and meta-analysis

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Comparison between high-flow nasal

cannula and noninvasive ventilation in

COVID-19 patients: a systematic review

Abstract

Background: High-flow nasal cannula (HFNC) and noninvasive ventilation (NIV) are important treatment approaches for acute hypoxemic respiratory failure (AHRF) in coronavirus disease 2019 (COVID-19) patients. However, the differential impact of HFNC *versus* NIV on clinical outcomes of COVID-19 is uncertain.

Objectives: We assessed the effects of HFNC *versus* NIV (interface or mode) on clinical outcomes of COVID-19.

Methods: We searched PubMed, EMBASE, Web of Science, Scopus, MedRxiv, and BioRxiv for randomized controlled trials (RCTs) and observational studies (with a control group) of HFNC and NIV in patients with COVID-19-related AHRF published in English before February 2022. The primary outcome of interest was the mortality rate, and the secondary outcomes were intubation rate, PaO_2/FiO_2 , intensive care unit (ICU) length of stay (LOS), hospital LOS, and days free from invasive mechanical ventilation [ventilator-free day (VFD)].

Results: In all, 23 studies fulfilled the selection criteria, and 5354 patients were included. The mortality rate was higher in the NIV group than the HFNC group [odds ratio (OR) = 0.66, 95% confidence interval (CI): 0.51-0.84, p = 0.0008, $l^2 = 60\%$]; however, in this subgroup, no significant difference in mortality was observed in the NIV-helmet group (OR = 1.21, 95% CI: 0.63-2.32, p = 0.57, $l^2 = 0\%$) or NIV-continuous positive airway pressure (CPAP) group (OR = 0.77, 95% CI: 0.51-1.17, p = 0.23, $l^2 = 65\%$) relative to the HFNC group. There were no differences in intubation rate, Pa0₂/FiO₂, ICU LOS, hospital LOS, or days free from invasive mechanical ventilation (VFD) between the HFNC and NIV groups.

Conclusion: Although mortality was lower with HFNC than NIV, there was no difference in mortality between HFNC and NIV on a subgroup of helmet or CPAP group. Future large sample RCTs are necessary to prove our findings.

Registration: This systematic review and meta-analysis protocol was prospectively registered with PROSPERO (no. CRD42022321997).

Keywords: CPAP, COVID-19, helmet, high-flow nasal cannula, noninvasive mechanical ventilation

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Introduction

Patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may develop coronavirus disease 2019 (COVID-19) with viral pneumonia, acute hypoxemic respiratory failure (AHRF), or acute respiratory distress syndrome (ARDS) and may require hospital admission.^{1–3} About 15–30% of COVID-19 patients experience hypoxemia and progress to ARDS.⁴ These patients require oxygen and possibly ventilatory support, which can be delivered using different devices. Noninvasive oxygenation strategies, such as

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high-flow nasal cannula (HFNC) and noninvasive ventilation (NIV), have been widely adopted in patients with AHRF secondary to COVID-19.^{5,6}

HFNC is a noninvasive respiratory support modality that delivers warm, humidified oxygen at a maximum flow rate of 60–1001/min and up to 100% of the inspired oxygen fraction (FiO₂) through nasal probes.7 NIV refers to the application of mechanical ventilatory support using a nasal, oronasal, or full face mask or a helmet.8 HFNC and NIV are the main forms of treatment for AHRF and associated with favorable outcomes in COVID-19 patients.9 Many recent studies have compared the effects of HFNC and NIV in COVID-19 patients, but the use of HFNC versus NIV for COVID-19-related AHRF remains controversial.5,6 Current clinical practice is based on prior experience, personal medical opinion, and local availability. Therefore, this meta-analysis compared HFNC versus NIV with respect to the risk for mortality and intubation in patients with COVID-19-related AHRF.

Methods

Search strategy

We conducted a systematic review and meta-analysis according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations.¹⁰ PubMed, EMBASE, Web of Science, Scopus, ClinicalTrials.gov, MedRxiv, BioRxiv, and the Cochrane Central Register of Controlled Trials were searched for relevant studies published before February 2022. Two trained investigators (W.T. and Y.P.) independently performed the searches, screening, and identification. Discrepancies were resolved by discussion and consensus.

The search combinations adopted were as follows: ('Ventilation, Noninvasive' OR 'Non Invasive Ventilation' OR 'Ventilation, Non Invasive' OR 'Noninvasive Ventilation') OR ('HFNC' OR 'high-flow nasal cannula' OR 'high-flow nasal oxygen' OR 'high-flow oxygen') AND ('COVID 19' OR 'SARS CoV 2' OR '2019 Novel Coronavirus' OR '2019 nCoV' OR 'Coronavirus Disease 2019' OR 'Coronavirus Disease 19' OR 'Severe Acute Respiratory Syndrome Coronavirus 2 Infection' OR 'SARS Coronavirus 2 Infection' OR 'COVID 19 Pandemic OR COVID-19'). In addition, the reference lists of all primary studies and review

articles were evaluated to locate additional relevant studies.

Study selection

The inclusion criteria were as follows: randomized controlled trials (RCTs) and observational studies; adult patients (\geq 18 years old) with laboratory-confirmed COVID-19; HFNC compared with a control group receiving NIV; and outcomes, including aggregated mortality rate, intubation rate, or both.

The exclusion criteria were as follows: patients who did not meet the screening criteria; studies that were not in English or commentaries, reviews, or duplicate publications from the same study; and data that could not be extracted by the reported statistical methods or non-targeted outcomes.

The ultimate decision to include or exclude any study was made following a full-text review of the article by two investigators (W.T. and Y.P.) focusing on publication date, study type, study design, and outcomes. Discrepancies were resolved by consensus.

The primary outcome of interest was the mortality rate, and the secondary outcomes were the intubation rate, PaO_2/FiO_2 , intensive care unit (ICU) length of stay (LOS), hospital LOS, and days free from invasive mechanical ventilation [ventilator-free day (VFD)].

Data extraction and study quality

Using a standardized form, two investigators (W.T. and Y.P.) independently extracted data with no blinding of trials (e.g. authors, institutions, or publication sources). Some data not provided in the published reports were obtained by contacting authors by email. To assess the quality of eligible RCTs, we used the Cochrane collaboration risk of bias tool, which considers allocation sequence generation, concealment of allocation, masking of participants and investigators, incomplete outcome reporting, selective outcome reporting, and other sources of bias. Potential sources of bias were graded as high, low, or unclear to assign the studies to high, low, or moderate risk of bias groups. The Newcastle-Ottawa quality assessment scale (NOS) checklist was used to assess the quality of observational studies. Using this scale, each study was assessed on nine items and categorized into three groups, as follows: selection, comparability, and outcomes. Stars were awarded



Figure 1. Study flow diagram.

for each quality item, and the highest-quality studies were awarded nine stars. A study was considered to be of low, moderate, or high quality when it achieved 0-4, 5-7, or 8-9 stars, respectively.

Data synthesis and analysis

The meta-analysis was performed using available data from the primary studies with the RevMan Review Manager (version 5.4.1; Nordic Cochrane Review Centre, Copenhagen, Denmark). Dichotomous outcomes are presented as odds ratios (ORs) with 95% confidence intervals (CIs). Continuous outcomes are presented as weighted mean differences (MDs) and 95% CIs. Data were assessed in median-interquartile ranges and were transformed into standard mean difference formats for further comparison.

The results were analyzed using the randomeffects model and are presented in a forest plot. The I^2 statistical index (ranges from 0% to 100%) was used to measure heterogeneity among the studies in each analysis, with values of 25%, 50%, and 75% corresponding to degrees of low, moderate, and high heterogeneity, respectively. Publication bias was assessed using a funnel plot. In addition, subgroup analysis was performed to investigate the different effects of interface and mode of NIV on treatment outcomes. A *p*-value of less than 0.05 was considered to represent a significant difference.

Results

Search results

A total of 6394 relevant studies were obtained from the databases. After excluding duplicates and evaluating the full texts of articles, we identified 23 eligible studies^{9,11–32} (3 RCTs,^{20,24,26} 8 prospective observational studies,^{13,16,18,19,22,25,28,30} and 12 retrospective observational studies).^{9,11,12,14,15,17,21,23,27,29,31,32} The process of searching and screening is described in Figure 1. The main characteristics of the articles included in the meta-analysis are shown in Table 1.

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Table 1. Characteristics of included studies.

Author	Country	Study design	Setting	Study period	No. of patients Total (HFNC/ NIV)	Outcomesª
Alharthy <i>et al.</i> ¹¹	Saudi Arabia	Retrospective observational study	ICU	As of 30 April 2020	30 (15/15)	2
Alkouh <i>et al.</i> ¹²	Morocco	Retrospective observational study	ICU	1 March 2020–31 December 2021	233 (162/71)	12
Costa <i>et al.</i> 9	Brazil	Retrospective observational study	ICU	March 2020–April 2020	37 (23/14)	1245
COVID-ICU group ¹³	France, Belgium, Switzerland	Prospectively observational study	ICU	25 February 2020–4 May 2020	725 (567/158)	1245
Duan <i>et al.</i> ¹⁴	China	Retrospective observational study	Ward/ ICU	January 2020-March 2020	36 (23/13)	123
Fernández <i>et al.</i> ¹⁵	Spanish	Retrospective observational study	Ward/ ICU	1 March 2020–1 April 2020	594 (431/163)	12
Franco <i>et al.</i> ¹⁶	Italy	Prospectively observational study	ED/ICU	1 March 2021–1 April 2020	667 (163/507)	125
Gaulton <i>et al.</i> ¹⁷	US (most)	Retrospective observational study	ICU	MD	59 (42/17)	12
Ghani <i>et al.</i> ¹⁸	UK	Prospectively observational study	Non-ICU	March 2020–January 2021	130 (35/95)	12
Gough <i>et al.</i> ¹⁹	Ireland	Prospectively observational study	Non-ICU	March 2020–April 2020	117 (32/85)	12
Grieco <i>et al.</i> ²⁰	Italy	RCT, multicenter	ICU	October 2020–December 2020	109 (54/55)	123456
Mahroof <i>et al.</i> ²¹	UK	Retrospective observational study	ICU	MD	45 (32/13)	2
Menga <i>et al.</i> ²²	Italy	Prospectively observational study	ICU	12 March 2021–20 April 20	85 (24/61)	2
Nadeem <i>et al.</i> ²³	UK	Retrospective observational study	RSU	1 March 2020–28 February 2021	100 (44/56)	1
Nair <i>et al.</i> ²⁴	India	RCT, single center	ICU	Auguts 2020–December 2020	109 (55/54)	12356
Pearson <i>et al.</i> ²⁵	US	Prospectively observational study	ICU	1 March 2020–31 July 2020	62 (31/31)	12
Perkins et al. ²⁶	UK	RCT	Non-ICU	MD	797 (417/380)	124
Ranieri <i>et al.</i> 27	Italy	Retrospective observational study	MD	February 2020-December 2020	315 (184/131)	12
Rodrigues Santos <i>et al.</i> ²⁸	Egypt	Retrospective observational study	ICU	May 2020–August 2020	63 (37/26)	123

Table 1. (Continued)

Author	Country	Study design	Setting	Study period	No. of patients Total (HFNC/ NIV)	Outcomesª
Shoukri ²⁹	Portugal	Prospectively observational study	RICU	18 November 2020–18 February 2021	190 (139/51)	125
Sykes <i>et al.</i> ³⁰	UK	Prospectively observational study	Non-ICU	April 2020–March 2021	140 (48/92)	
Wendel Garcia <i>et al.</i> ³¹	Spain	Retrospective observational study	ICU	As of 1 October 2020	174 (87/87)	124
Wendel Garcia et al. ³²	Spain	Retrospective observational study	ICU	14 March 2020–15 April 2020	540 (439/101)	1246

ED, emergency department; HFNC, high-flow nasal cannula; ICU, intensive care unit; MD, missing data; NIV, noninvasive ventilation; No, number; RCT, randomized controlled trial; RICU, respiratory intermediate care units; RSU, respiratory support unit; UK, the United Kingdom; USA, the United States.

^aOutcome measures include: ① mortality rate; ② Intubation rate; ③ PaO₂/FiO₂; ④ ICU length of stay; ⑤ Hospital length of stay; and ⑥ days free from invasive mechanical ventilation.

Author	HFNC						NIV					
	Age	Male %	BMI, kg/m²	APACHE I	SOFA	P/F, mmHg	Age	male%	BMI, kg/ m²	APACHE II	SOFA	P/F, mmHg
Alharthy <i>et al.</i> ¹¹	46 (16.4)	86.7	24.3 (7.4)	MD	9 (1.6)	217.7 (34.4)	46.3 (13.9)	80	24.3 (7.4)	MD	9 (1.6)	214.7 (30.3)
Alkouh et al. ¹²	66.32 (12.8)	72.2	27.59 (4.7)	MD	MD	MD	64.7 (14.97)	69	27.5 (4.9)	MD	MD	MD
Costa <i>et al.</i> 9	65.3 (17.7)	91.3	29.4 (5.5)	11.2 (8.5)	3.7 (5.7)	MD	74.5 (19)	35.7	32.4 (4.7)	20.7 (12.4)	2.7 (1)	MD
COVID-ICU group ¹³	63.7 (12.6)	75	28 (4.5)	MD	3 (1.5)	105 (42.3)	64.3 (12)	71	28 (4.5)	MD	2.7 (1.5)	127.7 (62)
Duan et al.14	50 (14)	52	MD	10 (5)	4 [2]	165 (48)	65 (14)	92	MD	8 (2)	4 [1]	196 (46)
Fernández et al. ¹⁵	MD	MD	MD	MD	MD	MD	MD	MD	MD	MD	MD	MD
Franco et al. ¹⁶	65.7 (14.7)	69.9	MD	MD	2.5 (0.9)	166 (65)	69.08 (12.6)	69	MD	MD	3.5 (1.8)	147 (82.4)
Gaulton et al. ¹⁷	61 (16)	33.3	35.8 (9)	MD	MD	MD	56 (15)	82.3	34.8 (7.8)	MD	MD	MD
Ghani <i>et al.</i> ¹⁸	MD	68	MD	MD	MD	MD	MD	68	MD	MD	MD	MD
Gough et al.19	74 (28.7)	51.6	29.6 (7.8)	MD	MD	180.3 (150)	61.7 (13.6)	43.4	30.2 (5.3)	MD	MD	180.5 (101.3)
Grieco <i>et al.</i> ²⁰	62 (10.7)	84	28.3 (3.8)	MD	2.3 (0.8)	102 (33.5)	65 (11.4)	77	27.7 (3)	MD	2.3 (0.8)	104 (32)
Mahroof et al. ²¹	MD	MD	MD	MD	MD	MD	MD	MD	MD	MD	MD	MD
Menga et al. ²²	MD	MD	MD	MD	MD	MD	MD	MD	MD	MD	MD	MD
Nadeem et al. ²³	MD	MD	MD	MD	MD	MD	MD	MD	MD	MD	MD	MD

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Author	HFNC						NIV						
	Age	Male %	BMI, kg/m²	APACHE I	SOFA	P/F, mmHg	Age	male%	BMI, kg/ m²	APACHE II	SOFA	P/F, mmHg	
Nair et al. ²⁴	56.7 (13)	80	MD	MD	MD	112.1 (36)	56.2 (13)	64.8	MD	MD	MD	115.3 (42)	
Pearson et al. ²⁵	66 (12.4)	61.3	32.5 (9.5)	MD	3 (1.6)	MD	60.7 (18.7)	81.3	27.7 (4.8)	MD	2.3 (0.8)	MD	
Perkins <i>et al.</i> ²⁶	57.6 (13)	65.2	MD	MD	MD	138.5 (87.6)	56.7 (12.5)	68.4	MD	MD	MD	131.8 (67.8)	
Ranieri et al. ²⁷	62.7 (12.7)	78.3	27.7 (4.6)	MD	3 (1.5)	132.7 (41.8)	66.3 (10.5)	75.6	27.6 (3.2)	MD	2.3 (0.7)	148.7 (42.7)	
Rodrigues Santos et al. ²⁸	67.94 (7.82)	62.2	MD	9.8 (3.2)	3 (0.9)	191.1 (37.8)	64.1 (9.81)	65.4	MD	11 (3.2)	2.7 (0.8)	190.38 (42.47)	
Shoukri ²⁹	65.7 (12.2)	68.3	28.2 (5.7)	MD	MD	MD	69.6 (10.2)	68.6	29.5 (6.2)	MD	MD	MD	
Sykes <i>et al.</i> ³⁰	71.3 (13.9)	75	MD	MD	MD	77.3 (38.2)	70.7 (10.0)	60	MD	MD	MD	76.0 (34.5)	
Wendel Garcia <i>et al.</i> ³¹	64 (14.3)	75	28 (5.3)	9.7 (5.3)	5.3 (3)	124.7 (67.8)	65.7 (15.8)	71	26.3 (3.8)	11 (6.8)	5.7 (2.3)	133.3 (53.5)	
Wendel Garcia <i>et al.</i> ³²	62 (11.9)	68	28.3 (3.7)	MD	MD	MD	61.7 (12)	68	28.3 (3.8)	MD	MD	MD	

APACHE, acute physiology and chronic health evaluation; BMI, body mass index; HFNC, high-flow nasal cannula; MD, missing data; NIV, noninvasive ventilation; P/F, oxygenation index (Pa0₂/Fi0₂); SOFA, sequential organ failure assessment. Values are given as mean (standard deviation).

