Helmet noninvasive ventilation compared to facemask noninvasive ventilation and high-flow nasal cannula in acute respiratory failure: a systematic review and meta-analysis

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Helmet NIV may reduce mortality and intubation when compared to facemask NIV; however, large, well-designed RCTs are needed on this topic https://bit.ly/3i1rCnS

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Abstract

Background Although small randomised controlled trials (RCTs) and observational studies have examined helmet noninvasive ventilation (NIV), uncertainty remains regarding its role. We conducted a systematic review and meta-analysis to examine the effect of helmet NIV compared to facemask NIV or high-flow nasal cannula (HFNC) in acute respiratory failure.

Methods We searched multiple databases to identify RCTs and observational studies reporting on at least one of mortality, intubation, intensive care unit (ICU) length of stay, NIV duration, complications or comfort with NIV therapy. We assessed study risk of bias using the Cochrane Risk of Bias 2 tool for RCTs and the Ottawa–Newcastle Scale for observational studies, and rated certainty of pooled evidence using the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) framework.

Results We separately pooled data from 16 RCTs (n=949) and eight observational studies (n=396). Compared to facemask NIV, based on low certainty of evidence, helmet NIV may reduce mortality (relative risk 0.56, 95% CI 0.33–0.95) and intubation (relative risk 0.35, 95% CI 0.22–0.56) in both hypoxic and hypercapnic respiratory failure, but may have no effect on duration of NIV. There was an uncertain effect of helmet NIV on ICU length of stay and development of pressure sores. Data from observational studies were consistent with the foregoing findings but of lower certainty. Based on low and very low certainty data, helmet NIV may reduce intubation compared to HFNC, but its effect on mortality is uncertain.

Conclusions Compared to facemask NIV, helmet NIV may reduce mortality and intubation; however, the effect of helmet NIV compared to HFNC remains uncertain.

Introduction

The European Respiratory Society/American Thoracic Society clinical practice guidelines strongly recommend noninvasive ventilation (NIV) use for patients who have acute respiratory failure (ARF) due to

cardiogenic pulmonary oedema and exacerbations of chronic obstructive pulmonary disease (COPD), and conditionally recommend its use for patients with ARF due to other causes, including trauma, post-operative respiratory failure and those with immunocompromise [1]. For patients with ARF, NIV is typically applied with a facemask interface [2]. However, at higher airway pressures, the facemask interface may be difficult to tolerate and associated with air leaks, thus impairing oxygenation and limiting the mean airway pressure that can be applied to maintain lung recruitment [3]. Additionally, patients may not tolerate the facemask mask due to claustrophobia or facial pressure ulceration [4].

The helmet interface is a relatively new interface for NIV delivery. A transparent hood is positioned over the patient's head with a seal at the neck using a soft collar. The helmet reduces air leak due to better seal integrity at the neck and improves tolerability because there is no direct contact with the patient's face [5]. In patients with potentially infectious respiratory illness such as coronavirus disease 2019 (COVID-19), the reduced air leak and attendant decrease in droplet dispersion is especially valuable [6]. Furthermore, when compared to the facemask interface or high-flow nasal cannula (HFNC), the helmet reduces inspiratory effort, preserves lung volumes and allows for lower inspiratory support, possibly by mitigating air leak or allowing for more effective provision of positive end-expiratory pressure (PEEP) [3, 7, 8]. A recent JAMA Network meta-analysis comparing all noninvasive oxygenation strategies in patients with purely hypoxaemic respiratory failure demonstrated that helmet NIV may lower mortality and the need for intubation compared to conventional oxygen therapy [9]. However, only a small number of randomised controlled trials (RCTs) were included in the JAMA Network review [3, 5, 10–12] and it did not evaluate other patient-important outcomes such as complications, comfort or duration of NIV. Moreover, with a focus on only hypoxaemic respiratory failure, the effect of helmet NIV on the other forms of ARF remained uncertain. The COVID-19 pandemic has increased helmet NIV use [13]; however, uncertainty regarding the benefits and harms of helmet NIV in clinical practice remains. Given several recently published RCTs and observational studies evaluating helmet NIV, along with the shortfalls of the previous JAMA Network systematic review addressing the topic [9], we conducted a systematic review and meta-analysis to address the following research question: "In adult patients with ARF of all types, does use of helmet NIV reduce mortality, intubation rate, intensive care unit (ICU) length of stay and the risk of complications compared to facemask NIV or HFNC?".

Methods

We registered the protocol of this systematic review with PROSPERO (CRD42020222942) and report our findings using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist (supplementary table E1).

Search strategy and selection criteria

We performed a comprehensive search of the following databases from inception until 23 October 2020: MEDLINE, Embase, Web of Science, The Cochrane Library, International HTA Database, EBSCO CINAHL Complete, LILACS and WHO COVID-19 Global literature on coronavirus disease. The search was updated on 31 March 2021. We used keywords "noninvasive ventilation" or "oxygen inhalation therapy" or "oxygen therapy" or "respiratory insufficiency" or "respiratory insufficiency" or "adult respiratory distress syndrome" or "respiratory failure" or "acute respiratory failure" or "adult respiratory distress syndrome" or "continuous positive airway pressure" or "positive end-expiratory pressure" and "head protective devices" or "helmet". We did not exclude trials based on language or quality. We searched the bibliographies of included articles and prior meta-analyses on the topic. We consulted experts in the field to identify unpublished studies. A copy of our initial search strategy is included in the supplementary material.

Study selection

Two reviewers (D.C. and R.J.) screened citations independently and in duplicate in two stages: first examining the title and abstracts, and then the full text of selected citations. We captured reasons for study exclusion after reviewing the full texts of identified trials. A third reviewer (B.R.) adjudicated disagreements.

We included parallel group and crossover RCTs and observational studies that had an intervention and comparator cohort. We included studies that compared helmet NIV to NIV through another interface or HFNC in adult patients with ARF of any aetiology. Included studies had to report at least one of the following outcomes of interest: mortality, intubation rate, duration of mechanical ventilation, ICU length of stay, hospital length of stay, patient comfort, modality tolerance and NIV-related adverse events. We excluded observational studies without comparative analysis as well as case studies and case reports.

