臺北榮總胸腔部
呼吸感染免疫科

High flow nasal cannula vs NIV Current evidence in ICU

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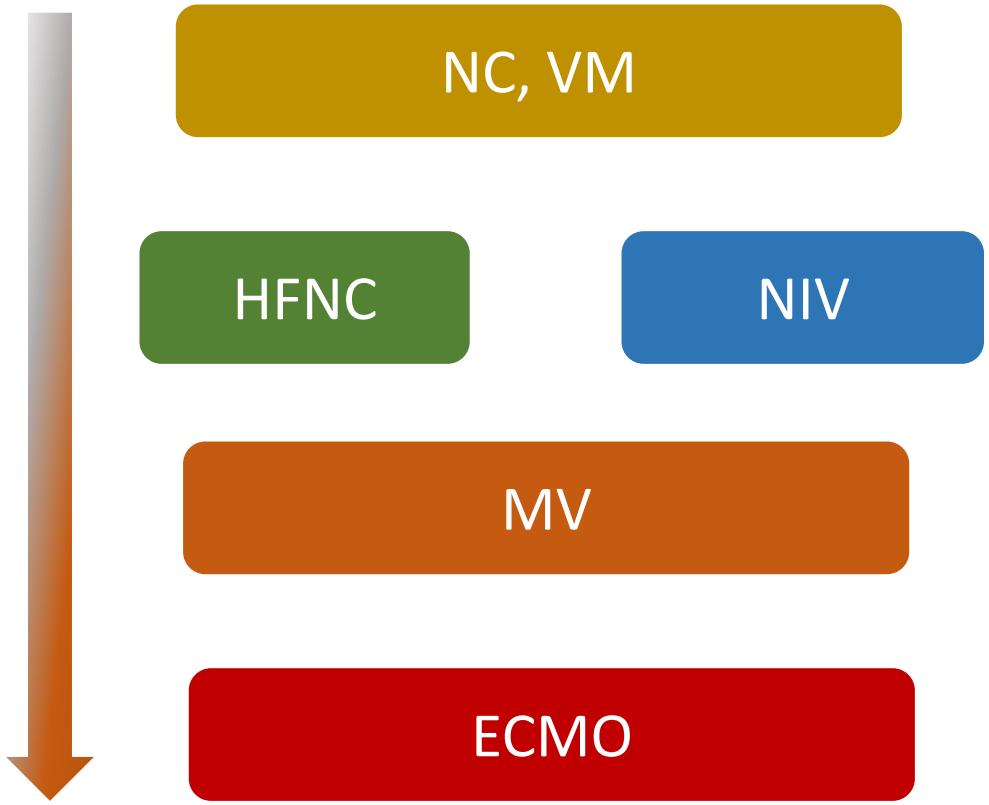
A typical scenario of oxygen therapy

- **A case of pneumonia with desaturation**
- **Marked respiratory distress require non-invasive ventilator support**
- **Respiratory failure requires intubation and mechanical ventilator support**
- **Disease recovery with weaning and extubation**
- **Refractory desaturation that need VV-ECMO**



高流量鼻導管健保給付規定(2021/12生效)

適應症

1.**急性缺氧性呼吸衰竭**（符合下列3項）:

(1) 當以 10L/min 或更高的流速供應氧氣至少 15 分鐘,P/F ratio≦300 時

(2) RR>25/min,呼吸困難或呼吸窘迫

(3) **PaCO2 ≤ 45 mmHg**

2.呼吸衰竭**拔管後,預防再次插管**使用。

(1)插管大於 24 小時的病人,且有高危險因子*

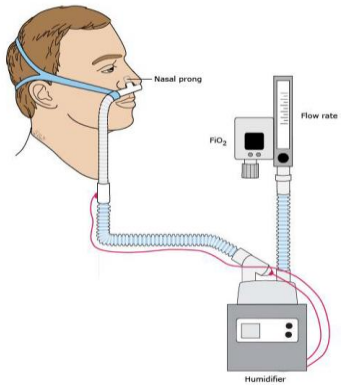
(*註:年紀大於 65 歲、APACHE II>12、BMI>30、呼吸道清除功能失效、困難脫離呼吸器病人、插管大於 7 天病人)

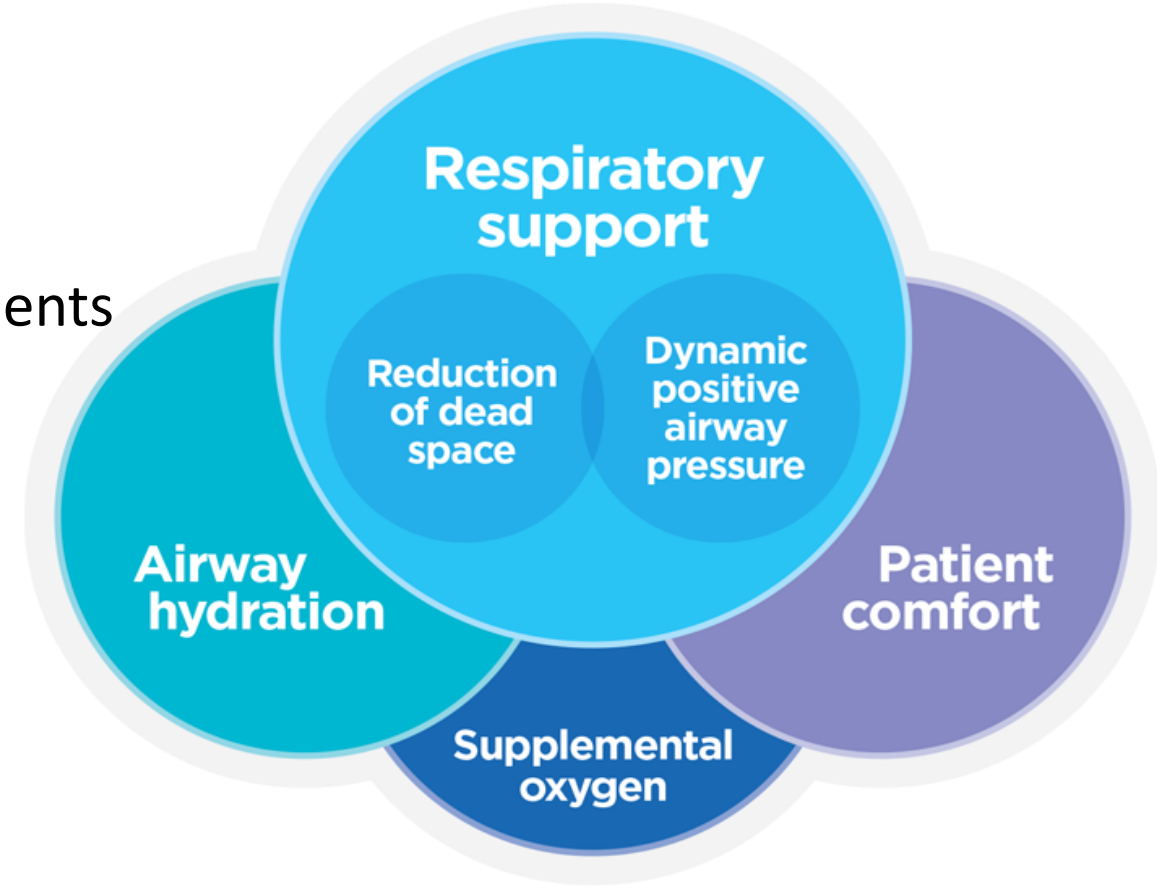
(2)經臨床負責醫師判定有再度呼吸衰竭可能

(3)**若臨床上認為拔管後應使用非侵襲性陽壓呼吸治療的病人,則不建議使用本項**

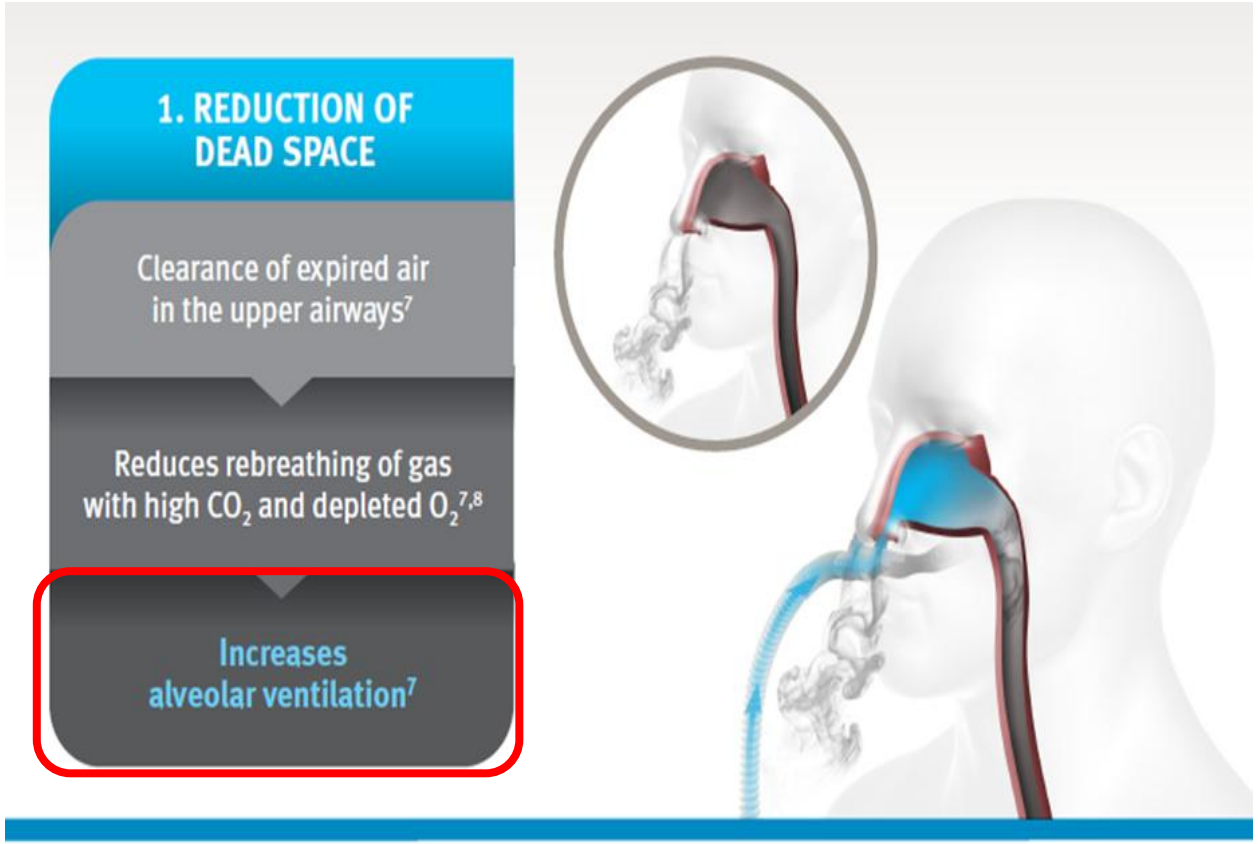
High Flow Nasal Oxygen Therapy

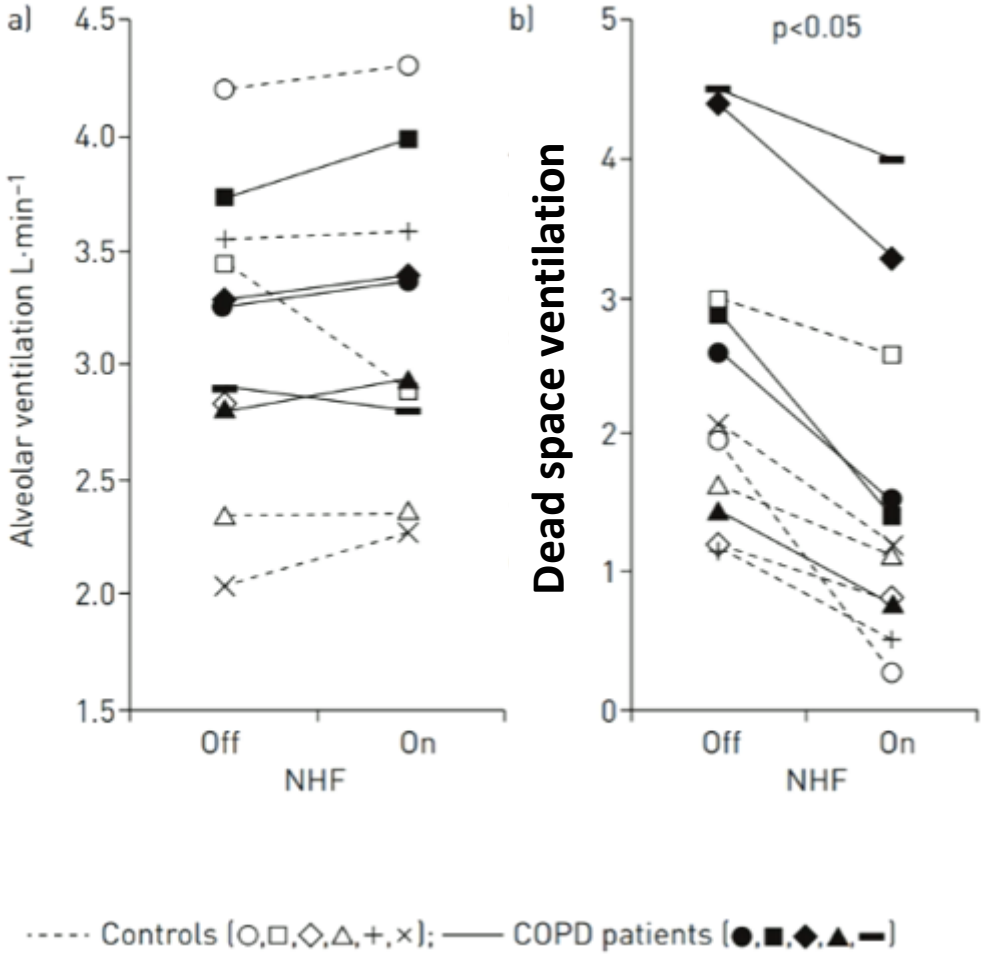
- "High-flow" "Oxygen" through "Nasal cannula"
  - High flow oxygen therapy: **HFOT**
  - High flow rate: ≥ inspiratory flow of the patients
  - Constant high FiO2 supply (up to 100%)
  - Better tolerance through nasal prone





Nasopharynx Dead Space Washout





30% of regular ventilation
(anatomical dead space)

Moller W, et al. J Appl Physiol 2015

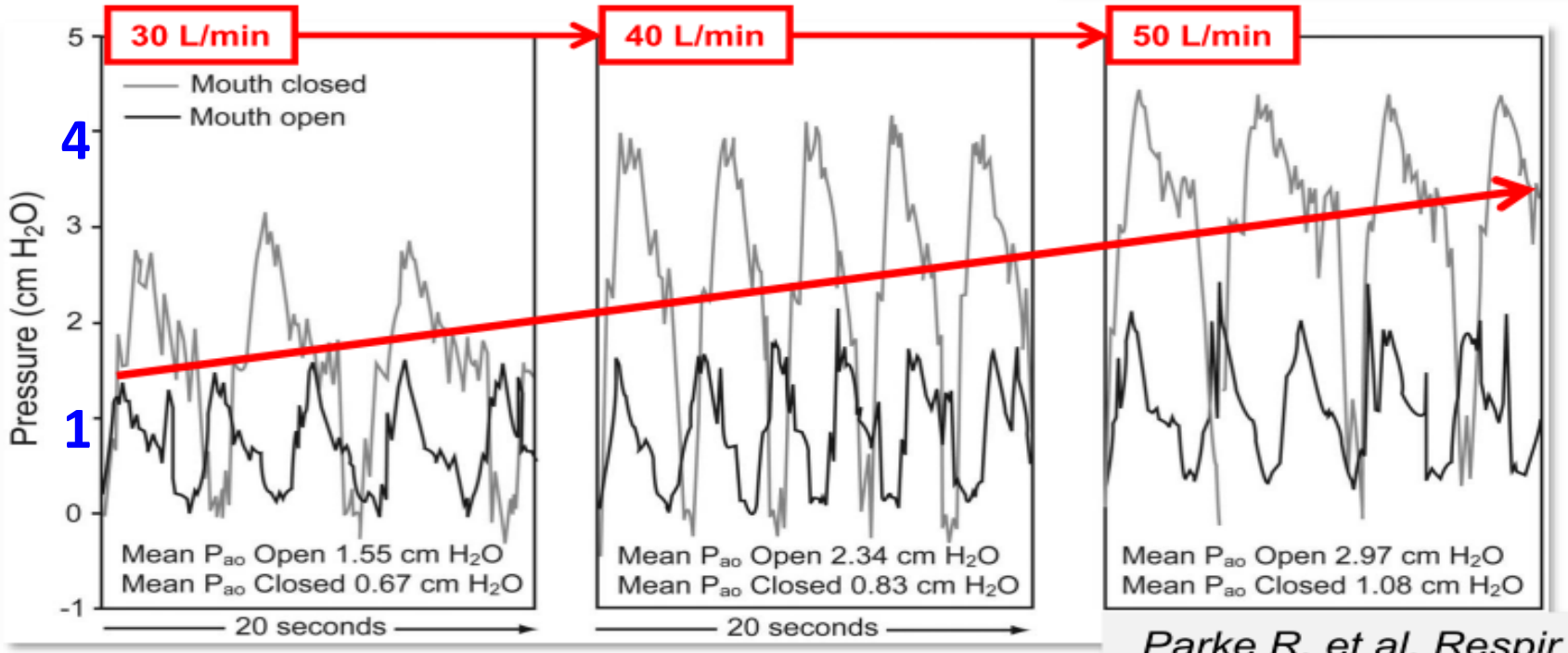
Small CPAP effect

Nasopharyngeal pressure (cmH_2O) [Flow 35 L/min]

	NHF Mouth Closed	NHF Mouth Open	FM Mouth Closed	FM Mouth Open
M	**2.7**	**1.2**	**0.2**	**0.1**
	±	±	±	±
SD	1.0	0.8	0.6	0.4

Flow dependent
Mouth closed important

Parke R, et al. Br J Anaest 2009;103:886-890



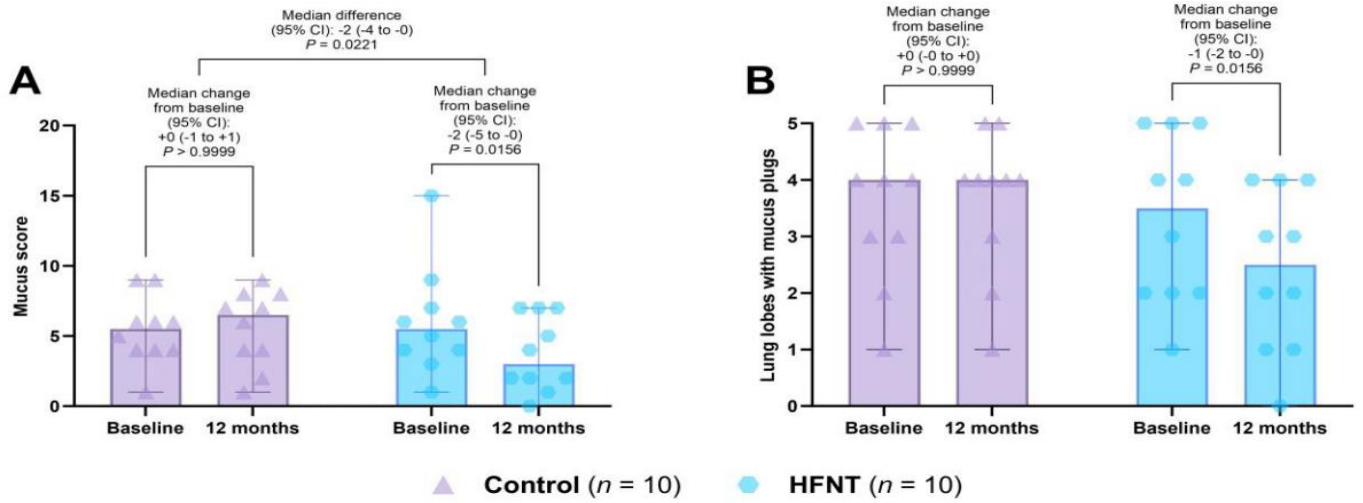
0.5-1 cmH2O per 10L/min

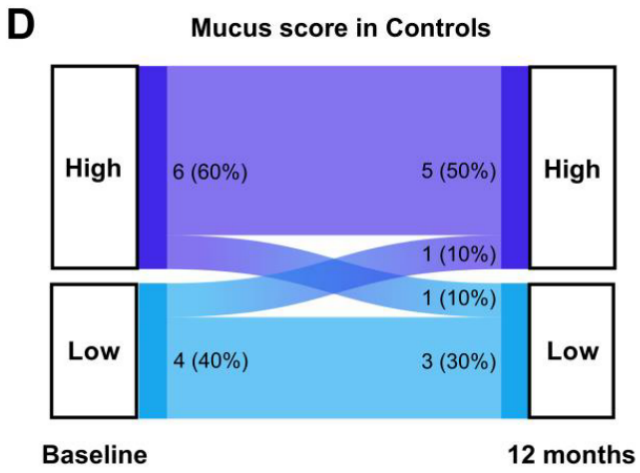
Loss of CPAP when mouth open

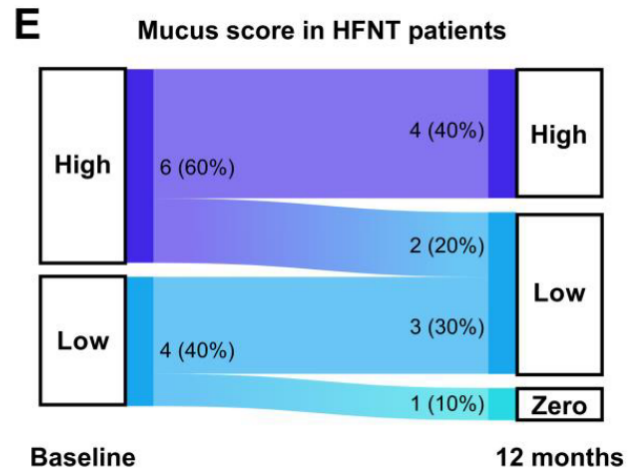
Parke R, et al. Respir Care 2011;56:1151-5

