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WORLDVIEWS ON EVIDENCE-BASED NURSING

REVIEW ARTICLE

Respiratory support in the emergency department a systematic review and meta-analysis

Jane O'Donnell PhD Candidate[1] | Alison Pirret NP, PhD[2] | Karen Hoare NP, PhD[2] | Rebecca Fenn NP[2] | Elissa McDonald PhD[2]

[1]Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand

[2]Massey University, Auckland, New Zealand

Correspondence
Jane O'Donnell, Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand.
Email: jane.odonnell@auckland.ac.nz

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Abstract

Background: An estimated 20% of emergency department (ED) patients require respiratory support (RS). Evidence suggests that nasal high flow (NHF) reduces RS need.

Aims: This review compared NHF to conventional oxygen therapy (COT) or noninvasive ventilation (NIV) in adult ED patients.

Method: The systematic review (SR) and meta-analysis (MA) methods reflect the Cochrane Collaboration methodology. Six databases were searched for randomized controlled trials (RCTs) comparing NHF to COT or NIV use in the ED. Three summary estimates were reported: (1) need to escalate care, (2) mortality, and (3) adverse events (AEs).

Results: This SR and MA included 18 RCTs ($n = 1874$ participants). Two of the five MA conclusions were statistically significant. Compared with COT, NHF reduced the risk of escalation by 45% (RR 0.55; 95% CI [0.33, 0.92], $p = .02$, NNT = 32); however, no statistically significant differences in risk of mortality (RR 1.02; 95% CI [0.68, 1.54]; $p = .91$) and AE (RR 0.98; 95% CI [0.61, 1.59]; $p = .94$) outcomes were found. Compared with NIV, NHF increased the risk of escalation by 60% (RR 1.60; 95% CI [1.10, 2.33]; $p = .01$); mortality risk was not statistically significant (RR 1.23, 95% CI [0.78, 1.95]; $p = .37$).

Linking Evidence to Action: Evidence-based decision-making regarding RS in the ED is challenging. ED clinicians have at times had to rely on non-ED evidence to support their practice. Compared with COT, NHF was seen to be superior and reduced the risk of escalation. Conversely, for this same outcome, NIV was superior to NHF. However, substantial clinical heterogeneity was seen in the NIV delivered. Research considering NHF versus NIV is needed. COVID-19 has exposed the research gaps and slowed the progress of ED research.

KEYWORDS
COVID-19, emergency, high-flow nasal cannula, meta-analysis, nasal high flow, oxygenation, respiratory, systematic review

INTRODUCTION

Clinicians in the emergency department (ED) use a variety of therapies to deliver respiratory support (RS) to their spontaneously breathing patients. Historically, RS has been provided with noninvasive ventilation (NIV) or conventional oxygen therapy (COT). Nasal high-flow (NHF) therapy presents clinicians with another option when making decisions about the RS of ED patients. All forms of RS have advantages and disadvantages that should be clinical decision-making considerations (Hardavella et al., 2019; Popowicz & Leonard, 2022; Table 1). Clinical decision-making theories describe the dynamic nature of decision-making and the requirement for adaptability when identifying factors which influence patient care and outcomes. The patient outcome considered by this systematic review is a requirement for RS or the escalation of RS. Recognizing a requirement for RS or its escalation corresponds with the model of hypothetico-deductive reasoning and normative theory (Pearson, 2013). This systematic review (SR) of NHF ED evidence was completed to provide an evidence base for clinical decision-making around the delivery of RS in the ED.

The review patient population

The diverse ED patient population presents many complex life-threatening conditions that require emergency care; respiratory failure (RF) is an example. Dyspnea, increased WOB, and poor oxygenation are common in RF. Typically, those with RF present with either an arterial oxygen tension (PaO_2) of <60 mmHg or an arterial carbon dioxide tension ($PaCO_2$) of >45 mmHg or both (Roussos & Koutsoukou, 2003). Spontaneously breathing ED patients who require RS were the population of interest for this SR.

The review intervention

Nasal high-flow therapy was the intervention considered in this SR. This intervention was compared to noninvasive ventilation (NIV) or conventional oxygen therapy (COT). The terminology describing NHF is globally inconsistent with >20 terms and >10 abbreviations in current use; some of the common examples include high-flow nasal cannula (HFNC) and high-flow oxygen (HFO; Heikkilä & Korppi, 2019). Whilst the abbreviation NHF was used in this SR, the search incorporated the other available equivalent terms. Nasal high-flow therapy provides humidified medical gas to the upper respiratory tract through a specialized nasal cannula (the interface). The NHF humidifier conditions the inspiratory gases (up to 37°C and 100% relative humidity) and provides the same balance of warmth and humidity, just like healthy lungs. For adults, NHF therapy can deliver humidified medical gas at flow rates between 10 and 70 L/min with a fraction of inspired oxygen (FiO_2) between 0.21 (21% oxygen) and 1.0 (100% oxygen). Flow rate and FiO_2 levels can be modified independently (Mauri, Turrini, et al., 2017). Evidence confirms that NHF can optimize patient oxygenation and reduce their work of breathing (WOB) by (1) limiting entrainment of room air, which decreases available FiO_2; (2) reducing physiological airway dead space; (3) flushing expired carbon dioxide (CO_2) from the upper airway; (4) providing a dynamic, positive airway pressure that augments functional residual capacity (FRC); and (5) airway humidification for improved comfort and sputum clearance (Mauri, Turrini, et al., 2017). Despite evidence describing these benefits, NHF use and delivery are inconsistent in the ED, and evidence-based guidance is limited (Mitsuyama et al., 2022).

