Philippine COVID-19 Living Clinical Practice Guidelines
Institute of Clinical Epidemiology, National Institutes of Health, UP Manila
In cooperation with the Philippine Society for Microbiology and Infectious Diseases
Funded by the Department of Health

EVIDENCE SUMMARY

Should non-invasive ventilation be used over high flow nasal cannula for patients with severe and critical COVID-19?

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RECOMMENDATION

We suggest the use of either high flow nasal cannula or non-invasive positive pressure ventilation in COVID-19 patients with hypoxemic respiratory failure in the absence of any indication for emergent invasive mechanical ventilation. *(Low certainty of evidence; Weak recommendation)*

Consensus Issues

The risk of aerosolization using non-invasive ventilation was not discussed in the identified studies, but case series and reports have suggested minimal risk for health care workers. Standard of procedure includes the use of filters in the expiratory limb tubing for non-invasive ventilation and use of face masks for patients on high flow nasal cannula. Physicians must be cognizant of the indications for intubation such as continued and progressive deterioration, and signs of respiratory failure.

Key Findings

Two randomized controlled trials were evaluated to compare the effect of non-invasive ventilation (NIV) and high flow nasal cannula (HFNC) oxygenation in improving clinical outcomes in COVID-19 patients with respiratory failure. Direct comparison of NIV in the form of helmet and face mask CPAP with HFNC in 218 COVID-19 patients with hypoxemia showed that reduction in mortality and need for endotracheal intubation were inconclusive. Certainty of evidence was low due to serious risk of bias and serious imprecision. Indirect mixed treatment comparison of NIV in the form of helmet CPAP and HFNC among COVID-19 patients with hypoxemia also showed no significant difference in terms of in-hospital mortality, need for mechanical ventilation, intensive care unit admission, and length of hospital stay.

Introduction

Non-invasive ventilation (NIV) has been one of the options in managing patients with acute respiratory failure. It decreases the need to escalate to invasive mechanical ventilation; however, its use in COVID-19 is still under investigation. Devices such as continuous positive airway pressure (CPAP), and bilevel positive airway pressure (BiPAP) can provide Positive End Expiratory Pressure (PEEP), which aids in decreasing inspiratory effort. Compared to HFNC, mask and helmet CPAP are able to provide higher levels of PEEP which can contribute to decreasing the incidence of invasive mechanical intubation.[1] A systemic review that included 31 journal articles and 5136 participants with different non-COVID-related etiologies of respiratory failure evaluated whether HFNC was superior to NIV in preventing mortality. The result did not reach statistical significance and there was no difference between the two interventions in terms

of length of hospital stay and the occurrence of adverse events such as barotrauma.[2] The practice of placing patients on non-invasive ventilation such as CPAP and BiPAP has not been widely used, with a recorded prevalence of 10% and 5.9% of patients in the United Kingdom and in the Philippines respectively.[3,4] Studies on non-COVID patients have demonstrated that HFNC or NIV offer physiological benefit for patients requiring respiratory support. [2] However, clinically beneficial improvement in patient outcomes such as prevention of invasive mechanical ventilation and reduction of mortality and their association with the use of NIV or HFNC among COVID-19 patients with respiratory failure remains to be unanswered. This review aims to evaluate the effectiveness of NIV compared with HFNC among COVID-19 patients with respiratory failure.

Review Methods

A comprehensive literature search was done as of 07 December 2021 on the use of NIV compared to HFNC in COVID-19 using Medline, Cochrane Library, Google Scholar, clinicaltrials.gov, and medRxiv (pre-prints) with the following keywords: “CPAP”, “non-invasive ventilation”, “high flow nasal cannula”, “COVID-19”, and “SARS-COV2”. All search yields were reviewed and appraised. Randomized controlled trials comparing NIV with HFNC in COVID-19 and respiratory failure were included.

Results

Direct Comparison of NIV versus HFNC

Two randomized controlled trials compared NIV and HFNC among COVID-19 patients with hypoxemic respiratory failure.[5,6] The trials enrolled 218 adult patients admitted to the intensive care unit (ICU). One study [5] randomized patients to either NIV (as helmet CPAP) or HFNC while the other study [6] randomized patients to either NIV (as facemask or helmet CPAP) or HFNC. Both studies reported clinical outcomes such as mortality, need to shift to invasive mechanical ventilation, and clinical improvement. Pooled analysis showed that reduction in mortality was inconclusive (RR 1.28, 95% CI 0.77-2.12; moderate certainty). Certainty of evidence was downgraded to moderate due to serious imprecision. The need for mechanical ventilation between the two intervention groups was likewise inconclusive (RR 0.96, 95% CI 0.32-2.92; low certainty). Certainty of evidence was downgraded to low due serious risk of bias because of the lack of participant and study personnel blinding, and serious imprecision. In one RCT [6], no statistically significant improvement in median respiratory rate (NIV at 24 breaths per minute versus HFNC at 24 breaths per minute; p=0.57), median oxygen saturation (NIV at 96% versus HFNC at 96%; p=0.52) and median PF ratio (NIV at 153.60 versus HFNC at 118.33; p=0.10) were found at 24 hours after initiation of NIV or HFNC.

