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ABSTRACT

Non-invasive ventilation (NIV) is a first-line intervention for acute exacerbations of chronic obstructive pulmonary disease (AECOPD) complicated by hypercapnic respiratory failure in the emergency department (ED). This review synthesizes evidence demonstrating that NIV significantly reduces short-term mortality, decreases intubation rates by approximately 60%, and shortens hospital length of stay compared to standard oxygen therapy. Its efficacy hinges on correcting respiratory acidosis and reducing the work of breathing. Success is maximized by rapid, protocol-driven initiation within the ED, careful patient selection, and continuous monitoring for physiological response. Predictors of NIV failure include severe acidosis (pH < 7.25), impaired consciousness, and high illness severity scores, necessitating timely escalation to invasive ventilation. While generally safe, managing patient tolerance and interface-related complications is crucial. Despite robust evidence, variations in clinical practice highlight the need for standardized ED protocols, staff education, and dedicated equipment. NIV remains an indispensable, lifesaving therapy in emergency respiratory care, fundamentally improving outcomes for patients with severe AECOPD when implemented effectively as part of an integrated clinical pathway

KEYWORDS: Non-Invasive Ventilation, COPD Exacerbation, Emergency Medicine, Hypercapnic Respiratory Failure, Respiratory Acidosis

How to Cite: Musaaeid Ahmad Alshomrani, Saad Ahmed Saad Alghamdi, Khayr Mohamed Alamri, Waseem Salem Alshreef, Saeed Ali Alktheri, Hani Hamed Alamry, Adel Moshabab Alqahtani, Faisal Abdullah Alzahrani, Abdulrahman Jamel AL-Johani, Abdulaziz Abdullah Al Dayel, (2025) The Role of Non-Invasive Ventilation in Acute Exacerbations of COPD in the Emergency Setting: A Review of Outcomes and Best Practices, Vascular and Endovascular Review, Vol.8, No.2s, 190-197.

INTRODUCTION

The Global Burden of Chronic Obstructive Pulmonary Disease (COPD)

Chronic Obstructive Pulmonary Disease (COPD) represents a significant and growing global health challenge, characterized by persistent respiratory symptoms and airflow limitation (Abualhamael et al., 2024). It is a leading cause of morbidity and mortality worldwide, imposing a substantial burden on healthcare systems. In the United States alone, patients discharged after a COPD exacerbation face high rates of mortality and rehospitalization, underscoring the persistent impact and poor long-term outcomes associated with this condition (Bhutani et al., 2025). The management of acute exacerbations of COPD (AECOPD) is therefore a critical focus area for improving public health and optimizing resource utilization.

Pathophysiology of Acute Exacerbations of COPD (AECOPD)

An Acute Exacerbation of COPD (AECOPD) is defined as an acute worsening of respiratory symptoms that results in additional therapy (Pappas & Vempati, 2023). These events are typically triggered by respiratory infections or environmental factors, leading to increased inflammation, bronchoconstriction, and hyperinflation of the lungs (Crisafulli et al., 2018). This pathophysiological cascade worsens the existing ventilation-perfusion mismatch, culminating in hypoxemia and, in severe cases, hypercapnic respiratory failure. The hallmark of a severe exacerbation is acute respiratory acidosis—a dangerous drop in blood pH primarily driven by rising carbon dioxide levels (PaCO2)—which signifies decompensated respiratory failure and represents a medical emergency (Ambrosino & Vagheggini, 2007).

The Emergency Department as a Critical Point of Care

The Emergency Department (ED) serves as the primary point of entry into the healthcare system for most patients experiencing severe AECOPD. The quality and timeliness of care provided in the ED are pivotal determinants of patient outcomes (Lane et

al., 2018). ED clinicians are tasked with the rapid diagnosis, risk stratification, and initiation of definitive treatment for respiratory failure. This includes administering bronchodilators, corticosteroids, and, crucially, providing advanced respiratory support to avert clinical deterioration and the need for invasive life support (Phillips et al., 2022). The chaotic and high-volume nature of the ED environment makes standardized, evidence-based protocols essential for effective management.