Airway Humidity Matters

	TEMPERATURE	ABSOLUTE HUMIDITY**
MEDICAL GAS	15 °C	0.3 mg/L
ROOM	22 °C	7 mg/L
COLD BUBBLER	Ambient	16 mg/L [1]
PASSIVE HUMIDIFIER (HME)	25–30 °C	17–32 mg/L [2]
HEATED HUMIDIFIER	37 °C	44 mg/L







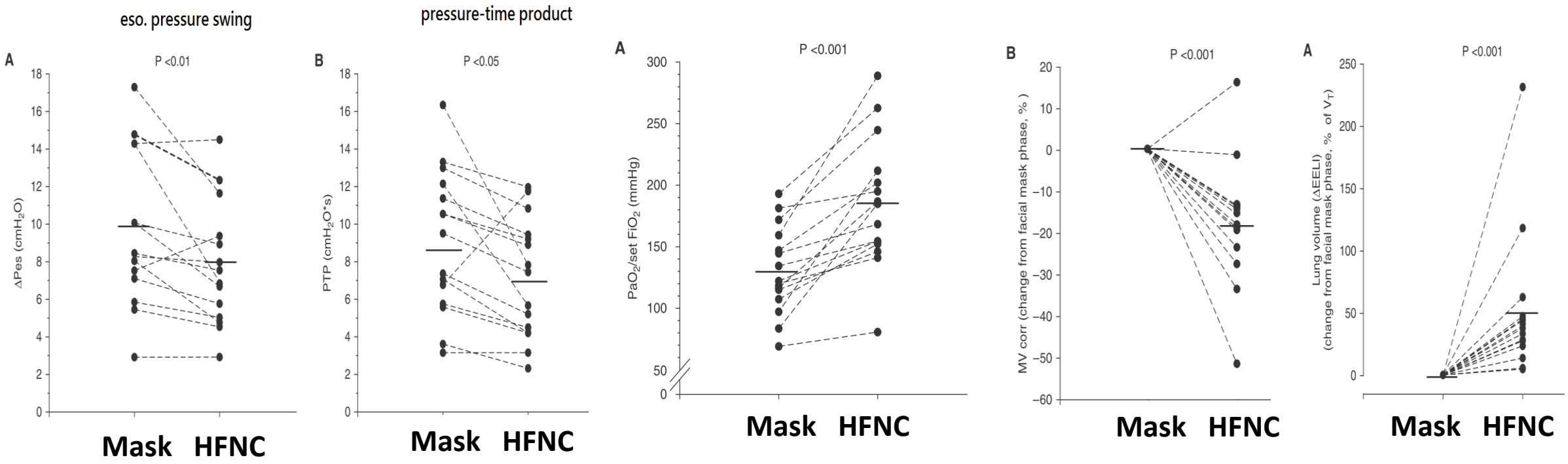
Crimi C, et al. ERJ Open Res 2024

Physiologic Effects of High-Flow Nasal Cannula in Acute Hypoxemic Respiratory Failure

15 patients with AHRF (PF ratio <300) in Italy

HFNC 40L/min vs. facial mask in the **same FiO2**

Inspiratory Effort | **Oxygenation** | **Min. ventilation** | **Lung volume**



Mauri T, et al. AJRCCM 2017

A summary of physiology

↓ Dead space ventilation preventing CO_2 rebreathing

Positive airway pressure (PEEP effect) > ↑ EELV and recruitment of alveoli

Resistance to expiratory flow > prolonged breathing cycles, ↓ RR

FLOW

↓ V_E

↓ WOB

(↓ CO2 production)

Improvement gas exchange

Oxygen delivery stable and optimal

Humidification

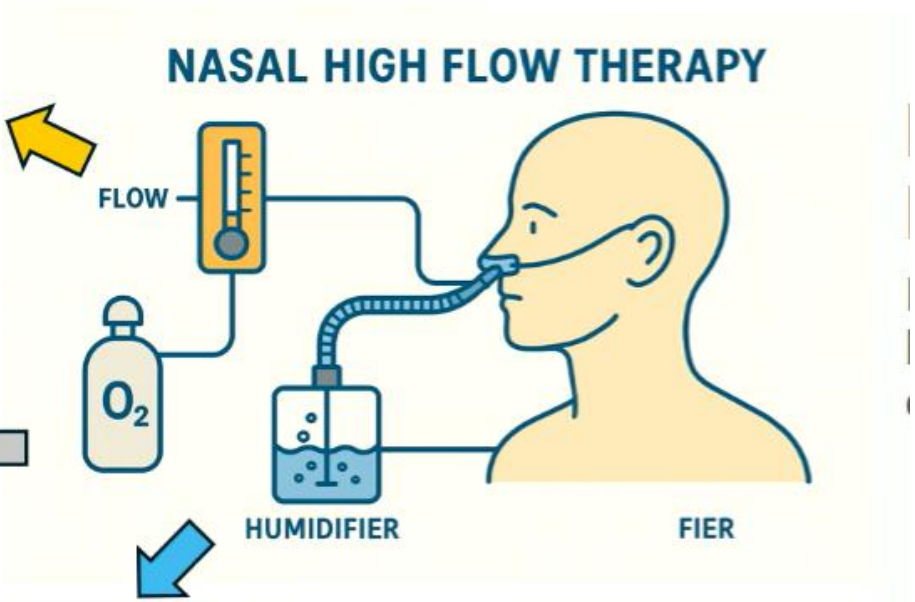


Figure produced with use of AI

HFNC

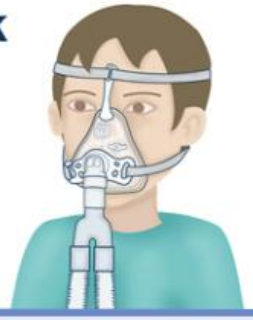
Physiological effects

- Accurate delivery of set FiO_2
- PEEP-effect proportional to flow
- Washout of airway dead space
- Reduction in inspiratory effort
- Enhanced comfort and tolerance

Indications

- De novo acute hypoxemic respiratory failure
- Post-extubation
- Mild hypercapnic respiratory failure?

Face Mask NIV



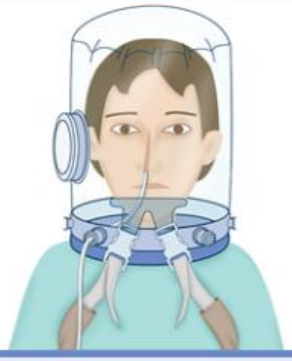
Physiological effects

- Accurate delivery of set FiO_2
- Alveolar recruitment (CPAP and NIV)
- Respiratory muscle unloading (NIV)
- Reduced left ventricular afterload (CPAP and NIV)

Indications

- Hypercapnic respiratory failure (NIV) and acute cardiogenic pulmonary edema (CPAP and NIV)
- Post extubation in hypercapnic and obese patients
- De novo acute hypoxemic respiratory failure?

Helmet NIV



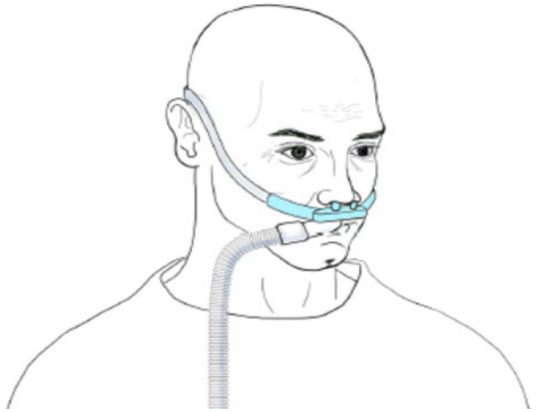
Physiological effects

- Accurate delivery of set FiO_2
- Alveolar recruitment (CPAP and NIV)
- Possible high PEEP in hypoxemic patients
- Reduced respiratory muscle workload (NIV)
- Reduced left ventricular afterload (CPAP and NIV)

Indications

- Acute cardiogenic pulmonary edema (CPAP and NIV)
- De novo acute hypoxemic respiratory failure
- Uncertain for hypercapnic patients (CO_2 rebreathing)

Rittayamai N, et al. ICM 2022

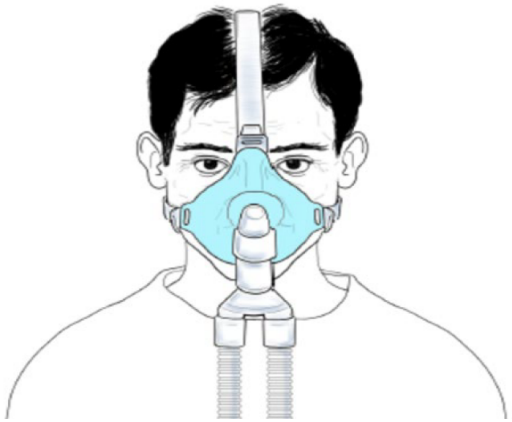


Benefits

- Matches inspiratory flow
- Delivers set F_iO_2
- Delivers fully conditioned gas
- Enhances comfort
- Provides positive airway pressure (up to 4 cmH_2O)
- Washout of nasopharyngeal dead space
- Reduces inspiratory effort

Pitfalls

- Small amount of PEEP delivered

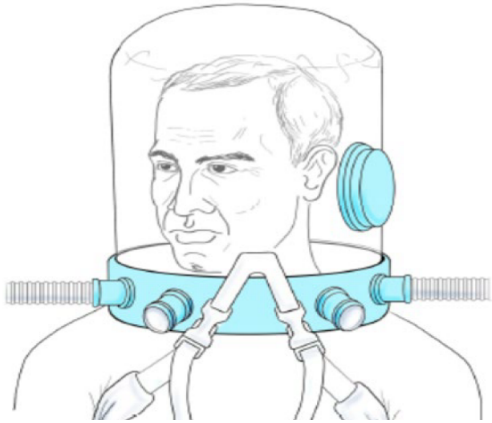


Benefits

- Delivers set FiO_2
- Delivers fully conditioned gas
- Provides PEEP to allow alveolar recruitment
- Provides PS (only for PSV) to unload inspiratory muscles
- Allows to monitor tidal volume (only PSV)

Pitfalls

- Skin ulcer
- Air leaks, difficult delivery of high PEEP
- Full inspiratory synchronization may increase P_L swings and tidal volume
- Poor tolerability: need for treatment interruptions



Benefits

- Delivers set FiO_2
- Provides high PEEP to allow alveolar recruitment and enhance ventilator homogeneity
- Continuous treatments with good tolerability
- Provides PS (only for PSV) to reduce inspiratory effort
- Asynchronous PS may prevent positive P_L swings

Pitfalls

- Impossibility to measure tidal volume
- Upper limbs edema, with possible vasal thrombosis

Grieco DL, et al. ICM 2021

Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure

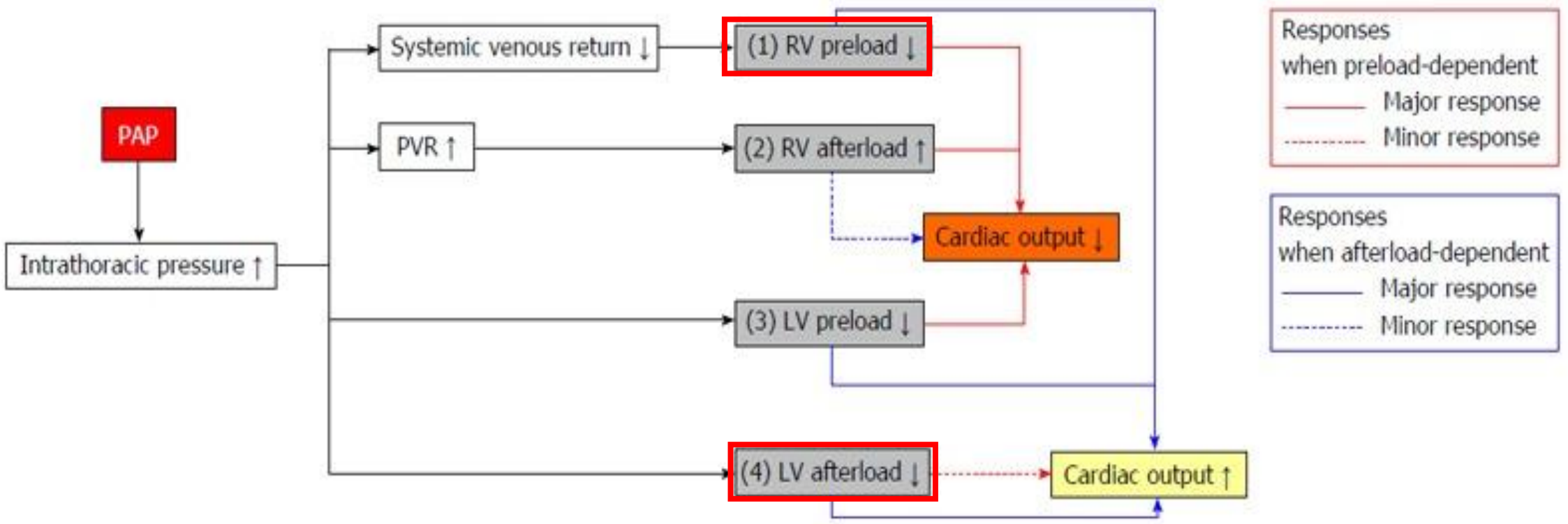
TABLE 2 Recommendations for actionable PICO questions

Clinical indication[#]	Certainty of evidence[¶]	Recommendation
Prevention of hypercapnia in COPD exacerbation	⊕⊕	Conditional recommendation against
Hypercapnia with COPD exacerbation	⊕⊕⊕⊕	Strong recommendation for
Cardiogenic pulmonary oedema	⊕⊕⊕	Strong recommendation for
Acute asthma exacerbation		No recommendation made
Immunocompromised	⊕⊕⊕	Conditional recommendation for
★ ***De novo* respiratory failure**		No recommendation made
Post-operative patients	⊕⊕⊕	Conditional recommendation for
Palliative care	⊕⊕⊕	Conditional recommendation for
Trauma	⊕⊕⊕	Conditional recommendation for
Pandemic viral illness		No recommendation made
Post-extubation in high-risk patients (prophylaxis)	⊕⊕	Conditional recommendation for
Post-extubation respiratory failure	⊕⊕	Conditional recommendation against
Weaning in hypercapnic patients	⊕⊕⊕	Conditional recommendation for

certainty of effect estimates: ⊕⊕⊕⊕, high; ⊕⊕⊕, moderate; ⊕⊕, low; ⊕, very low.

Rochwerg B, et al. ERJ 2017

Effects of Positive Airway Pressure on Hemodynamics



Kato et al. *World journal of cardiology 2014*

2021 ESC Heart Failure Guideline

ESC

- Blood pressure should be monitored regularly during non-invasive positive pressure ventilation.
- The increase in pulmonary vascular resistance and RV afterload may also be detrimental in RV dysfunction.

HFOT versus NIV: a randomised physiological crossover study of alveolar recruitment in acute respiratory failure

16 cases with de novo hypo resp failure

HFNC vs. NIV, **cross-over study**

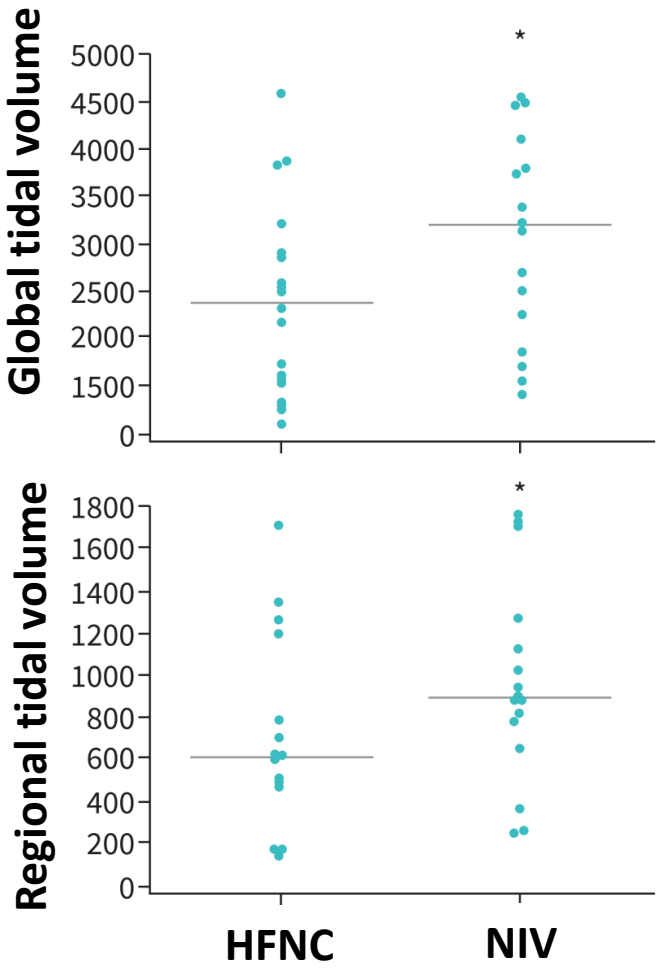


TABLE 2 Comparison between physiological effects of noninvasive ventilation (NIV) and high-flow nasal cannula (HFNC)

	NIV	HFNC	HFNC–NIV	
	Median (IQR)	Median (IQR)	Median (95% CI)	p-value[#]
V_T global (units)	3161 (1884–3805)	2323 (1497–2891)	−678.0 (−947.5– −322.0)	**0.001**
V_T ROI1 (units)	887 (657–1033)	590 (464–774)	−204.5 (−279.5– −122.0)	**0.0007**
V_T ROI2 (units)	686 (413–925)	445 (262–656)	−214.0 (−309.0– −130.0)	**0.0003**
V_T ROI3 (units)	743 (498–1008)	589 (271–909)	−118.5 (−221.5–0.0)	**0.04**
V_T ROI4 (units)	444 (318–861)	450 (286–664)	−93.5 (−200.0–7.5)	0.06
V_T consolidation (units)	778 (338–1002)	489 (198–783)	−133.0 (−215.0– −53.5)	**0.004**
Respiratory rate (breaths·min^{-1})	24 (22–27)	23 (21–26)	−2 (−4–4)	0.6
S_{pO_2}/F_{iO_2} ratio	167 (143–200)	163 (140–200)	−4.5 (−15.5– −2.0)	**0.001**
S_{pO_2} (%)	100 (98–100)	97 (96–100)	−2 (−3–0)	**0.010**
Heart rate (beats·min^{-1})	84 (68–98)	90 (78–104)	1 (−2–5)	0.8
SBP (mmHg)	119 (108–131)	125 (113–137)	3 (−1–11)	0.2
MAP (mmHg)	80 (76–89)	85 (77–94)	2 (−3–5)	0.6
Dyspnoea score (0–10)	5 (0–5)	5 (2–5)	0 (−1–1)	0.7
Patient comfort score (0–10)	4 (2–5)	5 (4–7)	0 (−1–4)	0.7

Artaud-Macari E, et al. ERJ Open 2021

Non-invasive ventilatory support and high-flow nasal oxygen as first-line treatment of acute hypoxemic respiratory failure and ARDS

