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► To cite this version:

Shannon Fernando, Alexandre Tran, Behnam Sadeghirad, Karen Burns, Eddy Fan, et al.. Noninvasive respiratory support following extubation in critically ill adults: a systematic review and network meta-analysis. *Intensive Care Medicine*, 2022, 48 (2), pp.137-147. 10.1007/s00134-021-06581-1 . hal-03452893

HAL Id: hal-03452893

<https://hal.science/hal-03452893v1>

Submitted on 28 Nov 2021

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Noninvasive respiratory support following extubation in critically ill adults: a systematic review and network meta-analysis

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Abstract

Purpose: Systematic review and network meta-analysis to investigate the efficacy of noninvasive respiratory strategies, including noninvasive positive pressure ventilation (NIPPV) and high-flow nasal cannula (HFNC), in reducing extubation failure among critically ill adults.

Methods: We searched databases from inception through October 2021 for randomized controlled trials (RCTs) evaluating noninvasive respiratory support therapies (NIPPV, HFNC, conventional oxygen therapy, or a combination of these) following extubation in critically ill adults. Two reviewers performed screening, full text review, and extraction independently. The primary outcome of interest was reintubation. We used GRADE to rate the certainty of our findings.

Results: We included 36 RCTs (6806 patients). Compared to conventional oxygen therapy, NIPPV (OR 0.65 [95% CI 0.52–0.82]) and HFNC (OR 0.63 [95% CI 0.45–0.87]) reduced reintubation (both moderate certainty). Sensitivity analyses showed that the magnitude of the effect was highest in patients with increased baseline risk of reintubation. As compared to HFNC, no difference in incidence of reintubation was seen with NIPPV (OR 1.04 [95% CI 0.78–1.38], low certainty). Compared to conventional oxygen therapy, neither NIPPV (OR 0.8 [95% CI 0.61–1.04], moderate certainty) or HFNC (OR 0.9 [95% CI 0.66–1.24], low certainty) reduced short-term mortality. Consistent findings were demonstrated across multiple subgroups, including high- and low-risk patients. These results were replicated when evaluating noninvasive strategies for prevention (prophylaxis), but not in rescue (application only after evidence of deterioration) situations.

Conclusions: Our findings suggest that both NIPPV and HFNC reduced reintubation in critically ill adults, compared to conventional oxygen therapy. NIPPV did not reduce incidence of reintubation when compared to HFNC. These findings support the preventative application of noninvasive respiratory support strategies to mitigate extubation failure in critically ill adults, but not in rescue conditions.

Keywords: Critical care medicine, Mechanical ventilation, Extubation failure, High-flow nasal cannula

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Introduction

Invasive mechanical ventilation is a widely used life-saving therapy for many critically ill patients [1, 2], but is also associated with important complications, including ventilator-induced lung injury, nosocomial infections [e.g., ventilator-associated pneumonia (VAP)], neuromuscular weakness, and delirium [3–5]. Furthermore, invasive mechanical ventilation requires substantial resource utilization, and is one of the most costly therapies provided in the intensive care unit (ICU) [6]. For all these reasons, providers seek timely and safe liberation of patients from mechanical ventilation [7].

Extubation failure is associated with important harms [8], including increased mortality [9, 10], and occurs in approximately 10–15% of extubated patients. Incidence is even higher (25–40%) in certain patient populations (e.g., patients with heart failure or chronic obstructive pulmonary disease) [7, 11]. To mitigate the risk of extubation failure, clinicians have used noninvasive respiratory support interventions in the post-extubation period to optimize gas exchange and decrease patients' oxygen cost of breathing [12]. These interventions [noninvasive positive pressure ventilation (NIPPV) and high-flow nasal cannula (HFNC)] have been shown to be efficacious in preventing initial intubation in patients with hypoxemic respiratory failure [13], but their efficacy in preventing post-extubation respiratory failure and reintubation is less clear. These support strategies may also be associated with increased patient discomfort and healthcare resource utilization [14]. Further to this, survey studies have demonstrated provider skepticism regarding the efficacy of these interventions [15]. As such, there is substantial practice variation worldwide in the application of such strategies, with overall limited use [16, 17].

We conducted a systematic review and network meta-analysis of randomized controlled trials (RCTs) to evaluate the relative efficacy of conventional oxygen therapy, NIPPV, HFNC, and the strategy of alternating NIPPV and HFNC during the post-extubation period in reducing extubation failure and short-term mortality among critically ill adults. We hypothesized that NIPPV, HFNC, and alternating NIPPV and HFNC would reduce extubation failure, as compared to conventional oxygen therapy.

Methods

We followed the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement extension for network meta-analysis [18, 19], and registered our protocol with the Open Science Framework (<https://www.osf.io/49xgd>).

In this network meta-analysis of 36 randomized trials and 6806 patients, we found that both NIPPV and HFNC reduced reintubation in the post-extubation period, compared to conventional oxygen therapy. Magnitude of benefit was increased among patients at highest risk of reintubation. The results supported the preventative or prophylactic application of noninvasive ventilation, but not use of these interventions for rescue.

Data sources and search strategy

We searched six databases (Medline, PubMed, EMBASE, Scopus, Web of Science, and the Cochrane Database of Systematic Reviews) from inception to October 11, 2021. An experienced health sciences librarian helped develop the search strategy (Supplemental Fig. 1). We conducted further surveillance searches using the 'related articles' feature [20], and performed a grey literature search, including screening the reference lists of all included studies, and subsequent guidelines on non-invasive ventilation.

Study selection

Two reviewers (SMF and AT) independently screened titles and abstracts identified through the searches using Covidence (Melbourne, Australia), and then independently assessed full texts of the selected articles from phase one. Reviewers resolved disagreements by discussion. We included English-language RCTs (parallel, cluster, or cross-over) meeting the following criteria: (1) enrolled adult patients (≥ 16 years of age); (2) conducted primarily ($\geq 70\%$ of patients) in an ICU setting; (3) randomized patients to receive NIPPV, HFNC, conventional oxygen therapy, or a combination of the above; (4) conducted in the post-extubation period, and evaluated these treatments for prevention (i.e. prophylactic application immediately post-extubation) or rescue (i.e. application only in patients developing symptoms and signs of respiratory failure post-extubation); and (5) reported at least one of the outcomes of interest. We excluded trials that: (1) were conducted in the emergency department, operating room, or post-anesthetic care unit; (2) evaluated the effect of these interventions on "weaning" (e.g. passing a spontaneous breathing trial) but did not provide data on extubation failure; (3) exclusively evaluated patients with self-extubation; (4) evaluated these interventions for transitioning to palliative care; and (5) randomized patients to liberation or post-extubation protocols, rather than treatments [21].

The primary outcome of interest was extubation failure, defined as reintubation using an endotracheal tube and recurrent invasive mechanical ventilation. In the absence of a widely accepted time-based definition of

“extubation failure” [11], we included trials that evaluated this outcome at any point during the index ICU admission. Other important outcomes included short-term mortality (28-day, 30-day, or in-hospital), incidence of VAP, patient discomfort (described as a binary outcome in the included trials), incidence of tracheostomy, time to re-intubation, ICU length of stay, and total hospital length of stay. For studies reporting length of stay as a median (with interquartile range), this was converted to a mean (with standard deviation), using appropriate methods [22].

