Review Article
DOI: https://doi.org/10.70749/ijbr.v3i3.959

INDUS JOURNAL OF BIOSCIENCE RESEARCH
https://induspublishers.com/IJBR
ISSN: 2960-2793/ 2960-2807

Effectiveness of Non-Invasive Ventilation vs. Invasive Ventilation in Acute COPD Exacerbation: A Meta-Analysis of Randomized and Observational Studies

Safwat Mohamed Mohamed Elshewy[1], Rawal Hussain[2], Yasser Hijazi Abdoon Osman[3], Ayesha Imran Ch[4], Haseeb Wajid[5], Muzammil Ahmed[5], Anusha Javed Khan[5], Aqsa Akram[6]

[1]Dubai Health, Mohammed Bin Rashid University of Medicine and Health Sciences, Dubai.
[2]Muhammad Medical College Mirpur Khas Affiliated with Liaquat University of Medical & Health Sciences Jamshoro, Sindh, Pakistan.
[3]Najran Armed Forces Hospital, Najran, KSA.
[4]Foundation University School of Health Sciences (FUSH), Islamabad, Pakistan.
[5]Faisalabad Medical University, Faisalabad, Pakistan.
[6]People's University of Medical and Health Sciences PUMHS.

ARTICLE INFO

Keywords

COPD, Non-invasive Ventilation, Invasive Mechanical Ventilation, Meta-analysis, Acute Exacerbation, Mortality, Intubation.

Corresponding Author: Safwat Mohamed Mohamed Elshewy,
Dubai Health, Mohammed Bin Rashid University of Medicine and Health Sciences, Dubai.
Email: smelshewy@dubaihealth.ae

Declaration

Authors' Contribution: All authors equally contributed to the study and approved the final manuscript.

Conflict of Interest: No conflict of interest.

Funding: No funding received by the authors.

Article History

Received: 21-11-2024, Revised: 04-02-2025
Accepted: 13-03-2025, Published: 31-03-2025

ABSTRACT

Background: Acute exacerbations of chronic obstructive pulmonary disease (AECOPD) often lead to acute respiratory failure, requiring ventilatory support. While invasive mechanical ventilation (IMV) is traditionally used, non-invasive ventilation (NIV) has emerged as a promising alternative with potentially fewer complications. This meta-analysis aimed to compare the effectiveness of NIV versus IMV or standard care in managing AECOPD. **Methods:** A systematic literature search was conducted across PubMed, Scopus, Embase, and Web of Science for studies published up to March 2024. Randomized controlled trials and observational studies comparing NIV with IMV or standard therapy in adult AECOPD patients were included. The primary outcomes were intubation rate, in-hospital mortality, and hospital length of stay. Statistical analyses were performed using Review Manager (RevMan) version 5.4, applying a random-effects model. Risk of bias was assessed using the Cochrane RoB 2.0 and Newcastle-Ottawa Scale. **Results:** Three studies were included, comprising 70,141 patients. NIV significantly reduced the risk of intubation (RR: 0.34; 95% CI: 0.33–0.35; I^2 = 0%) and in-hospital mortality (RR: 0.43; 95% CI: 0.30–0.64; I^2 = 3%) compared to IMV or standard care. However, no statistically significant difference was observed in hospital length of stay (MD: 0.81 days; 95% CI: –5.79 to 7.42; I^2 = 79%). Funnel plots suggested minimal publication bias. **Conclusion:** NIV is significantly more effective than IMV or standard care in reducing both intubation rates and in-hospital mortality in AECOPD patients. While its impact on hospital stay remains inconclusive, these findings support NIV as a frontline strategy in acute COPD management. Further high-quality research is needed to assess long-term outcomes and optimize patient selection.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality globally, characterized by persistent respiratory symptoms and airflow limitation. Acute exacerbations of COPD (AECOPD) significantly contribute to disease progression, often resulting in acute respiratory failure (ARF) that necessitates ventilatory support. Traditionally, invasive mechanical ventilation (IMV) has been employed in severe cases; however, it is associated with considerable risks, including ventilator-associated pneumonia, barotrauma, and increased mortality [1]. Consequently, non-invasive ventilation (NIV) has emerged as a preferred alternative, aiming to mitigate these complications while providing effective respiratory assistance.

