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Helmet Non-Invasive Ventilation compared to Facemask Non-Invasive Ventilation and High Flow Nasal Cannula in Acute Respiratory Failure: A systematic review and meta-analysis

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Take Home Message

Helmet NIV may reduce mortality and intubation when compared to facemask NIV, however, large well designed RCTs are needed on this topic.

Conflict of Interest/Competing Interests

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Abstract

Background: Although small randomized controlled trials (RCTs) and observational studies have examined helmet non-invasive 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, ICU length of stay, NIV duration, complications, or comfort with NIV therapy. We assessed study risk of bias (ROB) using the Cochrane ROB tool for RCTs and the Ottawa-Newcastle scale for observational studies and rated certainty of pooled evidence using GRADE.

Results: We separately pooled data from 16 RCTs (n=949) and 8 observational studies (n=396). Compared to facemask NIV, based on low certainty evidence, helmet NIV may reduce mortality (relative risk (RR) 0.56, 95% confidence interval (CI) (0.33 to 0.95)), and intubation (RR 0.35, 95% CI (0.22 to 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 on ICU length of stay and development of pressure sores. Data from observational studies was 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.

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

The protocol for this systematic review is registered with PROSPERO (CRD42020222942)

The ERS/ATS clinical practice guideline strongly recommends NIV use for patients who have acute respiratory failure (ARF) due to cardiogenic pulmonary edema and exacerbations of COPD and conditionally recommends 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 an 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 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)[7–9]. A recent JAMA network meta-analysis comparing all non-invasive oxygenation strategies in patients with purely hypoxemic respiratory failure demonstrated that helmet NIV may lower mortality and the need for intubation compared to COT[10]. However, only a small number of randomized control trials (RCTs) were included in this review[3, 5, 11–13], and it did not evaluate other patient important outcomes such as complications, comfort or duration of NIV. Moreover, with a focus on only hypoxemic

respiratory failure, the effect of helmet NIV on the other forms of acute respiratory failure remained uncertain. The COVID-19 pandemic has increased helmet NIV use[14], 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 systematic review addressing the topic, we conducted a systematic review and meta-analysis to address the following research question: In adult patients with acute respiratory failure of all types, does use of helmet NIV reduce mortality, intubation rate, 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 checklist (Supplementary Table 1).

Search Strategy and Selection Criteria

We performed a comprehensive search of following databases from inception until October 23, 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 March 31, 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 search strategy is included in the Supplementary Materials.

Study Selection

Two reviewers (DW, RJ) 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 (BR) 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 etiology. 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 (DC and RJ) working in pairs abstracted data in duplicate using a standardized data abstraction form. We collected data on trial characteristics, demographic data, interventional and control details, and outcomes. A third reviewer (BR) adjudicated disagreements where needed.

We assessed risk of bias (ROB) in duplicate using the modified Cochrane risk of bias tool 2 for RCTs[15]. We assessed each RCT using following domains: randomization sequence generation, allocation concealment, blinding, incomplete data, selective reporting, and other bias. For each domain, we rated ROB to be "low", "high", or "some concerns". The overall ROB for each trial was the highest risk attributed to any domain except for blinding (of the caregiver and patient specifically), as blinding is infeasible even with sham devices for these trials. For observational studies, we used the Newcastle-Ottawa scale[16] and assessed each cohort or case control study using the following domains: selection, comparability, exposure/outcome. For each domain, we rated ROB by a star system, whereby the greater number of stars, the lower the ROB. We assessed overall certainty of evidence for each outcome using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework[17]. 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 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^2 test, the I^2 statistic, and visual inspection of the forest plots [18]. We present results of dichotomous outcomes using relative risk (RR) and continuous outcomes as mean difference (MD) with 95% confidence intervals

(CIs). We also tabulated absolute differences with 95% CIs. We performed all statistical analysis using RevMan 5.3 (Cochrane Collaboration, Oxford) software.

We planned for five *a priori* subgroup analyses: (a) COPD/hypercapnic respiratory failure vs. non-COPD/hypercapnic respiratory failure patients (b) CHF/pulmonary edema patients vs. non CHF/pulmonary edema patients; (c) COVID-19 related ARF vs. non-COVID-19 related ARF patients; (d) immunocompromised patients vs. non-immunocompromised patients; and (e) high ROB studies vs. low ROB studies. *A priori,* we hypothesized that COPD patients, CHF patients, COVID-19 patients, immunocompromised patients and trials at high ROB 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, 19–32] and 8 observational studies (n= 396)[33–40] (Figure 1). We depict the characteristics of the included RCTs in Table 1 and the observational studies in Supplementary Table 4. RCTs included between 10 and 188 patients. Of the 16 included RCTs, 4 were crossover studies[7, 19, 21, 32] and 2 trials were only published in abstract form[25, 26]. Overall, 13 studies compared helmet NIV to facemask NIV where 3 trials compared helmet NIV to HFNC[7, 24, 26]. Three trials applied the helmet NIV in continuous positive airway pressure (CPAP) mode[22, 25, 26], and 13 trials applied bilevel helmet NIV[3, 7, 19–21, 23, 24, 27–32].

Six trials included patients with hypoxic respiratory failure, of which, one trial each focused on patients with ARDS[3], pulmonary edema[25], chest trauma[23], COVID-19[24] and two on mixed hypoxemic respiratory failure[7, 26]. Two trials examined patients with post-

extubation respiratory failure[21, 23], and the 8 remaining trials enrolled exclusively patients with hypercapnic respiratory failure/COPD[19, 20, 27–32]. In Supplementary Table 2a and 2c, we summarize the ROB for included RCTs. Six trials were adjudicated to have low or intermediate ROB[3, 7, 20, 23, 24, 28, 32], while the remainder were judged to be at high ROB.

Of the 8 observational studies, 4 were case control studies[34, 37, 39, 40] and 4 were cohort studies[33, 35, 36, 38]. Observational studies included between 20 and 99 patients. Three studies compared helmet NIV to HFNC[33, 36, 38] and 5 compared helmet NIV to facemask NIV. Four studies only used helmet CPAP as their intervention[33, 36, 38, 39], and 4 studies evaluated helmet NIV[34, 35, 37, 40]. Only one study examined patients with COPD[34], while the remaining 7 examined helmet NIV in patients with hypoxic respiratory failure. Of the studies evaluating hypoxic patient populations, 2 focused on patients with COVID-19 infection[33, 36], one evaluated patients with hematologic malignancies[39] and one assessed immunocompromised patients[40]. In Supplementary Table 2b, we summarize the ROB for the observational studies. Most studies were adjudicated to have low ROB except for 2 studies [33, 36] that did not match their comparison cohorts.

Outcomes

We summarized the GRADE certainties and pooled estimates for pooled outcomes in Supplementary Table 3.

Helmet NIV versus facemask NIV

Compared to facemask NIV, helmet NIV may reduce mortality (RR 0.56, 95% CI 0.33 to 0.95, low certainty, Figure 2) and intubation (RR 0.35, 95% CI 0.22 to 0.56, low certainty,

Figure 3). Observational data was consistent with these findings yet of lower certainty (e-Figure 1, e-Figure 2). Pooled data from RCTs suggested that helmet NIV has an uncertain effect on ICU LOS (MD 0.29 days less, 95% CI 2.31 days less to 1.74 days more, very low certainty evidence, 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 evidence, Figure 5). Observational data was again consistent with these findings but of lower certainty (e-Figure 4, e-Figure 5)

Helmet NIV has an uncertain effect on the risk of skin necrosis/pressure sores compared to facemask NIV (RR 0.60, 95% CI 0.19 to 1.37, ARR 8.1% lower, 95% CI 13.2% lower to 6.0% more, e-Figure 7, very low certainty). All other complications are summarized 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 summarized in Table 2.

Helmet NIV versus HFNC

Compared to HFNC, low certainty evidence from RCTs suggest that helmet NIV may reduce intubation (RR 0.59, 95% CI 0.39 to 0.91, e-Figure 6) but has an uncertain effect on mortality (RR 0.72, 95% CI 0.40 to 1.28, very low certainty, Figure 7).

The pooled estimates from observational studies for both intubation (RR 0.69, 95% CI 0.27 to 1.73, e-Figure 5) and mortality (RR 0.77, 95% CI 0.16 to 3.75, e-Figure 6) are consistent in demonstrating uncertainty based on very low certainty 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 hypoxemic respiratory failure or when comparing high versus low or intermediate ROB trials in pooled analysis from either RCTs or observational studies (Figure 3, e-Figure 2, e-Figure 8). For the outcome of intubation, we also did not identify any credible subgroup effects when comparing high versus low or intermediate ROB trials (e-Figure 11). 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).

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 (e-Figure 9, e-Figure 10). 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[14], 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 stay, duration of NIV, and adverse events such as facial ulceration is uncertain. There was limited evidence to compare helmet NIV

with HFNC, and therefore we conclude that high quality randomized clinical trials 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[41] (12 new studies including 7 new RCTs[7, 22, 23, 25, 26, 31, 32]). Despite this, all included trials and observational studies were small. For example, the largest trial examining helmet NIV use was a 188 patient RCT that compared helmet NIV to HFNC[26]. Further, 2 included trials were only published in abstract form[25, 26] and 2 trials were of a crossover design and only examined short term outcomes[7, 32]. Although pooled data from this systematic review suggests 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 endpoints due to infrequent and variable outcome reporting. Similarly, while current best 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[34, 42]. However, at least one study of helmet NIV has shown that adequate CO_2 clearance can be achieved with high gas flow rates[42] 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 hypoxemic 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 severe acute respiratory syndrome (SARS), the helmet may be a safer route to provide non-invasive respiratory support. To this end, simulation studies have demonstrated benefits of the helmet interface when compared to other non-invasive modes of respiratory support in the context of exhaled viral dispersion[6, 43], although this aerosolization has not 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 (NG) 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 (PSV) 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 (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 at al.[3] suggested that by reducing intubation and ICU length of stay, the helmet interface may actually be associated with cost saving; however, further clinical studies and a more comprehensive cost-effectiveness study is needed to confirm or refute these findings.

To 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 contextualization of results, and inclusion of 11 additional studies (including 8 RCTs) compared to a previously conducted review including 13 studies[41]. 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 analyzed 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 acute respiratory failure 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 acute respiratory failure.

Conclusion

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 hypoxemic and hypercapnic respiratory failure will be needed to help inform practice.