Data extraction and quality assessment

Two independent reviewers (D.C. and R.J.) working in pairs abstracted data in duplicate using a standardised data abstraction form. We collected data on trial characteristics, demographic data, interventional and control details, and outcomes. A third reviewer (B.R.) adjudicated disagreements where needed.

We assessed risk of bias in duplicate using the modified Cochrane Risk of Bias 2 tool for RCTs [14]. We assessed each RCT using the following domains: randomisation sequence generation, allocation concealment, blinding, incomplete data, selective reporting and other bias. For each domain, we rated risk of bias to be "low", "high" or "some concerns". The overall risk of bias for each trial was the highest risk attributed to any domain except for blinding (of the caregiver and patient specifically), as blinding is not feasible even with sham devices for these trials. For observational studies, we used the Newcastle–Ottawa Scale [15] and assessed each cohort or case–control study using the following domains: selection, comparability and exposure/outcome. For each domain, we rated the risk of bias by a star system, whereby the greater the number of stars, the lower the risk of bias. We assessed overall certainty of evidence for each outcome using the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) framework [16]. To assess for publication bias, we also created funnel plots for the outcomes of mortality and intubation.

Data analysis

We pooled RCTs and observational studies separately. In keeping with the GRADE methodology, when presenting pooled data from both RCTs and observational data, we focused on the results with the higher certainty. We used the DerSimonnian–Laird random effects model with inverse variance weighting to generate pooled treatment effects across studies. We assessed heterogeneity between trials using a combination of the Chi-squared test, the I^2 statistic and visual inspection of the forest plots [17]. We present results of dichotomous outcomes using relative risk (risk ratio) and continuous outcomes as mean difference (MD) with 95% confidence intervals. We also tabulated absolute differences with 95% confidence intervals. We performed all statistical analysis using RevMan 5.3 (Cochrane Collaboration, London, UK) software.

We planned for five *a priori* subgroup analyses: 1) COPD/hypercapnic respiratory failure *versus* non-COPD/hypercapnic respiratory failure patients, 2) congestive heart failure (CHF)/pulmonary oedema *versus* non-CHF/pulmonary oedema patients, 3) COVID-19-related ARF *versus* non-COVID-19-related ARF patients, 4) immunocompromised *versus* non-immunocompromised patients and 5) high *versus* low risk of bias studies. *A priori*, we hypothesised that COPD patients, CHF patients, COVID-19 patients, immunocompromised patients and trials at high risk of bias would show greater benefit with helmet NIV therapy.

Results

Search strategy and study characteristics

We reviewed 974 citations, and included 16 RCTs (n=949) [3, 7, 18–31] and eight observational studies (n=396) [32–39] (figure 1). We present the characteristics of the included RCTs in table 1 and the observational studies in supplementary table E4. RCTs included between 10 and 188 patients. Of the 16 included RCTs, four were crossover studies [7, 18, 20, 31] and two were only published in abstract form [24, 25]. Overall, 13 studies compared helmet NIV to facemask NIV and three trials compared helmet NIV to HFNC [7, 23, 25]. Three trials applied the helmet NIV in continuous positive airway pressure (CPAP) mode [21, 24, 25] and 13 trials applied bilevel helmet NIV [3, 7, 18–20, 22, 23, 26–31].

Six trials included patients with hypoxic respiratory failure, of which one trial each focused on patients with ARDS [3], pulmonary oedema [24], chest trauma [22] and COVID-19 [23], and two on mixed hypoxaemic respiratory failure [7, 25]. Two trials examined patients with post-extubation respiratory failure [20, 22] and the eight remaining trials enrolled exclusively patients with hypercapnic respiratory failure/COPD [18, 19, 26–31]. We summarise the risk of bias for the included RCTs in supplementary table E2a and c. Six trials were adjudicated to have low or intermediate risk of bias [3, 7, 19, 22, 23, 27, 31], while the remainder were judged to be at high risk of bias.

Of the eight observational studies, four were case–control studies [33, 36, 38, 39] and four were cohort studies [32, 34, 35, 37]. Observational studies included between 20 and 99 patients. Three studies compared helmet NIV to HFNC [32, 35, 37] and five studies compared helmet NIV to facemask NIV. Four studies only used helmet CPAP as their intervention [32, 35, 37, 38] and four studies evaluated helmet NIV [33, 34, 36, 39]. Only one study examined patients with COPD [33], while the remaining seven studies examined helmet NIV in patients with hypoxic respiratory failure. Of the studies evaluating hypoxic patient

