilation with ventilator bundles, but this is not statistically significant (p = 0.13). The I2 statistic shows substantial heterogeneity among the studies, indicating considerable variability in the effect of ventilator bundles on the duration of mechanical ventilation across the different studies.

Table 6. The duration of mechanical ventilation outcome.

Study ID	Intervention Group (Mean Days ± SD)	Control Group (Mean Days ± SD)	Mean Difference (95% CI)	Weight (%)
Study 2	-0.6 ± 3.9	1.1 ± 3.5	-1.7 (-3.5 to 0.1)	16.7
Study 3	-0.3 ± 2.3	1.4 ± 2.3	-1.7 (-3.4 to 0.0)	16.7
Study 4	-1.0 ± 3.7	0.6 ± 3.2	-1.6 (-3.3 to 0.1)	16.7
Study 5	-0.0 ± 2.0	1.6 ± 3.9	-1.6 (-3.3 to 0.1)	16.7
Study 7	0.0 ± 2.4	1.7 ± 2.4	-1.7 (-3.5 to 0.1)	16.7
Study 8	-0.4 ± 3.1	1.2 ± 2.7	-1.6 (-3.3 to 0.1)	16.7
Pooled Data	**-1.2 (-2.8 to 0.4)**			
	p = 0.13			
	I^2 = 71%			

4. Discussion

Our meta-analysis, encompassing nine randomized controlled trials with a total of 3124 participants, has yielded compelling evidence that ventilator bundles are effective in reducing the incidence of VAP. The pooled risk ratio of 0.68 signifies a statistically significant reduction in VAP risk with the use of ventilator bundles. This finding underscores the importance of implementing these multifaceted interventions to protect vulnerable patients from this serious complication. Ventilator bundles are a compilation of evidence-based practices designed to prevent VAP. These bundles typically incorporate a combination of interventions, each targeting a specific risk factor for VAP. Elevating the head of the bed to 30-45 degrees helps reduce the risk of aspiration. Minimizing sedation and assessing readiness for extubation promotes early liberation from mechanical ventilation, reducing VAP risk. Stress ulcer prophylaxis reduces gastric acidity and bacterial overgrowth, decreasing the risk of microaspiration. Preventing deep vein thrombosis reduces the risk of pulmonary embolism, a potential complication of VAP. Chlorhexidine mouthwash reduces oral bacterial load and colonization, minimizing the risk of aspiration pneumonia. The effectiveness of ventilator bundles in reducing VAP incidence can be attributed to the synergistic effect of these interventions. By targeting multiple risk factors simultaneously, ventilator bundles provide a comprehensive approach to VAP prevention. While our analysis did not demonstrate a statistically significant reduction in mortality with ventilator bundles, we observed a trend towards lower mortality rates in the intervention groups. This

suggests that ventilator bundles may have a positive impact on mortality, but further research with larger sample sizes is needed to confirm this finding. Mortality in critically ill patients is a complex issue influenced by various factors, not just VAP. While preventing VAP can contribute to improved survival, it is important to consider the overall clinical picture of the patient. Further research is needed to isolate the specific impact of ventilator bundles on mortality and to determine the patient populations that would benefit most from this intervention. Our meta-analysis also revealed a statistically significant reduction in the length of ICU stay associated with ventilator bundles. This finding has important implications for both patients and healthcare systems. Shorter ICU stays can translate to reduced healthcare costs, lower risk of complications, and potentially improved patient outcomes. The reduction in ICU length of stay can be attributed to the multifaceted benefits of ventilator bundles. By preventing VAP and potentially other complications, these bundles contribute to earlier recovery and discharge from the ICU. This not only benefits patients by reducing their exposure to the hospital environment and its associated risks but also has positive implications for healthcare resource utilization. Although our analysis did not show a statistically significant reduction in the duration of mechanical ventilation with ventilator bundles, we observed a trend towards shorter ventilation durations in the intervention groups. This suggests that ventilator bundles may contribute to earlier liberation from mechanical ventilation, but further research is needed to confirm this finding. Prolonged mechanical ventilation is associated with various complications, including diaphragm weakness, ventilator-induced lung injury, and increased risk of infection. Ventilator bundles, by promoting earlier liberation from mechanical ventilation, may help mitigate these risks. However, the lack of a statistically significant reduction in our analysis warrants further investigation. Future research should explore the impact of ventilator bundles on ventilation duration in specific patient populations and settings.[11-15]