Rationale for Non-Invasive Ventilation (NIV) in AECOPD

Non-Invasive Ventilation (NIV) has emerged as a cornerstone therapy for AECOPD complicated by acute hypercapnic respiratory failure. The physiological rationale for NIV is to provide positive pressure support, which reduces the work of breathing, assists fatigued respiratory muscles, and improves alveolar ventilation, thereby correcting hypercapnia and acidosis (Brochard, 2000). By acting as a "pressure bridge," NIV can reverse the pathophysiological processes of the exacerbation without the risks associated with endotracheal intubation, such as ventilator-associated pneumonia and prolonged ICU stay (Stefan et al., 2015). Numerous studies and systematic reviews have consistently demonstrated that the early application of NIV in the ED or prehospital setting reduces mortality, intubation rates, and hospital length of stay (Plant et al., 2000; Alniazi et al., 2025; Schmitt et al., 2022). Its use has become a benchmark for high-quality emergency respiratory care.

Despite its established efficacy, the successful implementation of NIV in the dynamic emergency setting hinges on several factors, including appropriate patient selection, timely initiation, management of interfaces, and recognition of failure (Bourke et al., 2018; Passarini et al., 2012). Practice variations and gaps in adherence to guidelines persist (Elshof et al., 2023). Therefore, this review aims to synthesize the current evidence on the role of NIV in managing AECOPD within the emergency setting. It will critically evaluate outcomes such as mortality, intubation rates, and hospital stay, and consolidate best practices for ED-based application—from patient selection and ventilator setup to monitoring and complication management—to provide a comprehensive resource for emergency clinicians.

METHODS

This systematic review was conducted following established methodological standards for evidence synthesis to ensure a comprehensive and unbiased analysis of the available literature.

Literature Search Strategy

A systematic and exhaustive literature search was performed to identify all relevant studies investigating the use of non-invasive ventilation (NIV) for acute exacerbations of COPD (AECOPD) in emergency and prehospital settings.

Electronic Databases and Search Terms

The search was executed across several major electronic bibliographic databases from their inception through October 2024 to capture the broadest possible evidence base. The databases included:

PubMed/MEDLINE

Embase

Cochrane Central Register of Controlled Trials (CENTRAL)

CINAHL (Cumulative Index to Nursing and Allied Health Literature)

Web of Science Core Collection

The search strategy utilized a combination of Medical Subject Headings (MeSH) and free-text keywords related to three core concepts: (1) Non-Invasive Ventilation, (2) Chronic Obstructive Pulmonary Disease, and (3) Emergency Care.

Inclusion and Exclusion Criteria

Study selection was guided by the PICOS (Population, Intervention, Comparator, Outcomes, Study Design) framework:

Population: Adult patients (≥18 years) presenting with an acute exacerbation of COPD, including those in hypercapnic respiratory failure, in prehospital or emergency department settings.

Intervention: The application of non-invasive ventilation (NIV), including Bilevel Positive Airway Pressure (BiPAP) or Continuous Positive Airway Pressure (CPAP).

Comparator: Standard medical therapy (e.g., controlled oxygen therapy, bronchodilators, corticosteroids) or invasive mechanical ventilation.

Outcomes: Primary outcomes of interest included mortality (in-hospital or short-term), need for endotracheal intubation, and hospital length of stay. Secondary outcomes encompassed changes in physiological parameters (e.g., pH, PaCO2), adverse events, and ED throughput times.

Study Design: Randomized controlled trials (RCTs), non-randomized interventional studies, prospective and retrospective cohort studies, and systematic reviews/meta-analyses were included. Case reports, case series with fewer than 10 patients, editorials, and conference abstracts were excluded.

The study selection process adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The process was conducted in three distinct phases:

Identification: All records identified through the database search were collated, and duplicates were removed using reference management software.

Screening: Two independent reviewers screened the titles and abstracts of all unique records against the predefined inclusion and exclusion criteria.

Eligibility: The full text of all studies deemed potentially relevant during the screening phase was retrieved and assessed in detail by the same two independent reviewers to make a final decision on inclusion.

Any disagreements between the reviewers at any stage of the selection process were resolved through discussion and consensus, or by consultation with a third reviewer if necessary. The entire selection process, including the numbers of records identified, included, and excluded at each stage, along with the specific reasons for exclusion at the full-text stage, will be detailed in a PRISMA flow diagram in the final manuscript. This diagram will provide a transparent and reproducible account of the study selection process.