Indirect Comparison of NIV and HFNC versus Conventional Oxygen Therapy (COT)

One randomized controlled trial [7] compared NIV (as facemask CPAP) to COT and HFNC to COT in 1272 adult COVID-19 patients with acute respiratory failure defined as peripheral oxygen saturation of 94% or below despite receiving oxygen support with fraction of inspired oxygen of at least 40%. Indirect mixed treatment comparison to determine the effect of NIV compared with HFNC showed higher ranking probability for NIV but inconclusive difference in terms of in-hospital mortality (RR 0.93, 95% CrI 0.57-1.49; moderate certainty), need for invasive mechanical ventilation (RR 0.82, 95% CrI 0.53-1.27; low certainty), ICU admission (RR 0.84; 95% CrI 0.61-1.11; low certainty), and length of hospital stay (MD -2.03, 95% CrI -6.27-2.13; low certainty). Findings in this indirect comparison were concordant with the results reported in the above randomized controlled trials [5,6] which directly compared NIV and HFNC. Certainty of evidence for in-hospital mortality was downgraded to moderate due to imprecision while certainty of

evidence for need for mechanical ventilation, ICU admission, and overall length of hospital stay were downgraded to low due to lack of blinding and imprecision.

Evidence to Decision

There is still insufficient evidence and a scarce amount of published randomized controlled trials on the effect of NIV in COVID-19. Though there is promising evidence on and benefits from the use of helmet CPAP, it is still unavailable in the Philippines and is only accessible in countries such as the United States and United Kingdom among others. Infection control issues such as aerosol generation in NIV is also a concern especially for healthcare workers. While the use of a helmet CPAP has minimal aerosol generation as long as there are no leaks [8-10], the use of a face mask CPAP may produce aerosols at the exhalation ports and also if there are air leaks on the face. Placement of filters in the expiratory tubing may mitigate aerosol leak without affecting the patient's breathing.[11] Adverse events may also occur in patients on NIV. Among the most common serious adverse events seen in patients on CPAP were pneumothorax and pneumomediastinum, the incidence of which has been reported at approximately 3-4%.[5,12]

Recommendations from Other Groups

Four Guidelines on the use of NIV in COVID-19 were identified. Their recommendations are summarized in the table below:

Group/Society or Network	Year	Recommendation	Level of Evidence/Strength of Recommendation
European Respiratory Journal [12]	2020	We suggest HFNC or non-invasive CPAP delivered through either a helmet or a face-mask for patients with COVID-19 and hypoxemic acute respiratory failure	Conditional Recommendation Very Low Certainty of Evidence
National Institutes of Health [13]	2021	In the absence of an indication for endotracheal intubation, the Panel recommends a closely monitored trial of NIPPV for adults with COVID-19 and acute hypoxemic respiratory failure and for whom HFNC is not available	BIIa
World Health Organization [14]	2021	In selected patients with COVID-19 and mild ARDS, a trial of HFNO, non-invasive	Conditional recommendation

		ventilation – continuous positive airway pressure (CPAP), bilevel positive airway pressure (BiPAP) may be used	
Surviving Sepsis Campaign [15]	2020	In adults with COVID-19 and acute hypoxemic respiratory failure, if HFNC is not available and there is no urgent indication for endotracheal intubation, we suggest a trial of NIPPV with close monitoring and short-interval assessment for worsening of respiratory failure	Weak
		We were not able to make a recommendation regarding the use of helmet NIPPV compared with mask NIPPV. It is an option, but we are not certain about its safety or efficacy in COVID-19	No recommendation

Research Gaps

More clinical trials comparing NIV with HFNC are needed to establish conclusive benefits especially on clinically important outcomes such as the reduction in mortality and reduction in mechanical ventilation. Furthermore, studies on the aerosol-generating effects associated with the use if NIV, which may increase transmission of infection to healthcare workers, should also be included as a safety outcome. Currently, there are 3 ongoing randomized controlled trials, which may further elucidate and provide evidence on its use and safety in preventing mortality.