Data extraction

One investigator (SMF) used a pre-designed data extraction form to collect the following variables: author information, publication year, eligibility criteria, and number of patients (Supplemental Table 1). Two investigators (SMF and AT) independently collected data related to descriptions of interventions and outcomes. Disagreements were resolved through discussion.

Risk of bias assessment

Two reviewers (SMF and AT) independently assessed the risk of bias of the studies, using a modified Cochrane Collaboration tool [23], that included sequence generation, allocation sequence concealment, blinding, missing outcome data, and other biases. Reviewers resolved disagreement through discussion.

Data synthesis and analysis

For each outcome and each pair of interventions, we calculated odds ratios (OR) and corresponding 95% confidence intervals (CIs). Initially, we performed conventional pairwise meta-analysis using a DerSimonian and Laird random-effects model for all comparisons with two RCTs or more [24]. We assessed heterogeneity for each direct comparison using visual inspection of forest plots, the I^2 statistic and the Chi-squared test. We evaluated the feasibility of conducting network meta-analysis by evaluating the: (1) availability of evidence (e.g. number of trials, number of interventions); (2) homogeneity of study designs, patients, and characteristics of interventions across the body of evidence (transitivity assumption); (3) structural properties of the network of evidence (e.g. connectivity); and (4) coherence in network (using the ‘design-by-treatment’ model), and in each closed loop of the network.

We performed frequentist random-effects network meta-analysis using multivariate meta-analysis assuming a common heterogeneity parameter [25, 26]. We confirmed the coherence assumption in the entire network using ‘design-by-treatment’ model (global test), as described by Higgins et al. [27]. We also used the side

splitting method to assess the presence of incoherence between direct and indirect estimates of the effect [28, 29]. For each outcome, we estimated ranking probabilities, the Surface Under the Cumulative Ranking Curve (SUCRA), and generated mean treatment rankings. For all direct comparisons, we assessed the small-study effect using Harbord’s test for binary outcomes and Egger’s test for continuous outcomes when 10 or more RCTs were available [30]. We conducted all analyses using STATA 16 (StataCorp, College Station, TX, USA).

Subgroups and sensitivity analyses

While most trials included mixed populations of critically ill patients, we expected that some trials had exclusively recruited particular patient populations. To explore these between-trial comparisons, we performed network meta-regression among pre-specified subgroups (mixed ICU patients, surgical patients, patients at “high risk” for extubation failure, patients with hypercapnic respiratory failure, and study continent) to assess for effect modification by subgroup. For any subgroup effect that was found to be statistically significant, we used the Instrument to assess the Credibility of Effect Modification Analyses (ICEMAN) to evaluate credibility [31]. Finally, to further assess these therapies across various conditions, we performed network meta-regression to adjust for baseline risk of reintubation among the included trials. The baseline risk for reintubation was generated using the incidence of reintubation among patients receiving conventional oxygen therapy in the included trials. Additionally, we performed a sensitivity analysis using a possible range of baseline risks for reintubation (range from 5 to 40%, supported by evidence and confirmed by our clinical experts) to estimate absolute risk reductions and number need to treat (NNT) for the outcome of reintubation.

Trials may also differ in timing of patient recruitment and application of noninvasive ventilation. Although we expected that most trials would test the efficacy of prophylactic or preventative noninvasive ventilation in the immediate post-extubation period, some trials may exclusively recruit patients with evidence of clinical deterioration prior to rescue application of noninvasive ventilation. Consequently, we performed sensitivity analyses only including trials evaluating the efficacy of noninvasive ventilation for prevention of reintubation following extubation. We additionally performed conventional meta-analysis among the trials that used noninvasive ventilation for rescue in patients with evidence of respiratory distress prior to application.

Assessment of certainty of evidence

We used the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach to assess the certainty of evidence for each comparison [32]. The certainty assessment addresses the domains of risk of bias, imprecision, inconsistency, indirectness, intransitivity, publication bias, and incoherence [32]. Imprecision for each comparison was assessed at the network level, and not at the level of the direct or indirect estimate. Given our presumption that blinding clinicians to noninvasive treatments would not be possible in the included trials, and that a lack of blinding might lead to potential differences in adjunctive therapies (e.g., suctioning, positioning) that might affect the outcome, we decided to rate down our GRADE certainty for subjective outcomes (e.g., extubation failure), but not objective outcomes (e.g., mortality). We applied a minimally contextualized approach to evaluate certainty in effect estimates and draw conclusions from network meta-analyses [33].

Results

Search results, study characteristics, and risk-of-bias

Of 6899 citations (Supplemental Fig. 2) identified in the search, we screened 6605 following removal of duplicates, and 58 underwent full-text review. We included 36 RCTs [34–69], examining 6806 patients (all ICU patients). Characteristics of the included trials are shown in Table 1, and detailed characteristics are shown in Supplemental Table 2. Of these, 29 studies (2129 patients, 31.3% of patients) investigated conventional oxygenation therapy (delivered via nasal prongs or facemask) [34–43, 45–47, 49–58, 60, 62, 63, 67–69], 24 studies (2149 patients, 31.3%) investigated NIPPV (using facemask interface) [34, 38, 40, 41, 43, 44, 46–51, 54–56, 59–61, 63, 64, 66–69], 18 studies (2189 patients, 32.2%) investigated HFNC [35–37, 39, 42, 44, 45, 48, 52, 53, 57–59, 61, 62, 64–66], and 1 study (339 patients, 5.0%) evaluated the combination of alternating NIPPV and HFNC [65]. Risk-of-bias assessments are shown in Supplemental Table 3. While the majority of trials were considered low risk-of-bias in most domains, all trials were considered to have probable high risk-of-bias with regard to blinding, given the practical inability to blind treating providers to noninvasive respiratory strategies.

Reintubation

The network plot for reintubation is displayed in Fig. 1, and the summary of findings, including network estimates, is shown in Table 2. We found that, compared to conventional oxygen therapy, both NIPPV (OR 0.65 [95% CI 0.52–0.82]; absolute risk difference – 5.18 [95% CI

Table 1 Characteristics of the 36 randomized clinical trials

Description	Overall (36 studies, n = 6806)	
	Number of studies (%)	Number of patients (%)
Continent of study		
Europe	14 (38.9)	4062 (59.7)
Asia	14 (38.9)	1596 (23.4)
North America	3 (8.3)	163 (2.4)
Australia	2 (5.6)	495 (7.3)
Multicontinental	3 (8.3)	490 (7.3)
Year of publication		
1995–1999	1 (2.8)	93 (1.4)
2000–2004	2 (5.6)	302 (4.4)
2005–2009	4 (11.1)	415 (6.1)
2010–2014	8 (22.2)	1317 (19.4)
2015–2021	21 (58.3)	4679 (68.7)
Sites		
Single center	19 (52.8)	1941 (28.5)
Multicenter	17 (47.2)	4865 (71.5)
Intensive care unit population		
Medical/mixed	14 (38.9)	2273 (33.4)
Surgical	10 (27.8)	2259 (33.2)
High-risk patients	7 (19.4)	1859 (27.3)
Hypercapnic respiratory failure	5 (13.9)	415 (6.1)
Interventions studied		
Conventional oxygen therapy	29 (80.6)	2129 (31.3)
Noninvasive positive pressure ventilation	24 (66.7)	2149 (31.6)
High-flow nasal cannula	18 (50)	2189 (32.2)
Combined noninvasive positive pressure ventilation and high-flow nasal cannula	1 (2.8)	339 (5)
Indication for noninvasive ventilation		
Prevention/prophylaxis	31 (86.1)	6092 (89.5)
Rescue	5 (13.9)	714 (10.5)