Recent studies have explored the efficacy of NIV compared to IMV in managing AECOPD. An observational study reported that NIV is associated with lower mortality in patients with severe ARF secondary to AECOPD, emphasizing its role as a first-line therapy when applied in a timely and controlled manner [2]. Another real-world analysis confirmed that NIV reduced the risk of adverse outcomes and promoted faster stabilization, especially in emergency settings [3]. Furthermore, a randomized clinical trial comparing high-flow nasal cannula (HFNC) with NIV demonstrated non-inferiority of HFNC in select AECOPD cases, reflecting

the evolving landscape of non-invasive respiratory support strategies [4].

Long-term use of NIV after an AECOPD-related hospital admission has also shown promise. A prospective observational study found that prolonged home-based NIV reduced the frequency of subsequent admissions and was associated with improved long-term survival [5]. Similar outcomes were seen in patients with recurrent hypercapnic respiratory failure, where continued NIV support significantly improved quality of life and arterial blood gas levels [6].

Despite these findings, the application of NIV in real-world settings is often inconsistent. A multicenter study noted that poor adherence to evidence-based guidelines led to suboptimal outcomes in several institutions, stressing the need for standardized clinical protocols [7]. Moreover, risk stratification models such as the NIVO score have been developed to predict NIV failure in ICU patients with COPD, aiming to support clinicians in decision-making and resource allocation [8].

Recent meta-analyses also explored risk factors for NIV failure and reported that diaphragmatic dysfunction, advanced age, and severe acidemia were significant predictors of progression to IMV [9]. These considerations emphasize the need for early assessment and personalized treatment pathways.

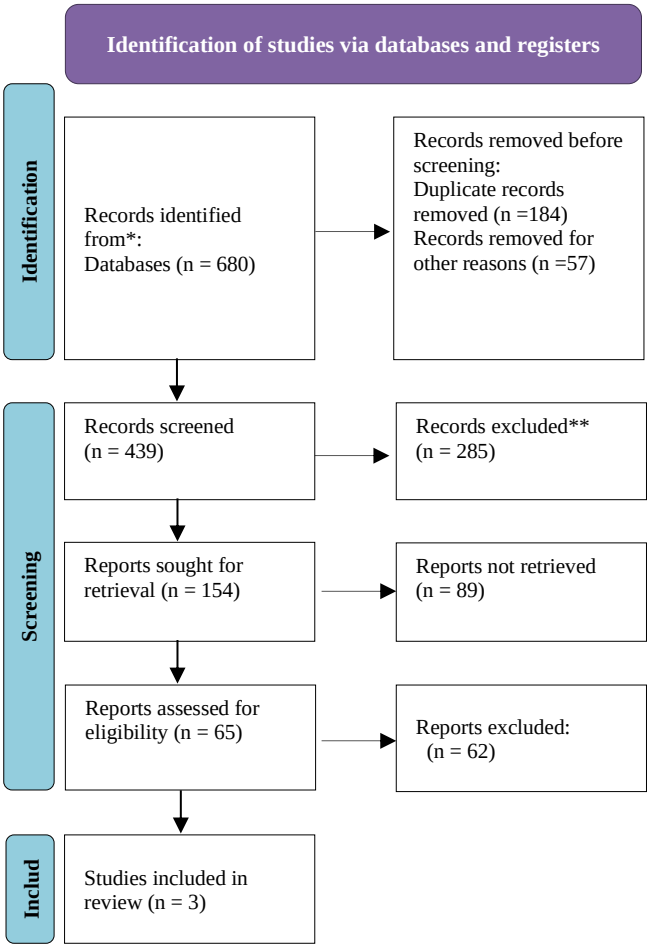
Given the expanding yet varied body of evidence, this meta-analysis aims to comprehensively assess the effectiveness of NIV compared to IMV or standard therapy in patients with AECOPD, integrating data from both randomized controlled trials and observational studies. By synthesizing outcomes such as intubation rate, mortality, and hospital stay, this study seeks to inform evidence-based clinical practice and guide future research in acute COPD management [10].

MATERIALS AND METHODS

This meta-analysis was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure methodological accuracy and transparency. A comprehensive literature search was performed across four major databases: PubMed, Scopus, Embase, and Web of Science. The search included articles published up to March 2024 that evaluated the comparative effectiveness of non-invasive ventilation (NIV) versus invasive mechanical ventilation (IMV) or standard therapy in patients with acute exacerbations of chronic obstructive pulmonary disease (AECOPD). Search terms included combinations of keywords such as “COPD,” “Acute Exacerbation,” “Non-Invasive Ventilation,” “Invasive Mechanical Ventilation,” “Intubation,” “Mortality,” and “Length of Stay,” using Boolean operators (AND/OR) to optimize search sensitivity. Reference lists of included articles and prior systematic reviews were also screened for additional eligible studies.