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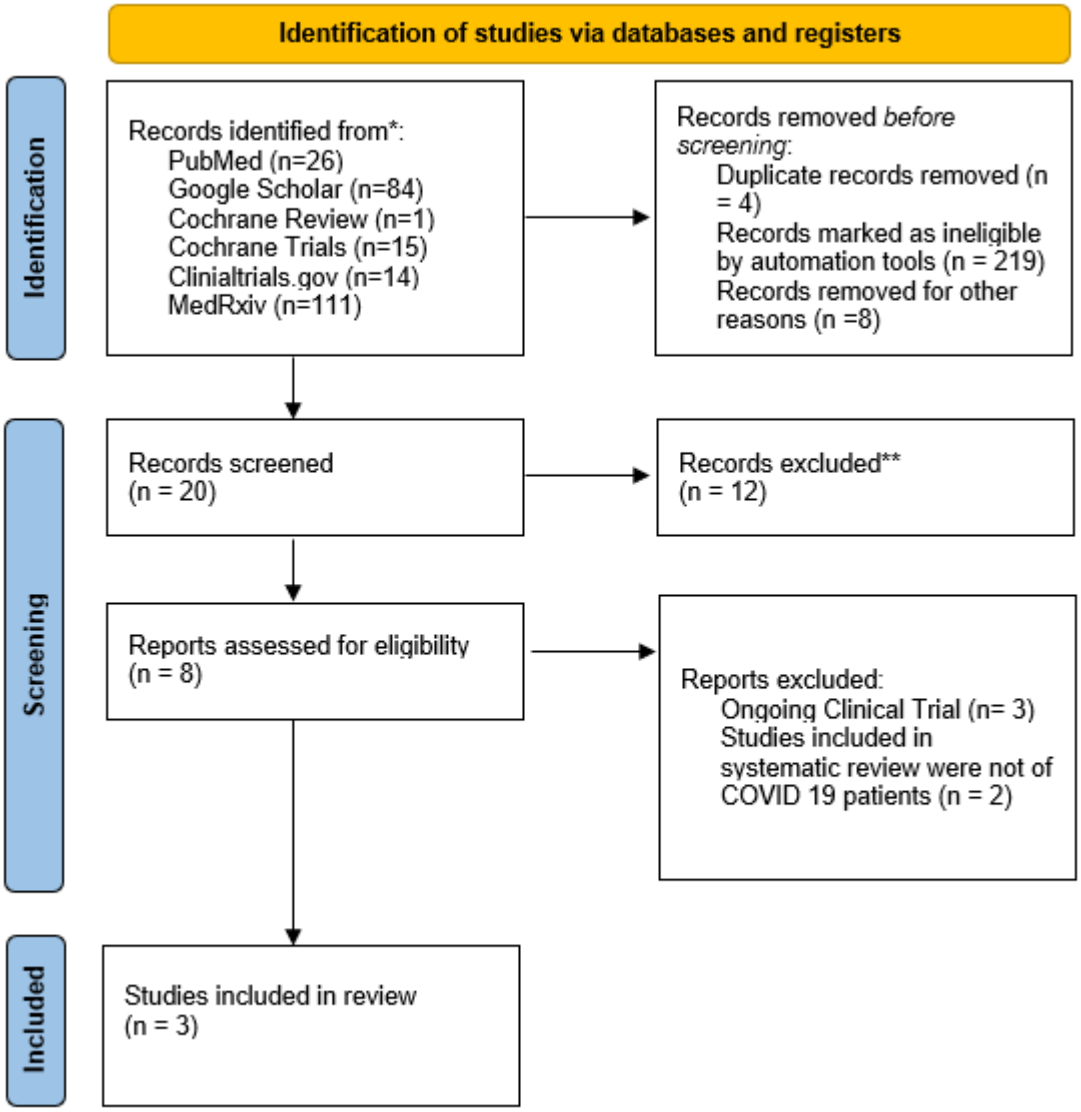
Appendix 1. Evidence to Decision

Table 1. Summary of initial judgements prior to the panel discussion (N=5)