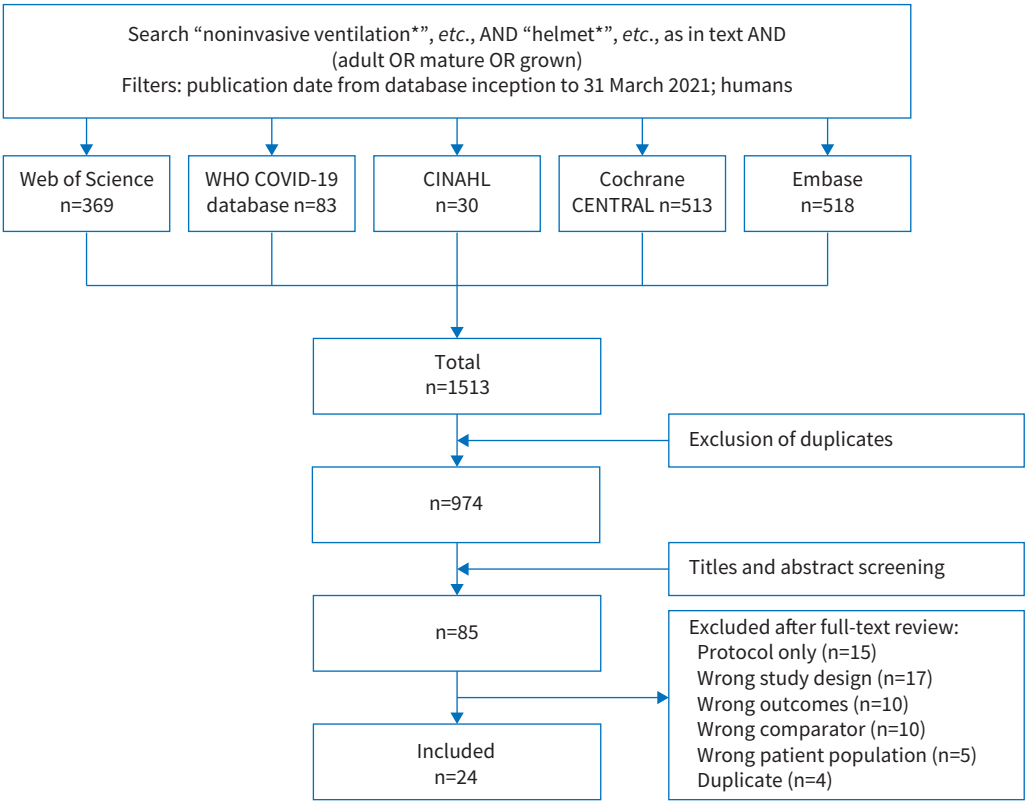

FIGURE 1 Study flowchart. WHO: World Health Organization.

populations, two focused on patients with COVID-19 infection [32, 35], one evaluated patients with haematological malignancies [38] and one assessed immunocompromised patients [39]. We summarise the risk of bias for the observational studies in supplementary table E2b. Most studies were adjudicated to have low risk of bias except for two studies [32, 35] that did not match their comparison cohorts.

Outcomes

We summarise the GRADE certainties and pooled estimates for pooled outcomes in supplementary table E3.

Helmet NIV versus *facemask NIV*

Compared to facemask NIV, helmet NIV may reduce mortality (relative risk 0.56, 95% CI 0.33–0.95; low certainty) (figure 2) and intubation (relative risk 0.35, 95% CI 0.22–0.56; low certainty) (figure 3). Observational data were consistent with these findings, yet of lower certainty (supplementary figures E1 and E2). Pooled data from RCTs suggested that helmet NIV has an uncertain effect on ICU length of stay (MD 0.29 days less, 95% CI 2.31 days less to 1.74 days more; very low certainty) (figure 4) and may have no effect on duration of NIV (MD 0.02 days less, 95% CI 0.15 days less to 0.11 days more; low certainty) (figure 5). Observational data were again consistent with these findings but of lower certainty (supplementary figures E4 and E5)

Helmet NIV has an uncertain effect on the risk of skin necrosis/pressure sores compared to facemask NIV (relative risk 0.50, 95% CI 0.19–1.37; absolute risk reduction 8.1% lower, 95% CI 13.2% lower to 6.0% higher; very low certainty) (supplementary figure E7). All other complications are summarised in table 2 as they were too variably reported to allow for pooling. The most common complications were skin necrosis/pressure sores and gastric distension. Similarly, whether and how patient comfort scales were documented across trials did not allow for statistical synthesis, so these are summarised in table 2.

Helmet NIV versus *HFNC*

Compared to HFNC, low certainty of evidence from RCTs suggests that helmet NIV may reduce intubation (relative risk 0.59, 95% CI 0.39–0.91) (figure 6), but has an uncertain effect on mortality (relative risk 0.72, 95% CI 0.40–1.28; very low certainty) (figure 7).

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TABLE 1 Characteristics of included randomised controlled trials

First author [ref.]	Year	Country	Type of helmet	Settings for helmet	Comparator	Settings for comparator	Total (n)	Select inclusion criteria	Outcomes recorded
Adi [24]	2019	Malaysia	Helmet CPAP	Not described	HFNC	Not described	188	Patients presenting to emergency department with cardiogenic pulmonary oedema	Intubation rate, mortality, patient comfort
Adi [25]	2018	Malaysia	Helmet CPAP	Not described	Facemask CPAP	Not described	123	Patients presenting with ARF	Patient comfort
Ali [26]	2011	Turkey	Helmet NIV (CaStar)	Started at PEEP 5–7 cmH_2O with pressure support 10 cmH_2O and adjusted until volumes of 6–8 $mL{\cdot}kg^{-1}$ obtained; F_{IO_2} titrated to keep S_{pO_2} >92%	Facemask NIV	Facemask NIV (set same way as helmet NIV)	30	Patients with COPD exacerbation	Intubation rate, ICU LoS, complications, patient comfort
Antonaglia [27]	2010	Italy	Helmet NIV (CaStar)	Inspiratory pressure increased (+20%) and finely tuned according to PVS until respiratory rate <30 $breaths{\cdot}min^{-1}$, accessory muscle activity disappeared, the patient was comfortable and leakage was minimised	Facemask NIV	Facemask NIV (set same way as helmet NIV)	40	Acute exacerbation of COPD investigated in semirecumbent position; patients had to undergo 2 h of facemask NIV	Intubation rate, ICU LoS, duration of MV, complications
Çakir Gürbüz [28]	2015	Turkey	Helmet NIV (CaStar)	Pressure support gradually increased by 2 cmH_2O steps during first hour of ventilation to observe adequate patient respiratory effort; F_{IO_2} rate also increased gradually up to 50% by 5% steps to obtain at least 92% S_{pO_2}; target V_T 6–8 $mL{\cdot}kg^{-1}$ during NIV	Facemask NIV	Facemask NIV (set same way as helmet NIV)	48	COPD patients admitted to respiratory ICU	Intubation rate, ICU LoS, duration of MV
Fasano [29]	2012	Italy	Helmet NIV (CaStar)	Not described	Full facemask NIV	Not described	31	COPD patients admitted to respiratory ICU for AHRF and supported with NIV	Intubation rate
Grieco [7]	2020	Italy	Helmet NIV (DiMAR)	Pressure support ventilation: initial pressure support 8–10 cmH_2O and then adjusted to permit peak inspiratory flow 100–150 $L{\cdot}min^{-1}$, up to a maximum of 20 cmH_2O; PEEP 10–12 cmH_2O; pressurisation time set to fastest possible	HFNC	Not described	15	AHRF defined by respiratory rate >25 $breaths{\cdot}min^{-1}$, need for supplemental O_2 to maintain 90% S_{pO_2} and evidence of pulmonary infiltrates on chest radiography or CT scan	Patient comfort