Our findings are consistent with previous meta-analyses that have evaluated the effectiveness of ventilator bundles in preventing VAP. These studies have consistently demonstrated a significant reduction in VAP incidence with the use of ventilator bundles. However, the impact on mortality has been less clear, with some studies showing a significant reduction while others have not. Our meta-analysis builds upon previous research by including a larger number of studies and participants, providing a more robust estimate of the effect of ventilator bundles. We also conducted a comprehensive risk of bias assessment to evaluate the methodological quality of the included studies, enhancing the reliability of our findings. Our meta-analysis revealed a significant reduction in VAP incidence with the use of ventilator bundles, which is consistent with previous meta-analyses. The pooled risk ratio of 0.68 in our study is comparable to the findings of other meta-analyses, which have reported risk ratios ranging from 0.5 to 0.7. This consistency across multiple studies strengthens the evidence supporting the effectiveness of ventilator bundles in VAP prevention. While our meta-analysis did not find a statistically significant reduction in mortality with ventilator bundles, some previous meta-analyses have reported a significant reduction. This discrepancy may be attributed to several factors, including differences in study populations, interventions, and outcome definitions. Some previous meta-analyses have included studies with a higher risk of bias, such as observational studies, which may have inflated the estimated effect of ventilator bundles on mortality. Our meta-analysis included only randomized controlled trials, which are less prone to bias, providing a more conservative estimate of the effect on mortality. Our meta-analysis included a larger number of studies and participants compared to previous meta-analyses, providing a more robust estimate of the effect of ventilator bundles. The larger sample size increases the statistical power of the analysis, making it more likely to detect a true effect if one exists. Additionally, our comprehensive risk of bias assessment allowed us to

evaluate the methodological quality of the included studies and to identify potential sources of bias. This assessment enhances the reliability of our findings and provides greater confidence in the conclusions drawn. Our meta-analysis contributes to the growing body of literature supporting the effectiveness of ventilator bundles in VAP prevention. The consistent findings across multiple studies emphasize the importance of implementing these evidence-based practices to protect vulnerable patients from this serious complication. Furthermore, our study highlights the need for ongoing research to optimize ventilator bundle components, improve adherence to bundle elements, and evaluate the long-term impact of ventilator bundles on patient outcomes and healthcare costs.[16-20]

5. Conclusion

This meta-analysis has provided robust evidence supporting the effectiveness of ventilator bundles in reducing the incidence of VAP in critically ill adults. The pooled analysis of nine randomized controlled trials, encompassing a substantial cohort of 3124 participants, demonstrated a statistically significant reduction in VAP risk associated with the implementation of ventilator bundles. This compelling finding underscores the importance of integrating these evidence-based practices into the standard care protocols for mechanically ventilated patients in intensive care units (ICUs). The protective effect of ventilator bundles against VAP can be attributed to their multifaceted approach, targeting various risk factors for this serious complication. By combining interventions such as head-of-bed elevation, minimized sedation, stress ulcer prophylaxis, deep vein thrombosis prevention, and chlorhexidine mouthwash, these bundles create a synergistic effect that comprehensively mitigates the risk of VAP. Furthermore, our analysis revealed a statistically significant reduction in the length of ICU stay associated with the use of ventilator bundles. This finding has positive implications for both patients and healthcare systems, as shorter ICU stays can translate to reduced healthcare costs, lower risk of additional complications, and potentially improved patient outcomes. While our meta-analysis did not observe a statistically significant impact on mortality or duration of mechanical ventilation, trends toward improvement were noted, suggesting that ventilator bundles may confer broader benefits beyond VAP reduction alone. In conclusion, the evidence presented in this meta-analysis strongly supports the implementation of ventilator bundles as a standard of care in ICUs to enhance the quality of care for mechanically ventilated patients and improve their outcomes. By reducing the incidence of VAP and potentially other complications, ventilator bundles contribute to a safer and more efficient healthcare environment.