– 8.09 to – 2.26]) and HFNC (OR 0.63 [95% CI 0.45–0.87]; absolute risk difference, – 3.84 [95% CI – 6.7 to – 0.98]) reduced the incidence of reintubation (moderate certainty). NIPPV had no effect on reintubation compared to HFNC (OR 1.04 [95% CI 0.78–1.38]; absolute risk difference – 1.34 [95% CI – 4.40 to 1.72], low certainty). The combination of alternating HFNC and NIPPV did not decrease the incidence of reintubation, as compared to NIPPV alone (OR 0.58 [95% CI 0.3–1.11]; absolute risk difference – 5.07 [95% CI – 13.38 to 3.24]), or HFNC alone (OR 0.6 [95% CI 0.33–1.08]; absolute risk difference – 6.41 [95% CI – 14.13 to 1.31]), based on low certainty evidence. Direct estimates, indirect estimates, and SUCRA table are shown in Supplemental Table 4.

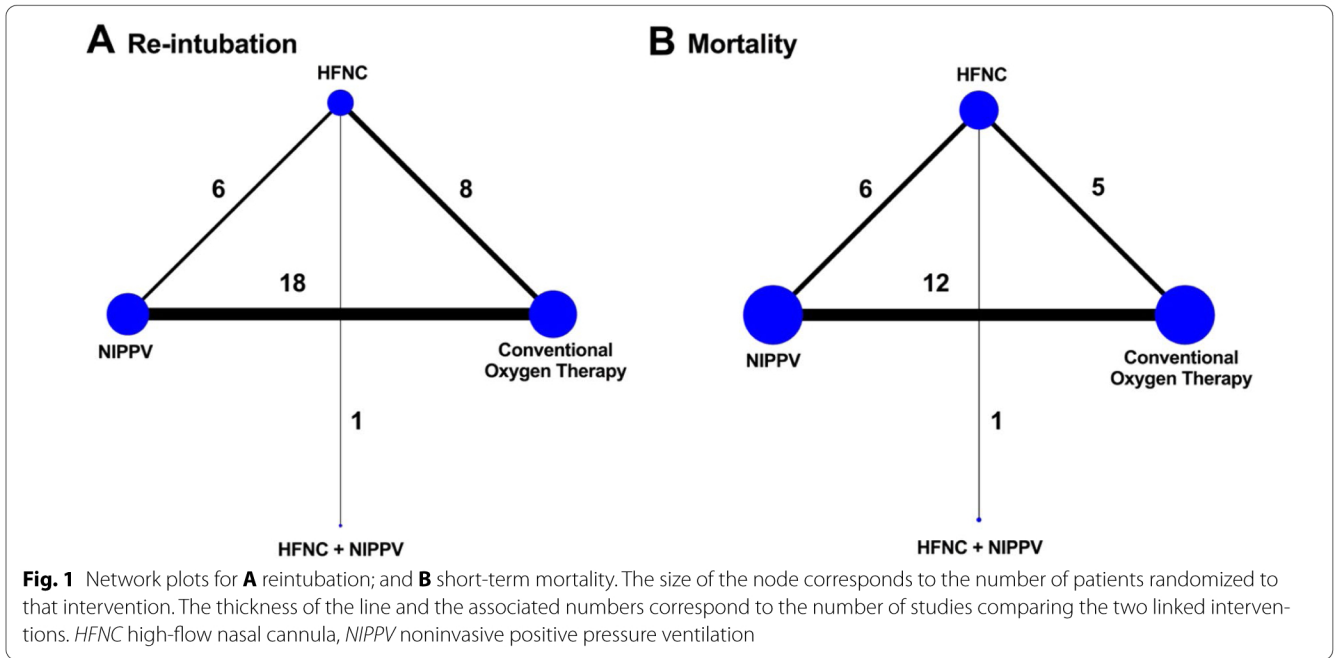


Table 2 Network and absolute estimates evaluating the efficacy of the interventions for prevention of reintubation in critically ill adults

Comparison	Network odds ratio (95% CI)	Absolute risk difference (95% CI)	Number needed to treat	GRADE
NIPPV vs conventional oxygen	0.65 (0.52–0.82)	– 5.18 (– 8.09 to – 2.26)	20 (13 to 45)	Moderate ^a
HFNC vs conventional oxygen	0.63 (0.45–0.87)	– 3.84 (– 6.7 to – 0.98)	26 (15 to 102)	Moderate ^a
NIPPV vs HFNC	1.04 (0.78–1.38)	– 1.34 (– 4.4 to 1.72)	N/A	Low ^{a,b}
HFNC + NIPPV vs conventional oxygen	0.38 (0.19–0.74)	– 10.25 (– 18.49 to – 2.01)	10 (6 to 50)	Moderate ^a
HFNC + NIPPV vs NIPPV	0.58 (0.3–1.11)	– 5.07 (– 13.38 to 3.24)	N/A	Low ^{a,b}
HFNC + NIPPV vs HFNC	0.6 (0.33–1.08)	– 6.41 (– 14.13 to 1.31)	N/A	Low ^{a,b}

NIPPV noninvasive positive pressure ventilation, HFNC high-flow nasal cannula, GRADE grading of recommendations assessment, development, and evaluation, OR odds ratio, CI confidence interval

^a Lowered for risk of bias

^b Lowered one level for imprecision as CIs don't exclude harm

Mortality

The efficacy of these treatments in preventing short-term all-cause mortality is depicted in the network plot (Fig. 2b), with summary findings displayed in Table 3. Compared to conventional oxygen therapy, neither NIPPV (OR 0.8 [95% CI 0.61–1.04]; absolute risk difference – 1.65 [95% CI – 3.81 to 0.5], moderate certainty), nor HFNC (OR 0.9 [95% CI 0.66–1.24]; absolute risk difference – 0.29 [95% CI – 1.58 to 1.01]), were associated with reduced short-term mortality, based on low certainty evidence. NIPPV did not reduce mortality compared to HFNC (OR 0.89 [95% CI 0.69–1.13]; absolute risk difference – 1.37 [95% CI – 3.47 to 0.72], moderate certainty). Direct estimates, indirect estimates, and SUCRA table are shown in Supplemental Table 4.