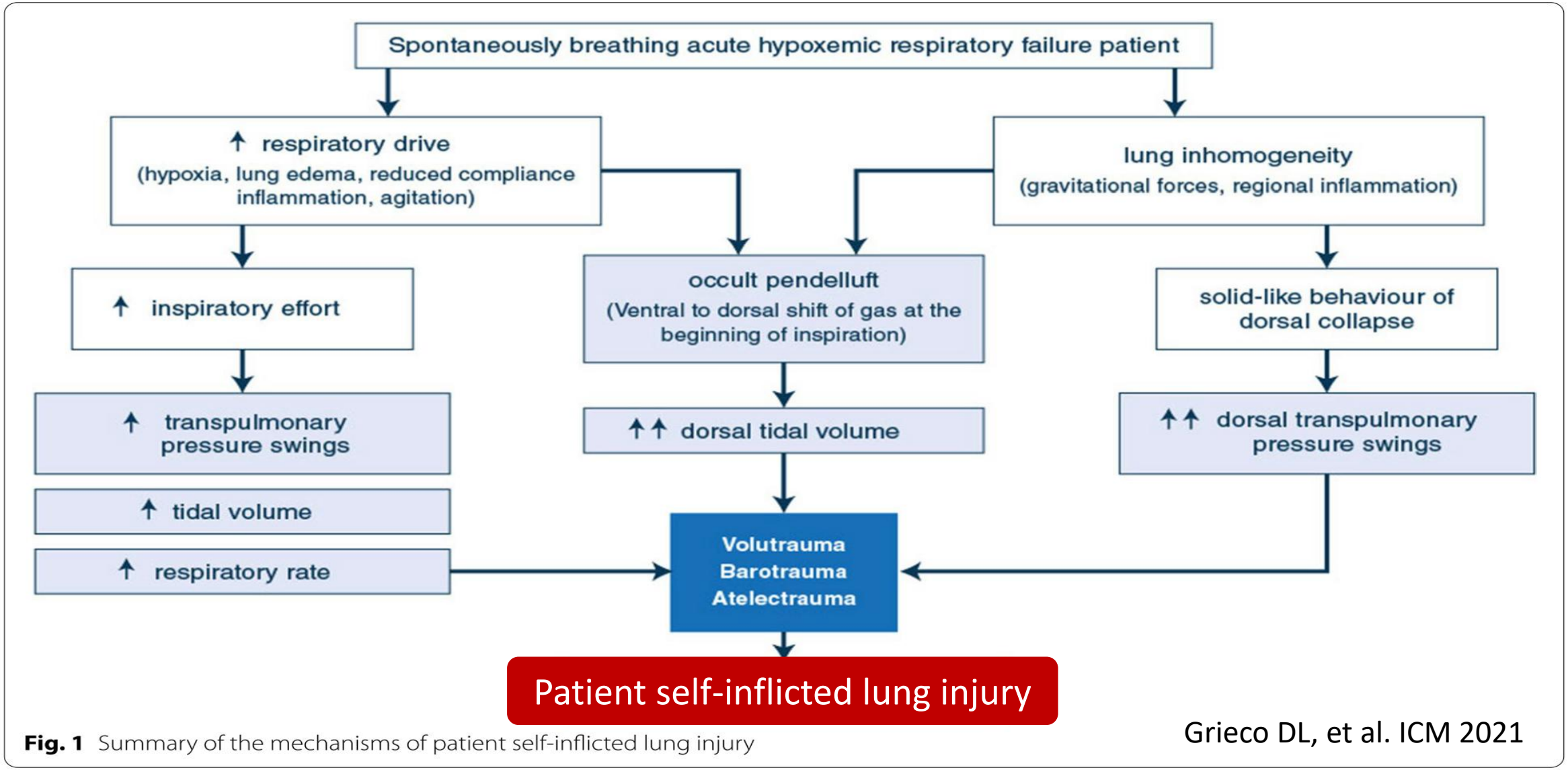


Fig. 1 Summary of the mechanisms of patient self-inflicted lung injury

Grieco DL, et al. ICM 2021

Feature	HFNC	Facemask NIV	Helmet NIV
PEEP effect	2–4 cm H_2O (low)	5–8 cm H_2O (moderate)	10–12 cm H_2O (high)
Inspiratory support pressure	None	PS 8–14 cm H_2O	PS 10–12 cm H_2O (partly damped by helmet compliance)
Transpulmonary pressure swings	Small	Large – marked ΔPL and high VT	Moderate – attenuated by pressure buffering
Tidal-volume control	Spontaneous, relatively low	Often > 9 mL/kg PBW → high risk	Hard to measure but ΔPES decreases
Overall P-SILI risk	★ Low	★★★ High	★★ Moderate-to-low (depends on settings and synchrony)

Grieco DL, et al. ICM 2021

ERS Clinical Practice Guidelines: high-flow nasal cannula in acute respiratory failure

Acute hypoxaemic respiratory failure

TABLE 2 Population, intervention, comparison, outcomes (PICO) questions and recommendations

1. Should HFNC or COT be used in patients with acute hypoxaemic respiratory failure?	The ERS task force suggests the use of HFNC over COT in patients with acute hypoxaemic respiratory failure (conditional recommendation, moderate certainty of evidence)
2. Should HFNC or NIV be used in patients with acute hypoxaemic respiratory failure?	The ERS task force suggests the use of HFNC over NIV in acute hypoxaemic respiratory failure (conditional recommendation, very low certainty of evidence)
3. Should HFNC or COT be used during breaks from NIV in patients with acute hypoxaemic respiratory failure?	The ERS task force suggests the use of HFNC over COT during breaks from NIV in patients with acute hypoxaemic respiratory failure (conditional recommendation, low certainty of evidence)
4. Should HFNC or COT be used in post-operative patients after extubation?	The ERS task force suggests the use of either COT or HFNC in post-operative patients at low risk of respiratory complications (conditional recommendation, low certainty of evidence)
5. Should HFNC or NIV be used in post-operative patients after extubation?	The ERS task force suggests the use of either HFNC or NIV in post-operative patients at high risk of respiratory complications (conditional recommendation, low certainty of evidence)

Oczkowski S, et al. Eur Respir J . 2022.

ERS Clinical Practice Guidelines: high-flow nasal cannula in acute respiratory failure

PICO question: Should HFNC or NIV be used in patients with acute hypoxaemic respiratory failure?

- We suggest the use of HFNC over NIV in patients with acute hypoxaemic respiratory failure (conditional recommendation, very low certainty of evidence)
- Subset of patients that NIV maybe preferable:
  - Increased work of breathing
  - Respiratory muscle fatigue
  - Congestive heart failure
  - The positive pressure of NIV may positively impact haemodynamics.

Oczkowski S, et al. Eur Respir J . 2022.

High-Flow Oxygen through Nasal Cannula in Acute Hypoxemic Respiratory Failure

NEJM GROUP

FLORALI study

Frat JP, et al. NEJM 2015

310 **ARDS** p's with PF ratio<300; HFNC vs. BiPAP vs facial mask O_2

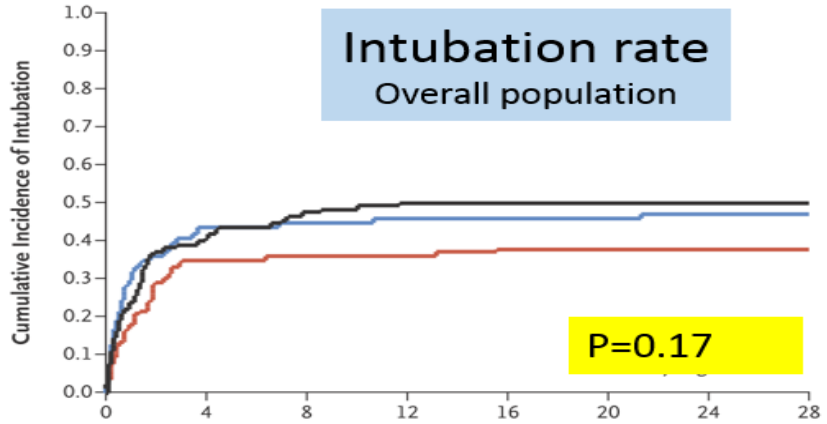
Exclude COPD/APE

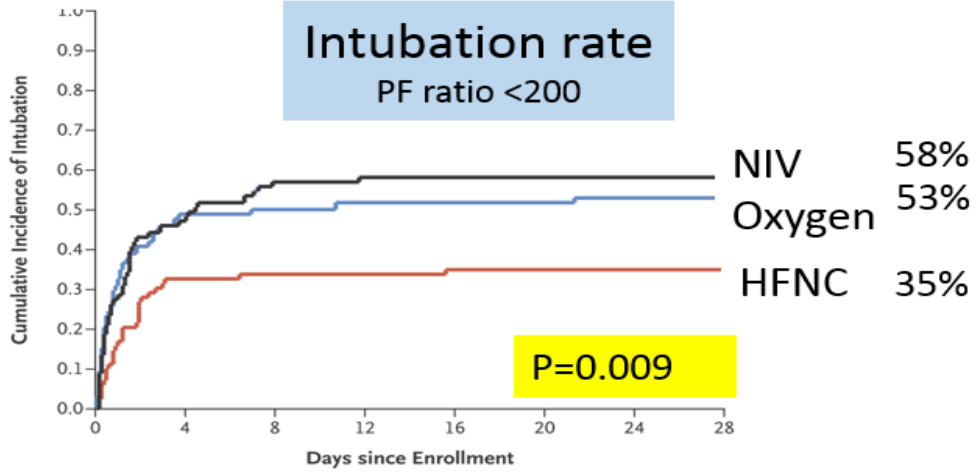
1st endpoint: 28 days intubation rate

Table 1. Characteristics of the Patients at Baseline, According to Study Group.*

Characteristic	High-Flow Oxygen (N=106)	Standard Oxygen (N=94)	Noninvasive Ventilation (N=110)
Arterial blood gas			
pH	7.43±0.05	7.44±0.06	7.43±0.06
Pao_2 — mm Hg	85±31	92±32	90±36
FIO_2 §	0.62±0.19	0.63±0.17	0.65±0.15
Pao_2:FIO_2 — mm Hg	157±89	161±73	149±72
$Paco_2$ — mm Hg	36±6	35±5	34±6

85%: pneumonia related





NIV worse than COT

High-Flow Oxygen through Nasal Cannula in Acute Hypoxemic Respiratory Failure

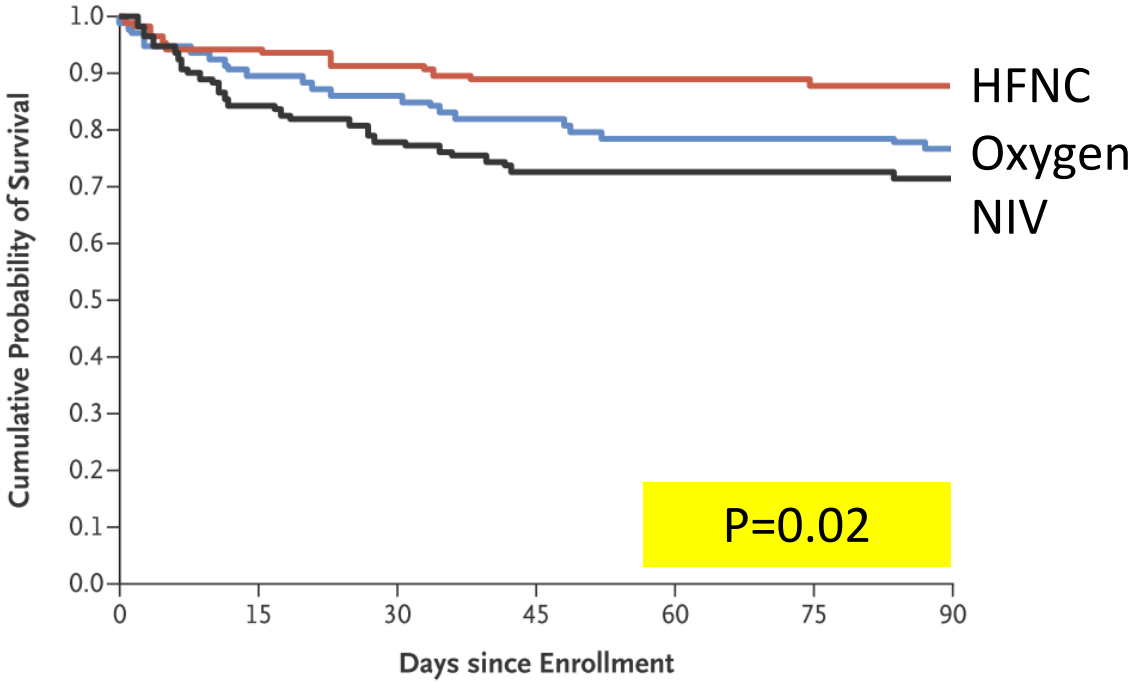
NEJM GROUP

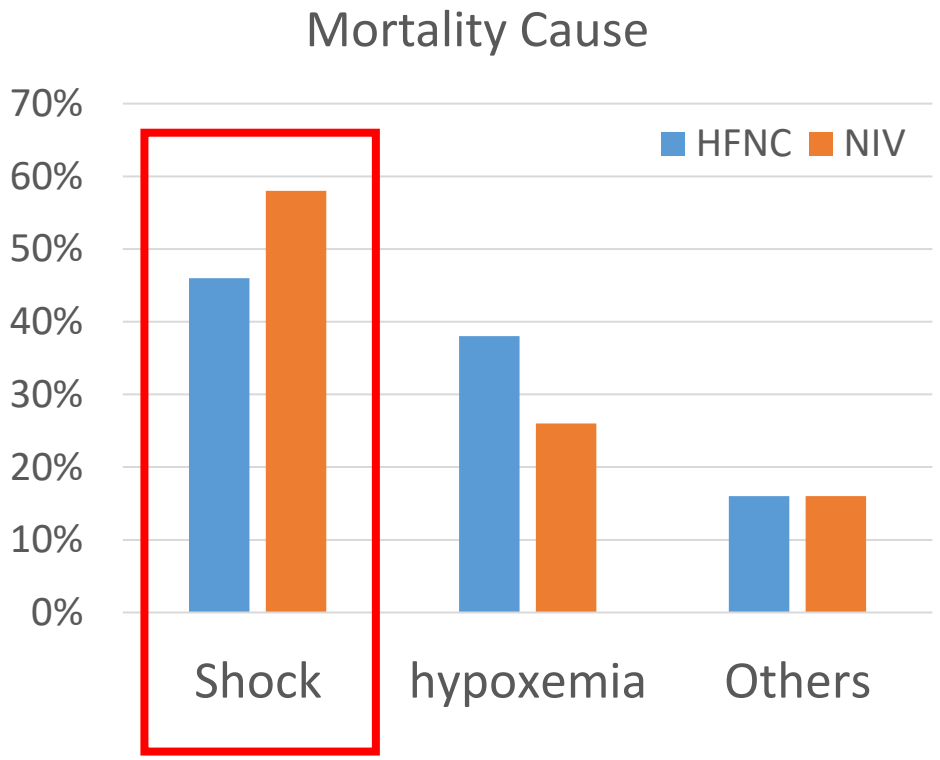
FLORALI study

310 ARDS p's with PF ratio<300; HFNC vs. BiPAP

1st endpoint: 28 days intubation rate

Survival rate, **Day 90**





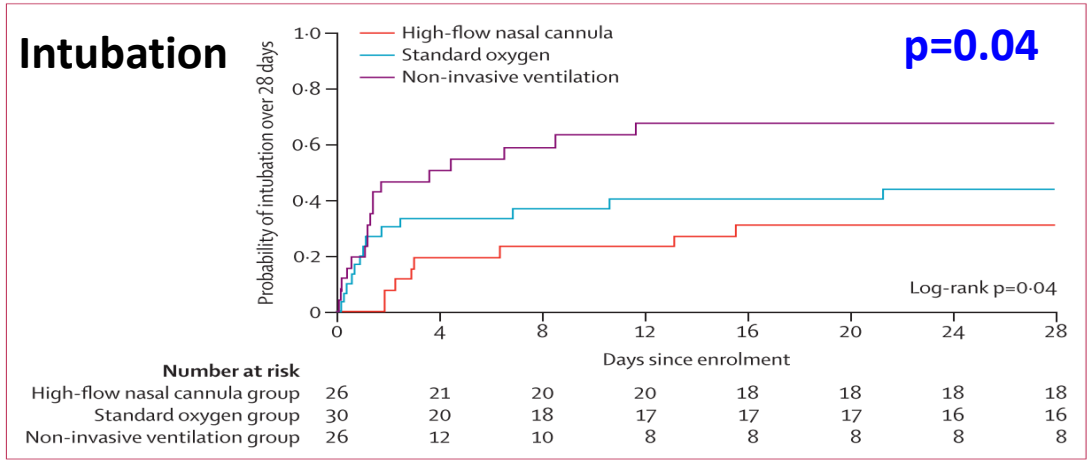
Frat JP, et al. NEJM 2015

Effect of non-invasive oxygenation strategies in immune-compromised patients with severe acute respiratory failure: a post-hoc analysis of a randomised trial

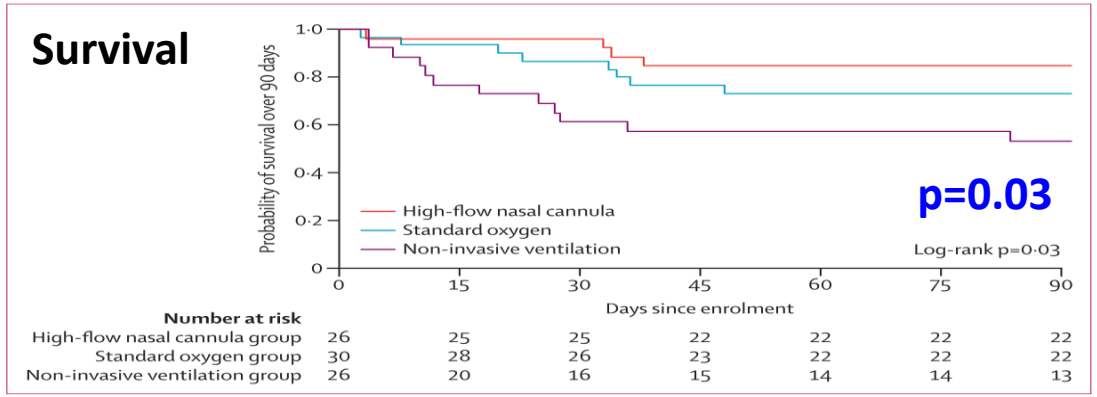
Post-hoc analysis of FLORALI study

82 immunocompromised cases: cancer, HIV, immunosuupresant

	Standard oxygen (n=30)	High-flow nasal cannula (n=26)	Non-invasive ventilation plus high-flow cannula (n=26)	p value
Outcomes				
Intubation	13 (43%)	8 (31%)	17 (65%)	0·04
Ventilator-free days at day 28	23 (10)	26 (6)	14 (13)	<0·0001
Intensive care unit mortality	6 (20%)	4 (15%)	11 (42%)	0·06
90-day mortality	8 (27%)	4 (15%)	12 (46%)	0·046



NIV
SOT
HFNC



HFNC
SOT
NIV

Frat JP, et al. Lancet Resp Med 2016

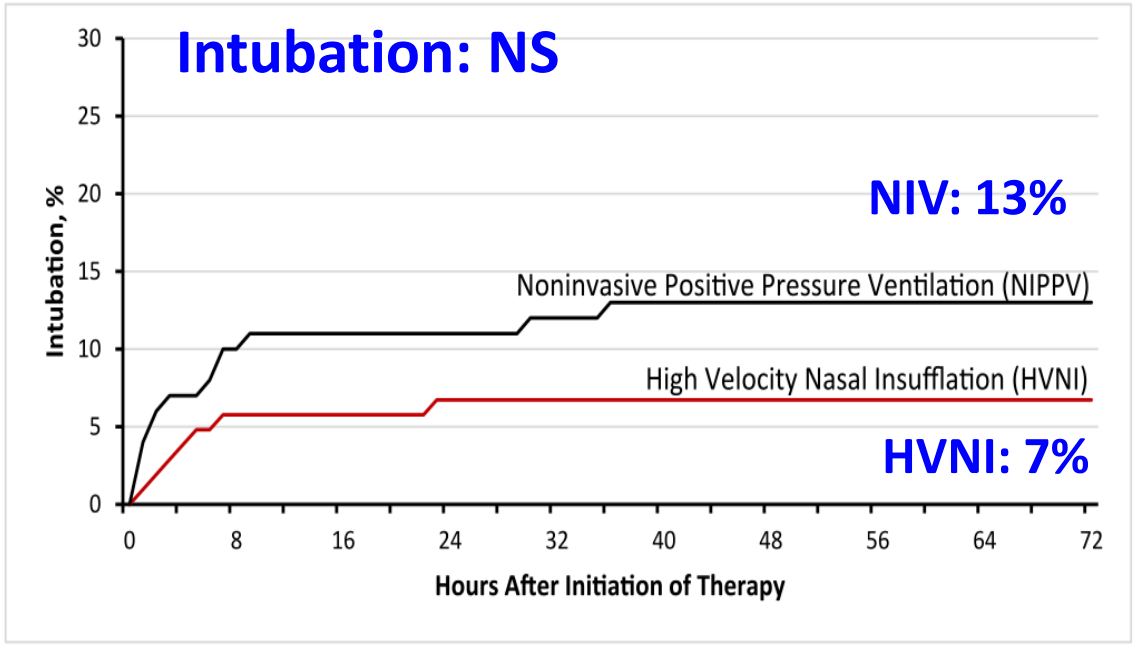
High-Velocity Nasal Insufflation in the Treatment of Respiratory Failure: A Randomized Clinical Trial