FACTORS	JUDGEMENT					RESEARCH EVIDENCE/ADDITIONAL CONSIDERATIONS
Problem	No	Yes (5)				• Non-invasive ventilation has been one of the options in managing patients with acute respiratory failure. It decreases the need to escalate to invasive mechanical ventilation, however, its use in COVID-19 is still under investigation.
Benefits	Large (2)	Moderate (3)	Small	Uncertain		• No significant difference in mortality with the use of NIV compared to HFNC, invasive mechanical ventilation rate. • No statistically significant improvement in median respiratory rate (NIV at 24 breaths per minute versus HFNC at 24 breaths per minute; p=0.57), median oxygen saturation (NIV at 96% versus HFNC at 96%; p=0.52) and median PF ratio (NIV at 153.60 versus HFNC at 118.33; p=0.10) were found at 24 hours after initiation of NIV or HFNC.
Harm	Large (1)	Small (2)	Uncertain (2)	No response		• Concerns: Infection control measures such as aerosol generation in NIV. • The use of a helmet CPAP has minimal aerosol generation as long as there are no leaks. • Adverse events on NIV: pneumothorax and pneumomediastinum reported at approximately 3-4%.

Certainty of Evidence	High	Moderate (1)	Low (4)	Very low			• Certainty of evidence was low due the risk of bias and imprecision
Balance of effects	Favors drug (1)	Does not favor drug (1)	Uncertain (3)				
Values	Important uncertainty or variability	Possibly important uncertainty or variability (4)	Possibly NO important uncertainty or variability (1)	No important uncertainty or variability			
Resources Required	Uncertain (3)	Large cost	Moderate Cost (2)	Negligible cost	Moderate savings	Large savings	
Certainty of evidence of required resources	No included studies (5)	Very low	Low	Moderate	High		
Cost effectiveness	No included studies (4)	Favors the comparison	Does not favor either the intervention or the comparison (1)	Favors the intervention			
Equity	Uncertain (2)	Reduced (1)	Probably no impact (1)	Increased (1)			
Acceptability	Uncertain (2)	No	Yes (3)				
Feasibility	Uncertain (3)	No	Yes (2)				

Appendix 2. PRISMA Flow Diagram



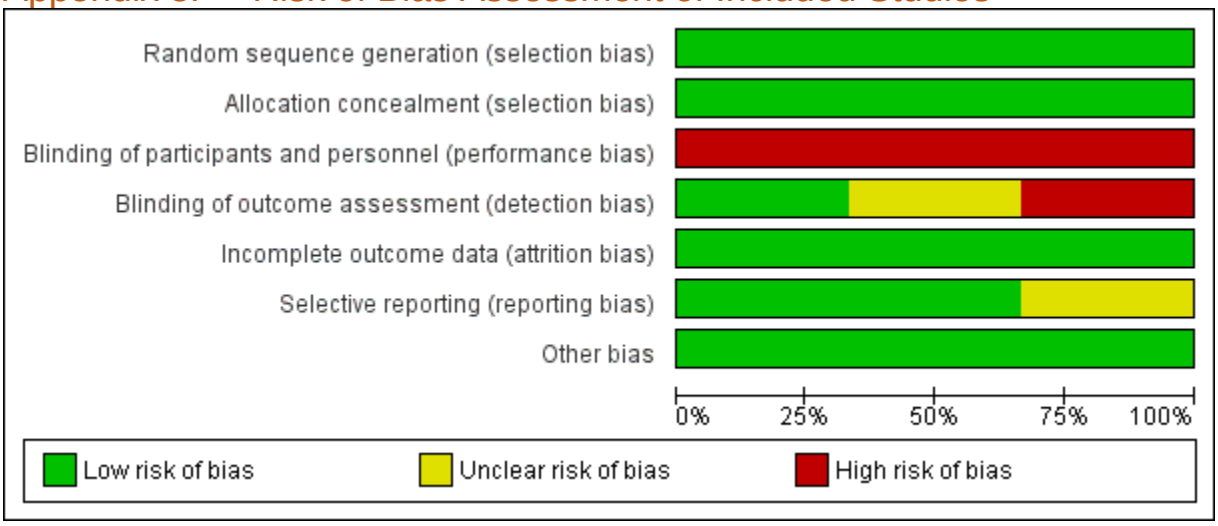
Appendix 3. Characteristics of Included Studies