Ventilator-associated pneumonia, discomfort, and other outcomes

Compared to conventional oxygen therapy, both NIPPV (OR 0.39 [95% CI 0.25–0.61]) and HFNC (OR 0.35 [95% CI 0.21–0.59]) were associated with a reduced incidence of VAP (moderate certainty) (Supplemental Table 5). As documented by clinician ratings or patient-reported experience, NIPPV was associated with increased patient discomfort (OR 30.89 [95% CI 1.48–645.7], low certainty), compared to conventional oxygen therapy (Supplemental Table 6). Finally, comparison between the treatments and outcomes including ICU length of stay (Supplemental Table 7) and incidence of tracheostomy (Supplemental Fig. 3) were uncertain, due to very low certainty of evidence.

Table 3 Network estimates evaluating the efficacy of the interventions for prevention of short-term all-cause mortality in critically ill adults

Comparison	Network odds ratio (95% CI)	Absolute risk difference (95% CI)	GRADE
NIPPV vs conventional oxygen	0.8 (0.61–1.04)	– 1.65 (– 3.81 to 0.5)	Moderate ^b
HFNC vs conventional oxygen	0.9 (0.66–1.24)	– 0.29 (– 1.58 to 1.01)	Low ^a
NIPPV vs HFNC	0.89 (0.69–1.13)	– 1.37 (– 3.47 to 0.72)	Moderate ^b
HFNC + NIPPV vs conventional oxygen	0.95 (0.56–1.62)	0.41 (– 5.36 to 6.18)	Low ^a
HFNC + NIPPV vs NIPPV	1.19 (0.73–1.95)	2.07 (– 3.93 to 8.07)	Low ^a
HFNC + NIPPV vs HFNC	1.05 (0.69–1.62)	0.7 (– 4.93 to 6.33)	Low ^a

NIPPV noninvasive positive pressure ventilation, HFNC high-flow nasal cannula, GRADE grading of recommendations assessment, development, and evaluation, OR odds ratio, CI confidence interval

Imprecision only incorporated at network level not at direct or indirect

^a Lowered two levels for imprecision as wide CIs don't exclude important harm

^b Lowered one level for imprecision as CIs don't exclude harm

Subgroup and sensitivity analyses

The results of network meta-regression among the subgroups of interest (proportion of surgical patients, proportion of “high risk” patients, proportion of hypercapnic patients, and by continent) for the outcomes of reintubation and short-term mortality are shown in Supplemental Tables 8–9. We did not find evidence of an effect modification among subgroups of patient populations, but did find evidence for statistically significant effect modification by continent of study publication, with trials conducted in Europe demonstrating greater efficacy of NIPPV and HFNC, as compared to conventional oxygen therapy. However, the credibility of this subgroup finding was judged to be low. Table 4 shows that compared to conventional oxygen, the predicted absolute effect of NIPPV, HFNC, and alternating HFNC and NIPPV for prevention of reintubation are highest in patients at increased baseline risk of reintubation.

The sensitivity analyses that only included studies testing the efficacy of noninvasive respiratory support for prevention or prophylaxis are shown in Supplemental

Tables 10–12, and are consistent with the primary analyses. Conversely, pairwise meta-analyses did not demonstrate benefit of noninvasive ventilation in reducing reintubation or death when provided as rescue therapy (Supplemental Figs. 4–5).

Discussion

Extubation failure is a critical outcome that is prognostically important (i.e., associated with mortality) and is patient-important [9, 10]. Therefore, treatments that may mitigate the risk of reintubation are of value to a variety of stakeholders [70]. Although noninvasive respiratory support in the post-extubation period has been studied, there is variation in its use in this setting [71], and providers have expressed skepticism in its efficacy [15]. In this context, we found evidence suggesting that both NIPPV and HFNC reduced reintubation in the post-extubation period compared to conventional oxygen therapy, with increased effect size in patients with the highest baseline risk for reintubation. These effects were present when noninvasive respiratory support

Table 4 Predicted absolute network estimates (with 95% confidence intervals) for efficacy of the interventions for prevention of reintubation in critically ill adults, using baseline risk for reintubation

Comparison	NIPPV (compared to conventional oxygen)		HFNC (compared to conventional oxygen)		HFNC + NIPPV (compared to conventional oxygen)	
	Absolute estimate ^a	NNT	Absolute estimate	NNT	Absolute estimate	NNT
5% risk of reintubation	– 1.69 (– 2.4 to – 0.81)	60 (42 to 124)	– 1.84 (– 2.74 to – 0.57)	55 (37 to 176)	– 3.09 (– 4.06 to – 1.11)	33 (25 to 91)
10% risk of reintubation	– 3.26 (– 4.64 to – 1.56)	31 (22 to 65)	– 3.56 (– 5.34 to – 1.09)	29 (19 to 92)	– 6.05 (– 8.04 to – 2.12)	17 (12 to 48)
20% risk of reintubation	– 6.02 (– 8.69 to – 2.82)	17 (12 to 36)	– 6.58 (– 10.09 to – 1.97)	16 (10 to 51)	– 11.53 (– 15.69 to – 3.86)	9 (7 to 26)
40% risk of reintubation	– 9.77 (– 14.63 to – 4.38)	11 (7 to 23)	– 10.73 (– 17.32 to 3.03)	N/A	– 20.21 (– 29.29 to – 6.08)	5 (4 to 17)

HFNC high-flow nasal cannula, NIPPV noninvasive positive pressure ventilation, NNT number needed to treat

^a Absolute estimates refer to the risk difference between the interventions (NIPPV, HFNC, and HFNC + NIPPV) and conventional oxygen therapy

was used prophylactically following extubation, but not when it was applied for rescue in patients who were deteriorating post-extubation. Finally, no difference between NIPPV and HFNC was detected in prevention of reintubation. These data have important implications for providers, patients, and clinical practice guidelines.

The most recent iteration of the European Respiratory Society and American Thoracic Society clinical practice guidelines on the use of NIPPV, published in 2017, provided a conditional recommendation (low certainty) for its use in high-risk patients post-extubation, and a conditional recommendation (low certainty) against the use of NIPPV in low-risk patients post-extubation [72]. These recommendations were based on evidence existing at the time of guideline development, which showed benefit of NIPPV only in selected populations. Use of post-extubation HFNC was addressed in the more recent European Society of Intensive Care Medicine guideline, which provided a conditional recommendation (low certainty) for its use in high-risk patients who had received invasive ventilation for more than 24 h [73].

Our work has important implications in this regard. Here, we found evidence suggesting that both NIPPV and HFNC reduced the incidence of extubation failure in heterogeneous cohorts of ICU patients, without effect modification in higher risk patients, as demonstrated in our subgroup analyses. This reduction in reintubation likely contributed to the lower incidence of VAP among patients receiving noninvasive ventilation. Previous work comparing the use of NIPPV during weaning against invasive ventilation has demonstrated its superiority in reducing mortality, while preventing weaning failure and reducing ICU length of stay [74]. Our review builds upon this existing work, and shows that NIPPV is likely superior to conventional oxygen therapy in reducing reintubation in the post-extubation period. Compared to the existing guideline recommendations, our results are aligned with and reinforced by more recent randomized data, supporting more widespread use of noninvasive ventilation in the post-extubation period. In light of these new trials and findings, updated guidelines are warranted.

