American Thoracic Society Documents

Noninvasive Respiratory Support for Adult Patients with Acute Respiratory Failure
An Official American Thoracic Society Clinical Practice Guideline

Neha N. Goel[1†], Bruno L. Ferreyro[2†*], Tyler Pitre[3], Kimberley Lewis[3,4], Collin Homer-Bouthiette[5], Federico Angriman[6], Leticia Kawano Dourado[7,8], Matthew Drake[9], Tammy L. Eaton[10,11], Cheryl L. Esbrook [12], Jean-Pierre Frat[13], Domenico L. Grieco[14,15], William LeTourneau[16], Jarrod Mosier[17], Bhakti K. Patel[18], Nida Qadir[19], Elisabeth Riviello[20], Oriol Roca[21,22], Theogene Twagirumugabe[23], Kelly C. Vranas[9,24], Laveena Munshi[2], Bram Rochwerg[3,4,25]; on behalf of the American Thoracic Society Assembly on Critical Care

Affiliations

1. Division of Pulmonary, Critical Care and Sleep Medicine, Icahn School of Medicine at Mount Sinai, New York, NY, USA
2. Interdepartmental Division of Critical Care Medicine, Sinai Health System, University of Toronto, Toronto, Ontario, Canada
3. Division of Respirology, Department of Medicine, University Health Network, University of Toronto, ON, Canada
4. Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, Ontario, Canada
5. Division of Pulmonary, Critical Care, and Sleep Medicine, Boston University School of Medicine, Boston, MA, USA
6. Department of Critical Care Medicine, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada
7. Hcor Research Institute, Hcor Hospital, Sao Paulo, Brazil
8. Pulmonary Division, Hospital das Clínicas – HCFMUSP, University of São Paulo, São Paulo, Brazil
9. Division of Pulmonary and Critical Care Medicine, Oregon Health & Science University, Portland, OR, USA
10. Department of Internal Medicine, Division of Hospital Medicine, Michigan Medicine, Ann Arbor, MI, USA
11. VA Center for Clinical Management Research, VA Ann Arbor Healthcare System, Ann Arbor, MI, USA
12. Department of Therapy Services, University of Chicago, Chicago, IL, USA
13. Service de Médecine Intensive-Réanimation, Centre Hospitalier Universitaire de Poitiers, Poitiers, France
14. Department of Anesthesiology and Intensive Care, Catholic University of the Sacred Heart, Rome, Italy

15. Department of Emergency, Intensive Care and Anesthesia. Fondazione Policlinico A. Gemelli IRCCS, Rome, Italy
16. Department of Respiratory Therapy, Mayo Clinic, Rochester, MN, USA
17. Departments of Emergency Medicine and Medicine, University of Arizona, Tucson, AZ, USA
18. Section of Pulmonary and Critical Care, Department of Medicine, University of Chicago, Chicago, IL, USA
19. Division of Pulmonary and Critical Care Medicine, David Geffen School of Medicine, University of California Los Angeles (UCLA), Los Angeles, CA, USA
20. Division of Pulmonary, Sleep, and Critical Care Medicine, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, USA
21. Department of Critical Care, Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat (Barcelona), Spain.
22. Ciber Enfermedades Respiratorias (Ciberes), Instituto de Salud Carlos III, Madrid, Spain
23. Department of Anesthesiology and Critical Care, University Teaching Hospital of Butare, University of Rwanda, Kigali, Rwanda
24. Core Investigator, Center to Improve Veteran Involvement in Care, VA Portland Health Care System, Portland, OR
25. Knowledge Centre, Hamilton Health Sciences, Hamilton, ON

*Corresponding author: Bruno L. Ferreyro, M.D., Ph.D., Sinai Health System and University Health Network, University of Toronto, 5-349 600 University Avenue, Ontario M5G 1X5, Canada. E-mail: bruno.ferreyro@utoronto.ca.

†Neha N. Goel and Bruno L. Ferreyro contributed equally to this work.

This official Clinical Practice Guideline of the American Thoracic Society was approved May 2026.

Abstract

Background: Acute hypoxemic and hypercapnic respiratory failure are among the most common reasons for ICU admission and need for invasive mechanical ventilation. Noninvasive respiratory support (NIRS) strategies—including high-flow nasal cannula (HFNC), noninvasive ventilation (NIV), and continuous positive airway pressure (CPAP)—may prevent intubation, improve outcomes, and reduce ICU utilization. However, there is uncertainty regarding optimal patient and modality selection, resulting in variable implementation. There are no clinical practice guidelines comprehensively

addressing the use of the different noninvasive respiratory support strategies across the spectrum of acute respiratory failure.

Objective: To update and develop new evidence-based clinical practice recommendations informing noninvasive respiratory support use, including HFNC, NIV and CPAP, in adults with acute respiratory failure.

Methods: A multidisciplinary panel used the GRADE approach to address four PICO questions related to the use of NIRS for hypoxemic and hypercapnic respiratory failure, preoxygenation for intubation, and post-extubation respiratory support. Recommendations were informed by several systematic reviews and network meta-analyses.

Results: The panel made a strong recommendation for HFNC and a conditional recommendation for NIV or CPAP for adults with acute hypoxemic respiratory failure with close monitoring for the need for escalation of respiratory support, based primarily on effects on need for intubation. For acute hypercapnic respiratory failure, the panel made a strong recommendation for NIV to reduce mortality and need for invasive mechanical ventilation, and a conditional recommendation for HFNC only in patients with less severe hypercapnia and with mild acidemia (e.g. pH > 7.25), provided that close monitoring and prompt escalation to NIV are available. The panel made a strong recommendation for HFNC or NIV for preoxygenation prior to endotracheal intubation to prevent peri-intubation hypoxemia. The panel also issued a risk-based recommendation, suggesting HFNC for low-risk patients and NIV for high-risk patients to reduce the need for re-intubation following extubation after critical illness.

Conclusions: Noninvasive respiratory support strategies are effective in improving outcomes in a range of clinical scenarios. We provide evidence-based recommendations, which can be further informed by patient risk, institutional capacity, and interface tolerance.

Keywords: noninvasive respiratory support, acute hypoxemic respiratory failure, acute hypercapnic respiratory failure, preoxygenation, post-extubation respiratory failure

Contents

Glossary

NIRS strategy	Standard oxygen therapy	High flow nasal cannula	CPAP	NIV[1]
Interface or device used	Cannula, venturi mask, NRB	Cannula, symmetric or asymmetric	Facemask (total facemask and oronasal masks) or Helmet	

1. Equivalent to non-invasive positive pressure ventilation (NIPPV) or bilevel NIV

Summary of Recommendations

This guideline provides evidence-based recommendations informing noninvasive respiratory support (NIRS) use in adults with acute respiratory failure. The panel addressed four high priority questions regarding standard oxygen, high-flow nasal cannula (HFNC), continuous positive airway pressure (CPAP), and noninvasive ventilation (NIV), across the following clinical conditions (Figure 1):

1. **Acute hypoxemic respiratory failure**,
2. **Acute hypercapnic respiratory failure**,
3. **Preoxygenation during endotracheal intubation**, and
4. **Post-extubation respiratory support**.

Given that NIV or CPAP can be applied with either a facemask or a helmet interface and due to potential physiological and clinical differences between these interfaces, we have specified in our recommendations where different interfaces might have different roles. Of note, these nuances are particularly important in the context of acute hypoxemic respiratory failure and acute hypercapnic respiratory failure. For the purposes of this guideline, “facemask” refers to interfaces applied directly to the patient’s face. These include oronasal masks, which cover the nose and mouth and are the most commonly used interface in acute respiratory failure, and total face masks, which cover the entire face. Nasal masks, which cover only the nose, are distinct and are rarely used in acute respiratory failure. In contrast, “helmet” refers to support delivered through a transparent hood that encloses the patient’s entire head and seals at the neck.

We either updated or performed *de novo* systematic reviews and network meta-analyses to inform each PICO question. Then, using the GRADE approach, a multidisciplinary panel used the Evidence-to-Decision (EtD) process to generate recommendations. Across conditions, NIRS strategies reduced the need for invasive mechanical ventilation and improved comfort compared with standard oxygen therapy, with the magnitude of benefit depending on the patient population and clinical context.

Recommendations:

Acute hypoxemic respiratory failure

- **We recommend HFNC as compared to standard oxygen therapy** for adults with *de novo* acute hypoxemic respiratory failure (*strong recommendation, moderate certainty*).

- **We suggest NIV via facemask or helmet as compared to standard oxygen therapy** for adults with *de novo* acute hypoxemic respiratory failure (*conditional recommendation, low certainty*).
- **We suggest CPAP via facemask or helmet as compared to standard oxygen therapy** for adults with *de novo* acute hypoxemic respiratory failure (*conditional recommendation, low certainty*).

Acute hypercapnic respiratory failure

- **We recommend NIV via facemask as compared to standard oxygen therapy** for adults with acute hypercapnic respiratory failure (*strong recommendation, moderate certainty*).
- **We suggest HFNC** as an alternative to NIV **as compared to standard oxygen therapy** for patients with acute hypercapnic respiratory failure and mild acidemia (e.g. pH > 7.25) provided that monitoring and escalation to NIV are promptly available (*conditional recommendation, low certainty*).

Preoxygenation:

- **We recommend using HFNC or NIV via facemask as compared to standard oxygen therapy** for preoxygenation in adults with acute respiratory failure undergoing endotracheal intubation (*strong recommendation, moderate certainty*).
- **We make no recommendation for or against HFNC compared with NIV** for preoxygenation in adults with acute respiratory failure undergoing endotracheal intubation.

Post-Extubation:

- **We suggest using HFNC or NIV via facemask as compared to standard oxygen therapy** in patients extubated in the intensive care unit after critical illness (*conditional recommendation, moderate certainty*).
- **We suggest using NIV via facemask as compared to standard oxygen therapy or HFNC** in patients extubated in the intensive care unit after critical illness at high-risk of extubation failure (e.g., age > 65 years, obesity, hypercapnia, prolonged mechanical ventilation, or severe illness, among others) (*conditional recommendation, moderate certainty*).

Implementation should be tailored to patient risk, disease severity, interface tolerance, resource availability, and provider familiarity with interface (helmet vs. facemask etc.). Note that the vast majority of the evidence emanates from resource-rich settings. These recommendations emphasize early initiation, close monitoring, and timely escalation

when NIRS fails. Future research should refine patient selection, optimal settings for each device, monitoring and escalation of patients on NIRS, and combined or sequential use of HFNC and NIV in certain clinical contexts.

Introduction

Acute respiratory failure is a leading cause of hospital admissions and need for intubation and mechanical ventilation (1). Noninvasive respiratory support (NIRS) offers an alternative to invasive mechanical ventilation (IMV) (2). NIRS strategies include high-flow nasal cannula (HFNC), noninvasive ventilation (NIV) delivered via facemask or helmet, and continuous positive airway pressure (CPAP) delivered via facemask or helmet interfaces. HFNC is defined as the delivery of heated, humidified gas (typically an oxygen–air mixture with adjustable FiO_2) at high flow rates, most commonly via nasal cannula. However, the comparative effectiveness between these different modalities for each specific clinical context remains unclear.

Prior guidelines have addressed clinical recommendations regarding the use of NIRS primarily from the perspective of the device or modality. The European Society of Intensive Care Medicine (ESICM) (3) and the European Respiratory Society–American Thoracic Society (ERS–ATS) (4, 5) guidelines provided evidence-based recommendations for specific interventions, such as CPAP, HFNC or NIV, and for defined syndromes such as acute respiratory distress syndrome (6). Since the development of those guidelines, new evidence from randomized controlled trials (RCTs) has emerged which warrants re-evaluation of existing recommendations and integration of updated data across conditions and modalities of support.

Accordingly, this American Thoracic Society Clinical Practice Guideline seeks to provide an evidence-based framework examining NIRS use in adults within the spectrum of acute respiratory failure, ranging from the prevention of intubation to support provided following liberation from invasive mechanical ventilation. The guideline is structured around physiologic categories—acute hypoxemic respiratory failure, acute hypercapnic respiratory failure, preoxygenation during endotracheal intubation, and post-extubation support—reflecting the underlying pathophysiology and therapeutic goals rather than specific disease etiologies. For example, the hypoxemic respiratory failure PICO encompasses diverse conditions that result in impaired oxygenation, irrespective of the precipitating diagnosis. Similarly, the hypercapnic respiratory failure PICO includes studies enrolling patients with ventilatory deficiencies, including but not limited to chronic obstructive pulmonary disease (COPD) exacerbation. Within each of these PICO domains, we examined and described the individual underlying conditions represented in the included trials, and when able, evaluated whether treatment effects varied across these populations. We summarize and appraise evidence for different NIRS modalities for each of these domains and highlight key areas where evidence remains insufficient.

The intended audience includes clinicians, respiratory therapists, and advanced practice providers caring for adults with acute respiratory failure in acute care settings. Ultimately, this guideline aims to improve the safety, consistency, and quality of care delivered to these patients, while identifying priorities for future research to address remaining knowledge gaps.

Methods

Guideline Development Committee Composition

Content experts were assembled by the co-chairs of the guideline (BF, NG) to compose a multidisciplinary guideline panel. This panel included pulmonary and critical care physicians, emergency medicine clinicians, respiratory therapists, physical and occupational therapists, methodologists, and patient representatives with lived experience of acute respiratory failure. Members were selected to ensure diverse expertise across the domains of NIRS, clinical research and evidence synthesis, expertise in health systems and implementation, and representatives from low- and middle-income countries. Methodologic support was provided by experienced methodologists (BR, TP, CHB, KL) with expertise in Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology and with prior involvement in ATS guideline development (7–11). The panel was responsible for defining the scope, selecting the final PICO questions, interpreting the evidence, and drafting recommendations. The panel met primarily by video conference, with one in-person meeting held during the 2025 ATS International Conference. All sessions were recorded and distributed, allowing members who were unable to attend to review proceedings and contribute asynchronously.

Conflict of Interest Disclosure and Management

All members completed COI disclosures at initiation and throughout development (12). Financial and intellectual potential conflicts were reviewed by the ATS Documents Development and Implementation Committee and managed by the co-chairs; members with relevant COIs abstained from related discussions and votes.

PICO Question Development and Outcome Prioritization

The panel co-chairs proposed several potential topics related to the management of NIRS. Through iterative discussion and consensus, the panel identified four priority clinical questions addressing the use of NIRS in adult patients with acute respiratory failure. Each question was structured using the PICO (Population, Intervention, Comparator, Outcome) framework (13). The four actionable PICO questions focused on NIRS strategies for adult patients with 1. Acute hypoxemic respiratory failure; 2. Acute hypercapnic respiratory failure; 3. Patients requiring preoxygenation during endotracheal intubation; and 4. Post-extubation NIRS (Figure 1).

Panel members were presented with a list of potential outcomes compiled by the co-chairs and the methodology team and were invited to propose additional outcomes of

interest, which were subsequently collated. Panelists then rated each outcome based on its importance for clinical decision-making from a patient's perspective, using a 1–9 scale (where 1 indicates not important and 9 indicates critically important) (14) . Eight outcomes were designated as critical to clinical decision-making and were subsequently prioritized during evidence synthesis and recommendation generation: (1) long-term mortality (90-day or 6-month), (2) short-term mortality (28-day, ICU, or hospital), (3) cardiac arrest, (4) need for intubation, (5) long-term disability or increased care needs at discharge, (6) health-related quality of life at 3 and 6 months, (7) need for extracorporeal membrane oxygenation (ECMO), and (8) need for reintubation. Patient comfort and tolerance received a mean rating of 6.55 and were classified as important, but not critical, outcomes. Recognizing that comfort influences patient adherence to NIRS, we evaluated and reported comfort in the PICO domains where data were available and considered it in the Evidence-to-Decision (Etd) discussions.

Literature Search and Study Selection

For each of the PICO questions, we either performed *de novo* reviews, or updated previously published systematic reviews and network meta-analyses conducted by members of this guideline panel (15–17). Each PICO incorporated a comprehensive electronic search which included Embase*, Cochrane CENTRAL, Web of Science,* and *Scopus* to identify relevant RCTs. We did not place any limits based on language or publication status. For two of the four PICO questions (acute hypoxemia and post-extubation respiratory support), we formally updated previously published systematic reviews and network meta-analyses (15, 17) that had been conducted by members of this guideline panel. These analyses were updated through comprehensive literature searches from the last search date of the original reviews, and newly identified studies underwent duplicate screening, data extraction, and risk-of-bias assessment consistent with the methods applied in the original analyses. For the other PICO questions (acute hypercapnia and preoxygenation), we conducted new systematic reviews and evidence synthesis to support this guideline effort (16). For all systematic reviews (either updated or *de novo*), two independent reviewers screened all citations in two stages (titles, abstracts, and then full texts) in duplicate using Covidence software (Melbourne, Australia). Similarly, we assessed individual study's risk of bias independently and in duplicate using the modified Cochrane risk of bias tool (18, 19). Because blinding of patients and clinicians is generally not feasible in trials evaluating NIRS strategies, this limitation was considered in the GRADE risk-of-bias assessments and may influence the interpretation of some outcomes, in particular for endotracheal intubation.