Author	HFNC										
	Setting	Intervention	Duration, days	NIV mode	NIV interface	Setting	Intervention	Duration, days			
Alharthy et al. ¹¹	Mean flow rate, 60 l/min; median FiO ₂ , 40%	Received HFNC	9 (3.3)	CPAP	Helmet	Mean flow rate, 45 l/ min; median FiO ₂ , 40%	Received helmet- CPAP	8.3 (4.1)			
Alkouh et al. ¹²	Flow rate, 60–80 l/ min; FiO ₂ , maintain SpO ₂ \ge 92%	Received HFNC	MD	MD	MD	MD	Received NIV	MD			
Costa <i>et al</i> 9	Flow rate, 40–50 l/ min; Fi0 ₂ , maintain Sp0 ₂ >92%	Received HFNC	MD	BiPAP	Face mask	$\begin{array}{l} PEE \geq & 8cmH_20;PS,\\ for \; a \; TV \leq & 8ml/kg;\\ FiO_2, \;maintain\; SpO_2\\ > & 92\% \end{array}$	Received NIV	MD			
COVID-ICU group ¹³	Flow rate, 50 (40–60) l/min; FiO ₂ , 70 (60–90) %	HFNC was the most invasive treatment	MD	MD	Face mask	PEEP, 7 (6–8) cmH ₂ 0; PS, 8 (6–10) cmH ₂ 0; FiO ₂ , 60 (50–80)%	NIV was the most invasive treatment	MD			
Duan <i>et al.</i> ¹⁴	Flow rate: 30–60 l/ min; FiO ₂ , maintain SpO ₂ >93%	HFNC as first-line therapy	4.5 (5.3)	CPAP/BiPAP	Face mask	Initial: CPAP or PEEP, 4 cmH ₂ 0; initial inspiratory pressure, 8–10 cmH ₂ 0; FiO ₂ , maintain SpO ₂ >93%	NIV as first-line therapy	7.1 (4.6)			
Fernández et al. ¹⁵	MD	HFNC only		CPAP/BiPAP	Face mask	MD	NIV and/or CPAP with or without HFNC	MD			
Franco et al. ¹⁶	MD	Received HFNC	MD	CPAP/BiPAP	MD	MD	Received CPAP or NIV	MD			

Author	HFNC			NIV				
	Setting	Intervention	Duration, days	NIV mode	NIV interface	Setting	Intervention	Duration, days
Gaulton, 2020 ¹⁷	Flow rate, 40–60 l/ min; FiO ₂ , maintain SpO ₂ >92%	HFNC as first-line therapy	MD	CPAP	Helmet	CPAP, 5–10 cmH ₂ 0; FiO ₂ , maintain SpO ₂ >92%	Helmet as first-line therapy. Patients on helmet therapy were provided breaks with intervening HFNC use	MD
Ghani <i>et al.</i> ¹⁸	Initial flow rate, 60 l/min; FiO ₂ , maintain SpO ₂ 92–96%	Received HFNC	MD	CPAP	Face mask	PEEP, 8 (6–12) cmH ₂ O; FiO ₂ , maintain SpO ₂ 92–96%	Received CPAP	MD
Gough et al. ¹⁹	Flow rate, capped at 30 l/min, limiting PEEP to <3 cmH ₂ 0	Received HFNC	MD	CPAP	Face mask	PEEP≥10cmH ₂ 0	Received CPAP	MD
Grieco et al. ²⁰	Initial flow rate, 60 l/min; Fi0 ₂ , maintain SpO ₂ 92–98%	Randomized	≥2	BiPAP	Helmet	PEEP, 10–12 cmH ₂ 0; initial PS, 10– 12 cmH ₂ 0; Fi0 ₂ , maintain SpO ₂ 92–98%	Randomized. After interruption of NIV, patients underwent continuous Venturi mask or HFNC	≥
Mahroof et al. ²¹	MD	Initial mode of support was HFNC	MD	MD	MD	MD	Initial mode of support was NIV	MD
Menga et al. ²²	MD	HFNC as first-line treatment	MD	Bipap	Helmet/ Face mask	MD	NIV as first-line treatment	MD
Nadeem et al. ²³	MD	Received HFNC	MD	CPAP/BiPAP	MD	MD	Received CPAP or NIV	MD
Nair <i>et al.</i> ²⁴	Initial: flow rate, 50 l/min; FiO ₂ , 1.0, target SpO ₂ >94%	HFNC only	MD	BiPAP	MD	$\begin{array}{l} {\sf PEEP, 5-10 cmH_20;} \\ {\sf PS, 10-20 cmH_20;} \\ {\sf FiO_2, 0.5-1.0, target} \\ {\sf SpO_2 > 94\%} \end{array}$	Received NIV	MD
Pearson et al. ²⁵	MD	HFNC as initial therapy	MD	CPAP	Helmet	MD	Helmet NIV as initial therapy	MD
Perkins et al. ²⁶	MD	Randomized. Crossover was observed between allocated treatment arms	3.7 (4.1)	СРАР	Face mask	MD	Randomized. Crossover was observed between allocated treatment arms	3.5 (4.6)
Ranieri et al. ²⁷	Flow rate, 55 (50–60) l/min	Patients initially treated for ≥12 continuous hours with HFNC using gas flows ≥40 l/ min	MD	BiPAP	MD	PEEP, 10 (10–12) cmH ₂ 0 PS, 10 (10–12) cmH ₂ 0	Patients initially treated with NIV with PEEP ≥5 cmH ₂ 0	MD
Rodrigues Santos <i>et al.</i> 28	Flow rate, 30–60 l/ min; FiO ₂ , maintain SpO ₂ >93%	HFNC as initial therapy	5.53 (1.11)	Bipap	Face mask	Initial PEEP, 4 cmH ₂ 0; initial inspiratory pressure, 8–10 cmH ₂ 0; FiO ₂ , maintain SpO ₂ >93%	NIV as initial therapy	5.86 (1.10)
Shoukri ²⁹	Maximum: flow, 59.2 (1.0) l/min; FiO ₂ , 0.9 (0.1), SpO ₂ , 92–96%	Received HFNC	5.5 (4.4)	MD	Face mask	Maximum: CPAP/ EPAP, 10.0 (1.9) cmH ₂ O; IPAP, 14.8 (2.4) cmH ₂ O; FiO ₂ , 1.0 (0.1), SpO ₂ , 92–96%	Received CPAP or NIV	5.2 (4.3)
Sykes <i>et al.</i> ³⁰	Mean FiO ₂ , 79.5 (23) %	HFNC was the highest level of treatment	6 (9.8)	СРАР	Face mask	Mean FiO ₂ , 83.8 (26.1) %	CPAP with or without HFNC	9 (17.4)

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Author	HFNC		NIV						
	Setting	Intervention	Duration, days	NIV mode	NIV interface	Setting	Intervention	Duration, days	
Wendel Garcia <i>et al.</i> ³¹	Flow rate >30 l/ min; mean Fi0 ₂ , 60 [44-80]%	HFNC was maximal respiratory support at ICU admission	MD	MD	MD	MD	NIV was maximal respiratory support at ICU admission	MD	
Wendel Garcia <i>et al.</i> ³²	Flow rate >30 l/ min; mean Fi0 ₂ ≥50%	HFNC only	MD	MD	Face mask	Mean FiO ₂ , at least 50%	NIV only	MD	

BiPAP, bi-level positive airway pressure; CPAP, continuous positive airway pressure; EPAP, expired positive airway pressure; FiO₂, Fraction of inspiration O₂; HFNC, high-flow nasal cannula; ICU, intensive care unit; IPAP, inspired positive airway pressure; MD, missing data; NIV, noninvasive ventilation; PEEP, positive end-expiratory pressure; PS, pressure support; SpO₂, oxygen saturation; TV, tidal volume.

Values are given as mean (standard deviation).

Literature quality and bias assessment

The quality evaluation results of the three RCTs^{20,24,26} are shown in Figure 2. None of the included studies were performed with double blinding. Two studies were considered to have an unclear risk of bias. The 20 observatio nal^{9,11–19,21–23,25,27–32} studies were assessed using the NOS checklist, and the results are shown in the Table 2. All studies were of medium quality (\geq 5 stars) or above, and 10 were considered high quality (\geq 8 stars). We generated a funnel plot for intubation and mortality rates; visual inspection of this plot indicated no evidence of publication bias for intubation rate, but we did observe a possible bias for mortality rate (Figure 3).

Clinical outcomes

A total of 5354 patients participated in the 23 studies^{9,11-32} of the present meta-analysis, all of whom were adult COVID-19 patients. The patients were admitted to different hospital settings and received noninvasive respiratory support at the time of admission. In 4 studies,^{11,17,20,25} a helmet was applied, in 11 studies,^{9,13-15,18,19,26,28,29,30,32} a face mask was used, 1 study²² reported applying both a helmet and a face mask, 7 studies^{12,16,21,23,24,27,31} did not report whether a helmet or a facemask was used, in 6 studies,^{9,20,22,24,27,29} BiPAP was applied, 7 studies^{11,17-19,25,26,30} featured CPAP, 4 studies^{14-16,23} reported applying both BiPAP and CPAP, and 6 studies^{12,13,21,28,31,32} did not report whether they applied BiPAP or CPAP (Table 1).

A total of 5196 patients participated in 20 studies^{9,12–20,23–32} that reported mortality, and the pooled estimates demonstrated that mortality rate was lower in HFNC groups than in NIV groups [OR=0.66, 95% CI: 0.51–0.84, p=0.0008, I^2 =60%, Figure 4(a)]. However, in subgroup analysis, no significant differences in mortality were observed in the HFNC group relative to NIV-helmet group [OR=1.21, 95% CI: 0.63–2.32, p=0.57, I^2 =0%, Figure 5(a)] or the NIV-CPAP group [OR=0.77, 95% CI: 0.51–1.17, p=0.23, I^2 =65%, Figure 5(b)], but significant differences in mortality were observed in the HFNC group relative to the NIV-facemask group [OR=0.58, 95% CI: 0.41–0.81, p=0.001, I^2 =63%, Figure 5(a)] or the NIV-BiPAP group [OR=0.60, 95% CI: 0.45–0.79, p=0.0003, I^2 =5%, Figure 5(b)].

Intubation was reported in 5114 patients in 21 studies^{9,11–22,24–29,31,32} and pooled estimates demonstrated that there were no significant differences in the intubation rate between the HFNC and NIV groups [OR=0.93, 95% CI: 0.73–1.20, p=0.59, $I^2=63\%$, Figure 4(b)]. No significant differences in intubation requirements were found in subgroup analyses by interface [helmet: OR=1.54, 95% CI: 0.72–3.29, p=0.27, $I^2=55\%$; facemask: OR=0.81, 95% CI: 0.57–1.15, p=0.24, $I^2=65\%$, Figure 5(c)] or mode [CPAP: OR=0.90, 95% CI: 0.57–1.40, p=0.62, $I^2=66\%$; BiPAP: OR=1.16, 95% CI: 0.85–1.58, p=0.35, $I^2=35\%$, Figure 5(d)] relative to the HFNC group.

 PaO_2/FiO_2 ratio (24 h after treatment) was reported in 317 patients in four studies,^{14,20,24,29} and no significant differences were found between the HFNC group and NIV group [MD=-22.63, 95% CI: -47.21 to 1.95, p=0.07, $I^2=64\%$, Figure 6(a)]. A total of 2382 patients from six











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 Table 2.
 The NOS quality of included studies.

Study	Selectio	on			Compar	ability	Outcom	е		Total	Quality
	REC	SNEC	AE	DO	SC	AF	A0	FU	AFU		
Alharthy <i>et al.</i> ¹¹	1	1	1	1	1	1	1	0	1	8	High
Alkouh <i>et al.</i> ¹²	1	1	1	1	0	0	0	1	1	6	Moderate
Costa <i>et al.</i> 9	1	1	1	1	1	1	0	1	1	8	High
COVID-ICU group ¹³	1	1	1	1	1	1	1	1	1	9	High
Duan <i>et al.</i> ¹⁴	1	1	1	1	1	1	1	1	1	9	High
Fernández <i>et al.</i> ¹⁵	1	1	1	1	0	0	1	1	1	5	Moderate
Franco <i>et al.</i> ¹⁶	1	1	1	1	1	1	1	1	1	8	High
Gaulton <i>et al.</i> ¹⁷	1	1	1	1	1	0	1	0	1	7	Moderate
Ghani <i>et al.</i> ¹⁸	1	1	1	1	1	1	0	1	1	8	High
Gough et al. ¹⁹	1	1	1	1	0	0	1	0	1	6	Moderate
Mahroof <i>et al.</i> ²¹	1	1	1	1	0	0	1	0	1	5	Moderate
Menga <i>et al.</i> ²²	1	1	1	1	1	1	0	0	0	6	Moderate
Nadeem <i>et al.</i> ²³	1	1	1	1	1	1	0	0	1	7	Moderate
Pearson <i>et al.</i> ²⁵	1	1	1	1	1	1	1	0	1	7	Moderate
Ranieri <i>et al.</i> 27	1	1	1	1	1	1	1	1	1	9	High
Rodrigues Santos <i>et al.</i> ²⁸	1	1	1	1	1	1	1	0	1	8	High
Shoukri ²⁹	1	1	1	1	1	0	1	0	1	7	Moderate
Sykes <i>et al.</i> ³⁰	1	1	1	1	1	1	1	0	1	8	High
Wendel Garcia <i>et al.</i> ³¹	1	1	1	1	1	1	0	1	0	7	Moderate
Wendel Garcia <i>et al.</i> ³²	1	1	1	1	1	1	1	0	1	8	High

AE, ascertainment of exposure; AF, study controls for any additional factors; AFU, adequacy of follow-up of cohorts [>90%]; AO, assessment of outcome; DO, demonstration that outcome of interest was not present at start of study; FU, follow-up long enough for outcomes to occur; REC, representativeness of the exposed cohort; SC, study controls for age, sex; SNEC, selection of the non-exposed cohort.

'1' means that the study is satisfied with the item and '0' means the opposite situation.

studies^{9,13,20,26,31,32} reported ICU LOS, and no significant differences were found between those two groups [MD=0.31, 95% CI: -0.81 to 1.43, p=0.59, $I^2=0\%$, Figure 6(b)]. The results were similar for hospital LOS: no difference in this value was reported in a total of 1840 patients in six studies^{9,13,16,20,24,28} between those two groups [MD=0.76, 95% CI: -0.33 to 1.85, p=0.17, $I^2=0\%$, Figure 6(c)]. A total of 758 patients in three studies^{20,24,32} reported VFD, and again there

were no significant differences between those two groups [MD=0.17, 95% CI: -2.63 to 2.96, p=0.91, P=55%, Figure 6(d)].

Discussion

In this meta-analysis of 23 studies with 5354 patients who were hospitalized for COVID-19, NIV was associated with higher mortality than HFNC. However, no significant differences in



Figure 4. Mortality (a) and intubation (b) for included studies. HFNC, high-flow nasal cannula; NIV, noninvasive ventilation.