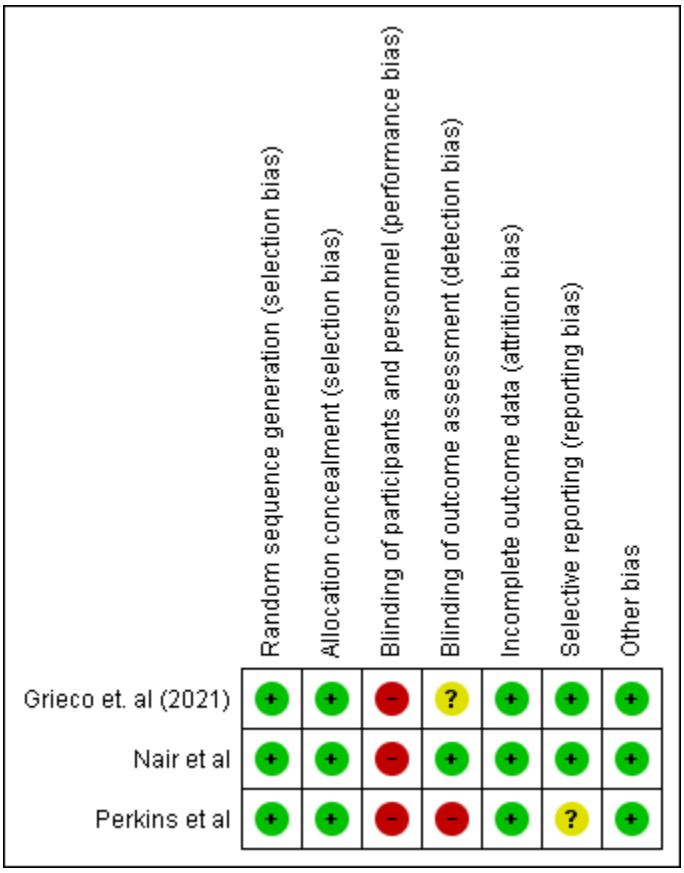
Study ID Title Author	Study Design	Setting/Country	Total number of Patients Included	Population	Intervention	Comparator/Control	Outcomes
Effect of Helmet Noninvasive Ventilation VS High-Flow Nasal Oxygen on Days Free of Respiratory Support in Patients with COVID_19 and Moderate to Severe Hypoxemic Respiratory Failure The HENIVOT Randomized Clinical Trial Grieco et. al March 2021	Investigator-initiated 2-group open label, multicenter randomized clinical trial	Italy	n=109	All adult patients admitted in the intensive care units with acute hypoxemic respiratory failure and diagnosed with COVID-19 Inclusion Criteria: PaO2/FiO2 equal or below 200 Partial pressure of arterial carbon dioxide equal to or lower than 45 mmHg Absence of history of chronic respiratory failure or moderate to severe cardiac insufficiency (NYHA >II or LV ejection fraction of <50%) Exclusion Criteria: Acute exacerbation of chronic pulmonary disease Kidney failure	Non-invasive ventilation was delivered by a compressed gas-based ventilator connected to the helmet through a bi-tube circuit Initial pressure support between 10 and 12 cm H2) eventually increased to ensure a peak inspiratory flow ot 100L//min Positive ed expiratory pressure between 10 and 12 cm H2) and FiO2 titrated to obtain SpO2 between 92 and 98%	High flow nasal cannula for 48 hours Gas flow initially set at 60L/min and decreased in case of intolerance, FIO2 titrated to obtain peripheral oxygen saturation as mea sured by pulse oximetry (SpO2) between 92% and 98%, and humidification chamber was set at 37 °C or 34 °C according to the patient's comfort.	Primary Outcome Number of days free of respirator support within 28 days after enrollment Secondary outcome: proportion of patients who required endotracheal intubation within 28 days from study enrollment, number of days free of invasive mechanical ventilation at days 28 and 60 Intensive care unit mortality In hospital mortality 28 and 60 day mortality Intensive care unit length of stay and hospital length of stay 90-day mortality Quality of life after 6 and 12 hours