Continued

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TABLE 1 Continued

First author [ref.]	Year	Country	Type of helmet	Settings for helmet	Comparator	Settings for comparator	Total (n)	Select inclusion criteria	Outcomes recorded
Grieco [23]	2021	Italy	Helmet NIV (DiMAR or CaStar)	Ventilator set in pressure support mode: initial pressure support 10–12 cmH_2O, eventually increased to ensure peak inspiratory flow 100 $L{\cdot}min^{-1}$; PEEP 10–12 cmH_2O; F_{IO_2} titrated to obtain S_{pO_2} 92–98%	HFNC	Flow initially set at 60 $L{\cdot}min^{-1}$ and eventually decreased in case of intolerance, F_{IO_2} titrated to obtain S_{pO_2} 92–98% and humidification chamber set at 37°C or 34°C according to patient comfort	109	COVID-19 patients with moderate to severe hypoxaemic respiratory failure (P_{aO_2}/F_{IO_2} ⩽200)	Intubation rate, mortality, ICU LoS, complications, patient comfort
Liu [30]	2020	China	Helmet NIV	Not described	Facemask NIV	Facemask NIV (set same way as helmet NIV)	26	COPD exacerbation with respiratory failure as defined by study protocol	Intubation, mortality, complications
Liu [22]	2020	China	Helmet NIV (CaStar)	Pressure initially set at 8 cmH_2O, PEEP 5 cmH_2O and F_{IO_2} 40%; according to patient's clinical symptoms and S_{pO_2}, NIV supports sequentially increased in 1–2 cmH_2O increments; if respiratory distress and S_{pO_2} did not improve, F_{IO_2} progressively increased in 5% increments to achieve S_{pO_2} >92%	Facemask NIV	Facemask NIV (set same way as helmet NIV)	59	Within 72 h of chest trauma confirmed by imaging with moderate to severe hypoxaemic respiratory failure as defined by study protocol	Intubation rate, mortality, ICU LoS, duration of MV, complications
Longhini [31]	2019	China	Helmet NIV (CaStar)	Same PEEP applied during pressure support through a face mask trial and upper P_{aw} limit to obtain same overall P_{aw} applied during pressure support through a face mask trial; trigger sensitivity 0.5 V, whereas default cycling was 70% of the peak electrical activity of the diaphragm, as fixed by the company; F_{IO_2} set to maintain S_{pO_2} 90–94%	Full facemask NIV	Ventilator set as previously clinically indicated by attending physician; inspiratory pressure support 8 cmH_2O to obtain V_T 6–8 $mL{\cdot}kg^{-1}$ ideal body weight, with fastest rate of pressurisation and cycling that was 25–50% of peak inspiratory flow	10	History of COPD admitted to ICU for exacerbation and ARF as defined by study protocol	Patient comfort
Navalesi [18]	2007	Italy	Helmet NIV (CaStar)	Inspiratory assistance of 12 cmH_2O, delivered using the highest pressurisation rate, above PEEP 5 cmH_2O, was used for all patients; preceded by periods of spontaneous unassisted breathing through a mouthpiece with nostrils closed by a nose-clip and ventilator set in CPAP mode at 5 cmH_2O; F_{IO_2} set to obtain O_2 saturation 93–96% during first trial of spontaneous unassisted breathing and never changed throughout study period; all trials lasted 30 min	Facemask NIV	Facemask NIV (set same way as helmet NIV)	10	History of COPD, chronic hypercapnic respiratory failure, long-term NIV *via* nasal mask in accordance to study protocol for ⩾6 months with recent exacerbation	Patient comfort

Continued

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TABLE 1 Continued

First author [ref.]	Year	Country	Type of helmet	Settings for helmet	Comparator	Settings for comparator	Total (n)	Select inclusion criteria	Outcomes recorded
Patel [3]	2016	USA	Helmet NIV (SeaLong)	PEEP increased in increments of 2–3 cmH_2O to improve O_2 saturation to >90% at F_{IO_2} ⩽60%, if possible; inspiratory pressure increased in increments of 2–3 cmH_2O to obtain a respiratory rate of <25 breaths·min^{-1} and disappearance of accessory muscle activity	Facemask NIV	Facemask NIV (set same way as helmet NIV)	83	ARDS patients as defined by Berlin criteria requiring facemask NIV	Intubation rate, mortality, ICU LoS, hospital LoS, complications
Pisani [19]	2015	Italy	Helmet NIV (CaStar)	PEEP >5 cmH_2O and inspiratory pressure support of ⩾16 cmH_2O, keeping flow rate >30 L·min^{-1} inside helmet; other pressure increments made to keep respiratory rate <20 breaths·min^{-1} and minimising, by visual inspection, occurrence of accessory muscle recruitment; fastest rate of pressurisation and cycling-off flow threshold from 25% to 50% of the peak inspiratory flow were also set; further changes eventually made according to ABGs	Facemask NIV	Ventilator settings decided according to usual practice: maximal tolerated inspiratory pressure to obtain V_T 6–8 mL·kg^{-1} body weight and PEEP 3–5 cmH_2O	80	History of COPD and AHRF as defined by study protocol admitted to the ICU	Intubation rate, complications, patient comfort
Vargas [20]	2009	France	Helmet NIV (CaStar)	Pressure support adjusted initially during 5 min of NIV with facemask, before starting recordings; level of pressure support increased gradually until expired V_T 6–8 mL·kg^{-1} body weight; PEEP set at 4–5 cmH_2O	Facemask NIV	Facemask NIV (set same way as helmet NIV)	11	Patients intubated for >48 h who tolerated spontaneous breathing trial after recovery from acute disease	Patient comfort
Yang [21]	2015	China	Helmet CPAP (CaStar)	F_{IO_2} adjusted to 40–50% and PEEP adjusted to 8–10 cmH_2O in order to maintain S_{pO_2} >95%	Facemask NIV	Initial parameters: inspiration pressure 10–20 cmH_2O; expiration pressure 0–4 cmH_2O; F_{IO_2} 60–100%; inspiration: expiration 1:1.5 to 1:2; time for pressure increase 0.5–1 s; parameters adjusted gradually according to clinical outcomes and patient tolerance	40	Patients who underwent surgery for Stanford type A aortic dissection and had ARF as per study protocol	Intubation rate, mortality, ICU LoS, hospital LoS, duration of MV, complications