Specific search terms, inclusion/exclusion criteria, and further evidence synthesis details are provided within each PICO section of this document. Of note, several relevant trials were published following completion of the evidence synthesis and EtD processes for this guideline, including the RENOVATE trial (20) and the SOHO trial

(21). Although these studies represent important contributions to the field of NIRS, the panel felt confident that inclusion of these trials would not lead to meaningful changes in pooled estimates, conclusions, or recommendations. For transparency, and comprehensiveness, these studies are discussed in the relevant PICO sections.

Evidence Synthesis Approach

We extracted data from included studies (again for both updated and de novo reviews) using standardized case report forms. We performed frequentist random-effects network meta-analysis using R (*netmeta* package) for each of the four PICO questions, with treatment effects expressed as relative risk ratios (RRs) for dichotomous outcomes and mean differences (MD) for continuous outcomes, each with 95% confidence intervals (CIs) (22). When feasible, the network meta-analyses for each PICO comprised six distinct treatment nodes: standard oxygen therapy, HFNC, facemask NIV, helmet NIV, helmet CPAP, and facemask CPAP. For ease of presentation, given the sparsity of data for some networks, we present some analyses by collapsing the interface through which NIV or CPAP was delivered (helmet or facemask). We rated the certainty of evidence for each comparison and outcome using the GRADE approach. We categorized certainty as *high*, *moderate*, *low*, or *very low*. For each PICO question, we generated summary-of-findings tables and network diagrams illustrating treatment effects, and certainty of evidence.

For each of the four PICO questions, the panel prospectively identified key subgroups based on biological plausibility, prior evidence, and anticipated sources of heterogeneity (e.g., patient risk profile, setting where interventions were deployed, and underlying etiology of respiratory failure). These subgroups were evaluated within each corresponding network meta-analysis. The credibility of observed subgroup effects was assessed using the ICEMAN (Instrument to assess the Credibility of Effect Modification Analyses) framework, which incorporates both statistical tests and a structured appraisal of clinical plausibility and consistency (23).

Recommendation Formulation Process

We developed recommendations using the GRADE EtD framework, which systematically considers the balance of desirable and undesirable effects, the certainty of evidence, patient values and preferences, and factors related to resource use, feasibility, equity, and acceptability (24). Panel discussions were iterative and evidence-based, and draft recommendations were refined through structured consensus. All EtD meetings were held via video conference, and recordings were shared with the full panel so that members who could not attend could review discussions and provide input asynchronously. Each recommendation was classified as strong or conditional based on the overall balance of these considerations, and we used GRADE approved language to frame recommendations.

In alignment with the GRADE methodology, the panel had planned to hold formal votes if consensus could not be achieved through discussion. Ultimately, this was unnecessary, as all recommendations were agreed upon through iterative deliberation.

Manuscript Preparation

We prepared the manuscript in accordance with ATS procedures outlined in the *ATS Handbook for Guideline Development* and established standards for trustworthy guideline development from Institute of Medicine (25). The co-chairs prepared the guideline manuscript, synthesizing the evidence summaries and panel deliberations into an integrated draft. All panel members reviewed the document, and their feedback was incorporated through multiple iterative revisions. In addition, the co-chairs held a dedicated meeting with the patient representative to review the recommendations, ensuring that patient perspectives were accurately reflected and integrated into the final guideline. All recommendations and supporting materials were reviewed by the ATS Documents Development and Implementation Committee (DDIC) and approved by the ATS Board of Directors before publication.

PICO 1: Acute Hypoxemic Respiratory Failure

Question 1: Should we use HFNC, NIV (via helmet or facemask) or CPAP (via helmet or facemask) versus standard oxygen therapy for patients with *de novo* acute hypoxemic respiratory failure?

Recommendations

- **We recommend HFNC as compared to standard oxygen therapy** for adults with *de novo* acute hypoxemic respiratory failure (*strong recommendation, moderate certainty*) (Figure 2).
- **We suggest NIV via facemask or helmet as compared to standard oxygen therapy** for adults with *de novo* acute hypoxemic respiratory failure (*conditional recommendation, low certainty*).
- **We suggest CPAP via facemask or helmet as compared to standard oxygen therapy** for adults with *de novo* acute hypoxemic respiratory failure (*conditional recommendation, low certainty*).

We make no recommendation for or against HFNC or CPAP compared with NIV for adults with *de novo* acute hypoxemic respiratory failure; selection between these modalities should be based on patient characteristics, operator expertise, and local resources.

Background

Acute hypoxemic respiratory failure is a leading cause of admission to intensive care units and is associated with high morbidity and mortality (1). Standard oxygen therapy is often insufficient to correct severe hypoxemia and decrease work of breathing, and many patients require escalation to IMV. Over the past two decades, a range of NIRS strategies - including HFNC, NIV (via a helmet or facemask interface) and CPAP (also via a helmet or facemask interface) have been increasingly used as strategies to improve gas exchange, reduce work of breathing, and decrease the risk of intubation (2).

These modalities differ from standard oxygen therapy in their ability to deliver higher and more reliable inspired oxygen fractions, provide varying degrees of positive airway pressure, and improve comfort. HFNC delivers heated and humidified oxygen at flow rates up to 60 L/min or higher, which reduces anatomical dead space and generates low levels of positive end-expiratory pressure (26). NIV applies positive pressure via a

sealed interface (facemask or helmet), improving alveolar recruitment and unloading respiratory muscles but at the expense of greater complexity and potential intolerance. Previous guidelines have suggested possible benefit of NIRS strategies for selected patients with acute hypoxemic respiratory failure; however, since those publications, new RCTs and several large network meta-analyses have provided updated evidence summaries (15).

Evidence Summary

We included 39 RCTs (n=2913 patients) examining NIRS strategies in patients with *de-novo* acute hypoxemic respiratory failure (27–66), including some studies of COVID-19 related acute hypoxemic respiratory failure (27, 29, 30, 32–41, 43–46, 48–54, 56–61, 63–73). Among the 39 randomized trials included: 17 evaluated facemask NIV, 8 evaluated facemask CPAP, 5 evaluated helmet NIV, 2 evaluated helmet CPAP, and 15 evaluated HFNC. Pooled analysis demonstrated that HFNC (RR 0.81, 95% CI 0.67 to 0.97; low certainty) may reduce mortality compared with standard oxygen therapy, whereas helmet NIV (RR 0.72, 95% CI 0.48 to 1.07; very low certainty), facemask NIV (RR 0.93, 95% CI 0.75 to 1.14; very low certainty), helmet CPAP (RR 0.76, 95% CI 0.51 to 1.12; low certainty), and facemask CPAP (RR 1.01, 95% CI 0.73 to 1.40; low certainty) had uncertain effects on mortality compared with standard oxygen therapy. (29, 30, 34–41, 43–46, 48–51, 53, 54, 56–61, 63–65). Finally, HFNC had an uncertain effect on mortality compared to facemask NIV (RR 0.84, 95% CI 0.69 to 1.02, very low certainty)

For intubation, HFNC (RR 0.76, 95% CI 0.64 to 0.89; moderate certainty), helmet CPAP (RR 0.53, 95% CI 0.35 to 0.79; moderate certainty), and helmet NIV (RR 0.22, 95% CI 0.11 to 0.43; moderate certainty) probably reduce the need for intubation, whereas facemask NIV (RR 0.79, 95% CI 0.67 to 0.93; low certainty) and facemask CPAP (RR 0.77, 95% CI 0.59 to 1.01; low certainty) may reduce the risk of intubation compared with standard oxygen therapy (27, 29, 30, 33–41, 43–46, 48–52, 54, 56–60, 63–65, 73). Patient comfort may be highest with HFNC compared to standard oxygen therapy (MD +1.3 points on a 10-point scale, 95% CI –0.64 to 3.5; low certainty) (27, 29, 32, 34, 35, 38, 39, 51, 60, 69, 72). Comfort differences for helmet and facemask NIV were small and variable, reflecting challenges with titrating appropriate ventilator settings, interface tolerance, skin injury, or noise. Evidence for other outcomes, including cardiac arrest, length of stay, and duration of noninvasive support, was of mostly very low certainty and did not demonstrate important between-group differences. We examined a number of pre-defined subgroups, which failed to demonstrate credible subgroup effects, including baseline severity of hypoxemia, disease etiology (COVID-19, pneumonia, or mixed), immune status, and clinical setting (ICU vs non-ICU).

Of note, the RENOVATE (20) and SOHO (21) trials were published after completion of the evidence synthesis and EtD) processes for this guideline. RENOVATE is directly relevant to PICO questions 1 and 2, whereas SOHO is relevant to PICO question 1. After review, the panel felt confident that inclusion of the RENOVATE trial to the pooled results would not lead to tangible changes to the pooled estimates, conclusions, or recommendations. More recently, the SOHO trial represents an important contribution to the field of noninvasive respiratory support and demonstrated that HFNC reduced the risk of endotracheal intubation without a clear signal of mortality benefit, in keeping with our evidence synthesis findings.

Justification and Implementation Considerations

The panel determined that the desirable effects of HFNC clearly outweighed the undesirable effects compared with standard oxygen therapy. HFNC reduces the need for intubation with minimal harms. HFNC is easy to implement, well tolerated, and enables patient communication, oral nutrition, and secretion clearance while maintaining comfort. For these reasons and given the consistency of benefit across RCTs and settings, the panel issued a strong recommendation for the use of HFNC as the first-line noninvasive oxygenation strategy in adults with *de-novo* acute hypoxemic respiratory failure of any etiology. However, the panel emphasized that this strong recommendation applies to HFNC compared with standard oxygen therapy. Evidence comparing HFNC and NIV remains limited and of low certainty, and therefore no recommendation was made for this comparison. Selection between HFNC and NIV should be individualized based on patient characteristics, clinician expertise, and institutional resources.

The undesirable effects associated with HFNC were considered trivial or small. Increased oxygen consumption from the oxygen delivery system and occasional prolongation of therapy duration were the main concerns. Interruptions in electrical power in settings without a reliable electricity supply or uninterruptible backup systems may limit the use of NIRS outside the ICU. These disadvantages were offset by the reduction in intubation rates and the potential for shorter ICU stays. During the COVID-19 pandemic, the scalability of HFNC, relative ease of use, and minimal staff burden further supported its widespread adoption. However, data directly comparing the environmental impact, including carbon footprint, of HFNC versus NIV or IMV are limited, and these considerations were weighed alongside clinical benefits during the panel's deliberations.

In contrast, facemask and helmet NIV were judged to offer smaller or more uncertain net benefit. These modalities may reduce the need for intubation and may decrease mortality, but they can cause more discomfort and require specialized expertise to prevent complications or delayed intubation. Facemask NIV can cause patient discomfort, air leaks, and skin injury, while helmet NIV requires specific interfaces and

institutional familiarity that may not be readily available outside selected centers. The use of helmet NIV varies substantially across regions and practice settings, reflecting differences in availability, regulatory approval, device familiarity, and local experience. In addition, multiple helmet designs exist, and performance characteristics—including seal integrity, pressurization capability, noise, and comfort—may differ between devices. These factors should be considered when interpreting trial results and when implementing helmet NIV in clinical practice.

In some patients, NIRS may fail to adequately reduce inspiratory effort, resulting in persistently high transpulmonary pressures and tidal volumes that may increase the risk of lung injury and contribute to treatment failure. This concern has been most extensively described in the context of NIV, particularly when high inspiratory effort combined with positive pressure leads to larger tidal volumes. While similar physiologic considerations may apply to HFNC in patients with persistently elevated respiratory drive, clinical evidence supporting this risk is limited (74). In addition, NIRS may have important implications for other aspects of care, including impaired oral intake and speech, delayed mobilization, patient discomfort, and potential delays in escalation to invasive mechanical ventilation. These considerations highlight the importance of close monitoring, timely reassessment of treatment response, and readiness to escalate support when clinically indicated. These modalities may be appropriate for selected patients or when applied in centers with sufficient expertise and staffing. Given these considerations, the panel provided a conditional recommendation for the use of facemask or helmet NIV over standard oxygen therapy.

Implementation of all NIRS requires attention to monitoring and setting. Patients initiated on HFNC should be closely observed for non-improving or worsening gas exchange, persistent tachypnea, or signs of respiratory muscle fatigue (75). Those requiring high flows or FiO_2 should ideally be managed in a unit capable of close supervision. For any NIRS modality, continuous monitoring is essential to detect early signs of treatment failure. Institutions should establish protocols defining criteria for intubation, escalation pathways, and staff training.

Resource considerations vary across health systems. HFNC requires adequate oxygen infrastructure and disposable interfaces, which may pose challenges in resource-limited settings (76). During periods of high demand, such as the COVID-19 pandemic, oxygen supply constraints can limit widespread use. Nevertheless, economic analyses suggest that HFNC is cost-effective when the reduction in intubation and ICU stay are considered (77). Helmet NIV, though associated with higher upfront equipment costs and training requirements, may reduce resource utilization in centers with established expertise.

Uncertainties and Research Priorities

Several important uncertainties persist regarding the optimal use of noninvasive oxygenation for acute hypoxemic respiratory failure. First, further evidence is needed to determine which patient populations derive the greatest benefit from each strategy. Subgroup analyses to date have not identified consistent effect modifiers, but larger, harmonized datasets could clarify whether specific phenotypes—such as patients with moderate versus severe hypoxemia, high inspiratory effort, inflammatory status, or differing etiologies—respond differently to these interventions (78).

Second, the comparative effectiveness of HFNC versus NIV remains unresolved, as most RCTs have compared each modality separately with standard oxygen therapy. While direct head-to-head RCTs are required to determine whether one approach should be preferred for patient subsets or stages of disease, the comparative effectiveness studies will also be complicated by the experience, biases, and culture of included institutions and regions.

Third, physiologic concerns regarding patient-self-inflicted lung injury during spontaneous breathing under noninvasive support remain inadequately addressed(79). Future RCTs could integrate physiologic and biologic monitoring—such as assessment of inspiratory effort, drive, or inflammatory state—to identify thresholds for safe application and timely transition to invasive ventilation.

Fourth, long-term outcomes, including post-ICU functional recovery, quality of life, and neurocognitive sequelae, have not been well studied. The impact of these interventions on healthcare resource utilization beyond the ICU—such as rehabilitation needs or readmissions—also warrants investigation.

Fifth, research in broader settings, including low- and middle-income countries, is necessary to determine generalizability, cost-effectiveness, and feasibility (80).

Finally, the role of helmet NIV deserves focused evaluation. Although some studies and meta-analyses suggest favorable effects on oxygenation and intubation, effect estimates vary across trials, and much of the early evidence comes from single-center studies conducted in experienced centers. More recent multicenter trials have not consistently demonstrated superiority of helmet over other noninvasive strategies (66). Additional adequately powered, pragmatic trials are needed to confirm reproducibility and clarify which patient populations may derive the greatest benefit.

PICO 2: Acute Hypercapnic Respiratory Failure

Question 2: In adult patients with acute hypercapnic respiratory failure, should we use standard oxygen therapy, HFNC, NIV (via facemask or helmet) or CPAP (via facemask or helmet)?

Recommendations

- **We recommend NIV via facemask as compared to standard oxygen therapy** for adults with acute hypercapnic respiratory failure (*strong recommendation, moderate certainty*) (Figure 3).
  We suggest HFNC as an alternative to NIV **as compared to standard oxygen therapy** for patients with acute hypercapnic respiratory failure and mild acidemia (e.g. pH > 7.25) provided that monitoring and escalation to NIV are promptly available (*conditional recommendation, low certainty*).

Background

Acute or acute on chronic respiratory failure occurs in the presence of ventilatory failure – when the respiratory system is unable to meet ventilatory demand and maintain adequate carbon dioxide clearance – resulting in respiratory acidosis (81, 82) This imbalance may reflect reduced effective alveolar ventilation, increased physiologic dead space, airflow limitation, dynamic hyperinflation, altered respiratory drive, and ventilation-perfusion abnormalities, which together increase the work of breathing and promote respiratory muscle fatigue. If untreated, this process may lead to progressive ventilatory failure. COPD exacerbations are the most common cause of hypercapnic respiratory failure; however, this can also occur in the context of asthma, cardiogenic pulmonary edema, obesity-related hypoventilation, drug-induced hypoventilation, or neuromuscular disorders that impair ventilatory mechanics.