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Table 1: Characteristics of Included Randomized Control Trials

Author	Year	Country	Type of Helmet	Settings for Helmet	Comparator	Settings Used Comparator	Total (n)	Select Inclusion Criteria	Outcomes Recorded
Adi et al.	2019	Malaysia	Helmet CPAP	Not Described	High Flow Nasal Canula	Not Described	188	Patients presenting to ED with cardiogenic pulmonary edema	Intubation Rate, Mortality, Patient Comfort
Adi and Salleh	2018	Malaysia	Helmet CPAP	Not Described	Facemask CPAP	Not Described	123	Patients presenting with acute respiratory failure	Patient Comfort
Ali et al.	2011	Turkey	Helmet NIV (CaStar)	Started at PEEP 5-7 with Pressure Support 10 cm H20 and adjusted until volumes of 6-8 ml/kg obtained. Fio2 titrated to keep SPO2>92%	Facemask NIV	Facemask NIV (set same way as helmet NIV)	30	Patients with COPDe	Intubation Rate, ICU Length of Stay, Complications, Patient Comfort
Antogali a et al.	2010	Italy	Helmet NIV (CaStar)	Inspiratory pressure was increased (+20%) and finely tuned according to the patient-ventilator synchrony until the respiratory rate was less than 30 bpm, accessory muscle activity disappeared, the patient was comfortable, and leakage was minimized.	Facemask NIV	Facemask NIV (set same way as helmet NIV)	40	Acute exacerbation of COPD was investigated in the semi recumbent position. Patients had to undergo 2 hours of Facemask NIV	Intubation Rate, ICU length of Stay, Duration of Mechanical Ventilation, Complications
Cakir Gurbuz et al.	2015	Turkey	Helmet NIV (CaStar)	Pressure Support was gradually increased by 2 cm H20 steps during the first hour of ventilation to observe adequate patient respiratory effort. The FiO2 rate was also increased gradually up to 50% by 5% steps to obtain at least 92% SpO2. Target 6–8 mL/kg tidal volume during the NIMV procedure.	Facemask NIV	Facemask NIV (set same way as helmet NIV)	48	COPD patients admitted to the respiratory intensive care unit	Intubation Rate, ICU Length of Stay, Duration of Mechanical Ventilation
Fasano et al.	2012	Italy	Helmet NIV (CaStar)	Not Described	Full Facemask NIV	Not Described	31	COPD patients admitted to a Respiratory Intensive Care Unit (RICU) for AHRF and supported with NIV	Intubation Rate
Grieco et al.	2020	Italy	Helmet NIV (DiMAR)	Pressure-support ventilation: initial pressure support was 8–10 cm H2O and then adjusted to permit a peak inspiratory flow of 100–150 L/min, up to a maximum of 20 cm H2O; PEEP was 10–12 cm H2O; pressurization time was set to the fastest possible	High Flow Nasal Canula	Not Described	15	Acute hypoxic respiratory failure defined by respiratory rate >25 breaths per minute, need for supplemental oxygen to maintain 90% SpO2, and evidence of pulmonary infiltrates on chest X-ray or computed tomography scan	Patient Comfort
Grieco et al.	2021	Italy	Helmet NIV (DiMAR + CaStar)	The ventilator was set in pressure support mode, with the following settings: initial pressure support between 10 and 12 cm H2O, eventually increased to ensure a peak inspiratory flow of 100 L/min; positive end-expiratory pressure between 10 and 12 cm H2O; and Fio2 titrated to obtain Spo2 between 92% and 98%	High Flow Nasal Canula	Flow was initially set at 60 L/min and eventually decreased in case of intolerance, Fio2 titrated to obtain peripheral oxygen saturation as measured by pulse oximetry (Spo2) between 92% and 98%, and humidification chamber was set at 37 °C or 34 °C according to the patient's comfor	109	COVID-19 patients with moderate to severe hypoxemic respiratory failure (PF ratio <200)	Intubation Rate, Mortality, ICU Length of stay, Complications, Patient Comfort
Liu et al.	2020	China	Helmet NIV	Not Described	Facemask NIV	Facemask NIV (set same way as helmet group)	26	COPD exacerbation with respiratory failure as defined by study protocol	Intubation, Mortality, Complications

Liu et al.	2020	China	Helmet NIV (CaStar)	Pressure was initially set at 8 cm H2O, positive end-expiratory pressure at 5 cm H2O, and FiO2 at 40%. According to the patient's clinical symptoms and their percutaneous blood oxygen saturation (SpO2), NIV supports were sequentially increased in 1–2-cm H2O increments. If respiratory distress and SpO2 did not improve, FiO2 was progressively increased in 5% increments to achieve an SpO2 > 92%.	Facemask NIV	Facemask NIV (set same way as helmet group)	59	Within 72 hours of chest trauma confirmed by imaging with moderate to severe hypoxemic respiratory failure as defined by the study protocol	Intubation Rate, Mortality, ICU Length of Stay, Duration of Mechanical Ventilation, Complications
Longhini et al.	2019	China	Helmet NIV (CaStar)	The same PEEP applied during the pressure support through a face mask trial and an upper airway pressure (Paw) limit to obtain the same overall Paw applied during the pressure support through a face mask trial. The trigger sensitivity was set at 0.5 V, whereas the default cycling was 70% of the peak electrical activity of the diaphragm (EAdi), as fixed by the company. FIO2 was set to maintain peripheral (SpO2) between 90% and 94%.	Full Facemask NIV	Full face mask NIV (The ventilator was set as previously clinically indicated by the attending physician. Inspiratory pressure support was 8 cm H2O to obtain a tidal volume of 6 – 8 mL/kg of ideal body weight, with the fastest rate of pressurization and cycling that was between 25 and 50% of peak inspiratory flow.)	10	History of COPD admitted to ICU for exacerbation and acute respiratory failure as defined by the study protocol	Patient Comfort
Navalesi et al.	2007	Italy	Helmet NIV (CaStar)	Inspiratory assistance of 12 cmH2O, delivered using the highest pressurization rate, above a positive end expiratory pressure (PEEP) of 5 cmH2O, was used for all patients. This was preceded by periods of spontaneous unassisted breathing through a mouthpiece with the nostrils closed by a nose-clip and the ventilator set in continuous positive airway pressure (CPAP) mode at 5 cmH2O. FiO2 was set to obtain an oxygen saturation ≥ 93% and ≤ 96% during the first trial of spontaneous unassisted breathing and never changed throughout the study period. All the trials lasted 30 min.	Facemask NIV	Facemask NIV (set same way as helmet group)	10	History of COPD, chronic hypercapnic respiratory failure, long-term NIV via nasal mask as accordance to study protocol for at least 6 months with recent exacerbation	Patient Comfort
Patel et al.	2016	USA	Helmet NIV SeaLong	PEEP was increased in increments of 2 to 3 cm H2O to improve oxygen saturation to more than 90% at an inspired oxygen fraction (FIO2) of 60% or less, if possible. Inspiratory pressure was increased in increments of 2 to 3 cm H2O to obtain a respiratory rate of less than 25/min and disappearance of accessory muscle activity.	Facemask NIV	Facemask NIV (set same way as helmet group)	83	ARDS patients as defined by the Berlin criteria requiring facemask NIV	Intubation Rate, Mortality, ICU length of Stay, Hospital Length of Stay, Complications
Pisani et al.	2015	Italy	Helmet NIV (CaStar)	Set a positive end-expiratory pressure (PEEP) of >5 cmH2O and an inspiratory pressure support of ⩾16 cmH2O, keeping a flow rate >30 L·min-1 inside the helmet; other pressure increments were made to keep respiratory rate <20 breaths per min and minimising, by visual inspection, the occurrence of accessory muscle recruitment. The fastest rate of pressurisation and a cycling-off flow threshold from 25% to 50% of the peak inspiratory flow were also set. Further changes were eventually made according to ABGs.	Facemask NIV	Facemask NIV (The ventilator settings were decided according to the usual practice: maximal tolerated inspiratory pressure to obtain a tidal volume of 6–8 mL·kg-1 of body weight and PEEP between 3 and 5 cmH2O)	80	History of COPD and acute hypoxic respiratory failure as defined by the study protocol admitted to the ICU	Intubation Rate, Complications, Patient Comfort

Vargas et al.	2009	France	Helmet NIV (CaStar)	Pressure support was adjusted initially during 5 minutes of noninvasive ventilation with the facemask, before starting the recordings. The level of pressure support was increased gradually until the expired tidal volume (VT) was 6 to 8 mL/kg of body weight. PEEP was set at 4 to 5 cm H2O.	Facemask NIV	Facemask NIV (set same way as helmet group)	11	Patients intubated for more than 48 hours who tolerated spontaneous breathing trial after recovery from acute disease	Patient Comfort
Yang et al.	2015	China	Helmet CPAP (CaStar)	The FiO2 was adjusted to 40–50%, and PEEP was adjusted to 8–10 cm H2O in order to maintain pulse oxygen saturation (SpO2)>95%.	Facemask NIV	Facemask NIV (initial parameters: inspiration pressure [IPAP], 10–20 cm H2O; expiration pressure [EPAP], 0–4 cm H2O; FIO2, 60–100%; inspiration: expiration, 1:1.5 to 1:2; and time for pressure increase, 0.5–1 s). All these parameters were adjusted gradually according to the clinical outcomes and patient tolerance)	40	Patients who underwent surgery for Stanford type A aortic dissection and had acute respiratory failure as per study protocol	Intubation Rate, Mortality, ICU length of Stay, Hospital Length of Stay, Duration of Mechanical Ventilation, Complications