The review comparators

This SR involved two RS comparators, the so-called noninvasive ventilation (NIV) and conventional oxygen therapy (COT). Noninvasive ventilation (NIV) RS provides pressurized gas flows to spontaneously breathing patients. The options for RS pressure include continuous positive airway pressure (CPAP), where the pressure delivered is constant, or bi-level-positive airway pressure (BiPAP). The term BiPAP is sometimes used in practice to mean NIV. During BiPAP, there are two pressure settings: (1) inhalation (IPAP) and (2) exhalation (EPAP). BiPAP RS respects the pressure differential across the breathing cycle. Various NIV interfaces are positioned on the face or nose; these include helmets, full FM, and nasal masks. Noninvasive RS requires a reliable interface seal. Noninvasive ventilation is challenging to tolerate and requires expertise to deliver (Popowicz & Leonard, 2022). Conventional oxygen therapy RS includes nasal cannula (NC), face masks (FM), and nonrebreathing masks (NRM). Typically, low flows of <15 L/min of O_2 are provided and it is not heated or humidified, rather it is dry and cool. These interfaces are common; they are relatively inexpensive and easy to use (Popowicz & Leonard, 2022).

The review outcomes

Respiratory support may reduce the need to escalate care. Escalating care may include one or a combination of RS therapies: COT, NHF, NIV (Table S1), or invasive ventilation (INV). This SR compared the NHF intervention with NIV or COT for three SR outcomes: (1) *need to escalate care*, defined as the need to progress to NHF, NIV, or INV; (2) mortality; and (3) adverse event (AE) rates. Delayed RS escalation of RF patients is associated with increased mortality and morbidity (Roca et al., 2019; Slutsky & Ranieri, 2013).

METHODS

The PICO(S) theoretical framework was used to abstract and structure the SR question (Clephas & Heesen, 2022). The question asked in this SR was: "In adult ED patients requiring RS, what is the effect of RS with NHF compared to other forms of RS on patient outcomes?"

TABLE 1 Advantages and disadvantages of respiratory support therapies and interfaces compared (Hardavella et al., 2019; Popowicz & Leonard, 2022).

RS therapy	Flow (L/min)	FiO_2%	Indications	Advantages	Disadvantages
Nasal Cannula[a]	1–6	24–40 varies with entrainment	Spontaneous breathing Domiciliary O_2	Low cost Easy to use Mouth not obstructed	Gas not heated & humidified Unknown FiO_2 Cannot reduce WOB No dead space washout
Face Mask[a]	5–10	35–60 Varies with entrainment	Spontaneous breathing Nebulization	Low cost Easy to use	Gas not heated & humidified Unknown FiO_2 Claustrophobic Limited therapy Mouth obstructed Cannot reduce WOB No dead space washout
Venturi Mask[a]	2–15	24–50 Varies with entrainment	Spontaneous breathing	Low cost Easy to use	Gas not heated & humidified Variable FiO_2 Claustrophobic Mouth obstructed Cannot reduce WOB No dead space washout
Nonrebreather Mask[a]	10–15	24–50 Varies with entrainment	Spontaneous breathing	Low cost Easy to use	Gas not heated & humidified Variable FiO_2 Claustrophobic Mouth obstructed Cannot reduce WOB No dead space washout
Nasal high flow	10–70	21–100	Spontaneous breathing Respiratory failure	Fixed FiO_2 Open system Gas heated and humidified Improves mucous clearance Mouth not obstructed Meets insp flow demand PEEP Flushes dead space Can reduce WOB	Complex Noise High cost
Noninvasive ventilation	10–60	21–100	Spontaneous breathing Respiratory Failure	High costs Fixed FiO_2 Closed system Gas heated and humidified May improve mucous clearance Meets insp flow demand IPAP EPAP Can reduce WOB	Known AE High cost Complex Claustrophobic Uncomfortable Increases dead space Mouth obstructed Many contraindications: Facial trauma ± deformity Upper airway obstruction or bleed Reduced GCS </10 Inability to protect the airway

Abbreviations: AE, Adverse Event; Expiratory Positive Airway Pressure, EPAP; FiO_2, Fraction of Inspired Oxygen Percentage; Flow L/min FiO_2, Flow of gas liters per minute; GCS, Glasgow Coma Score; IPAP, Inspiratory Positive Airway Pressure; PEEP, Positive End Expiratory Pressure; RS, Respiratory Support; WOB, Work of Breathing.

[a]Conventional Oxygen Therapy.

The SR was completed as per its registered protocol (O'Donnell et al., 2022) and the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist (Page et al., 2021).

Study literature search and inclusion criteria

The scope and methods of this review precluded the inclusion of qualitative studies or nonrandomized trials, much like Cochrane SR of interventions (Higgins et al., 2023). The SR inclusion criteria were (1) RCT set in ED, (2) reporting on adults >18 years, and (3) comparing NHF versus COT or NIV. The exclusion criteria were (1) non-English, (2) non-RCT, and (3) gray literature due to its high risk of bias (RoB; Adams et al., 2016). The sensitivity of the search for NHF evidence was low given all the numerous names and acronyms for NHF (Heikkilä & Korppi, 2019). In consultation with two subject librarians, a search strategy was designed to locate RCTs for potential inclusion. The strategy included keywords and Medical Subject Headings (Table S2). The search was executed in six databases, two conference proceedings, and two clinical trial registries (SI Search Strategies).