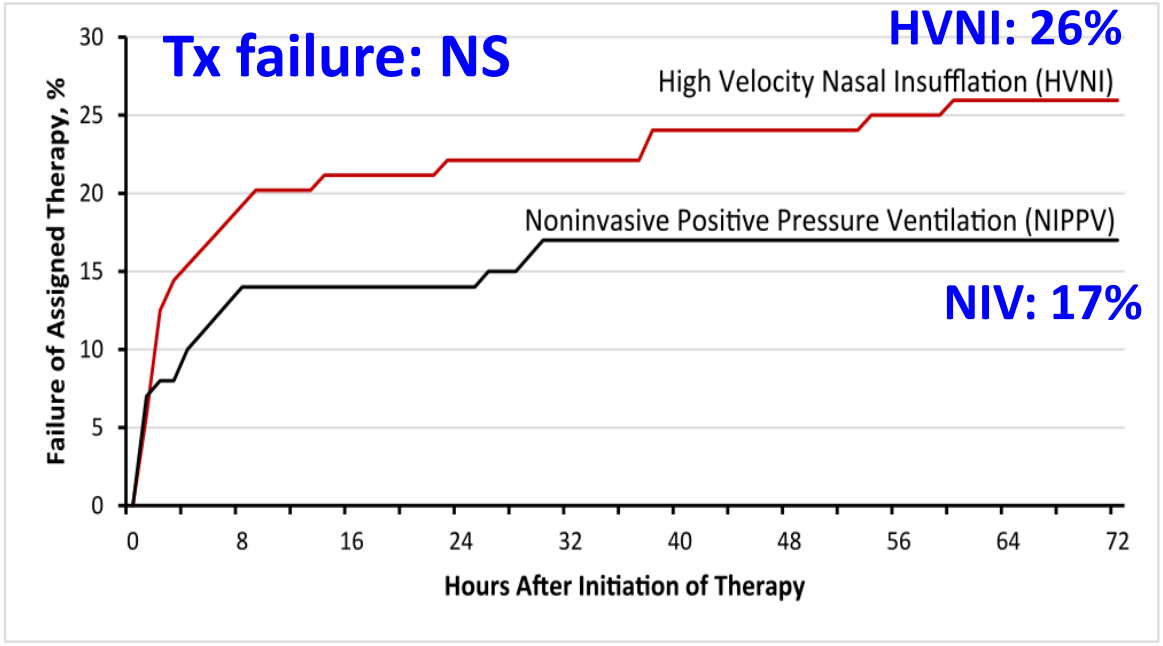
204 patients with RF in ED

HVNI (35L/min, 100%) vs. **NIV** (I/E: 10/5)

1st endpoint: therapy failure at 72 h

Mixed population: hypoxic (13%), COPDAE (28%), CHF (21%)





HFNC is non-inferior to NIV

Doshi P, et al. Ann Emerg Med 2018

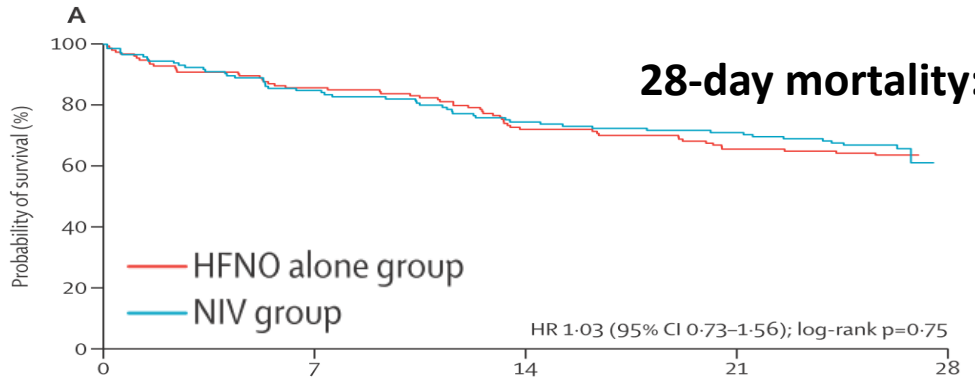
HFNC alone or alternating with NIV in critically ill immunocompromised patients with acute respiratory failure: a randomised controlled trial

Open label RCT in ICUs of France/Italy

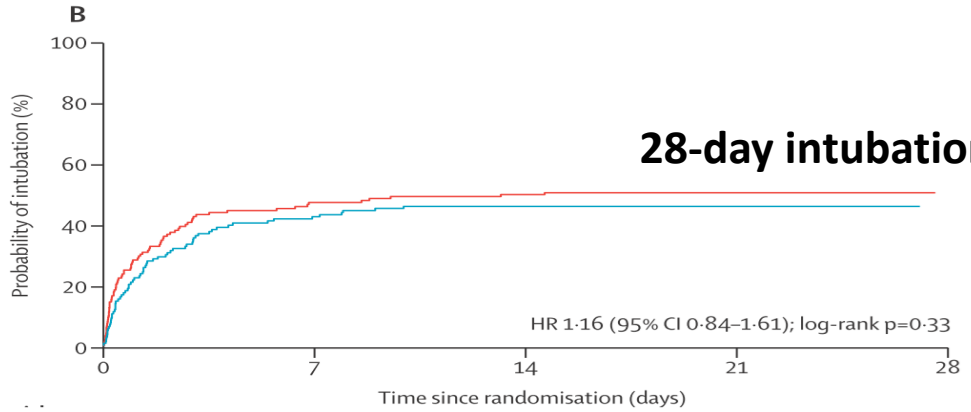
Immune compromise with hypoxemic RF

1st endpoint: 28-Day mortality

	HFNO alone group (n=154)	NIV group (n=145)
Age, years	62 (13)	65 (12)
Underlying conditions		
Haematological malignancy	78 (51%)	73 (50%)
Solid cancer	35 (23%)	38 (26%)
AIDS	7 (5%)	5 (3%)
Solid organ transplant recipient	20 (13%)	15 (10%)
Other	14 (9%)	14 (10%)
Corticosteroids or immunosuppressive therapy	95 (62%)	95 (66%)
Leucopenia or neutropenia	26 (17%)	18 (12%)
Allogeneic stem cell transplant recipient	11 (7%)	12 (8%)
Autologous stem cell transplant recipient	14 (9%)	4 (3%)
Haematological malignancy or leucopenia or neutropenia (strata)	81 (53%)	75 (52%)



28-day mortality: NS



28-day intubation: NS

Coudroy R, et al. Lancet Res Med 2022

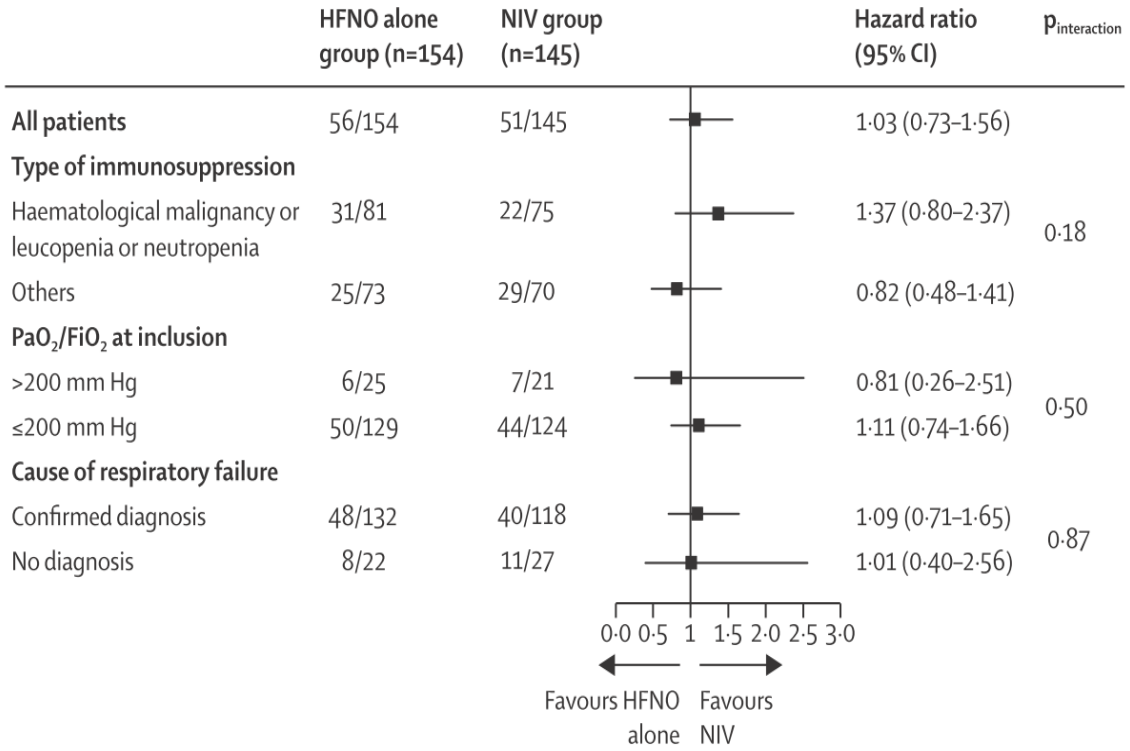
HFNC alone or alternating with NIV in critically ill immunocompromised patients with acute respiratory failure: a randomised controlled trial

Open label RCT in ICUs of France/Italy

Immune compromise with hypoxemic RF

1st endpoint: 28-Day mortality

	HFNO alone group (n=154)	NIV group (n=145)	p value
Primary outcome			
Mortality at day 28	56 (36%)	51 (35%)	0·83
Secondary outcomes			
Intubation at day 28	78 (51%)	67 (46%)	0·44
Mortality of intubated patients in the ICU	40/78 (51%)	43/67 (64%)	-
Mortality			
In the ICU	45 (29%)	49 (34%)	0·39
In hospital	63 (41%)	60 (41%)	0·93
At day 90	67 (44%)	63 (43%)	0·99
Respiratory parameters 1 h after treatment initiation			
PaO_2/FiO_2, mm Hg	143 (76)	199 (91)	<0·001
Respiratory rate, breaths per min	27 (7)	29 (8)	0·059
Change in discomfort scale, mm	−4 (−18 to 4)	0 (−16 to 17)	0·040
Time to intubation, h [n]	20 (5 to 58) [78]	29 (9 to 72) [67]	0·24



Coudroy R, et al. Lancet Res Med 2022

High-Flow Nasal Oxygen vs Noninvasive Ventilation in Patients With Acute Respiratory Failure: The RENOVATE Randomized Clinical Trial

Multicenter RCT in Brazil, non-inferior design

HFNC (**n=883**) vs. NIV (**n=883**) in acute respiratory failure

1st endpoint: **intubation/death at day 7**

Non-inferior margin: **10%**→ OR **1.55**

Table 2. Adherence to Trial Therapy and Co-Interventions

	Patient group with acute respiratory failure									
	Nonimmunocompromised with hypoxemia **N=485**		Immunocompromised with hypoxemia **N=50**		COPD exacerbation with respiratory acidosis **N=77**		Acute cardiogenic pulmonary edema **N=272**		Hypoxemic COVID-19 **N=882**	
	High-flow nasal oxygen (n = 249)[a]	Noninvasive ventilation (n = 236)[b]	High-flow nasal oxygen (n = 28)[a]	Noninvasive ventilation (n = 22)[b]	High-flow nasal oxygen (n = 35)[a]	Noninvasive ventilation (n = 42)[b]	High-flow nasal oxygen (n = 136)[a]	Noninvasive ventilation (n = 136)[b]	High-flow nasal oxygen (n = 435)[a]	Noninvasive ventilation (n = 447)[b]
Trial respiratory support during first 3 d										
Received assigned therapy, No. (%)	223 (89.6)	205 (86.9)	26 (92.9)	20 (90.9)	30 (85.7)	37 (88.1)	130 (95.6)	131 (96.3)	415 (95.4)	415 (92.8)
Time receiving therapy, median (IQR), d	2 (1-3)	1 (1-3)	3 (1-3)	2 (1-3)	1 (1-3)	1.5 (1-3)	1 (1-2)	1 (1-2)	3 (1-3)	2 (1-3)
Crossed over to another therapy, No. (%)[c]	23 (9.2)	5 (2.1)	1 (3.6)	0	8 (22.9)	0	7 (5.1)	0	39 (9.0)	34 (7.6)

Using days: 1-3 days

JAMA 2025; 330 (10):875

High-Flow Nasal Oxygen vs Noninvasive Ventilation in Patients With Acute Respiratory Failure: The RENOVATE Randomized Clinical Trial

Multicenter RCT in Brazil, non-inferior design

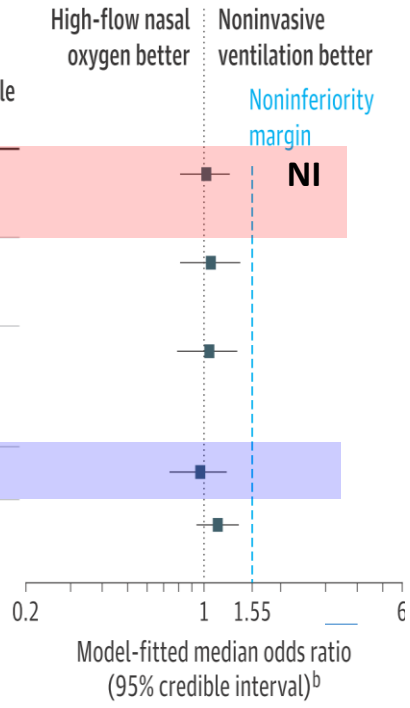
HFNC (n=883) vs. NIV (n=883) in acute respiratory failure

1st endpoint: intubation/death at day 7

Primary analysis

A Analysis of the primary outcome[a]

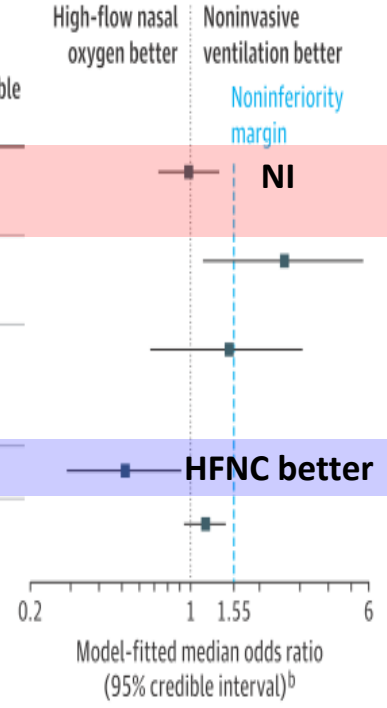
Patients with acute respiratory failure	No./total (%) High-flow nasal oxygen	No./total (%) Noninvasive ventilation	Model-fitted median odds ratio (95% credible interval)[b]
Nonimmunocompromised with hypoxemia	81/249 (32.5)	78/236 (33.1)	1.02 (0.81-1.26)
Immunocompromised with hypoxemia	16/28 (57.1)	8/22 (36.4)	1.07 (0.81-1.39)
Chronic obstructive pulmonary disease exacerbation with respiratory acidosis	10/35 (28.6)	11/42 (26.2)	1.05 (0.79-1.36)
Acute cardiogenic pulmonary edema	14/136 (10.3)	29/136 (21.3)	0.97 (0.73-1.23)
Hypoxemic COVID-19	223/435 (51.3)	210/447 (47.0)	1.13 (0.94-1.38)



Post hoc analysis

B Post hoc analysis of the primary outcome[f]

Patients with acute respiratory failure	No./total (%) High-flow nasal oxygen	No./total (%) Noninvasive ventilation	Model-fitted median odds ratio (95% credible interval)[b]
Nonimmunocompromised with hypoxemia	81/249 (32.5)	78/236 (33.1)	0.98 (0.73-1.33)
Immunocompromised with hypoxemia	16/28 (57.1)	8/22 (36.4)	2.56 (1.14-5.68)
Chronic obstructive pulmonary disease exacerbation with respiratory acidosis	10/35 (28.6)	11/42 (26.2)	1.48 (0.67-3.09)
Acute cardiogenic pulmonary edema	14/136 (10.3)	29/136 (21.3)	0.52 (0.29-0.91)
Hypoxemic COVID-19	223/435 (51.3)	210/447 (47.0)	1.16 (0.94-1.43)



JAMA 2025; 330 (10):875

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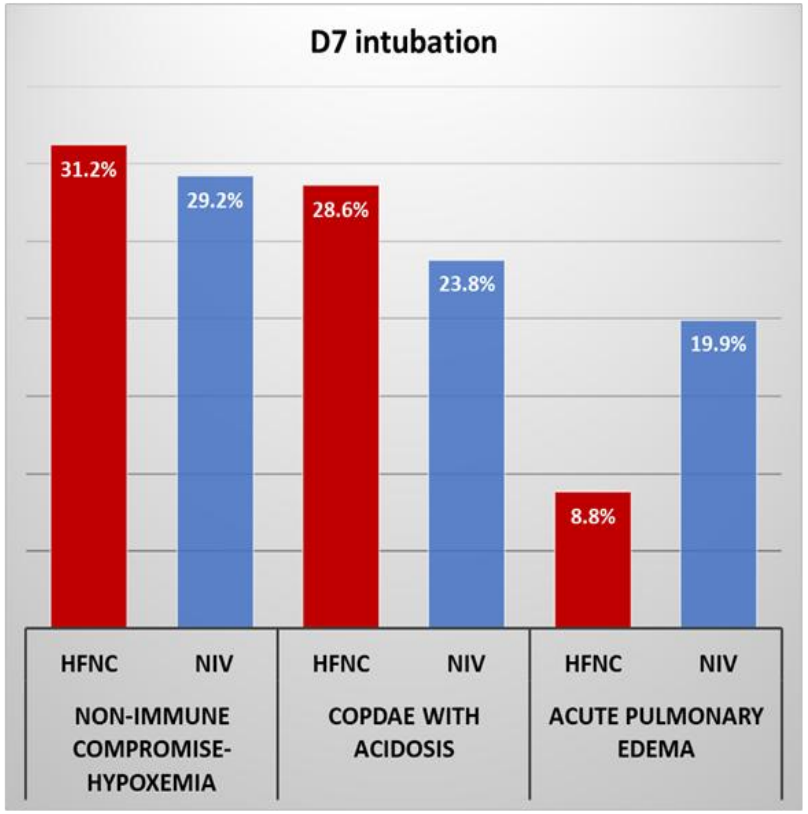
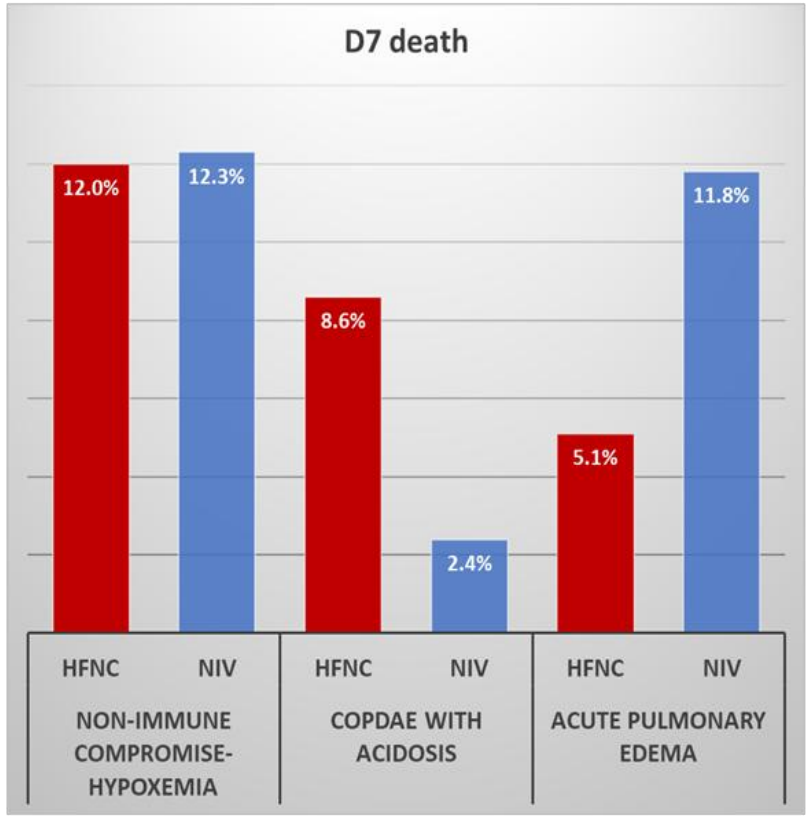
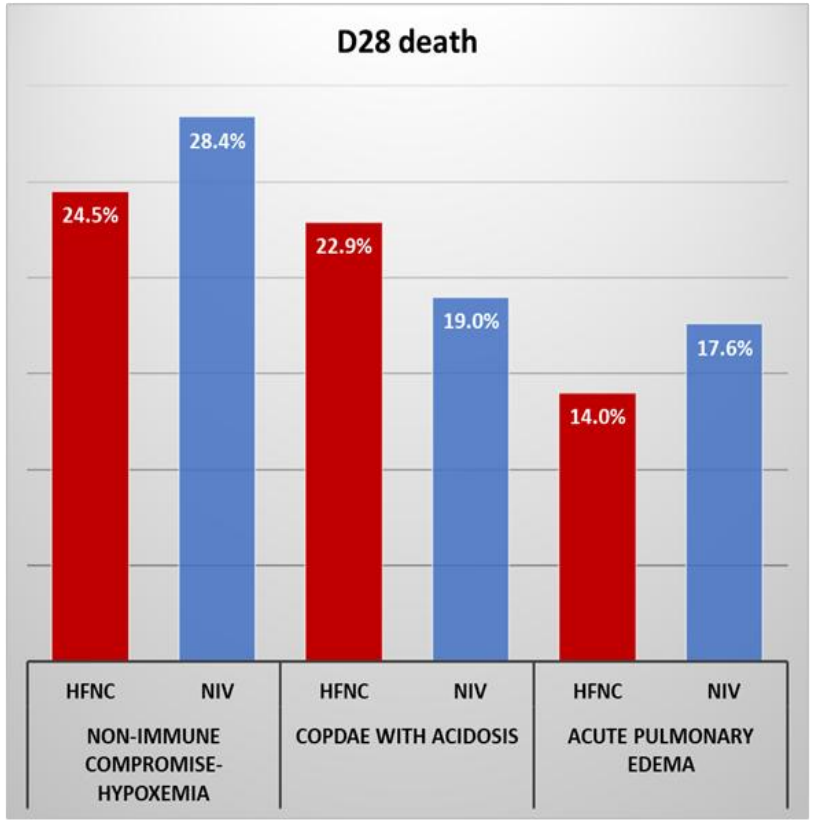






JAMA 2025; 330 (10):875

EDITORIAL

Is High-Flow Oxygen the Standard for All Patients With Acute Respiratory Failure?