(a)	HENC	10/	Odda Patio	Odda Patio	(b)		HFNC	N	VIV		Odds Ratio	Odds Ratio
Study or Subgroup	Events Total Even	ts Total Weight	M-H. Random, 95% CI	M-H. Random, 95% Cl	` '	Study or Subgroup	Events T	otal Even	ts Total	Weight M	I-H, Random, 95% CI	M-H, Random, 95% Cl
1.1.1 Helmet						1.1.1 Helmet						
Gaulton,2021	8 42	1 17 1.9%	3.76 [0.43, 32.71]			Alharthy,2020	2	15	3 15	2.3%	0.62 [0.09, 4.34]	
Grieco,2021	10 54	12 55 6.5%	0.81 [0.32, 2.08]			Gaulton,2021 Grieco 2021	22	42 54	3 17	7 2%	2.87 [1.20, 20.53]	
Pearson,2021 Subtotal (95% CI)	18 31	15 31 6.0%	1.48 [0.54, 4.02]	-		Menga.2021	15	24 2	27 42	5.5%	0.93 [0.33, 2.62]	
Total events	36	103 14.376	1.21 [0.03, 2.32]			Pearson, 2021	15	31	17 31	5.8%	0.77 [0.28, 2.10]	
Heterogeneity: Tau ² = 0.00;	Chi2 = 1.91, df = 2 (P =	: 0.38); l ² = 0%				Subtotal (95% CI)		166	160	24.6%	1.54 [0.72, 3.29]	•
Test for overall effect: Z = 0	.56 (P = 0.57)					Total events	82		65			
						Heterogeneity: Tau ^e = 0.39 Test for overall effect: 7 = 1	$P_{\rm r}$; Chi ² = 8.82, 1 11 (P = 0.2)	, df = 4 (P =	= 0.07); l* =	55%		
1.1.2 Face mask	A 44	0 00 0 78	4 00 10 04 40 501			Teat for overall endor. 2 -	1.11(1 - 0.2	.,				
COV/ID-ICLL group 2021	106 567	5 158 12.7%	1.82 [0.31, 10.58]	-		1.1.2 Face mask						
Duan.2021	1 23	1 13 1.2%	0.55 [0.03, 9.52]			costa,2022	16	23	8 14	3.9%	1.71 [0.43, 6.83]	
Fernández,2021	69 431	17 163 11.8%	0.47 [0.31, 0.72]			COVID-ICU group,2021	242	567 7	77 158	11.0%	0.78 [0.55, 1.12]	-
Ghani,2021	12 35	54 95 7.6%	0.40 [0.18, 0.89]			Duan,2021	4	23	2 13	2.5%	1.16 [0.18, 7.38]	
Gough,2021	16 32	19 85 7.6%	0.73 [0.32, 1.66]			Fernandez,2021 Chapi 2021	259	431 10	44 05	6.0%	0.83 [0.57, 1.21]]
Perkins,2021	78 415	33 378 12.4%	1.16 [0.80, 1.67]			Gough 2021	14	32	40 85	7.0%	0.88 [0.39, 1.98]	
Rodrigues Santos, 2021	38 139	1 26 128	0.24 [0.12, 0.48]			Menga,2021	15	24	10 19	4.5%	1.50 [0.44, 5.09]	
Sykes 2021	27 48	5 92 86%	0.86 (0.43 1.75)			Perkins,2021	170	414 12	26 377	11.5%	1.39 [1.04, 1.85]	-
WendelGarcia, 2022	106 439	37 101 11.4%	0.55 [0.35, 0.87]	-		Rodrigues Santos, 2021	23	139	8 51	6.6%	1.07 [0.44, 2.56]	
Subtotal (95% CI)	2180	1185 85.5%	0.58 [0.41, 0.81]	•		Shoukri,2021	4	37	3 26	3.2%	0.93 [0.19, 4.55]	
Total events	457 3	96				WendelGarcia, 2022	307	439 8	1102	8.5%	0.31 [0.17, 0.59]	
Heterogeneity: Tau ² = 0.17;	Chi ² = 27.31, df = 10 (P = 0.002); ² = 63%				Total events	1060	5	12	73.476	0.01 [0.07, 1.10]	
Test for overall effect: Z = 3.	.19 (P = 0.001)					Heterogeneity: Tau ² = 0.18	3: Chi ² = 28.9	1. df = 10 (F	P = 0.001);	² = 65%		
Total (95% CI)	2307	1288 100.0%	0.65 [0.47.0.89]	•		Test for overall effect: Z = 1	1.16 (P = 0.24	4)				
Total events	493 4	24	0100 [0111] 0100]	-								
Heterogeneity: Tau ² = 0.18;	Chi2 = 33.41, df = 13 (P = 0.001); 2 = 61%	t.			Total (95% CI)	2	330	1262	100.0%	0.95 [0.69, 1.32]	•
Test for overall effect: Z = 2	.66 (P = 0.008)		(0.01 0.1 1 10 100 Eavours [HENC] Eavours [NIV]		Total events	1142	57	77			
Test for subaroup difference	rs: Chi ² = 3.85. df = 1 (P = 0.05), l ² = 74.0%		ravous (mito) i avous (mit)		Heterogeneity: Tau ^e = 0.22	$2; Chi^2 = 42.4$	7, df = 15 (F	P = 0.0002); l ^z = 65%		0.002 0.1 1 10 500
						Test for subgroup difference	ces: Chif = 2 :	$^{\prime}$ df = 1 (F	P = 0 13) I	² = 55.3%		Favours [HFNC] Favours [NIV]
(a)					(\mathbf{A})							
					(u)							
	HFNC NIV		Odds Ratio	Odds Ratio			HFNC	NIV	/		Odds Ratio	Odds Ratio
Study or Subgroup Ex	HFNC NIN vents Total Events	Total Weight N	Odds Ratio I-H, Random, 95% Cl	Odds Ratio M-H, Random, 95% Cl		Study or Subgroup E	HFNC Events Tota	NIV al Events	Total V	Veight M-	Odds Ratio H. Random. 95% Cl	Odds Ratio M-H. Random, 95% Cl
Study or Subgroup Ev 2.1.1 CPAP	HFNC NIV vents Total Events	Total Weight M	Odds Ratio I-H, Random, 95% Cl	Odds Ratio M-H, Random, 95% Cl	2	Study or Subgroup E	HFNC Events Tota	NIV al Events	Total V	Veight M-	Odds Ratio H. Random. 95% Cl	Odds Ratio M-H. Random, 95% Cl
Study or Subgroup Ex 2.1.1 CPAP Duan,2021	HFNC NIV vents Total Events	Total Weight M	Odds Ratio I-H. Random, 95% CI 0.60 [0.02, 17.22]	Odds Ratio M-H. Random, 95% Cl	-	Study or Subgroup E 2.1.1 CPAP Alharthy,2020 Duap 2021	HFNC Events Tota 2 1: 4 2:	NIV al Events 5 3	Total V	Veight M- 1.5%	Odds Ratio H. Random. 95% Cl 0.62 [0.09, 4.34] 0.63 [0.05, 7, 75]	Odds Ratio M-H. Random. 95% Cl
Study or Subgroup Ev 2.1.1 CPAP Duan,2021 Fernández,2021	HFNC NIV vents Total Events 1 23 0 69 431 20 26 183 100	Total Weight N 4 0.6% 58 7.9% 330 9.2%	Odds Ratio 1-H, Random, 95% Cl 0.60 [0.02, 17.22] 0.36 [0.20, 0.66] 0.44 [0.27, 0.71]	Odds Ratio M-H, Random, 95% Cl	-	Study or Subgroup E 2.1.1 CPAP Alharthy,2020 Duan,2021 Fernández 2021	HFNC Events Tota 2 1: 4 2: 259 43	NIV al Events 5 3 3 1 1 43	7 Total V 15 4 58	Veight M- 1.5% 1.0% 7.6%	Odds Ratio H. Random. 95% Cl 0.62 [0.09, 4.34] 0.63 [0.05, 7.75] 0.53 [0.28, 0.98]	Odds Ratio M-H. Random, 95% Cl
Study or Subgroup Ev 2.1.1 CPAP Duan,2021 Fernández,2021 Franco.2020 Gaulton 2021	HFNC NIX vents Total Events 1 23 0 69 431 20 26 163 100 8 42 1	Total Weight N 4 0.6% 58 7.9% 330 9.2% 17 1.4%	Odds Ratio 1-H. Random, 95% Cl 0.60 [0.02, 17.22] 0.36 [0.20, 0.66] 0.44 [0.27, 0.71] 3.76 [0.43, 32 71]	Odds Ratio M-H, Random, 95% CI		Study or Subgroup E 2.1.1 CPAP Alharthy,2020 Duan,2021 Fernández,2021 Franco,2020	HFNC Events Tota 2 1: 4 2: 259 43 47 16:	NIV al Events 5 3 3 1 1 43 3 82	7 Total V 15 4 58 330	Veight M- 1.5% 1.0% 7.6% 9.9%	Odds Ratio H. Random. 95% Cl 0.62 [0.09, 4.34] 0.63 [0.05, 7.75] 0.53 [0.28, 0.98] 1.23 [0.80, 1.87]	Odds Ratio M-H. Random, 95% Cl
Study or Subgroup Ex 2.1.1 CPAP Duan,2021 Fernández,2021 Franco,2020 Gaulton,2021 Ghani,2021	HFNC NIV 1 23 0 69 431 20 26 163 100 8 42 1 12 35 54	Total Weight N 4 0.6% 58 7.9% 330 9.2% 17 1.4% 95 6.0%	Odds Ratio 1-H, Random, 95% Cl 0.60 [0.02, 17.22] 0.36 [0.20, 0.66] 0.44 [0.27, 0.71] 3.76 [0.43, 32.71] 0.40 [0.18, 0.89]	Odds Ratio M-H, Random, 95% Cl	-	Study or Subgroup E 2.1.1 CPAP Alharthy,2020 Duan,2021 Fernández,2021 Franco,2020 Gaulton,2021	HFNC Events Tota 2 1: 4 2: 259 43 47 16: 22 4:	NIV al Events 5 3 3 1 1 43 3 82 2 3	7 Total V 15 4 58 330 17	Veight M- 1.5% 1.0% 7.6% 9.9% 2.8%	Odds Ratio H. Random, 95% Cl 0.62 [0.09, 4.34] 0.63 [0.05, 7.75] 0.53 [0.28, 0.98] 1.23 [0.80, 1.87] 5.13 [1.28, 20.53]	Odds Ratio
Study or Subgroup Ex 2.1.1 CPAP Duan,2021 Fernández,2021 Franco,2020 Gaulton,2021 Ghani,2021 Gough,2021	HFNC NIX vents Total Events 1 23 0 69 431 20 26 163 100 8 42 1 12 35 54 16 32 49	Total Weight M 4 0.6% 58 7.9% 58 7.9% 330 9.2% 17 1.4% 95 6.0% 85 5.9% 5.9%	Odds Ratio 1-H, Random, 95% Cl 0.60 [0.02, 17.22] 0.36 [0.20, 0.66] 0.44 [0.27, 0.71] 3.76 [0.43, 32.71] 0.40 [0.18, 0.89] 0.73 [0.32, 1.66]	Odds Ratio	-	Study or Subgroup E 2.1.1 CPAP Alharthy, 2020 Duan, 2021 Fernández, 2021 Franco, 2020 Gaulton, 2021 Ghani, 2021	HFNC <u>Events Tota</u> 2 1: 4 2: 259 43 47 16: 22 4: 6 3:	NIV 5 3 3 1 1 43 3 82 2 3 5 44	/ Total V 15 4 58 330 17 95	Veight M- 1.5% 1.0% 7.6% 9.9% 2.8% 4.7%	Odds Ratio H. Random. 95% Cl 0.62 [0.09, 4.34] 0.63 [0.05, 7.75] 0.53 [0.28, 0.98] 1.23 [0.80, 1.87] 5.13 [1.28, 20.53] 0.24 [0.09, 0.63]	Odds Ratio M-H. Random. 95% Cl
Study or Subgroup Et 2.1.1 CPAP Duan,2021 Fernández,2021 Gauton,2021 Gauton,2021 Ghani,2021 Gough,2021 Nadeem,2021	HFNC NIV 1 23 0 69 431 20 26 163 100 8 42 1 12 35 54 35 44 36	Total Weight N 4 0.6% 58 7.9% 330 9.2% 17 1.4% 95 6.0% 85 5.9% 53 5.1% 53 5.1%	Odds Ratio 1-H, Random, 95% Cl 0.60 [0.02, 17.22] 0.36 [0.20, 0.66] 0.44 [0.27, 0.71] 3.76 [0.43, 32.71] 0.40 [0.18, 0.89] 0.73 [0.32, 1.66] 1.84 [0.72, 4.67]	Odds Ratio M-H. Random, 95% Cl	-	Study or Subgroup E 2.1.1 CPAP Alharthy,2020 Duan,2021 Fernández,2021 Franco,2020 Gaulton,2021 Ghani,2021 Gough,2021	HFNC 2 1: 4 2: 259 43 47 16: 22 4: 6 3: 14 3:	NIV 5 3 3 1 1 43 3 82 2 3 5 44 2 40	/ Total // 15 4 58 330 17 95 85	Veight M- 1.5% 1.0% 7.6% 9.9% 2.8% 4.7% 5.7%	Odds Ratio H. Random, 95% Cl 0.62 [0.09, 4.34] 0.63 [0.05, 7.75] 0.53 [0.28, 0.98] 1.23 [0.80, 1.87] 5.13 [1.28, 20.53] 0.24 [0.09, 0.63] 0.88 [0.39, 1.98]	Odds Ratio
Study or Subgroup Ev 2.1.1 CPAP Duan.2021 Fernández.2021 Franco.2020 Gaulton.2021 Ghani.2021 Gough.2021 Nadeem.2021 Pearson.2021	HFNC NIV rents Total Events 1 23 0 69 431 20 26 163 100 8 42 1 12 35 54 16 32 49 35 44 35 18 31 15	Total Weight N 4 0.6% 58 7.9% 330 9.2% 31 17 1.4% 95 6.0% 85 5.9% 53 5.1% 31 4.6%	Odds Ratio 1-H. Random, 95% Cl 0.60 [0.02, 17.22] 0.36 [0.20, 0.66] 0.44 [0.27, 0.71] 3.76 [0.43, 32.71] 0.40 [0.18, 0.89] 0.73 [0.32, 1.66] 1.84 [0.72, 4.67] 1.48 [0.54, 4.02]	Odds Ratio M-H. Random, 95% Cl	-	Study or Subgroup E 2.1.1 CPAP Alharthy,2020 Duan,2021 Fernández,2021 Gnaiton,2021 Ghani,2021 Gough,2021 Pearson,2021	HFNC Events Tota 2 19 4 22 259 43 47 16 22 44 6 33 14 33 15 3	NIV al Events 5 3 3 1 1 43 3 82 2 3 5 44 2 40 1 17	/ Total V 15 4 58 330 17 95 85 31	Veight M- 1.5% 1.0% 7.6% 9.9% 2.8% 4.7% 5.7% 4.5%	Odds Ratio H. Random. 95% Cl 0.62 [0.09, 4.34] 0.63 [0.05, 7.75] 1.23 [0.80, 1.87] 5.13 [1.28, 20.53] 0.24 [0.09, 0.63] 0.88 [0.39, 1.98] 0.77 [0.28, 2.10]	Odds Ratio
Study or Subgroup Ev 2.1.1 CPAP Duan.2021 Franco.2020 Gaulton.2021 Ghant.2021 Ghant.2021 Nadeem.2021 Nadeem.2021 Pearson.2021 Perkins.2021	HFNC NIV. 1 23 00 69 431 20 26 163 100 8 42 1 12 35 54 16 32 49 35 44 35 18 31 15 78 415 63	Total Weight N 4 0.6% 58 7.9% 330 9.2% 17 1.4% 95 6.0% 85 5.9% 53 5.1% 31 4.6% 378 10.5% 10.5%	Odds Ratio 1:H. Random. 95% C1 0.60 [0.02, 17.22] 0.36 [0.20, 0.66] 0.44 [0.27, 0.71] 3.76 [0.43, 32.71] 0.40 [0.18, 0.89] 0.73 [0.32, 1.66] 1.84 [0.72, 4.67] 1.48 [0.54, 4.02] 1.16 [0.80, 1.67]	Odds Ratio M-H, Random, 95% Cl	-	Study or Subgroup E 2.1.1 CPAP Alharthy.2020 Duan.2021 Franco.2020 Gaulton.2021 Ghani.2021 Gough.2021 Pearson.2021 Pearson.2021 Pearson.2021	HFNC 2 1: 4 2: 259 43 47 16: 22 4: 6 3: 14 3: 15 3 170 41:	NIV al Events 5 3 3 1 1 43 3 82 2 3 5 44 2 40 1 17 4 126	7 Total V 15 4 58 330 17 95 85 31 377 1022	Veight M- 1.5% 1.0% 7.6% 9.9% 2.8% 4.7% 5.7% 4.5% 11.5% 10.4%	Odds Ratio H. Random. 95% Cl 0.62 [0.09, 4.34] 0.63 [0.05, 7.75] 0.53 [0.26, 0.98] 1.23 [0.80, 1.87] 5.13 [1.28, 20.53] 0.24 [0.09, 0.63] 0.88 [0.39, 1.98] 0.77 [0.28, 2.10] 1.39 [1.04, 1.85] 0.29 [1.04, 1.85]	Odds Ratio M-H. Random. 95% Cl
Study or Subgroup Ex 2.1.1 CPAP Duan.2021 Fernindez.2021 Gaulton.2021 Ghani,2021 Ghani,2021 Gaugh.2021 Naddem.2021 Pearson.2021 Perkins.2021 Sykes.2021	HFNC NIV 1 23 0 69 431 20 26 163 100 8 42 1 12 35 54 35 44 36 18 31 15 78 415 63 27 48 55	Total Weight N 4 0.6% 58 7.9% 330 9.2% 17 1.4% 95 6.0% 53 5.1% 31 4.6% 31 4.6% 92 6.9% 92 6.9%	Odds Ratio 14.1, Random, 95% Cl 0.60 [0.02, 17, 22] 0.36 [020, 0.66] 0.44 [0.27, 0.71] 3.76 [0.43, 32,71] 0.40 [0.18, 0.89] 0.73 [0.32, 1.66] 1.84 [0.72, 4.67] 1.48 [0.54, 4.02] 1.16 [0.80, 1.67] 0.86 [0.43, 1.75]	Odds Ratio M-H. Random, 95% CI	-		HFNC 2 1: 4 2: 259 43 47 16: 22 4: 6 3: 14 3: 15 3 170 41: 118/ 520	NIV al Events 5 3 3 1 1 43 3 82 2 3 5 44 2 40 1 17 4 126 5 5 5 5 4 2 40 1 17 4 126 5 5 5 5 5 4 5 5 4 4 2 2 5 5 5 4 4 5 5 5 5 5 5 5 5 5 5 5 7 8 7 5 7 8 7 8 7	7 Total 7 15 4 58 330 17 95 85 31 377 1012	Veight M- 1.5% 1.0% 7.6% 9.9% 2.8% 4.7% 5.7% 4.5% 11.5% 49.1%	Odds Ratio H. Random. 95% CI 0.62 [0.09, 4.34] 0.63 [0.05, 7.75] 0.53 [0.28, 0.98] 1.23 [0.80, 1.87] 5.13 [1.28, 20.53] 0.24 [0.09, 0.63] 0.24 [0.09, 0.63] 0.88 [0.39, 1.88] 0.77 [0.28, 2.10] 1.39 [1.04, 1.85] 0.90 [0.57, 1.40]	Odds Ratio
Study or Subgroup Ex 2.1.1 CPAP Duan.2021 Franciadez.2021 Franco.2020 Gaulton.2021 Ghani,2021 Ghani,2021 Nadeem.2021 Person.2021 Person.2021 Subtotal (95% CI)	HFNC NIV 1 23 00 69 431 20 26 163 100 8 42 1 12 35 54 16 32 49 35 44 36 18 31 15 78 415 655 1264 55	Total Weight N 4 0.6% 58 7.9% 330 9.2% 17 1.4% 95 6.0% 85 5.9% 53 5.1% 31 4.6% 378 10.5% 92 6.9% 1143 58.1% 58.1%	Odds Ratio 1.41, Random, 95% C1 0.60 [0.02, 17, 22] 0.36 [0.20, 0.66] 0.44 [0.27, 0.71] 3.76 [0.43, 32,71] 0.40 [018, 0.89] 0.73 [0.32, 1.66] 1.84 [0.54, 4.02] 1.16 [0.80, 1.67] 0.65 [0.43, 1.75] 0.77 [0.51, 1.17]	Odds Ratio M-H, Random, 95% Cl	-	Study or Subgroup E 2.1.1 CPAP Alharthy, 2020 Duan, 2021 Fernindez, 2021 Fernandez, 2020 Gauthon, 2021 Gauthon, 2021 Gough, 2021 Peerson, 2021 Peerson, 2021 Petrins, 2021 Subtotal (65% CI) Total events Heteronpetitier target = 0.2	HFNC 2 1: 4 22 259 43 47 16: 22 4: 6 3: 14 3: 15 3 170 41: 1186 539 24: Chi ² = 23	NIV al Events 5 3 3 1 1 43 3 82 2 3 5 44 2 40 1 17 4 126 5 359 80 df = 8	7 Total V 15 4 58 300 17 95 85 31 377 1012 (P = 0.000	Veight M- 1.5% 1.0% 7.6% 9.9% 2.8% 4.7% 5.7% 4.5% 11.5% 49.1% 2.68%	Odds Ratio H. Random. 95% Cl 0.62 [0.09, 4.34] 0.63 [0.05, 7.75] 0.53 [0.28, 0.98] 1.23 [0.80, 1.87] 0.53 [1.28, 20.53] 0.24 [0.09, 0.63] 0.88 [0.39, 1.98] 0.77 [0.28, 2.10] 1.39 [1.04, 1.85] 0.90 [0.57, 1.40]	Odds Ratio
Study or Subgroup Exit 21.1 CPAP Duan.2021 Fernindez.2021 Franco.2020 Gaudro.2021 Gaudro.2021 Ghanl.2021 Gaudro.2021 Nadzen.2021 Persins.2021 Sylex.2021 Sylex.2021 Sylex.2021 Sylex.2021 Sylex.2021 Sylex.2021 Subtotal (6% G) Total events	HFNC NIX vents Total Events 1 23 0 69 431 20 26 163 100 8 42 1 12 35 544 36 31 15 78 415 63 27 48 55 264 290 363 290 393 45	Total Weight N 4 0.6% 58 7.9% 330 9.2% 95 6.0% 85 5.9% 531 4.6% 378 10.5% 92 6.9% 1143 58.1%	Odds Ratio H.H. Random. 95% Cl 0.60 [0.02, 17.22] 0.36 [0.20, 0.66] 0.44 [0.27. 0.71] 3.76 [0.43, 32.71] 0.40 [0.18, 0.89] 0.73 [0.32, 1.66] 1.84 [0.72, 4.67] 1.48 [0.54, 4.02] 1.16 [0.80, 1.67] 0.66 [0.43, 1.75] 0.66 [0.43, 1.75]	Odds Ratio	-	Study or Subgroup F 2.1.1 CPAP Alnarthy 2020 Duan.2021 Franciacz.2021 Franciacz.2021 Gaulton.2020 Gaulton.2020 Gharil.2021 Gharju.2021 Pearson.2021 Perkins.2021 Subjol.201 Perkins.2021 Subjol.201 Perkins.2021 Subjol.201 Subjol.201 Perkins.2021 Subjol.201 Perkins.2021 Total events Heitorogeneity: Tau ² = 0.2 Test for overall effect.2 Test for overall effect.2	HFNC 2 11 4 22 259 43 47 16 22 43 14 33 15 3 170 41 1184 539 24; Chi ² = 23 0.49 (P = 0	NIV al Events 5 3 3 1 1 43 3 82 2 3 5 44 2 40 1 17 4 126 6 5 359 8.0, df = 8 .62)	7 Total V 15 4 58 330 17 95 85 31 377 1012 (P = 0.002	Veight M- 1.5% 1.0% 7.6% 9.9% 2.8% 4.7% 5.7% 5.7% 4.5% 11.5% 49.1% 21,12 = 66%	Odds Ratio H, Random, 95% Cl 0.62 (0.9, 4.34) 0.63 (0.05, 7.75) 0.53 (0.28, 0.98) 1.23 (0.80, 1.67) 5.13 (1.28, 20.53) 0.24 (0.09, 0.63) 0.24 (0.09, 0.63) 0.24 (0.09, 0.63) 0.24 (0.03, 1.98) 0.24 (0.03, 1.98) 0	Odds Ratio