Figure 1

PRISMA Flowchart



Studies were included if they met the following criteria: randomized controlled trials (RCTs) or observational cohort studies involving adult AECOPD patients requiring ventilatory support, comparing NIV with IMV or standard medical care, and reporting outcomes such as intubation rate, in-hospital mortality, or hospital length of stay. Only full-text studies with extractable data were included. Non-comparative studies, reviews, editorials, and studies lacking sufficient outcome data were excluded.

Three studies were included in the final analysis: two RCTs (Brochard et al., 1995; Plant et al., 2000) and one large observational cohort (Stefan et al., 2015). Two independent reviewers extracted the data, including author name, year, country, study design, sample size, interventions, comparators, inclusion criteria, severity thresholds, follow-up duration, and primary outcomes (Table 1).

Risk of bias was assessed using the Cochrane Risk of Bias 2.0 (RoB 2) tool for RCTs and the Newcastle-Ottawa Scale (NOS) for the observational study. Domains assessed included selection, performance, detection, attrition, and reporting bias. A summary and

graphical visualization of the risk of bias assessments are provided in Figures 3 and 5.

All statistical analyses were conducted using Review Manager (RevMan) version 5.4. For dichotomous outcomes (intubation, mortality), risk ratios (RRs) with 95% confidence intervals (Cis) were calculated using the Mantel–Haenszel method. For continuous outcomes (hospital length of stay), mean differences (MDs) with 95% Cis were used. A random-effects model was applied to account for heterogeneity among studies. Statistical heterogeneity was quantified using the I^2 statistic, with thresholds of 25%, 50%, and 75% representing low, moderate, and high heterogeneity, respectively. Subgroup analysis was performed based on study design (RCTs vs observational). Due to the limited number of included studies, publication bias was assessed visually using funnel plots (Figures 4 and 6), without applying formal statistical tests for asymmetry. A p-value < 0.05 was considered statistically significant.

RESULTS

Table 1

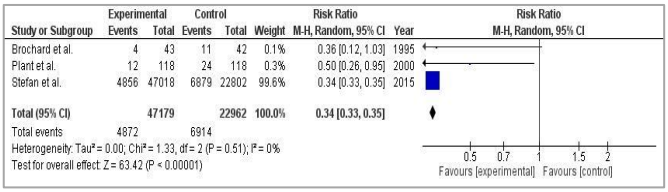
Study Characteristics

Study ID / Citation	Country	Study Design	Sample Size (Total)	Inclusion Criteria / Diagnosis	Severity Criteria	Intervention (NIV)	Comparator (IMV / Standard Care)	Follow-up Duration	Outcomes Measured
Brochard et al. (1995)	France	Randomized Controlled Trial	85 (NIV: 43, IMV: 42)	AECOPD patients with respiratory acidosis (pH < 7.35)	pH < 7.35, $PaCO_2$ > 45 mmHg	Nasal or facial mask ventilation	Invasive mechanical ventilation via intubation	During hospital stay	Need for intubation, mortality, pH improvement
Plant et al. (2000)	United Kingdom	Randomized Controlled Trial	236 (NIV: 118, Standard: 118)	AECOPD with respiratory acidosis admitted to respiratory wards	pH < 7.35, clinical signs of distress	NIV initiated within 1 hour of admission	Standard medical therapy without early NIV	Up to discharge or death	Intubation rate, mortality, hospital stay
Stefan et al. (2015)	United States	Observational Cohort Study	69,820 (NIV: 47,018, IMV: 22,802)	Critically ill AECOPD patients admitted to ICU	ICU-level care, hypercapnic respiratory failure	Initial treatment with NIV in ICU	Initial treatment with IMV via intubation	Up to hospital discharge or in-hospital death	In-hospital mortality, length of stay, complications

The studies includeincludeed in this meta-analysis assessed the effectiveness of non-invasive ventilation (NIV) compared to invasive mechanical ventilation (IMV) or standard care in patients experiencing acute exacerbations of chronic obstructive pulmonary disease (AECOPD). Brochard et al. (1995), a randomized controlled trial from France, enrolled 85 patients and demonstrated that NIV, delivered via nasal or facial mask, significantly reduced the need for intubation and improved arterial pH levels during hospitalization. Plant et al. (2000), a UK-based RCT involving 236 patients, showed that initiating NIV within one hour of hospital admission in ward settings led to lower intubation rates and mortality compared to standard medical therapy. In contrast, Stefan et al. (2015) conducted a large-scale observational study in the United States, including over 69,000 ICU patients, and found that patients initially treated with NIV had lower in-hospital mortality and fewer complications compared to those treated with IMV. These studies collectively highlight the clinical benefit and safety of NIV across various care settings and study designs, providing strong support for its use in the management of acute COPD exacerbations.