NIV reduces inspiratory effort, improves alveolar ventilation, and corrects acidosis without endotracheal intubation (83) Randomized controlled trials and previous ATS guidelines have established NIV as the standard of care for COPD exacerbations with acidosis, demonstrating reductions in intubation rates and mortality compared with standard oxygen therapy (4, 84). HFNC can provide heated, humidified gas at high flows, which has been shown to reduce anatomical dead space, provide mild increases in positive pressure, lower respiratory rate and work of breathing per minute, improve ciliary function and secretion clearance, and improve patient comfort (85). Recent RCTs have suggested that in certain populations with mild to moderate hypercapnia, HFNC may achieve outcomes comparable to NIV. HFNC may also be used between NIV sessions instead of standard oxygen therapy.

Evidence Summary

We included 43 RCTs (n=5354 patients) evaluating NIRS strategies in patients with hypercapnic respiratory failure (82, 86–124). Most trials enrolled patients with hypercapnic respiratory failure due to COPD (33 RCTs) (82, 86, 88, 92–100, 102–105, 107, 109, 111, 113, 115–119, 121–124), with six in acute cardiogenic pulmonary edema (ACPE) (90, 91, 101, 110, 112) and four with mixed etiologies (87, 106, 114). Participants had moderate hypercapnia (median pH 7.31, mean $PaCO_2$ 65 ± 12 mm Hg), a mean age of 71 years, and 38% were women. Studies were conducted across diverse settings—11 in wards, 10 in emergency departments, 10 in ICUs, 6 in mixed settings, and 6 trials did not report the setting. The network included 23 RCTs comparing NIV with standard oxygen therapy, 12 comparing NIV with HFNC, 3 comparing NIV with CPAP, 3 comparing HFNC with standard oxygen therapy, 1 comparing CPAP with standard oxygen therapy, and 1 comparing helmet versus facemask NIV. Given limited evidence, analyses did not distinguish between helmet versus facemask NIV and the panel only made recommendations on NIV via facemask for this PICO question. Of note, the majority of the HFNC studies were conducted in patient with mild hypercapnia and the majority of the CPAP studies are older and included mixed populations or predominantly patients with acute cardiogenic pulmonary edema.

Pooled analysis demonstrates that HFNC reduces hospital mortality (RR 0.39, 95% CI 0.17 to 0.87; high certainty) while NIV (RR 0.47, 95% CI 0.34 to 0.65; moderate certainty) and CPAP (RR 0.33, 95% CI 0.12 to 0.94; moderate-certainty) probably reduce mortality compared to standard oxygen therapy. The effect of NIV versus HFNC on mortality was uncertain (RR 1.21, 95% CI 0.56 to 2.60; very low certainty). NIV (RR 0.43, 95% CI 0.32 to 0.56; moderate certainty), CPAP (RR 0.38, 95% CI 0.17 to0.88; moderate certainty), and HFNC (RR 0.38, 95% CI 0.24 to 0.59; moderate certainty) probably decrease the need for intubation compared to standard oxygen therapy. The relative effect on intubation between NIV and HFNC was uncertain (RR 1.14, 95% CI 0.77 to1.68; very low certainty).

Compared with standard oxygen therapy, NIV (MD 1.47 days fewer, 95% CI 0.24 to 2.70 days fewer; moderate certainty) and HFNC (MD 1.83 days fewer, 95% CI 0.04 to 3.63 days fewer; moderate certainty) probably shorten hospital length of stay while CPAP may have little or no effect on hospital length of stay (MD 0.03 days more, 95% CI 3.33 days fewer to 3.39 days more; low certainty). However, notably, while this pooled analysis was across severities of hypercapnia and acidemia, the majority of the trials with HFNC were conducted only in patients with mild hypercapnia and without significant acidemia. All three modalities may improve gas exchange compared with standard oxygen therapy, reducing $PaCO_2$ by - 3.26 mm Hg (95% CI –5.55 to –0.97) for

NIV, –5.25 mm Hg (95% CI –10.69 to 0.19) for CPAP, and –3.31 mm Hg (95% CI –6.37 to –0.24) for HFNC (all low certainty). NIV (RR 7.26, 95% CI 2.50 to 21.08; moderate certainty) and HFNC (RR 3.47, 95% CI 0.84 to14.31; moderate certainty) probably improve treatment tolerance, whereas CPAP may improve tolerance (RR 4.78, 95% CI 1.50 to15.23; low certainty), compared to standard oxygen therapy.

Evidence regarding serious adverse events—including cardiac arrest, aspiration, or interface-related complications—was limited and of very low certainty. No signal indicated excess harm with any modality. The panel prospectively identified four subgroups for consideration: (1) location of care (emergency department, hospital ward, step-down unit, or ICU); (2) underlying etiology (COPD vs. non-COPD); (3) asthma; and (4) severity of hypercapnia. There were no credible subgroup effects.

Justification and Implementation Considerations

Moderate certainty evidence demonstrates consistent reductions in mortality and intubation with NIV compared with standard oxygen therapy. In this group, NIV corrects acidosis, decreases work of breathing, and improves survival, reflecting both physiologic advantages and extensive clinical experience. Evidence supporting HFNC or CPAP in severe hypercapnia is indirect and of low certainty. Accordingly, the panel reaffirmed a strong recommendation for early NIV initiation in all patients with hypercapnic respiratory failure.

For patients with mild hypercapnia or acidemia (pH ≥ 7.25), evidence suggests that both NIV and HFNC probably reduce mortality and the need for intubation to a similar extent. Although HFNC is often perceived as more comfortable, pooled analyses did not confirm a meaningful difference, and the ventilatory unloading achieved with NIV may itself improve comfort and dyspnea. An additional consideration is the underlying mechanism of hypercapnic respiratory failure. In settings where hypercapnia is potentially rapidly reversible (e.g., COPD exacerbations or transient opioid-related hypoventilation), noninvasive strategies such as HFNC may be more appropriate. In contrast, when the mechanism of hypercapnia is not rapidly reversible (e.g. obesity hypoventilation or neuromuscular disease), these approaches may be less effective. Accordingly, application of this recommendation should be guided by the etiologies represented in the trials informing the evidence base.

Notably, while ACPE was represented in the included trials within the hypercapnic respiratory failure domain, it was not evaluated as a standalone clinical entity with a dedicated PICO question. The physiology and optimal noninvasive strategy for acute cardiogenic pulmonary edema — particularly the well-established and distinct role of CPAP in this population — may differ substantially from other causes of hypercapnic respiratory failure. Clinicians should interpret these recommendations in the context of

the predominant trial populations (primarily COPD exacerbation) and exercise independent clinical judgment when applying these recommendations to patients with ACPE.

The trials evaluating CPAP in acute hypercapnic respiratory failure are largely older studies with methodological limitations, often enrolling heterogeneous patient populations. These limitations reduce confidence in the applicability of their findings to current practice. CPAP is also not commonly used in current practice for hypercapnic respiratory failure, particularly in patients with COPD exacerbation. Given these limitations, the panel decided not to make a recommendation for or against CPAP.

The panel recognized that most HFNC studies enrolled patients with mild to moderate disease severity, and often permitted crossover to NIV, potentially biasing results toward an apparent benefit. Therefore, the panel interpreted findings according to disease severity and with a note for escalation to NIV as needed. In this specific population, HFNC and NIV showed similar desirable effects, whereas in patients with more severe acidosis, NIV remains the preferred first-line therapy, reflecting both its physiological advantages and higher-certainty supporting evidence. Study heterogeneity across emergency departments, wards, and ICUs, as well as limited representation of specific subgroups such as cardiogenic pulmonary edema or obesity hypoventilation, further reduced confidence in generalizability. Across studies, one-third of patients initially treated with HFNC required escalation to NIV, underscoring the need for close monitoring and predefined escalation criteria.

Optimal HFNC parameters for hypercapnic failure remain uncertain. Flow rates in the range of 30–40 L/min have been suggested based on physiologic rationale and limited clinical data; however, robust comparative evidence is lacking (85). The potential impact of higher flow rates on dynamic hyperinflation, CO_2 retention, or patient effort remains incompletely understood. Accordingly, flow should be individualized based on clinical response, and further studies are needed to define optimal HFNC dosing strategies in hypercapnic respiratory failure (125). Accordingly, the panel discussions highlighted the importance of also paying attention to the flows employed during HFNC therapy, since this might prove clinically relevant.

Implementation should reflect expertise, infrastructure, and patient acuity. NIV requires trained staff, patient coaching, continuous monitoring, and is best delivered in ICUs or intermediate-care units where rapid intubation can be performed if needed. HFNC is now increasingly used in emergency and ward settings. The panel highlighted that patients with acute hypercapnia receiving HFNC therapy still necessitate strict vigilant observation, clear escalation pathways, and ready availability of NIV. Resource considerations may influence feasibility. NIV can be implemented using reusable ventilators and typically single-patient-use interfaces; in some resource-constrained

settings, certain components may be reused according to local infection prevention policies and availability. In contrast, HFNC depends on disposable circuits, which may constrain its use in low-resource environments.

Uncertainties and Research Priorities

Comparative studies directly evaluating HFNC and NIV in patients with more severe hypercapnia (pH < 7.25) are needed, as existing RCTs have primarily enrolled patients with moderate acidosis, leaving uncertainty about the safety and effectiveness of HFNC in more severe disease. Future studies should also evaluate protocolized escalation from HFNC to NIV and its effects on outcomes and resource use. Most existing HFNC RCTs allowed crossover to NIV, which may have influenced apparent effectiveness and made it difficult to isolate the true effect of each therapy, and might reflect the benefit of combined therapy.

Further investigation is needed to determine the influence of interface design on clinical outcomes, including studies comparing helmet and facemask NIV in hypercapnic respiratory failure, as well as emerging interface technologies such as asymmetrical high-flow cannulas. These studies should assess not only gas exchange and treatment success but also adverse events, which could not be adequately evaluated with the available evidence and warrant further investigation. Research should also clarify the role of NIV and HFNC in hypercapnia from non-COPD etiologies, including obesity hypoventilation, opioid toxicity, neuromuscular disease, and cardiogenic pulmonary edema, as these populations are underrepresented in current evidence.

Finally, the panel highlighted the need for physiologic and implementation research to define optimal HFNC settings in hypercapnia, including appropriate flow ranges, FiO_2 titration, and cannula design. Future research should also evaluate the feasibility, oxygen consumption, and sustainability of these interventions in resource-limited and low- and middle-income settings, where access to high oxygen flow, uninterrupted power supply in non-ICU wards, clean water, and disposables may be constrained.

PICO 3: Preoxygenation during Endotracheal Intubation

Question 3: In adult patients who are undergoing endotracheal intubation, should we use HFNC, NIV, or standard oxygen therapy to improve outcomes during the procedure?

Recommendations

- **We recommend using HFNC or NIV via facemask as compared to standard oxygen therapy** for preoxygenation in adults with acute respiratory failure undergoing endotracheal intubation (*strong recommendation, moderate certainty*) (Figure 4).
- **We make no recommendation for or against HFNC compared with NIV** for preoxygenation in adults with acute respiratory failure undergoing endotracheal intubation.

Background

Endotracheal intubation is a high-risk procedure associated with high rates of complications including severe hypoxemia, cardiac arrest, and mortality (126) . The goal of preoxygenation is to boost the oxygenation reserve, which increases the safe apnea time, while the patient is undergoing intubation and thereby reduce hypoxemia and other adverse events (127, 128). Traditional preoxygenation strategies, such as facemask or bag-valve-mask oxygenation, may be insufficient to maintain oxygenation in acutely ill patients with hypoxemia, which has led to several RCTs exploring alternate preoxygenation strategies for patients with respiratory failure requiring intubation.

While numerous RCTs have compared NIV or HFNC individually with standard oxygen therapy, few have directly evaluated these modalities compared to each other or in combination. Following the recent publication of the PREOXI RCT (134), the panel prioritized this PICO question to update clinical guidance on peri-intubation oxygenation.

Evidence Summary

We included 15 RCTs (n=3,420) examining noninvasive respiratory strategies in patients undergoing intubation (129–143). The network compared three primary oxygenation strategies used for preoxygenation immediately before intubation: NIV (predominantly bilevel positive-pressure ventilation via facemask), HFNC, and standard oxygen therapy. Facemask, bag-valve-mask, and non-rebreather oxygenation were

grouped under standard oxygen therapy due to physiological and pragmatic equivalence. Seven RCTs compared HFNC with standard oxygen therapy, four compared NIV with standard oxygen therapy, two compared NIV directly with HFNC, and one evaluated a combined NIV + HFNC strategy versus either modality alone. Most studies enrolled critically ill adults requiring endotracheal intubation in the ICU or emergency department, with three additional trials in surgical populations (two emergency and one elective). The median age across studies ranged from 40 to 78 years; 40% of participants were women, and the mean body mass index (BMI) ranged between 23 and 30 kg/m². Approximately one-quarter of patients had chronic lung disease.

Pooled analysis demonstrated that NIV (RR 0.51, 95% CI 0.39 to 0.65; high certainty) and HFNC (RR 0.69, 95% CI 0.54 to 0.88; high certainty) decreased the risk of peri-intubation hypoxemia compared to standard oxygen therapy. When compared head-to-head, NIV probably reduced hypoxemia compared to HFNC (RR 0.73, 95% CI 0.55 to 0.98; moderate certainty). There was little to no effect on mortality when comparing NIV (RR 0.94; 95% CI 0.83 to 1.08, low certainty) or HFNC (RR 0.86; 95% CI 0.73 to 1.01, low-certainty) to standard oxygen therapy. There was an uncertain effect regarding first-pass intubation success comparing between modalities (all very low certainty). Serious adverse events—including aspiration, cardiac arrest, and hemodynamic instability—were probably less frequent with NIV compared to standard oxygen therapy (RR 0.30, 95% CI 0.12 to 0.77; moderate certainty), whereas HFNC may have little or no effect on adverse effects compared with standard oxygen therapy (RR 0.95, 95% CI 0.60 to 1.51; low certainty).

The panel prospectively identified patients who received neuromuscular blockade versus those that did not during intubation as a key subgroup. This subgroup was chosen because differences in apnea duration, airway control, and oxygen consumption between paralyzed and non-paralyzed patients could influence the effectiveness of preoxygenation strategies. No credible subgroup effects were observed comparing paralyzed versus not paralyzed patients on peri-intubation hypoxemia.

Justification and Implementation Considerations

Peri-intubation hypoxemia is a common and clinically important event in critically ill adults, given its association with cardiac arrest and hemodynamic instability. The consistent reduction in hypoxemia across studies using either NIV or HFNC was therefore judged to be a meaningful and desirable effect, even in the absence of mortality or first-pass success benefits.

The relative effects of NIV and HFNC are uncertain. The PREOXI trial compared NIV with standard oxygen/bag mask ventilation for preoxygenation of patients undergoing

endotracheal intubation. Despite this being the largest study to date; its exclusion of patients already receiving NIV and its reassignment of patients on HFNC to other modalities is not aligned with real-world ICU practice, in particular where HFNC is widely used in patients with acute hypoxemic respiratory failure and keeping this device in place once the decision to intubate is made might be pragmatic.

The panel also discussed emerging combined or sequential strategies (e.g., NIV for preoxygenation followed by continued HFNC during laryngoscopy). Such approaches may theoretically optimize alveolar recruitment and prolong apneic oxygenation, though their efficacy remains uncertain and warrants further investigation.

Implementation feasibility was a central consideration. Both NIV and HFNC require specialized equipment, adequate oxygen supply, and trained personnel capable of rapid setup and monitoring. These requirements can pose challenges during emergent or time-sensitive intubations, particularly in resource-limited environments. Importantly, initiation of NIV or HFNC should not delay necessary or emergent endotracheal intubation. In patients with impending respiratory arrest, severe hemodynamic instability, or inability to protect the airway, prompt intubation remains the priority. Noninvasive preoxygenation strategies are most appropriate when there is sufficient time and clinical stability to allow safe application without compromising timely airway management. NIV necessitates appropriate mask fitting and pressure titration, while HFNC relies on high-flow oxygen infrastructure and heated humidification. Because most trials were conducted in high-resource centers, the applicability of findings to low- and middle-income or rural settings remains uncertain.

Both modalities incur moderate costs, which varies by institution—HFNC may be less expensive where infrastructure is already installed; NIV may require greater initial investment in equipment and interfaces. In facilities equipped with current-generation ICU ventilators capable of delivering IMV, NIV, and HFNC on the same platform, implementation may be simplified, as clinicians can transition directly between modalities without changing devices. However, this capability may not be available in all settings, particularly in institutions using older ventilator systems or with limited infrastructure.