Study or Subgroup E1 2.1.1 CPAP Duan,2021 Femiandaz,2021 Franco.2020 Gaution.2021 Gauton.2021 Gough.2021 Nodeem,2021 Persina.2021 Subjoact Sykes.2021 Sykes.2021 Total events Heterogeneity: Tau* = 0.22 Total events Heterogeneity: Tau* = 0.27	HFRC NIN varis Total Events 1 23 00 69 431 20 26 163 100 8 42 1 12 35 54 35 44 36 178 415 63 290 393 5; Chi*=25.96; dr=9 12 (LP = 0.23) 12 (LP = 0.24)	Total Weight A 4 0.6% 58 7.9% 330 9.2% 17 1.4% 95 6.0% 53 5.1% 378 10.5% 92 6.9% 1143 58.1% (P = 0.002); I ² = 65%	Odds Ratio 1:H. Random, 95% Cf1 0:60 [0.02, 17,22] 0:36 [0.20, 0.66] 0:44 [0.27, 0.71] 0:76 [0.43, 32,71] 0:40 [0.18, 0.89] 1:76 [0.43, 0.27] 0:73 [0.32, 1.66] 1:84 [0.72, 4.67] 1:48 [0.54, 4.02] 1:16 [0.80, 1.67] 0.67 [0.51, 1.17]	Odds Ratio M-H, Random, 95% Cl	-	Study or Subgroup E 2.1.1 CPAP Anarthy 2020 Duan.2021 Fernandez.2021 Franco.2020 Gaulino.2021 Gaulino.2021 Gough.2021 Pearson.2021 Perkins.2021 Subtotal (95% CI) Total events Heterogeneity: Tau' = 0.2 Test for overall effect: Z =	HFNC Events Tota 2 11: 4 2: 259 43 47 16 22 4: 6 33 14 3: 15 3 170 41. 1184 539 24; Chi ² = 23 e 0.49 (P = 0	NIV al Events 5 3 3 1 1 43 3 82 2 3 5 44 2 40 1 17 4 126 6 5 359 .80, df = 8 .62)	7 Total V 15 4 58 330 17 95 85 31 377 1012 (P = 0.002	Veight M- 1.5% 1.0% 7.6% 9.9% 2.8% 4.7% 5.7% 4.5% 11.5% 49.1% 9.1° = 66%	Odds Ratio H. Random, 95% CI 0.62 [0.09, 4.34] 0.63 [0.05, 7.75] 0.53 [0.05, 7.75] 1.23 [0.80, 1.87] 5.13 [1.28, 20.53] 0.24 [0.09, 0.53] 0.24 [0.09, 0.53] 0.77 [0.28, 2.10] 0.39 [0.47, 1.40]	Odds Ratio
Study or Subgroup Etit 2.1.1 CPAP Duran, 2021 Ferraindez, 2021 Franco. 2020 Gaudon, 2021 Ghani, 2021 Ghani, 2021 Gough, 2021 Nadeem, 2021 Persins, 2021 Sykes, 2021 Subtotal (6% G) Total events Heterogenenity: Tau * = 0.22 Test for overall effect; Z = Test for overall effect; Z =	HFRC NIN 1 23 0 69 431 20 26 163 100 28 42 1 16 32 49 35 44 36 18 31 56 126 35 249 35 1264 32 290 320 20% 32 290 32, CM* 25,96, df = 9 32 1,21 (P = 0,23)	Total Weight A 4 0.6% 58 7.9% 330 9.2% 17 1.4% 95 6.0% 53 5.1% 314 4.6% 378 10.5% 1143 58.1% (P=0.002); I ² = 65%	Odds Ratio LH, Random, 95% CI 0.60 [0.02, 17,22] 0.36 [0.20, 0.66] 0.44 [0.27, 0.71] 0.47 [0.43, 23,271] 0.47 [0.43, 23,271] 0.49 [0.18, 0.89] 0.73 [0.32, 1.66] 1.44 [0.24, 4.02] 1.48 [0.44, 1.02] 1.48 [0.44, 1.02] 1.48 [0.44, 1.17] 0.86 [0.43, 1.17] 0.87 [0.51, 1.17]	Odds Ralio M-H. Random, 95% Cl	-	Study or Subgroup E 2.11. (PAP Alnarthy 2020 Duan.2021 Francio.2021 Francio.2020 Gaulton.2021 Gaulton.2021 Ghani.2021 Gough.2021 Pearson.2021 Perkins.2021 Subtotal (95% CI) Subtotal (95% CI) Total events Test for overall effect: Z = 2.1.2 BiPAP	HFNC Events Tota 2 1: 4 2: 259 43 47 16 6 3: 14 3: 15 3; 170 41: 118/ 539 24; Chi ^p = 23 e 0.49 (P = 0	NIV al Events 5 3 3 1 1 43 3 82 2 3 5 44 4 2 40 1 17 4 126 6 359 .80, df = 8 .62)	7 Total Y 15 4 58 330 17 95 85 31 377 1012 (P = 0.002	Veight M- 1.5% 1.0% 1.0% 7.6% 9.9% 2.8% 4.7% 5.7% 4.5% 11.5% 49.1% 2); ² = 66%	Odds Ratio H. Random. 95% CI 0.62 [0.09, 4.34] 0.63 [0.05, 7.76] 0.53 [0.28, 0.98] 1.23 [0.80, 1.87] 5.13 [1.28, 20.53] 0.24 [0.09, 0.63] 0.24 [0.09, 0.63] 0.24 [0.09, 0.63] 0.24 [0.09, 0.63] 0.24 [0.09, 0.63] 0.77 [0.28, 2.10] 1.39 [1.04, 1.65] 0.90 [0.57, 1.40]	Odds Ratio
Study or Subgroup Ei 21.1 CPAP Duan.2021 Famiondor.2021 Famo.2020 Gaulion.2021 Gaulion.2021 Gough.2021 Nadoem.2021 Nadoem.2021 Nadoem.2021 Subschaft Subschaft Dear.2021 Subschaft Total events Heterogeneity: Tau ² = 0.25 Total events Test for ovenitifiere: Z = 21.2 BIPAP Para	HFRC NIN reants Total Events 1 23 0 68 421 20 28 163 12 36 42 1 16 32 49 35 44 36 18 31 15 78 415 63 27 48 55 280 383 5 35 4.4 56 290 383 5 280 383 5 291 383 5 292 383 5 291 383 4.7 392 5 5.6 1.21 (P = 0.23) 12 1	Total Weight A 4 0.6% 58 7.9% 330 9.2% 17 1.4% 95 6.0% 53 5.1% 378 10.5% 92 6.9% 1143 58.1% (P = 0.002); I ² = 65%	Odds Ratio LH. Random. 95% CL 0.36 (0.20, 17.22) 0.36 (0.20, 0.66) 0.44 (0.27, 0.27) 0.47 (0.43, 0.27) 0.47 (0.43, 0.27) 0.47 (0.13, 0.28) 0.48 (0.14, 0.27, 4.67) 1.48 (0.54, 4.67) 1.48 (0.54, 4.67) 1.48 (0.54, 4.67) 1.48 (0.54, 1.67) 0.66 (0.43, 1.77) 0.66 (0.43, 1.77) 0.67 (0.54, 1.17)	Odds Ratio M-H. Random, 95% CI	=	Study of Subgroup E 2.1.1 CPAP Almarthy 2020 Duan.2021 Francialez.2021 Francialez.2021 Ghani.2021 Gaulion.20201 Ghani.2021 Person.20201 Subtotal (85% Cf) Total events Heterogeneity. Tau" = 0.2 Test for overall effect: Z = 2.1.2 BiPAP costa_2022	HFNC Events Tota 2 1: 4 2: 259 43 47 16 22 4: 6 3: 14 3: 15 3 170 41: 118/ 539 = 0.49 (P = 0 16 2:	NIV al Events 5 3 3 1 1 43 3 82 2 3 5 44 4 2 40 1 17 4 126 6 5 359 .80, df = 8 .62) 3 8	7 Total Y 15 4 58 330 17 95 85 31 377 1012 (P = 0.002 14	Veight M- 1.5% 1.0% 1.0% 7.6% 9.9% 2.8% 4.7% 5.7% 5.7% 45% 11.5% 49.1% 2); 2 = 66% 2.8%	Odds Ratio H, Random. 35% CI 0.62 (0.06, 4.34) 0.53 (0.05, 7.59) 1.53 (0.26, 7.09) 1.53 (0.26, 7.09) 1.54 (0.26, 0.63) 0.24 (0.06, 0.63) 0.24 (0.06, 0.63) 0.24 (0.06, 0.23) 0.24 (0.06, 0.23) 0.24 (0.06, 0.23) 0.24 (0.06, 0.23) 0.26 (0.57, 1.46) 1.77 (0.43, 6.83)	Odds Ratio
Study or Subaroup Etit 2.1.1 CPAP Duran, 2021 Ferraindez, 2021 Franco. 2020 Gaudino2021 Gaudino2021 Ghani, 2021 Gough, 2021 Persina2021 Sylees, 2021 Subtocal (19% CI) Total events HeterogenenityTau? = 0.22 Test for overall effect: Z = 2.1.2 Bi/AP costa, 2022	HFRC NIN rents Total Events 1 23 0 69 431 20 26 163 100 26 163 10 16 32 49 35 44 36 18 31 15 7 48 55 122 35 54 30 27 48 20 33 3 3 14 3	Total Weight N 4 0.6% 58 7.9% 330 9.2% 17 1.4% 95 6.0% 53 5.1% 53 5.1% 53 5.1% 311 4.6% 378 10.5% 1143 58.1% (P = 0.002); P = 65% 23 2.0%	Odds Ratio LH. Random. 95% CL 0.60 (10.2, 17, 22) 0.36 (10.2, 17, 22) 0.44 (10.27, 0.71) 3.76 (10.43, 32,71) 3.76 (10.43, 32,71) 0.40 (10.43, 32,71) 1.84 (10.72, 4.67) 1.84 (10.72, 4.67) 1.84 (10.72, 4.67) 1.84 (10.54, 4.02) 1.16 (10.81, 0.54) 0.77 (10.51, 1.17) 0.86 (10.43, 1.15) 0.77 (10.51, 1.15)	Odds Ralio M-H. Random, 95% Cl	-	Study or Subgroup E 2.11.10PAP Alnarthy.2020 Duan.2021 Ferniandez.2021 Ferniandez.2021 Gaulton.2020 Gaulton.2021 Ghani.2021 Gaugh.2021 Pearson.2021 Perkins.2021 Subtotal (95% CI) Subtotal (95% CI) Total events Test for overall effect: Z = 2.1.2 BiPAP costa.2022 Duan.2021	HFNC Events Tota 2 1: 4 2: 259 43 47 16 22 4: 6 3: 14 3: 15 3 170 41: 1188 539 24: Chi ² = 23 = 0.49 (P = 0 16 2: 4 2: 24 2: 4 2: 259 43 14 3: 15 3: 10 4: 11 18 16 2: 4 2: 16 2: 17 16 16 2: 17 16 16 2: 17 16 16 2: 17 16 16 2: 16 2: 17 16 16 2: 17 16 16 2: 17 16 16 2: 16 2: 17 16 16 2: 17 16 16 2: 18 2: 18 2: 18 2: 18 2: 18 2: 19 2: 19 2: 19 2: 10 2:	NIV al Events 5 3 3 1 1 43 3 82 2 3 5 44 2 40 1 17 4 126 6 5 359 80, df = 8 .62) 3 8 3 1 1 5 5 4 4 126 5 5 3 5 3 1 1 7 4 4 12 5 3 5 3 5 3 5 4 4 5 5 3 5 4 4 5 5 3 5 4 4 5 5 3 5 4 4 5 5 3 5 4 4 5 5 5 3 5 4 4 5 5 5 3 5 4 4 5 5 5 4 4 5 5 5 4 4 5 5 5 4 4 5 5 5 4 4 5 5 5 4 4 5 5 5 4 4 5 5 5 4 4 5 5 5 4 4 5 5 5 4 4 5 5 5 4 4 5 5 5 4 4 5 5 5 4 4 5 5 5 4 4 5 5 5 5 5 4 4 5	/ Total V 15 4 58 330 17 95 85 31 377 1012 (P = 0.002 14 9 14 9	Yeight M- 1.5% 1.0% 7.6% 9.9% 2.8% 4.7% 4.5% 11.5% 11.5% 49.1% 2); ? = 666% 2.8% 1.1% 11.5%	Odds Ratio H. Random. <u>95% CI</u> 0.62 (0.06, 4.34) 0.63 (0.05, 7.75) 0.53 (0.28, 0.98) 1.23 (0.08, 0.28, 0.28) 1.128, 20.53 0.24 (0.09, 0.63) 0.24 (0.09, 0.63) 0.24 (0.09, 0.63) 0.24 (0.09, 0.63) 0.24 (0.09, 0.63) 0.24 (0.09, 0.63) 0.24 (0.09, 0.63) 1.39 (1.04, 1.65) 0.90 (0.57, 1.40)	Odds Ratio
Study or Subgroup Ei 21.1 CPAP Duan.2021 Ferraindize.2021 Ferraindize.2020 Gaudin.2021 Ghani.2021 Ghani.2021 Ghani.2021 Subsci.2021 Subsci.2021 Persina.2021 Subsci.2021 Syles.2021 Subsci.2021 Total events Heterogeneity: Tau* = 0.21 Test for ovents Test for ovents Test for ovents Test.2022 Duan.2021 Duan.2021	HFNC NIN reants Total Events 1 23 0 69 431 20 28 13 10 26 13 10 26 13 12 35 44 31 35 44 55 27 48 55 290 233 344 3 14 33 1 23 1	Total Waight 1 4 0.6% 58 7.9% 330 9.2% 17 1.4% 95 6.0% 83 5.1% 10.5% 31 4.6% 378 10.5% 92 6.9% 1143 58.1% (P = 0.002); I ² = 65% 23 2.0% 9 0.8%	Odds Ratio LH. Random. 96% CL 0.36 (0.02, 17.22) 0.36 (0.20, 0.66) 0.44 (0.27, 0.71) 0.47 (0.73, 0.27) 0.47 (0.73, 0.27) 0.47 (0.73, 0.23, 1.86) 1.48 (0.44, 4.02) 1.48 (0.44,	Odds Ratio M-H. Random, 95% CI	_	Study of Subgroup E 2.1.1 CPAP Almarthy 2020 Duna.2021 Fernindez.2021 Fernindez.2021 Gaulton.2021 Ghani.2021 Ghani.2021 Ghani.2021 Pearton.2021 Pearton.2021 Pearton.2021 Pearton.2021 Total events Subtotal (95% GI) Total events 2.1.2 Bir/Brd Francio.2021 Duna.2021 Pearton.2021 Pearton.2021 Pearton.2021	HFNC Events Tota 2 1: 4 2: 259 43 47 16: 22 4: 6 33 14 3: 14 3: 14 3: 15 3 170 41. 118 539 24; Chi ² = 23 = 0.49 (P = 0 16 2: 4 2: 259 43 377 45: 16 3: 16 3: 170 45: 18 4: 18 4:	NIV al Events 5 3 3 1 1 43 3 82 2 3 5 44 2 40 0 1 17 4 126 6 3 5 8 80, df = 8 .62) 3 8 3 1 1 62 2 0	/ Total V 15 4 58 330 17 95 85 31 377 1012 (P = 0.002 14 9 105 47	Veight M- 1.5% 1.0% 1.0% 7.6% 2.8% 4.7% 4.5% 11.5% 49.1% 2); I² = 66% 2.8% 1.1% 9.7% 0.0%	Odds Ratio H. Random. 95% CI 0.62 (0.06, 4.34) 0.53 (0.26, 0.98) 1.23 (0.65, 7.58) 1.53 (0.80, 1.67) 0.54 (0.28, 0.98) 0.54 (0.28, 0.53) 0.24 (0.06, 0.53) 0.24 (0.06, 0.53) 0.26 (0.57, 1.40] 0.58 (0.31, 64, 1.65) 1.04 (0.68, 1.61) 1.04 (0.68, 1.61)	Odds Ratio
Study or Subaroup Etit 2.1.1 CPAP Duran, 2021 Fernández, 2021 Franco. 2020 Gaulton, 2021 Gaulton, 2021 Ghani, 2021 Syless, 2021 Subaro, 2021 Persina, 2021 Varbaro, 2021 Syless, 2021 Subaro, 2021 Subaro, 2021 Heterogenenity, Tau ² = 0.25 Test for overall effect; Z = 2.1.2 BIPAP costa, 2022 Duan, 2021 Pernández, 2021	HFNC NIN reants Total Events 1 23 0 69 431 20 28 163 100 8 42 1 12 35 54 16 32 49 35 44 36 178 415 63 290 383 24 200 383 (1) 35 44 36 12 50 1264 290 383 (3) 35 (4) 36 12 (2) (4) 12 (1) (2) 3 14 3 1 23 1 23 14 27	Total Weight № 4 0.6% 58 7.9% 330 9.2% 17 1.4% 95 6.0% 85 5.9% 53 5.1% 92 6.9% 314 4.6% 378 10.5% 92 6.9% 1143 58.1% (P = 0.002); I ² = 65% 9 0.8% 9 0.8%	Odds Ratio LH. Random. 95% CL 0.60 (10 2, 17, 22) 0.36 (10 20, 066) 0.44 (0 27, 071) 3.76 (0 43, 32,71) 3.76 (0 43, 32,71) 0.40 (0 18, 0.89) 0.73 (0 43, 32,71) 1.84 (0 72, 4.67) 1.84 (0 54, 4.02) 1.84 (0 72, 4.67) 1.46 (0 54, 4.02) 1.66 (0 54, 0.12) 0.77 (0.54), 1.175 0.66 (0 43, 1.75) 0.77 (0.54), 1.056] 0.36 (0 02, 6.53) 0.35 (0 33, 0.056)	Odds Raiio M-H. Random, 95% Cl	_	Study or Subgroup E 2.11.10PAP Alharthy.2020 Duan.2021 Ferniandez.2021 Ferniandez.2021 Glaution.2021 Glaution.2021 Ghari.2021 Deks.2021 Pearson.2021 Perkins.2021 Subtotal (95% CI) Subtotal (95% CI) Total events Heterogeneity: Tau ² = 0.2 2.1.2 BiPAP costa.2022 Duan.2021 Ferniandez.2021 Ferniandez.2021 Franco.2020 Costa.2020	HFNC Events Tota 2 1: 4 2: 259 43: 47 16: 22 4: 6 3: 14 3: 15 3: 17 41: 118: 539 24: Chi ² = 23 24: Chi ² = 23 16 2: 4 2: 24: Chi ² = 23 16 2: 4 2: 24: Chi ² = 23 16 2: 4 2: 17 4: 18 5: 18 5:	NIV al Events 5 3 3 1 1 43 3 82 2 3 5 44 2 40 1 17 4 126 5 359 80, df = 8 .62) 3 8 3 1 1 62 3 49 4 15	/ Total V 15 4 58 330 17 95 85 31 377 1012 (P = 0.002 14 9 105 177 5 5 17 95 1012	Veight M- 1.5% 1.0% 7.6% 9.9% 2.8% 4.7% 5.7% 4.5% 45.7% 4.5% 49.1% 2.8% 1.15% 1.15% 2.8% 9.7	Odds Ratio H. Random. <u>95% Cl</u> 0.62 (0.04, 3.44) 0.63 (0.05, 7.75) 1.53 (1.28, 0.98) 1.23 (0.80, 1.87) 0.54 (0.28, 20.53) 0.24 (0.09, 0.63) 0.28 (0.33, 1.98) 0.77 (0.28, 2.10) 1.39 (10.44, 1.85) 0.90 (0.57, 1.40)	Odds Ratio
Study or Subgroup Ei 21.1 CFAP Duan.2021 Ferraindez.2021 Ferraindez.2020 Gaudro.2021 Gaudro.2021 Ghani.2021 Gaudro.2021 Sylacz.2021 Sylacz.2021 Total events Total events Heterogenalty: Tau' = 0.22 Total events Heterogenalty: Tau' = 0.22 Total events Heterogenalty: Tau' = 0.22 Duan.2021 Fast for ovenall effect: Z = 2.1.2 BIPAP Costa.2022 Duan.2021 Faraoc.20202 Duan.2021 Faraoc.20202 Duan.2021	HFNC NIN reants Total Events 1 23 0 69 431 200 28 183 100 28 183 100 28 183 100 35 44 46 55 415 63 200 203 303 5, Ch# = 25.96, cf = 9 12 3 14 3 1 23 1 68 31 15 200 203 31 3 14 3 3 14 3 20 163 54	$\begin{array}{c} \hline Total Weight h \\ 4 & 0.6\% \\ 58 & 7.9\% \\ 330 & 9.2\% \\ 17 & 1.4\% \\ 95 & 6.0\% \\ 53 & 5.1\% \\ 53 & 5.1\% \\ 53 & 5.1\% \\ 1143 & 58.1\% \\ 1143 & 58.1\% \\ 1143 & 58.1\% \\ (P=0.002); P=65\% \\ 23 & 2.0\% \\ 9 & 0.8\% \\ 105 & 8.9\% \\ 105 & 8.9\% \\ 17 = 6.7\% \end{array}$	Odds Ratio LH. Random. 96% CI 0.00 (0.02, 17.22) 0.44 (0.27, 0.71) 0.44 (0.27, 0.71) 0.49 (0.16, 0.89) 0.49 (0.16, 0.89) 0.49 (0.16, 0.89) 0.49 (0.16, 0.16) 1.49 (0.44, 4.02) 1.49 (0.44, 4.02) 1.49 (0.44, 4.02) 1.49 (0.44, 4.02) 1.49 (0.44, 4.02) 1.56 (0.04, 1.75) 0.57 (0.54, 1.77) 0.57 (0.54, 1.77) 0.56 (0.03, 0.15) 0.56 (0.23, 0.53) 0.55 (0.33, 0.51) 0.43 (0.23, 0.73)	Odds Ratio	_	Study or Subgroup F 2.1.1 (PAP P Almarthy 2020 Dun.2021 Fernindez.2021 Franco.2020 Gaulton.2021 Gaulton.2021 Graution.2021 Genzin.2021 Pearson.2021 Pearson.2021 Perkins.2021 Subtotal (95% CI) Subtotal (95% CI) Subtotal (95% CI) 2.1.2 Bir/AP Colar avents C1.2 Bir/AP colar.2021 Fernindez.2021 Fernindez.2021 Fernindez.2021 Giraco.2021 Marca 2021 Giraco.2021	HFNC Events Tota 2 1: 2 59 43 4 2 4: 2 59 43 47 16 22 48 7 16 539 24; Chi ² = 23 259 16 2 4 259 43 47 16 28 5 259 43 15	NIV al Events 5 3 3 1 1 43 3 82 2 3 5 44 2 40 1 17 4 126 6 359 80, df = 8 .62) 3 8 3 1 1 62 3 49 4 15 4 37 1 62 3 49 4 37 1 62 1 7 1 62 1 62 1 62 1 7 1 62 1 62 1 62 1 62 1 7 1 62 1 7 1 62 1 7 1 7 1 7 1 62 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7	/ Total V 15 4 58 330 17 95 31 1012 (P = 0.002 14 9 105 177 55 61	<pre>/eight M- 1.5% 1.0% 9.9% 2.8% 4.7% 5.7% 4.5% 49.1% 2.8% 49.1% 2.8% 49.1% 2.8% 49.1% 5.9% 4.6%</pre>	Odds Ratio H. Random. 95% CI 0.62 (0.06, 4.34) 0.53 (0.26, 0.09) 1.32 (0.06, 7.78) 1.32 (0.80, 1.67) 0.54 (0.28, 0.29) 0.34 (0.09, 0.53) 0.24 (0.09, 0.53) 0.24 (0.09, 0.53) 0.24 (0.09, 0.53) 1.39 (1.04, 1.65) 0.39 (0.57, 1.40) 1.39 (1.04, 1.65) 0.39 (0.57, 1.40)	Odds Ratio
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Study or Subgroup Ex 21.1 CFAP Duna.2021 Fernindrez.2021 Fernindrez.2021 Franco.2020 Gaudro.2021 Ghand.2021 Ghand.2021 Ghand.2021 Sylexe.2021 Sylexe.2021 Sylexe.2021 Subdool (65% G) Total events Heterogenehy: Tau' = 0.22 Test for overall effect: Z = 21.2 Bi/AP costa.2022 Dane.2021 Fernindrez.2021 Fernindrez.2021 Fernindrez.2021 Fernindrez.2021 Farnoc.2020 Dane.2021 Nadeem.2021 Nadeem.2021 Nadeem.2021 Dane.2021 Nadeem.2021	HFNC NIN reants Total Events 1 23 0 69 431 20 28 163 100 8 42 1 12 35 54 112 35 54 35 44 56 178 415 63 200 303 50 35 44 35 12 55 1264 200 303 35 31 1 23 1 23 1 1 23 1 5 44 12 5 44 12 26 163 44 10 54 41 25 44 11 16 5 5	Total Weight h 4 0.6% 6% 58 7.9% 7 330 9.2% 17 1.4% 95 6.0% 95 6.9% 93 5.1% 1 4.6% 378 10.5% 92 6.9% 92 6.9% 1143 58.1% (CP 0.002); μ = 65% 9 0.8% 105 8.9% 1.1% 55 5.0% 35 3.1% 5.5% 55 5.0%	Odds Raio LH. Random. 95% CI 0.40 (0.20, 72.22) 0.30 (0.20, 72.22) 0.41 (0.27, 0.27) 0.41 (0.27, 0.27) 0.41 (0.27, 0.27) 0.41 (0.27, 0.27) 0.41 (0.14, 0.28) 0.42 (0.14, 0.28) 0.42 (0.14, 0.28) 0.44 (0.14, 0.28) 0.44 (0.14, 0.28) 0.44 (0.14, 0.28) 0.45 (0.14, 0.14) 0.45 (0.14, 0.14) 0.45 (0.14, 0.14) 0.45 (0.24, 0.14)	Odds Raiio M-H. Random 95% Cl		Study or Subgroup F 2.1.1 (PAP Alnarthy 2020 Duan.2021 Franca.2021 Franca.2020 Gaulton.2021 Gaulton.2021 Ghani.2021 Gaulton.2021 Pearson.2021 Perkins.2021 Subtotal (95% CI) Stuttotal (95% CI) Subtotal (95% CI) Subtotal (95% CI) Subtotal (95% CI) </td <td>HFNC Events Tota 2 11 4 2 259 43 47 16 22 44 6 3 15 3 16 3 539 24; ChiP = 23 259 43 4 2 259 43 4 2 259 43 47 16 28 5 15 5 15 5 15 5 112 18</td> <td>NIV al Events 5 3 3 1 4 3 82 2 3 5 44 4 2 400 1 17 4 126 6 359 80, df = 8 .62) 3 8 3 1 1 62 3 49 4 55 4 37 5 25 4 67 4 57 5 25 5 4 6 10 1 62 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7</td> <td>/ Total V 15 4 58 330 17 95 85 31 377 1012 (P = 0.002 (P = 0.002 14 9 105 177 561 54 131</td> <td>(eight M- 1.5% 1.0% 7.6% 9.9% 2.8% 4.7% 5.7% 4.5% 4.5% 4.5% 4.5% 4.5% 4.5% 4.5% 9.3% 5.9% 9.3% 5.9%</td> <td>Odds Ratio H. Random. <u>95% CI</u> 0.52 [0.06, 4.34] 0.53 [0.28, 0.98] 1.23 [0.80, 1.87] 0.53 [0.28, 0.98] 1.23 [0.80, 1.87] 0.24 [0.09, 0.63] 0.24 [0.09, 0.63] 0.24 [0.09, 0.63] 0.25 [0.28, 2.10] 0.26 [0.14, 1.85] 0.90 [0.57, 1.40] 1.71 [0.43, 6.83] 1.68 [0.16, 17.52] 1.04 [0.68, 1.61] 1.06 [0.66, 1.70] 2.87 [1.28, 6.83] 1.06 [0.61, 1.28] 1.06 [0.64, 1.28] 1.06 [0.64, 1.28] 0.43 [0.20, 0.97] 1.40 [0.89, 2.20]</td> <td>Odds Ratio</td>	HFNC Events Tota 2 11 4 2 259 43 47 16 22 44 6 3 15 3 16 3 539 24; ChiP = 23 259 43 4 2 259 43 4 2 259 43 47 16 28 5 15 5 15 5 15 5 112 18	NIV al Events 5 3 3 1 4 3 82 2 3 5 44 4 2 400 1 17 4 126 6 359 80, df = 8 .62) 3 8 3 1 1 62 3 49 4 55 4 37 5 25 4 67 4 57 5 25 5 4 6 10 1 62 1 7 1 7 1 7 1 7 1 7 1 7 1 7 1 7	/ Total V 15 4 58 330 17 95 85 31 377 1012 (P = 0.002 (P = 0.002 14 9 105 177 561 54 131	(eight M- 1.5% 1.0% 7.6% 9.9% 2.8% 4.7% 5.7% 4.5% 4.5% 4.5% 4.5% 4.5% 4.5% 4.5% 9.3% 5.9% 9.3% 5.9%	Odds Ratio H. Random. <u>95% CI</u> 0.52 [0.06, 4.34] 0.53 [0.28, 0.98] 1.23 [0.80, 1.87] 0.53 [0.28, 0.98] 1.23 [0.80, 1.87] 0.24 [0.09, 0.63] 0.24 [0.09, 0.63] 0.24 [0.09, 0.63] 0.25 [0.28, 2.10] 0.26 [0.14, 1.85] 0.90 [0.57, 1.40] 1.71 [0.43, 6.83] 1.68 [0.16, 17.52] 1.04 [0.68, 1.61] 1.06 [0.66, 1.70] 2.87 [1.28, 6.83] 1.06 [0.61, 1.28] 1.06 [0.64, 1.28] 1.06 [0.64, 1.28] 0.43 [0.20, 0.97] 1.40 [0.89, 2.20]	Odds Ratio