CPAP: continuous positive airway pressure; HFNC: high-flow nasal cannula; A(H)RF: acute (hypoxic) respiratory failure; NIV: noninvasive ventilation; PEEP: positive end-expiratory pressure; F_{IO_2}: inspiratory oxygen fraction; S_{pO_2}: peripheral oxygen saturation; COPD: chronic obstructive pulmonary disease; ICU: intensive care unit; LoS: length of stay; PVS: patient–ventilator synchrony; MV: mechanical ventilation; V_T: tidal volume; CT: computed tomography; P_{aO_2}: arterial oxygen tension; P_{aw}: airway pressure; ARDS: acute respiratory distress syndrome; ABG: arterial blood gas.

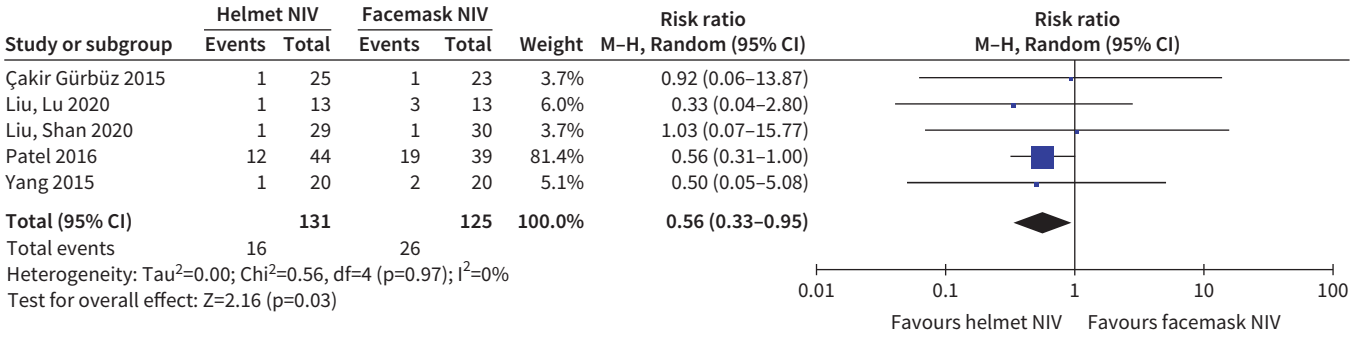

FIGURE 2 Effect of helmet noninvasive ventilation (NIV) compared to facemask NIV on mortality. Randomised controlled trial data only. M–H, Random: Mantel–Haenszel random effects method.

The pooled estimates from observational studies for both intubation (relative risk 0.69, 95% CI 0.27–1.73) (supplementary figure E5) and mortality (relative risk 0.77, 95% CI 0.16–3.75) (supplementary figure E6) are consistent in demonstrating uncertainty based on very low certainty of evidence.

Subgroup and sensitivity analysis

For the outcome of intubation, we did not identify credible subgroup effects when comparing patients with hypercapnic respiratory failure to those with hypoxaemic respiratory failure or when comparing high *versus* low or intermediate risk of bias trials in pooled analysis from either RCTs or observational studies (figure 3, and supplementary figures E2 and E8). For the outcome of intubation, we also did not identify any credible subgroup effects when comparing high *versus* low or intermediate risk of bias trials (supplementary figure E11). The remaining pre-planned subgroup analyses were not feasible due to lack of study-level aggregate data (only one study included immunocompromised patients and two included patients with COVID-19).