Equity and access were additional concerns. Broad recommendation of noninvasive oxygenation could widen disparities if access to devices, oxygen supply, or trained staff is uneven. Successful implementation will depend on adapting protocols to local context, ensuring adequate staff training, and planning infrastructure to support safe and equitable use.

Uncertainties and Research Priorities

The existing evidence comparing NIV and HFNC is predominantly indirect, and there is a need for large, adequately powered randomized trials directly comparing NIV and HFNC in patients undergoing intubation for acute respiratory failure. Future trials should account for variation in pre-intubation care, including patients who proceed directly to intubation after failure of NIRS without additional preoxygenation strategies, to better reflect real-world practice across different healthcare settings.

Further investigation is warranted examining combination and sequential approaches, such as NIV for preoxygenation followed by HFNC for apneic oxygenation during laryngoscopy, which may optimize both recruitment and continuous oxygen delivery. Studies should also assess the effect of these strategies on patient-important outcomes, including peri-intubation cardiac arrest and long-term neurological sequelae. We also need to standardize definitions of hypoxemia in the peri-intubation setting and more granular data about adverse events, including aspiration and cardiac arrest.

Additional research is needed to evaluate the implementation and cost-effectiveness of HFNC and NIV across diverse clinical environments, particularly in low- and middle-income countries where resources may limit feasibility. Studies should also explore how patient-level factors—such as severity of respiratory failure, obesity, and comorbidities—modify treatment response, to support risk-stratified and individualized approaches to peri-intubation oxygenation. Finally, future investigations should examine the impact of standardized preoxygenation and intubation protocols, including device and settings, on clinical outcomes and resource utilization.

PICO 4: Post-Extubation Respiratory Support

In adult patients who are extubated in the intensive care unit after critical illness, should we use HFNC, NIV (either through a facemask or helmet interface), CPAP (either through a facemask or helmet interface) or standard oxygen therapy to improve outcomes?

Recommendations

- **We suggest using HFNC or NIV via facemask as compared to standard oxygen therapy** in patients extubated in the intensive care unit after critical illness (*conditional recommendation, moderate certainty*) (Figure 5).

- **We suggest using NIV via facemask as compared to standard oxygen therapy or HFNC** in patients extubated in the intensive care unit after critical illness at high-risk of extubation failure (e.g., age >65 years, obesity, hypercapnia, prolonged mechanical ventilation, or severe illness, among others) (*conditional recommendation, moderate certainty*).

Remark: Those patients who are at very low risk (e.g. oxygenating well, post operative from non-thoracic or abdominal surgery, no previous respiratory or cardiac disease, short duration of invasive mechanical ventilation, good cough and minimal secretions) could be extubated to standard low flow oxygen or even room air.

Background

Extubation is a critical transition in the care of mechanically ventilated patients. Despite clinical stability at the time of extubation, 10–20% of patients require reintubation, which is associated with increased mortality, prolonged ICU stay, and complications such as ventilator-associated events. NIRS strategies have been studied in several RCTs for preventing and treating post-extubation respiratory failure and decreasing the need for reintubation, particularly in high-risk patients (144–147) . However, the optimal strategy remains unclear, especially across different patient populations and practice settings.

Evidence Summary

We included 53 RCTs (n=5,304) in the evidence summary evaluating post-extubation NIRS (148–200). Nearly half of the trials were conducted in Europe. Participant mean ages ranged from 34 to 77 years; 63 % were men. Most studies (44 trials, 83%) assessed prophylactic use immediately after planned extubation, whereas only 9 (17%) examined rescue use after post-extubation respiratory failure. Thirty-six percent enrolled mixed medical–surgical ICU populations, and the remainder focused on surgical or medical cohorts (predominantly COPD or sepsis). Several trials specifically targeted high-risk groups such as those with obesity, chronic hypercapnia, or prolonged mechanical ventilation. Across these studies, 35 RCTs compared NIV with standard oxygen therapy, 17 compared HFNC with standard oxygen therapy, 9 directly compared HFNC and NIV, and 2 evaluated alternating or combined HFNC–NIV strategies. NIV was the predominant strategy used in these studies.

Based on pooled analysis, we found that NIV (RR 0.75, 95% CI 0.63 to 0.88; moderate certainty) probably reduced re-intubation while HFNC (RR 0.80, 95% CI 0.64 to 1.00; low certainty) may reduce re-intubation compared with standard oxygen therapy. The effect of NIV versus HFNC on re-intubation was uncertain (RR 0.93, 95% CI 0.76 to 1.15; very low certainty). Both HFNC (RR 0.87, 95% CI 0.71 to 1.06, low certainty) and NIV (RR 0.88, 95% CI 0.74 to 1.04, low certainty) may reduce short-term mortality as

compared to standard oxygen therapy with possibly no difference between the two modalities (RR 1.01, 95% CI 0.85 to 1.20; low certainty).

HFNC may reduce the need for tracheostomy (RR 0.35, 95% CI 0.15 to 0.84; low certainty) with possibly no effect on hospital length of stay (MD 0.51 days fewer, 95% CI 0.17 to 0.85 days fewer, low certainty) compared to standard oxygen therapy, NIV probably increases discomfort compared with standard oxygen therapy (risk difference [RD] +14.5 %, 95% CI +7.5 to +21.4 %, moderate certainty), and HFNC probably reduced discomfort compared with NIV (RD –12.2 %, 95% CI –17.8 to –6.6 %; moderate certainty). The impact of HFNC and NIV on adverse events, compared with standard oxygen therapy, was uncertain.

Subgroup analyses suggested that baseline risk and timing of therapy modified treatment effects. Among high-risk patients (Table 1), NIV was more effective than HFNC at preventing reintubation and post-extubation respiratory failure (subgroup interaction p = 0.006). HFNC reduced re-intubation when used prophylactically compared to standard oxygen therapy; but when HFNC was used as rescue therapy, it may increase the risk of reintubation compared to standard oxygen therapy (subgroup interaction p= 0.001). HFNC increased re-intubation risk versus NIV in rescue use but not when used prophylactically (subgroup interaction p=0.03). These subgroups effects were judged to be of low to moderate credibility. No subgroup effects were observed for other outcomes of interest.

Justification and Implementation Considerations

Discussion focused on the established role of NIV for high-risk patients and the emerging evidence supporting HFNC in broader post-extubation populations. Both strategies reduced re-intubation compared with standard oxygen therapy when used prophylactically, but direct comparisons were few and underpowered, yielding low certainty for relative effectiveness. Across studies, NIV appeared more effective in high-risk groups, whereas HFNC provided similar benefit to NIV in lower-risk patients with greater comfort and tolerance. Subgroup analyses also found that NIV demonstrated greater benefit in preventing re-intubation in patients with hypercapnia post extubation. This supports preferential use of NIV in high-risk patients, especially those with hypercapnia.

Most evidence is derived from prophylactic use immediately after extubation, where both NIV and HFNC reduced re-intubation. Evidence for rescue therapy after the onset of respiratory failure was sparse and less consistent, particularly for HFNC, and therefore these recommendations should not apply to the use of these strategies as rescue therapies in patients with respiratory failure following extubation. The panel also considered alternating or sequential HFNC–NIV strategies, but data from only two small studies were insufficient to support recommendations. However, maintaining NIV alone

for prolonged durations post extubation was deemed challenging and rarely achieved in the real-world setting, leading the panel to note that NIV with HFNC breaks might be an optimal strategy for implementation.

Implementation feasibility and resource use were key considerations. NIV can often be delivered using existing ventilators but requires staff expertise, close monitoring, and patient cooperation. HFNC demands continuous high-flow oxygen and single-use heated circuits, increasing demand on oxygen supply and cost but offering simpler setup and improved patient comfort. Relative burden depends on institutional context—HFNC may be less costly where systems are already installed, whereas NIV may be more practical in units equipped for ventilatory support. In resource-limited settings, both modalities may strain oxygen supply and staffing, underscoring the need for context-specific implementation.

Equity concerns were highlighted. Wider recommendation of HFNC or NIV could exacerbate disparities between well-resourced and under-resourced hospitals if access to devices, reliable oxygen, or trained staff is uneven. Equitable implementation will require locally adapted protocols, training, and infrastructure investment to ensure safe and consistent use. Although the recommendation applies broadly, implementation should reflect patient risk profile and local resource availability, and universal application in all extubated patients may not be necessary in every setting

In summary, both HFNC and NIV reduce post-extubation re-intubation without increasing adverse events. NIV remains preferred for high-risk patients, while HFNC is an acceptable alternative for lower-risk patients, or those where interface tolerance might be a concern. Combination strategies cannot yet be recommended due to insufficient evidence. Modality selection should be individualized based on patient risk, tolerance, clinician expertise, and resource availability.

Uncertainties and Research Priorities

The panel identified several important gaps in the current evidence base that should guide future research on NIRS following extubation. Although both HFNC and NIV reduce re-intubation compared with conventional oxygen therapy, uncertainty remains regarding their optimal application, duration of use post extubation, patient selection, and sequencing.

Future trials should define and consistently apply standardized criteria for high-risk patients—including age, illness severity, duration of mechanical ventilation, obesity, airway compromise, secretion burden, and chronic cardiopulmonary comorbidities—to enable meaningful comparisons and risk stratification. The substantial heterogeneity in

how “high-risk” populations were defined across existing studies limited the ability to tailor recommendations to specific subgroups.

Well-designed randomized controlled trials are needed to directly compare HFNC and NIV across both prophylactic and rescue applications, with clearly defined thresholds for initiation, duration, and escalation to invasive ventilation. Research should also determine whether the preventive benefits observed in high-risk patients translate into improved long-term outcomes, including mortality, functional recovery, and health-related quality of life.

The potential value of combination or sequential therapy—for example, alternating or transitioning between HFNC and NIV based on patient tolerance and response—should be assessed in pragmatic, protocolized trials. Existing data from two small studies were insufficient to determine whether such strategies provide additive benefit or improved comfort and adherence.

Finally, implementation and feasibility studies are needed to guide safe, cost-effective application across diverse care settings. Comparative evaluations should address staffing requirements, workflow efficiency, and cost-effectiveness, particularly in resource-limited environments where access to equipment, oxygen infrastructure, and respiratory therapy support varies widely. Evaluations of low-cost or simplified HFNC systems and reusable interfaces could help improve accessibility in low- and middle-income settings.

Discussion

Noninvasive respiratory support strategies consistently provide moderate clinical benefit compared with standard oxygen therapy across a range of acute respiratory failure syndromes. Their primary advantage lies in reducing the need for invasive mechanical ventilation and peri-intubation complications rather than large effects on mortality. These benefits are clinically meaningful yet depend on appropriate expertise, close monitoring, and systems capable of timely escalation. In addition, it is worth noting that a reduction in the need for invasive mechanical ventilation could translate to a mortality benefit in low- and middle-income country settings where safe mechanical ventilation is often unavailable for most patients and associated with several complications, though adequate resources to safely implement these strategies are also critical components when examining effectiveness (80). Certainty of evidence was limited by heterogeneity in study population, variability in intervention protocols and frequent crossover between different modalities within individual RCTs. Most studies were performed in high-resource settings under close supervision, which constrained generalizability. As a result of these limitations, several of the recommendations on this guideline are conditional rather than strong.

Feasibility emerged as a key determinant of overall confidence in the interventions. HFNC requires reliable oxygen infrastructure, heated humidification, and disposable circuits, which may strain oxygen supply and increase cost, particularly in resource-limited settings. Nonetheless, HFNC could actually use *less* oxygen than standard oxygen, as evidenced by a study in East Africa in children (201). NIV requires experienced clinicians for mask fitting, ventilatory settings titration, and continuous monitoring to detect intolerance or deterioration. Both interventions may increase staff workload and prolong ICU or step-down unit stay, particularly when escalation decisions are delayed. These practical realities, rather than uncertainty in physiologic rationale, contributed to the predominance of conditional recommendations in this guideline. Equity considerations were an important component in formulating these recommendations. Access to NIRS varies widely across hospitals and regions, and universal implementation without adaptation to local resources risks exacerbating disparities. Sustainable application requires context-specific planning, including use of reusable equipment and standardized escalation and weaning protocols. Institutions should ensure consistent monitoring and early recognition of NIRS failure to prevent harm from delayed intubation. The balance of benefits and harms favors NIRS strategies in most scenarios. Adverse effects—such as interface discomfort, skin injury, and potential delay in escalation—are infrequent and were generally outweighed by the benefits of reduced intubation and improved patient comfort.

These recommendations align closely with and extend prior international guidance. The 2017 ATS/ERS guideline and GOLD 2024 report reaffirm NIV as the standard of care for acute hypercapnic respiratory failure, with strong evidence for reduced mortality and intubation among patients with COPD exacerbations. Notably, the 2017 ATS/ERS guideline made no recommendation for or against NIV in de novo acute hypoxemic respiratory failure due to limited and uncertain evidence at that time. In contrast, the current guideline reflects the accumulation of newer randomized trials and network meta-analyses, which now support a strong recommendation for HFNC and a conditional recommendation for NIV in this population. Similarly, the ESICM High-Flow Oxygen Statement and SCCM Airway Management Guidelines support the use of HFNC or NIV for preoxygenation during intubation, depending on local expertise and patient factors. The current guideline integrates and updates these domains across the full trajectory of acute respiratory failure -from initial presentation through extubation and recovery.

This work has several strengths. All four PICO questions were informed by comprehensive network meta-analyses, enabling simultaneous comparison of multiple interventions within a unified analytical framework. The panel adhered to GRADE methodology and included broad international representation across clinicians, respiratory therapists, methodologists, and implementation experts practicing in varied health systems. A patient representative contributed to reviewing recommendations and assessing their acceptability and feasibility; however, engagement occurred later in the process rather than from the outset, which represents a limitation. Additional limitations include limited data from low- and middle-income countries, where infrastructure and staffing realities differ substantially. Despite these constraints, the guideline provides a comprehensive, evidence-based framework to guide the safe, effective, and equitable use of NIRS across diverse care environments.

The effectiveness of these recommendations depends more on consistent and physiological bedside practice than on device choice. Institutional efforts should focus on ensuring staff proficiency, streamlined workflows, and well-defined escalation pathways rather than rapid adoption of new technologies. Early recognition of treatment failure, defined escalation thresholds, and readiness for timely intubation remain essential to patient safety. Monitoring frameworks need to be more clearly defined and should include frequent assessment of gas exchange, work of breathing, and comfort; structured documentation of therapy adjustments; and routine and protocolized evaluation for weaning. In lower-resource settings, pragmatic implementation may require a phased introduction of NIRS, prioritizing deployment in areas with trained personnel, and sufficient monitoring capacity to ensure safety and effectiveness.

In summary, NIRS modalities confer moderate, reproducible benefits in improving patients' outcomes but are constrained by feasibility, cost, and infrastructure requirements that vary widely across care environments. The conditional nature of several recommendations reflects these real-world challenges rather than uncertainty about the physiological benefits. Future research should focus on refining patient selection, defining standardized monitoring and escalation criteria, and evaluating combined or sequential use of HFNC and NIV. Implementation studies addressing cost-effectiveness, oxygen utilization, and workforce implications will be crucial to ensuring equitable and sustainable adoption of NIRS worldwide.

Conclusion

Noninvasive respiratory support provides consistent, moderate benefit across the spectrum of acute respiratory failure. Compared with standard oxygen therapy, these modalities reduce the need for invasive mechanical ventilation, improve comfort, and may modestly reduce mortality in selected populations. These benefits are clinically meaningful but context-dependent, and their impact in practice depends on timely initiation, skilled personnel, and readiness to escalate care when failure occurs.

These recommendations establish NIRS as an essential component of evidence-based care for acute respiratory failure, consistent with prior international guidelines from the American Thoracic Society, European Respiratory Society, European Society of Intensive Care Medicine, and the Society of Critical Care Medicine. Together, these recommendations emphasize that the success of NIRS depends on appropriate patient selection, careful monitoring, and defined escalation thresholds rather than a single preferred device or interface.

Editor's note
The American Thoracic Society's Quality Improvement and Implementation Committee reviewed the guideline recommendations for performance measure development suitability. The NIV for acute hypercapnic respiratory failure clinical recommendation was deemed potentially appropriate for performance measure development.

Subcommittee
This official clinical practice guideline was prepared by an *ad hoc* subcommittee of the ATS Assembly on Critical Care.