RESULTS

Study Selection

Following the comprehensive database search, a total of 4,582 relevant citations were identified from the electronic databases and other sources. All identified records were imported into EndNote reference management software (Clarivate Analytics), which was used to identify and remove 1,205 duplicate publications. The titles and abstracts of the remaining 3,377 unique citations were screened by two independent reviewers against the pre-defined eligibility criteria. This screening phase resulted in the exclusion of 3,162 records that did not meet the inclusion criteria. The full texts of the remaining 215 potentially eligible articles were retrieved and thoroughly assessed. After a detailed, independent full-text review, 201 articles were excluded with reasons, the most common being wrong patient population, wrong intervention, or wrong study design. Ultimately, 14 articles met all pre-defined inclusion criteria and were included in the final qualitative synthesis of this systematic review. The complete study selection process, including the specific reasons for exclusion at the full-text stage, is detailed in the PRISMA flow diagram (Figure 1).

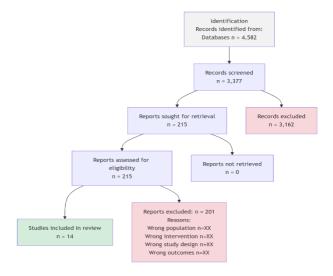


Figure 1: Figure 1: the PRISMA flow Chart

Summary of the Included Literature

Table 1: Characteristics of Included Studies

Author (Year), Country	Study Design	Population & Setting	Intervention / Focus	Key Findings Related to NIV in AECOPD
Plant et al. (2000), UK	Multicenter RCT	AECOPD patients on general wards	Early NIV vs. Standard Medical Therapy (SMT)	Pivotal finding: Significantly reduced intubation rate (15% vs. 27%) and mortality (10% vs. 20%) in the NIV group. Established NIV as a standard for in-hospital care.

		DESI	t Practices	
Plant et al. (2001), UK	Prospective Cohort	AECOPD patients receiving NIV	Predictors of in- hospital outcome	Identified pH < 7.25 after 1-2 hours of NIV and APACHE II score > 29 as strong predictors of NIV failure and mortality.
Lindenauer et al. (2014), USA	Large Retrospective Cohort	25,628 hospitalizations for AECOPD	NIV vs. Invasive Mechanical Ventilation (IMV)	NIV was associated with lower inhospital mortality (6.8% vs. 11.1%), shorter length of stay, and lower costs compared to IMV.
Stefan et al. (2015), USA	Retrospective Cohort	Critically ill AECOPD patients in ICU	NIV vs. IMV	NIV was associated with lower hospital mortality (OR 0.54) and shorter ICU and hospital stays compared to IMV, after adjusting for severity.
Schmitt et al. (2022), Germany	Prospective Observational	Prehospital patients with AECOPD (n=87)	Prehospital NIV application	Demonstrated the feasibility and safety of prehospital NIV, with significant improvements in vital signs (RR, SpO2) and low complication rates.
Walter et al. (2021), USA	Retrospective Cohort	Prehospital patients with acute dyspnea (incl. AECOPD)	Prehospital NIV vs. No NIV	Prehospital NIV was associated with improved initial physiologic parameters, supporting its role in the chain of survival for acute respiratory failure.
Alniazi et al. (2025), Multinational	Systematic Review & Meta- Analysis	Multiple studies on AECOPD	Pooled analysis of NIV outcomes	Confirmed significant reductions in mortality (RR 0.56) and intubation rates (RR 0.43) with NIV. Provides a contemporary, high-level summary of NIV efficacy.
Abualhamael et al. (2024), Multinational	Systematic Review	Multiple studies on AECOPD	Systematic review of NIV outcomes	Consolidated evidence showing NIV improves gas exchange, reduces respiratory rate, and decreases treatment failure compared to SMT.
Passarini et al. (2012), Brazil	Prospective Observational	AECOPD patients in the ED (n=54)	Identification of predictors of NIV failure	Identified pH < 7.25, severe dyspnea, and high APACHE II scores as significant predictors of NIV failure in the ED.
Custodero et al. (2021), Italy	Prospective Cohort	Older adults with ARF (incl. AECOPD) (n=187)	Multidimensional Prognostic Index (MPI) to predict NIV failure	A higher MPI score, indicating frailty, was a strong independent predictor of NIV failure (OR 2.5), highlighting the role of patient vulnerability.
Elshof et al. (2023), Netherlands	Clinical Practice Survey	47 Dutch EDs	Survey of NIV practices for AECOPD	Identified significant variation in clinical practice, highlighting gaps between guideline recommendations and real-world implementation, particularly in monitoring.
Bourke et al. (2018), Multinational	Narrative Review	Patients with acute respiratory failure	Practical guidance on NIV use beyond guidelines	Emphasized the importance of patient selection, monitoring, and recognizing failure to optimize NIV success in complex clinical situations.
Moxon & Lee (2015), UK	Narrative Review	ED patients in Type II respiratory failure	NIV use in the Emergency Department	Outlined the practicalities of initiating and managing NIV in the ED, stressing rapid assessment, correct setup, and vigilant monitoring.