Table 2: Complications of NIV

Author	Definition of Complication	Complications in Helmet Group	Complication in Comparator Group	Scale Used	Comfort Score in Helmet Group (mean, SD)	Comfort Score in Comparator Group (mean, SD)
Adi et al.	Not Recorded	Not Recorded	Not Recorded	Likert score (mean rank)	2	2
Adi and Salleh	Not Recorded	Not Recorded	Not Recorded	Likert score (mean rank)	67.8	55.7
Ali et al.	Erythema and Pressure Sores	0 of 15	1 of 15	HUS (1h and 2h)	3.5 (0.6) and 3.2 (0.7)	2.6 (0.9) and 2.2 (0.7)
Antogalia et al.	Metabolic complications; sepsis and pneumonia; tracheostomy	4/20; 2/20; 0/20	3/20; 4/20; 1/20	Not Recorded	Not Recorded	Not Recorded
Cakir Gurbuz et al.	Face laceration, Erythema, Axillary erythema, and Laceration	9/25	14/23	Not Recorded	Not Recorded	Not Recorded
Fasano et al.	Not Recorded	Not Recorded	Not Recorded	Not Recorded	Not Recorded	Not Recorded
Grieco et al.	Not Recorded	Not Recorded	Not Recorded	Dyspnea VAS	3 (2.2)	8 (2.2)
Grieco et al	VAP, barotrauma	14/54 and 2/54	18/55 and 2/55	Dyspnea VAS	1.9 (2.0)	2.5 (2.2)
Liu et al.	Total and Skin Lesions	3/15 and 9/15	8/15 and 4/15	Not Recorded	Not Recorded	Not Recorded
Liu et al.	Skin lesion and Gastric Distension	2/29 and 0/29	0/30 and 1/30	Not Recorded	Not Recorded	Not Recorded
Longhini et al.	Not Recorded	Not Recorded	Not Recorded	0 to 10 scale with 0 being least comfortable	7 (1.5)	5 (0.4)
Navalesi et al.	Not Recorded	Not Recorded	Not Recorded	1 to 5 scale with 1 being least comfortable	3 (1.5)	3 (0.8)
Patel et al.	Mask Deflation and Skin Ulceration	2/44 and 3/44	0/39 and 3/39	Not Recorded	Not Recorded	Not Recorded
Pisani et al.	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	Dyspnea VAS (at 2 hours)	4.3 (2.1)	3.3 (2.0)
Vargas et al.	Not Recorded	Not Recorded	Not Recorded	Not Recorded	Not Recorded	Not Recorded
Yang et al.	Skin lesions and Gastric distension	0/20 and 0/20	7/20 and 5/20	Not Recorded	Not Recorded	Not Recorded
Alharthy et al.	Not Recorded	Not Recorded	Not Recorded	Not Recorded	Not Recorded	Not Recorded
Antonelli et al.	Skin Necrosis, Gastric Distension, and Eye Irritation Cumulative	0/33; 0/33; 0/33	7/10; 3/66; 4/66	Not Recorded	Not Recorded	Not Recorded
Antonelli et al.	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 et al.	Skin Necrosis and VAP	1/25 and 1/25	1/25 and 7/25	Not Recorded	Not Recorded	Not Recorded
Gaulton et al.	Not Recorded	Not Recorded	Not Recorded	Not Recorded	Not Recorded	Not Recorded
Giovini et al.	Not Recorded	Not Recorded	Not Recorded	Not Recorded	Not Recorded	Not Recorded
Principi et al.	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 et al.	Total; Skin Necrosis; Gastric Distension	6/19; 2;/19; 0/19	10/17; 9/17; 1;17	Not Recorded	Not Recorded	Not Recorded

Figure Legends

Figure 1: Prisma Study Flow

Figure 2: Effect of helmet NIV compared to facemask NIV on mortality. RCT data only. DF = degrees of freedom.

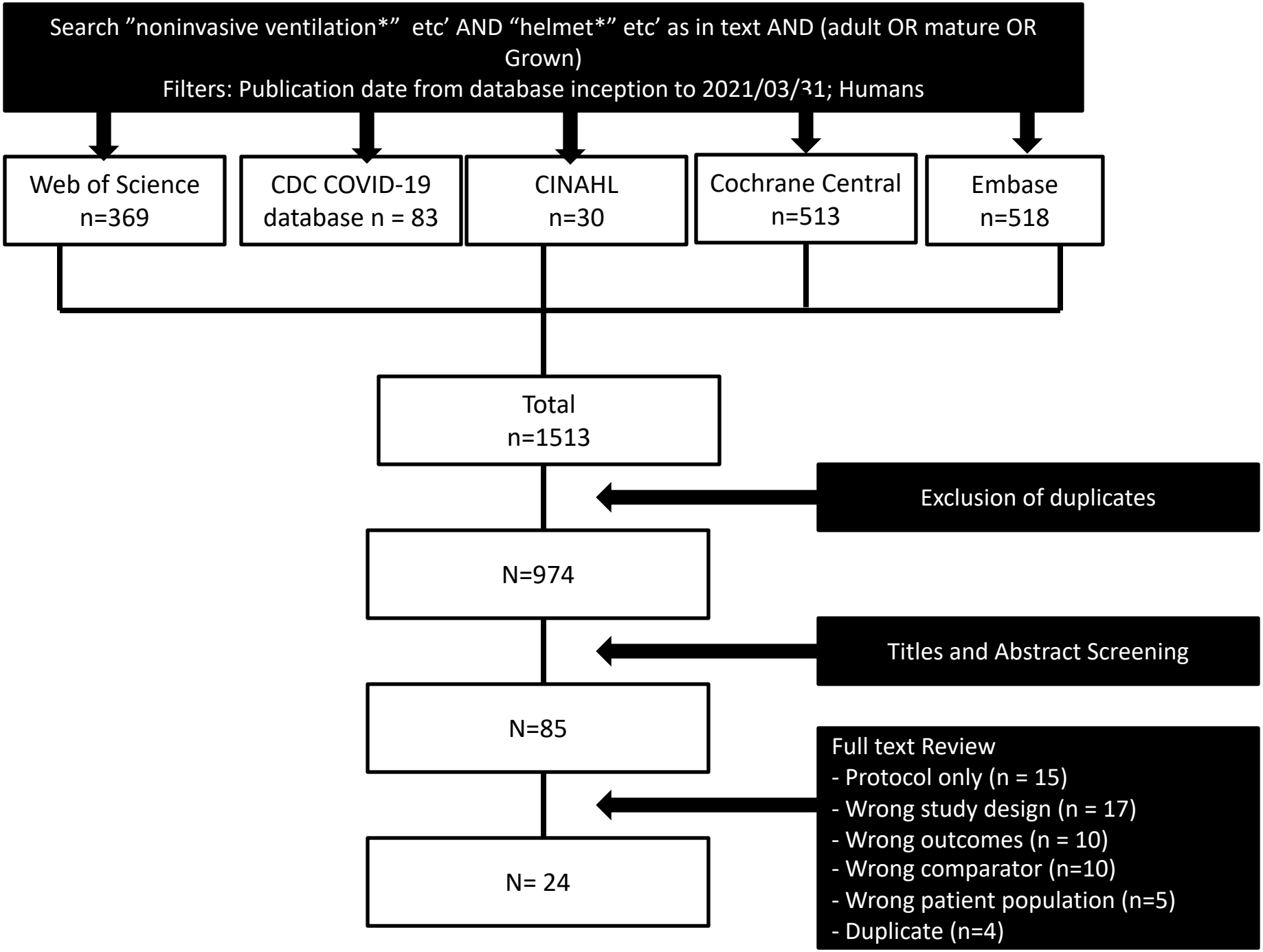
Figure 3: Effect of helmet NIV compared to facemask NIV on intubation. RCT data only. Studies subdivided by type of respiratory failure. DF = degrees of freedom.

Figure 4: Effect of helmet NIV compared to facemask NIV on ICU length of stay. RCT data only. Df = degrees of freedom

Figure 5: Effect of helmet NIV compared to facemask NIV on duration of NIV. RCT data only. Df = degrees of freedom

Figure 6: Effect of helmet NIV compared to high flow nasal cannula on intubation. RCT data only. Df = degrees of freedom

Figure 7: Effect of helmet NIV compared to high flow nasal cannula on mortality. RCT data only. Df = degrees of freedom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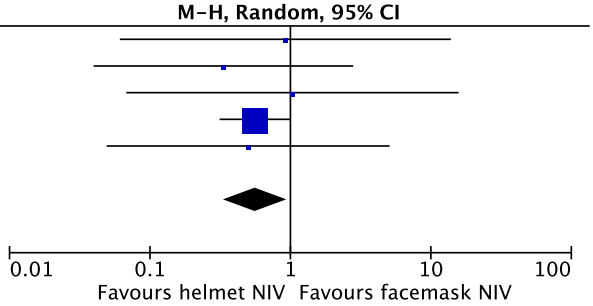
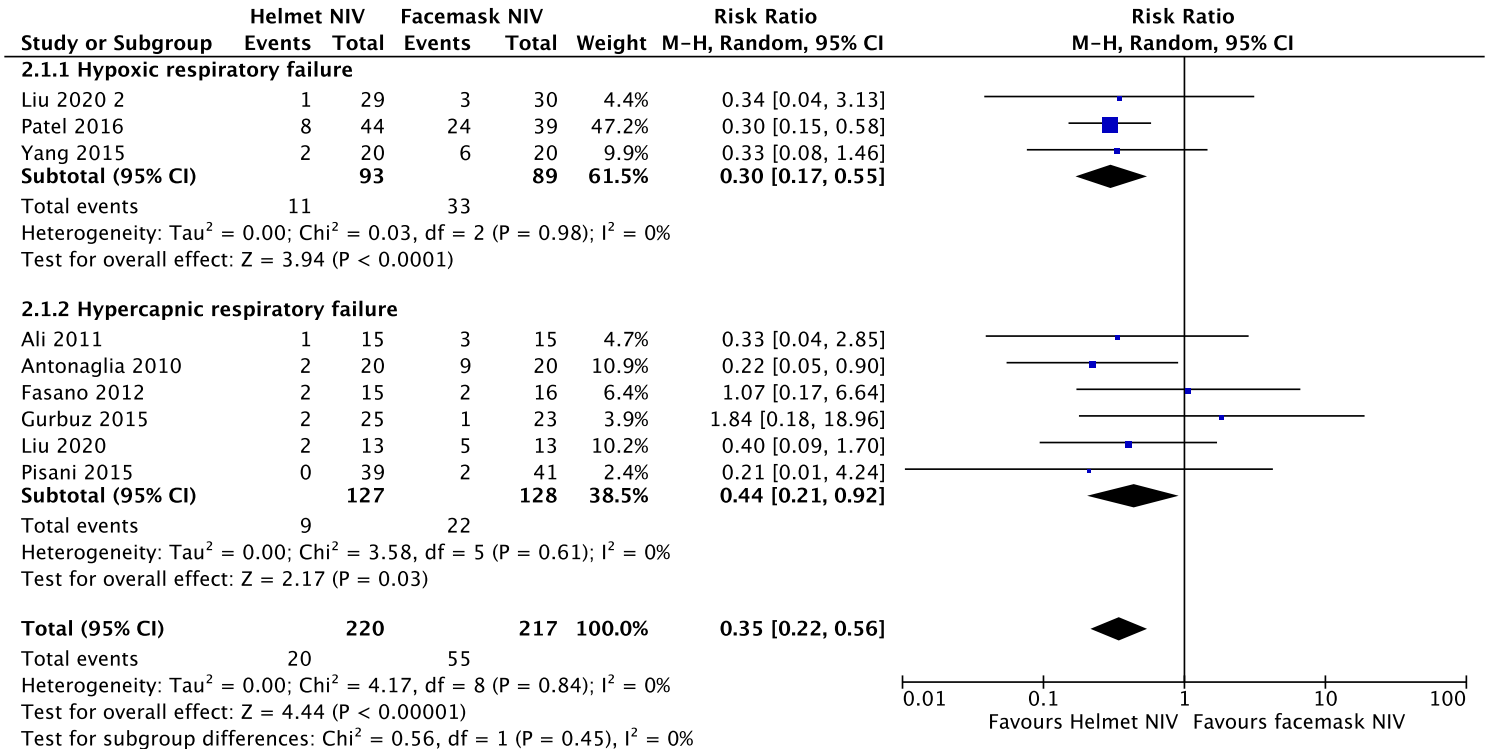
Filters: Publication date from database inception to 2021/03/31; Humans
Web of Science n=369
CDC COVID-19 database n = 83
CINAHL n=30
Cochrane Central n=513
Embase n=518
Total n=1513
Exclusion of duplicates
N=974
Titles and Abstract Screening
N=85
Full text Review
- Protocol only (n = 15)
- Wrong study design (n = 17)
- Wrong outcomes (n = 10)
- Wrong comparator (n=10)
- Wrong patient population (n=5)
- Duplicate (n=4)
N= 24