Members of the subcommittee are as follows:

Bruno L. Ferreyro, M.D., Ph.D. (*Co-Chair*)
Neha N. Goel, M.D., M.S.C.R. (*Co-Chair*)
Federico Angriman, M.D., M.Sc.*
Leticia Kawano Dourado, M.D., Ph.D.*
Matthew Drake, M.D., Ph.D.*
Tammy L. Eaton, Ph.D., M.Sc.*
Cheryl L. Esbrook, O.T.R./L.*
Jean-Pierre Frat, M.D., Ph.D.*
Domenico L. Grieco, M.D.*
Collin Homer-Bouthiette, M.D.†
William LeTourneau, M.A., R.R.T.*
Kimberley Lewis, M.D., M.Sc.†

Jarrod Mosier, M.D.*
Laveena Munshi, M.D., M.Sc.*
Bhakti K. Patel, M.D.*
Tyler Pitre, M.D. Ph.D.†
Nida Qadir, M.D.*
Jason Rissman‡
Elisabeth Riviello, M.D., M.P.H.*
Oriol Roca, M.D., Ph.D.*
Bram Rochwerg, M.D., M.Sc.§
Theogene Twagirumugabe, M.D., Ph.D.*
Kelly C. Vranas, M.D., M.C.R.*

*Panel member.
†Methodologist.
‡Patient representative who provided critical input on patient-centered outcomes, feasibility, and acceptability of the recommendations.
§Lead methodologist.

Conflicts of interest

N.N.G. received research support from NIH/NHLBI. B.L.F. served as a speaker for University of Toronto. L.K.D. received research support from Brazilian Ministry of Health and Fisher & Paykel. M.D. served on an advisory committee for AstraZeneca, GlaxoSmithKline, Merck, Sanofi, Trevi; served as a consultant for AstraZeneca, GlaxoSmithKline; served as a speaker for AstraZeneca, Chiesi, GlaxoSmithKline, Merck, Regeneron, Trevi, UpToDate; received research support from NIH, Pacific Northwest Biomedical Innovation Co-laboratory. J.P.F. served on an advisory committee for SOS oxygene; served as a speaker for Fisher & Paykel; received travel support from Fisher & Paykel, SOS oxygene; received research support from Fisher & Paykel, Fondation du Souffle, SOS oxygene. D.L.G. served as a speaker for Draeger, Fisher and Paykel, General Electric, Nihon Kohden; received travel support from Fisher & Paykel; received research support from Fisher & Paykel, General Electric. W.L.T. served as a speaker and received travel support from American Association for Respiratory Care; received royalties from Medbridge. J.M. holds a patent for virtual reality environment adapted to model the mammalian airway for intubation and airway management; served as national course director for Airway Management Education Center; received travel support from Fisher & Paykel; received research support from NHLBI. B.K.P. served on an advisory committee for Getinge; received honoraria from Merck and Chest Foundation; received research support from NIH/NHLBI. E.R. served as a board member of Global Critical Care Consortium; served on a data safety monitoring board for STARS trial; served as a speaker for University of Pennsylvania; received research support from Butterfly Ultrasound, Fisher & Paykel, Wellcome Trust. O.R. holds stock in Tesai Care SL; served as a consultant for Getinge, Telesair, Hamilton Medical AG; served on a data safety monitoring board for Confidence trial,

Overcool trial; served as a speaker for Fisher & Paykel, Hamilton Medical AG, Medtronic; received research support from European Society of Intensive Care Medicine, Hamilton Medical AG, Timpel. T.T. received research support from Fisher & Paykel and Wellcome Trust. T.P., K.L., C.H.B., F.A., T.L.E., C.L.E., N.Q., K.C.V., L.M., B.R. reported no commercial or relevant non-commercial interests from ineligible companies.

References

1. Bellani G, Laffey JG, Pham T, Fan E, Brochard L, Esteban A, *et al.* Epidemiology, Patterns of Care, and Mortality for Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries. *JAMA* 2016;315:788–800.

2. Munshi L, Mancebo J, Brochard LJ. Noninvasive Respiratory Support for Adults with Acute Respiratory Failure. *N Engl J Med* 2022;387:1688–1698.

3. Rochwerg B, Einav S, Chaudhuri D, Mancebo J, Mauri T, Helviz Y, *et al.* The role for high flow nasal cannula as a respiratory support strategy in adults: a clinical practice guideline. *Intensiv Care Med* 2020;46:2226–2237.

4. Rochwerg B, Brochard L, Elliott MW, Hess D, Hill NS, Nava S, *et al.* Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure. *European Respiratory Journal* 2017;50:.

5. Oczkowski S, Ergan B, Bos L, Chatwin M, Ferrer M, Gregoretti C, *et al.* ERS clinical practice guidelines: high-flow nasal cannula in acute respiratory failure. *Eur Respir J* 2022;59:2101574.

6. Grasselli G, Calfee CS, Camporota L, Poole D, Amato MBP, Antonelli M, *et al.* ESICM guidelines on acute respiratory distress syndrome: definition, phenotyping and respiratory support strategies. *Intensiv Care Med* 2023;49:727–759.

7. Guyatt GH, Oxman AD, Schünemann HJ, Tugwell P, Knottnerus A. GRADE guidelines: A new series of articles in the Journal of Clinical Epidemiology. *J Clin Epidemiology* 2011;64:380–382.

8. Rochwerg B, Alhazzani W, Jaeschke R. Clinical meaning of the GRADE rules. *Intensiv Care Med* 2014;40:877–9.

9. Brignardello-Petersen R, Izcovich A, Rochwerg B, Florez ID, Hazlewood G, Alhazanni W, *et al.* GRADE approach to drawing conclusions from a network meta-analysis using a partially contextualised framework. *BMJ* 2020;371:m3907.

10. Puhan MA, Schünemann HJ, Murad MH, Li T, Brignardello-Petersen R, Singh JA, *et al.* A GRADE Working Group approach for rating the quality of treatment effect estimates from network meta-analysis. *BMJ : Br Méd J* 2014;349:g5630.

11. Brignardello-Petersen R, Mustafa RA, Siemieniuk RAC, Murad MH, Agoritsas T, Izcovich A, *et al.* GRADE approach to rate the certainty from a network meta-analysis: addressing incoherence. *J Clin Epidemiology* 2019;108:77–85.

12. American Thoracic Society. Policy for management of financial conflicts of interest in the development of ATS Clinical Practice Guidelines. 2015;at <https://www.thoracic.org/statements/document-development/resources/cpg-specific-coi-policy.pdf>.

13. Guyatt GH, Oxman AD, Kunz R, Atkins D, Brozek J, Vist G, *et al.* GRADE guidelines: 2. Framing the question and deciding on important outcomes. *J Clin Epidemiology* 2011;64:395–400.

14. Needham DM, Sepulveda KA, Dinglas VD, Chessare CM, Friedman LA, O. 3rd Bingham C, *et al.* Core Outcome Measures for Clinical Research in Acute Respiratory Failure Survivors. An International Modified Delphi Consensus Study. *Am J Respir Crit Care Med* 2017;196:1122–1130.

15. Pitre T, Zeraatkar D, Kachkovski GV, Leung G, Shligold E, Dowhanik S, *et al.* Noninvasive Oxygenation Strategies in Adult Patients With Acute Hypoxemic Respiratory Failure A Systematic Review and Network Meta-Analysis. *CHEST* 2023;164:913–928.

16. Pitre T, Liu W, Zeraatkar D, Casey JD, Dionne JC, Gibbs KW, *et al.* Preoxygenation strategies for intubation of patients who are critically ill: a systematic review and network meta-analysis of randomised trials. *Lancet Respir Med* 2025;doi:10.1016/s2213-2600(25)00029-3.

17. Fernando SM, Tran A, Sadeghirad B, Burns KEA, Fan E, Brodie D, *et al.* Noninvasive respiratory support following extubation in critically ill adults: a systematic review and network meta-analysis. *Intensiv Care Med* 2022;48:137–147.

18. Mansournia MA, Higgins JPT, Sterne JAC, Hernán MA. Biases in Randomized Trials. *Epidemiology* 2017;28:54–59.

19. Guyatt G, busse J. Methods Commentary: Risk of Bias in Randomized Trials 1. at <https://www.distillersr.com/resources/methodological-resources/risk-of-bias-commentary>.

20. Authors RI and the Bricn, Francio F, Weigert RM, Mattei EDB, Grion CMC, Festti J, *et al.* High-Flow Nasal Oxygen vs Noninvasive Ventilation in Patients With Acute Respiratory Failure. *JAMA* 2025;333:875–890.

21. Frat J-P, Quenot J-P, Guitton C, Coudroy R, Gacouin A, Badie J, *et al.* High-Flow or Standard Oxygen in Acute Hypoxemic Respiratory Failure. *N Engl J Med* 2026;doi:10.1056/nejmoa2516087.

22. Balduzzi S, Rücker G, Nikolakopoulou A, Papakonstantinou T, Salanti G, Efthimiou O, *et al.* netmeta: An R Package for Network Meta-Analysis Using Frequentist Methods. *J Stat Softw* 2023;106:1–40.

23. Schandelmaier S, Briel M, Varadhan R, Schmid CH, Devasenapathy N, Hayward RA, *et al.* Development of the Instrument to assess the Credibility of Effect Modification Analyses (ICEMAN) in randomized controlled trials and meta-analyses. *CMAJ* 2020;192:E901–E906.

24. Li S-A, Alexander PE, Reljic T, Cuker A, Nieuwlaat R, Wiercioch W, *et al.* Evidence to Decision framework provides a structured "roadmap" for making GRADE guidelines recommendations. *J Clin Epidemiology* 2018;104:103–112.

25. Clinical Practice Guidelines We Can Trust. 2011;doi:10.17226/13058.

26. Nishimura M. High-Flow Nasal Cannula Oxygen Therapy in Adults: Physiological Benefits, Indication, Clinical Benefits, and Adverse Effects. *Respir Care* 2016;61:529–541.

27. Agmy G, Adam M, Hsanen EHM, Mahmoud MA. High-flow nasal cannula versus noninvasive ventilation in the prevention of escalation to invasive mechanical ventilation in patients with acute hypoxemic respiratory failure. *Egypt J Chest Dis Tuberc* 2022;71:81–87.

28. Al-Hashim AH, Reesi AA, Lawati NMA, Burad J, Khabori MA, Chandwani J, *et al.* Comparison of Noninvasive Mechanical Ventilation With High-Flow Nasal Cannula, Face-Mask, and Helmet in Hypoxemic Respiratory Failure in Patients With COVID-19: A Randomized Controlled Trial*. *Crit Care Med* 2023;51:1515–1526.

29. Andino R, Vega G, Pacheco SK, Arevalillo N, Leal A, Fernández L, *et al.* High-flow nasal oxygen reduces endotracheal intubation: a randomized clinical trial. *Ther Adv Respir Dis* 2020;14:1753466620956459.

30. Antonelli M, Conti G, Bufi M, Costa MG, Lappa A, Rocco M, *et al.* Noninvasive Ventilation for Treatment of Acute Respiratory Failure in Patients Undergoing Solid Organ Transplantation: A Randomized Trial. *JAMA* 2000;283:235–241.

31. Arabi YM, Tlayjeh H, Aldekhyl S, Al-Dorzi HM, Abdukahil SA, Harbi MKA, *et al.* Helmet Non-Invasive Ventilation for COVID-19 Patients (Helmet-COVID): study protocol for a multicentre randomised controlled trial. *BMJ Open* 2021;11:e052169.

32. Artaud-Macari E, Bubenheim M, Bouar GL, Carpentier D, Grangé S, Boyer D, *et al.* High-flow oxygen therapy versus noninvasive ventilation: a randomised physiological crossover study of alveolar recruitment in acute respiratory failure. *ERJ Open Res* 2021;7:00373–02021.

33. Azevedo J, Montenegro W, Leitao A, Silva M, Prazeres J, Maranhao J. High flow nasal cannula oxygen (hfnc) versus non-invasive positive pressure ventilation (nippv) in acute hypoxemic respiratory failure. a pilot randomized controlled trial. *Intensiv Care Med Exp* 2015;3:A166.

34. Azoulay E, Lemiale V, Mokart D, Nseir S, Argaud L, Pène F, *et al.* Effect of High-Flow Nasal Oxygen vs Standard Oxygen on 28-Day Mortality in Immunocompromised Patients With Acute Respiratory Failure: The HIGH Randomized Clinical Trial. *JAMA* 2018;320:2099.

35. Brambilla AM, Aliberti S, Prina E, Nicoli F, Forno MD, Nava S, *et al.* Helmet CPAP vs. oxygen therapy in severe hypoxemic respiratory failure due to pneumonia. *Intensiv Care Med* 2014;40:942–949.

36. Bouadma L, Mekontso-Dessap A, Burdet C, Merdji H, Poissy J, Dupuis C, *et al.* High-Dose Dexamethasone and Oxygen Support Strategies in Intensive Care Unit Patients With Severe COVID-19 Acute Hypoxemic Respiratory Failure. *JAMA Intern Med* 2022;182:906–916.

37. CONFALONIERI M, POTENA A, CARBONE G, PORTA RD, TOLLEY EA, MEDURI GU. Acute Respiratory Failure in Patients with Severe Community-acquired Pneumonia. *Am J Respir Crit Care Med* 1999;160:1585–1591.

38. Coudroy R, Frat J-P, Ehrmann S, Pène F, Decavèle M, Terzi N, *et al.* High-flow nasal oxygen alone or alternating with non-invasive ventilation in critically ill immunocompromised patients with acute respiratory failure: a randomised controlled trial. *Lancet Respir Med* 2022;10:641–649.

39. Crimi C, Noto A, Madotto F, Ippolito M, Nolasco S, Campisi R, *et al.* High-flow nasal oxygen versus conventional oxygen therapy in patients with COVID-19 pneumonia and mild hypoxaemia: a randomised controlled trial. *Thorax* 2023;78:354–361.

40. Delclaux C, L'Her E, Alberti C, Mancebo J, Abroug F, Conti G, *et al.* Treatment of Acute Hypoxemic Nonhypercapnic Respiratory Insufficiency With Continuous Positive Airway Pressure Delivered by a Face Mask: A Randomized Controlled Trial. *JAMA* 2000;284:2352–2360.

41. Elagamy AE, Taha SS, Elfawy DM. High flow nasal cannula versus non- invasive ventilation in prevention of intubation in immunocompromised patient with acute hypoxemic respiratory failure. *Egypt J Anaesth* 2021;37:432–439.

42. Elkheshen OM, El-Shaarawy DE, El-Baradey GF, Bahr HM. Comparison between nasal high-flow oxygen therapy and noninvasive ventilation on the outcome of patients with chronic interstitial lung disease complicated with acute respiratory failure. *Egypt J Chest Dis Tuberc* 2024;73:65–70.

43. Ferrer M, Esquinas A, Leon M, Gonzalez G, Alarcon A, Torres A. Noninvasive Ventilation in Severe Hypoxemic Respiratory Failure. *Am J Respir Crit Care Med* 2003;168:1438–1444.

44. Frat J-P, Quenot J-P, Badie J, Coudroy R, Guitton C, Ehrmann S, *et al.* Effect of High-Flow Nasal Cannula Oxygen vs Standard Oxygen Therapy on Mortality in Patients With Respiratory Failure Due to COVID-19. *JAMA* 2022;328:1212–1222.

45. Frat J-P, Thille AW, Mercat A, Girault C, Ragot S, Perbet S, *et al.* High-Flow Oxygen through Nasal Cannula in Acute Hypoxemic Respiratory Failure. *N Engl J Med* 2015;372:2185–2196.

46. Grieco DL, Menga LS, Cesarano M, Rosà T, Spadaro S, Bitondo MM, *et al.* Effect of Helmet Noninvasive Ventilation vs High-Flow Nasal Oxygen on Days Free of Respiratory Support in Patients With COVID-19 and Moderate to Severe Hypoxemic Respiratory Failure. *JAMA* 2021;325:1731–1743.

47. Hao J, Liu J, Pu L, Li C, Zhang M, Tan J, *et al.* High-Flow Nasal Cannula Oxygen Therapy versus Non-Invasive Ventilation in AIDS Patients with Acute Respiratory Failure: A Randomized Controlled Trial. *J Clin Med* 2023;12:1679.

48. He H, Sun B, Liang L, Li Y, Wang H, Wei L, *et al.* A multicenter RCT of noninvasive ventilation in pneumonia-induced early mild acute respiratory distress syndrome. *Crit Care* 2019;23:300.

49. Hernandez G, Fernandez R, Lopez-Reina P, Cuena R, Pedrosa A, Ortiz R, *et al.* Noninvasive ventilation reduces intubation in chest trauma-related hypoxemia: a randomized clinical trial. *Chest* 2009;137:74–80.

50. Hilbert G, Gruson D, Vargas F, Valentino R, Gbikpi-Benissan G, Dupon M, *et al.* Noninvasive Ventilation in Immunosuppressed Patients with Pulmonary Infiltrates, Fever, and Acute Respiratory Failure. *N Engl J Med* 2001;344:481–487.