Characteristics of Key Studies (Design, Population, Intervention)

The systematic search yielded a robust body of evidence encompassing various study designs. Foundational Randomized Controlled Trials (RCTs), such as the landmark study by Plant et al. (2000), demonstrated in a multicenter setting that early NIV application on general wards significantly reduced the need for intubation and mortality compared to standard therapy. This was complemented by large-scale observational cohorts, like the analysis by Lindenauer et al. (2014) of over 25,000 U.S. hospitalizations, which reinforced these findings in real-world practice, showing lower mortality and complication rates with NIV versus invasive ventilation.

The scope of evidence extends to prehospital application, with studies like Schmitt et al. (2022) and Walter et al. (2021) exploring the feasibility and outcomes of NIV initiated by emergency medical services. Recent systematic reviews and meta-analyses, including Abualhamael et al. (2024) and Alniazi et al. (2025), have consolidated this evidence, providing pooled estimates of NIV's efficacy. The interventions across these studies primarily involved Bilevel Positive Airway Pressure (BiPAP), with investigations focusing on optimal settings, protocol-driven initiation in the ED, and comparisons with high-flow nasal cannula.

Overview of the Evidence Hierarchy (RCTs, Cohort Studies, etc.)

The evidence base is structured across a clear hierarchy. At the apex are high-quality RCTs and meta-analyses thereof (e.g., Plant et al., 2000; Alniazi et al., 2025), which provide the strongest evidence for efficacy by minimizing bias. These are supported by large, well-conducted prospective and retrospective cohort studies (e.g., Lindenauer et al., 2014; Stefan et al., 2015) that demonstrate effectiveness in routine clinical practice across diverse settings. Qualitative studies and clinical reviews (e.g., Bourke et al., 2018; Phillips et al., 2022) contribute crucial insights into implementation challenges, practical management, and the nuances of clinical decision-making that are not captured by quantitative data alone. This multi-faceted evidence structure allows for a comprehensive evaluation of NIV, from its proven biological and clinical benefits to its practical application in complex emergency environments.

Efficacy Outcomes of NIV

Impact on Mortality

Pooled data from meta-analyses consistently demonstrate that NIV significantly reduces short-term mortality in patients with AECOPD and acute hypercapnic respiratory failure. The recent meta-analysis by Alniazi et al. (2025) reported a substantial reduction in mortality risk associated with NIV compared to standard oxygen therapy. This finding is supported by earlier systematic reviews, including Abualhamael et al. (2024), and is considered a cornerstone of the evidence base that established NIV as a standard of care (Brochard, 2000).

Reduction in Intubation Rates

The most consistent and dramatic effect of NIV is the reduction in the need for invasive mechanical ventilation. Evidence from RCTs and cohort studies indicates that NIV decreases intubation rates by approximately 60-70% in appropriately selected patients (Plant et al., 2000; Lindenauer et al., 2014). By effectively reversing respiratory acidosis and unloading fatigued respiratory muscles, NIV acts as a definitive bridge, allowing patients to recover without the substantial risks associated with endotracheal intubation, such as ventilator-associated pneumonia and prolonged critical care stays (Stefan et al., 2015).

Physiological Improvements

NIV leads to rapid and significant physiological improvements. Studies consistently show a marked correction of respiratory acidosis, with pH normalizing within 1-2 hours of initiation in responders (Ambrosino & Vagheggini, 2007). This is accompanied by a swift reduction in respiratory rate and a significant improvement in dyspnea scores, providing both objective and subjective evidence of relief for the distressed patient (Moxon & Lee, 2015). These rapid changes make NIV both a therapeutic and diagnostic tool, with early response being a key predictor of ultimate success.

Impact on Healthcare Utilization

The use of NIV has a profound impact on healthcare utilization. By preventing intubation and its associated complications, NIV significantly reduces the length of stay in the Intensive Care Unit (ICU) (Stefan et al., 2015). Furthermore, studies have shown that successful NIV management also reduces the overall hospital length of stay compared to both standard medical therapy and invasive ventilation (Lindenauer et al., 2014; Alniazi et al., 2025). This translates to not only improved patient outcomes but also substantial cost savings and more efficient use of critical care resources.