Further to this, our review evaluated heterogeneity of treatment effect, which has implications for the application of our findings. Of note, the effect size of these interventions was greatest for patients at highest baseline risk of reintubation. For example, as compared to conventional oxygen, NIPPV had a NNT for prevention of reintubation of 60 among patients with a 5% baseline risk of reintubation, but a NNT of 11 in patients with a 40% baseline risk. This is important in evaluating the use of these therapies relative to their resource use and individual costs. That is, routine use of noninvasive ventilation may be considered in high-risk patient populations,

but the purported benefits may not outweigh associated resource use and costs in low-risk populations.

We performed further sensitivity analyses comparing the use of noninvasive respiratory support therapies for prevention/prophylaxis, or rescue of symptomatic patients. Our findings were replicated among trials evaluating use of noninvasive ventilation for prevention or prophylaxis, supporting the efficacy of these therapies in this context. However, we did not find similar efficacy of noninvasive ventilation in the rescue of symptomatic patients post-extubation. We found only one ICU trial demonstrating benefit of NIPPV in the rescue setting [46], and this trial was conducted in post-operative patients where post-extubation hypoxemia is most likely secondary to atelectasis, and where NIPPV has been shown to have some evidence of benefit in ward patients [75, 76]. In mixed ICU populations, rescue use of NIPPV post-extubation was not beneficial, and indeed may be associated with harm [38]. Together, our work importantly differentiates between these two clinical indications, and identifies disparate conclusions favouring use in prophylactic application, but not rescue.

Our findings were less conclusive when examining the differences in effect between NIPPV and HFNC. Although HFNC does have some theoretical benefits compared to NIPPV (e.g., improved patient comfort, and fewer hemodynamic consequences), we found no difference in terms of reintubation or mortality for NIPPV compared to HFNC. HFNC generally consumes fewer healthcare resources and is more suitable for use outside the ICU setting, while NIPPV is typically applied in an ICU or step-down unit [52]. Whether NIPPV is superior to HFNC in this context remains unclear, underscoring the need for further trials. Finally, we evaluated the alternating combination of HFNC and NIPPV, and found that it did not reduce the incidence of reintubation, compared to either alone (low certainty evidence). For now, the use of this combination could be considered efficacious in patients at high risk of extubation failure (as shown in the HIGH-WEAN trial [65]), and if tolerated, could be considered over either NIPPV or HFNC alone.

This review has several strengths, including a broad search, and a pre-registered protocol. We included 36 RCTs with over 6800 patients. We conducted rigorous subgroup and sensitivity analyses to test the robustness of our findings across populations and indications, and applied GRADE to rate the certainty of estimates. There are also important limitations. First, all included trials were judged to be at potentially high risk-of-bias for blinding, as blinding of treating clinicians to treatment allocation among noninvasive respiratory support interventions is difficult. However, we accounted

for this through GRADE ratings, downrating confidence for subjective outcomes (e.g., reintubation). The results of network meta-analyses may potentially be influenced by indirect evidence, which may have issues related to transitivity. However, in this review, we did not find issues with intransitivity, and the network estimates were largely driven by direct data, with coherent indirect data. Second, the included trials enrolled heterogeneous subgroups, as well as combined studies evaluating various indications for noninvasive ventilation (prevention vs. rescue). However, we mitigated concerns related to this through important subgroup and sensitivity analyses, which indicate the scenarios where noninvasive respiratory support may be of greatest benefit. Unfortunately, there were some sources of heterogeneity (such as definition of “extubation failure”, definition of “VAP”, or proportion of patients with obesity) that could not be accounted for by secondary analyses, and must be taken into consideration. Third, we included only English-language RCTs. Finally, trials did not report costs such as consumables, clinician time, and other aspects of resource utilization, which may influence practice or policy decisions.

Conclusion

Our results suggest that both NIPPV and HFNC are efficacious in reducing the incidence of reintubation, compared to conventional oxygen therapy. The magnitude of treatment effect of these interventions is highest in patients at increased baseline risk of reintubation. Finally, these therapies appear efficacious in prophylactic application, but not for rescue in symptomatic patients following extubation. Taken together, our study has important implications for clinicians caring for mechanically ventilated adults, and should prompt re-evaluation of guidelines for the use of noninvasive respiratory support for the treatment of critically ill patients post-extubation.

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Author contributions

SMF, AJES, and BR conceived the study idea. SMF and BR coordinated the systematic review. SMF and AT designed the search strategy. SMF and AT screened abstracts and full texts. SMF and AT acquired the data and judged risk of bias in the studies. BS verified the data and performed the analyses. BR created the GRADE evidence profiles. All authors interpreted the data analyses. All authors co-wrote and revised the manuscript for intellectual content. All authors provided their final approval for manuscript submission. AJES and BR contributed equally as co-senior authors. All authors agree to be accountable for all aspects of the work. SMF is guarantor.

Funding

None.

Declarations

Conflicts of interest

SMF has no conflicts to report. AT has no conflicts to report. BS reports receiving funding from PIPRA AG, outside of the submitted work. KEAB is supported by a Physician Services Incorporated-50 Mid-Career Clinical Award. EF reports receiving personal fees from ALung Technologies, Baxter, Boehringer-Ingelheim, Fresenius Medical Care, and MC3 Cardiopulmonary, outside of the submitted work. DB reports receiving research support from ALung Technologies, outside of the submitted work, and was previously on their medical advisory board. He has been on the medical advisory boards for Baxter, Abiomed, Xenios, and Hemovent. LM has no conflicts to report. ECG is supported by an Early Career Investigator Award from the Canadian Institutes of Health Research. DJC is supported by a Canada Research Chair in Critical Care Knowledge Translation. RAF is the H. Barrie Fairley Professor of Critical Care at the University Health Network and Interdepartmental Division of Critical Care Medicine at the University of Toronto. MSH has no conflicts to report. PC has no conflicts to report. SJ reports receiving personal fees from Drager, Fisher & Paykel, Medtronic, and Baxter, outside of the submitted work. MHM has no conflicts to report. AWT reports receiving grants from the French Ministry of Health and personal fees from Fisher & Paykel, Maquet-Getinge, GE Healthcare, and Covidien, outside of the submitted work. NDF reports consulting for Baxter and Xenios, outside of the submitted work. ASS reports consulting for Baxter and Xenios, outside of the submitted work. LJB has no conflicts to report. AJES holds patents related to multiorgan variability analysis, and has shares in Therapeutic Monitoring Systems Inc., outside of the submitted work. BR has no conflicts to report.

Ethics approval

Not required.