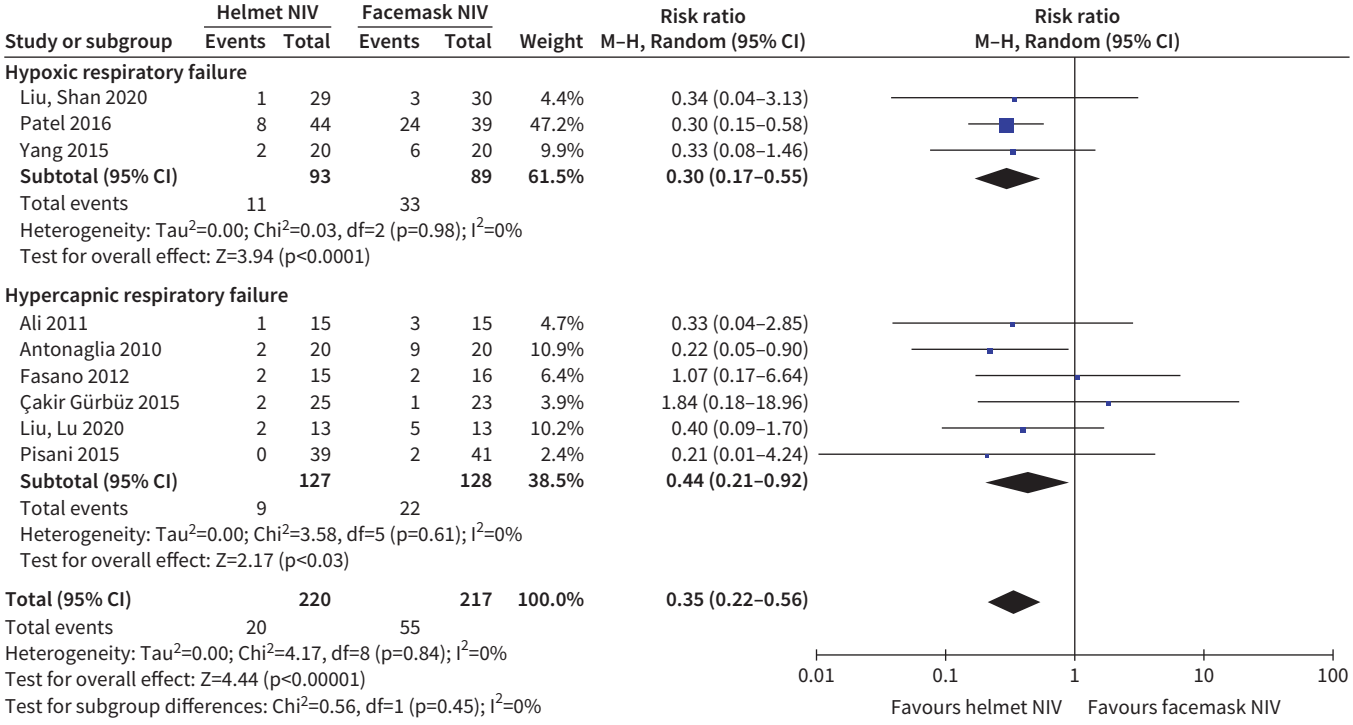

FIGURE 3 Effect of helmet noninvasive ventilation (NIV) compared to facemask NIV on intubation. Randomised controlled trial data only. Studies subdivided by type of respiratory failure. M–H, Random: Mantel–Haenszel random effects method.

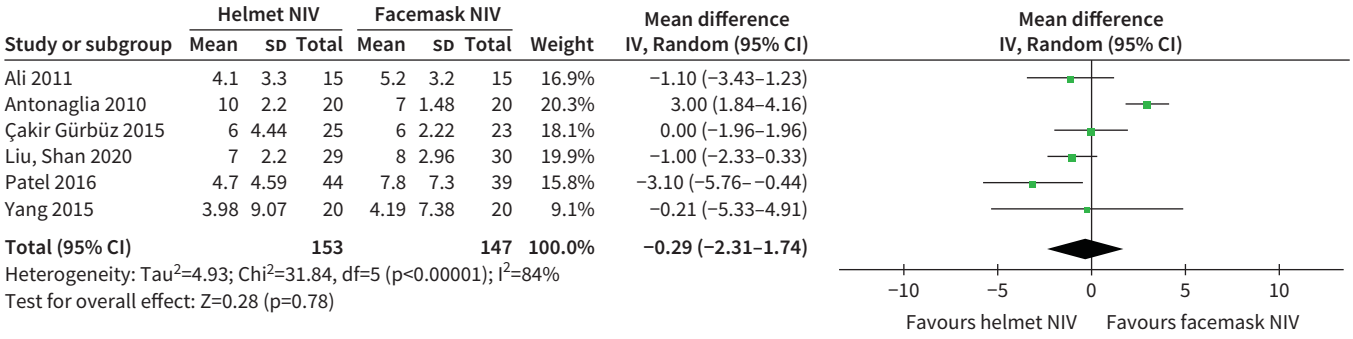

FIGURE 4 Effect of helmet noninvasive ventilation (NIV) compared to facemask NIV on intensive care unit length of stay (days). Randomised controlled trial data only. IV, Random: inverse variance random effects method.

Publication bias

There was minimal publication bias for the comparison of helmet NIV to facemask NIV in terms of the outcomes of mortality and intubation (supplementary figures E9 and E10). We did not perform funnel plots for the comparison of helmet NIV to HFNC due to the small number of included studies.

Discussion

Although the use of helmet NIV has steadily increased [13], the evidence supporting its use remains sparse. This systematic review and meta-analysis found that while available studies demonstrate that helmet NIV may be associated with lower intubation rates and mortality compared to facemask NIV, the certainty of these estimates remains low. The effect of helmet NIV on other clinically important outcomes, including ICU length of stay, duration of NIV and adverse events such as facial ulceration, is uncertain. There was limited evidence to compare helmet NIV to HFNC and therefore we conclude that high-quality RCTs are required to establish the net clinical benefits or harms of helmet NIV.

Compared to previous reviews, this systematic review and meta-analysis adds a number of new studies examining the role of helmet NIV in ARF [40] (12 new studies including seven new RCTs [7, 21, 22, 24, 25, 30, 31]). Despite this, all included trials and observational studies were small. For example, the largest trial examining helmet NIV use was an RCT of 188 patient that compared helmet NIV to HFNC [25]. Furthermore, two included trials were only published in abstract form [24, 25], and two trials were of a crossover design and only examined short-term outcomes [7, 31]. Although pooled data from this systematic review suggest that helmet NIV may be preferable to facemask NIV, the information size and event rates are low, contributing to important imprecision which limits the strength of inferences that can be made. Comparisons between the effects of helmet NIV *versus* HFNC are even more uncertain. Overall, this systematic review highlights the critical need for large, high-quality RCTs comparing helmet NIV to both facemask NIV and HFNC, including patient-important outcomes and attention to possible adverse events.