Study data extraction

A data extraction form was developed to collect data comparing NHF, NIV (either continuous positive airway pressure (CPAP) or BiPAP), and all types of COT reporting on the three SR primary outcomes. Two reviewers used the data collection form to capture three categories of data: (1) study characteristics, (2) study outcomes, and (3) data for the risk of RoB assessment. One SR reviewer verified these extracted data prior to their synthesis and analysis. Covidence and RevMan platforms were used to support data extraction and RoB assessment (Review Manager, 2023). Two SR reviewers completed critical appraisals of the included studies, including the RoB assessments. The RoB assessment used the Cochrane RoB tool (Higgins et al., 2023). Six domains of bias were considered: (1) random sequence generation, (2) allocation concealment, (3) outcome assessment blinding, (4) incomplete outcome data, (5) selective reporting, and (6) other biases. Any RoB assessment for blinding was limited to outcome assessments as RS interventions cannot be blinded. The same Cochrane tool was used to classify RoB as *low*, *unclear*, or *high* for each domain. Evidence was classified as low RoB only if all bias domains were deemed low risk. The final RoB rating was the highest risk assigned to any risk domain.

Study data analysis

This SR analysis included a series of meta-analyses (MA) and a narrative synthesis (NS). The NS provided a descriptive summary of the review findings (Popay et al., 2005). In contrast, the MAs used numerical data to describe the overall or absolute treatment effects, where independent study data were able to be extracted and systematically merged. Study data were entered into RevMan Web (Cochrane Collaboration, 2020) for analysis. The reviewers employed well-established, systematic methods to manage differences in sample size and heterogeneity in the study approaches and reported treatment effects. These methods determined the sensitivity of SR findings and tested the methods' reliability (Higgins et al., 2023). Two estimates of treatment effect were completed: (1) risk ratio (RR) for dichotomous outcomes and (2) number needed to treat (NNT). The 95% confidence interval (CI) was used to describe the precision of effect for these two estimates. The threshold for statistical significance of the estimates was $p < .05$. As is now convention, both p values and z scores were reported. The z score reflects the magnitude of the treatment effect irrespective of sample size (Clephas & Heesen, 2022).

The standard unit of analysis for all outcomes was per participant as opposed to a treatment period. For example, pairwise comparisons were completed for multiple intervention studies, and multiple interventions were combined for analysis into a single intervention group. As per Cochrane methods, when multiple time points were reported in a single study, the most relevant time points preintervention, baseline, and first recorded time point postintervention were used (Higgins et al., 2023). The recorded first-time points after implementation of the interventions were inconsistent across the included studies.

As it is not uncommon for RCTs to have missing outcome data (Wood et al., 2004), therefore, every included study was appraised for missing data. If there had been a study with >20% of their primary outcome data missing, then its impact upon the MA would have been considered by sensitivity analysis.

The fixed-effect Mantel–Haenszel model was used to estimate the pooled overall adjusted RR and applied to MAs with no significant heterogeneity (Higgins et al., 2023). For completeness, the random effects model was also used to test whether the effects seen were consistent across both models (Figure S1).

Three forms of heterogeneity were explored. First, reviewers used their clinical judgment to examine sources of clinical heterogeneity. Second, methodological heterogeneity was explored during the RoB appraisal and the visual examination of the MA forest plots. Finally, the *I*-squared (I^2) statistic, chi-square (χ^2) test, with associated p values collectively considered statistical heterogeneity. The degree of heterogeneity was categorized using the I^2 statistic: 0%–40%, *not important*; 30%–60%, *moderately important*; 50%–90%, *substantially important*; and >90%, *considerably important* (Higgins et al., 2023). The I^2 statistic and their reported CIs helped determine if the data pooling was valid in MA with small numbers of included studies (von Hippel, 2015). The power of the χ^2 test for homogeneity is low if the number of studies within an MA is small, so a 10% significance level was set for probability in this SR (Higgins et al., 2023).

The Recommendations, Assessment, Development, and Evaluations (GRADE) method informed MA certainty by considering

within-study methodological bias, directness, heterogeneity, precision of effect estimates, and publication bias (Schünemann et al., 2008). The summary of findings (SOF) table (Table 1) presents pooled estimates and certainty of SR findings for the three primary outcomes (Schünemann et al., 2008).

RESULTS

Study selection and characteristics

The final search on July 15, 2023, yielded $n=2412$ citations. The abstracts and titles were screened, and $n=242$ full manuscripts were considered. Eighteen of the full manuscripts met the SR protocol inclusion criteria applied by two reviewers (Figure S2; Attia et al., 2017; Bell et al., 2015; Chua et al., 2022; Cortegiani et al., 2020; Doshi et al., 2018, 2020; Geng et al., 2020; Haywood et al., 2019; Hsu et al., 2020; Jones et al., 2016; Kim et al., 2020; Ko et al., 2020; Makdee et al., 2017; Osman et al., 2021; Raeisi et al., 2019; Rittayamai et al., 2015; Ruangsomboon et al., 2020, 2021). All included study characteristics are detailed in Table S3. No included studies were deemed to have high RoB, whereby the bias was such that the results may be invalidated (Table S4). Because more than 10 studies were included in the MA (NHF vs. COT), an assessment of publication bias was performed by visually inspecting the symmetry within the funnel plot for the escalation outcome; publication bias was not evident (Figure S3).