Study or Subaroup Etit 21.1 CPAP Duan.2021 Fernández.2021 Franco.2020 Gaulton.2021 Gaulton.2021 Ghani.2021 Gough.2021 Nadcem.2021 Syles.2021 Subboli.0251 Gough.2021 Valor.2021 Syles.2021 Subboli.0251 Total events Heterogenenity: Tau" = 0.21 Heterogenenity: Tau" = 0.22 2.1.2 BIPAD.2021 Dam.2021 Parandez.2020 Greice.2021 France.2020 Greice.2021 Ratieri.2021 Nadeem.2021 Nadeem.2021 Nadeem.2021 Ratieri.2021 Nadeem.2021	HFNC NIN reants Total Events 1 23 0 09 431 20 26 163 100 8 42 1 12 35 54 16 32 49 35 44 36 178 415 63 290 124 52 123 1 15 124 52.96.df = 9 121(P = 0.23) 1 123 1 123 1 123 1 123 1 123 1 123 1 123 1 123 1 125 163 125 163 125 163 13 14 13 15 15 44 16 55 17 25	7 Total Weight A 4 0.6% 58 7.9% 330 9.2% 17 1.4% 85 5.9% 95 6.0% 53 5.1% 378 10.5% 92 6.9% 92 6.9% 1143 58.1% (P=0.002); I ² = 65% 1143 58.1% (P=0.002); I ² = 65% 105 8.9% 105 8.9% 5 5.0% 5 5.0% 5 1.1% 54 6.1% 54 6.1% 55 8.5% 54 6.1% 55 8.5% 55 8.5% 56 8.5% 57 8.5% 57 8.5% 58 8.5% 59 8.5% 50	Odds Ratio LH. Random. 95% CI. 0.60 (10.20, 17.22) 0.36 (0.20, 0.66) 0.44 (0.27, 0.27) 3.76 (0.43, 92.71) 3.76 (0.43, 92.71) 1.48 (0.72, 4.67) 1.48 (0.52, 4.67) 1.48 (0.54, 4.02) 1.69 (0.43, 1.75) 0.77 (0.45, 1.17) 0.86 (0.43, 1.75) 0.36 (0.02, 6.53) 0.36 (0.02, 6.53) 0.43 (0.22, 0.73) 0.43 (0.22, 0.73) 0.44 (0.22, 1.05)	Odds Ralio M-H, Bandom, 95% Cl	_	Study or Subgroup F 2.11.10PAP Alharthy.2020 Duan.2021 Fermindez.2021 Fermindez.2021 Glaulton.2021 Gaulton.2021 Ghari.2021 Ghari.2021 Barbor.2021 Perkins.2021 Subtotal (95% CI) Tobal events Hetercgeneity: Taul* = 0.2 Test.1cr overail effect: Z = 2.12 BirAP Costa.2022 Duan.2021 Fernindez.2021 Franco.2020 Merga.2021 Merga.2021 Raireid.2021 Raireid.2021 Raireid.2021 Shoukri.2021	HFNC Events Tota 2 1: 4 2: 259 43 47 16 22 4: 6 3 15 3 170 41. 188 5.39 24; ChiP = 23. 2.49 (P = 0 16 2: 25.9 4.3 47 16 28 5 12 15 15 2 15 2 15 2 15 2 15 2 15 2 15 4 3 3	NIV al Events 5 3 3 1 4 3 3 82 2 3 5 44 4 2 4 0 1 17 4 126 5 359 3 62 3 49 4 15 4 37 5 25 4 37 7 3 8	/ Total V 15 4 58 330 17 95 85 31 377 1012 (P = 0.002 (P = 0.002 14 9 105 61 177 55 61 12 54 137 26	Veight M- 1.5% 7.6% 9.9% 4.7% 5.7% 4.5% 11.5% 11.5% 11.5% 2.8% 2.8% 2.8% 5.9% 5.9% 4.6% 5.9% 9.3%	Odds Ratio H. Random. <u>85% CI</u> 0.62 (0.06, 4.34) 0.53 (0.28, 0.98) 1.23 (0.05, 7.75) 7.15 (1.28, 20.53) 0.24 (0.09, 0.53) 0.24 (0.09, 0.53) 0.24 (0.09, 0.53) 0.24 (0.09, 0.53) 1.39 (10.4, 1.85] 0.90 (0.57, 1.40] 1.59 (10.4, 1.85] 0.90 (0.57, 1.40] 1.04 (0.66, 1.61) 1.04 (0.62, 1.20) 0.43 (0.23, 0.97) 1.40 (0.89, 2.20) 0.33 (0.19, 4.55)	Odds Ratio
Study or Subgroup Etit 2.1.1 CPAP Dum.2021 Fernindraz.2021 Fernindraz.2020 Gaudro.2021 Gaudro.2021 Ghani.2021 Gaudro.2021 Parsion.2021 Sylex.2021 Sylex.2021 Sylex.2021 Subtotal (6% CI) Total events Heterogeneity: Travit = 0.22 Test for overall effect: Z = 2.1.2 BIPAP costa.2022 Dura.2021 Faraco.2020 Grideo.2021 Faraco.2021 Faraco.2021 Raineri.2021 Naiz.2021 Raineri.2021	HFNC NIN reants Total Events 1 23 0 69 431 200 28 163 100 8 42 10 12 35 54 16 32 49 35 44 56 78 115 57 280 339 (cH = 25, 96, cf = 9 1,21 (P = 0,23) 12 35 1 23 1 7 1 23 1 1 290 393 14 3 1 23 1 1 291 131 14 3 1 23 1 10 54 10 54 12 13 16 55 25 25 3 14 3 16 16 55 25 35 137 1 17	Total Weight Λ 4 0.6% 8 58 7.9% 3330 9.2% 330 9.2% 3330 9.2% 331 9.2% 5 5.6% 53 5.1% 53 5.1% 378 10.5% 92 6.9% 92 6.9% 1143 58.1% (P = 0.002): µ = 65% 9 0.8% 105 8.9% 105 8.9% 107 8.7% 3 1.1% 55 5.0% 3 1.1% 54 6.1% 13 8.5% 26 0.9% 26 0.9%	Odds Ratio LH. Random. 95% CI 0.60 (10.20, 72.22) 0.36 (10.20, 72.22) 0.44 (10.27, 0.27) 3.76 (10.43, 0.27) 0.44 (10.27, 0.71) 3.76 (10.43, 0.27) 0.40 (10.18, 0.89) 0.73 (10.43, 0.27) 1.49 (10.72, 467) 1.49 (10.72, 467) 1.49 (10.72, 467) 1.49 (10.54, 0.22) 0.77 (10.51, 1.17) 0.56 (10.43, 1.75) 0.77 (10.51, 1.17) 0.55 (10.31, 0.54) 0.36 (10.22, 53) 0.55 (10.31, 0.54) 0.43 (10.22, 2.08) 7.76 (10.33, 95.68) 0.44 (10.22, 2.105) 0.78 (10.33, 95.68) 0.44 (10.22, 1.15)	Odds Raiio		Study or Subgroup F 2.1.1 (PAP Alnarthy 2020 Duan.2021 Franca.2021 Franca.2020 Gaulton.2021 Gaulton.2021 Ghani.2021 Ghani.2021 Pearson.2021 Perkins.2021 Subtotal (95% CI) Total events Test for overall effect: 2 = 2.1.2 BiPAP costa.2022 Duan.2021 Fernandez.2021 Fernandez.2021 Grieco.2021 Merga.2021 Nair.2021 Shubir, 2021 Shubir, 2021 Shubir, 2021 Shubir, 2021	HFNC Events Tota 2 1: 4 2: 259 43 47 16: 22 44 6 3: 15 3 170 41-1 180 539 24: Chi* = 23. 16 2: 259 43. 47 16: 28 0.49 (P = 0) 16 2: 259 43. 47 16: 28 55.9 15 2 15 2 15 15 112 18 4 3 99 99	NNV al Events 5 3 1 1 43 3 82 2 3 5 44 2 40 1 17 4 126 6 359 80, df = 8 62) 3 8 3 8 3 9 4 9 4 15 5 525 4 37 5 255 4 69 7 3 4	Total V 15 4 58 330 17 95 85 31 377 1012 (P = 0.002 (P = 0.002 (P = 0.002 (P = 0.002 14 9 105 177 55 61 131 26 632	Veight M- 1.5% 1.0% 7.6% 9.9% 5.7% 5.7% 4.7% 5.7% 11.5% 4.5% 9.9% 2.8% 11.1% 9.7% 9.3% 5.9% 5.9% 5.9% 9.5% 2.2%	Odds Ratio H. Random. <u>95% CI</u> 0.52 [0.09, 4.34] 0.53 [0.28, 0.99] 1.23 [0.80, 1.87] 0.53 [0.28, 0.98] 1.23 [0.80, 1.87] 0.24 [0.09, 0.53] 0.24 [0.09, 0.53] 0.24 [0.09, 0.53] 0.24 [0.09, 0.53] 1.39 [1.04, 1.85] 0.90 [0.57, 1.40] 1.39 [1.04, 1.85] 0.90 [0.57, 1.40] 1.06 [0.64, 1.752] 1.04 [0.68, 1.61] 1.06 [0.64, 1.752] 1.04 [0.68, 1.61] 1.06 [0.64, 1.752] 1.04 [0.68, 1.61] 1.06 [0.64, 1.28] 0.39 [0.20, 0.97] 1.40 [0.89, 2.20] 0.33 [0.19, 4.55]	Odds Ratio
Study or Subaroup Etit 21.1 CPAP Duan.2021 Fernández.2021 Franco.2020 Gaulton.2021 Gaulton.2021 Ghani.2021 Subaro.2021 Persins.2021 Subaro.2021 Subaro.2021 Subaro.2021 Subaro.2021 Subaro.2021 Subaro.2021 Subaro.2021 Tast for overall effect.2 = 2.1.2 BIPAO.2021 Duan.2021 Perrindez.2021 Franco.2020 Gault.2021 Perandez.2020 Galdon.2021 Ratier.2021 Ratier.2021 Nataken.2021 Nataken.2021 Subbotal (Edst. G1) Subaker.2021	HFNC NIN reants Total Events 1 23 0 09 431 20 26 163 100 8 42 1 12 35 54 16 32 49 35 44 36 178 415 63 290 123 1 290 123 1 1 23 1 1 23 1 1 23 1 1 23 1 1 23 1 1 23 1 1 23 1 1 23 1 1 23 1 1 23 1 1 24 1 25 44 1 16 55 25 35 144 25	7 Total Weight A 4 0.6% 58 7.9% 330 9.2% 17 1.4% 85 5.9% 95 6.0% 53 5.1% 378 10.5% 92 6.9% 92 6.9% 1143 58.1% (P=0.002); I ² = 65% 1143 58.1% (P=0.002); I ² = 65% 105 8.9% 3 1.1% 54 6.1% 54 6.1% 54 6.1%	Odds Ratio LH. Random. 95% CI 0.60 (10.27, 12.21) 0.36 (10.20, 0.66) 0.44 (10.27, 0.27) 0.44 (10.27, 0.27) 1.376 (10.43, 92.71) 1.34 (10.72, 4.67) 1.48 (10.52, 4.67) 1.48 (10.54, 4.02) 1.69 (10.43, 1.75) 0.77 (10.43, 10.54) 0.36 (10.45, 1.15) 0.36 (10.25, 6.53) 0.55 (10.33, 0.56) 0.43 (10.22, 0.73) 0.43 (10.22, 0.73) 0.45 (10.22, 0.75) 0.45 (10.22, 1.02) 0.45 (10.22, 1.02) 0.45 (10.22, 1.02) 0.45 (10.24, 1.12) 0.45 (10.24, 1.12) 0.45 (10.24, 1.12)	Odds Raiio M-H, Random, 95% Cl		Study or Subgroup F 2.1.1 (PAP Alharthy 2020 Duan,2021 Franco,2020 Gaulton,2021 Graniton,2021 Graulton,2021 Ghari,2021 Perkins,2021 Subtotal (95% CI) Tobal events Heierogeneity: Taul* = 0.2 Tobal events Fernindez: Ze Perkins,2021 Fernindez: Ze Perkins,2021 Franco,2020 Pernindez: Ze Pernindez: Ze Pernindez	HFNC Events Tota 2 1: 4 2: 259 43 47 16 24 47 539 1184 539 24: Chi* 24: Chi* 23 16 2 24: Chi* 23 16 2 259 43 24: Chi* 23 16 2 47 16 28 5 15 2 15 2 15 2 16 2 47 16 112 18 4 3 112 18 4 3 99 500	NNV al Events 5 3 1 1 43 3 82 2 3 5 44 2 40 1 17 4 126 6 359 .80, df = 8 .62) 3 8 3 1 1 62 3 49 4 15 4 37 5 25 4 37 5 25 4 37 5 25 4 37 5 25 4 37 5 25 4 37 5 25 4 37 5 25 2 4 4 37 5 25 2 5 2 5 2 5 2 5 2 5 2 5 2	Total V Total V 15 4 58 330 17 95 85 31 377 1012 (P = 0.002 14 9 105 177 56 61 54 131 26 632	Veight M- 1.5% 9.9% 2.8% 4.7% 5.7% 4.5% 11.5% 49.1% 2.8% 4.5% 11.5% 49.1% 9.7% 5.9% 4.6% 5.9% 5.9% 5.9% 5.9% 5.9% 5.5% 5.9% 5.5% 5.9%	Odds Ratio H. Random. 35% CI 0.62 (0.06, 4.34) 0.53 (0.28, 0.98) 1.23 (0.05, 7.75) 7.15 (1.28, 20.53) 0.24 (0.09, 0.53) 0.24 (0.09, 0.53) 0.24 (0.09, 0.53) 0.24 (0.09, 0.53) 1.39 (10.44, 1.85) 0.99 (0.57, 1.40) 1.59 (10.44, 1.85) 0.99 (0.57, 1.40) 1.04 (0.66, 1.61) 1.04 (0.68, 1.61) 1.04 (0.89, 2.20) 0.43 (0.23, 0.97) 1.40 (0.89, 2.20) 0.33 (0.19, 4.55) 1.16 (0.45, 1.58)	Odds Ratio
Study or Subgroup Etit 2.1.1 CPAP Duran, 2021 Fernándoz, 2021 Fernándoz, 2021 Gradom, 2021 Gradom, 2021 Gradom, 2021 Gradom, 2021 Persina, 2021 Sykes, 2021 Subtotal (69% CI) Total events Heterogenenity: Trau* = 0.22 Test for overall effect: Z = 2.1.2 BIPAP costa, 2022 Duan, 2021 Faraco, 2020 Gradem, 2021 Faraco, 2020 Duan, 2021 Faraco, 2021 Naice, 2021 Rarieri, 2021 Shoukri, 2021 Rarieri, 2021 Subtotal (69% CI) Total events	HFNC NIN reants Total Events 1 2.3 0 69 431 20 28 163 100 8 42 1 12 35 54 16 32 49 35 44 36 78 415 63 200 383 54 05 1264 10 5 (44 36 12 35 (41 63 37 14 35 (44 36 (50) 1264 12 200 333 14 3 10 54 12 11 10 54 12 23 11 13 14 12 15 52 12 14 16 55 25 35 184 32 11 105	Total Weight ♪ 4 0.6% 58 7.9% 330 9.2% 331 9.2% 330 9.2% 330 9.2% 331 9.2% 95 6.0% 85 5.9% 92 6.9% 92 6.9% 1143 58.1% (cP = 0.002); l ² = 65% 23 2.0% 9 0.8% 105 8.9% 105 8.9% 105 8.9% 105 8.9% 131 8.5% 54 6.1% 131 8.5% 583 41.9%	Odds Ralio LH. Random. 95% CI 0.66 (10.02, 97.22) 0.36 (10.02, 97.22) 0.44 (10.27, 0.27) 3.76 (10.43, 92.7) 1.376 (10.43, 92.7) 1.34 (10.72, 46.7) 1.48 (10.72, 46.7) 1.48 (10.72, 46.7) 1.48 (10.54, 0.22) 0.77 (10.51, 1.17) 0.86 (10.43, 1.75) 0.77 (10.51, 1.17) 0.36 (10.43, 1.75) 0.36 (10.24, 5.33) 0.36 (10.24, 5.33) 0.48 (10.22, 2.08) 7.78 (10.33, 95.68) 0.36 (10.33, 22, 2.08) 7.78 (10.33, 95.68) 0.48 (10.22, 2.105) 0.73 (10.33, 95.68) 0.48 (10.22, 2.105) 0.73 (10.33, 95.68) 0.48 (10.22, 2.105) 0.73 (10.43, 11.53) 0.49 (10.24, 11.53) 0.49 (10.45, 0.79)	Odds Raiio M-H. Random, 95% Cl	_	Study or Subgroup E 2.11.0PAP Alnarthy.2020 Duan.2021 Franco.2020 Franco.2020 Gaulton.2021 Gaulton.2021 Ghani.2021 Pearson.2021 Pearson.2021 Perkins.2021 Subtotal (95% CI) Total events Heterogeneity: Tau* = 0.2 Pearson.2021 Fernández.2021 Franco.2020 Grieco.2021 Merga.2021 Nair.2021 Ranieri.2021 Shubici.2021 Subtotal (95% CI) Total events	HFNC Events Tota 2 1: 4 2: 259 43 47 16 22 4: 6 3: 15 3 170 41. 539 24: Chi ² = 23 16 2: 255 43 47 16 28 5 15 2 15 5 112 18 99 500 07: Chi ² = 12 12	NNV al Events 5 3 3 1 1 43 3 82 2 3 4 4 02 5 44 4 126 6 359 359 4 126 6 359 350, df = 8 62) 3 1 1 62 3 3 1 1 62 3 3 1 3 4 9 4 15 4 5 2 5 2 5 2 5 2 5 2 6 9 4 2 8 9 4 4 9 8 8 8 8 8 9 8 8 9 8 9 8 9 8 9 8 9	/ Total V 15 4 58 330 17 95 31 17 95 31 37 1012 (P = 0.002 (P = 0.014) (P = 0.014)	Veight M- 1.5% 1.5% 7.6% 9.9% 2.8% 4.7% 5.7% 5.7% 4.5% 4.5% 4.5% 4.5% 9.1% 9.3% 5.9% 4.6% 5.9% 4.6% 5.9% 5	Odds Ratio H. Random. <u>95% CI</u> 0.62 [0.09, 4.34] 0.63 [0.05, 778] 1.53 [0.28, 0.98] 1.23 [0.80, 1.87] 0.28 [0.38], 1.88] 0.77 [0.28, 2.10] 0.28 [0.39, 1.98] 0.77 [0.28, 2.10] 1.39 [1.04, 1.85] 0.90 [0.57, 1.40] 1.39 [1.04, 1.85] 1.06 [0.65, 1.70] 2.87 [1.29, 6.38] 1.06 [0.65, 1.70] 2.87 [1.29, 6.38] 1.40 [0.88, 2.20] 0.33 [0.19, 4.55] 1.46 [0.45, 1.58]	Odds Ratio
Study or Subaroup Et 21.1 CPAP Duan.2021 Fernández.2021 Franco.2020 Gaulton.2021 Gaulton.2021 Gaudon.2021 Subaro.2021 Persina.2021 Subaro.2021 Subaro.2021 Subaro.2021 Subaro.2021 Subaro.2021 Subaro.2021 Subaro.2021 Subaro.2021 Subaro.2021 Cat.2 Tast for overall effect.2 2.1.2 BIAP cota.2020 Grade.2021 Faranco.2020 Grade.2021 Faranco.2020 Grade.2021 Faranco.2020 Grade.2021 Farano.2020 Grade.2021 Subator.2021 Subator.2021 Nair.2021 Subator.2021 Subator.2021 Subator.2021 Subator.2021 Subator.2021 Subator.2021 Subator.2021 Subator.2021 Subator.2021 Subator.2055 Grade.2021 Subator.2055 Grade.2021 Subator.2055 Grade.2021 Subator.2055	HFNC NIN reants Total Events 1 23 0 69 431 20 28 163 100 8 42 1 12 35 54 16 32 49 35 44 38 27 48 55 280 128 43 20 123 1 41 78 415 63 1 23 1 44 38 1 23 1 44 39 1 23 1 44 31 27 26 163 54 41 16 55 25 35 14 41 16 55 25 35 184 32 1 37 1 1005 1005 1005 1005 1005 1005 1005 1005 1005 1005 1005	$\begin{array}{c} \hline Total Waight h \\ 4 & 0.6\% \\ 58 & 7.9\% \\ 330 & 9.2\% \\ 17 & 1.4\% \\ 95 & 6.0\% \\ 85 & 5.9\% \\ 83 & 5.1\% \\ 378 & 10.5\% \\ 314 & 4.6\% \\ 378 & 10.5\% \\ 1143 & 58.1\% \\ (P = 0.002); I^2 = 65\% \\ \hline \\ 23 & 2.0\% \\ 9 & 0.8\% \\ 105 & 8.9\% \\ 55 & 5.0\% \\ 54 & 6.1\% \\ 54 & 6.1\% \\ 563 & 4.1.9\% \\ 26 & 0.3\%; I^2 = 5\% \\ \end{array}$	Odds Ratio LH. Random. 96% CI 0.60 (0.02, 17.22) 0.36 (0.20, 0.67) 0.44 (0.27, 0.71) 0.47 (0.73, 0.27) 0.47 (0.73, 0.27) 0.47 (0.73, 0.23, 1.86) 1.48 (0.44, 4.67) 1.48 (0.45, 4.67) 0.48 (0.45, 0.73) 0.41 (0.32, 0.04) 0.43 (0.26, 0.73) 0.43 (0.26, 0.73) 0.44 (0.22, 1.05) 0.46 (0.44, 1.163) 0.66 (0.44, 0.77)	Odds Raiio M-H. Random, 95% CI		Study of Subgroup E 2.1.1 CPAP 2.1.1 CPAP Almarthy 2020 Dun, 2021 Fernindez, 2021 Franco, 2020 Gaulton, 2021 Ghani 2021 Ghani 2021 Ghani 2021 Pearson, 2021 Pearson, 2021 Pearson, 2021 Subtotal (95% CI) Total events Heterogeneity: Tau* = 0.2 2.1.2 Bir/AD Pearson, 2021 Dun, 2021 Pearson, 2021 Pernandez, 2021 Prana, 2021 Merga, 2021 Merga, 2021 Shoukri, 2021 Subtotal (95% CI) Shoukri, 2021 Shoukri, 2021 Shoukri, 2021<	HFRC Events Tota 2 1: 4 2: 259 43 47 16 22 4 6 33 14 3: 15 3 17 18 539 24; Chi ² = 23 0 0.49 (P = 0 0 0.49 (P = 0 16 2: 4 2: 259 43 47 16 28 5 15 5 15 5 15 5 15 5 15 5 15 5 15 5 1	NNV al Events 5 3 3 1 1 433 3 82 2 3 5 44 2 40 1 17 4 126 6 359 80, df = 8 3 8 3 1 1 62 3 49 4 15 4 37 5 25 4 37 5 25 4 49 7 3 4 269 7 3 269 226, df = 8 3.55)	/ Total V 15 330 17 95 85 331 377 1012 1012 1012 1012 1012 1012 1012 1012 1012 1012 1012 (P = 0.002 (P = 0.14) (P = 0.14)	Aright M- 1.5% 1.0% 7.6% 9.9% 2.8% 4.7% 5.7% 4.5% 11.5% 49.1% (2); I' = 666% 9.7% 9.7% 9.3% 5.9% 2.8% 5.9% 2.9% 5.9% 5.9% 2.2% 50.9% (; I' = 35%) ; I' = 35%	Odds Ratio H. Random. 35% CI 0.62 (0.06, 4.34) 0.63 (0.05, 7.58) 0.53 (0.28, 0.98) 1.23 (0.80, 1.67) 0.54 (0.28, 0.53) 0.24 (0.06, 0.53) 0.24 (0.06, 0.53) 0.26 (0.05, 7.140] 1.39 [1.04, 1.65] 1.39 [1.04, 1.65] 1.36 [0.16, 17.52] 1.36 [0.16, 17.52] 1.36 [0.66, 1.71] 1.36 [1.04, 1.68, 1.61] 1.36 [1.04, 1.26, 1.61] 1.36 [1.04, 1.26] 1.36 [1.04, 1.26] 1.46 [0.85, 1.36]	Odds Ratio