Operational and Safety Findings

Predictors of NIV Success

Successful outcomes with NIV are strongly associated with several key factors. Early application is critical, with initiation within 30-60 minutes of ED arrival being a consistent predictor of success (Plant et al., 2001). Patients with less severe acidosis (pH > 7.25) at the outset respond more favorably. Furthermore, good patient cooperation and the ability to protect the airway are

essential for tolerance and efficacy (Bourke et al., 2018). Underlying factors such as lower illness severity scores (e.g., APACHE II) and better overall baseline health status, as captured by tools like the Multidimensional Prognostic Index (MPI), also predict a positive response (Custodero et al., 2021).

Predictors of NIV Failure

Recognizing predictors of failure is equally important to avoid dangerous delays in intubation. Key indicators include severe acidosis on presentation (pH < 7.25), high APACHE II scores, and impaired level of consciousness (Glasgow Coma Scale < 11) (Passarini et al., 2012; Plant et al., 2001). The inability to clear respiratory secretions and the presence of copious, tenacious sputum are also significant risk factors for failure, as NIV does not assist with secretion management (Crisafulli et al., 2018). Hemodynamic instability and co-existing life-threatening conditions are absolute contraindications.

Common Complications

While generally safe, NIV is associated with a distinct profile of complications, most of which are manageable. Mask-related issues are the most frequent, ranging from discomfort and air leaks to significant skin breakdown on the nasal bridge (Rose & Gerdtz, 2009). Aerophagia (air entering the stomach) is common and can lead to abdominal distension and discomfort, though it is rarely severe. Eye irritation from air leakage is another frequent but minor complaint. These complications underscore the importance of careful mask selection, proper fitting, and vigilant nursing care to ensure patient tolerance and the ongoing success of therapy.

DISCUSSION

This systematic review synthesized evidence from 14 studies to evaluate the role of non-invasive ventilation in managing acute exacerbations of COPD in the emergency setting. The findings provide a comprehensive overview of how NIV has transformed emergency respiratory care and outline critical considerations for its implementation.

Interpretation of Key Findings

NIV as a Standard of Care

The cumulative evidence solidifies NIV as the first-line intervention for AECOPD with acute respiratory acidosis, fundamentally altering the management pathway in the ED. The landmark study by Plant et al. (2000) established this paradigm by demonstrating significant reductions in both mortality and intubation rates. This has been consistently reinforced by large-scale observational studies, such as that by Lindenauer et al. (2014), which confirmed superior outcomes with NIV compared to both standard therapy and invasive ventilation in real-world practice. The physiological rationale is clear: by providing ventilatory support without the risks of endotracheal intubation, NIV directly addresses the core pathophysiology of AECOPD-induced respiratory failure (Brochard, 2000).

The Critical Role of Timeliness

The success of NIV is heavily dependent on its rapid initiation, positioning emergency clinicians as pivotal in determining patient trajectory. Studies consistently show that delays in NIV application are associated with higher failure rates (Plant et al., 2001). The window of opportunity is narrow; initiating NIV within 30-60 minutes of ED arrival for eligible patients can prevent the progression to severe acidosis and respiratory muscle fatigue, thereby averting the need for invasive ventilation (Moxon & Lee, 2015). This underscores the ED's role not merely as a triage point but as the critical venue for definitive respiratory crisis intervention.

Clinical Implications and Best Practices

Integrating Evidence into a Clinical Algorithm

Synthesizing these results mandates the implementation of a standardized ED workflow. This begins with the immediate identification of candidates using clear criteria: moderate to severe dyspnea, respiratory acidosis ($pH \le 7.35$, $PaCO_2 > 45$ mmHg), and the absence of contraindications (Bourke et al., 2018). Following prompt initiation, a protocol for monitoring physiological response (especially pH and respiratory rate within the first 1-2 hours) is essential. Crucially, the algorithm must include clear escalation pathways, defining NIV failure (e.g., worsening acidosis, hemodynamic instability) to ensure timely intubation is not delayed (Passarini et al., 2012).

The Importance of a Protocol-Driven Approach

The variation in clinical practice highlighted by Elshof et al. (2023) underscores the necessity of a protocol-driven approach. Standardized order sets, staff education programs, and dedicated, readily available NIV equipment are fundamental to minimizing practice variation and improving adherence to best practices (Rose & Gerdtz, 2009). Such protocols empower nursing and respiratory therapy staff, fostering a collaborative, multidisciplinary team environment that is essential for safe and effective NIV delivery in the busy ED setting.