Meta-analysis findings

The SR involved pooling $n=1874$ participant data sets within five MA. All MA compared NHF to either COT or NIV. However, the reported mix of NIV interfaces and ventilator settings dictates that all MA findings (NHF versus NIV) must be cautiously viewed.

Requirement to escalate care in ED patients—NHF versus COT

For the comparison NHF versus COT and the outcome need for escalation, the MA confirmed that NHF reduces the need for escalation by 45% (RR 0.55; 95%; CI [0.33, 0.92]; $z=2.26$, $p=.02$; $I^2=0\%$; 9 RCTs, $n=991$, NNT = 32; Figure 1). An absolute effect of 3% (95% CI [1, 5]) fewer NHF ED patients will need escalation of care if they receive NHF versus COT. For completeness, the random effects model demonstrated consistency in the effects seen (RR 0.58; 95% CI [0.34, 0.99]; $z=2.00$, $p=.05$; $I^2=0\%$; Figure S3).

Requirement to escalate care in ED patients—NHF Versus NIV

For the comparison of NHF versus NIV and the outcome need for escalation, the MA confirms that NHF increases the need for escalation by 60% (RR 1.60; 95% CI [1.10, 2.33]; $z=2.48$, $p=.01$; $I^2=22\%$;

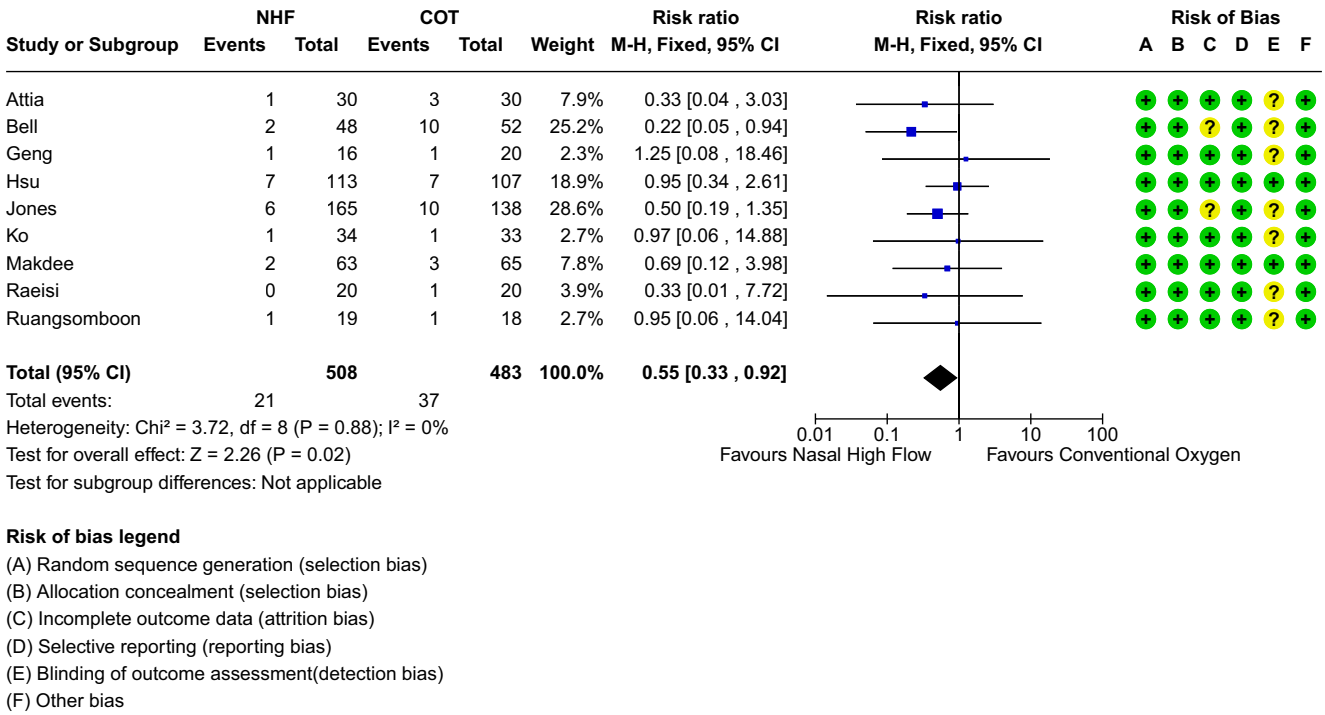


FIGURE 1 Forest plot: Requirement to escalate care in ED patients—NHF versus COT. COT, conventional oxygen therapy; ED, emergency department; NHF, nasal high flow..