Study or Subgroup Etit 2.1.1 CPAP Duran, 2021 Ferraindez, 2021 Ferrainedez, 2020 Gaudon, 2021 Gaudon, 2021 Ghani, 2021 Gough, 2021 Nadeem, 2021 Persins, 2021 Sykes, 2021 Subtotal (69% G) Total events Heterogeneity: Tau ² = 0.21 Test for overall effect; Z = 2.1.2 BiPAP costa, 2022 Dura, 2021 Ferraindez, 2021 France, 2020 Griece, 2021 Nadeem, 2021 Nader, 2021 Rainei, 2021 Shoukri, 2021 Rainei, 2021 Subtotal (69% G) Total events Heterogeneity: Tau ² = 0.07 Total events	HFNC NIN Numents Total Events 1 23 0 69 431 20 28 163 100 8 42 1 12 35 54 16 32 49 35 44 36 178 415 63 200 363 (14 35 (17 60 (12) (17) (13) (12) (17) (13) (12) (17) (13) (12) (17) (13) (12) (14) (13) (12) (14) (13) (12) (14) (13) (12) (14) (13) (12) (14) (15) (15) (15) (15) (15) (15) (15) (16) (16) (16) (10) (16) (16)	$\begin{array}{c} \hline Total Weight h \\ 4 & 0.6\% \\ 58 & 7.9\% \\ 330 & 9.2\% \\ 330 & 9.2\% \\ 330 & 9.2\% \\ 330 & 9.2\% \\ 95 & 6.0\% \\ 85 & 5.9\% \\ 53 & 5.1\% \\ 311 & 4.6\% \\ 92 & 6.9\% \\ 1143 & 58.1\% \\ 1143 & 58.1\% \\ 105 & 8.9\% \\ 105 & 8.$	Odds Ralio LH. Random. 95% CL 0.66 (10.2.7,22) 0.36 (0.10.2.7,22) 0.44 (0.27,07) 3.76 (0.43,027) 1.376 (0.43,027) 1.34 (0.72,467) 1.48 (0.72,467) 1.48 (0.72,467) 1.48 (0.54,402) 1.16 (0.80,167) 0.68 (0.43,175) 0.77 (0.51,1.17) 0.68 (0.43,175) 0.77 (0.51,1.17) 0.55 (0.33,016) 0.55 (0.33,016) 0.36 (0.22,6.53) 0.48 (0.22,1.05) 0.48 (0.24,1.163) 0.66 (0.44,0.79)	Odds Raiio M-H. Random, 95% Cl		Study or Subgroup E 2.11.0PAP Alnarthy 2020 Dun.2021 Franco.2020 Franco.2020 Gaulton.2021 Gaulton.2021 Ghani.2021 Ghani.2021 Bearson.2021 Perkins.2021 Subtotal (95% CI) Total events Heterogeneity: Tau* = 0.2 Pearson.2021 Fernández.2021 Fernández.2021 Fernández.2021 Fernández.2021 Shubich.2021 Nair.2021 Shubich.2021 Shubich.2021 Shubich.2021<	$\begin{array}{c} \text{HFNC} \\ \text{Events Tots} \\ 2 & 1: \\ 4 & 2: \\ 2299 & 43 \\ 47 & 16 \\ 22 & 4; \\ 6 & 33 \\ 14 & 3; \\ 15 & 3 \\ 15 & 3 \\ 15 & 3 \\ 170 & 41 \\ 1188 \\ 24; Chi^2 = 2, \\ 4 & 2; \\ 259 & 43 \\ 47 & 16 \\ 28 & 5 \\ 15 & 2 \\ 259 & 43 \\ 47 & 16 \\ 28 & 5 \\ 15 & 2 \\ 259 & 43 \\ 47 & 16 \\ 28 & 5 \\ 15 & 2 \\ 259 & 43 \\ 47 & 16 \\ 28 & 5 \\ 112 & 18 \\ 4 & 2 \\ 259 & 43 \\ 47 & 16 \\ 28 & 5 \\ 112 & 18 \\ 4 & 9 \\ 99 \\ 90 \\ 70 \\ 70 \\ Chi^2 = 12 \\ 0.94 \\ (P = 0 \\ 0 \\ 70 \\ 10 \\ (P = 0 \\ 0 \\ 0 \\ (P = 0 \\ 0 \\ 0 \\ (P = 0 \\ (P = 0 \\ 0 \\ (P = 0 \\ 0 \\ (P = 0 \\$	NIVU 1 Events 5 3 3 1 1 43 3 62 2 3 5 44 1 26 5 24 1 26 6 359 8 3 1 1 62 2 3 8 3 1 1 62 2 3 8 3 1 1 62 2 5 25 5 2 5 25 5 25 25 5 25 25 5 25 25 5 25 25 7 3 4 4 37 7 3 4 269 6 226, df = 8 5 26 7 3 7 3 7 3 7 3 7 3 7 3 7 3 7 3	/ Total V 15 4 58 330 17 17 95 337 1012 (P = 0.002 (P = 0.002 14 9 9 9 105 61 131 26 632 (P = 0.14) (P = 0.012) (P = 0.012)	Aright M. 1.5% 1.0% 7.6% 9.9% 2.8% 4.7% 5.7% 4.5% 4.5% 9.7% 9.1% 9.7% 9.7% 9.3% 9.7% 9.3% 9.7% 9.5% 2.2% 5.9% 5.9% 2.2% 50.9% ; P = 35%	Odds Ratio H. Random. <u>95% CI</u> 0.62 (0.06, 4.34) 0.63 (0.05, 778) 1.32 (0.06, 778) 1.32 (0.08, 0.87) 1.32 (0.08, 0.87) 0.24 (0.09, 0.63) 0.24 (0.09, 0.63) 0.24 (0.09, 0.63) 0.25 (0.28, 2.10) 0.26 (0.16, 17.52) 1.06 [0.64, 1.752] 1.04 (0.68, 1.61) 1.06 [0.64, 1.752] 1.04 (0.68, 1.61) 1.06 [0.64, 1.752] 1.04 (0.68, 1.61) 1.06 [0.64, 1.752] 1.06 [0.04, 1.286] 0.33 (0.20, 0.97) 1.16 [0.08, 1.56]	Odds Ratio
Study or Subgroup Ei 21.1 CFAP Duan.2021 Ferraindez.2021 Ferraindez.2020 Gaudro.2021 Gaudro.2021 Ghani.2021 Gaudro.2021 Subsci.2021 Sylexs.2021 Sylexs.2021 Sylexs.2021 Subsci.2021 Sylexs.2021 Subsci.2021 Subsci.2021 Test for overall effect: Z = 2.1.2 BIPAP costa.2022 Duan.2021 Fernindez.2021 Fernindez.2021 Nadeem.2021 Nadeem.2021 Nadeem.2021 Substotal (65% G) Total events Heterogeneity: Tau = 0.07 Heterogeneity: Tau = 0.07 Total events Heterogeneity: Tau = 0.07 Total events	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	$\begin{array}{c} \hline Total Waight h \\ 4 & 0.6\% \\ 58 & 7.9\% \\ 330 & 9.2\% \\ 17 & 1.4\% \\ 95 & 6.0\% \\ 53 & 5.1\% \\ 53 & 5.1\% \\ 53 & 5.1\% \\ 378 & 10.5\% \\ 92 & 6.9\% \\ 1143 & 58.1\% \\ 92 & 6.9\% \\ 1143 & 58.1\% \\ 105 & 8.9\% \\ 105 & 8.9\% \\ 105 & 8.9\% \\ 105 & 8.9\% \\ 105 & 8.9\% \\ 105 & 8.9\% \\ 105 & 8.9\% \\ 105 & 8.9\% \\ 105 & 8.9\% \\ 105 & 8.9\% \\ 105 & 8.9\% \\ 105 & 8.9\% \\ 105 & 8.9\% \\ 105 & 8.9\% \\ 105 & 8.1\%$	Odds Ratio LH. Random. 96% CI 0.40 (0.02, 97.22) 0.40 (0.27, 0.71) 0.40 (0.27, 0.71) 0.40 (0.18, 0.29) 0.73 (0.33, 1.86) 1.44 (0.14, 4.02) 1.46 (0.44, 4.02) 1.46 (0.45, 4.02) 1.66 (0.45, 0.73) 0.45 (0.23, 0.53) 0.45 (0.23, 0.53) 0.45 (0.24, 0.23) 0.45 (0.24, 0.23) 0.45 (0.24, 0.25) 0.45 (0.24, 1.03) 0.66 (0.44, 1.03) 0.66 (0.44, 0.07)	Odds Raiio M-H. Random, 95% CI		Study or Subgroup F 2.1.1 (PAP P 2.1.1 (PAP P Almarthy 2020 Dun.2021 Fernindez.2021 Franco.2020 Gaulton.2021 Gaulton.2021 Pearson.2021 Pearson.2021 Pearson.2021 Pearson.2021 Petriss.2021 Subtotal (95% CI) Colla events 2.1.2 Bir/AD Hotercogeneity: Tau? = 0.2 2.1.2 Bir/AD Pearson.2021 Fernindez.2021 Fernindez.2021 Fernindez.2021 Marga.2021 Nair 2021 Subtotal (95% CI) Total events Hetercogeneity: Tau? = 0.0 Total events Marga.2021 Subtotal (95% CI) Total (95% CI) Total (95% CI)	HFRC Events Tots 2 11 2 4 2 259 43 47 16 22 4 4 259 43 14 33 15 41 15 31 15 41 170 41 180 539 19 24; Ch≓ = 23 47 16 22 259 43 47 16 22 59 43 47 16 29 500 07; Ch≓ = 12 0,94 (P = 0 0,94 (P =	NUTURE 5 3 3 1 1 43 3 1 1 43 3 2 2 3 3 2 2 40 1 17 4 126 5 3 5 44 4 126 6 3 5 44 126 6 3 5 44 126 6 3 5 44 126 7 3 4 4 151 4 51 4 52 4 69 9 7 3 4 52 4 69 9 7 3 4 52 4 69 9 7 3 3 6 8 3 5 4 4 126 5 5 7 7 3 7 3 7 3 7 5 7 5 7 7 3 7 5 7 7 3 7 5 7 7 3 7 7 5 7 7 7 7 3 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7	/ Total V 15 4 58 330 17 77 95 531 1012 (P = 0.002 (P = 0.14) 1644 1	Aright M- 1.5% 1.0% 7.6% 9.9% 2.8% 4.7% 5.7% 4.5% 11.5% 49.1% 2.8% 1.1% 9.7% 5.9% 5.9% 5.9% 5.9% 5.9% 5.9% 9.5% 2.8% 00.0%	Odds Ratio H. Random. <u>95% CI</u> 0.62 (0.06, 4.34) 0.53 (0.26, 0.98) 1.32 (0.80, 1.67) 1.33 (0.80, 1.67) 0.54 (0.28, 0.28) 0.74 (0.06, 0.54) 0.58 (0.38, 1.58) 0.77 (0.28, 2.10) 0.58 (0.38, 1.58) 0.77 (0.28, 2.10) 1.39 (1.04, 1.65) 0.90 (0.57, 1.40) 1.59 (1.04, 1.65) 1.04 (0.68, 161) 1.05 (0.66, 1.752) 1.04 (0.68, 161) 1.05 (0.66, 1.752) 1.04 (0.68, 161) 1.05 (0.65, 1.752) 1.04 (0.68, 151) 1.05 (0.55, 1.58) 1.46 (0.55, 1.58)	Odds Ratio
Study or Subgroup Etit 2.1.1 CPAP Duran, 2021 Fernández, 2021 Fernández, 2020 Gaudino. 2021 Gaudino. 2021 Ghani, 2021 Gough, 2021 Nadeem, 2021 Persina, 2021 Sylexe, 2021 Subject, 2021 Subject, 2021 Subject, 2021 Test for overall effect; Z = 2.1.2 Bi/AP Costa, 2022 Dura, 2021 Pernández, 2021 Franco. 2020 Dana, 2021 Faraco, 2020 Dana, 2021 Substotal (85% CI) Total events Heterogenenity, Tau* = 0.21 Substotal (85% CI) Total events Heterogenenity, Tau* = 0.21 Total events Heterogenenity, Tau* = 0.21 Total events	HFNC NIN NIN Events 1 23 0 09 431 20 28 163 100 8 42 1 12 35 54 16 32 49 35 44 36 178 415 63 270 38 56 126 55 1264 10 54 12 3 14 3 1 09 431 27 16 12 35 44 1 10 54 12 15 12 14 3 1 23 105 105 12 15 12 11 16 55 25 35 18 32 7 1 1005 1005 156 156 156 156 105 156	$\begin{array}{c} \hline Total Weight h \\ 4 & 0.6\% \\ 58 & 7.9\% \\ 300 & 92\% \\ 310 & 92\% \\ 310 & 92\% \\ 311 & 1.4\% \\ 85 & 5.9\% \\ 85 & 5.9\% \\ 53 & 5.1\% \\ 314 & 1.6\% \\ 92 & 6.9\% \\ 92 & 6.9\% \\ 1143 & 58.1\% \\ 1143 & 58.1\% \\ 105 & 8.9\% \\$	Odds Ratio LH. Random. 95% CL 0.60 (10.2, 17.22) 0.36 (0.10.2, 17.22) 0.44 (0.27, 0.71) 3.76 (0.43, 9.271) 3.76 (0.43, 9.271) 3.76 (0.43, 9.271) 1.44 (0.72, 4.671 1.48 (0.54, 4.02) 0.77 (0.54, 1.172) 0.77 (0.54, 1.172) 0.77 (0.54, 1.152) 0.35 (0.33, 0.26) 0.36 (0.22, 6.53) 0.36 (0.23, 2.200) 7.78 (0.53, 9.568) 0.36 (0.44, 1.163) 0.66 (0.44, 1.163) 0.66 (0.44, 1.163) 0.66 (0.44, 0.77)	Odds Raiio M-H. Bandom, 95% Cl		Study or Subgroup E 2.11.1CPAP Alnarthy.2020 Dun.2021 Franco.2020 Ferniandez.2021 Franco.2020 Gaulton.2021 Ghani.2021 Ghani.2021 Ghani.2021 Pearson.2021 Pearson.2021 Total events Heterogeneity: Tau* = 0.2 Total events Test for overall effect: z = 2.1.2 BiPAP costa.2022 Duna.2021 Fernandez.2021 Fernandez.2021 Grieco.2021 Marinel.2021 Shutotal.2021 Subtotal (6%5 CI) Subtotal effect: z = Total events Heterogeneity: Tau* = 0.2 Heterogeneity: Tau* = 0.2 Total events	HFNC Events Tots 2 1: 4 2 259 43 47 16 22 4 6 3 15 3 170 41 118 15 3 9 24; Chi ² = 25 9 44 2 259 43 47 2 16 2 2 4 2 259 43 47 2 16 2 2 4 2 259 43 47 2 16 2 2 5 9 16 2 2 5 9 15 2 2 5 15 2 15 5 5 15 2 15 5 5 15 2 2 15 5 5 12 2 15 5 5 15 2 2 15 5 5 5 112 18 4 3 3 99 500 07; Chi ² = 12 99 500 27 18 19 218 4 13 29 15 2 2 15 2 2 2 15 5 2 2 15 2 2 15 2 2 2 15 3 2 2 15 2 2 2 5 15 3 2 2 5 15 3 2 2 5 15 2 2 2 5 15 3 2 2 5 15 3 2 2 5 15 3 2 2 5 15 3 2 2 5 15 3 2 2 5 15 2 2 15 2 2 5 15 2 2 15 5 2 2 15 5 2 2 15 5 2 2 15 5 2 2 15 5 2 2 15 15 2 2 15 15 2 2 15 15 2 2 15 15 2 15 15 2 2 15 15 2 15 15 15 2 15 15 15 15 15 15 15 15 15 15 15 15 15 1	NUV 5 3 1 1 43 1 1 43 2 2 3 2 2 3 2 2 4 2 40 1 2 4 126 5 44 4 126 6 359 6 4 4 126 6 2 3 8 359 6 4 4 126 6 2 2 3 4 4 126 6 2 2 5 4 4 5 126 7 3 1 1 6 225 7 3 4 4 269 6 225 4 5 4 5 4 5 4 5 5 4 4 4 126 5 25 5 4 4 4 126 5 25 5 4 5 4 5 4 5 4 5 4 5 4 5 4 5 4 5 4 5	/ Total V 15 4 58 330 17 17 95 585 31 177 1012 (P = 0.002 14 9 105 117 105 117 105 117 105 61 131 128 632 (P = 0.022 (P = 0.024) 131 147 157 167 17 17 105 17 17 105 107 107 107 107 107 107 107 107	Arright M- 1.5% 1.0% 1.0% 1.0% 2.8% 4.7% 5.7% 4.5% 4.5% 2.8% 1.1% 9.7% 9.3% 5.9% 4.6% 5.9%	Odds Ratio H. Random. <u>95% CI</u> 0.62 [0.09, 4.34] 0.63 [0.05, 778] 1.23 [0.80, 167] 1.23 [0.80, 167] 1.23 [0.80, 167] 0.28 [0.39, 1.98] 0.77 [0.28, 2.10] 1.39 [1.04, 1.68] 0.77 [0.28, 2.10] 1.39 [1.04, 1.68] 0.77 [0.28, 2.10] 1.39 [0.41, 1.68] 0.79 [0.67, 1.40] 0.57 [1.26, 6.13] 1.66 [0.61, 712] 1.66 [0.61, 712] 1.66 [0.61, 712] 1.66 [0.61, 712] 1.66 [0.61, 712] 1.66 [0.62, 1.76] 0.33 [0.10, 0.55, 1.36] 1.68 [0.35, 1.36]	Odds Ratio
Study or Subgroup Ex 21.1 CPAP Dun.2021 Fernindrez.2021 Fernindrez.2021 Franco.2020 Gaudro.2021 Gaudro.2021 Ghani.2021 Ghani.2021 Gough.2021 Nadeom.2021 Persins.2021 Sylexe.2021 Subtotal (65% CI) Total events Hetrogonnity: Tau? = 0.22 Test for overall effect.2 = 2.1.2 BI/AP costs.2022 Dun.2021 Persinsc.2021 Franco.2020 Grieco.2021 Raineri.2021 Shoukra.2021 Raineri.2021 Shoukra.2021 Raineri.2021 Total effect.2 = Total effect.2 = Total events Hetrogonnity: Tau? = 0.01 Heterogeneity: Tau? = 0.01 Total events Heterogeneity: Tau? = 0.01 Total events Heterogeneity: Tau? = 0.01 Total events	HFNC NIN verants Total Events 1 23 0 69 431 20 28 163 100 8 42 1 12 35 54 112 35 54 35 44 56 12 35 54 78 415 63 200 333 (chi = 26, 6), cf = 9 3 14 3 69 431 27 28 163 54 10 54 12 3 14 3 69 431 27 10 54 12 10 54 12 11 1005 156 12 16 55 13 17 1 1005 156 156 10 54 16 11 1005 </td <td>Total Weight b 4 0.6% 58 7.9% 330 9.2% 17 1.4% 95 6.0% 93 5.1% 11 4.6% 92 6.9% 92 6.9% 92 6.9% 93 5.1% (CP = 0.002); I² = 65% 105 8.9% 107 8.7% 65 5.0% 3 1.1% 54 6.1% 131 8.5% 583 41.9% 29 0.39; I² = 5% 1726 100.0%</td> <td>0.445 Ratio LH. Random. 95% CI 0.36 (0.02, 17.22) 0.44 (0.27, 021) 0.44 (0.27, 021) 0.44 (0.27, 021) 0.44 (0.27, 021) 0.45 (0.24, 0.43, 0.27) 0.44 (0.14, 0.43) 0.45 (0.14, 0.43) 0.45 (0.14, 0.43) 0.45 (0.14, 0.43) 0.45 (0.14, 0.14) 0.45 (0.14, 0.</td> <td>Odds Raiio</td> <td></td> <td>Study or Subproup F 2.11 (PAP 2.11 (PAP Alnarthy 2020 Duan.2021 Franca.2020 Franca.2020 Gaulton.2021 Franca.2020 Ghani.2021 Ghani.2021 Pearson.2021 Pearson.2021 Perkins.2021 Subtotal (95% CI) Total events Pearson.2021 Perandez.2021 Franca.2020 Ordinez.2021 Franca.2020 Gride.2021 Subtotal (95% CI) Total events Heterogeneity. Tau² = 0 Heterogeneity. Tau² = 0 Total events Heterogeneity. Tau² = 0 Total events</td> <td>$\begin{array}{r} \mbox{HFNC} \\ \hline \mbox{Events} \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \$</td> <td>NUTURE 5 3 3 1 1 43 2 2 3 42 2 400 1 17 3 82 2 400 1 432 5 344 4 126 5 3 8 3 1 1 622 3 9 0 628 669 0 628 60 0 7 0 7 0 7 0 7 0 7 0 7 0 7 0</td> <td>/ Total V 15 4 58 330 17 1072 (P = 0.002 9 1072 (P = 0.002 9 1072 (P = 0.002 1072 (P = 0.002 1072 (P = 0.002 (P = 0.014) 1644 1 (P = 0.014) 1644 (P = 0.014) 1644 1644 17 17 17 17 17 17 17 17 17 17</td> <td>Keight M-: 1.5% 1.0% 1.0% 7.0% 9.9% 2.8% 2.8% 5.7% 9.9% 2.8% 1.15% 5.7% 9.7% 9.7% 9.7% 9.7% 9.7% 9.5% 5.9% 5.9% 5.9% 5.9% 5.9% 5.9% 5.9% 5.9% 5.9% 5.9% 5.9% 5.9% 5.9% 5.9% 0.9% 2.2% 0.9% 5.9% 0.9% 5.9%</td> <td>Odds Ratio H. Random. <u>95% CI</u> 0.52 [0.09, 4.34] 0.53 [0.28, 0.99] 1.23 [0.80, 1.87] 0.54 [0.28, 0.99] 1.23 [0.80, 1.87] 0.24 [0.09, 0.63] 0.24 [0.09, 0.63] 0.24 [0.09, 0.63] 1.39 [1.04, 1.85] 0.90 [0.57, 1.40] 1.71 [0.43, 6.83] 1.39 [1.04, 1.85] 1.90 [0.41, 2.86] 0.90 [0.57, 1.40] 1.06 [0.61, 172] 1.04 [0.68, 1.61] 1.06 [0.61, 172] 1.04 [0.68, 1.61] 1.06 [0.61, 122] 1.06 [0.61, 2.20] 0.33 [0.20, 0.97] 1.40 [0.88, 2.20] 0.33 [0.19, 4.55] 1.16 [0.45, 1.58]</td> <td>Odds Ratio</td>	Total Weight b 4 0.6% 58 7.9% 330 9.2% 17 1.4% 95 6.0% 93 5.1% 11 4.6% 92 6.9% 92 6.9% 92 6.9% 93 5.1% (CP = 0.002); I ² = 65% 105 8.9% 107 8.7% 65 5.0% 3 1.1% 54 6.1% 131 8.5% 583 41.9% 29 0.39; I ² = 5% 1726 100.0%	0.445 Ratio LH. Random. 95% CI 0.36 (0.02, 17.22) 0.44 (0.27, 021) 0.44 (0.27, 021) 0.44 (0.27, 021) 0.44 (0.27, 021) 0.45 (0.24, 0.43, 0.27) 0.44 (0.14, 0.43) 0.45 (0.14, 0.43) 0.45 (0.14, 0.43) 0.45 (0.14, 0.43) 0.45 (0.14, 0.14) 0.45 (0.14, 0.	Odds Raiio		Study or Subproup F 2.11 (PAP 2.11 (PAP Alnarthy 2020 Duan.2021 Franca.2020 Franca.2020 Gaulton.2021 Franca.2020 Ghani.2021 Ghani.2021 Pearson.2021 Pearson.2021 Perkins.2021 Subtotal (95% CI) Total events Pearson.2021 Perandez.2021 Franca.2020 Ordinez.2021 Franca.2020 Gride.2021 Subtotal (95% CI) Total events Heterogeneity. Tau ² = 0 Heterogeneity. Tau ² = 0 Total events	$\begin{array}{r} \mbox{HFNC} \\ \hline \mbox{Events} \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \$	NUTURE 5 3 3 1 1 43 2 2 3 42 2 400 1 17 3 82 2 400 1 432 5 344 4 126 5 3 8 3 1 1 622 3 9 0 628 669 0 628 60 0 7 0 7 0 7 0 7 0 7 0 7 0 7 0	/ Total V 15 4 58 330 17 1072 (P = 0.002 9 1072 (P = 0.002 9 1072 (P = 0.002 1072 (P = 0.002 1072 (P = 0.002 (P = 0.014) 1644 1 (P = 0.014) 1644 (P = 0.014) 1644 1644 17 17 17 17 17 17 17 17 17 17	Keight M-: 1.5% 1.0% 1.0% 7.0% 9.9% 2.8% 2.8% 5.7% 9.9% 2.8% 1.15% 5.7% 9.7% 9.7% 9.7% 9.7% 9.7% 9.5% 5.9% 5.9% 5.9% 5.9% 5.9% 5.9% 5.9% 5.9% 5.9% 5.9% 5.9% 5.9% 5.9% 5.9% 0.9% 2.2% 0.9% 5.9% 0.9% 5.9%	Odds Ratio H. Random. <u>95% CI</u> 0.52 [0.09, 4.34] 0.53 [0.28, 0.99] 1.23 [0.80, 1.87] 0.54 [0.28, 0.99] 1.23 [0.80, 1.87] 0.24 [0.09, 0.63] 0.24 [0.09, 0.63] 0.24 [0.09, 0.63] 1.39 [1.04, 1.85] 0.90 [0.57, 1.40] 1.71 [0.43, 6.83] 1.39 [1.04, 1.85] 1.90 [0.41, 2.86] 0.90 [0.57, 1.40] 1.06 [0.61, 172] 1.04 [0.68, 1.61] 1.06 [0.61, 172] 1.04 [0.68, 1.61] 1.06 [0.61, 122] 1.06 [0.61, 2.20] 0.33 [0.20, 0.97] 1.40 [0.88, 2.20] 0.33 [0.19, 4.55] 1.16 [0.45, 1.58]	Odds Ratio
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BiPAP, bi-level positive airway pressure; CPAP, continuous positive airway pressure; HFNC, high-flow nasal cannula; NIV, noninvasive ventilation.