Jean-Pierre Frat, MD, PhD; Sylvain Le Pape, MD, PhD; Arnaud W. Thille, MD, PhD

- HFNC is non-inferior to NIV in preventing intubation or death across most causes of acute respiratory failure
- HFNC can be considered a safe initial “bridge” therapy while clinicians identify the underlying etiology of respiratory failure
- Individualized treatment decisions rather than a one-size-fits-all approach in respiratory support for acute respiratory failure

EDITORIAL

Reevaluating Respiratory Support in Acute Respiratory Failure—Insights From the RENOVATE Trial and Implications for Practice

Yonathan Freund, MD, PhD; Amelie Vromant, MD

- Due to heterogeneity, small subgroup sizes, and a wide noninferiority margin, the results should be viewed as hypothesis-generating rather than practice-changing
- The broad noninferiority margin and lack of improvement in secondary or patient-centered outcomes limit the clinical certainty and clinical application
- Patient-centered and patient-reported outcomes are needed in future studies to determine whether HFNC offers true benefits

HFNC in post-extubation patients

ERS Clinical Practice Guidelines: high-flow nasal cannula in acute respiratory failure

post-extubation patients

TABLE 2 Population, intervention, comparison, outcomes (PICO) questions and recommendations

6. Should HFNC or COT be used in nonsurgical patients after extubation?	The ERS task force suggests the use of HFNC over COT in nonsurgical patients after extubation (conditional recommendation, low certainty of evidence)
7. Should HFNC or NIV be used in nonsurgical patients after extubation?	The ERS task force suggests the use of NIV over HFNC for patients at high risk of extubation failure, unless there are absolute or relative contraindications to NIV (conditional recommendation, moderate certainty of evidence)
8. Should HFNC or NIV be used in patients with acute hypercapnic respiratory failure?	The ERS task force suggests a trial of NIV prior to use of HFNC in patients with COPD and acute hypercapnic respiratory failure (conditional recommendation, low certainty of evidence)

HFNC: high-flow nasal cannula; COT: conventional oxygen therapy; NIV: noninvasive ventilation; ERS: European Respiratory Society.

Oczkowski S, et al. Eur Respir J . 2022.

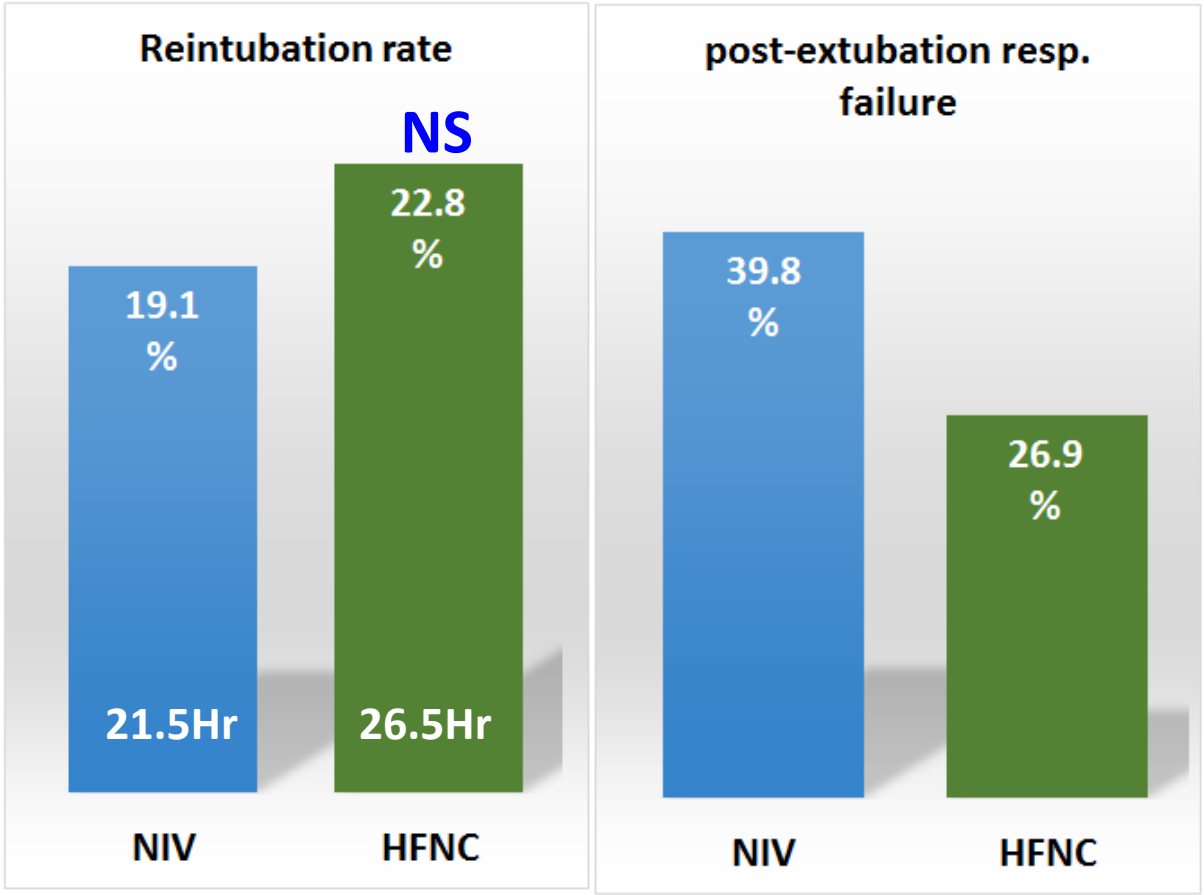
Effect of Postextubation HFNC vs NIV on Reintubation and Postextubation Respiratory Failure in High-Risk Patients: A Randomized Clinical Trial

604 patients from 3 centers in Spain

- **High-risk extubation failure**
  - Age **> 65** years old
  - **Heart failure** for mechanical ventilation
  - Moderate to **severe COPD**
  - **APACHE II > 12** on extubation day
  - **BMI>30**
  - High risk of laryngeal edema
  - Inability to deal with **respiratory secretions**
  - **Difficult or proloned weaning**
  - 2 or more comorbilidies
  - **Mechanical ventilation for more than 7 days**

- Randomize to HFNC or NIV for **24 hours**

- **Primary endpoints**
  - **Reintubation** within 72 hours

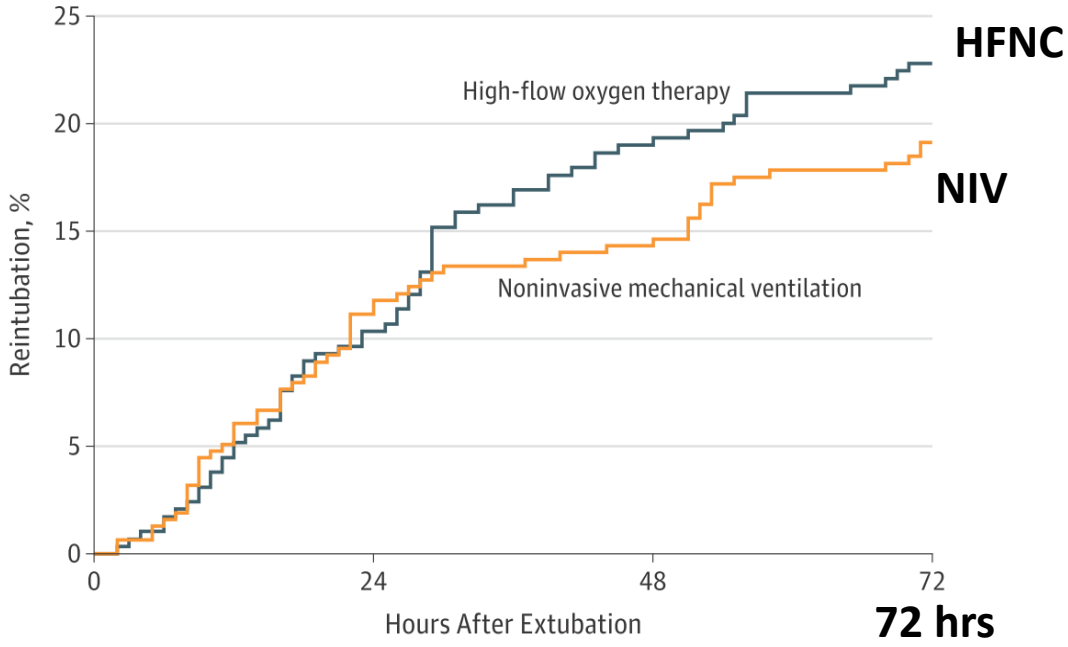


Hernandez G, et al. JAMA 2016

Effect of Postextubation HFNC vs NIV on Reintubation and Postextubation Respiratory Failure in High-Risk Patients: A Randomized Clinical Trial

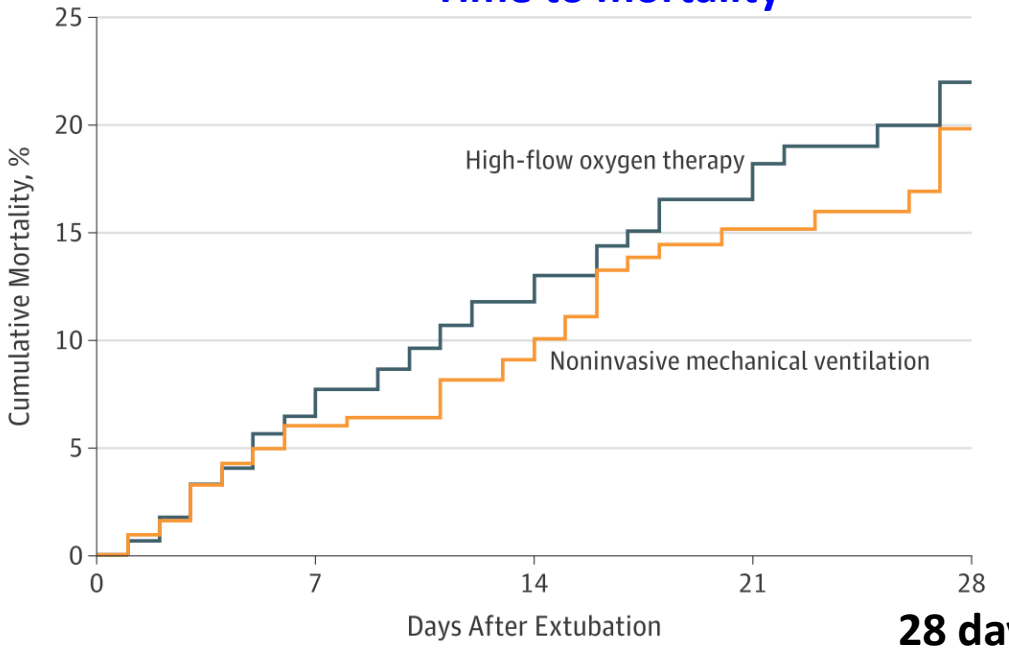
604 patients from 3 centers in Spain

Time to reintubation



72 hrs

Time to mortality



28 days

HFNC is non-inferior to NIV for preventing reintubation in high risk population

Hernandez G, et al. JAMA 2016

Effect of Postextubation HFNC vs NIV on Reintubation and Postextubation Respiratory Failure in High-Risk Patients: A Randomized Clinical Trial

JAMA

Randomized clinical trial in 3 ICUs in Spain

HFN or NIV 24 hrs after extubation

Outcome	NIV	NHF	Absolute difference between groups (95% CI)
Median time to reintubation, hr (IQR)	21.5 (10 to 47)	26.5 (14 to 39)	-5 (-34 to 24)
Outcome	**NIV**	**NHF**	**P value**
Reintubations due to hypercapnic respiratory failure, n (%)	8 (2.5%)	6 (2%)	p = 0.63
Median ICU length of stay, days (IQR)	4 (2 to 9)	3 (2 to 7)	p = 0.048
Adverse events requiring treatment discontinuation for >18 hr, n (%)	135 (42.9)	0 (0)	p < 0.001

Hernandez G, et al. JAMA 2016

Effect of postextubation NIV with active humidification vs HFNC on reintubation in patients at very high risk for extubation failure: a randomized trial

Prospective RCT in 2 ICUs | s/p MV with **≥4 risk factor** | NIV vs. HFNC ≥ 48 hrs | 1st endpoint: reintubate in 7 days

	NIV (*n* = 92)	HFNC (*n* = 90)
Age, mean (SD), y	60.9 (14.3)	59.9 (15.4)
Men, n (%)	67 (72.8)	50 (55.6)
APACHE II at ICU admission, median (IQR)[a]	19 (16.3–24)	19 (15–23)
Length of MV before extubation, median (IQR), days	4.5 (2–9)	5.5 (2–10)
Diagnosis at admission[e]		
Respiratory primary failure	59 (64.8)	49 (54.4)
SARS COVID-19[f]	12 (13.1)	15 (16.7)
Hemodynamic failure	53 (57.6)	57 (63.3)
Neurologic failure	44 (47.8)	57 (63.3)
Trauma	15 (16.3)	15 (16.7)
Surgical	19 (20.7)	28 (31.1)

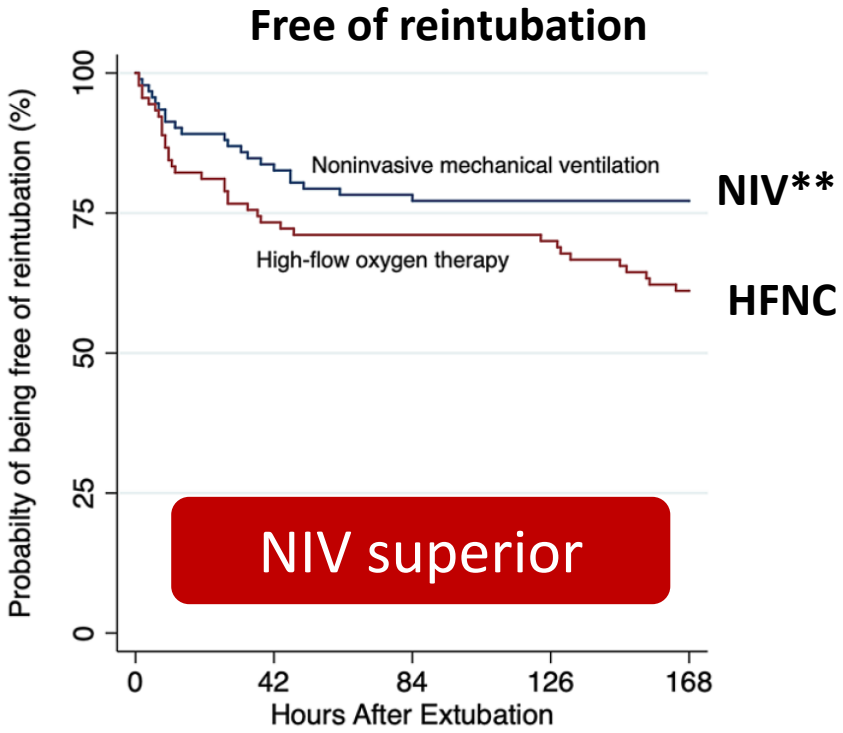
	NIV (*n* = 92)	HFNC (*n* = 90)
High-risk factors for reintubation, no (%)		
Age > 65 y	42 (45.7)	41 (45.6)
Heart failure as primary indication for MV	25 (27.2)	6 (6.7)
COPD	28 (30.4)	14 (15.6)
APACHE II > 12 on extubation day[a]	53 (57.6)	56 (62.2)
Body mass index > 30[c]	49 (53.3)	46 (51.1)
Airway patency problems	33 (35.9)	31 (34.4)
Inability to deal with respiratory secretions	31 (33.7)	47 (52.2)
Difficult or prolonged weaning[d]	60 (66.7)	59 (64.1)
≥ 2 comorbidities	75 (81.5)	61 (67.8)
Prolonged MV	36 (39.1)	43 (47.8)
Hypercapnia at the end of the SBT	47 (51.1)	27 (30)
High-risk factors, median (IQR)	5 (4–6)	4 (4–6)

Hernandez G, et al. ICM 2022

Effect of postextubation NIV with active humidification vs HFNC on reintubation in patients at very high risk for extubation failure: a randomized trial

Prospective RCT in 2 ICUs | s/p MV with ≥4 risk factor | NIV vs. HFNC ≥ 48 hrs | 1st endpoint: reintubate in 7 days

	NIV ($n=92$)	HFNC ($n=90$)	Difference between groups (95%CI), p
Primary outcome, n (%)			
All-cause reintubation	21 (22.8)	35 (38.9)	−16.0 (−29.2 to −0.3), $p=0.019$
Secondary outcomes			
Postextubation respiratory failure, *n* (%)	40 (43.5)	40 (44.4)	−0.9 (−15.4–13.5), $p=0.896$
Ventilator-associated tracheobronchitis, *n* (%	0 (0)	1 (1.1)	−1.1 (−3.3–1.1), $p=0.495$
Sepsis, *n* (%)	4 (4.3)	3 (3.3)	1 (−5.5–7.6), $p=1.000$
Multiorgan failure, *n* (%)	3 (3.3)	2 (2.2)	1 (−4.5–6.6), $p=1.000$
ICU mortality, *n* (%)	12 (13)	4 (4.4)	9.7 (−1.1–18.7), $p=0.356$
Intolerance to therapy, *n* (%)	19 (20.7)	8 (8.9)	11.7 (1.6–21.9), $p=0.026$
Nasal discomfort, *n* (%)	18 (19.6)	6 (6.7)	12.9 (3.3–22.5), $p=0.010$
Facial skin ulcer, *n* (%)	4 (4.3)	0 (0)	4.3 (0.1–8.5), $p=0.045$
Exploratory outcomes			
Reintubation rate at 5 d, *n* (%)	21 (23.3)	26 (28.8)	0.321
Time to reintubation at 5 d, median (IQR), h	27 (6–47)	10 (6.5–28)	0.029



NIV**

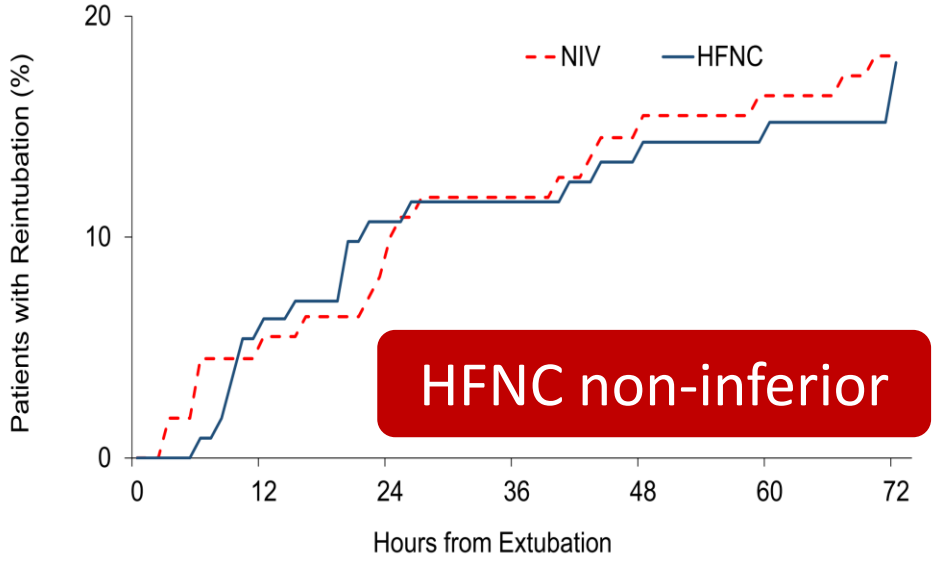
HFNC

Hernandez G, et al. ICM 2022

High-flow nasal oxygen cannula vs. noninvasive mechanical ventilation to prevent reintubation in sepsis: a randomized controlled trial

Single center RCT in Thailand | Sepsis/septic shock with MV >48 hr | HFNC (n=112) vs. NIV (n=110)