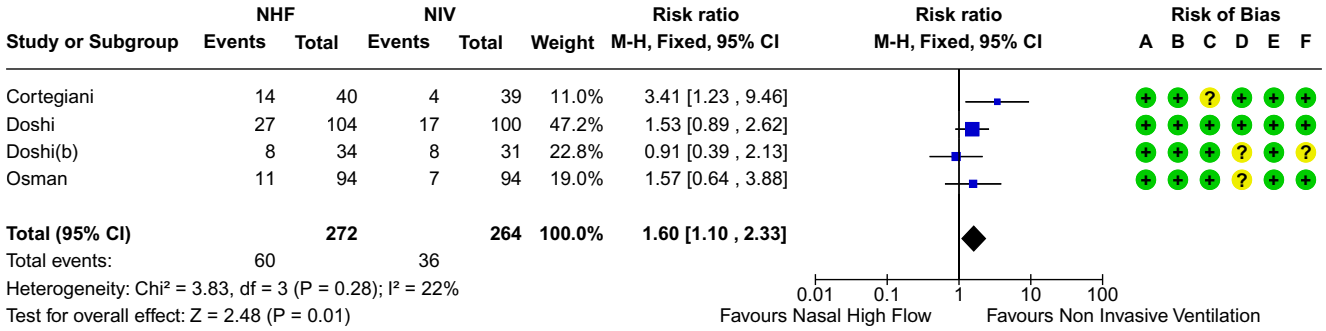


FIGURE 2 Forrest plot: Requirement to escalate care in ED patient—NHF versus NIV. NHF, nasal high flow; NIV, noninvasive ventilation.

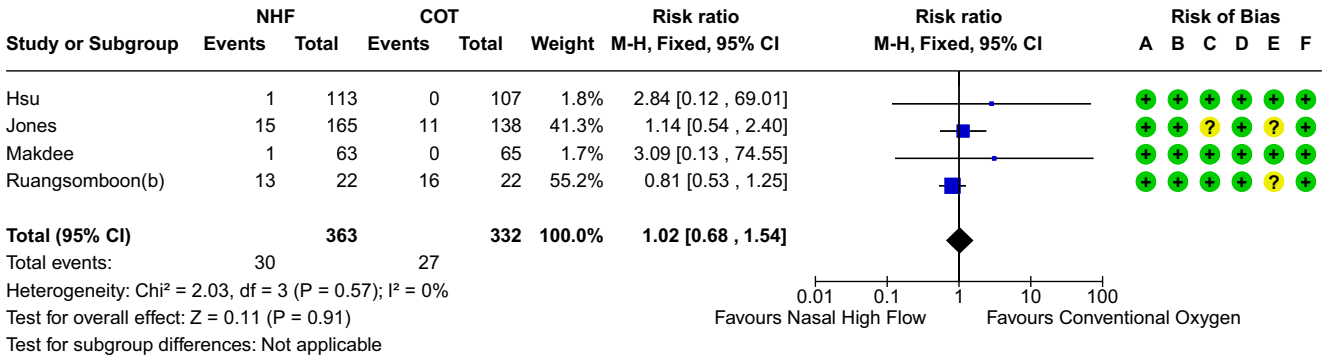


FIGURE 3 Forrest plot: Mortality rate in hospital (up to 90 days) NHF versus COT. COT, conventional oxygen therapy; NHF, nasal high flow.

4 RCTs, $n = 536$, NNT = 13; Figure 2). The absolute effect reported suggests that 8% (95% CI [1, 17]) more ED patients may require escalation if they receive NHF versus NIV. The I^2 of 22% suggests that heterogeneity was not important.

Mortality of ED patients—NHF versus COT

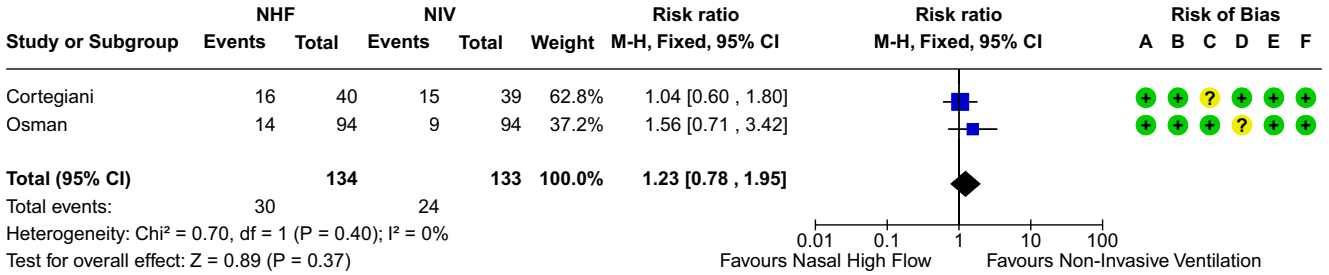
For the comparison NHF versus COT and the outcome mortality, the MA findings were not significantly different (RR 1.02; 95% CI [0.68, 1.54]; $z = 0.11$ $p = .91$, $I^2 = 0\%$; 4 RCTs, $n = 695$; Figure 3). The absolute effect reported suggests that 1% (95% CI [2, 4]) more ED patients may have increased mortality rates with NHF versus COT.

Mortality of ED patients—NHF Versus NIV

For the comparison NHF versus NIV and the outcome mortality, the MA findings were not significantly different (RR 1.23, 95% CI [0.78, 1.95]; $z = 0.89$, $p = 0.37$; $I^2 = 0\%$; 2 RCTs, 267 patients; Figure 4).