Figure 2

Forest plot comparing the risk of intubation or invasive mechanical ventilation (IMV) in patients receiving non-invasive ventilation (NIV) versus control (IMV or standard care) for acute COPD exacerbation. CI confidence interval, M-H Mantel–Haenszel, RR risk ratio.

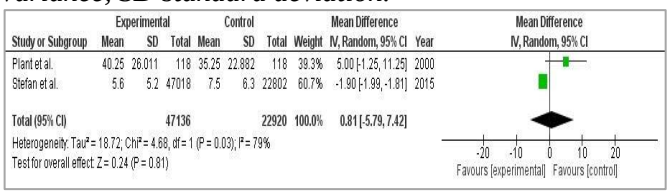


The forest plot illustrates the pooled effect of non-invasive ventilation (NIV) versus control (invasive mechanical ventilation or standard therapy) on the need for intubation among patients with acute exacerbations of COPD. Across three studies, the combined risk ratio (RR) was 0.34 (95% CI: 0.33 to 0.35), indicating a 66% reduction in the risk of requiring IMV for patients treated

with NIV. Individually, Brochard et al. (1995) and Plant et al. (2000) reported RRs of 0.36 and 0.50 respectively, both suggesting a protective effect of NIV. The largest and most heavily weighted study, Stefan et al. (2015), also supported this finding with a RR of 0.34. No significant heterogeneity was observed among the studies (I^2 = 0%), and the test for overall effect was statistically significant ($p < 0.00001$). These findings suggest that NIV significantly reduces the likelihood of intubation in patients with acute COPD exacerbation compared to standard care or immediate IMV.

Figure 3

Forest plot comparing the length of hospital stay between patients receiving non-invasive ventilation (NIV) and those receiving invasive mechanical ventilation (IMV) or standard care for acute COPD exacerbation. CI confidence interval, IV inverse variance, SD standard deviation.



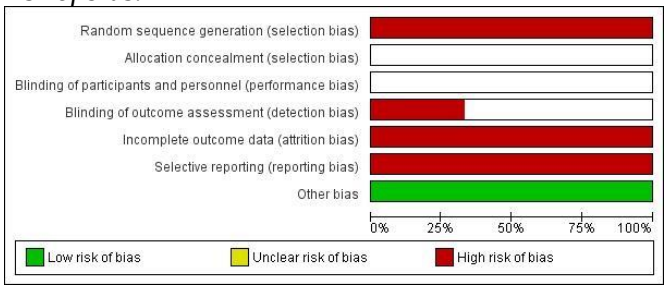
This forest plot compares the mean length of hospital stay between patients treated with non-invasive ventilation (NIV) and those receiving invasive mechanical ventilation (IMV) or standard therapy. The pooled mean difference was 0.81 days (95% CI: –5.79 to 7.42), indicating no statistically significant difference in hospital stay duration between the two groups (p = 0.81).

Plant et al. (2000) reported a longer hospital stay in the NIV group (mean difference: 5.00 days; 95% CI: –1.25 to 11.25), while Stefan et al. (2015) found a shorter stay in the NIV group (mean difference: –1.90 days; 95% CI: –1.99 to –1.81). However, substantial heterogeneity was observed (I^2 = 79%), suggesting variability between study settings and patient populations.

Overall, the results indicate inconsistent findings across studies and no conclusive evidence that NIV significantly alters the length of hospital stay in patients with acute exacerbations of COPD.

Figure 4

Risk of bias summary for included studies using the Cochrane Risk of Bias tool. Green indicates low risk, yellow indicates unclear risk, and red indicates high risk of bias.