Many questions regarding the net clinical benefits of helmet NIV remain. Although some trials and studies reported complications and patient-reported comfort with helmet NIV, we were unable to pool the majority of data on these end-points due to infrequent and variable outcome reporting. Similarly, while current best

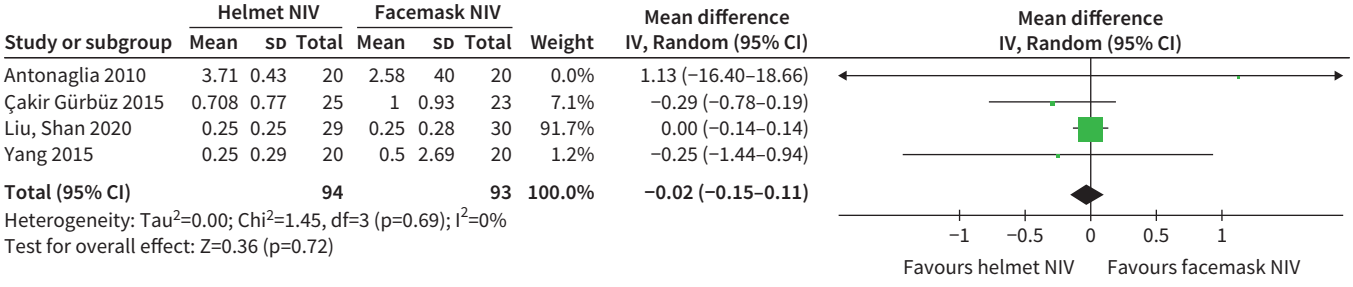

FIGURE 5 Effect of helmet noninvasive ventilation (NIV) compared to facemask NIV on duration of NIV (days). Randomised controlled trial data only. IV, Random: inverse variance random effects method.

TABLE 2 Complications of noninvasive ventilation

First author [ref.]	Definition of complication	Complications		Scale used	Comfort score	
		Helmet group	Comparator group		Helmet group	Comparator group
Adi [24]	Not recorded	Not recorded	Not recorded	Likert score (mean rank)	2	2
Adi [25]	Not recorded	Not recorded	Not recorded	Likert score (mean rank)	67.8	55.7
Ali [26]	Erythema and pressure sores	0/15	1/15	PTS (1 and 2 h)	3.5±0.6 and 3.2±0.7	2.6±0.9 and 2.2±0.7
Antonaglia [27]	Metabolic complications; sepsis and pneumonia; tracheostomy	4/20; 2/20; 0/20	3/20; 4/20; 1/20	Not recorded	Not recorded	Not recorded
Çakir Gürbüz [28]	Face laceration, erythema, axillary erythema and laceration	9/25	14/23	Not recorded	Not recorded	Not recorded
Fasano [29]	Not recorded	Not recorded	Not recorded	Not recorded	Not recorded	Not recorded
Grieco [7]	Not recorded	Not recorded	Not recorded	Dyspnoea VAS	3±2.2	8±2.2
Grieco [23]	VAP; barotrauma	14/54; 2/54	18/55; 2/55	Dyspnoea VAS	1.9±2.0	2.5±2.2
Liu [30]	Total complications; skin lesions	3/13; 9/13	8/13; 4/13	Not recorded	Not recorded	Not recorded
Liu [22]	Skin lesions; gastric distension	2/29; 0/29	0/30; 1/30	Not recorded	Not recorded	Not recorded
Longhini [31]	Not recorded	Not recorded	Not recorded	0–10 scale (0=least comfortable)	7±1.5	5±0.4
Navalesi [18]	Not recorded	Not recorded	Not recorded	1–5 scale (1=least comfortable)	3±1.5	3±0.8
Patel [3]	Mask deflation; skin ulceration	2/44; 3/44	0/39; 3/39	Not recorded	Not recorded	Not recorded
Pisani [19]	Noise; claustrophobia; gastric distension; vomit; sweat; tightness	4/39; 2/29; 2/39; 0/39; 0/39; 3/39	0/44; 1/44; 2/44; 1/44; 0/44; 5/44	Dyspnoea VAS (at 2 h)	4.3±2.1	3.3±2.0
Vargas [20]	Not recorded	Not recorded	Not recorded	Not recorded	Not recorded	Not recorded
Yang [21]	Skin lesions; gastric distension	0/20; 0/20	7/20; 5/20	Not recorded	Not recorded	Not recorded
Alharthy [32]	Not recorded	Not recorded	Not recorded	Not recorded	Not recorded	Not recorded
Antonelli [34]	Skin necrosis; gastric distension; eye irritation cumulative	0/33; 0/33; 0/33	7/66; 3/66; 4/66	Not recorded	Not recorded	Not recorded
Antonelli [33]	Skin breakdown; conjunctivitis; gastric distension; intolerance; DVT; total	0/33; 0/33; 0/33; 0/33; 1/33; 0/33	4/33; 2/33; 0/33; 6/33; 0/33; 12/33	Not recorded	Not recorded	Not recorded
Conti [36]	Skin necrosis; VAP	1/25; 1/25	1/25; 7/25	Not recorded	Not recorded	Not recorded
Gaulton [35]	Not recorded	Not recorded	Not recorded	Not recorded	Not recorded	Not recorded
Giovini [37]	Not recorded	Not recorded	Not recorded	Not recorded	Not recorded	Not recorded
Principi [38]	Skin necrosis; gastric distension; eye irritation	0/17; 0/17; 0/17	2/17; 0/17; 2/17	Not recorded	Not recorded	Not recorded
Rocco [39]	Total; skin necrosis; gastric distension	6/19; 2/19; 0/19	10/17; 9/17; 1/17	Not recorded	Not recorded	Not recorded

Data are presented as n/N or mean±SD, unless otherwise stated. PTS: patient tolerance scale; VAP: ventilator-associated pneumonia; VAS: visual analogue scale; DVT: deep vein thrombosis.

trial evidence supports the use of facemask NIV in selected populations (patients with COPD, CHF, immunocompromised, *etc.*) [1], there is currently a relative dearth of evidence regarding the effects of helmet NIV in these patient populations. Specifically in patients with hypercapnic respiratory failure, worsening hypercapnia, ventilator asynchrony and under-assistance are common concerns [33, 41]. However, at least one study of helmet NIV has shown that adequate carbon dioxide clearance can be achieved with high gas flow rates [41] and a few others have shown that helmet NIV reduces inspiratory effort [7, 8]. Regardless, to address the aforementioned concerns, we compared patients with hypercapnic respiratory failure *versus* those with hypoxaemic ARF in a pre-specified subgroup analysis. Although we did not find any credible subgroup effects based on available data, imprecision and low number of events underscore the need for further investigation.