51. Lemiale V, Mokart D, Resche-Rigon M, Pène F, Mayaux J, Faucher E, *et al.* Effect of Noninvasive Ventilation vs Oxygen Therapy on Mortality Among Immunocompromised Patients With Acute Respiratory Failure: A Randomized Clinical Trial. *JAMA* 2015;314:1711–1719.

52. Lemiale V, Mokart D, Mayaux J, Lambert J, Rabbat A, Demoule A, *et al.* The effects of a 2-h trial of high-flow oxygen by nasal cannula versus Venturi mask in immunocompromised patients with hypoxemic acute respiratory failure: a multicenter randomized trial. *Crit Care* 2015;19:380.

53. MARTIN TJ, HOVIS JD, COSTANTINO JP, BIERMAN MI, DONAHOE MP, ROGERS RM, *et al.* A Randomized, Prospective Evaluation of Noninvasive Ventilation for Acute Respiratory Failure. *Am J Respir Crit Care Med* 2000;161:807–813.

54. MENDİL NA, TEMEL Ş, YÜKSEL RC, GÜNDOĞAN K, ESER B, KAYNAR L, *et al.* THE USE OF HIGH-FLOW NASAL OXYGEN VS. STANDARD OXYGEN THERAPY IN HEMATOLOGICAL MALIGNANCY PATIENTS WITH ACUTE RESPIRATORY FAILURE IN HEMATOLOGY WARDS. *Turk J Méd Sci* 2021;51:1756–1763.

55. Nagata K, Yokoyama T, Tsugitomi R, Nakashima H, Kuraishi H, Ohshimo S, *et al.* Continuous positive airway pressure versus high-flow nasal cannula oxygen therapy for acute hypoxemic respiratory failure: A randomized controlled trial. *Respirology* 2024;29:36–45.

56. Nair PR, Haritha D, Behera S, Kayina CA, Maitra S, Anand RK, *et al.* Comparison of High-Flow Nasal Cannula and Noninvasive Ventilation in Acute Hypoxemic Respiratory Failure Due to Severe COVID-19 Pneumonia. *Respir Care* 2021;66:1824–1830.

57. Ospina-Tascón GA, Calderón-Tapia LE, García AF, Zarama V, Gómez-Álvarez F, Álvarez-Saa T, *et al.* Effect of High-Flow Oxygen Therapy vs Conventional Oxygen Therapy on Invasive Mechanical Ventilation and Clinical Recovery in Patients With Severe COVID-19. *JAMA* 2021;326:2161–2171.

58. Patel BK, Wolfe KS, Pohlman AS, Hall JB, Kress JP. Effect of Noninvasive Ventilation Delivered by Helmet vs Face Mask on the Rate of Endotracheal Intubation in Patients With Acute Respiratory Distress Syndrome: A Randomized Clinical Trial. *JAMA* 2016;315:2435.

59. Perkins GD, Ji C, Connolly BA, Couper K, Lall R, Baillie JK, *et al.* Effect of Noninvasive Respiratory Strategies on Intubation or Mortality Among Patients With Acute Hypoxemic Respiratory Failure and COVID-19. *JAMA* 2022;327:546–558.

60. Saxena A, Nazir N, Pandey R, Gupta S. Comparison of Effect of Non-invasive Ventilation Delivered by Helmet vs Face Mask in Patients with COVID-19 Infection: A Randomized Control Study. *Indian J Crit Care Med : Peer-Rev, Off Publ Indian Soc Crit Care Med* 2022;26:282–287.

61. Squadrone V, Massaia M, Bruno B, Marmont F, Falda M, Bagna C, *et al.* Early CPAP prevents evolution of acute lung injury in patients with hematologic malignancy. *Intensiv Care Med* 2010;36:1666–1674.

62. Thota B, Samantaray A, Vengamma B, Mangu HR, Alladi M, Kalawat U. A randomised controlled trial of high-flow nasal oxygen versus non-rebreathing oxygen face mask therapy in acute hypoxaemic respiratory failure. *Indian J Anaesth* 2022;66:644–650.

63. Wermke M, Schiemanck S, Höffken G, Ehninger G, Bornhäuser M, Illmer T. Respiratory failure in patients undergoing allogeneic hematopoietic SCT—a randomized trial on early non-invasive ventilation based on standard care hematology wards. *Bone Marrow Transplant* 2012;47:574–580.

64. Wysocki M, Tric L, Wolff MA, Gertner J, Millet H, Herman B. Noninvasive Pressure Support Ventilation in Patients With Acute Respiratory Failure. *Chest* 1993;103:907–913.

65. Zhan Q, Sun B, Liang L, Yan X, Zhang L, Yang J, *et al.* Early use of noninvasive positive pressure ventilation for acute lung injury. *Crit Care Med* 2012;40:455–460.

66. Arabi YM, Aldekhyl S, Qahtani SA, Al-Dorzi HM, Abdukahil SA, Harbi MKA, *et al.* Effect of Helmet Noninvasive Ventilation vs Usual Respiratory Support on Mortality Among Patients With Acute Hypoxemic Respiratory Failure Due to COVID-19. *JAMA* 2022;328:1063–1072.

67. Bell N, Hutchinson CL, Green TC, Rogan E, Bein KJ, Dinh MM. Randomised control trial of humidified high flow nasal cannulae versus standard oxygen in the emergency department. *Emerg Med Australas* 2015;27:537–541.

68. Cosentini R, Brambilla AM, Aliberti S, Bignamini A, Nava S, Maffei A, *et al.* Helmet Continuous Positive Airway Pressure vs Oxygen Therapy To Improve Oxygenation in Community-Acquired Pneumonia A Randomized, Controlled Trial. *Chest* 2010;138:114–120.

69. Doshi P, Whittle JS, Bublewicz M, Kearney J, Ashe T, Graham R, *et al.* High-Velocity Nasal Insufflation in the Treatment of Respiratory Failure: A Randomized Clinical Trial. *Ann Emerg Med* 2018;72:73-83.e5.

70. Jones PG, Kamona S, Doran O, Sawtell F, Wilsher M. Randomized Controlled Trial of Humidified High-Flow Nasal Oxygen for Acute Respiratory Distress in the Emergency Department: The HOT-ER Study. *Respir Care* 2016;61:291–299.

71. Kyeremanteng K, Gagnon L-P, Robidoux R, Thavorn K, Chaudhuri D, Kobewka D, *et al.* Cost Analysis of Noninvasive Helmet Ventilation Compared with Use of Noninvasive Face Mask in ARDS. *Can Respir J* 2018;2018:6518572.

72. Spoletini G, Mega C, Pisani L, Alotaibi M, Khoja A, Price LL, *et al.* High-flow nasal therapy vs standard oxygen during breaks off noninvasive ventilation for acute respiratory failure: A pilot randomized controlled trial. *J Crit Care* 2018;48:418–425.

73. Squadrone V, Coha M, Cerutti E, Schellino MM, Biolino P, Occella P, *et al.* Continuous Positive Airway Pressure for Treatment of Postoperative Hypoxemia: A Randomized Controlled Trial. *JAMA* 2005;293:589–595.

74. Schifino G, Vega ML, Pisani L, Prediletto I, Catalanotti V, Comellini V, *et al.* Effects of non-invasive respiratory supports on inspiratory effort in moderate-severe COVID-19 patients. A randomized physiological study. *Eur J Intern Med* 2022;100:110–118.

75. Freeman H, Vranas KC, Tuthill S, Drake MG. High-Flow Nasal Cannula Liberation: Who, When, and How? *CHEST* 2025;168:1152–1161.

76. Botta M, Caritg O, Meenen DMP van, Pacheco A, Tsonas AM, Mooij WE, *et al.* Oxygen Consumption with High-Flow Nasal Oxygen versus Mechanical Ventilation— An International Multicenter Observational Study in COVID–19 Patients (PROXY–COVID). *Am J Trop Med Hyg* 2023;108:1035–1041.

77. Etges APB da S, Marcolino MAZ, Bianchini L, Kawano-Dourado L, Negrelli K, Gurgel R, *et al.* Economic analysis of high-flow nasal oxygen compared with noninvasive ventilation in patients with acute respiratory failure: results from the RENOVATE randomized clinical trial. *Respir Med* 2025;247:108270.

78. Blot P-L, Chousterman BG, Santafè M, Cartailler J, Pacheco A, Magret M, *et al.* Subphenotypes in patients with acute respiratory distress syndrome treated with high-flow oxygen. *Crit Care* 2023;27:419.

79. Brochard L, Slutsky A, Pesenti A. Mechanical Ventilation to Minimize Progression of Lung Injury in Acute Respiratory Failure. *Am J Respir Crit Care Med* 2017;195:438–442.

80. Twagirumugabe T, Gashame DF, Uwamahoro DL, Riviello E. Advanced non-invasive respiratory support in resource-constrained settings: a narrative review. *Crit Care* 2025;29:492.

81. Vital FMR, Ladeira MT, Atallah AN. Non-invasive positive pressure ventilation (CPAP or bilevel NPPV) for cardiogenic pulmonary oedema. *Cochrane Database Syst Rev* 2013;CD005351.doi:10.1002/14651858.cd005351.pub3.

82. Brochard L, Mancebo J, Wysocki M, Lofaso F, Conti G, Rauss A, *et al.* Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. *N Engl J Med* 1995;333:817–22.

83. Demoule A, Brochard L, Dres M, Heunks L, Jubran A, Laghi F, *et al.* How to ventilate obstructive and asthmatic patients. *Intensiv Care Med* 2020;46:2436–2449.

84. Ram FS, Picot J, Lightowler J, Wedzicha JA. Non-invasive positive pressure ventilation for treatment of respiratory failure due to exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2004;CD004104.doi:10.1002/14651858.cd004104.pub3.

85. Pintaudi G, Cutuli SL, Rosà T, Michi T, Cardu A, Bongiovanni F, *et al.* High-Flow Nasal Oxygen in Patients with Acute Hypercapnic Respiratory Failure: A Narrative Review of the Physiological Rationale and Clinical Evidence. *J Clin Med* 2024;13:6350.

86. Avdeev SN, Tret'iakov AV, Grigor'iants RA, Kutsenko MA, Chuchalin AG. [Study of the use of noninvasive ventilation of the lungs in acute respiratory insufficiency due exacerbation of chronic obstructive pulmonary disease]. *Anesteziol Reanimatol* 1998;45–51.

87. Aziz AAAE, Abdelaal GA, Gasad HR, Tawadros BB. High velocity nasal insufflation versus non-invasive ventilation in acute respiratory failure: a comparative study. *Egypt J Chest Dis Tuberc* 2024;73:161–168.

88. Barbe F, Togores B, Rubi M, Pons S, Maimo A, Agusti A. Noninvasive ventilatory support does not facilitate recovery from acute respiratory failure in chronic obstructive pulmonary disease. *Eur Respir J* 1996;9:1240–1245.

89. Bardi G, Pierotello R, Desideri M, Valdisserri L, Bottai M, Palla A. Nasal ventilation in COPD exacerbations: early and late results of a prospective, controlled study. *Eur Respir J* 15:98–104.

90. Belenguer-Muncharaz A, Mateu-Campos L, González-Luís R, Vidal-Tegedor B, Ferrándiz-Sellés A, Árguedas-Cervera J, *et al.* Non-Invasive Mechanical Ventilation Versus Continuous Positive Airway Pressure Relating to Cardiogenic Pulmonary Edema in an Intensive Care Unit. *Arch Bronconeumol* 2017;53:561–567.

91. Bellone A, Vettorello M, Monari A, Cortellaro F, Coen D. Noninvasive pressure support ventilation vs. continuous positive airway pressure in acute hypercapnic pulmonary edema. *Intensiv Care Med* 2005;31:807–811.

92. Bott J, Carroll MP, Conway JH, Keilty SEJ, Ward EM, Brown AM, *et al.* Randomised controlled trial of nasal ventilation in acute ventilatory failure due to chronic obstructive airways disease. *Lancet* 1993;341:1555–1557.

93. Carrera M, Marín JM, Antón A, Chiner E, Alonso ML, Masa JF, *et al.* A controlled trial of noninvasive ventilation for chronic obstructive pulmonary disease exacerbations. *J Crit Care* 2009;24:473.e7–14.

94. Çelikel T, Sungur M, Ceyhan B, Karakurt S. Comparison of Noninvasive Positive Pressure Ventilation With Standard Medical Therapy in Hypercapnic Acute Respiratory Failure. *Chest* 1998;114:1636–1642.

95. Chen J, Wang X. Effect of noninvasive positive pressure ventilation in the treatment of acute exacerbation of chronic obstructive pulmonary disease [in Chinese]. *Zhonghua Jie He He Hu Xi Za Zhi (Chinese Journal of Tuberculosis and Respiratory Diseases)* 28:232–236.

96. Cong Y, Li H, Wang W, et.al. Observation on the effect of high-flow nasal cannula oxygen therapy in acute exacerbation of chronic obstructive pulmonary disease with type II respiratory failure [in Chinese]. *Chinese Journal of Respiration and Critical Care Medicine (中国呼吸与危重监护杂志)* 2019;18:420–424.

97. Cortegiani A, Longhini F, Madotto F, Groff P, Scala R, Crimi C, *et al.* High flow nasal therapy versus noninvasive ventilation as initial ventilatory strategy in COPD exacerbation: a multicenter non-inferiority randomized trial. *Crit Care* 2020;24:692.

98. Dhamija A, Tyagi P, Caroli R, Rahman MU, Vijayan V-K. Noninvasive ventilation in mild to moderate cases of respiratory failure due to acute exacerbation of chronic obstructive pulmonary disease. *Saudi Méd J* 2005;26:887–90.

99. Dikensoy O, Ikidag B, Filiz A, Bayram N. Comparison of non-invasive ventilation and standard medical therapy in acute hypercapnic respiratory failure: a randomised controlled study at a tertiary health centre in SE Turkey. *Int J Clin Pr* 2002;56:85–88.

100. Doshi PB, Whittle JS, Dungan G, Volakis LI, Bublewicz M, Kearney J, *et al.* The ventilatory effect of high velocity nasal insufflation compared to non-invasive positive-pressure ventilation in the treatment of hypercapneic respiratory failure: A subgroup analysis. *Hear Lung* 2020;49:610–615.

101. Gray A, Goodacre S, Newby DE, Masson M, Sampson F, Nicholl J, *et al.* Noninvasive Ventilation in Acute Cardiogenic Pulmonary Edema. *N Engl J Med* 2008;359:142–151.

102. Haciosman O, Ergenc H, Az A, Dogan Y, Sogut O. A high-flow nasal cannula versus noninvasive ventilation in acute exacerbations of chronic obstructive pulmonary disease. *Am J Emerg Med* 2025;87:38–43.

103. Keenan SP, Powers CE, McCormack DG. Noninvasive positive-pressure ventilation in patients with milder chronic obstructive pulmonary disease exacerbations: a randomized controlled trial. *Respir care* 2005;50:610–6.

104. Khilnani GC, Saikia N, Banga A, Sharma SK. Non-invasive ventilation for acute exacerbation of COPD with very high PaCO2: A randomized controlled trial. *Lung India : Off Organ Indian Chest Soc* 2010;27:125–130.

105. Khouaja I, Ghedira H. Nasal non-invasive positive pressure ventilation for moderate exacerbation of chronic obstructive pulmonary disease (COPD) treated in a Tunisian medical ward. *European Respiratory Society* 40:P2032.

106. Kramer N, Meyer TJ, Meharg J, Cece RD, Hill NS. Randomized, prospective trial of noninvasive positive pressure ventilation in acute respiratory failure. *Am J Respir Crit Care Med* 1995;151:1799–1806.

107. Li X-Y, Tang X, Wang R, Yuan X, Zhao Y, Wang L, *et al.* High-Flow Nasal Cannula for Chronic Obstructive Pulmonary Disease with Acute Compensated Hypercapnic Respiratory Failure: A Randomized, Controlled Trial. *Int J Chronic Obstr Pulm Dis* 2020;15:3051–3061.

108. Liu L, Qiu H, Zheng R, Yang Y. [Prospective randomized controlled clinical study of early use of noninvasive positive pressure ventilation in the treatment for acute exacerbation of chronic obstructive pulmonary disease]. *Zhongguo wei zhong bing ji jiu yi xue Chin Crit care Med Zhongguo weizhongbing jijiuyixue* 2005;17:477–80.

109. Matuska P, Pilarová O, Merta Z, Skricková J. [Non-invasive ventilation support in patients with acute exacerbation of chronic obstructive pulmonary disease (COPD)]. *Vnitrni Lék* 2006;52:241–8.

110. Moritz F, Brousse B, Gellée B, Chajara A, L'Her E, Hellot M-F, *et al.* Continuous positive airway pressure versus bilevel noninvasive ventilation in acute cardiogenic pulmonary edema: a randomized multicenter trial. *Ann Emerg Med* 2007;50:666–75, 675.e1.