Study or Subgroup	Helmet NIV Events	Total	Facemask NIV Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Gurbuz 2015	1	25	1	23	3.7%	0.92 [0.06, 13.87]
Liu 2020	1	13	3	13	6.0%	0.33 [0.04, 2.80]
Liu 2020 2	1	29	1	30	3.7%	1.03 [0.07, 15.77]
Patel 2016	12	44	19	39	81.4%	0.56 [0.31, 1.00]
Yang 2015	1	20	2	20	5.1%	0.50 [0.05, 5.08]
Total (95% CI)		**131**		**125**	**100.0%**	**0.56 [0.33, 0.95]**
Total events	16		26			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.56$, df = 4 (P = 0.97); $I^2 = 0\%$

Test for overall effect: Z = 2.16 (P = 0.03)

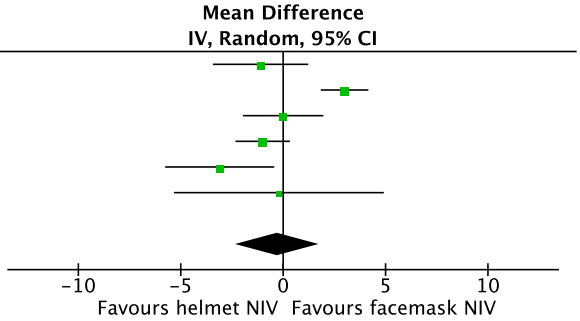



Helmet NIV
Facemask NIV
Risk Ratio
Risk Ratio
Study or Subgroup
Events Total Events Total Weight M-H, Random, 95% CI
M-H, Random, 95% CI
2.1.1 Hypoxic respiratory failure
Liu 2020 2 1 29 3 30 4.4% 0.34 [0.04, 3.13]
Patel 2016 8 44 24 39 47.2% 0.30 [0.15, 0.58]
Yang 2015 2 20 6 20 9.9% 0.33 [0.08, 1.46]
Subtotal (95% CI) 93 89 61.5% 0.30 [0.17, 0.55]
Total events 11 33
Heterogeneity: Tau² = 0.00; Chi² = 0.03, df = 2 (P = 0.98); I² = 0%
Test for overall effect: Z = 3.94 (P < 0.0001)
2.1.2 Hypercapnic respiratory failure
Ali 2011 1 15 3 15 4.7% 0.33 [0.04, 2.85]
Antonaglia 2010 2 20 9 20 10.9% 0.22 [0.05, 0.90]
Fasano 2012 2 15 2 16 6.4% 1.07 [0.17, 6.64]
Gurbuz 2015 2 25 1 23 3.9% 1.84 [0.18, 18.96]
Liu 2020 2 13 5 13 10.2% 0.40 [0.09, 1.70]
Pisani 2015 0 39 2 41 2.4% 0.21 [0.01, 4.24]
Subtotal (95% CI) 127 128 38.5% 0.44 [0.21, 0.92]
Total events 9 22
Heterogeneity: Tau² = 0.00; Chi² = 3.58, df = 5 (P = 0.61); I² = 0%
Test for overall effect: Z = 2.17 (P = 0.03)
Total (95% CI) 220 217 100.0% 0.35 [0.22, 0.56]
Total events 20 55
Heterogeneity: Tau² = 0.00; Chi² = 4.17, df = 8 (P = 0.84); I² = 0%
Test for overall effect: Z = 4.44 (P < 0.00001)
Test for subgroup differences: Chi² = 0.56, df = 1 (P = 0.45), I² = 0%
0.01
0.1
1
10
100
Favours Helmet NIV
Favours facemask NIV

Study or Subgroup	Helmet NIV Mean	SD	Total	Facemask NIV Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Ali 2011	4.1	3.3	15	5.2	3.2	15	16.9%	-1.10 [-3.43, 1.23]
Antonaglia 2010	10	2.2	20	7	1.48	20	20.3%	3.00 [1.84, 4.16]
Gurbuz 2015	6	4.44	25	6	2.22	23	18.1%	0.00 [-1.96, 1.96]
Liu 2020 2	7	2.2	29	8	2.96	30	19.9%	-1.00 [-2.33, 0.33]
Patel 2016	4.7	4.59	44	7.8	7.3	39	15.8%	-3.10 [-5.76, -0.44]
Yang 2015	3.98	9.07	20	4.19	7.38	20	9.1%	-0.21 [-5.33, 4.91]
Total (95% CI)			**153**			**147**	**100.0%**	**-0.29 [-2.31, 1.74]**

Heterogeneity: $Tau^2 = 4.93$; $Chi^2 = 31.84$, df = 5 ($P < 0.00001$); $I^2 = 84\%$

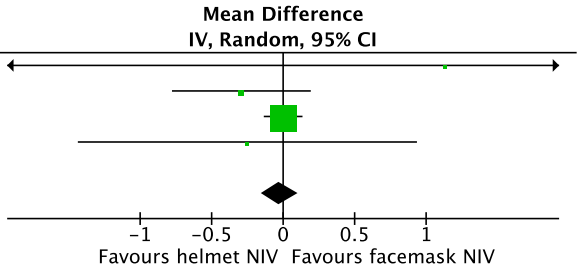
Test for overall effect: Z = 0.28 (P = 0.78)



Study or Subgroup	Helmet NIV Mean	SD	Total	Facemask NIV Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Antonaglia 2010	3.71	0.43	20	2.58	40	20	0.0%	1.13 [-16.40, 18.66]
Gurbuz 2015	0.708	0.77	25	1	0.93	23	7.1%	-0.29 [-0.78, 0.19]
Liu 2020 2	0.25	0.25	29	0.25	0.28	30	91.7%	0.00 [-0.14, 0.14]
Yang 2015	0.25	0.29	20	0.5	2.69	20	1.2%	-0.25 [-1.44, 0.94]
Total (95% CI)			**94**			**93**	**100.0%**	**-0.02 [-0.15, 0.11]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.45$, df = 3 (P = 0.69); $I^2 = 0\%$

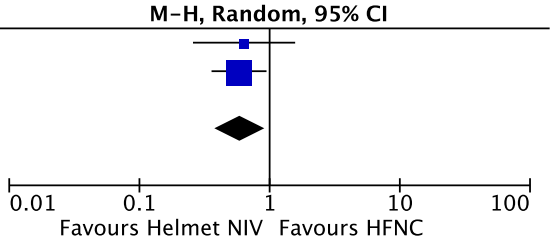
Test for overall effect: Z = 0.36 (P = 0.72)



Study or Subgroup	Helmet NIV Events	Total	HFNC Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Adi 2019	7	94	11	94	22.5%	0.64 [0.26, 1.57]
Grieco 2021	16	54	28	55	77.5%	0.58 [0.36, 0.95]
Total (95% CI)		**148**		**149**	**100.0%**	**0.59 [0.39, 0.91]**
Total events	23		39			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.03$, df = 1 (P = 0.86); $I^2 = 0\%$

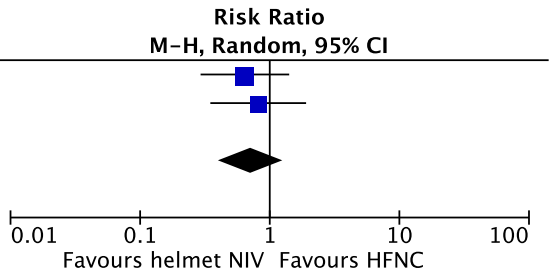
Test for overall effect: Z = 2.39 (P = 0.02)



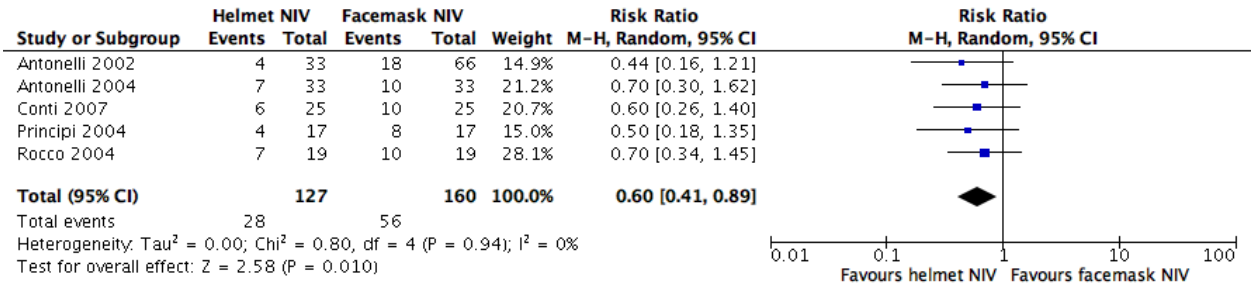
Study or Subgroup	Helmet NIV Events	Total	HFNC Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Adi 2019	9	94	14	94	53.9%	0.64 [0.29, 1.41]
Grieco 2021	8	54	10	55	46.1%	0.81 [0.35, 1.91]
Total (95% CI)		**148**		**149**	**100.0%**	**0.72 [0.40, 1.28]**
Total events	17		24			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.16$, df = 1 (P = 0.69); $I^2 = 0\%$