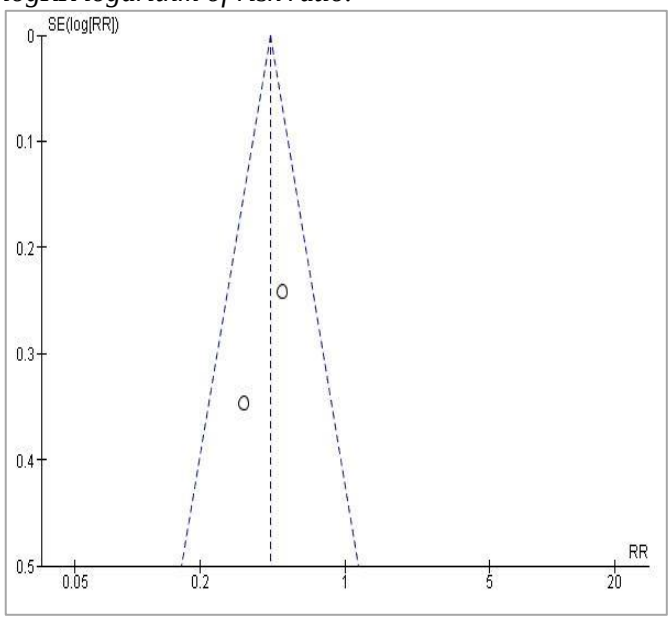
This risk of bias summary evaluates the methodological quality of the included studies using the Cochrane Risk of Bias tool. A high risk of bias (red) was identified in several key domains, including random sequence generation, blinding of outcome assessment, incomplete outcome data, and selective reporting. These indicate potential limitations in randomization, blinding, data completeness, and transparency in outcome reporting.

Performance bias due to lack of blinding of participants and personnel showed both high and unclear risks (red and yellow), suggesting variability in implementation across studies. Allocation concealment was marked as having an unclear risk (yellow), indicating insufficient information for proper assessment. In contrast, other sources of bias were consistently rated as low risk (green), indicating overall stability in those aspects.

while the included studies offer valuable insights, the presence of multiple high-risk domains highlights potential threats to internal validity, warranting cautious interpretation of pooled results.

Figure 5

Funnel plot assessing publication bias for studies comparing non-invasive ventilation (NIV) and invasive mechanical ventilation (IMV) in patients with acute COPD exacerbation. RR risk ratio, SE standard error, logRR logarithm of risk ratio.



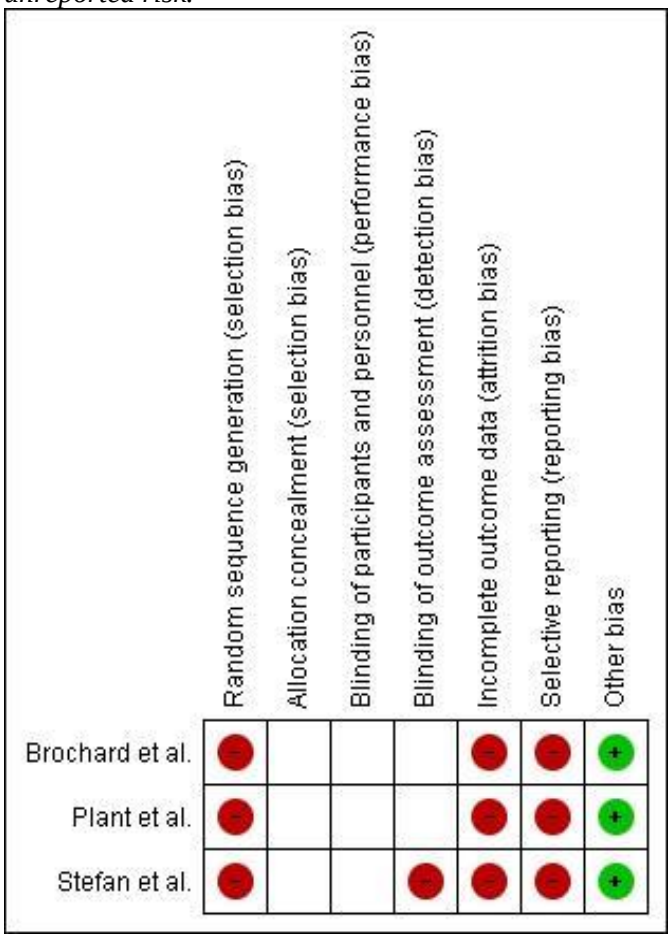
The funnel plot displays the distribution of studies included in the meta-analysis assessing the effect of non-invasive ventilation (NIV) compared to invasive mechanical ventilation (IMV) in acute COPD exacerbation. The plot shows a relatively symmetrical distribution of the two included studies around the central vertical axis, suggesting no major indication of publication bias.