111. Nava S, Grassi M, Fanfulla F, Domenighetti G, Carlucci A, Perren A, *et al.* Non-invasive ventilation in elderly patients with acute hypercapnic respiratory failure: a randomised controlled trial. *Age Ageing* 2011;40:444–450.

112. Nava S, Carbone G, DiBattista N, Bellone A, Baiardi P, Cosentini R, *et al.* Noninvasive Ventilation in Cardiogenic Pulmonary Edema. *Am J Respir Crit Care Med* 2003;168:1432–1437.

113. Pantazopoulos I, Boutlas S, Mavrovounis G, Papalampidou A, Papagiannakis N, Kontou M, *et al.* Nasal high flow or noninvasive ventilation? navigating hypercapnic COPD exacerbation treatment: A randomized noninferiority clinical trial. *Respir Med* 2024;232:107762.

114. Papachatzakis Y, Nikolaidis PT, Kontogiannis S, Trakada G. High-Flow Oxygen through Nasal Cannula vs. Non-Invasive Ventilation in Hypercapnic Respiratory Failure: A Randomized Clinical Trial. *Int J Environ Res Public Heal* 2020;17:5994.

115. Pisani L, Mega C, Vaschetto R, Bellone A, Scala R, Cosentini R, *et al.* Oronasal mask versus helmet in acute hypercapnic respiratory failure. *Eur Respir J* 2015;45:691–699.

116. Plant P, Owen J, Elliott M. Early use of non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease on general respiratory wards: a multicentre randomised controlled trial. *Lancet* 2000;355:1931–1935.

117. Rezaei A, Fakharian A, Ghorbani F, Idani Esmaeil, Abedini A, Jamaati H. Comparison of high-flow oxygenation with noninvasive ventilation in COPD exacerbation: A crossover clinical trial. *Clin Respir J* 2021;15:420–429.

118. Saeed AM, Wagih KM, Hussein NA. Evaluation of nasal optiflow device in the management of chronic obstructive pulmonary disease patients with acute excerbations. *Egypt J Bronchol* 2015;9:34–42.

119. Samaria J, Srivastava S. Study of pH Changes in Patient of Acute Exacerbation of COPD on Conventional Treatment Versus on NIPPV. *A39 COPD EXACERBATIONS* 2009;A1499.doi:10.1164/ajrccm-conference.2009.179.1_meetingabstracts.a1499.

120. Sklar MC, Dres M, Rittayamai N, West B, Grieco DL, Telias I, *et al.* High-flow nasal oxygen versus noninvasive ventilation in adult patients with cystic fibrosis: a randomized crossover physiological study. *Ann Intensiv Care* 2018;8:85.

121. Tan D, Wang B, Cao P, Wang Y, Sun J, Geng P, *et al.* High flow nasal cannula oxygen therapy versus non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease with acute-moderate hypercapnic respiratory failure: a randomized controlled non-inferiority trial. *Crit Care* 2024;28:250.

122. Wang J, Jiang HY, Li Q. Randomized controlled study of HFNC and NPPV in the treatment of AECOPD combined with type II respiratory failure. *Chin J Integr Med* 2019;39:945–948.

123. Xia J, Gu S, Lei W, Zhang J, Wei H, Liu C, *et al.* High-flow nasal cannula versus conventional oxygen therapy in acute COPD exacerbation with mild hypercapnia: a multicenter randomized controlled trial. *Critical Care* 2022;26:109.

124. Yamane DP, Jones CW, Wilkerson RG, Oliver JJ, Shahamatdar S, Loganathan A, *et al.* High-velocity nasal insufflation versus noninvasive positive pressure ventilation for moderate

acute exacerbation of chronic obstructive pulmonary disease in the emergency department: A randomized clinical trial. *Acad Emerg Med* 2025;32:403–413.

125. Mauri T, Alban L, Turrini C, Cambiaghi B, Carlesso E, Taccone P, *et al.* Optimum support by high-flow nasal cannula in acute hypoxemic respiratory failure: effects of increasing flow rates. *Intensiv Care Med* 2017;43:1453–1463.

126. Russotto V, Myatra SN, Laffey JG, Tassistro E, Antolini L, Bauer P, *et al.* Intubation Practices and Adverse Peri-intubation Events in Critically Ill Patients From 29 Countries. *JAMA* 2021;325:1164–1172.

127. DeMasi SC, Casey JD, Semler MW. Evidence-based Emergency Tracheal Intubation. *Am J Respir Crit Care Med* 2025;211:1156–1164.

128. Weingart SD. Preoxygenation, Reoxygenation, and Delayed Sequence Intubation in the Emergency Department. *J Emerg Med* 2011;40:661–667.

129. Baillard C, Prat G, Jung B, Futier E, Lefrant JY, Vincent F, *et al.* Effect of preoxygenation using non-invasive ventilation before intubation on subsequent organ failures in hypoxaemic patients: a randomised clinical trial. *Br J Anaesth* 2018;120:361–367.

130. Baillard C, Fosse J-P, Sebbane M, Chanques G, Vincent F, Courouble P, *et al.* Noninvasive Ventilation Improves Preoxygenation before Intubation of Hypoxic Patients. *Am J Respir Crit Care Med* 2006;174:171–177.

131. Chua MT, Ng WM, Lu Q, Low MJW, Punyadasa A, Cove ME, *et al.* Pre- and apnoeic high-flow oxygenation for rapid sequence intubation in the emergency department (the Pre-AeRATE trial): A multicentre randomised controlled trial. *Ann Acad Med, Singap* 2022;51:149–160.

132. Cırıl MF, Akarca M, Akoglu EU, Ozturk TC, Onur Ö. High-Flow Nasal Cannula versus Bag Valve Mask for Preoxygenation during Rapid Sequence Intubation in the Emergency Department: A Single-Center, Prospective, Randomized Controlled Trial. *Prehospital Disaster Med* 2024;39:45–51.

133. Frat J-P, Ricard J-D, Quenot J-P, Pichon N, Demoule A, Forel J-M, *et al.* Non-invasive ventilation versus high-flow nasal cannula oxygen therapy with apnoeic oxygenation for preoxygenation before intubation of patients with acute hypoxaemic respiratory failure: a randomised, multicentre, open-label trial. *Lancet Respir Med* 2019;7:303–312.

134. Gibbs KW, Semler MW, Driver BE, Seitz KP, Stempek SB, Taylor C, *et al.* Noninvasive Ventilation for Preoxygenation during Emergency Intubation. *N Engl J Med* 2024;390:2165–2177.

135. Guitton C, Ehrmann S, Volteau C, Colin G, Maamar A, Jean-Michel V, *et al.* Nasal high-flow preoxygenation for endotracheal intubation in the critically ill patient: a randomized clinical trial. *Intensiv Care Med* 2019;45:447–458.

136. Jaber S, Monnin M, Girard M, Conseil M, Cisse M, Carr J, *et al.* Apnoeic oxygenation via high-flow nasal cannula oxygen combined with non-invasive ventilation preoxygenation for intubation in hypoxaemic patients in the intensive care unit: the single-centre, blinded, randomised controlled OPTINIV trial. *Intensiv Care Med* 2016;42:1877–1887.

137. Li J, Liu B, Zhou Q, Ni H, Liu M, Deng K. Pre-oxygenation with high-flow oxygen through the nasopharyngeal airway compared to facemask on carbon dioxide clearance in emergency adults: a prospective randomized non-blinded clinical trial. *Eur J Trauma Emerg Surg* 2024;50:1051–1061.

138. Merry AF, Waart H van, Allen SJ, Baker PA, Cumin D, Frampton CMA, *et al.* Ease and comfort of pre-oxygenation with high-flow nasal oxygen cannulae vs. facemask: a randomised controlled trial. *Anaesthesia* 2022;77:1346–1355.

139. Rosén J, Frykholm P, Fors D. High-flow nasal cannula versus face mask for preoxygenation in obese patients: A randomised controlled trial. *Acta Anaesthesiol Scand* 2021;65:1381–1389.

140. Simon M, Wachs C, Braune S, Heer G de, Frings D, Kluge S. High-Flow Nasal Cannula Versus Bag-Valve-Mask for Preoxygenation Before Intubation in Subjects With Hypoxemic Respiratory Failure. *Respir Care* 2016;61:1160–1167.

141. Sjöblom A, Broms J, Hedberg M, Lodenius Å, Furubacke A, Henningsson R, *et al.* Pre-oxygenation using high-flow nasal oxygen vs. tight facemask during rapid sequence induction. *Anaesthesia* 2021;76:1176–1183.

142. Vourc'h M, Asfar P, Volteau C, Bachoumas K, Clavieras N, Egreteau P-Y, *et al.* High-flow nasal cannula oxygen during endotracheal intubation in hypoxemic patients: a randomized controlled clinical trial. *Intensiv Care Med* 2015;41:1538–1548.

143. Vourc'h M, Huard D, Penndu ML, Deransy R, Surbled M, Malidin M, *et al.* High-flow oxygen therapy versus facemask preoxygenation in anticipated difficult airway management (PREOPTI-DAM): an open-label, single-centre, randomised controlled phase 3 trial. *eClinicalMedicine* 2023;60:101998.

144. Taran S, Angriman F, Pinto R, Ferreyro BL, Amaral ACK-B, Registry TICO. Discordances Between Factors Associated With Withholding Extubation and Extubation Failure After a Successful Spontaneous Breathing Trial*. *Crit Care Med* 2021;49:2080–2089.

145. Frutos-Vivar F, Ferguson ND, Esteban A, Epstein SK, Arabi Y, Apezteguía C, *et al.* Risk Factors for Extubation Failure in Patients Following a Successful Spontaneous Breathing Trial. *Chest* 2006;130:1664–1671.

146. Angriman F, Amaral ACKB, Fan E, Taran S, McCredie VA, Baker A, *et al.* Timing of Extubation in Adult Patients with Acute Brain Injury. *Am J Respir Crit Care Med* 2025;211:339–346.

147. Pham T, Heunks L, Bellani G, Madotto F, Aragao I, Beduneau G, *et al.* Weaning from mechanical ventilation in intensive care units across 50 countries (WEAN SAFE): a multicentre, prospective, observational cohort study. *Lancet Respir Med* 2023;11:465–476.

148. Abrard S, Rineau E, Seegers V, Lebrec N, Sargentini C, Jeanneteau A, *et al.* Postoperative prophylactic intermittent noninvasive ventilation versus usual postoperative care for patients at high risk of pulmonary complications: a multicentre randomised trial. *Br J Anaesth* 2023;130:e160–e168.

149. Arora G, Arshad Z, Prakash R, Sharma M, Singh GP, Kohli M. High-Flow Nasal Cannula as an Alternate Weaning Strategy: A Randomized Controlled Trial. *Cureus* 2023;15:e36511.

150. Belenguer-Muncharaz A, Mateu-Campos M-L, Vidal-Tegedor B, Ferrándiz-Sellés M-D, Micó-Gómez M-L, Altaba-Tena S, *et al.* Ventilación no invasiva versus oxigenoterapia convencional tras fracaso de la extubación en pacientes de alto riesgo en una unidad de cuidados intensivos: un ensayo clínico pragmático. *Rev Bras Ter Intensiv* 2021;33:362–373.

151. Brainard J, Scott BK, Sullivan BL, Fernandez-Bustamante A, Piccoli JR, Gebbink MG, *et al.* Heated humidified high-flow nasal cannula oxygen after thoracic surgery — A randomized prospective clinical pilot trial. *J Crit Care* 2017;40:225–228.

152. Cho JY, Kim H-S, Kang H, Kim S-H, Choe KH, Lee KM, *et al.* Comparison of Postextubation Outcomes Associated with High-Flow Nasal Cannula vs. Conventional Oxygen Therapy in Patients at High Risk of Reintubation: a Randomized Clinical Trial. *J Korean Méd Sci* 2020;35:e194.

153. Corley A, Bull T, Spooner AJ, Barnett AG, Fraser JF. Direct extubation onto high-flow nasal cannulae post-cardiac surgery versus standard treatment in patients with a BMI ≥30: a randomised controlled trial. *Intensiv Care Med* 2015;41:887–894.

154. Elghonemy AAAM, Korraa E, Mohammed RM. Effectiveness of high-flow nasal cannula versus noninvasive ventilation and conventional oxygen therapy in patients weaned from invasive mechanical ventilation. *Egypt J Bronchol* 2024;18:102.

155. Esteban A, Frutos-Vivar F, Ferguson ND, Arabi Y, Apezteguía C, González M, *et al.* Noninvasive Positive-Pressure Ventilation for Respiratory Failure after Extubation. *N Engl J Med* 2004;350:2452–2460.

156. Fernandez R, Subira C, Frutos-Vivar F, Rialp G, Laborda C, Masclans JR, *et al.* High-flow nasal cannula to prevent postextubation respiratory failure in high-risk non-hypercapnic patients: a randomized multicenter trial. *Ann Intensiv Care* 2017;7:47.

157. Ferrer M, Valencia M, Nicolas JM, Bernadich O, Badia JR, Torres A. Early Noninvasive Ventilation Averts Extubation Failure in Patients at Risk. *Am J Respir Crit Care Med* 2006;173:164–170.

158. Ferrer M, Sellarés J, Valencia M, Carrillo A, Gonzalez G, Badia JR, *et al.* Non-invasive ventilation after extubation in hypercapnic patients with chronic respiratory disorders: randomised controlled trial. *Lancet* 2009;374:1082–1088.

159. Futier E, Paugam-Burtz C, Godet T, Khoy-Ear L, Rozencwajg S, Delay J-M, *et al.* Effect of early postextubation high-flow nasal cannula vs conventional oxygen therapy on hypoxaemia in patients after major abdominal surgery: a French multicentre randomised controlled trial (OPERA). *Intensiv Care Med* 2016;42:1888–1898.

160. Girault C, Bubenheim M, Abroug F, Diehl JL, Elatrous S, Beuret P, *et al.* Noninvasive Ventilation and Weaning in Patients with Chronic Hypercapnic Respiratory Failure. *Am J Respir Crit Care Med* 2011;184:672–679.

161. Hernández G, Vaquero C, González P, Subira C, Frutos-Vivar F, Rialp G, *et al.* Effect of Postextubation High-Flow Nasal Cannula vs Conventional Oxygen Therapy on Reintubation in Low-Risk Patients: A Randomized Clinical Trial. *JAMA* 2016;315:1354.

162. Hernández G, Vaquero C, Colinas L, Cuena R, González P, Canabal A, *et al.* Effect of Postextubation High-Flow Nasal Cannula vs Noninvasive Ventilation on Reintubation and Postextubation Respiratory Failure in High-Risk Patients: A Randomized Clinical Trial. *JAMA* 2016;316:1565.

163. Hernández G, Paredes I, Moran F, Buj M, Colinas L, Rodríguez ML, *et al.* Effect of postextubation noninvasive ventilation with active humidification vs high-flow nasal cannula on reintubation in patients at very high risk for extubation failure: a randomized trial. *Intensiv Care Med* 2022;48:1751–1759.

164. Hernández G, Dianti J, Paredes I, Moran F, Marquez M, Calle A, *et al.* Humidified Noninvasive Ventilation versus High-Flow Therapy to Prevent Reintubation in Patients with Obesity: A Randomized Clinical Trial. *Am J Respir Crit Care Med* 2025;211:222–229.

165. Jaaly EA, Fiorentino F, Reeves BC, Ind PW, Angelini GD, Kemp S, *et al.* Effect of adding postoperative noninvasive ventilation to usual care to prevent pulmonary complications in patients undergoing coronary artery bypass grafting: A randomized controlled trial. *J Thorac Cardiovasc Surg* 2013;146:912–918.

166. Jaber S, Lescot T, Futier E, Paugam-Burtz C, Seguin P, Ferrandiere M, *et al.* Effect of Noninvasive Ventilation on Tracheal Reintubation Among Patients With Hypoxemic Respiratory Failure Following Abdominal Surgery: A Randomized Clinical Trial. *JAMA* 2016;315:1345.

167. Jaber S, Pensier J, Futier E, Paugam-Burtz C, Seguin P, Ferrandiere M, *et al.* Noninvasive ventilation on reintubation in patients with obesity and hypoxemic respiratory failure following abdominal surgery: a post hoc analysis of a randomized clinical trial. *Intensiv Care Med* 2024;50:1265–1274.

168. Jiang J, Kao S, Wang S. Effect of early application of biphasic positive airway pressure on the outcome of extubation in ventilator weaning. *Respirology* 1999;4:161–165.