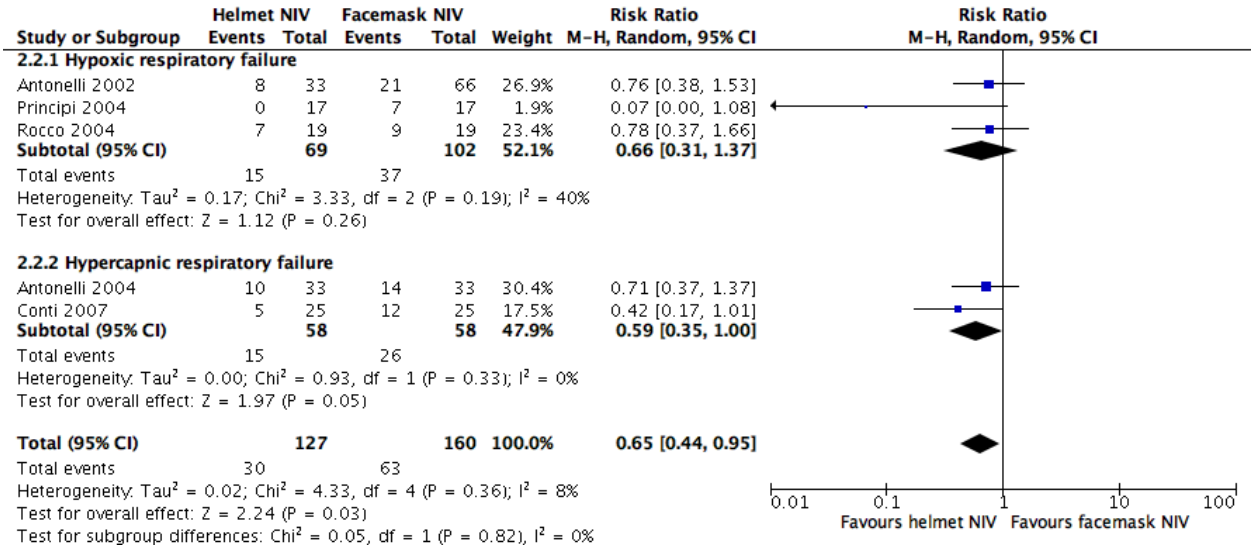
Test for overall effect: Z = 1.13 (P = 0.26)



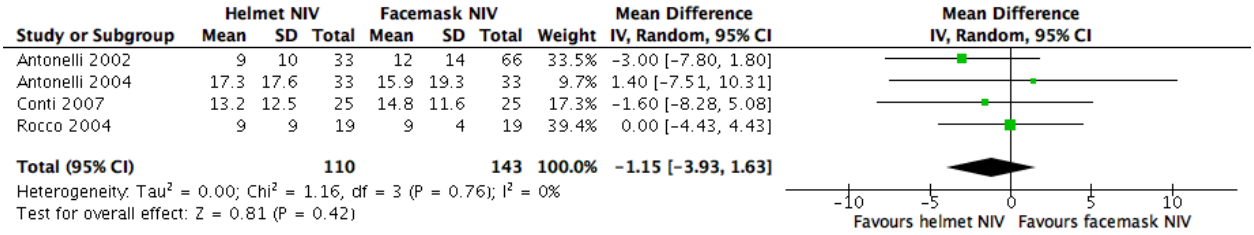
e-Figure 1: Effect of helmet NIV compared to facemask NIV on mortality. Observational data only. Df = degrees of freedom



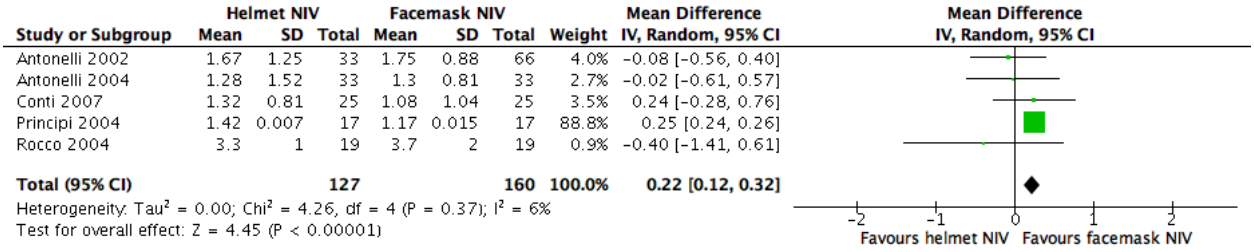
e-Figure 2: Effect of helmet NIV compared to facemask NIV on intubation. Observational data only. Studies are grouped by type of respiratory failure. Df = degrees of freedom



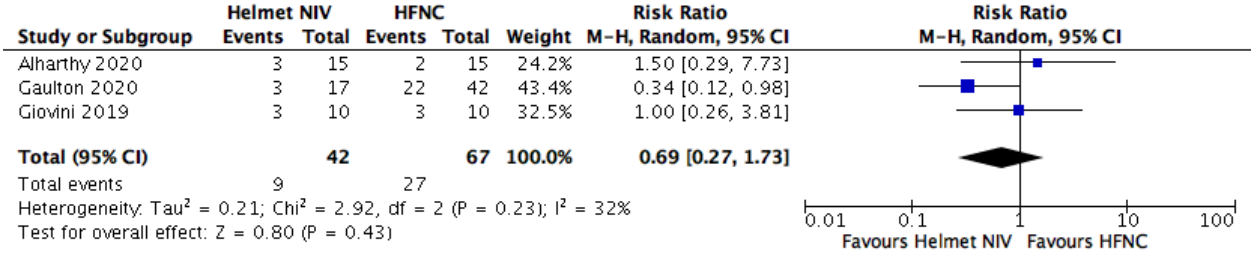
e-Figure 3: Effect of helmet NIV compared to facemask NIV on ICU length of stay. Observational data only. Df = degrees of freedom



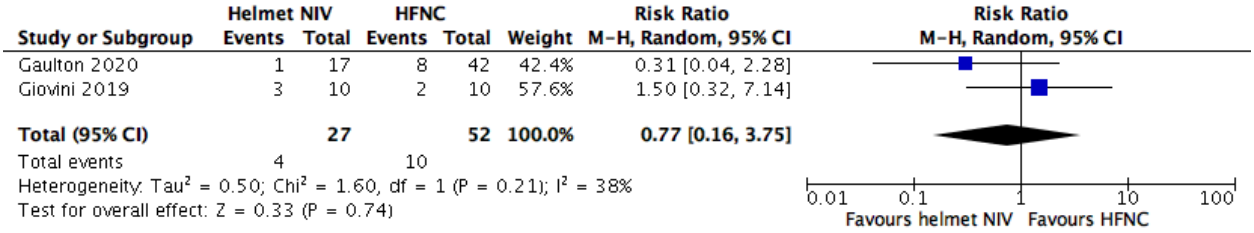
e-Figure 4: Effect of helmet NIV compared to facemask NIV on duration of NIV. Observational data only. Df = degrees of freedom



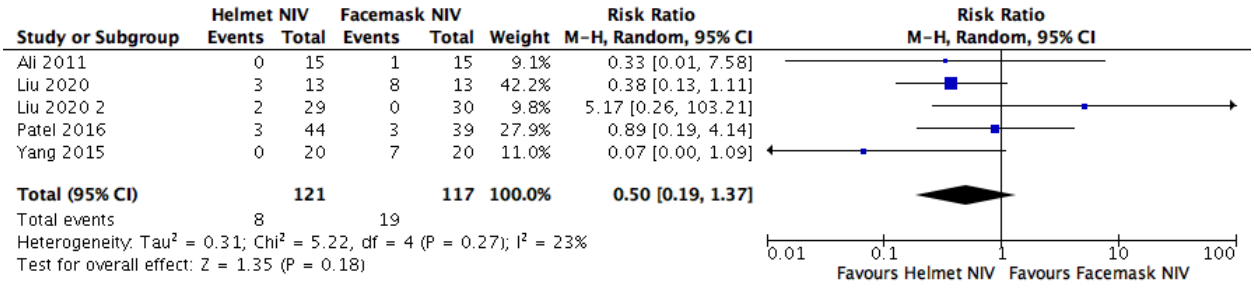
e-Figure 5: Effect of helmet NIV compared to high flow nasal cannula on intubation. Observational data only. Df = degrees of freedom



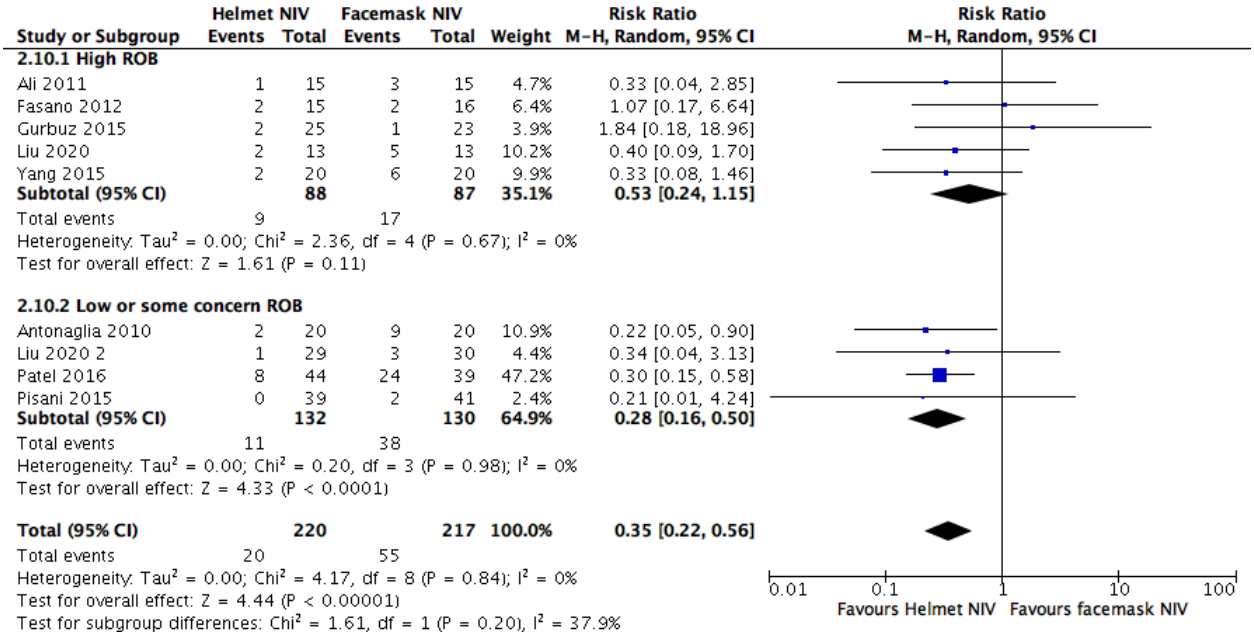
e-Figure 6: Effect of helmet NIV compared to high flow nasal cannula on mortality. Observational data only. Df = degrees of freedom