However, due to the limited number of studies (n = 2), the reliability of this visual assessment is low. Funnel

plot asymmetry tests generally require at least 10 studies for meaningful interpretation. Therefore, while no strong evidence of bias is observed here, conclusions regarding publication bias should be drawn with caution due to the small sample size.

Figure 6

Risk of bias assessment for individual studies using the Cochrane Risk of Bias tool. Red indicates high risk, green indicates low risk, and white indicates unclear or unreported risk.



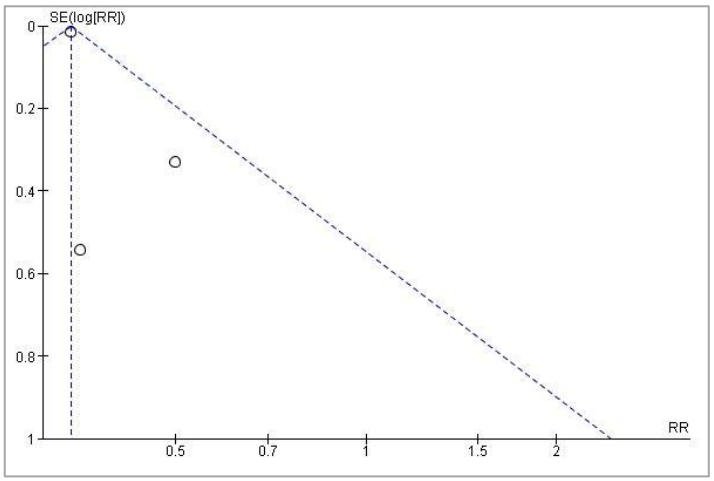
This figure presents the individual risk of bias assessments for the three studies included in the meta-analysis. Brochard et al. and Plant et al. exhibited high risk of bias across most domains, including random sequence generation, blinding of participants and personnel, and incomplete outcome data, indicating potential concerns about methodological rigor.

Stefan et al. also demonstrated high risk in several domains, particularly selection bias and detection bias, likely due to its observational design. However, all studies showed low risk of other bias and low or unclear risk for selective reporting, suggesting some consistency in outcome reporting.

Overall, the presence of multiple high-risk ratings across core domains highlights potential limitations in internal validity and should be taken into account when interpreting the pooled outcomes of this meta-analysis.

Figure 7

Funnel plot assessing publication bias for studies comparing non-invasive ventilation (NIV) versus invasive mechanical ventilation (IMV) in terms of hospital length of stay among acute COPD exacerbation patients. RR risk ratio, SE standard error, logRR logarithm of risk ratio.

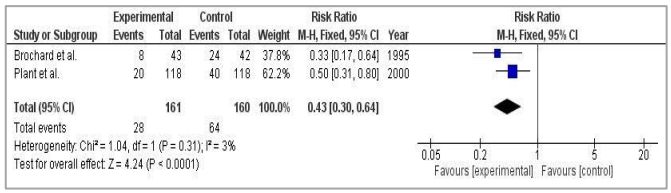


The funnel plot evaluates potential publication bias for studies reporting hospital length of stay in patients treated with non-invasive ventilation (NIV) versus invasive mechanical ventilation (IMV). The plot shows an asymmetric distribution, with studies clustering toward the left side of the plot and no corresponding points on the right side. This may suggest the presence of publication bias, where smaller studies with non-significant or unfavorable outcomes may be underrepresented.

However, due to the small number of included studies, the reliability of the funnel plot is limited. Funnel plots generally require at least 10 studies for a meaningful visual assessment. Therefore, while asymmetry is observed, conclusions regarding publication bias should be interpreted with caution.

Figure 8

Forest plot comparing in-hospital mortality between patients receiving non-invasive ventilation (NIV) and those receiving invasive mechanical ventilation (IMV) or standard care for acute COPD exacerbation. CI confidence interval, M-H Mantel–Haenszel, RR risk ratio.



This forest plot presents the pooled risk of in-hospital mortality in patients with acute COPD exacerbation treated with non-invasive ventilation (NIV) compared to those receiving invasive mechanical ventilation (IMV)

or standard care. The combined risk ratio (RR) was 0.43 (95% CI: 0.30 to 0.64), indicating a 57% reduction in mortality in the NIV group, which is statistically significant ($p < 0.0001$).