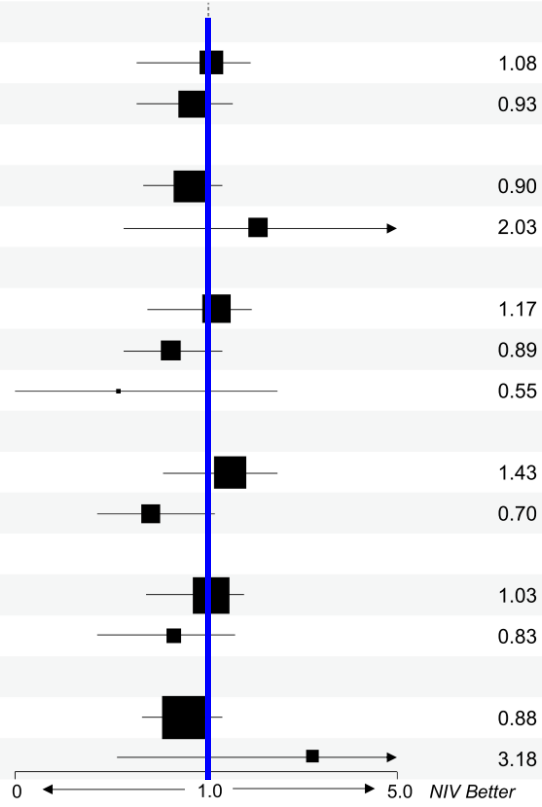
1st endpoint: reintubation in 72 hrs



No. at risk							
NIV	110	104	99	97	93	92	90
HFNC	112	105	100	99	96	95	92

Subgroup Analysis of Reintubation at 72 Hours

Subgroup	HFNC (N=112) *N with event/total N of patients (%)*	NIV (N=110)	Relative risk (95% CI)
Age			
Age ≤65 years	8/52 (15.4)	7/52 (13.5)	1.08 (0.61-1.93)
Age >65 years	12/60 (20.0)	13/58 (22.4)	0.93 (0.61-1.43)
Source of infection			
Pneumonia	13/65 (20.0)	18/75 (24.0)	0.90 (0.64-1.28)
Non-pneumonia	7/47 (14.9)	2/35 (5.7)	2.03 (0.58-7.09)
Cause of intubation			
Shock related respiratory failure	12/64 (18.8)	9/61 (14.8)	1.17 (0.69-1.98)
Hypoxic respiratory failure	7/39 (17.9)	10/45 (22.2)	0.89 (0.56-1.41)
Hypercapnic respiratory failure	1/9 (11.1)	1/4 (25.0)	0.55 (0.10-2.95)
Duration of intubation			
≤7 days	15/75 (20.0)	8/67 (11.9)	1.43 (0.79-2.57)
>7 days	5/37 (13.5)	12/43 (27.9)	0.70 (0.47-1.04)
Weaning method			
Pressure support	13/76 (17.1)	14/86 (16.3)	1.03 (0.69-1.53)
T-piece	7/36 (19.4)	6/24 (25)	0.83 (0.42-1.66)
Body mass index, kg/m^2			
Body mass index < 30 kg/m^2	16/100 (16.0)	19/95 (20.0)	0.88 (0.62-1.24)
Body mass index < 30 kg/m^2	4/12 (33.3)	1/15 (6.7)	3.18 (0.54-18.89)



Tongyoo S et al., Annals of Intensive Care 2021

Effect of Postextubation HFNO With NIV vs HFNO Alone on Reintubation Among Patients at High Risk of Extubation Failure: A Randomized Clinical Trial

Thille AW, et al. JAMA 2019

POPULATION

425 Men 216 Women

Adults at high risk of failure to extubate, ie, older than 65 years or with an underlying cardiac or respiratory disease

Mean age: 70 years

LOCATIONS

30
ICUs in France

INTERVENTION

648 Patients randomized
641 Patients analyzed

306

High-flow nasal oxygen alone

High-flow nasal oxygen alone for at least 48 hours with a flow of 50 L/min

342

High-flow nasal oxygen with NIV

High-flow nasal oxygen with NIV with a first session ≥4 hours and minimal duration ≥12 hours/day within 48 hours

PRIMARY OUTCOME

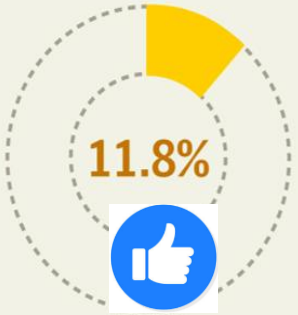
Proportion of patients reintubated at day 7

FINDINGS

Reintubation rate at day 7

High-flow nasal oxygen alone
55 of 302 patients

High-flow nasal oxygen with NIV
40 of 339 patients



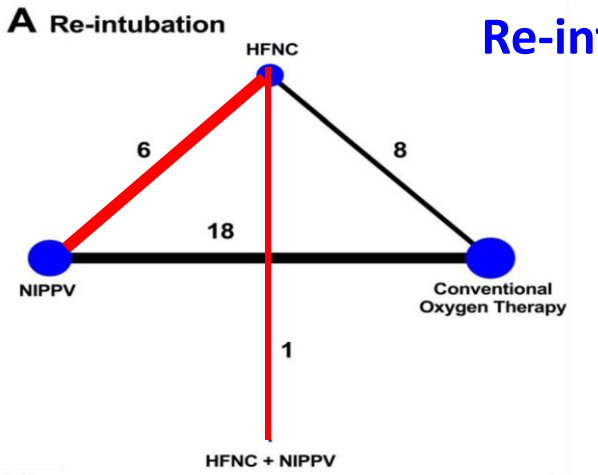
Between-group difference,
−6.4%
(95% CI, −12.0% to −0.9%)

Noninvasive respiratory support following extubation in critically ill adults: a systematic review and network meta-analysis

6806 cases from 36 RCTs

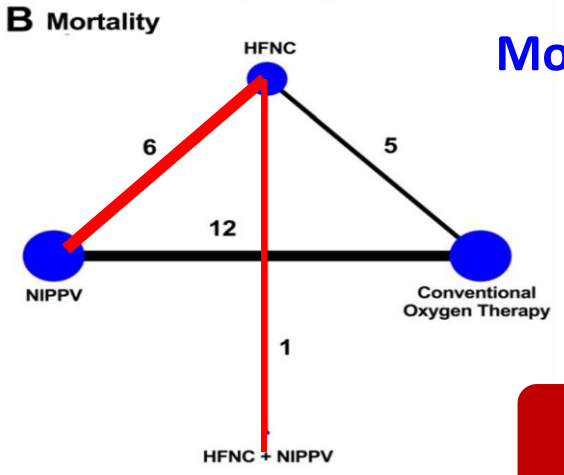
NIPPV vs. HFNC vs. HFNC+NIV vs. O2

Fernando SM, et al. ICM 2022



Re-intubate

Comparison	Network odds ratio (95% CI)		Number needed to treat	GRADE
NIPPV vs conventional oxygen	0.65 (0.52–0.82)		20 (13 to 45)	Moderate[a]
HFNC vs conventional oxygen	0.63 (0.45–0.87)		26 (15 to 102)	Moderate[a]
NIPPV vs HFNC	1.04 (0.78–1.38)	NS	N/A	Low[a,b]
HFNC + NIPPV vs conventional oxygen	0.38 (0.19–0.74)		10 (6 to 50)	Moderate[a]
HFNC + NIPPV vs NIPPV	0.58 (0.3–1.11)	NS	N/A	Low[a,b]
HFNC + NIPPV vs HFNC	0.6 (0.33–1.08)	NS	N/A	Low[a,b]



Mortality

Comparison	Network odds ratio		Absolute risk difference (	GRADE
NIPPV vs conventional oxygen	0.8 (0.61–1.04)		– 1.65 (– 3.81 to 0.5)	Moderate[b]
HFNC vs conventional oxygen	0.9 (0.66–1.24)		– 0.29 (– 1.58 to 1.01)	Low[a]
NIPPV vs HFNC	0.89 (0.69–1.13)	NS	– 1.37 (– 3.47 to 0.72)	Moderate[b]
HFNC + NIPPV vs conventional oxygen	0.95 (0.56–1.62)		0.41 (– 5.36 to 6.18)	Low[a]
HFNC + NIPPV vs NIPPV	1.19 (0.73–1.95)	NS	2.07 (– 3.93 to 8.07)	Low[a]
HFNC + NIPPV vs HFNC	1.05 (0.69–1.62)	NS	0.7 (– 4.93 to 6.33)	Low[a]

No difference in subgroups. Prophylaxis is better than rescue

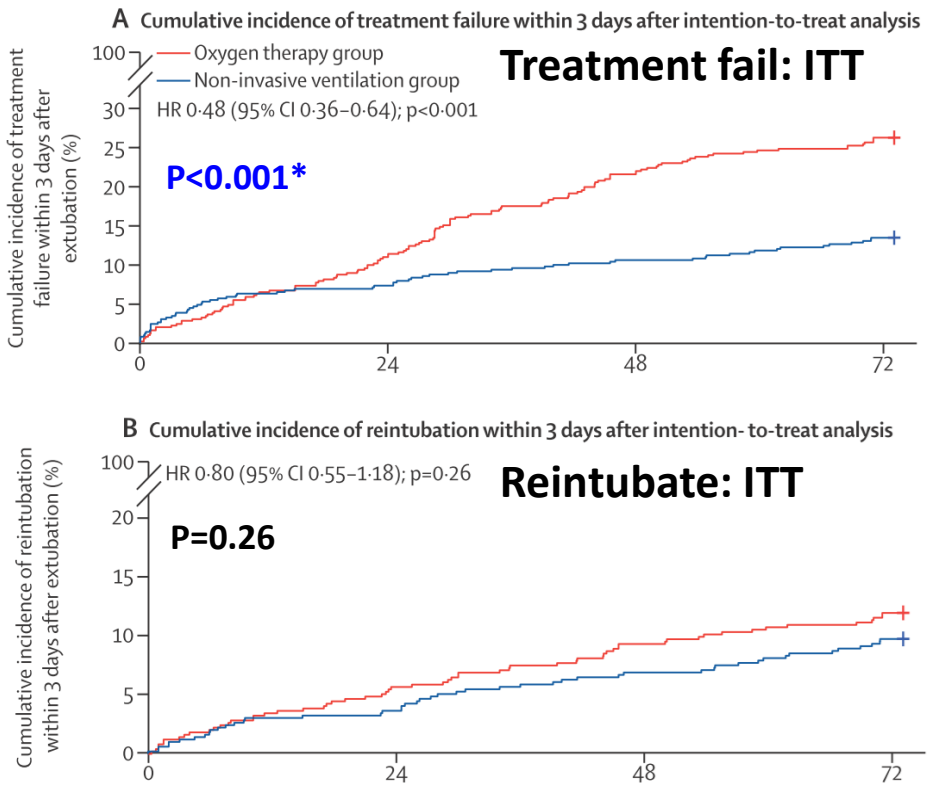
Effect of NIV after extubation in critically ill patients with obesity in France: a multicentre, unblinded, pragmatic randomised clinical trial

RCT, 39 ICUs in France

NIV alternate with HFNC/COT (n=466) vs. Oxygen group: (HFNC, n=234 or COT, n=239)

1st endpoint: 3 days treatment failure-reintubate, switch, discontinue

N=981

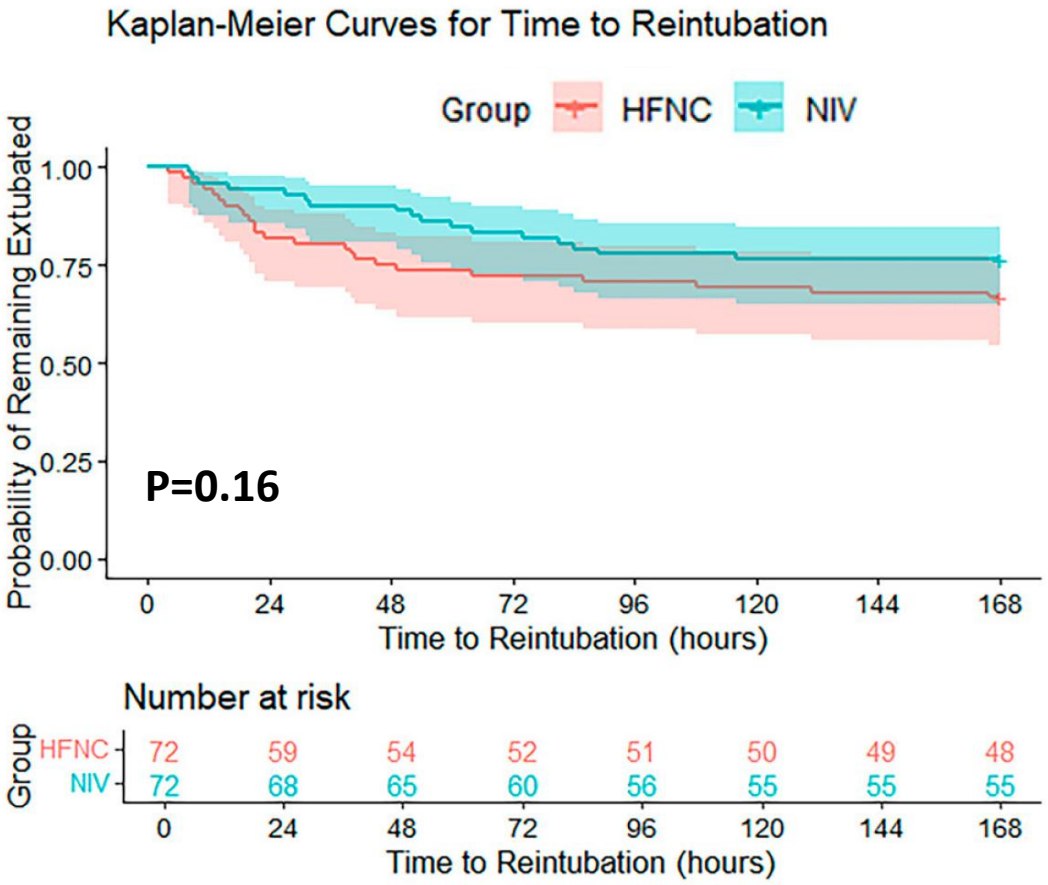


	NIV group (n=490)	Oxygen therapy group (n=491)		Relative risk (95% CI)	p value
Primary outcome: treatment failure	66 (13%)	130 (26%)	**	0·43 (0·31 to 0·60)	<0·0001
Reintubation within 3 days after extubation	48 (10%)	59 (12%)	NS	0·80 (0·53 to 1·19)	0·26
Switch to the other study treatment*	0	67 (14%)	**	0·0064 (0·0004 to 0·10)	<0·0001
Premature discontinuation of study treatment†	18 (4%)	4 (1%)		4·2 (1·5 to 12·0)	0·002
Exploratory‡					
Reintubation within 7 days after extubation	68/489 (14%)	77/490 (16%)		0·87 (0·61 to 1·23)	0·94
ICU mortality	29/486 (6%)	31/490 (6%)		0·94 (0·56 to 1·58)	0·94

De Jong A, et al. Lancet Resp Med 2023

Humidified NIV versus High-Flow Therapy to Prevent Reintubation in Patients with Obesity: A Randomized Clinical Trial

RCT in 2 ICUs in Spain | BMI >30 + <3 risk factors | NIV vs. HFNC ≥ 48 hrs | 1st endpoint: reintubate in 7 days



Variable	HFNC (*n* = 72)	NIV (*n* = 72)	*P* Value
Primary outcome			
All-cause reintubation within the first 7 d, *n* (%)	24 (33.3)	17 (23.6)	0.268
Secondary outcomes			
Postextubation respiratory failure, *n* (%)	24 (33.3)	28 (38.9)	0.603
Hospital LOS, median (25th–75th percentile), d	22.5 (10.0–40.5)	28.5 (19.0–38.5)	0.066
ICU LOS, median (25th–75th percentile), d	6.5 (3–17)	11 (6–20)	0.022
ICU mortality, *n* (%)	8 (11.1)	10 (13.9)	0.801
Hospital mortality, *n* (%)	8 (11.1)	10 (13.9)	0.801
Intolerance to therapy, *n* (%)	3 (4.2)	11 (15.3)	0.049
Facial skin ulcer, *n* (%)	0 (0)	2 (2.8)	0.476

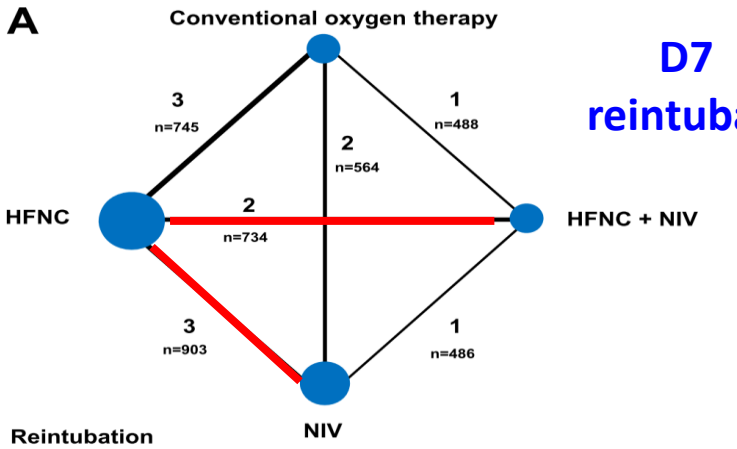
Hernandez G, et al. AJRCCM 2025

Noninvasive respiratory support following extubation in critically ill adults with obesity: a systematic review and network meta-analysis

1993 cases from 7 RCTs

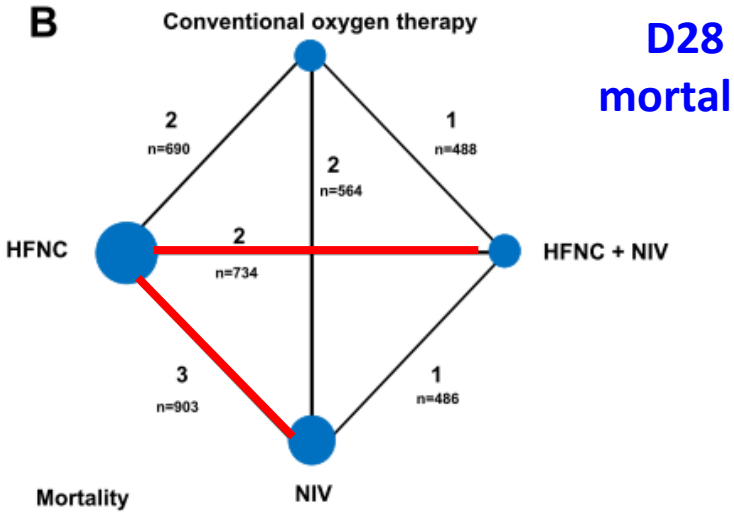
NIV vs. HFNC vs. NIV/HFNC vs. COT

1st endpoint: reintubation in 7 days



D7 reintubate

Comparison	Network risk ratio (95% CI)	p-value		Number needed to treat	Grade
NIV vs COT	0.45 (0.23; 0.88)	0.02		11 (8–50)	Moderate[a]
HFNC vs COT	0.79 (0.40; 1.59)	0.51		NA	Low[a,b]
NIV vs HFNC	0.57 (0.32; 1.02)	0.06	NS	NA	Very low[a,b,c]
NIV + HFNC vs COT	0.36 (0.16; 0.82)	0.01		10 (7–33)	Moderate[a]
NIV + HFNC vs NIV	0.80 (0.38; 1.72)	0.57		NA	Very low[a,b,c]
NIV + HFNC vs HFNC	0.46 (0.23; 0.90)	0.02	**	14 (10–77)	Moderate[a]



D28 mortality

Comparison	Network risk ratio (95% CI)	p-value		Number needed to treat	Grade
NIV vs COT	0.41 (0.13; 1.25)	0.12		NA	Low[a,b]
HFNC vs COT	1.32 (0.43; 4.10)	0.63		NA	Very low[a,b,c]
NIV vs HFNC	0.31 (0.13; 0.74)	<0.01	**	15 (12–40)	Low[a,c]
NIV + HFNC vs COT	0.40 (0.11; 1.43)	0.16		NA	Low[a,b]
NIV + HFNC vs NIV	0.97 (0.29; 3.19)	0.96		NA	Very low[a,b,c]
NIV + HFNC vs HFNC	0.30 (0.10; 0.89)	0.03	**	15 (11–90)	Moderate[a]

Pensier J, et al. eClinicalMedicine 2025

ERS Clinical Practice Guidelines: high-flow nasal cannula in acute respiratory failure

PICO question 7: Should HFNC or NIV be used in nonsurgical patients after extubation?

Recommendation 7

We suggest the use of NIV over HFNC after extubation for patients at high risk of extubation failure unless there are relative or absolute contraindications to NIV (conditional recommendation, moderate certainty of evidence).