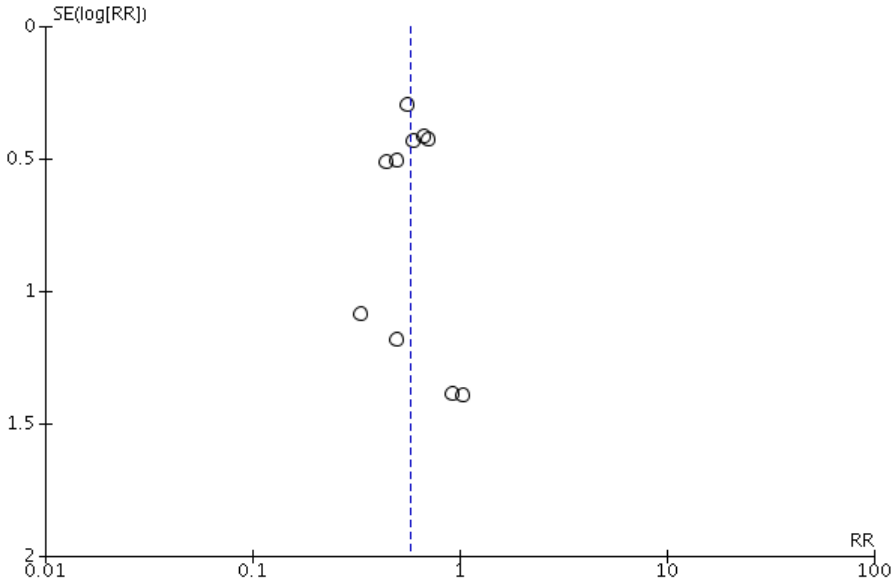
e-Figure 7: Effect of helmet NIV compared to facemask NIV on facial pressure sores. RCT data only. Df = degrees of freedom



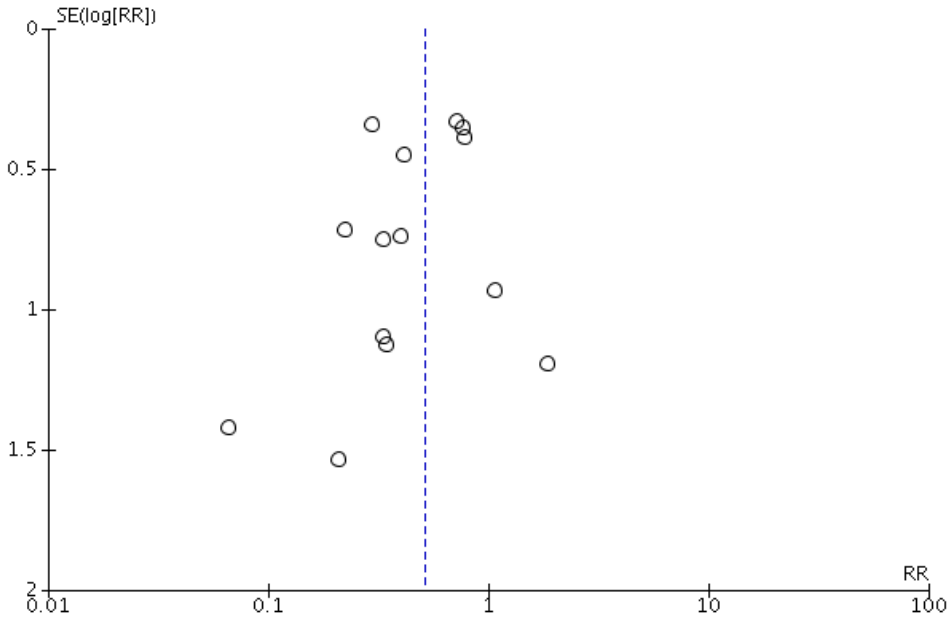
e-Figure 8: Effect of helmet NIV compared to facemask NIV on intubation. Studies are group by risk of bias. RCT data only. Df = degrees of freedom



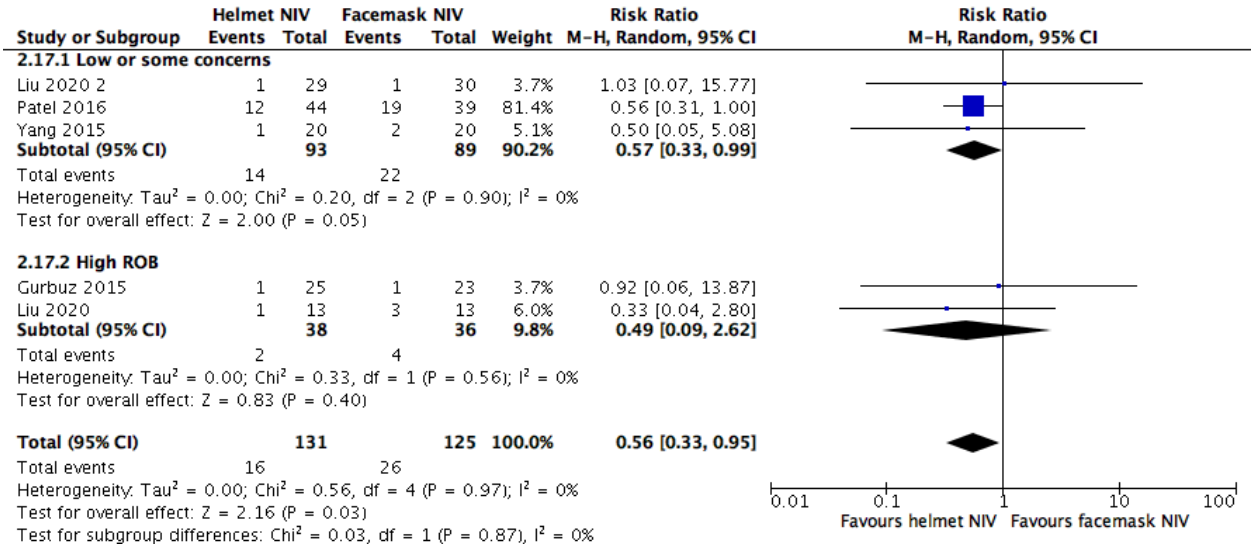
e-Figure 9: Funnel plot of helmet NIV compared to facemask NIV for the outcome of mortality



e-Figure 10: Funnel plot of helmet NIV compared to facemask NIV for the outcome of intubation



e-Figure 11: Effect of helmet NIV compared to facemask NIV on mortality. Studies are group by risk of bias. RCT data only. Df = degrees of freedom



Supplementary Table 1: PRISMA checklist

	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	4
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	7
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	7
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	7, Supplementary materials
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	9
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	8
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	9

Supplementary Table 1: PRISMA checklist

Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	9
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	9

Supplementary Table 2A: Risk of bias for RCTs for outcome of mortality

Study	Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall Bias for the outcome of Mortality
Adi, 2019	Some concerns	High	Low	Low	Some concerns	High
Gurbuz, 2015	Some concerns	High	Low	Low	Some concerns	High
Grieco, 2021	Low	Low	Low	Low	Low	Low
Liu 2020	Some concerns	Low	Low	Low	Some concerns	High
Patel 2016	Low	Low	Low	Low	Low	Low
Liu 2020 (2)	Low	Low	Low	Low	Low	Low
Yang 2015	Low	Low	Low	Low	Some concerns	Some concerns

Supplementary Table 2b: Risk of bias for observational studies

Study	Selection	Comparability	Outcome/Exposure
Alharthy, 2020	****	-	***
Antonelli, 2002	****	**	***
Antonelli, 2004	****	**	***
Conti, 2007	****	**	***
Gaulton, 2020	***	-	***
Giovini, 2019	****	**	***
Principi, 2004	****	**	***
Rocco, 2004	****	**	***

Supplementary Table 2c: Risk of bias for RCTs for outcome of intubation

Study	Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall Bias for the outcome of Intubation
Adi, 2019	Some concerns	High	Low	Low	Some concerns	High
Ali, 2011	Some concerns	High	Low	Low	Some concerns	High
Antogalia, 2010	Low	Low	Low	Low	Some concerns	Some concerns
Gurbuz, 2015	Some concerns	High	Low	Low	Some concerns	High
Fasano, 2012	Some concerns	High	Low	Low	Some concerns	High
Grieco, 2021	Low	Low	Low	Low	Low	Low
Liu 2020	Some concerns	Low	Low	Low	Some concerns	High
Patel 2016	Low	Low	Low	Low	Low	Low
Pisani 2015	Low	Low	Low	Low	Low	Low
Liu 2020 (2)	Low	Low	Low	Low	Low	Low
Yang 2015	Some concerns	Low	Low	Low	Some concerns	High

Supplementary Table 3: GRADE Summary of Findings Table

Question: Helmet NIV compared to oronasal NIV for respiratory failure

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Helmet NIV	oronasal NIV	Relative (95% CI)	Absolute (95% CI)		
Mortality (RCT)												
5	randomised trials	not serious	not serious	not serious	very serious [a]	none	16/131 (12.2%)	26/125 (20.8%)	**RR 0.56** (0.33 to 0.95)	**92 fewer per 1,000** (from 139 fewer to 10 fewer)	⨁⨁◯◯ LOW	CRITICAL
Intubation (RCT)												
9	randomised trials	serious [b]	not serious	not serious	serious [a]	none	20/220 (9.1%)	55/217 (25.3%)	**RR 0.35** (0.22 to 0.56)	**165 fewer per 1,000** (from 198 fewer to 112 fewer)	⨁⨁◯◯ LOW	CRITICAL
ICU LOS (RCT)												
6	randomised trials	serious [b]	serious [c]	not serious	serious [a]	none	153	147	-	MD **0.29 lower** (2.31 lower to 1.74 higher)	⨁◯◯◯ VERY LOW	IMPORTANT
Duration of NIV (RCT)												
4	randomised trials	serious [b]	not serious	not serious	serious [a]	none	94	93	-	MD **0.02 lower** (0.15 lower to 0.11 higher)	⨁⨁◯◯ LOW	IMPORTANT
Pressure sores (RCT)												
5	randomised trials	serious [b]	not serious	not serious	very serious [a,d]	none	8/121 (6.6%)	19/117 (16.2%)	**RR 0.50** (0.19 to 1.37)	**81 fewer per 1,000** (from 132 fewer to 60 more)	⨁◯◯◯ VERY LOW	IMPORTANT
Intubation (observational studies)												
5	observational studies	not serious	not serious	not serious	serious [a]	none	30/127 (23.6%)	63/160 (39.4%)	**RR 0.65** (0.44 to 0.95)	**138 fewer per 1,000** (from 221 fewer to 20 fewer)	⨁◯◯◯ VERY LOW	CRITICAL
Mortality (observational studies)												
5	observational studies	not serious	not serious	not serious	serious [a]	none	27/127 (21.3%)	55/160 (34.4%)	**RR 0.59** (0.40 to 0.88)	**141 fewer per 1,000** (from 206 fewer to 41 fewer)	⨁◯◯◯ VERY LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Helmet NIV	oronasal NIV	Relative (95% CI)	Absolute (95% CI)		
ICU LOS (observational studies)												
4	observational studies	not serious	not serious	not serious	very serious [a,d]	none	110	143	-	MD **1.15 lower** (3.93 lower to 1.63 higher)	⨁◯◯◯ VERY LOW	IMPORTANT
Duration of NIV (Observational studies)												
5	observational studies	not serious	not serious	not serious	serious [a]	none	127	160	-	MD **0.22 higher** (0.12 higher to 0.32 higher)	⨁◯◯◯ VERY LOW	IMPORTANT