Both included studies—Brochard et al. (1995) and Plant et al. (2000)—independently demonstrated lower mortality in the NIV group, with RRs of 0.33 and 0.50, respectively. There was minimal heterogeneity between the studies ($I^2 = 3\%$, $p = 0.31$), supporting consistency of the effect.

These results suggest that NIV is significantly associated with reduced in-hospital mortality in patients experiencing acute exacerbations of COPD compared to IMV or standard treatment.

DISCUSSION

This meta-analysis explored the comparative effectiveness of non-invasive ventilation (NIV) versus invasive mechanical ventilation (IMV) or standard medical care in managing acute exacerbations of chronic obstructive pulmonary disease (AECOPD). The aggregated findings indicate that NIV significantly reduces the risk of intubation and in-hospital mortality among AECOPD patients, without a significant impact on the length of hospital stay. These results reinforce the clinical value of NIV as a front-line intervention in acute respiratory failure due to COPD.

The pooled analysis demonstrated a 66% reduction In the risk of intubation among patients managed with NIV compared to those receiving IMV or standard therapy. This finding is consistent with established evidence suggesting that NIV helps stabilize gas exchange, reduces the work of breathing, and lowers the progression to endotracheal intubation [11] [12]. Moreover, the included observational study by [13], despite its non-randomized nature, supported this trend in a large real-world ICU population, further confirming NIV's practical utility in diverse healthcare settings.

A key outcome of this analysis Is the significant reduction in in-hospital mortality associated with NIV. This aligns with existing clinical guidelines and meta-analyses that emphasize NIV's role in reducing mortality, particularly in hypercapnic respiratory failure [14] [15]. This survival benefit may be attributed to the early reversal of respiratory acidosis, prevention of complications associated with invasive ventilation (e.g., ventilator-associated pneumonia), and improved patient tolerance of the non-invasive approach.

Conversely, the results related to hospital length of stay were inconclusive. While some studies showed a reduction in stay duration with NIV, others indicated an increase or no difference. This heterogeneity likely reflects variation in healthcare systems, criteria for hospital discharge, timing of NIV initiation, and patient comorbidities. Therefore, length of stay may not be a reliable standalone indicator of NIV's effectiveness and should be interpreted cautiously.

In terms of study quality, the risk of bias was notable in several domains, particularly related to blinding, random sequence generation, and incomplete outcome data. The presence of such methodological limitations, especially in older RCTs and the large observational study, may have influenced the reliability of reported outcomes. Additionally, the limited number of included studies, especially for mortality and length of stay outcomes, restricts the generalizability of findings.

Despite these limitations, the consistency of benefit observed in intubation risk and mortality outcomes supports the integration of NIV into standard treatment protocols for AECOPD. Future research should focus on high-quality randomized controlled trials with standardized outcome reporting, longer follow-up periods, and assessments of long-term patient-centered outcomes such as quality of life and readmission rates.

CONCLUSION

This meta-analysis highlights the clinical effectiveness of non-invasive ventilation (NIV) in managing acute exacerbations of chronic obstructive pulmonary disease (AECOPD). NIV significantly reduces both the need for invasive mechanical ventilation and in-hospital mortality, supporting its role as a first-line intervention in patients presenting with acute respiratory failure. Although its impact on hospital length of stay remains inconclusive, the consistent benefits observed in key clinical outcomes reinforce the utility of NIV across various care settings. Further large-scale randomized trials with rigorous methodological design are needed to evaluate long-term outcomes and guide evidence-based implementation of NIV in diverse healthcare environments.

REFERENCE

1. Elshof, J., Vonk, J. M., Van Der Pouw, A., Van Dijk, C., Vos, P., Kerstjens, H. A., Wijkstra, P. J., & Duiverman, M. L. (2023). Clinical practice of non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. *Respiratory Research, 24*(1). https://doi.org/10.1186/s12931-023-02507-1
2. Gao, Y., Yuan, B., Fan, P., Li, M., & Chen, J. (2024). Risk prediction models for non-invasive ventilation failure in patients with chronic obstructive pulmonary disease: A systematic

review. *Medicine*, *103*(51), e40588. https://doi.org/10.1097/md.0000000000040588