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Figure 6. The secondary outcomes for included studies: (a) PaO₂/FiO₂, (b) ICU length of stay, (c) hospital length of stay, and (d) days free from invasive mechanical ventilation.

HFNC, high-flow nasal cannula; NIV, noninvasive ventilation.

mortality were observed between the NIV-helmet group and the NIV-CPAP group compared with HFNC group. There were also no significant differences in the intubation rate, PaO₂/FiO₂, ICU LOS, hospital LOS, and VFD between the HFNC and NIV groups.

Noninvasive respiratory support, including the use of HFNC and NIV, has increasingly been used in the management of COVID-19-associated acute respiratory failure.5,6 A literature review found that HFNC can reduce the need for intubation in patients with COVID-19 and can decrease the LOS in the ICU as well as complications related to mechanical ventilation.33 A populationbased study involving 1400 patients found a similar 60-day mortality risk for patients undergoing immediate invasive mechanical ventilation (IMV) and those intubated after an NIV trial,³⁴ suggesting that NIV can be safely used in patients with COVID-19 AHRF. However, questions remain about the utility, safety, and outcome benefit of noninvasive respiratory strategies, as there was little high-quality evidence. In patients who do not have COVID-19, the European Respiratory Society recommends HFNC therapy to patients with hypoxic respiratory failure over conventional nasal cannula therapy and NIV.35 Since then, many studies have compared HFNC and NIV and have produced conflicting findings in patients with COVID-19^{13,18,20} for these patients, there is not enough evidence to prove which approach is better.