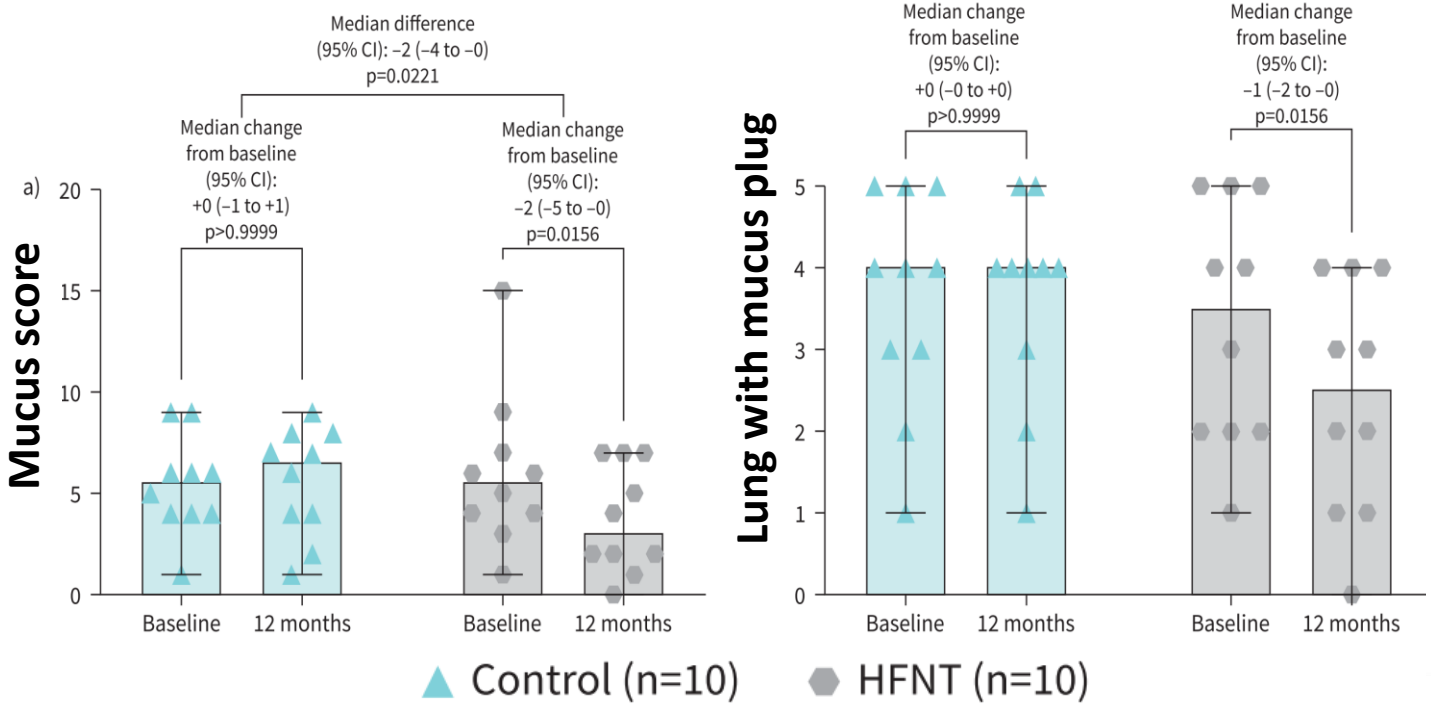
Justification

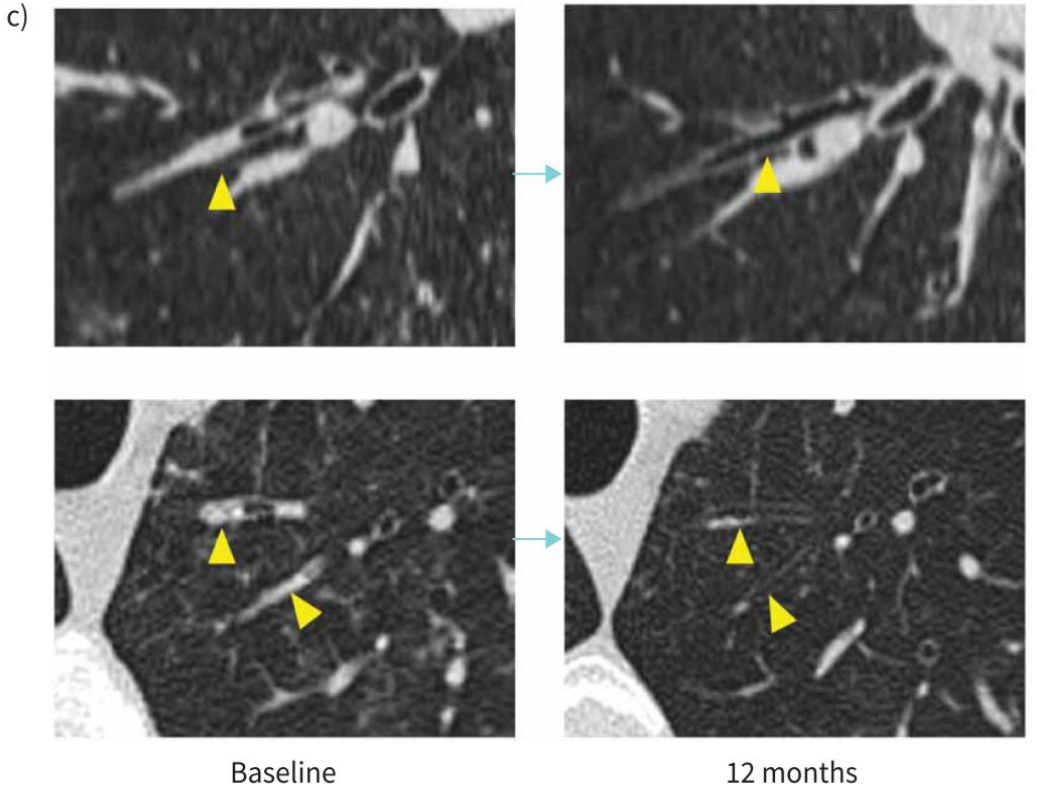
HFNC appears to result in small, but probably clinically important increased risk of reintubation (~4%) compared to NIV in nonsurgical patients at high risk of extubation failure. However, compared to NIV, HFNC slightly improves patient comfort. Therefore, in patients who are intolerant or have contraindications to NIV, HFNC may be an alternative to NIV for preventing post-extubation respiratory failure. NIV interspaced with HFNC breaks between NIV sessions is a strategy that may be effective to further improve oxygenation and reduce post-extubation respiratory failure by gaining the benefits of NIV, with increased comfort from HFNC [113]. The task force judges that the large majority of the patients would value avoiding reintubation over the increased comfort of HFNC, and, thus, in patients without any contraindications, NIV would generally be preferred. There is limited evidence related to costs for both NIV and HFNC, and these are likely to vary between centres.

Oczkowski S, et al. Eur Respir J . 2022.

Impact of long-term high-flow nasal therapy on mucus plugs in patients with bronchiectasis

20 bronchiectasis cases | 10 with home HFNC vs. 10 without HFNC | Chest CT before and after 12 months





Crimi C, et al. ERJ Open Research 2025

An Index Combining Respiratory Rate and Oxygenation to Predict Outcome of Nasal High-Flow Therapy

$$\text{ROX Index} = \frac{SPO_2/FIO_2}{\text{Respiratory Rate}}$$

4.88

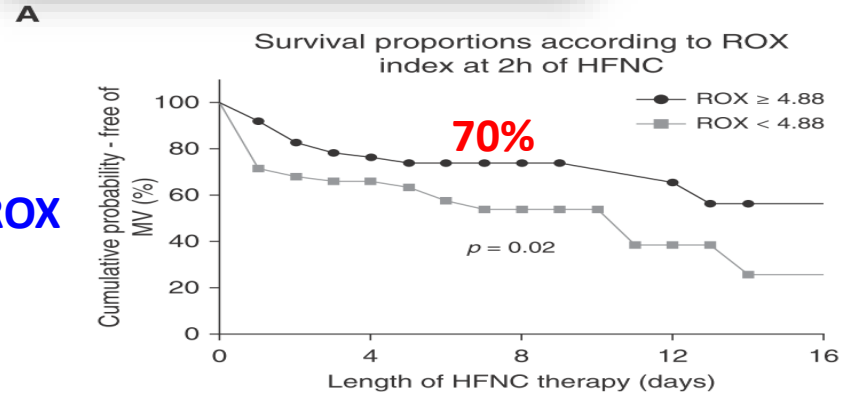
2-yr multicenter prospective observational study

patients with pneumonia treated with HFNC

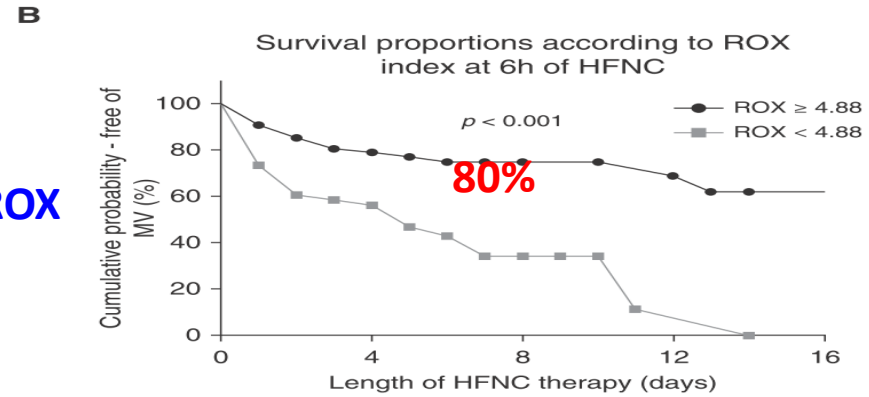
Table 3. Diagnostic Accuracy of Different Respiratory Variables at Different Time Points of Need for MV in Patients Treated with HFNC in the Validation Cohort

Variable	Time	AUROC	95% CI	*P* Value
ROX index	Prior to HFNC	0.659	0.566–0.751	0.001
	2 h	0.679	0.594–0.763	<0.001
	6 h	0.703	0.616–0.790	<0.001
	12 h	0.752	0.664–0.840	<0.001
	18 h	0.755	0.662–0.847	<0.001
	24 h	0.801	0.709–0.893	<0.001

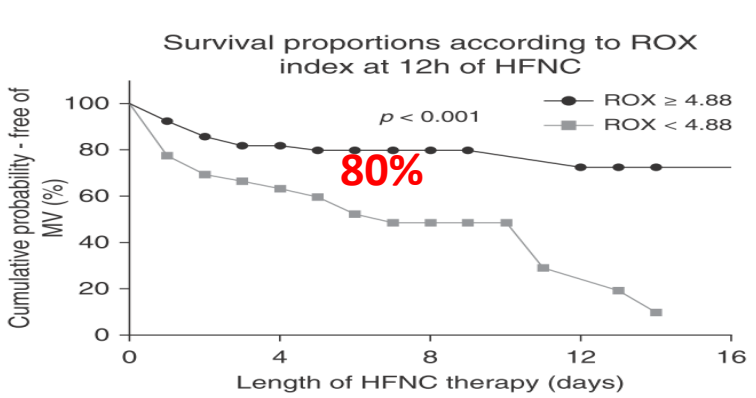
2H ROX



6H ROX

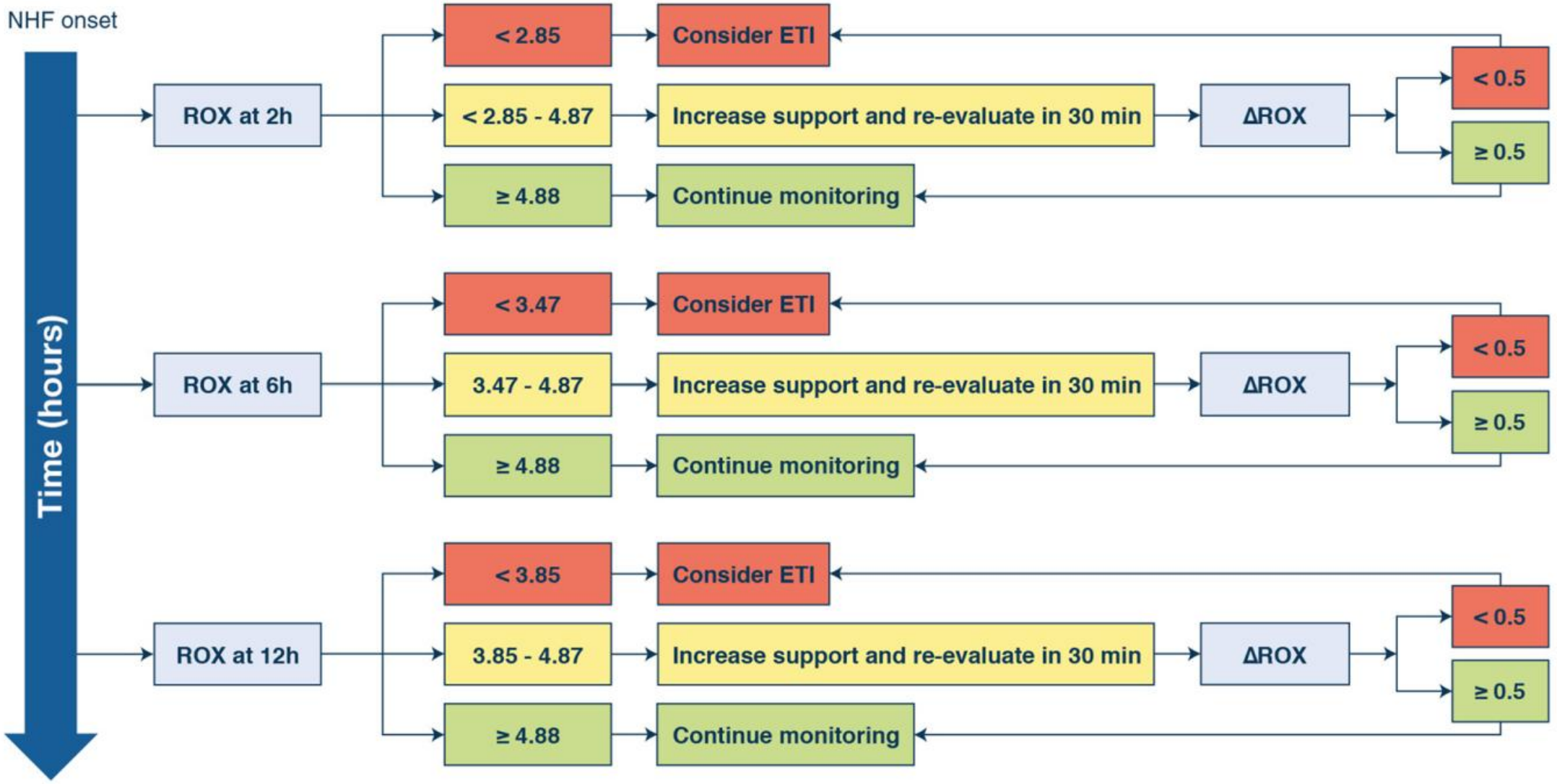


12H ROX



ROX can identify patients with risk for intubation

Roca O, et al. AJRCCM 2019



Close monitoring still required in patients with ROX ≥ **4.88**

Ricard JD, et al. ICM 2020

High Flow Nasal Cannula

Settings

Flow Rate

Set the highest tolerated

Best expressed as

$$\frac{\text{Flow}}{\text{Peak tidal inspiratory flow (PTIF)}}$$

Desirable range 1 - 1.7
PTIF in AHRF ~ 30 L/min

FiO_2

Titrate for SpO_2 targets
88-92% (hypercapnic)
92-96% (hypoxemic)

Temperature

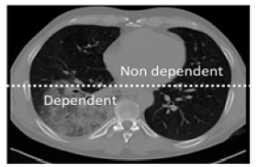
Choose the highest tolerated based on comfort

Type of nasal prongs

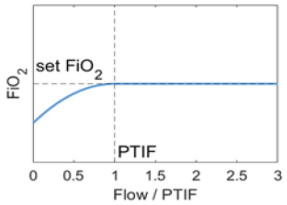
Larger size for hypoxemic patients
Asymmetrical prongs for those with higher respiratory drive

Physiological effects

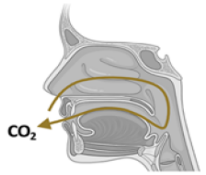
↑ EELV



↑ Alveolar FiO_2



↑ CO_2 wash-out



↑ Comfort

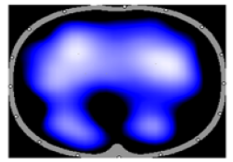
↑ Humidification

Close monitoring with dynamic assessment of physiology!!

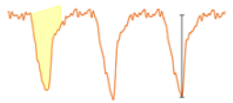
Monitoring

Advanced/Research

EIT



Esophageal pressure



+ Complexity –

ICU

PaO_2 / FiO_2

$PaCO_2$

Out-of-ICU

SpO_2/FiO_2

ROX index

Respiratory rate

Accesory muscles use

Dyspnea

Comfort

Roca O, et al. ICM 2024

The Take Away……

- Both HFNC and NIV provide non-invasive ventilatory support
  - Pros of **HFNC**: constant FiO2, small PEEP, reduce WOB, lower risk of P-SILI, comfort
  - Pros of **NIV**: reliable PEEP with alveolar recruitment, muscle unloading, reduce LV afterload

- ERS 2022 guidelines
  - Recommend HFNC over NIV in acute hypoxemic respiratory failure
  - Recommend NIV over HFNC in high-risk post extubation patients
  - Clinical data are controversial
  - HFNC can be used as a “bridge” therapy

- Prevention is always better than rescue

- NIV alternate with HFNC may offer benefits

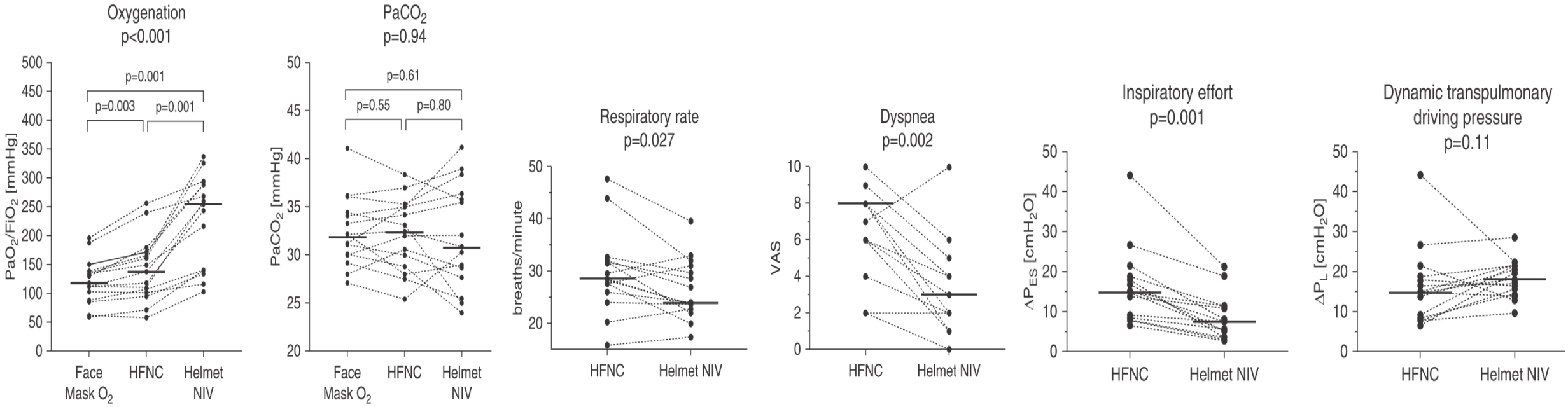
- Frequent evaluation after applying HFNC is important: never delay intubation

Physiological Comparison of High-Flow Nasal Cannula and Helmet Noninvasive Ventilation in Acute Hypoxemic Respiratory Failure

15 hypoxiemic pt with PF ratio<200

Helmet NIV (PEEP >10, PS 10-15) vs. HFNC (50L/min)

Randomize crossover



Grieco DL, et al. AJRCCM 2020

Effect of Helmet Noninvasive Ventilation vs High-Flow Nasal Oxygen on Days Free of Respiratory Support in Patients With COVID-19 and Moderate to Severe Hypoxemic Respiratory Failure

HENIVOT trial

110 COVID patients with PF ratio ≤ 200

Helmet NIV (PEEP >10, PS 10-12) vs. HFNC (60L/min)