References

1. Wunsch H, Linde-Zwirble WT, Angus DC, Hartman ME, Milbrandt EB, Kahn JM (2010) The epidemiology of mechanical ventilation use in the United States. *Crit Care Med* 38:1947–1953
2. Adhikari NK, Fowler RA, Bhagwanjee S, Rubenfeld GD (2010) Critical care and the global burden of critical illness in adults. *Lancet* 376:1339–1346
3. Klompas M (2013) Complications of mechanical ventilation—the CDC’s new surveillance paradigm. *N Engl J Med* 368:1472–1475
4. Dres M, Dubé BP, Mayaux J, Delemazure J, Reuter D, Brochard L, Similowski T, Demoule A (2017) Coexistence and impact of limb muscle and diaphragm weakness at time of liberation from mechanical ventilation in medical intensive care unit patients. *Am J Respir Crit Care Med* 195:57–66
5. Zaal IJ, Devlin JW, Peelen LM, Slooter AJ (2015) A systematic review of risk factors for delirium in the ICU. *Crit Care Med* 43:40–47
6. Dasta JF, McLaughlin TP, Mody SH, Piech CT (2005) Daily cost of an intensive care unit day: the contribution of mechanical ventilation. *Crit Care Med* 33:1266–1271
7. Burns KEA, Rizvi L, Cook DJ, Lebovic G, Dodek P, Villar J, Slutsky AS, Jones A, Kapadia FN, Gattas DJ, Epstein SK, Pelosi P, Kefala K, Meade MO (2021) Ventilator weaning and discontinuation practices for critically ill patients. *JAMA* 325:1173–1184
8. Thille AW, Cortés-Puch I, Esteban A (2013) Weaning from the ventilator and extubation in ICU. *Curr Opin Crit Care* 19:57–64
9. Thille AW, Harrois A, Schortgen F, Brun-Buisson C, Brochard L (2011) Outcomes of extubation failure in medical intensive care unit patients. *Crit Care Med* 39:2612–2618
10. Frutos-Vivar F, Esteban A, Apezteguia C, González M, Arabi Y, Restrepo MI, Gordo F, Santos C, Alhashemi JA, Pérez F, Peñuelas O, Anzueto A (2011) Outcome of reintubated patients after scheduled extubation. *J Crit Care* 26:502–509
11. Thille AW, Richard JC, Brochard L (2013) The decision to extubate in the intensive care unit. *Am J Respir Crit Care Med* 187:1294–1302
12. De Jong A, Casey JD, Myatra SN (2020) Focus on noninvasive respiratory support before and after mechanical ventilation in patients with acute respiratory failure. *Intensive Care Med* 46:1460–1463
13. Ferreyro BL, Angriman F, Munshi L, Del Sorbo L, Ferguson ND, Rochweg B, Ryu MJ, Saskin R, Wunsch H, da Costa BR, Scales DC (2020) Association of noninvasive oxygenation strategies with all-cause mortality in adults with acute hypoxemic respiratory failure: a systematic review and meta-analysis. *JAMA* 324:57–67
14. Vignaux L, Vargas F, Roeseler J, Tassaux D, Thille AW, Kossowsky MP, Brochard L, Jolliet P (2009) Patient-ventilator asynchrony during non-invasive ventilation for acute respiratory failure: a multicenter study. *Intensive Care Med* 35:840–846
15. Nuzzo EA, Kahn JM, Girard TD (2020) Provider perspectives on preventive postextubation noninvasive ventilation for high-risk intensive care unit patients. *Ann Am Thorac Soc* 17:246–249
16. Schnell D, Timsit JF, Darmon M, Vesin A, Goldgran-Toledano D, Dumenil AS, Garrouste-Orgeas M, Adrie C, Bouadma L, Planquette B, Cohen Y, Schwebel C, Soufir L, Jamali S, Souweine B, Azoulay E (2014) Noninvasive mechanical ventilation in acute respiratory failure: trends in use and outcomes. *Intensive Care Med* 40:582–591
17. Esteban A, Frutos-Vivar F, Muriel A, Ferguson ND, Peñuelas O, Abraira V, Raymondos K, Rios F, Nin N, Apezteguia C, Violi DA, Thille AW, Brochard L, González M, Villagomez AJ, Hurtado J, Davies AR, Du B, Maggiore SM, Pelosi P, Soto L, Tomacic V, D’Empaire G, Matamis D, Abroug F, Moreno RP, Soares MA, Arabi Y, Sandi F, Jibaja M, Amin P, Koh Y, Kuiper MA, Bülow HH, Zeggwagh AA, Anzueto A (2013) Evolution of mortality over time in patients receiving mechanical ventilation. *Am J Respir Crit Care Med* 188:220–230
18. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D (2021) The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 372:n71
19. Hutton B, Salanti G, Caldwell DM, Chaimani A, Schmid CH, Cameron C, Ioannidis JP, Straus S, Thorlund K, Jansen JP, Mulrow C, Catalá-López F, Gøtzsche PC, Dickersin K, Boutron I, Altman DG, Moher D (2015) The PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions: checklist and explanations. *Ann Intern Med* 162:777–784
20. Sampson M, Shojania KG, McGowan J, Daniel R, Rader T, Iansavichene AE, Ji J, Ansari MT, Moher D (2008) Surveillance search techniques identified the need to update systematic reviews. *J Clin Epidemiol* 61:755–762
21. Casey JD, Vaughan EM, Lloyd BD, Billas PA, Jackson KE, Hall EJ, Toporek AH, Buell KG, Brown RM, Richardson RK, Rooks JC, Buie RB, Wang L, Lindsell CJ, Ely EW, Self WH, Bernard GR, Rice TW, Semler MW (2021) Protocolized post-extubation respiratory support to prevent reintubation: a randomized clinical trial. *Am J Respir Crit Care Med* 204:294–302
22. Hozo SP, Djulbegovic B, Hozo I (2005) Estimating the mean and variance from the median, range, and the size of a sample. *BMC Med Res Methodol* 5:13
23. Guyatt GH, Busse JW, Modification of cochrane tool to assess risk of bias in randomized trials. <https://www.evidencepartners.com/resources/methodological-resources/>. Accessed 15 Oct 2021
24. DerSimonian R, Laird N (1986) Meta-analysis in clinical trials. *Control Clin Trials* 7:177–188
25. White IR (2015) Network meta-analysis. *Stata J* 15:951–985
26. White IR, Barrett JK, Jackson D, Higgins JP (2012) Consistency and inconsistency in network meta-analysis: model estimation using multivariate meta-regression. *Res Synth Methods* 3:111–125
27. Higgins JP, Jackson D, Barrett JK, Lu G, Ades AE, White IR (2012) Consistency and inconsistency in network meta-analysis: concepts and models for multi-arm studies. *Res Synth Methods* 3:98–110
28. Higgins JP, Thompson SG, Deeks JJ, Altman DG (2003) Measuring inconsistency in meta-analyses. *BMJ* 327:557–560
29. Lu G, Ades AE (2006) Assessing evidence inconsistency in mixed treatment comparisons. *J Am Stat Assoc* 101:447–459
30. Harbord RM, Egger M, Sterne JA (2006) A modified test for small-study effects in meta-analyses of controlled trials with binary endpoints. *Stat Med* 25:3443–3457
31. Schandelmaier S, Briel M, Varadhan R, Schmid CH, Devasenapathy N, Hayward RA, Gagnier J, Borenstein M, van der Heijden G, Dahabreh IJ, Sun X, Sauerbrei W, Walsh M, Ioannidis JPA, Thabane L, Guyatt GH (2020) Development of the Instrument to assess the Credibility of Effect Modification Analyses (ICEMAN) in randomized controlled trials and meta-analyses. *CMAJ* 192:E901–e906
32. Brignardello-Petersen R, Bonner A, Alexander PE, Siemieniuk RA, Furukawa TA, Rochweg B, Hazlewood GS, Alhazzani W, Mustafa RA, Murad MH, Puhon MA, Schünemann HJ, Guyatt GH (2018) Advances in the GRADE approach to rate the certainty in estimates from a network meta-analysis. *J Clin Epidemiol* 93:36–44
33. Brignardello-Petersen R, Florez ID, Izcovich A, Santesso N, Hazlewood G, Alhazzani W, Yepes-Nuñez JJ, Tomlinson G, Schünemann HJ, Guyatt GH (2020) GRADE approach to drawing conclusions from a network meta-analysis using a minimally contextualised framework. *BMJ* 371:m3900
34. Al Jaaly E, Fiorentino F, Reeves BC, Ind PW, Angelini GD, Kemp S, Shiner RJ (2013) 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* 146:912–918
35. Brainard J, Scott BK, Sullivan BL, Fernandez-Bustamante A, Piccoli JR, Gebbink MG, Bartels K (2017) Heated humidified high-flow nasal cannula oxygen after thoracic surgery—a randomized prospective clinical pilot trial. *J Crit Care* 40:225–228
36. Cho JY, Kim HS, Kang H, Kim SH, Choe KH, Lee KM, Shin YM (2020) 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 Med Sci* 35:e194
37. Corley A, Bull T, Spooner AJ, Barnett AG, Fraser JF (2015) Direct extubation onto high-flow nasal cannulae post-cardiac surgery versus standard treatment in patients with a BMI \geq 30: a randomised controlled trial. *Intensive Care Med* 41:887–894
38. Esteban A, Frutos-Vivar F, Ferguson ND, Arabi Y, Apezteguia C, González M, Epstein SK, Hill NS, Nava S, Soares MA, D’Empaire G, Alía I, Anzueto A (2004) Noninvasive positive-pressure ventilation for respiratory failure after extubation. *N Engl J Med* 350:2452–2460
39. Fernandez R, Subira C, Frutos-Vivar F, Rialp G, Laborada C, Masclans JR, Lesmes A, Panadero L, Hernandez G (2017) High-flow nasal cannula to