In our meta-analysis, we found that there were no differences in intubation rate, PaO_2/FiO_2 , ICU

LOS, hospital LOS, or VFD between the NIV and HFNC group, but mortality was significantly higher among COVID-19 patients in the NIV group, consistent with three recent meta-analyses.^{36–38} Whether this was because of the delayed intubation and increased mortality in the NIV group is still unclear. In general, the role of NIV is indeed controversial. The success of NIV, however, depends on several factors, such as, for example, the underlying causes of AHRF, patient cooperation, staff experience, interface, mode, and so forth.⁸ Our meta-analysis included more studies than recent meta-analyses; more importantly, we performed subgroup analyses to evaluate the factors affecting the efficiency of NIV.

NIV ventilates by applying positive pressure to the lungs through a mask or a helmet. In the pre-COVID-19 era, a meta-analysis demonstrated that helmet NIV may reduce mortality and the need for intubation relative to conventional oxygen therapy in patients with purely AHRF.39 Nonetheless, all included trials and observational studies were small, and helmet NIV was not compared with HFNC. In one other recent metaanalysis of adult patients with AHRF of all types, it was found that relative to facemask NIV, helmet NIV may reduce mortality and intubation; however, the effects of helmet NIV compared with HFNC remain uncertain.⁴⁰ The use of helmet NIV has steadily increased throughout the COVID-19 pandemic,¹⁰ Our meta-analysis found that there were no differences in mortality rate between helmet NIV and HFNC, while face mask NIV had a higher mortality than HFNC. Previous study found that helmet NIV may be more comfortable and allow the application of a more 'protective' ventilation with higher PEEP (i.e. $8-12 \text{ cmH}_2\text{O}$) and lower pressure support values with fewer air leaks and interruptions.^{39,41} However, only two small sample size RCTs^{20,26} and one observational study¹⁷ comparing helmet NIV and HFNC were included in the analysis, and there was no study to comparing the differences of mode and ventilator parameters between helmet NIV and face mask NIV. High-quality RCTs in COVID-19 patients comparing helmet NIV with both face mask NIV and HFNC are needed, including patient-important outcomes and attention to possible adverse events.

NIV can deliver airflow through the CPAP and BiPAP modes. Largely because of an early negative report,42 CPAP remains largely undocumented in ARDS. Recently, one multicenter adaptive RCT compared the use of CPAP, HFNC, and standard oxygen therapy. The results showed that treating hospitalized COVID-19 patients who had AHRF with continuous CPAP reduced the need for IMV.26 Our meta-analysis found that there were no differences in mortality between CPAP and HFNC, while BiPAP had a higher mortality than HFNC. This may be for two reasons. On the one hand, patients' conditions may have been relatively mild in the CPAP group; for these patients, medical personnel often choose the CPAP mode first as the majority of patients with COVID-19 who are offered continuous CPAP therapy (83-97%) can tolerate the treatment.43,44 On the other hand, the risks of BiPAP include delayed intubation, large tidal volumes, and injurious transpulmonary pressures;⁶ many guidelines describe BiPAP as the first-line treatment for AHRF caused by acute exacerbations of chronic obstructive pulmonary disease or acute cardiogenic pulmonary edema.45 RCTs with large samples to compare CPAP with BiPAP or HFNC based on patient populations in COVID-19 patients are still lacking.

Therefore, routinely offering HFNC as the main form of noninvasive respiratory support for patients with respiratory failure due to COVID-19 may not be recommendable.⁴⁶ We need to fully consider the underlying cause of AHRF, the severity and cooperation of patients, and the advantages of each noninvasive oxygen strategy. For patients with COVID-19-associated AHRF, the way forward may be a stepwise treatment approach that is based on patient status/commodities, includes several consecutive ventilation strategies,⁴⁷ uses multiple oxygen strategies based on patients' lifestyle and oxygenation status, and uses objective criteria when observing patients.

The present study had several limitations. First, our results were based mostly on cohort and case-control studies, and the quality of the evidence in these studies was low. The lack of RCTs may have reduced overall accuracy and increased heterogeneity. Some variables are likely skewed and would best be reported as medians with interquartile ranges and compared using a non-parametric statistical test, but this may be related to the original data provided by the included study. Second, few studies have been conducted on the use of a helmet in COVID-19 patients, and high-quality RCTs comparing helmet NIV to both face mask NIV and HFNC are needed. Third, population-based studies of evaluation of CPAP and BiPAP are lacking, such as BiPAP for COVID-19associated AHRF patients with COPD and cardiogenic pulmonary edema, or CPAP for COVID-19 patients with purely AHRF. For this reason, we could not conduct subgroup analysis based on the patient population.

Conclusion

In this meta-analysis, we found although mortality was lower with HFNC than NIV, there was no difference in mortality between HFNC and NIV on a subgroup of helmet or CPAP group. The lack of RCTs may have reduced overall accuracy and increased heterogeneity. Future large sample RCTs are necessary to prove our findings.

Declarations

Ethics approval and consent to participate Not applicable.

Consent for publication

Not applicable.

Author contributions

Yun Peng: Formal analysis; Methodology; Resources; Writing – original draft; Writing – review & editing.

Bing Dai: Formal analysis; Resources; Writing – original draft; Writing – review & editing.

Hong-wen Zhao: Formal analysis; Resources; Writing – original draft; Writing – review & editing.

Wei Wang: Formal analysis; Resources; Writing – original draft; Writing – review & editing.

Jian Kang: Formal analysis; Resources; Writing – original draft; Writing – review & editing.

Hai-jia Hou: Formal analysis; Resources; Supervision; Writing – original draft; Writing – review & editing.

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Competing interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Availability of data and materials Not applicable.

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