The ability to provide a better seal compared to a facemask mask and not obscure a full facial view also provides the helmet with a few unique applications. For pandemic-related illnesses, such as COVID-19 and

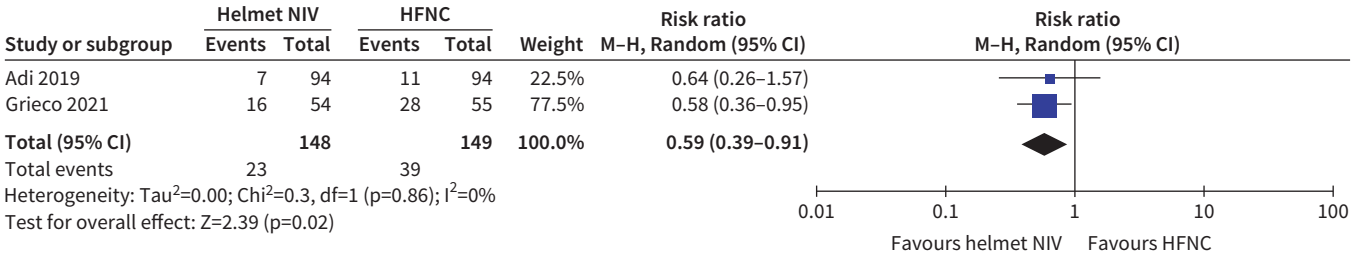

FIGURE 6 Effect of helmet noninvasive ventilation (NIV) compared to high-flow nasal cannula (HFNC) on intubation. Randomised controlled trial data only. M–H, Random: Mantel–Haenszel random effects method.

severe acute respiratory syndrome, the helmet may be a safer route to provide noninvasive respiratory support. To this end, simulation studies have demonstrated benefits of the helmet interface when compared to other noninvasive modes of respiratory support in the context of exhaled viral dispersion [6, 42], although this aerosolisation has not been rigorously evaluated in patients. For patients with ARF who are post-extubation, HFNC can be concurrently applied with helmet NIV and other nasal respiratory support devices. Moreover, helmet NIV permits a full facial view, speaking and nasogastric feeding tubes, which is often not possible with facemask NIV. Whether these features translate into enhanced comfort, fewer cutaneous complications and other benefits remains unknown, as patient-reported outcomes are lacking in this field. In addition, both CPAP and pressure support ventilation modes have been used with helmet NIV for various causes of respiratory failure. While it is likely that certain modes will provide no benefit for certain conditions (*e.g.* CPAP for COPD), the ideal mode for each cause of respiratory failure remains unknown. Finally, the cost-effectiveness of this new technology has not been examined. Although the helmet interface costs more than the traditional facemask interface, a previous costing study based on the RCT by Patel *et al.* [3] suggested that by reducing intubation and ICU length of stay, the helmet interface may actually be associated with cost savings; however, further clinical studies and a more comprehensive cost-effectiveness study is needed to confirm or refute these findings.

To the best of our knowledge, this is the largest and most comprehensive systematic review and meta-analysis to assess helmet NIV compared to facemask NIV and HFNC. Strengths of this study include pre-registration, incorporation of a comprehensive search, assessment of GRADE certainty allowing for appropriate contextualisation of results and inclusion of 12 additional studies (including seven RCTs) compared to a previously conducted review including 13 studies [40]. This review also has limitations. First, the total number of included patients and the number of events are small. Second, by including all studies that compared helmet NIV to either HFNC or facemask NIV, there was considerable clinical and methodological heterogeneity across trials, which nonetheless was not associated with statistical heterogeneity (inconsistency) for most outcomes. Acknowledging different design features informing this review, we analysed studies that compared helmet NIV to facemask NIV and HFNC separately, and RCTs and observational studies separately. However, considerable clinical heterogeneity remained as we were unable to conduct most predefined subgroup analyses due to insufficient data. In particular, we were unable to separate studies that examined hypoxic respiratory failure by the underlying varying pathophysiological mechanisms. While this highlights the need for further study on how specific causes of ARF respond to helmet NIV, the lack of inconsistency across our outcomes of interest seems to suggest that the effect of helmet NIV is likely similar regardless of the cause of ARF.

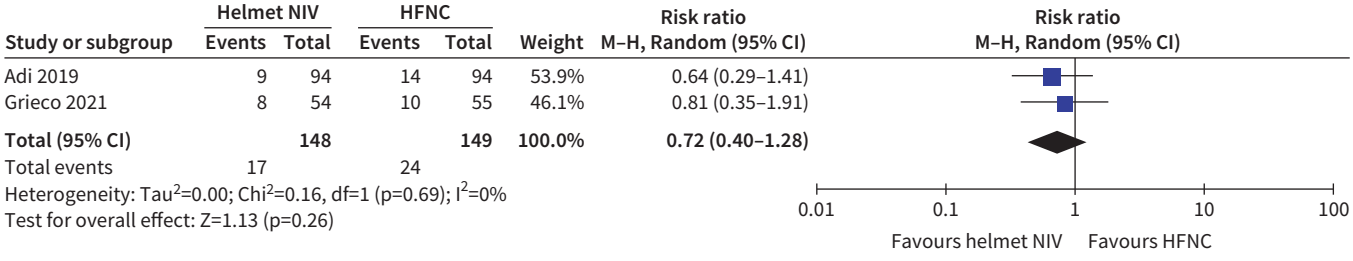

FIGURE 7 Effect of helmet noninvasive ventilation (NIV) compared to high-flow nasal cannula (HFNC) on mortality. Randomised controlled trial data only. M–H, Random: Mantel–Haenszel random effects method.

Conclusions

Compared to facemask NIV, helmet NIV may reduce mortality and intubation; however, the effect of helmet compared to HFNC remains uncertain. As application of this technology increases, large, well-designed RCTs comparing helmet NIV to both facemask NIV and HFNC in patients with both hypoxaemic and hypercapnic respiratory failure will be needed to help inform practice.

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