Rate of adverse events in ED

The inconsistent and poor reporting of AEs was reflected in measures of heterogeneity (such as I^2). The reported AEs for NHF versus COT included thoracic and cervical discomfort, feeling hot, apnea, reduction in Glasgow Coma Scale (GCS) score of two or more points, reduction in



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Incomplete outcome data (attrition bias)
(D) Selective reporting (reporting bias)
(E) Blinding of outcome assessment(detection bias)
(F) Other bias

FIGURE 4 Forrest plot: mortality rate in hospital (up to 90 days) NHF versus NIV. NHF, nasal high flow; NIV, noninvasive ventilation.

GCS with CO_2 retention, unpleasant smell, temperature too warm, and chest discomfort (Jones et al., 2016; Makdee et al., 2017; Rittayamai et al., 2015). For this comparison of NHF versus COT, the MA findings were not statistically significantly different for AEs (RR 0.98; 95% CI [0.61, 1.59]; $z = 0.07$, $p = .94$, $I^2 = 68\%$; 5 RCTs, $n = 721$; Figure 5). The I^2 of 68% was deemed substantially important and anticipated due to its inherent clinical heterogeneity. A single study reported no difference in AEs for the NHF versus NIV; this study described discomfort and poor tolerance (Cortegiani et al., 2019, 2020).

The GRADE certainty assessment and summary of findings for the included studies for three primary outcomes relating to the two comparisons NHF versus COT and NHF versus NIV are outlined in Table 2.

DISCUSSION

Key results

This SR included 18 RCTs ($n = 1752$ patients) and reported on three outcomes when NHF was compared to NIV or COT. Two of the five MAs were conclusive (Figures 1 and 2). Compared with COT, NHF reduces the risk of escalation by 45%; however, its effect on the risk of mortality or AEs remains unclear. Compared with NIV, NHF increased the risk of escalation by 60% but not mortality.

Interpretation

This SR demonstrates the requirement for adaptability when identifying decision-making factors which influence patient care and outcomes such as the need to escalate care (Pearson, 2013). It is important to remember that ED patients requiring RS are at high risk of needing escalation of care, and NHF may disguise their deterioration and ED clinicians should be cognizant of this when making clinical decisions (Ricard et al., 2019). Patients in the ED receiving NHF must be carefully monitored to avoid delays in care escalation. However, the SR conclusions for RS contrast, when NHF is compared to COT and the need to escalate patient care is reduced is of high clinical significance. However, the advantage of NIV over NHF remains unclear. The variation in patient clinical conditions, age, respiratory rate, intervention interfaces, flow rates, and FiO_2 could account for these unclear findings, and there was less available data to analyze some of the outcomes in this SR. Subgroup analyses based on patient clinical conditions, age, respiratory rate, NHF flow rates, and FiO_2, were proposed. However, very few RCTs reported separate outcome data for these subgroups. Additionally, no RCTs reported cost–benefit outcomes such as reduced ED length of stay. These factors limit the generalizability of the current SR of ED RCT findings to ED practice.

Generalizability

Evidence-based practice (EBP) theory incorporates the best research evidence, patient preference, and clinician expertise (Sackett, 1997). Initially, patient preference and clinician expertise informed NHF use; recently, the rapid emergence of NHF evidence has been influential, however, its generalizability is questionable. Establishing the efficacy of NHF in practice has demonstrated a legitimate EBP process. This process now refers to evidence from across the evidence hierarchy and across the gamut of quantitative and qualitative methodologies. The NHF evidence describing the clinical outcomes seen is rapidly emerging and highly cited. As of January 2024, the top 48 NHF publications have been cited 8670 times (mean = 180), with the most cited study ($n = 2371$) considering ARF (Frat et al., 2015). Some of these emergent publications have included the much-cited NHF SRs and clinical guidelines (Rochwerg et al., 2020). Many of the published ED SRs include evidence from outside the ED which limits their genuine generalizability in this setting. The common themes considered were coronavirus disease 2019 (62%), ARF (19%), postextubation care (6%), prediction outcomes (4%), supporting intubation (4%), delaying escalation (2%),