CI: Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

Explanations

a. very low event numbers which are far below optimal information size
b. high proportion of the included studies have high ROB
c. High I squared with variable effects across studies
d. wide confidence intervals that don't exclude serious benefit or harm

Question: Helmet NIV compared to HFNC for respiratory failure

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Helmet NIV	HFNC	Relative (95% CI)	Absolute (95% CI)		
Mortality (RCTs)												
2	randomised trials	serious [a]	not serious	not serious	very serious [b,c]	none	17/148 (11.5%)	24/149 (16.1%)	**RR 0.72** (0.40 to 1.28)	**45 fewer per 1,000** (from 97 fewer to 45 more)	⨁◯◯◯ VERY LOW	CRITICAL
Intubation (RCTs)												
2	randomised trials	serious [a]	not serious	not serious	serious [c]	none	23/148 (15.5%)	39/149 (26.2%)	**RR 0.59** (0.39 to 0.91)	**107 fewer per 1,000** (from 160 fewer to 24 fewer6)	⨁⨁◯◯ LOW	CRITICAL
Mortality (Observational studies)												
2	observational studies	not serious	not serious	not serious	serious [b,c]	none	4/27 (14.8%)	10/52 (19.2%)	**RR 0.77** (0.16 to 3.75)	**44 fewer per 1,000** (from 162 fewer to 529 more)	⨁◯◯◯ VERY LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Helmet NIV	HFNC	Relative (95% CI)	Absolute (95% CI)		
Intubation (Observational studies)												
3	observational studies	not serious	not serious	not serious	serious [b]	none	9/42 (21.4%)	27/67 (40.3%)	**RR 0.69** (0.27 to 1.73)	**125 fewer per 1,000** (from 294 fewer to 294 more)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. One out of two included studies have high ROB
b. wide confidence intervals that do not exclude serious benefit or harm
c. very low event numbers which are far below optimal information size as only two small studies are included.

Supplementary Table 4: Characteristics of Included Cohort and Case Series Studies

Author	Year	Country	Type of Helmet	Settings Used for Helmet	Comparator	Settings Used for Comparator	Total (n)	Select Inclusion Criteria	Outcomes
Alharthy et al.	2020	Saudi Arabia	H-CPAP	CPAP at high flow rates to prevent rebreathing (median flow rate 45 L/min) with a median fraction of inspired oxygen of 40%.	High Flow Nasal Canula	Adjusted at a median flow rate of 60 L/min and median fraction of inspired oxygen of 40%.	30	Adult patients with confirmed COVID-19 requiring higher support than standard oxygen	Intubation Rate
Antonelli et al.	2002	Italy	H-NIV (CaStar)	Once the helmet was positioned, pressure support was increased in increments of 2–3 cm H2O to obtain the patient comfort, a respiratory rate lower than 25 breaths/min, and the disappearance of accessory muscle activity (as evaluated by palpating the sternocleidomastoid muscle). PEEP was increased in increments of 2–3 cm H2O up to 10–12 cm H2O to assure a peripheral oxygen saturation of at least 92% with the lowest FIO2 possible.	Facemask NIV	Not Described	99	Non-COPD patients with acute respiratory failure as defined by study protocol	Intubation Rate, Mortality, ICU Length of Stay, Duration of Mechanical Ventilation, Complications
Antonelli et al.	2004	Italy	H-NIV (CaStar)	After the mask was secured, the initial level of 10 cmH2O pressure support was gradually increased in increments of 2–3 cmH2O to obtain a respiratory rate of less than 25 breaths/min, disappearance of accessory muscle activity (evaluated by palpating the sternocleidomastoid muscle),12 and patient comfort. PEEP was set at5–7 cmH2O to counterbalance the intrinsic PEEP level.	Facemask NIV	Not Described	66	Patients with acute decompensation of COPD eligible for treatment with NPPV admitted to ICU	Intubation Rate, Mortality, ICU Length of Stay, Duration of Mechanical Ventilation, Complications
Conti et al.	2007	Italy	H-NIV (CaStar)	Started with 10 cm H2O of pressure support, with progressive stepwise increase of 2-3 cm H2O, according to patient comfort, to obtain a respiratory rate 25 breaths/min and the disappearance of accessory muscle activity or paradoxical abdominal motion. Positive end-expiratory pressure (PEEP) was increased in steps of 2–3 cm H2O, up to a maximum of 12 cm H2O, to maintain the arterial oxygen saturation over 90% with the lowest possible FIO2.	Facemask NIV	Not Described	50	Patients who developed post operative acute respiratory failure after abdominal surgery admitted to the ICU	Intubation Rate, Mortality, ICU Length of Stay, Duration of Mechanical Ventilation, Complications
Gaulton et al.	2020	USA	H-CPAP SeaLong	CPAP between 5 - 10 cm H2O and FiO2 titrated to keep >92%.	High Flow Nasal Canula	HFNC was adjusted at a median flow rate of 60 L/min and median fraction of inspired oxygen of 40%.	59	Patients with body mass index greater than or equal to 25 kg/m2 and were candidates for non-invasive respiratory support as per study protocol	Intubation Rate, Mortality
Giovini et al.	2019	Italy	H-CPAP	Not Described	High Flow Nasal Canula	Not Described	20	Patients with moderate ARDS as defined y Berlin criteria	Intubation Rate, Mortality

Principi et al.	2004	Italy	H-CPAP (CaStar)	High-flow CPAP (Vital Signs, Brighton, UK) was set at 8 cmH2O with FIO2 0.6 controlled by means of an oximeter (Miniox II Oxygen Monitor, Catalyst Research Owings Mills, Md., USA).	Facemask CPAP	Facemask CPAP (same settings as helmet group)	34	Patients presenting with dyspnea, tachypnea, use of accessory muscles, and paradoxical abdominal motion, with infiltrates on chest radiography	intubation Rate, Mortality, Duration of Mechanical Ventilation, Complications
Rocco et al.	2004	Italy	H-NIV (CaStar)	The ventilator was set with pressure support of 10 cm H2O, and the level of pressure support was progressively increased in increments of 2 to 3 cm H2O to obtain patient comfort, an RR 25 breaths/min, and the disappearance of accessory muscle activity. Positive end-expiratory pressure (PEEP) was increased by 2 to 3 cm H2O, up to a maximum level of 12 cm H2O to maintain the arterial oxygen saturation 90% with the lowest Fio2 possible.	Facemask NIV	Facemask NIV (same settings as helmet group)	38	Immunocompromised patients with hypoxemic acute respiratory failure and pulmonary infiltrates admitted to ICU	Intubation Rate, Mortality, ICU Length of Stay, Duration of Mechanical Ventilation, Complications

Non-Invasive Ventilation (NIV) Helmet – SR – Literature Search

Research Question(s)

1. In all patients with acute respiratory failure, does the use of helmet NIV reduce mortality, intubation rate and days of MV compared to oro-nasal NIV and high flow nasal cannula (HFNC).
   Patient – All adult patients acute with respiratory failure of any type or etiology
   Intervention – NIV delivered by helmet interface
   Control – Oro-nasal NIV or high flow nasal cannula
   Outcome – mortality, intubation, invasive mechanical ventilator free days, duration of mechanical ventilation, duration of NIV, ICU length of stay, hospital length of stay, patient comfort and adverse events
      -for mortality, we will capture closest to 30 days or if not available, hospital mortality
      -for intubation, we will capture any need for intubation during index hospitalization

Seed Articles:

- Ferreyro BL, et al. Association of noninvasive oxygenation strategies with all-cause mortality in adults with acute hypoxemic respiratory failure: a systematic review and meta-analysis. JAMA. 2020 Jul 7;324(1):57-67. https://pubmed.ncbi.nlm.nih.gov/32496521/
- Patel BK, et al. Effect of noninvasive ventilation delivered by helmet vs face mask on the rate of endotracheal intubation in patients with acute respiratory distress syndrome: a randomized clinical trial. JAMA. 2016;315(22):2435-2441. https://pubmed.ncbi.nlm.nih.gov/27179847/

Search by: Kaitryn Campbell (kcampbel@stjosham.on.ca)
Requestor: Dipayan Chaudhuri (dipayan.chaudhuri@medportal.ca)
Date(s): 2020 Oct 23
Limits: NOT case reports; Human NOT Animal
Databases: Ovid Medline [ppez] & Embase [oemezd]; Web of Science; The Cochrane Library; International HTA database (https://database.inahta.org/); EBSCO CINAHL Complete; LILACS; WHO COVID-19 Global literature on coronavirus disease (https://search.bvsalud.org/global-literature-on-novel-coronavirus-2019-ncov/)
Filters: None
Output: RIS (931 results total after duplicates removed)

Concept #1: Noninvasive Ventilation, etc.

Noninvasive Ventilation/
Oxygen Inhalation Therapy/ use ppez
Oxygen Therapy/ use oemezd
((non-invasive* OR noninvasive*) ADJ3 (oxygen* OR O2 OR ventilat*)).tw,kf,kw.

Respiratory Insufficiency/ use ppez
Respiratory Distress Syndrome, Adult/ use ppez
Respiratory Failure/ use oemezd
Acute Respiratory Failure/ use oemezd
Adult Respiratory Distress Syndrome/ use oemezd
((lung? OR respiratory OR respiration OR pulmonary OR ventilator?) ADJ2 (depress* OR insufficien* OR fail* OR deficien* OR disturb* OR dysfunction* OR compromis*)).tw,kf,kw.
(((acute OR adult*) ADJ respiratory distress) OR ARDS OR ARDSS).tw,kf,kw.