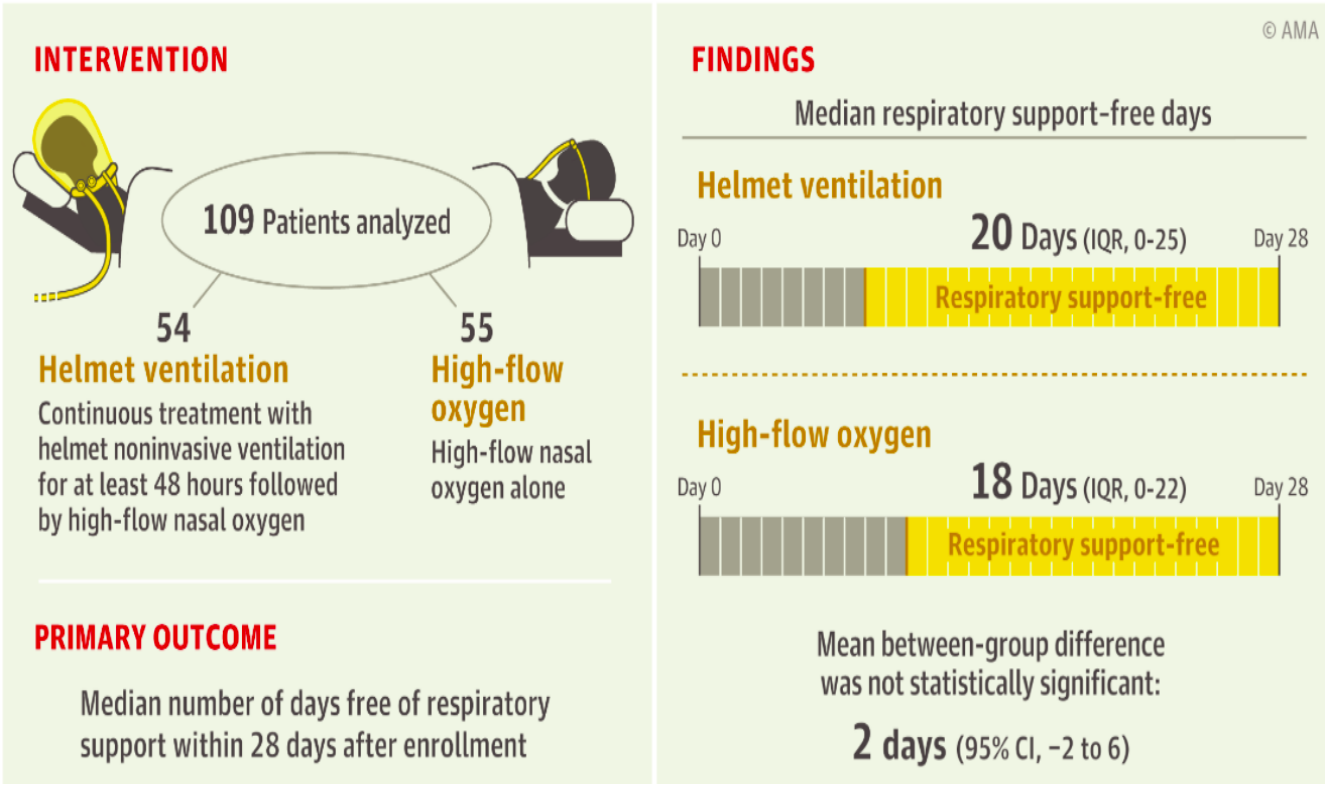
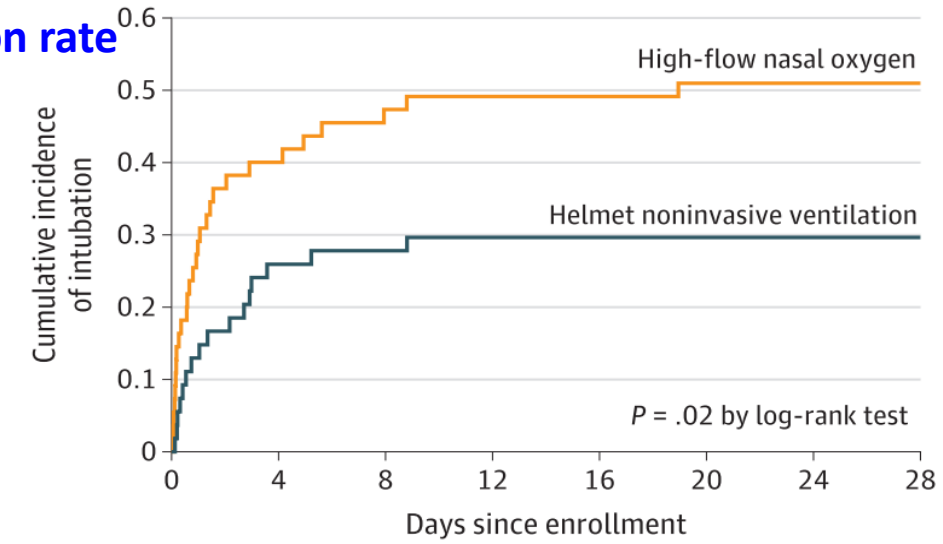


Figure 3. Cumulative Incidence of Intubation Over Time in the Helmet Noninvasive Ventilation and High-Flow Nasal Oxygen Groups to Day 28

Intubation rate



Grieco DL, et al. JAMA 2021

Effect of Postextubation High-Flow Nasal Cannula vs Noninvasive Ventilation on Reintubation and Postextubation Respiratory Failure in High-Risk Patients

JAMA

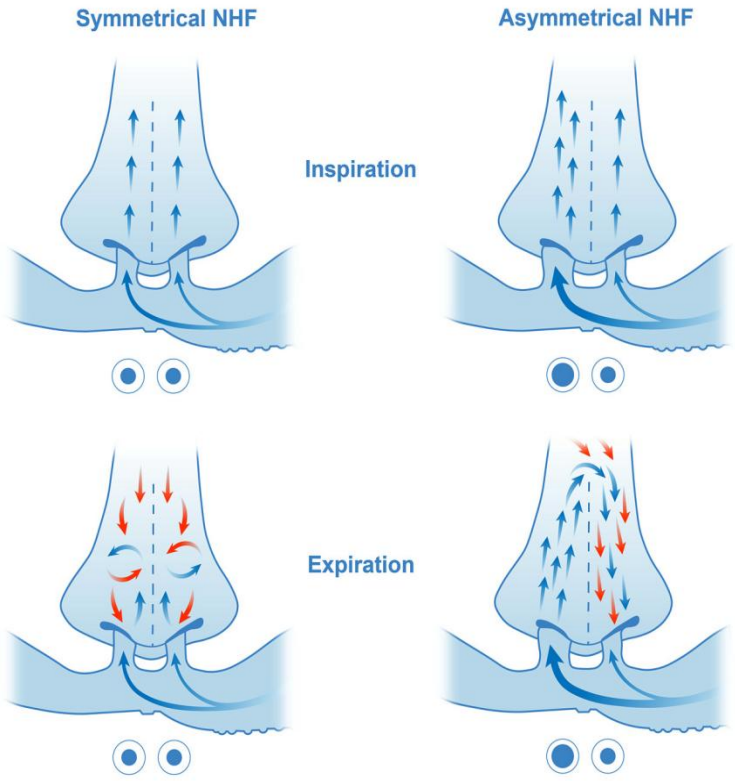
Randomized clinical trial in 3 ICUs in Spain

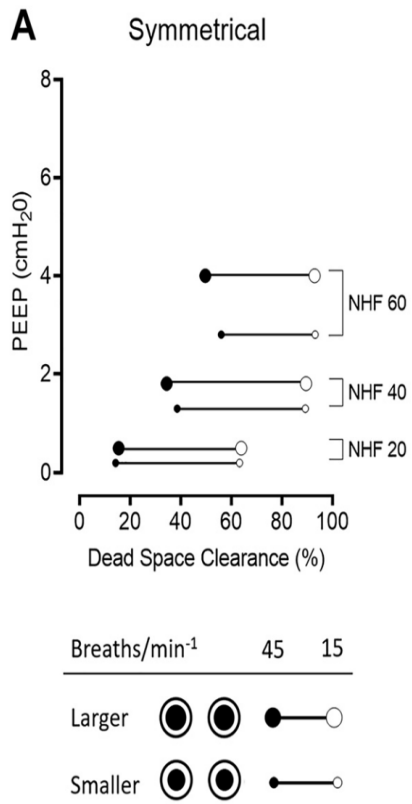
HFN or NIV 24 hrs after extubation

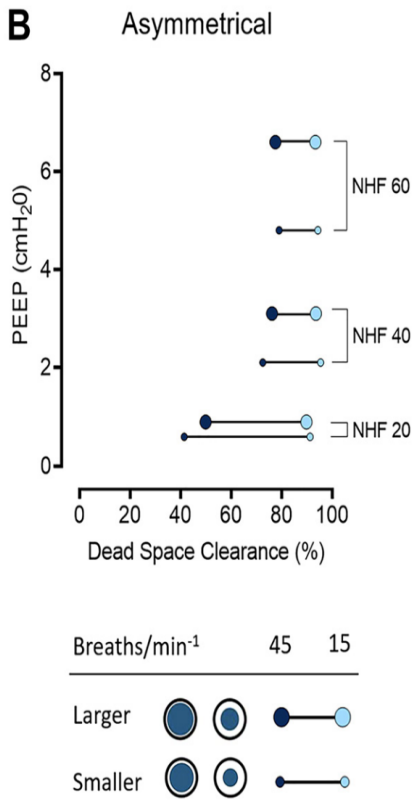
Outcome	NIV	NHF	Absolute difference between groups (95% CI)
Median time to reintubation, hr (IQR)	21.5 (10 to 47)	26.5 (14 to 39)	-5 (-34 to 24)
Outcome	**NIV**	**NHF**	**P value**
Reintubations due to hypercapnic respiratory failure, n (%)	8 (2.5%)	6 (2%)	p = 0.63
Median ICU length of stay, days (IQR)	4 (2 to 9)	3 (2 to 7)	p = 0.048
Adverse events requiring treatment discontinuation for >18 hr, n (%)	135 (42.9)	0 (0)	p < 0.001

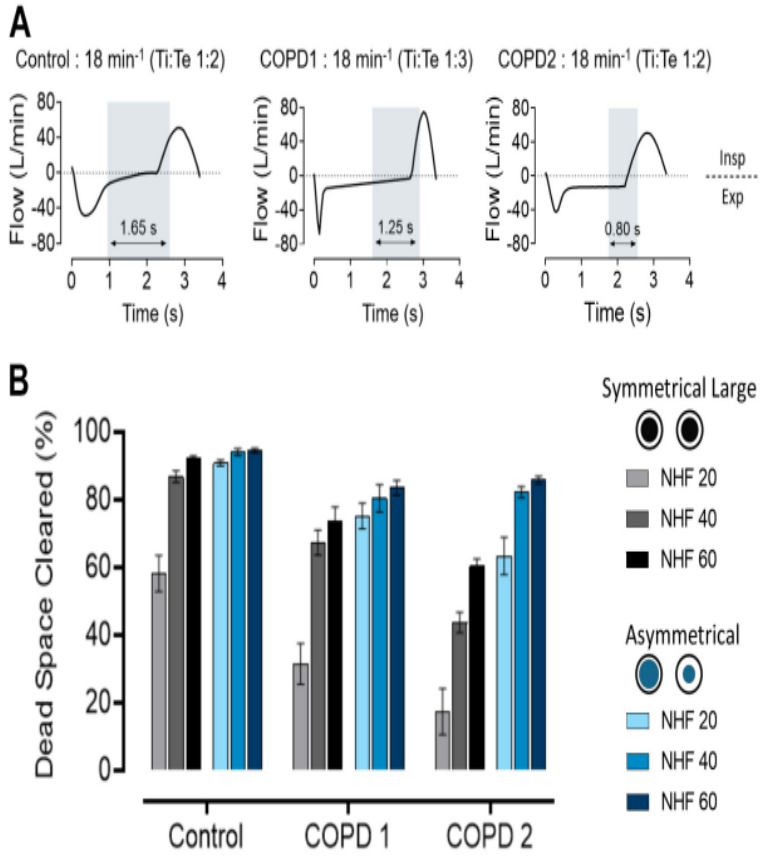
Hernandez G, et al. JAMA 2016

Asymmetrical nasal high flow ventilation improves clearance of CO2 from the anatomical dead space and increases positive airway pressure



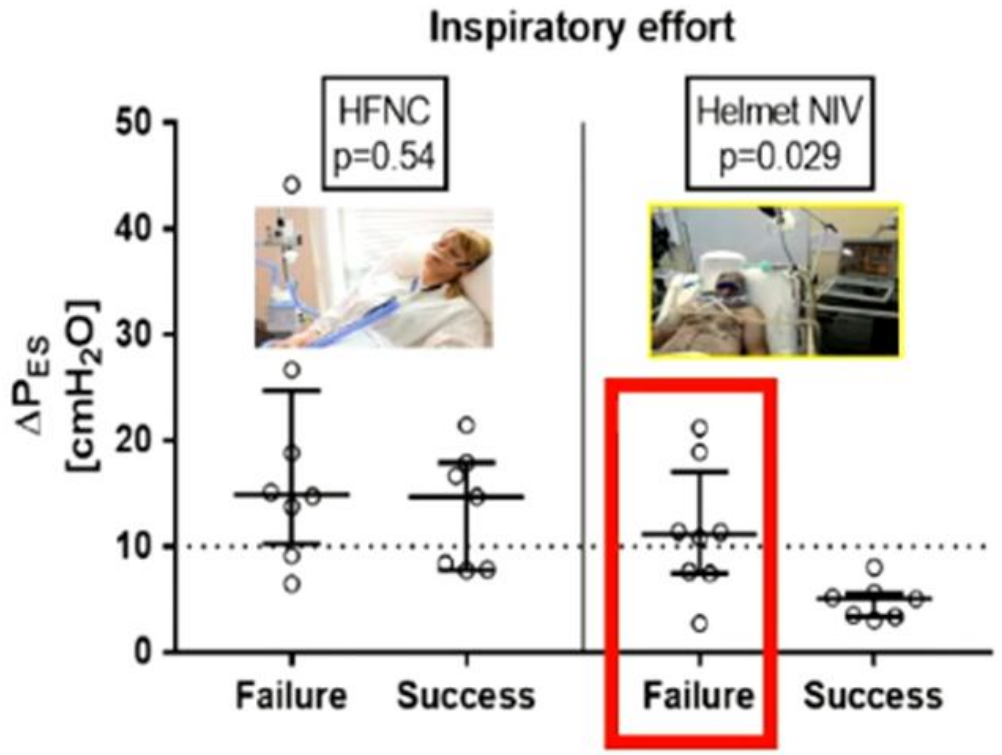


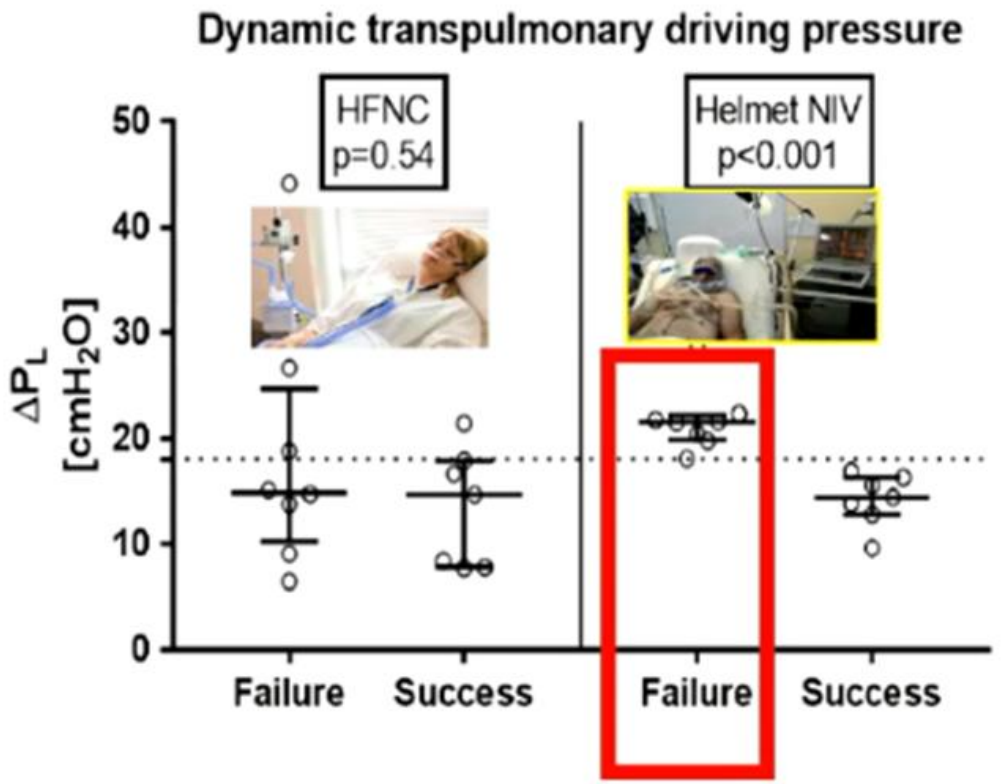




Tatkov S, et al. J Appl Physio 2023

Lower risk of P-SILI in HFNC vs. NIV-helmet





P-SILI: patient self-inflicted lung injury

Grieco DL, et al. AJRCCM 2019

ESICM guidelines on acute respiratory distress syndrome: definition, phenotyping and respiratory support strategies

- Question 3.2: In non-mechanically ventilated patients with AHRF not due to cardiogenic pulmonary edema or acute exacerbation of COPD, does HFNO compared to non-invasive ventilation reduce mortality or intubation?

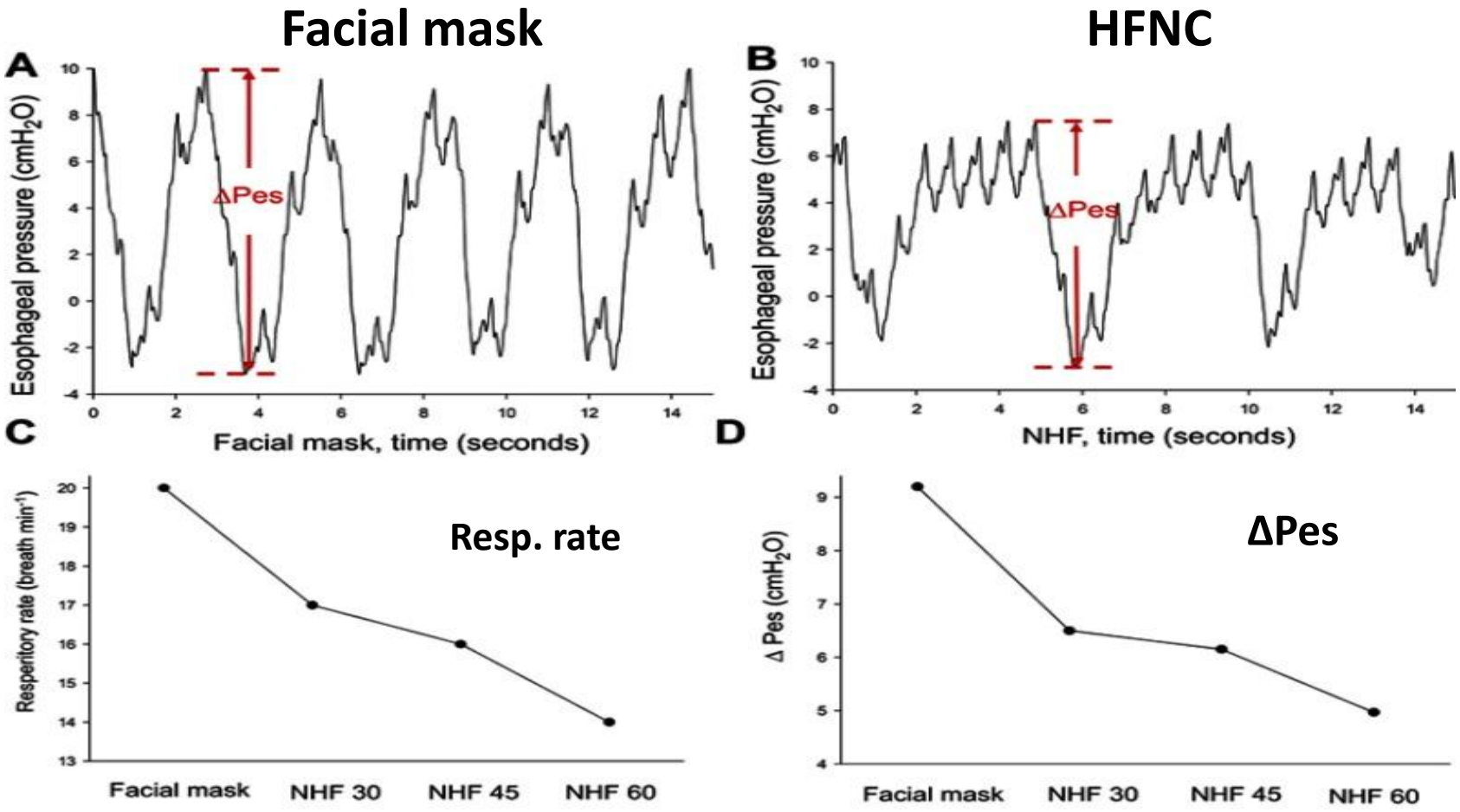
- Recommendation 3.2:
  - We are unable to make a recommendation for or against the use of HFNO compared to continuous positive airway pressure (CPAP)/NIV to reduce intubation or mortality in the treatment of unselected patients with acute hypoxemic respiratory failure not due to cardiogenic pulmonary edema or acute exacerbation of COPD.
  - We suggest that CPAP/NIV can be considered instead of HFNO for the treatment of AHRF due to COVID-19 to reduce the risk of intubation (weak recommendation, high level of evidence), but no recommendation can be made for whether CPAP/NIV can decrease mortality compared to HFNO in COVID-19.

Grasselli G, et al. ICM 2023

FLORALI vs. RENOVATE

	FLORALI	RENOVATE (hypoxic group)
Case number	310	485
Inclusion	PaO2 <300 in >10L O2	SpO2 <90 or PaO2<60
Exclusion	Neutropenia	Immunocompromised
Design	Multicenter, RCT	Multicenter, RCT, non-inferior (10% margin)
1st endpoint	Intubation in 28 days	Intubate/death in 7 days
PF ratio	Mean 156 (77% <200)	Median 191-194
Resp rate	33±6	28 (26-31)
Severity	SAPS II: 25	SAPS III: 60
Pneumonia	80%	Not reported
NIV setting	Target volume 7-10ml/kg	Target volume 6-9ml/kg
HFNC/NIV days	>2 days	HFNC 2 days/NIV 1 day
Outcome		
Intubation rate	28 days: 38% vs. 50%**	7 days: 31% vs. 29%
28D mortality	11% vs. 25%	24.5% vs. 28.4%
90D mortality	12% vs. 23%	29.7% vs. 33.9%
28 days MV free	24 days vs. 19 days	Median: 28 das vs. 28 days

HFNC decrease inspiratory efforts and P-SILI



Decreased esophageal pressure swing

Less risk of P-SILI

Reduce respiratory effort

P-SILI: patient- self inflicted lung injury

Mauri T, et al. Open Access Emerg Med. 2019