- prevent postextubation respiratory failure in high-risk non-hypercapnic patients: a randomized multicenter trial. *Ann Intensive Care* 7:47
40. Ferrer M, Valencia M, Nicolas JM, Bernadich O, Badia JR, Torres A (2006) Early noninvasive ventilation averts extubation failure in patients at risk: a randomized trial. *Am J Respir Crit Care Med* 173:164–170
 41. Ferrer M, Sellarés J, Valencia M, Carrillo A, Gonzalez G, Badia JR, Nicolas JM, Torres A (2009) Non-invasive ventilation after extubation in hypercapnic patients with chronic respiratory disorders: randomised controlled trial. *Lancet* 374:1082–1088
 42. Futier E, Paugam-Burtz C, Godet T, Khojy-Ear L, Rozenccwajg S, Delay JM, Verzilli D, Dupuis J, Chanques G, Bazin JE, Constantin JM, Pereira B, Jaber S (2016) 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). *Intensive Care Med* 42:1888–1898
 43. Girault C, Bubenheim M, Abroug F, Diehl JL, Elatrous S, Beuret P, Rich-ecoeur J, L'Her E, Hilbert G, Capellier G, Rabbat A, Besbes M, Guérin C, Guiot P, Bénichou J, Bonmarchand G (2011) Noninvasive ventilation and weaning in patients with chronic hypercapnic respiratory failure: a randomized multicenter trial. *Am J Respir Crit Care Med* 184:672–679
 44. Hernández G, Vaquero C, Colinas L, Cuenca R, González P, Canabal A, Sanchez S, Rodríguez ML, Villasclaras A, Fernández R (2016) 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* 316:1565–1574
 45. Hernández G, Vaquero C, González P, Subira C, Frutos-Vivar F, Rialp G, Laborda C, Colinas L, Cuenca R, Fernández R (2016) Effect of postextubation high-flow nasal cannula vs conventional oxygen therapy on reintubation in low-risk patients: a randomized clinical trial. *JAMA* 315:1354–1361
 46. Jaber S, Lescot T, Futier E, Paugam-Burtz C, Seguin P, Ferrandiere M, Lasocki S, Mimoz O, Hengy B, Sannini A, Pottecher J, Abback PS, Riu B, Belafia F, Constantin JM, Masseret E, Beaussier M, Verzilli D, De Jong A, Chanques G, Brochard L, Molinari N (2016) Effect of noninvasive ventilation on tracheal reintubation among patients with hypoxemic respiratory failure following abdominal surgery: a randomized clinical trial. *JAMA* 315:1345–1353
 47. Jiang JS, Kao SJ, Wang SN (1999) Effect of early application of biphasic positive airway pressure on the outcome of extubation in ventilator weaning. *Respirology* 4:161–165
 48. Jing G, Li J, Hao D, Wang T, Sun Y, Tian H, Fu Z, Zhang Y, Wang X (2019) 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 Health* 42:217–225
 49. Keenan SP, Powers C, McCormack DG, Block G (2002) Noninvasive positive-pressure ventilation for postextubation respiratory distress: a randomized controlled trial. *JAMA* 287:3238–3244
 50. Khilnani GC, Galle AD, Hadda V, Sharma SK (2011) Non-invasive ventilation after extubation in patients with chronic obstructive airways disease: a randomised controlled trial. *Anaesth Intensive Care* 39:217–223
 51. Kindgen-Milles D, Müller E, Buhl R, Böhner H, Ritter D, Sandmann W, Tarnow J (2005) Nasal-continuous positive airway pressure reduces pulmonary morbidity and length of hospital stay following thoracoabdominal aortic surgery. *Chest* 128:821–828
 52. Maggiore SM, Idone FA, Vaschetto R, Festa R, Cataldo A, Antonicelli F, Montini L, De Gaetano A, Navalesi P, Antonelli M (2014) Nasal high-flow versus Venturi mask oxygen therapy after extubation. Effects on oxygenation, comfort, and clinical outcome. *Am J Respir Crit Care Med* 190:282–288
 53. Matsuda W, Hagiwara A, Uemura T, Sato T, Kobayashi K, Sasaki R, Okamoto T, Kimura A (2020) High-flow nasal cannula may not reduce the re-intubation rate compared with a large-volume nebulization-based humidifier. *Respir Care* 65:610–617
 54. Mohamed KAE, Abdalla MH (2013) Role of noninvasive ventilation in limiting re-intubation after planned extubation. *Egypt J Chest Dis Tuberc* 62:669–674
 55. Nava S, Gregoretti C, Fanfulla F, Squadrone E, Grassi M, Carlucci A, Beltrame F, Navalesi P (2005) Noninvasive ventilation to prevent respiratory failure after extubation in high-risk patients. *Crit Care Med* 33:2465–2470
 56. Ornico SR, Lobo SM, Sanches HS, Deberaldini M, Tófoli LT, Vidal AM, Schettino GP, Amato MB, Carvalho CR, Barbas CS (2013) Noninvasive ventilation immediately after extubation improves weaning outcome after acute respiratory failure: a randomized controlled trial. *Crit Care* 17:R39
 57. Parke R, McGuinness S, Dixon R, Jull A (2013) Open-label, phase II study of routine high-flow nasal oxygen therapy in cardiac surgical patients. *Br J Anaesth* 111:925–931
 58. Song HZ, Gu JX, Xiu HQ, Cui W, Zhang GS (2017) The value of high-flow nasal cannula oxygen therapy after extubation in patients with acute respiratory failure. *Clinics (Sao Paulo)* 72:562–567
 59. Stéphan F, Barrucand B, Petit P, Rézaiguia-Delclaux S, Médard A, Delannoy B, Cosserant B, Flicoteaux G, Imbert A, Pilorge C, Bérard L (2015) High-flow nasal oxygen vs noninvasive positive airway pressure in hypoxemic patients after cardiothoracic surgery: a randomized clinical trial. *JAMA* 313:2331–2339
 60. Su CL, Chiang LL, Yang SH, Lin HI, Cheng KC, Huang YC, Wu CP (2012) Preventive use of noninvasive ventilation after extubation: a prospective, multicenter randomized controlled trial. *Respir Care* 57:204–210
 61. Tan D, Walline JH, Ling B, Xu Y, Sun J, Wang B, Shan X, Wang Y, Cao P, Zhu Q, Geng P, Xu J (2020) 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* 24:489
 62. Tatsuishi W, Sato T, Kataoka G, Sato A, Asano R, Nakano K (2020) High-flow nasal cannula therapy with early extubation for subjects undergoing off-pump coronary artery bypass graft surgery. *Respir Care* 65:183–190
 63. Thanthitaweevat V, Muntham D, Chirakalwasan N (2018) Targeted-volume noninvasive ventilation reduces extubation failure in postextubated medical intensive care unit patients: a randomized controlled trial. *Indian J Crit Care Med* 22:639–645
 64. Theerawit P, Natpobsuk N, Petnak T, Sutherasan Y (2020) 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* 63:117–123
 65. Thille AW, Muller G, Gacouin A, Coudroy R, Decavèle M, Sonnevile R, Beloncle F, Girault C, Dangers L, Lautrette A, Cabasson S, Rouzé A, Vivier E, Le Meur A, Ricard JD, Razazi K, Barberet G, Lebert C, Ehrmann S, Sabatier C, Bourenne J, Pradel G, Bailly P, Terzi N, Dellamonica J, Lacave G, Danin P, Nanadoumgar H, Gibelin A, Zanre L, Deye N, Demoule A, Maamar A, Nay MA, Robert R, Ragot S, Frat JP (2019) 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* 322:1465–1475
 66. Tongyoo S, Tantibundit P, Daorattanachai K, Viarasilpa T, Permpikul C, Udompanturak S (2021) High-flow nasal oxygen cannula vs. noninvasive mechanical ventilation to prevent reintubation in sepsis: a randomized controlled trial. *Ann Intensive Care* 11:135
 67. Vargas F, Clavel M, Sanchez-Verlan P, Garnier S, Boyer A, Bui HN, Clouzeau B, Sazio C, Kerchache A, Guisset O, Benard A, Asselineau J, Gauche B, Gruson D, Silva S, Vignon P, Hilbert G (2017) Intermittent noninvasive ventilation after extubation in patients with chronic respiratory disorders: a multicenter randomized controlled trial (VHYPER). *Intensive Care Med* 43:1626–1636
 68. Vaschetto R, Longhini F, Persona P, Ori C, Stefani G, Liu S, Yi Y, Lu W, Yu T, Luo X, Tang R, Li M, Li J, Cammarota G, Bruni A, Garofalo E, Jin Z, Yan J, Zheng R, Yin J, Guido S, Della Corte F, Fontana T, Gregoretto C, Cortegiani A, Giarratano A, Montagnini C, Cavuto S, Qiu H, Navalesi P (2019) Early extubation followed by immediate noninvasive ventilation vs. standard extubation in hypoxemic patients: a randomized clinical trial. *Intensive Care Med* 45:62–71
 69. Yang Y, Liu N, Sun L, Zhou Y, Yang Y, Shang W, Li X (2016) Noninvasive positive-pressure ventilation in treatment of hypoxemia after extubation following type-A aortic dissection. *J Cardiothorac Vasc Anesth* 30:1539–1544
 70. Goligher EC, Peñuelas O (2021) Post-extubation respiratory support: of clinical trials and clinical decisions. *Am J Respir Crit Care Med* 204(3):245–247
 71. Crimi C, Noto A, Princi P, Esquinas A, Nava S (2010) A European survey of noninvasive ventilation practices. *Eur Respir J* 36:362–369
 72. Rochweg B, Brochard L, Elliott MW, Hess D, Hill NS, Nava S, Navalesi PMOTSC, Antonelli M, Brozek J, Conti G, Ferrer M, Guntupalli K, Jaber S,