Continuous Positive Airway Pressure/ use ppez
Positive End Expiratory Pressure/ use oemezd
(continuous positive airway pressure OR CPAP OR nCPAP OR CPPB OR CPPV OR continuous positive pressure ventilation OR CPPV OR airway pressure release ventilation OR APRV OR ((bi-level OR bilevel) ADJ2 positive airway pressure) OR (hyperbaric ADJ (respiration OR ventilation)) OR

(positive pressure ADJ (breathing OR respiration OR ventilation)) OR positive endexpiratory pressure breathing OR PEEP).tw,kf,kw.
å
Concept #2: Helmet
Head Protective Devices/ use ppez
exp Helmet/ use oemezd
helmet*.tw,kf,kw.

exp animals/
exp animal experimentation/ OR exp animal experiment/
exp models animal/
nonhuman/
exp vertebrate/ OR exp vertebrates/
or/
exp humans/
exp human experimentation/ OR exp human experiment/
or/
25 not 28

(Case Reports.pt. OR *Case Report/) NOT (case series.ti. AND (Case Reports.pt. OR *Case Report/))

Ovid

Database(s): **Embase** 1974 to 2020 October 22, OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

Search Strategy:

#	Searches	Results
1	Noninvasive Ventilation/	12868
2	Oxygen Inhalation Therapy/ use ppez	14575
3	Oxygen Therapy/ use oemezd	30522
4	((non-invasive* or noninvasive*) adj3 (oxygen* or O2 or ventilat*)).tw,kf,kw.	25627
5	Respiratory Insufficiency/ use ppez	32369
6	Respiratory Distress Syndrome, Adult/ use ppez	19909
7	Respiratory Failure/ use oemezd	68775
8	Acute Respiratory Failure/ use oemezd	12805
9	Adult Respiratory Distress Syndrome/ use oemezd	39543
10	((lung? or respiratory or respiration or pulmonary or ventilator?) adj2 (depress* or insufficien* or fail* or deficien* or disturb* or dysfunction* or compromis*)).tw,kf,kw.	180943
11	(((acute or adult*) adj respiratory distress) or ARDS or ARDSS).tw,kf,kw.	61262
12	Continuous Positive Airway Pressure/ use ppez	7288
13	Positive End Expiratory Pressure/ use oemezd	55218
14	(continuous positive airway pressure or CPAP or nCPAP or CPPB or CPPV or continuous positive pressure ventilation or CPPV or airway pressure release ventilation or APRV or ((bi-level or bilevel) adj2 positive airway pressure) or (hyperbaric adj (respiration or ventilation)) or (positive pressure adj (breathing or respiration or ventilation)) or positive endexpiratory pressure breathing or PEEP).tw,kf,kw.	64104
15	or/1-14 [Noninvasive Ventilation, etc. Concept]	408808
16	Head Protective Devices/ use ppez	3598
17	exp Helmet/ use oemezd	5703
18	helmet*.tw,kf,kw.	12414
19	or/16-18 [Helmet Concept]	14658
20	exp animals/	49787816
21	exp animal experimentation/ or exp animal experiment/	2630293
22	exp models animal/	2002835
23	nonhuman/	6362133
24	exp vertebrate/ or exp vertebrates/	48451569
25	or/20-24	51664560
26	exp humans/	40330743
27	exp human experimentation/ or exp human experiment/	534778
28	or/26-27	40333169
29	25 not 28	11333047
30	15 and 19 [Noninvasive Ventilation, etc.+ Helmet]	670
31	30 not 29 [Noninvasive Ventilation, etc.+ Helmet, Human NOT Animal Filter applied]	652
32	(Case Reports.pt. or *Case Report/) not (case series.ti. and (Case Reports.pt. or *Case Report/))	2144091
33	31 not 32 [Noninvasive Ventilation, etc.+ Helmet, Human NOT Animal Filter applied, Case Reports removed]	622
34	remove duplicates from 33 [Final results, Human NOT Animal, Case Reports & duplicates removed]	426

Web of Science

Set	Results	Search Terms
# 25	326	#24 AND #18 Indexes=SCI-EXPANDED, CPCI-S, ESCI Timespan=All years
# 24	9,501	#23 OR #22 OR #21 OR #20 OR #19
# 23	2,041	AK=helmet*
# 22	6,684	AB=helmet*
# 21	3,996	TI=helmet*
# 20	9,296	TS=helmet*
# 19	331	TS=Head Protective Devices
# 18	112,258	#17 OR #16 OR #15 OR #14 OR #13 OR #12 OR #11 OR #10 OR #9 OR #8 OR #7 OR #6 OR #5 OR #4 OR #3 OR #2 OR #1
# 17	5,966	AK=(continuous positive airway pressure OR CPAP OR nCPAP OR CPPB OR CPPV OR continuous positive pressure ventilation OR CPPV OR airway pressure release ventilation OR APRV OR ((bi-level OR bilevel) NEAR/2 positive airway pressure) OR (hyperbaric NEAR/1 (respiration OR ventilation)) OR (positive pressure NEAR/1 (breathing OR respiration OR ventilation)) OR positive endexpiratory pressure breathing OR PEEP)
# 16	17,782	AB=(continuous positive airway pressure OR CPAP OR nCPAP OR CPPB OR CPPV OR continuous positive pressure ventilation OR CPPV OR airway pressure release ventilation OR APRV OR ((bi-level OR bilevel) NEAR/2 positive airway pressure) OR (hyperbaric NEAR/1 (respiration OR ventilation)) OR (positive pressure NEAR/1 (breathing OR respiration OR ventilation)) OR positive endexpiratory pressure breathing OR PEEP)
# 15	12,327	TI=(continuous positive airway pressure OR CPAP OR nCPAP OR CPPB OR CPPV OR continuous positive pressure ventilation OR CPPV OR airway pressure release ventilation OR APRV OR ((bi-level OR bilevel) NEAR/2 positive airway pressure) OR (hyperbaric NEAR/1 (respiration OR ventilation)) OR (positive pressure NEAR/1 (breathing OR respiration OR ventilation)) OR positive endexpiratory pressure breathing OR PEEP)
# 14	10,459	TS=Continuous Positive Airway Pressure
# 13	8,234	AK=(((acute OR adult*) NEAR/1 respiratory distress) OR ARDS OR ARDSS)
# 12	16,163	AB=(((acute OR adult*) NEAR/1 respiratory distress) OR ARDS OR ARDSS)
# 11	12,237	TI=(((acute OR adult*) NEAR/1 respiratory distress) OR ARDS OR ARDSS)
# 10	7,119	AK=((lung? OR respiratory OR respiration OR pulmonary OR ventilator?) NEAR/2 (depress* OR insufficien* OR fail* OR deficien* OR disturb* OR dysfunction* OR compromis*))
# 9	44,619	AB=((lung? OR respiratory OR respiration OR pulmonary OR ventilator?) NEAR/2 (depress* OR insufficien* OR fail* OR deficien* OR disturb* OR dysfunction* OR compromis*))
# 8	15,389	TI=((lung? OR respiratory OR respiration OR pulmonary OR ventilator?) NEAR/2 (depress* OR insufficien* OR fail* OR deficien* OR disturb* OR dysfunction* OR compromis*))
# 7	7,886	TS=Respiratory Distress Syndrome, Adult
# 6	6,679	TS=Respiratory Insufficiency
# 5	3,255	AK=((non-invasive* OR noninvasive*) NEAR/3 (oxygen* OR O2 OR ventilat*))
# 4	6,556	AB=((non-invasive* OR noninvasive*) NEAR/3 (oxygen* OR O2 OR ventilat*))
# 3	5,713	TI=((non-invasive* OR noninvasive*) NEAR/3 (oxygen* OR O2 OR ventilat*))
# 2	1,211	TS=Oxygen Inhalation Therapy
# 1	8,419	TS=Noninvasive Ventilation

The Cochrane Library

ID	Search	Hits
#1	MeSH descriptor: [Noninvasive Ventilation] this term only	241
#2	MeSH descriptor: [Oxygen Inhalation Therapy] this term only	1157
#3	((non-invasive* OR noninvasive*) NEAR3 (oxygen* OR O2 OR ventilat*)):ti,ab,kw	0
#4	MeSH descriptor: [Respiratory Insufficiency] this term only	1577
#5	((lung? OR respiratory OR respiration OR pulmonary OR ventilator?) NEAR2 (depress* OR insufficien* OR fail* OR deficien* OR disturb* OR dysfunction* OR compromis*)):ti,ab,kw OR (((acute OR adult*) NEXT respiratory distress) OR ARDS OR ARDSS):ti,ab,kw	2826
#6	MeSH descriptor: [Continuous Positive Airway Pressure] this term only	1074
#7	(continuous positive airway pressure OR CPAP OR nCPAP OR CPPB OR CPPV OR continuous positive pressure ventilation OR CPPV OR airway pressure release ventilation OR APRV OR ((bi-level OR bilevel) NEAR2 positive airway pressure) OR (hyperbaric NEXT (respiration OR ventilation)) OR (positive pressure NEXT (breathing OR respiration OR ventilation)) OR positive endexpiratory pressure breathing OR PEEP):ti,ab,kw	9922
#8	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7	1694300
#9	MeSH descriptor: [Head Protective Devices] explode all trees	97
#10	(helmet*):ti,ab,kw	459
#11	#9 OR #10	476
#12	#8 AND #11 in Trials	468

EBSCO CINAHL Complete

#	Query	Results
S11	S7 AND S10	26
S10	S8 OR S9	2,980
S9	TI helmet* OR AB helmet*	2,157
S8	(MH "Head Protective Devices")	2,098
S7	S1 OR S2 OR S3 OR S4 OR S5 OR S6	41,268
S6	TI (continuous positive airway pressure OR CPAP OR nCPAP OR CPPB OR CPPV OR continuous positive pressure ventilation OR CPPV OR airway pressure release ventilation OR APRV OR ((bi-level OR bilevel) N2 positive airway pressure) OR (hyperbaric N1 (respiration OR ventilation)) OR (positive pressure N1 (breathing OR respiration OR ventilation)) OR positive endexpiratory pressure breathing OR PEEP) OR AB (continuous positive airway pressure OR CPAP OR nCPAP OR CPPB OR CPPV OR continuous positive pressure ventilation OR CPPV OR airway pressure release ventilation OR APRV OR ((bi-level OR bilevel) N2 positive airway pressure) OR (hyperbaric N1 (respiration OR ventilation)) OR (positive pressure N1 (breathing OR respiration OR ventilation)) OR positive endexpiratory pressure breathing OR PEEP)	8,111
S5	(MH "Continuous Positive Airway Pressure")	5,335
S4	TI ((lung? OR respiratory OR respiration OR pulmonary OR ventilator?) N2 (depress* OR insufficien* OR fail* OR deficien* OR disturb* OR dysfunction* OR compromis*)) OR AB ((lung? OR respiratory OR respiration OR pulmonary OR ventilator?) N2 (depress* OR insufficien* OR fail* OR deficien* OR disturb* OR dysfunction* OR compromis*)) OR TI (((acute OR adult*) N1 respiratory distress) OR ARDS OR ARDSS) OR AB (((acute OR adult*) N1 respiratory distress) OR ARDS OR ARDSS)	22,824
S3	(MH "Respiratory Failure") OR (MH "Respiratory Distress Syndrome+")	10,890
S2	TX (non-invasive* OR noninvasive*) N3 (oxygen* OR O2 OR ventilat*)	3,999
S1	(MH "Pressure Support Ventilation") OR (MH "Positive Pressure Ventilation+")	11,309

International HTA database (https://database.inahta.org/)
=0 relevant results

"Head Protective Devices"[mhe] OR (helmet*)

LILACS (http://bases.bireme.br/cgi-bin/wxislind.exe/iah/online/?IsisScript=iah/iah.xis&base=LILACS&lang=i&form=F)
=0 relevant results

helmet* [all]

WHO COVID-19 Global literature on coronavirus disease (https://search.bvsalud.org/global-literature-on-novel-coronavirus-2019-ncov/)
=40 results

helmet* [all]