3. Von Düring, S., Chevalley, B., Wozniak, H., Desmettre, T., Quintard, H., Suppan, L., & Fehlmann, C. A. (2025). Clinical factors associated with the use of NIV in the pre-hospital setting in adult patients treated for acute COPD exacerbation: a single-center retrospective cohort study. *BMC Emergency Medicine*, *25*(1). https://doi.org/10.1186/s12873-025-01193-0
4. Du, Y., Zhang, H., Ma, Z., Liu, J., Wang, Z., Lin, M., Ni, F., Li, X., Tan, H., Tan, S., Chai, Y., & Zhong, X. (2023). High-Flow Nasal Oxygen versus Noninvasive Ventilation in Acute Exacerbation of Chronic Obstructive Pulmonary Disease Patients: A Meta-Analysis of Randomized Controlled Trials. *Canadian Respiratory Journal*, *2023*, 1–12. https://doi.org/10.1155/2023/7707010
5. Hedsund, C., Ankjærgaard, K. L., Sonne, T. P., Tønnesen, P., Hansen, E. F., Andreassen, H. F., Berg, R. M. G., Jensen, J. S., & Wilcke, J. T. (2023). Long-term non-invasive ventilation for COPD patients following an exacerbation with acute hypercapnic respiratory failure: a randomized controlled trial. *European Clinical Respiratory Journal*, *10*(1). https://doi.org/10.1080/20018525.2023.2257993
6. Kaminska, M., Adam, V., & Orr, J. E. (2024). Home Noninvasive ventilation in COPD. *CHEST Journal*, *165*(6), 1372–1379. https://doi.org/10.1016/j.chest.2024.01.030
7. Elshof, J., Vonk, J. M., Van Der Pouw, A., Van Dijk, C., Vos, P., Kerstjens, H. A., Wijkstra, P. J., & Duiverman, M. L. (2023b). Clinical practice of non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. *Respiratory Research*, *24*(1). https://doi.org/10.1186/s12931-023-02507-1
8. Alzaabi, O., Guerot, E., Planquette, B., Diehl, J., & Soumagne, T. (2024). Predicting outcomes in patients with exacerbation of COPD requiring mechanical ventilation. *Annals of Intensive Care*, *14*(1). https://doi.org/10.1186/s13613-024-01394-z
9. Elsayed, A. A., Neanaa, E. H. M., & Beshey, B. N. (2022, December 31). Diaphragmatic impairment as a predictor of invasive ventilation in acute exacerbation of chronic obstructive pulmonary disease patients. https://egja.journals.ekb.eg/article_387825.html
10. Ralf, E., Heine, A., Obst, A., Koerner, K., Hustig-Kittler, V., Boesche, M., Elhadad, M., Stubbe, B., & Westhoff, M. (2023). Acute COPD exacerbation treatment with noninvasive ventilation. *Scientific Reports*, *13*(1). https://doi.org/10.1038/s41598-023-33871-z
11. Brochard, L., Mancebo, J., Wysocki, M., Lofaso, F., Conti, G., Rauss, A., Simonneau, G., Benito, S., Gasparetto, A., Lemaire, F., Isabey, D., & Harf, A. (1995). Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. *New England Journal of Medicine*, *333*(13), 817–822. https://doi.org/10.1056/nejm199509283331301
12. Plant, P., Owen, J., & Elliott, M. (2000). Early use of non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease on general respiratory wards: a multicentre randomised controlled trial. *The Lancet*, *355*(9219), 1931–1935. https://doi.org/10.1016/s0140-6736(00)02323-0
13. Stefan, M. S., Nathanson, B. H., Lagu, T., Priya, A., Pekow, P. S., Steingrub, J. S., Hill, N. S., Goldberg, R. J., Kent, D. M., & Lindenauer, P. K. (2016). Outcomes of Noninvasive and Invasive Ventilation in Patients Hospitalized with Asthma Exacerbation. *Annals of the American Thoracic Society*, *13*(7), 1096–1104. https://doi.org/10.1513/annalsats.201510-701oc
14. Ram, F., Picot, J., Lightowler, J., & Wedzicha, J. (2003). Non-invasive positive pressure ventilation for treatment of respiratory failure due to exacerbations of chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews*. https://doi.org/10.1002/14651858.cd004104.pub2
15. Osadnik, C. R., Tee, V. S., Carson-Chahhoud, K. V., Picot, J., Wedzicha, J. A., & Smith, B. J. (2017b). Non-invasive ventilation for the management of acute hypercapnic respiratory failure due to exacerbation of chronic obstructive pulmonary disease. *Cochrane Library*, *2017*(7). https://doi.org/10.1002/14651858.cd004104.pub4