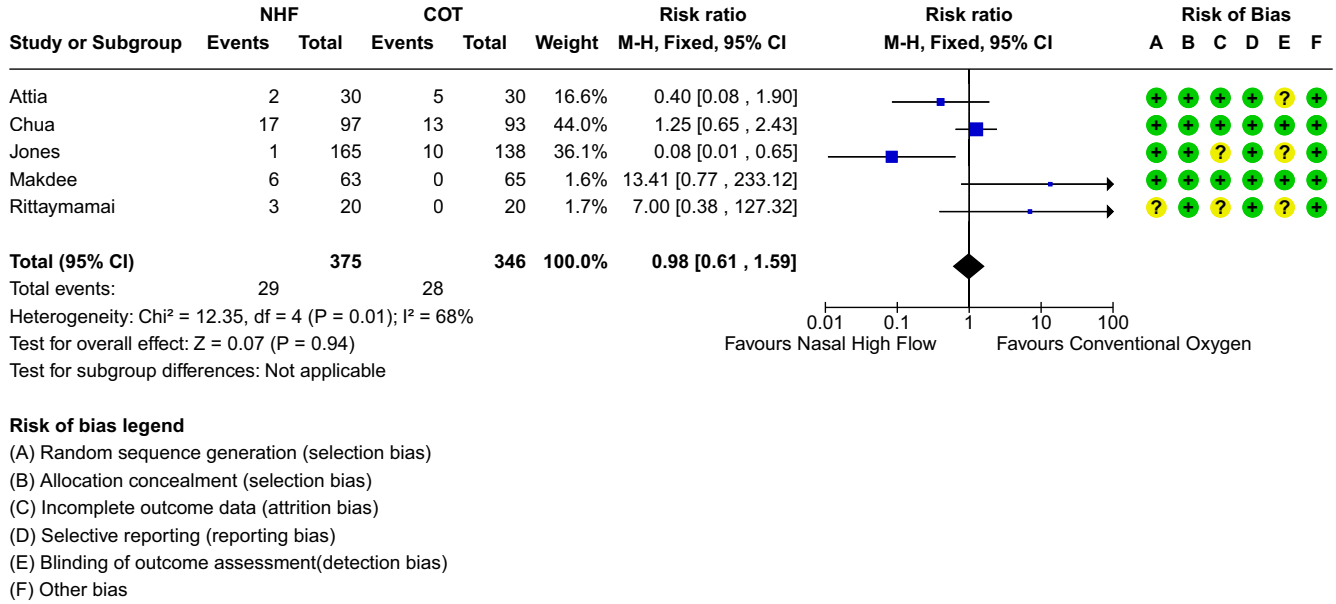


FIGURE 5 Forrest plot: adverse event in ED NHF versus COT. COT, conventional oxygen therapy; ED, emergency department; NHF, nasal high flow.

and postoperative support (2%). Evidence sourced using a variety of methods suggests that NHF RS provides favorable clinical outcomes to spontaneously breathing patients with various respiratory conditions in many settings including for adults in the ICU (Table 3).

The COVID-19 pandemic impacted all ED research and healthcare delivery (Khanna et al., 2023). The lack of robust evidence for RS in the ED was demonstrated during the pandemic when RS therapies were often indicated for those with RF secondary to COVID-19 infection (Jarou et al., 2021). During this pandemic, evidence of varying quality emerged, some NHF studies could not be sustained, and contrasting opinions and resource constraints paralyzed care delivery in many countries (Roy et al., 2021). The need to inform practice with reliable, valid, and applicable evidence on RS in the ED is obvious, pandemic notwithstanding. One Colombian multicenter RCT compared NHF to COT in 220 ED and ICU patients with severe ARF due to COVID. This study demonstrated the superiority of NHF over COT for avoiding escalation to INV (hazard ratio, 0.62; 95% CI [0.39, 0.96]; $p = .03$; Ospina-Tascón et al., 2021).

As demonstrated, there is limited research available in the ED, where patients first present to the hospital. However, it must be acknowledged that conducting research in the ED is challenging (Graham, 2019). Consequently, ED clinicians using NHF often rely on evidence drawn from other settings such as the ICU and or their own experience with the therapy (Marjanovic et al., 2020).

Limitations

This SR and its protocol have followed the Cochrane methodology to minimize its bias and limitations (Higgins et al., 2023). This SR did not include non-RCTs or qualitative evidence. Including these types of studies could have added further dimensions to the review findings. SRs are meant to be iterative as they require updating as new evidence emerges. However, secondary to COVID-19, ED evidence has been slow to emerge. As such, this SR includes the most recent data on ED patients and from RCTs based in the ED. The limitations of this SR include (1) insufficient data to consider subgroups; (2) use of outcome data impacted by imprecision for all outcomes; (3) including studies only published in English; and (4) use of data that had unavoidable RoB linked to the inability to fully blind participants, clinicians, and researchers.

Areas for potential research

While the reviewers acknowledge that conducting RCTs in the ED is challenging (Price et al., 2020), ED researchers are compelled to conduct rigorous, adequately powered ED RCTs that qualify for inclusion in future SRs. These studies should explore NHF cost–benefit and NHF use in different patient clinical conditions, age, respiratory rate, differing NHF flow rates, and FiO_2.

Linking evidence to action

- Evidence-based decision-making regarding RS in the ED is challenging.
- ED clinicians have at times had to rely on non-ED evidence to support their practice.
- Compared with COT, NHF was seen to be superior and reduced the risk of escalation.
- Conversely, for this same outcome, NIV was superior to NHF. However, substantial clinical heterogeneity was seen in the NIV delivered.

TABLE 2 GRADE assessment of certainty.

Certainty of assessment						No. of patients		Effect				
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	NHF	COT	Relative (95% CI)	Absolute (95% CI)	Certainty	Importance	Other considerations
Escalation of care NHF vs. COT												
12	RCTs	Serious	Not serious	Not serious	Serious	21/560 (3.8%)	37/537 (6.9%)	RR 0.55 (0.33 to 0.92)	3 fewer per 100 (from 5 fewer to 1 fewer)	Moderate ⊕⊕⊕◯	CRITICAL	None
Mortality NHF vs. COT												
12	RCTs	Serious	Not serious	Not serious	Serious	30/560 (5.4%)	27/537 (5.0%)	RR 1.11 (0.79 to 1.56)	1 more per 100 (from 1 fewer to 3 more)	Moderate ⊕⊕⊕◯	CRITICAL	None
Adverse event NHF vs. COT												
6	RCTs	Serious	Not serious	Not serious	Serious	29/423 (6.9%)	28/398 (7.0%)	RR 0.98 (0.61 to 1.59)	0 fewer per 100 (from 3 fewer to 4 more)	Low ⊕⊕◯	CRITICAL	None
Escalation of care NHF vs. NIV												
5	RCTs	Serious	Not serious	Not serious	Serious	60/292 (20.5%)	36/284 (12.7%)	RR 1.60 (1.10 to 2.33)	8 more per 100 (from 1 more to 17 more)	Moderate ⊕⊕⊕◯	CRITICAL	None
Mortality NHF vs. NIV												
5	RCTs	Serious	Not serious	Not serious	Serious	30/292 (10.3%)	24/284 (8.5%)	Not estimable	–	Moderate ⊕⊕⊕◯	CRITICAL	None

Abbreviations: COT, conventional oxygen therapy; NHF, nasal high flow; NIV, noninvasive ventilation; RCT, randomized controlled trial; RR, relative risk.