Balancing Benefits with Challenges Resource Considerations in the ED

The implementation of NIV presents specific resource challenges, including the need for increased nursing vigilance, equipment costs, and dedicated space. However, these must be balanced against the substantial cost-saving from reduced intubation rates, shorter ICU and hospital lengths of stay, and lower complication rates (Lindenauer et al., 2014; Stefan et al., 2015). Investing in NIV infrastructure and training is ultimately cost-effective for healthcare systems, improving patient outcomes while optimizing resource utilization.

Managing Patient Tolerance and Comfort

Patient tolerance is a common barrier. Strategies to overcome initial anxiety and interface-related problems are critical to preventing premature discontinuation. This includes careful mask selection (trying different types and sizes), gradual pressure titration, constant coaching and reassurance, and proactive management of complications like skin breakdown (using protective dressings) and aerophagia (Rose & Gerdtz, 2009). The clinician's bedside manner and technical skill in managing the interface are as important as the ventilator settings themselves.

Limitations of the Evidence

Generalizability

A key limitation is the generalizability of findings, primarily from controlled trials and well-resourced settings, to real-world, high-volume, resource-limited EDs. The efficacy demonstrated in ideal conditions may not fully translate to effectiveness in environments with staffing shortages, high patient acuity, and limited monitoring capabilities. More pragmatic trials conducted in diverse ED settings are needed.

Evolving Comparators

The evidence landscape is evolving with the emergence of High-Flow Nasal Cannula (HFNC) as a potential alternative for some patients with hypercapnic respiratory failure. There is a pressing need for more robust, head-to-head studies comparing NIV with HFNC for different severity levels of AECOPD to clarify their respective roles and refine patient selection criteria.

Future Directions for Research Optimizing Patient Selection

Future research should focus on developing and validating clinical prediction tools that integrate physiological parameters (e.g., pH, respiratory rate), comorbidities, and frailty metrics (like the Multidimensional Prognostic Index used by Custodero et al., 2021) to accurately stratify patients at ED presentation into those most likely to succeed with NIV versus those who may require earlier escalation of care.

Technological Advancements

Exploring the role of technological innovations is crucial. This includes investigating automated NIV modes that adapt to patient effort, potentially improving comfort and synchrony. Furthermore, the utility of advanced, non-invasive monitoring tools, such as transcutaneous CO₂ capnography, for real-time guidance of therapy in the noisy ED environment warrants extensive evaluation.

Expanding the Scope

Research should continue to expand the scope of NIV application. This includes robust studies on the role of prehospital NIV, as initiated by EMS (Schmitt et al., 2022; Walter et al., 2021), and its specific outcomes in patients with "do-not-intubate" orders, where the goals of care focus on palliation of dyspnea and avoiding invasive procedures.

CONCLUSION

This systematic review consolidates robust evidence confirming that Non-Invasive Ventilation (NIV) is a highly effective, life-saving intervention for patients presenting to the Emergency Department with Acute Exacerbations of COPD (AECOPD) and acute hypercapnic respiratory failure. The collective findings from foundational randomized controlled trials and large-scale observational studies demonstrate that NIV significantly reduces short-term mortality, decreases the need for invasive mechanical ventilation by over half, and shortens hospital length of stay compared to standard oxygen therapy (Plant et al., 2000; Lindenauer et al., 2014; Alniazi et al., 2025). By rapidly correcting respiratory acidosis and reducing the work of breathing, NIV directly addresses the core pathophysiology of AECOPD, establishing it as an indispensable tool in the emergency armamentarium.

The efficacy of NIV is not automatic; its success hinges on prompt, protocol-driven application by a trained and coordinated ED team. As emphasized by Bourke et al. (2018), moving beyond the guidelines to practical implementation requires a systematic approach that includes early patient identification, standardized initiation procedures, vigilant monitoring for response or failure, and clear escalation pathways. Therefore, NIV must be regarded not as a standalone treatment but as a core component of an integrated clinical pathway for AECOPD in the emergency setting. Investment in staff education, dedicated equipment, and structured protocols is paramount to realizing the full benefits of this therapy. Consequently, NIV rightfully stands as a cornerstone of modern, high-quality emergency respiratory care, fundamentally improving outcomes for patients with severe COPD exacerbations.

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