Study ID Title Author	Study Design	Setting/Country	Total number of Patients Included	Population	Intervention	Comparator/Control	Outcomes
Comparison of High-Flow Nasal Cannula and Noninvasive Ventilation in Acute Hypoxemic Respiratory Failure due to Severe COVID-19 Pneumonia Nair et al September 2021	Single-center, prospective randomized controlled trial	India	n= 109	Adult patients 18-75 years old Severe COVID-19 pneumonia presenting with fever, cough, respiratory distress with frequency >30 breaths/min and/or room air SpO2 <90%	NIV with either mask/helmet device connected to an ICU ventilator with the setting of Pressure support of 10-20 cmH2O adjusted to obtain an expired tidal volume of 7-10 mL/kg of PBW and PEEP 5-10 cm H2O and FiO2 0.5-1 titrated to target SpO2 >94%	HFNC with large bore binasal prongs and high flow heated humidifier device. Initial flow set up was at 50lpm and FiO2 of 1.0 The flow and FiO2 were adjusted between 30-60lpm and 0.5-1.0 to maintain SpO2 of >94%	Primary Outcome: Early intubation rate Proportion of subjects requiring invasive mechanical ventilation at 48 hours of ICU admission Secondary Outcome Late intubation rate Early improvement in oxygenation In hospital mortality Proportion of patients requiring awake prone positioning
Study ID Title Author	**Study Design**	**Setting/Country**	**Total number of Patients Included**	**Population**	**Intervention**	**Comparator/Control**	**Outcomes**
Comparison of High-Flow Nasal Cannula and Noninvasive Ventilation in Acute Hypoxemic Respiratory Failure due to Severe COVID-19 Pneumonia Nair et al September 2021	Single-center, prospective randomized controlled trial	India	n= 109	Adult patients 18-75 years old Severe COVID-19 pneumonia presenting with fever, cough, respiratory distress with frequency >30 breaths/min and/or room air SpO2 <90%	NIV with either mask/helmet device connected to an ICU ventilator with the setting of Pressure support of 10-20 cmH2O adjusted to obtain an expired tidal volume of 7-10 mL/kg of PBW and PEEP 5-10 cm H2O and FiO2 0.5-1 titrated to target SpO2 >94%	HFNC with large bore binasal prongs and high flow heated humidifier device. Initial flow set up was at 50lpm and FiO2 of 1.0 The flow and FiO2 were adjusted between 30-60lpm and 0.5-1.0 to maintain SpO2 of >94%	Primary Outcome: Early intubation rate Proportion of subjects requiring invasive mechanical ventilation at 48 hours of ICU admission Secondary Outcome Late intubation rate Early improvement in oxygenation In hospital mortality Proportion of patients requiring awake prone positioning

Study ID Title Author	Study Design	Setting/Country	Total number of Patients Included	Population	Intervention	Comparator/Control	Outcomes
An adaptive randomized controlled trial of non-invasive respiratory strategies in acute respiratory failure patients with COVID-19 Perkins et. Al (2021) (PREPRINT)	Parallel group, open-label, three-arm, adaptive, randomized controlled trial	London, United Kingdom	1259	Adults >18 years old hospitalized with COVID-19 Acute respiratory failure defined as SpO2 of <94% despite receiving a fraction of inspired oxygen of at least 0.4 Deemed suitable for tracheal intubation of treatment escalation was required	Participants randomized to High Flow Nasal Cannula started treatment as soon as possible	Conventional oxygen therapy (via face mask or nasal cannulae)	Primary Outcome Composite outcome of tracheal intubation or mortality within 30-days of randomization Secondary Outcomes Incidence of tracheal intubation and mortality at 30 days Time to tracheal intubation Duration of invasive mechanical ventilation Time to death Mortality Incidence of intensive care unit admission Length of stay

Appendix 3. Risk of Bias Assessment of Included Studies





Appendix 4. Forest Plots

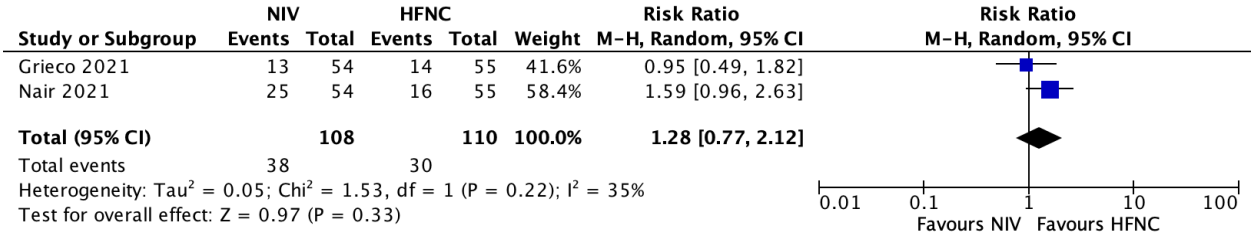


Figure 4-1 Forest plot for In-hospital Mortality

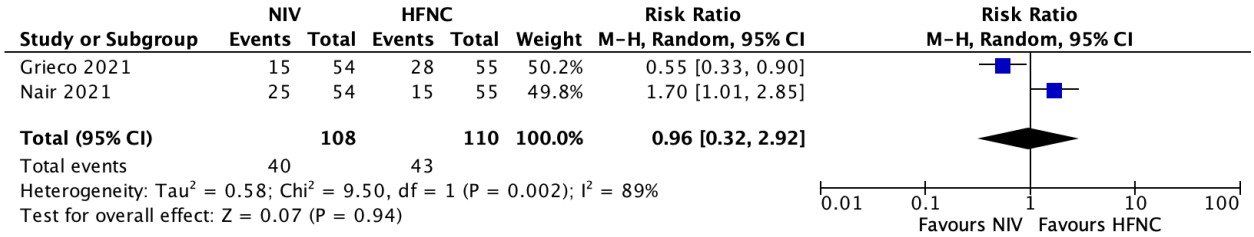


Figure 4-2 Forest plot for Need for Invasive Mechanical Ventilation

Appendix 5. League Tables for Bayesian Indirect Comparison

Table 5-1 League Table for In-hospital Mortality

Treatment effects for all studies: comparison of all treatment pairs.