TABLE 3 Described conditions and applications of nasal high-flow therapy—A summary.

Condition	Evidence	Evidence type	Setting
Acute Hypoxemic Respiratory Failure	Mauri, Alban, et al. (2017)	Cross Over RCT	ICU
Acute Hypoxemic Respiratory Failure	Colombo et al. (2022)	Observational Study	Ward
Acute Hypoxemic Respiratory Failure	Rochwerg et al. (2020)	Clinical Guideline	All
Acute Hypoxemic Respiratory Failure	Pitre et al. (2023)	Network Meta-Analysis	All
Acute Hypercapnic Respiratory Failure	Pilcher et al. (2017)	Cross Over RCT	Ward
Acute Hypercapnic Respiratory Failure	Ovtcharenko et al. (2022)	SR with MA	All
Acute Respiratory Distress Syndrome	Messika et al. (2015)	Observational Study	ICU
Postsurgical/postoperative	Stéphan et al. (2017)	Noninferiority RCT	ICU
Postextubation	Hernandez et al. (2016)	RCT	ICU
Postextubation	Rochwerg et al. (2020)	Clinical Guideline	All
Peri intubation (RSI)	Patel and Nouraei (2015)	Controlled Trial	OT
Peri Intubation	Rochwerg et al. (2020)	Clinical Guideline	All
Immunocompromised	Azoulay et al. (2018)	RCT	ICU
Immunocompromised	Wang et al. (2020)	SR	All
Dyspnea/Breathlessness	Bell et al. (2015)	RCT	ED
Pneumonia	Frat et al. (2015)	RCT	ICU
Chronic Obstructive Pulmonary Disease	Bräunlich et al. (2019)	RCT	Ward
Cariogenic Pulmonary Oedema	Makdee et al. (2017)	RCT	ED
Heart Failure	Makdee et al. (2017)	RCT	ED
Cystic Fibrosis	Sklar et al. (2018)	Cross Over RCT	Ward
Trauma	Mu et al. (2020)	Retrospective Study	Hospital
Carbon Monoxide Poisoning	Tomruk et al. (2019)	Observational Study	ED
Atelectasis	Suzuki and Takasaki (2014)	Case Report	Ward
Palliative (Do Not Intubate)	Peters et al. (2013)	Cohort Study	Ward
Bronchiectasis	Rea et al. (2010)	RCT	Home
Interstitial Lung Disease	Al Chikhanie et al. (2021)	Controlled Trial	Non-Hospital
Asthma	Ruangsomboon et al. (2021)	RCT	ED
As an alternative to NIV	Doshi et al. (2018)	RCT	ED
Conscious Sedation	Ayuse et al. (2020)	RCT	For ERCP
Resting During NIV	Rochwerg et al. (2020)	Clinical Guideline	All
Postoperative	Rochwerg et al. (2020)	Clinical Guideline	Postoperative
Dyspnea in cancer pts	Hui et al. (2021)	RCT	All
Endoscopy	Nay et al. (2021)	RCT	Outpatients
Bronchoscopy COPD	Sharma et al. (2023)	RCT	Outpatients
Bronchoscopy	Lucangelo et al. (2012)	Prospective Controlled Study	ICU

Abbreviations: ED, Emergency Department; ERCP, Endoscopic Retrograde Cholangio Pancreatography; ICU, Intensive Care Unit; OT, operating theater; RCT, randomized controlled trial; RSI, rapid sequence intubation.

- Research considering NHF versus NIV is needed.
- COVID-19 has exposed the research gaps and slowed the progress of ED research.

CONCLUSIONS

The findings in this SR and MA inform both clinical research and patient care by providing clinicians and researchers with an appraisal and synthesis of the collective RCT evidence of adults requiring RS in the ED. The RCTs included could be pooled using MA techniques, which increased the certainty of the findings and condensed the vast amount of data. However, only one SR comparison (NHF versus COT) could be fully resolved, thus confirming the evidence gaps.

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CONFLICT OF INTEREST STATEMENT

Prior to 2020, Jane O'Donnell was an employee of Fisher & Paykel Healthcare All other authors have no conflicts to declare.

DATA AVAILABILITY STATEMENT

Data sharing does not apply to this manuscript as no new data were created in this SR.

ORCID

Jane O'Donnell https://orcid.org/0000-0002-9554-5497
Alison Pirret https://orcid.org/0000-0001-8725-8490
Karen Hoare https://orcid.org/0000-0002-7123-5881
Rebecca Fenn https://orcid.org/0000-0002-4894-8357
Elissa McDonald https://orcid.org/0000-0002-3218-3468

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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