169. Jing G, Li J, Hao D, Wang T, Sun Y, Tian H, *et al.* Comparison of high flow nasal cannula with noninvasive ventilation in chronic obstructive pulmonary disease patients with hypercapnia in preventing postextubation respiratory failure: A pilot randomized controlled trial. *Res Nurs Heal* 2019;42:217–225.

170. Jong AD, Bignon A, Stephan F, Godet T, Constantin J-M, Asehnoune K, *et al.* Effect of non-invasive ventilation after extubation in critically ill patients with obesity in France: a multicentre, unblinded, pragmatic randomised clinical trial. *Lancet Respir Med* 2023;11:530–539.

171. Keenan SP, Powers C, McCormack DG, Block G. Noninvasive Positive-Pressure Ventilation for Postextubation Respiratory Distress: A Randomized Controlled Trial. *JAMA* 2002;287:3238–3244.

172. Ketan PS, Kumar R, AJ M, Ish P, Chakrabarti S, Gupta NK, *et al.* Post-extubation high-flow nasal cannula oxygen therapy versus non-invasive ventilation in chronic obstructive pulmonary disease with hypercapnic respiratory failure. *Monaldi Arch Chest Dis* 2023;94:.

173. Khilnani GC, Galle AD, Hadda V, Sharma SK. Non-Invasive Ventilation after Extubation in Patients with Chronic Obstructive Airways Disease: A Randomised Controlled Trial. *Anaesth Intensiv Care* 2010;39:217–223.

174. Kindgen-Milles D, Müller E, Buhl R, Böhner H, Ritter D, Sandmann W, *et al.* Nasal-Continuous Positive Airway Pressure Reduces Pulmonary Morbidity and Length of Hospital Stay Following Thoracoabdominal Aortic Surgery. *Chest* 2005;128:821–828.

175. Kumari N, Kumari B, Kumar S, Arun N, Kumari R. Effectiveness of high flow nasal cannula (HFNC) versus bilevel positive airway pressure (BiPAP) in preventing tracheal reintubation in patients with high risk of extubation failure in intensive care unit – A randomised comparative trial. *Indian J Anaesth* 2024;68:246–253.

176. Magdy DM, Metwally A. Direct Extubation to High-Flow Nasal Cannula versus Noninvasive Ventilation in Obese Subjects. *Respir Care* 2023;68:234–240.

177. Maggiore SM, Jaber S, Grieco DL, Mancebo J, Zakynthinos S, Demoule A, *et al.* High-Flow Versus VenturiMask Oxygen Therapy to Prevent Reintubation in Hypoxemic Patients after Extubation: A Multicenter Randomized Clinical Trial. *Am J Respir Crit Care Med* 2022;206:1452–1462.

178. Maggiore SM, Idone FA, Vaschetto R, Festa R, Cataldo A, Antonicelli F, *et al.* Nasal High-Flow versus Venturi Mask Oxygen Therapy after Extubation. Effects on Oxygenation, Comfort, and Clinical Outcome. *Am J Respir Crit Care Med* 2014;190:282–288.

179. Matsuda W, Hagiwara A, Uemura T, Sato T, Kobayashi K, Sasaki R, *et al.* High-Flow Nasal Cannula May Not Reduce the Re-Intubation Rate Compared With a Large-Volume Nebulization-Based Humidifier. *Respir Care* 2020;65:610–617.

180. Mohamed KAE, Abdalla MH. Role of non invasive ventilation in limiting re-intubation after planned extubation. *Egypt J Chest Dis Tuberc* 2013;62:669–674.

181. Nava S, Gregoretti C, Fanfulla F, Squadrone E, Grassi M, Carlucci A, *et al.* Noninvasive ventilation to prevent respiratory failure after extubation in high-risk patients* *Crit Care Med* 2005;33:2465–2470.

182. Ornico SR, Lobo SM, Sanches HS, Deberaldini M, Tófoli LT, Vidal AM, *et al.* Noninvasive ventilation immediately after extubation improves weaning outcome after acute respiratory failure: a randomized controlled trial. *Crit Care* 2013;17:R39.

183. Osterkamp JTF, Strandby RB, Henningsen L, Marcussen KV, Thomsen T, Mortensen CR, *et al.* Comparing the effects of continuous positive airway pressure via mask or helmet interface on oxygenation and pulmonary complications after major abdominal surgery: a randomized trial. *J Clin Monit Comput* 2023;37:63–70.

184. Parke R, McGuinness S, Dixon R, Jull A. Open-label, phase II study of routine high-flow nasal oxygen therapy in cardiac surgical patients. *Br J Anaesth* 2013;111:925–931.

185. Shang X, Wang Y. Comparison of outcomes of high-flow nasal cannula and noninvasive positive-pressure ventilation in patients with hypoxemia and various APACHE II scores after extubation. *Ther Adv Respir Dis* 2021;15:17534666211004235.

186. Song H-Z, Gu J-X, Xiu H-Q, Cui W, Zhang G-S. The value of high-flow nasal cannula oxygen therapy after extubation in patients with acute respiratory failure. *Clinics* 2017;72:562–567.

187. Stéphan F, Barrucand B, Petit P, Rézaiguia-Delclaux S, Médard A, Delannoy B, *et al.* High-Flow Nasal Oxygen vs Noninvasive Positive Airway Pressure in Hypoxemic Patients After Cardiothoracic Surgery: A Randomized Clinical Trial. *JAMA* 2015;313:2331–2339.

188. Su C-L, Chiang L-L, Yang S-H, Lin H-Y, Cheng K-C, Huang Y-CT, *et al.* Preventive Use of Noninvasive Ventilation After Extubation: A Prospective, Multicenter Randomized Controlled Trial. *Respir Care* 2012;57:204–210.

189. Tan D, Walline JH, Ling B, Xu Y, Sun J, Wang B, *et al.* High-flow nasal cannula oxygen therapy versus non-invasive ventilation for chronic obstructive pulmonary disease patients after extubation: a multicenter, randomized controlled trial. *Crit Care* 2020;24:489.

190. Tatsuishi W, Sato T, Kataoka G, Sato A, Asano R, Nakano K. High-Flow Nasal Cannula Therapy With Early Extubation for Subjects Undergoing Off-Pump Coronary Artery Bypass Graft Surgery. *Respir Care* 2020;65:183–190.

191. Thanthitaweewat V, Muntham D, Chirakalwasan N. Targeted-Volume Noninvasive Ventilation Reduces Extubation Failure in Postextubated Medical Intensive Care Unit Patients: A Randomized Controlled Trial. *Indian J Crit Care Med : Peer-Rev, Off Publ Indian Soc Crit Care Med* 2018;22:639–645.

192. Theerawit P, Natpobsuk N, Petnak T, Sutherasan Y. The efficacy of the WhisperFlow CPAP system versus high flow nasal cannula in patients at risk for postextubation failure: A Randomized controlled trial. *J Crit Care* 2021;63:117–123.

193. Theologou S, Ischaki E, Zakynthinos SG, Charitos C, Michopanou N, Patsatzis S, *et al.* High Flow Oxygen Therapy at Two Initial Flow Settings versus Conventional Oxygen Therapy in Cardiac Surgery Patients with Postextubation Hypoxemia: A Single-Center, Unblinded, Randomized, Controlled Trial. *J Clin Med* 2021;10:2079.

194. Thille AW, Coudroy R, Nay M-A, Gacouin A, Decavèle M, Sonneville R, *et al.* Beneficial Effects of Noninvasive Ventilation after Extubation in Obese or Overweight Patients: A Post Hoc Analysis of a Randomized Clinical Trial. *Am J Respir Crit Care Med* 2022;205:440–449.

195. Thille AW, Muller G, Gacouin A, Coudroy R, Decavele M, Sonneville R, *et al.* Effect of Postextubation High-Flow Nasal Oxygen With Noninvasive Ventilation vs High-Flow Nasal Oxygen Alone on Reintubation Among Patients at High Risk of Extubation Failure: A Randomized Clinical Trial. *JAMA* 2019;322:1465–1475.

196. Tongyoo S, Tantibundit P, Daorattanachai K, Viarasilpa T, Permpikul C, Udompanturak S. High-flow nasal oxygen cannula vs. noninvasive mechanical ventilation to prevent reintubation in sepsis: a randomized controlled trial. *Ann Intensiv Care* 2021;11:135.

197. Tseng C-W, Chao K-Y, Wu H-L, Lin C-C, Hsu H-S. Effectiveness of high-flow nasal cannulae compared with noninvasive positive-pressure ventilation in preventing reintubation in patients receiving prolonged mechanical ventilation. *Sci Rep* 2023;13:4689.

198. Vargas F, Clavel M, Sanchez-Verlan P, Garnier S, Boyer A, Bui H-N, *et al.* Intermittent noninvasive ventilation after extubation in patients with chronic respiratory disorders: a multicenter randomized controlled trial (VHYPER). *Intensiv Care Med* 2017;43:1626–1636.

199. Vaschetto R, Longhini F, Persona P, Ori C, Stefani G, Liu S, *et al.* Early extubation followed by immediate noninvasive ventilation vs. standard extubation in hypoxemic patients: a randomized clinical trial. *Intensiv Care Med* 2019;45:62–71.

200. Yang Y, Liu N, Sun L, Zhou Y, Yang Y, Shang W, *et al.* Noninvasive Positive-Pressure Ventilation in Treatment of Hypoxemia After Extubation Following Type-A Aortic Dissection. *J Cardiothorac Vasc Anesthesia* 2016;30:1539–1544.

201. Maitland K, Kiguli S, Olupot-Olupot P, Hamaluba M, Thomas K, Alaroker F, *et al.* Randomised controlled trial of oxygen therapy and high-flow nasal therapy in African children with pneumonia. *Intensiv Care Med* 2021;47:566–576.

Figure 1. Scope of Noninvasive Respiratory Support Clinical Practice Guideline

Figure 2. Recommendations for Noninvasive Respiratory Support for Acute Hypoxemic Respiratory Failure.

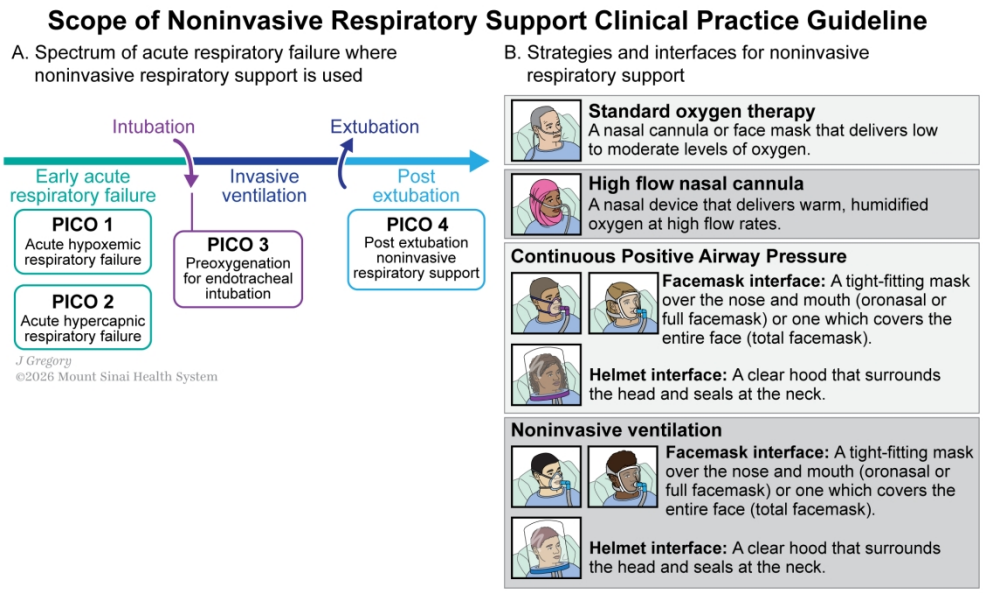
Figure 3. Recommendations for Noninvasive Respiratory Support for Acute Hypercapnic Respiratory Failure

Figure 4. Recommendations for Noninvasive Respiratory Support for Preoxygenation during Endotracheal Intubation

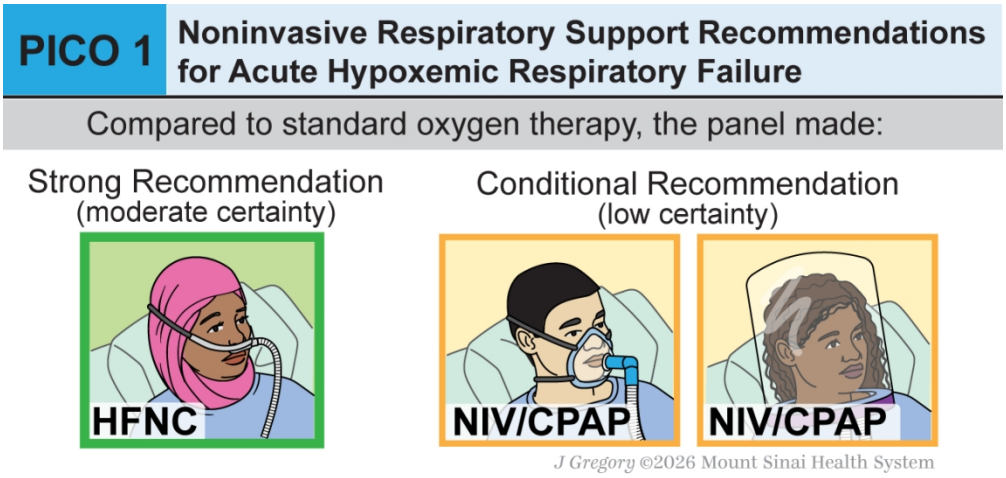
Figure 5. Recommendations for Noninvasive Respiratory Support Post-Extubation after Critical Illness

Table 1: High-Risk Features for Post-Extubation Respiratory Failure

Age ≥ 65 years of age
Cardiopulmonary disease (e.g. heart failure, moderate to severe COPD)
Acute Physiology and Chronic Health Evaluation (APACHE) II ≥ 12
Body Mass Index ≥ 30
Presence of airway patency problems or high risk of laryngeal edema
Inability to manage secretions: weak cough reflex or suctioning ≥ 2 times in 8 hours before extubation
Complex weaning
More than 2 comorbidities
Prolonged mechanical ventilation ≥ 7 days



186x112mm (300 x 300 DPI)



109x52mm (300 x 300 DPI)

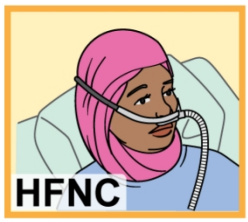
PICO 2 **Noninvasive Respiratory Support Recommendations for Acute Hypercapnic Respiratory Failure**

For patients with acute hypercapnic respiratory failure, compared to standard oxygen therapy, the panel made:

Strong Recommendation (moderate certainty)

For patients with mild acute hypercapnic respiratory failure with mild acidemia (e.g. ph ≥7.25), compared to standard oxygen therapy, the panel made:

Conditional Recommendation (low certainty)

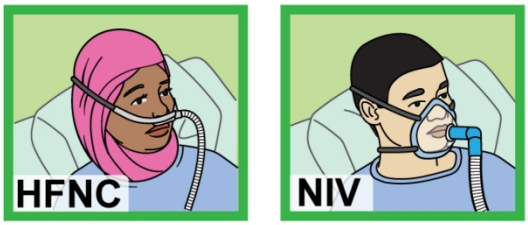


109x86mm (300 x 300 DPI)

PICO 3 **Noninvasive Respiratory Support Recommendations for Preoxygenation of Patients with Acute Respiratory Failure Undergoing Endotracheal Intubation**

Compared to standard oxygen therapy, the panel made:

Strong Recommendation (moderate certainty)

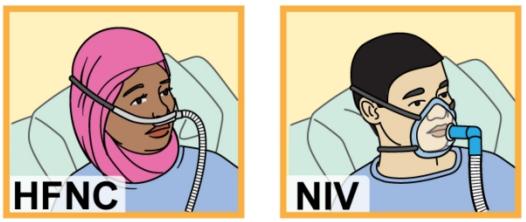


109x50mm (300 x 300 DPI)

PICO 4 **Noninvasive Respiratory Support Recommendations for Adult Patients Extubated after Critical Illness**

For patients extubated in the ICU after critical illness, compared to standard oxygen therapy, the panel made:

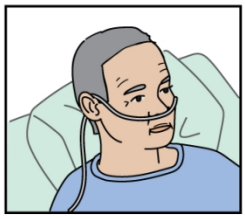
Conditional Recommendation (moderate certainty)



For patients extubated in the ICU after critical illness at high-risk of extubation failure, compared to high flow nasal oxygen and standard oxygen therapy, the panel made:

Conditional Recommendation (moderate certainty)

For patients who are at very low risk of extubation failure, it may be appropriate to use standard oxygen therapy or room air.



109x122mm (300 x 300 DPI)