	COT	HFNC	NIV
COT	COT	0.93 (0.67, 1.29)	0.86 (0.61, 1.21)
HFNC	1.08 (0.78, 1.49)	HFNC	0.93 (0.57, 1.49)
NIV	1.16 (0.82, 1.64)	1.07 (0.67, 1.75)	NIV

Treatment effects are expressed as relative risk (RR) with 95% credible intervals (95% CrI)

Table 5-2 League Table for Invasive Mechanical Intubation

Treatment effects for all studies: comparison of all treatment pairs.

	COT	HFNC	NIV
COT	COT	0.98 (0.73, 1.33)	0.81 (0.59, 1.11)
HFNC	1.02 (0.75, 1.37)	HFNC	0.82 (0.53, 1.27)
NIV	1.24 (0.9, 1.7)	1.22 (0.79, 1.88)	NIV

Treatment effects are expressed as relative risk (RR) with 95% credible intervals (95% CrI)

Table 5-3 League Table for ICU Admission

Treatment effects for all studies: comparison of all treatment pairs.

	COT	HFNC	NIV
COT	COT	1.04 (0.86, 1.26)	0.88 (0.72, 1.07)
HFNC	0.96 (0.79, 1.16)	HFNC	0.84 (0.64, 1.11)
NIV	1.14 (0.94, 1.39)	1.19 (0.9, 1.56)	NIV

Treatment effects are expressed as relative risk (RR) with 95% credible intervals (95% CrI)

Table 5-4 League Table for Length of Stay

Treatment effects for all studies: comparison of all treatment pairs.

	COT	HFNC	NIV
COT	COT	1.17 (-1.75, 4.18)	-0.84 (-3.79, 2.06)
HFNC	-1.17 (-4.18, 1.75)	HFNC	-2.03 (-6.27, 2.13)
NIV	0.84 (-2.06, 3.79)	2.03 (-2.13, 6.27)	NIV

Treatment effects are expressed as relative risk (RR) with 95% credible intervals (95% CrI)

Appendix 6. GRADE Evidence Profile

Table 6-1. GRADE Profile Table (Direct Comparison)

Certainty assessment							No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CPAP	HFNC	Relative (95% CI)	Absolute (95% CI)		
In hospital mortality												
2	randomised trials	not serious	not serious	not serious	serious[b]	none	38/108 (35.2%)	30/110 (27.3%)	**RR 1.28** (0.77 to 2.12)	**76 more per 1,000** (from 63 fewer to 305 more)	⨁⨁⨁◯ Moderate	CRITICAL
Need for intubation												
2	randomised trials	serious[a]	not serious	not serious	serious[b]	none	40/108 (37.0%)	43/110 (39.1%)	**RR 0.96** (0.32 to 2.92)	**16 fewer per 1,000** (from 266 fewer to 751 more)	⨁⨁◯◯ Low	CRITICAL

CI: confidence interval; **RR:** risk ratio

Explanations

a. Lack of patient blinding
b. Wide confidence interval

Table 6-2. GRADE Profile Table (Indirect Mixed Treatment Comparison)

Certainty assessment							No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CPAP	HFNC	Relative (95% CI)	Absolute (95% CI)		
In hospital mortality												
	randomised trials	not serious	not serious	not serious	serious[a]	none	**RR 0.93** (0.57 to 1.49)				⨁⨁⨁◯ Moderate	CRITICAL
Need for Invasive Mechanical Intubation												
	randomised trials	serious[b]	not serious	not serious	serious[a]	none	**RR 0.82** (0.53 to 1.27)				⨁⨁◯◯ Low	CRITICAL
Intensive Care Unit Admission												
	randomised trials	serious[b]	not serious	not serious	serious[a]	none	**RR 0.84** (0.61, 1.11)				⨁⨁◯◯ Low	CRITICAL
Length of Hospital Stay (DAYS)												
	randomised trials	serious[b]	not serious	not serious	serious[a]	none	**MD -2.03** (-6.27 to 2.13)				⨁⨁◯◯ Low	IMPORTANT