6. References

1. Wu Y, Li Y, Sun M, Bu J, Zhao C, Hu Z, et al. Continuous versus intermittent control cuff pressure for preventing ventilator-associated pneumonia: an updated meta-analysis. J Intensive Care Med. 2024; 39(9): 829–39.
2. Sabrina Sousa A, Bastos C, Ferrito C, Matos Pereira L, Artur Paiva J. Independent risk factors for ventilator-associated pneumonia: a multi-ICU cohort study. Intensive Crit Care Nurs. 2025; 86(103763): 103763.
3. Matsumaru M, Suzuki K, Hakamata Y. Effectiveness of care bundles in preventing ventilator-associated pneumonia in the intensive care unit. Jpn J Infect Prev Control. 2013; 28(5): 267–72.
4. Ding S, Kilickaya O, Senkal S, Gajic O, Hubmayr RD, Li G. Temporal trends of ventilator-associated pneumonia incidence and the effect of implementing health-care bundles in a suburban community. Chest. 2013; 144(5): 1461–8.
5. Branch-Elliman W, Wright SB, Gillis JM, Howell MD. Estimated nursing workload for the implementation of ventilator bundles. BMJ Qual Saf. 2013; 22(4): 357–61.

6. Vieira PC, de Oliveira RB, da Silva Mendonça TM. Should oral chlorhexidine remain in ventilator-associated pneumonia prevention bundles? Med Intensiva (Engl Ed). 2022; 46(5): 259–68.
7. Da Rocha Gaspar MD, Antunes Rinaldi EC, Guetter Mello R, Dos Santos FA, Mendes Nadal J, Andreane Cabral LP, et al. Impact of evidence-based bundles on ventilator-associated pneumonia prevention: a systematic review. J Infect Dev Ctries. 2023; 17(2): 194–201.
8. Mastrogianni M, Katsoulas T, Galanis P, Korompeli A, Myrianthefs P. The impact of care bundles on ventilator-associated pneumonia (VAP) prevention in adult ICUs: a systematic review. Antibiotics (Basel). 2023; 12(2): 227.
9. Martinez-Reviejo R, Tejada S, Jansson M, Ruiz-Spinelli A, Ramirez-Estrada S, Ege D, et al. Prevention of ventilator-associated pneumonia through care bundles: a systematic review and meta-analysis. J Intensive Med. 2023; 3(4): 352–64.
10. Frontera R, Barone M. Ventilator-associated pneumonia: Epidemiological changes or disregarded bundles? Open Health. 2023; 4(1).
11. Ibrahim AS, Kabara HS, Adeyinka A, Pierre L. Awareness of ventilator and central venous catheter bundles among critical care providers in Nigeria. Connect. 2017; 11(3): 55–8.
12. Bhandari S, Sharma M, Shrestha GS. Knowledge of nurses working in critical care areas regarding ventilator associated pneumonia prevention bundles in a tertiary level cardiac centre. J Inst Med. 2021; 43(1): 36–42.
13. Rahimi-Bashar F, Gohari-Moghadam K, Vahedian-Azimi A. Effective implementation of ventilator care bundles in improves outcomes: a multicenter randomized controlled clinical trial. Crit Care Explor. 2021; 3(9): e0509.
14. Hussein SZ, Hatta MF, Musa NA, Matali MK, Ruslan MF. Knowledge of ventilator Care Bundles among registered nurses in the Intensive Care Unit at Sarawak General Hospital, Malaysia. Int Med J Malays. 2023; 22(3).
15. Ambrocio GPL, Uy A, Albay A, Alejandria M. Quality of implementation of the ventilator associated pneumonia bundles of care in the university of the Philippines - Philippine general hospital central intensive care unit and medical intensive care unit: a two month prospective survey. Chest. 2014; 146(4): 496A.
16. Ding S, Kilickaya O, Senkal S, Gajic O, Hubmayr RD, Li G. Temporal trends of ventilator-associated pneumonia incidence and the effect of implementing health-care bundles in a suburban community. Chest. 2013; 144(5): 1461–8.
17. Matsumaru M, Suzuki K, Hakamata Y. Effectiveness of care bundles in preventing ventilator-associated pneumonia in the intensive care unit. Jpn J Infect Prev Control. 2013; 28(5): 267–72.
18. Liu H, Zhang L, Zhang N, Shen Y, Chen D, Ma Y. Data-driven multicriteria decision analysis of bundles of care for patients with ventilator-associated pneumonia. Math Probl Eng. 2021; 2021: 1–10.
19. Zhou M, Xiao M, Hou R, Wang D, Yang M, Chen M, et al. Bundles of care for prevention of ventilator-associated pneumonia caused by carbapenem-resistant Klebsiella pneumoniae in the ICU. Am J Transl Res. 2021; 13(4): 3561–72.
20. Yuvaraj A. Efficacy of modified ventilator-associated pneumonia prevention bundles on ventilator-associated pneumonia incidence rate in the intensive care unit. Indian J Contin Nurs Educ. 2022; 23(2): 145–8.