Keenan S, Mancebo J, Mehta S, Raoof SMOTTF (2017) Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure. *Eur Respir J* 50:1602426

73. Rochwerg B, Einav S, Chaudhuri D, Mancebo J, Mauri T, Helviz Y, Goligher EC, Jaber S, Ricard JD, Rittayamai N, Roca O, Antonelli M, Maggiore SM, Demoule A, Hodgson CL, Mercat A, Wilcox ME, Granton D, Wang D, Azoulay E, Ouanes-Besbes L, Cinnella G, Rauseo M, Carvalho C, Dessap-Mekontso A, Fraser J, Frat JP, Gomersall C, Grasselli G, Hernandez G, Jog S, Pesenti A, Riviello ED, Slutsky AS, Stapleton RD, Talmor D, Thille AW, Brochard L, Burns KEA (2020) The role for high flow nasal cannula as a respiratory support strategy in adults: a clinical practice guideline. *Intensive Care Med* 46:2226–2237
74. Burns KEA, Stevenson J, Laird M, Adhikari NKJ, Li Y, Lu C, He X, Wang W, Liang Z, Chen L, Zhang H, Friedrich JO (2021) Non-invasive ventilation

versus invasive weaning in critically ill adults: a systematic review and meta-analysis. *Thorax* 216993. <https://doi.org/10.1136/thoraxjnl-2021-216993>

75. Squadrone V, Cocha M, Cerutti E, Schellino MM, Biolino P, Occella P, Belloni G, Vilianis G, Fiore G, Cavallo F, Ranieri VM (2005) Continuous positive airway pressure for treatment of postoperative hypoxemia: a randomized controlled trial. *JAMA* 293:589–595
76. (2021) Postoperative continuous positive airway pressure to prevent pneumonia, re-intubation, and death after major abdominal surgery (PRISM): a multicentre, open-label, randomised, phase 3 trial. *Lancet Respir Med* 11:1221-1230