CI: confidence interval; **RR:** risk ratio; **MD:** mean difference

Explanations

a. Wide confidence interval
b. Lack of patient blinding

Appendix 7. Characteristics of Ongoing Clinical Trials

Title Identifier Expected Completion Date	Intervention	Comparator/Control	Patients/Population Recruited	Outcomes
Comparison of High Flow Nasal Cannula (HFNC), Face-mask Non-Invasive Ventilation (NIV) & Helmet NIV in COVID-19 ARDS Patients (NIV COVID19) NCT04715243 Ongoing Recruitment Estimated completion date: December 2021	HFNC	NIV	Inclusion Criteria: ● > 18 years of age ● confirmed COVID-19 ● Within 48 hours of presentation in the emergency department, high dependency area or intensive care unit (ICU) ● ARDS according to Berlin definition (P/F < 300) or O2 saturation < 90% or RR > 30/min) in room air ● Standard oxygen therapy at flow rate < 15L/min x 60 minutes	Primary Outcome Measures : 1. Rate of endotracheal intubation [Time Frame: within the study period with an average of one month.] The patient will be randomly assigned to one of the treatment arms. Then the patient will be followed up for one month for the primary outcome which is endotracheal intubation. Secondary Outcome Measures : 1. Hospital mortality [Time Frame: 90 days from the hospital mortality.] Number of patients who survived compared to who died in each intervention 2. Hospital length of stay [Time Frame: Through out the study completion. An average of 90 days.] total number of days patients remain in the hospital as inpatient in each intervention 3. Ventilator free days [Time Frame: Through out the study completion. An average of 90 days.] number of days patients remain off intervention (invasive or non-invasive)

High Flow Nasal Oxygen Versus Continuous Positive Airway Pressure Helmet Evaluation: A Randomized Crossover Trial in COVID-19 Pneumonia *COVIDNOCHE Trial (HFNO Versus CPAP Helmet) in COVID-19 Pneumonia (COVIDNOCHE)* NCT04381923 Not yet recruiting Estimated study completion: December 2022	HFNC	Hemet CPAP	Inclusion Criteria: ● Adult patients with confirmed COVID-19 with an Sp02 < 92% on ≥ 6 liters NC admitted to a Penn Medicine advanced respiratory unit. An advanced respiratory unit is a unit capable of non-invasive respiratory support such as an ICU or intermediate care unit.	Primary Outcome Measures : 1. Ventilator-Free Days (VFD) [Time Frame: 28 days] VFD is the number of days alive and free of mechanical ventilation in the first 28 days after study enrollment. Death before 28 days will be assigned a VFD equal to 0 to penalize non-survival. In cases of repeated intubation and extubation, periods free from invasive ventilation and lasting at least 24 consecutive hours will be calculated and summed. Timing of intubation and extubation will be captured in hours, and the number of hours a patient received invasive ventilation will be used to calculate duration of ventilation. Secondary Outcome Measures : 1. ICU and Hospital Length of Stay [Time Frame: 28 days] Days spent in the ICU and hospital after time of enrollment 2. Intubation [Time Frame: 28 days] Incidence and time to intubation in days after the time of enrollment 3. Renal Replacement Therapy (RRT) [Time Frame: 28 days]

				Incidence of RRT after the time of enrollment 4. Mortality [Time Frame: 28 days, 90 days] Death from any cause during after the time of enrollment
Comparison of efficacy of HighFlow Nasal Cannula with Continuous Positive Airway Pressure in prevention of Invasive mechanical ventilation in COVID 19 patients with Acute Respiratory Distress Syndrome in Critical Care Unit- A Randomized Control Study - COVID HFNC CTRI/2021/04/032501 Not yet recruiting Estimated completion date:	HFNC	NIV	Inclusion criteria: All COVID -19 positive patients (by RT-PCR) with paO2/Fio2 (P/F) â?? 150 to 250, with good sensorium, stable hemodynamics and pH > 7.2	Primary outcome: To compare the efficacy of High Flow Nasal Cannula and Non Invasive Ventilation -Continuous Positive Airway Pressure in reducing need for invasive mechanical ventilation in patients with ARDS in COVID-19.Timepoint: 24 hours Secondary outcome: Ability of ROX index to identify COVID 19 patients on HFNC requiring invasive mechanical ventilation.Timepoint: 24 hours Ability to alleviate dyspnoea as assessed by modified Borg scaleTimepoint: 24 hours Patientâ??s compliance to therapy - comfort / noise level, ability to proneTimepoint: 24 hours