NIPPV and HFNC for critically ill patients

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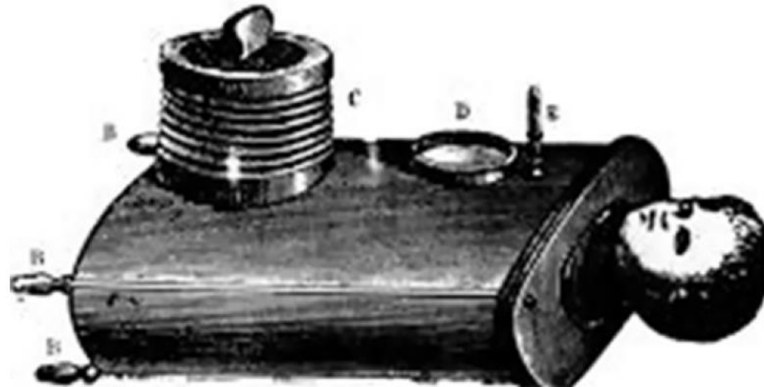
Outlines

- Current device of non-invasive respiratory support
- Indications of non-invasive respiratory support
- Parameters predicting failure of non-invasive respiratory support.

Devices of non-invasive respiratory support

- Negative pressure ventilator



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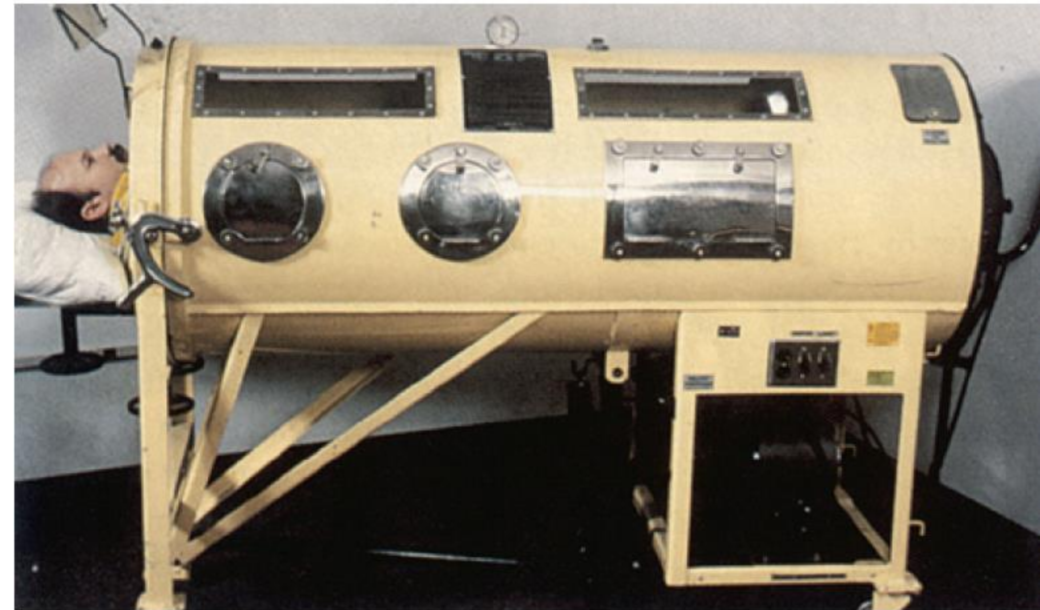


EGAN’S FUNDAMENTALS OF RESPIRATORY CARE, TWELFTH EDITION

Non-invasive respiratory support

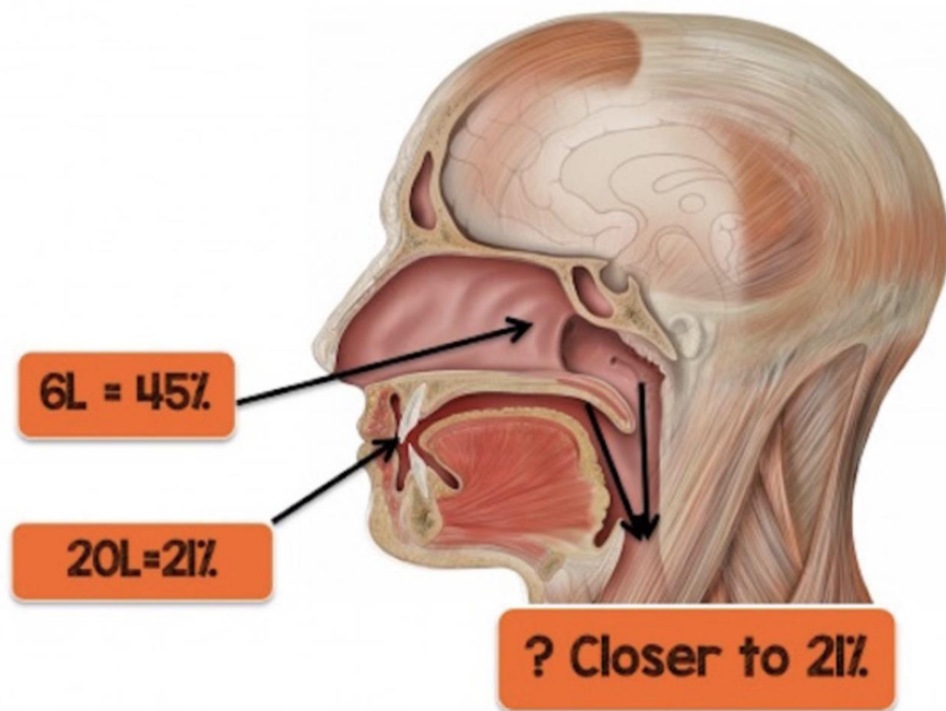
- Conventional oxygen therapy (COT)
  - ✓Nasal cannula
  - ✓Simple mask
  - ✓Non-rebreathing mask
  - ✓Venturi mask
- **High-flow nasal cannula (HFNC)**
- **Pressure support non-invasive ventilation (NIV)**

HFNC

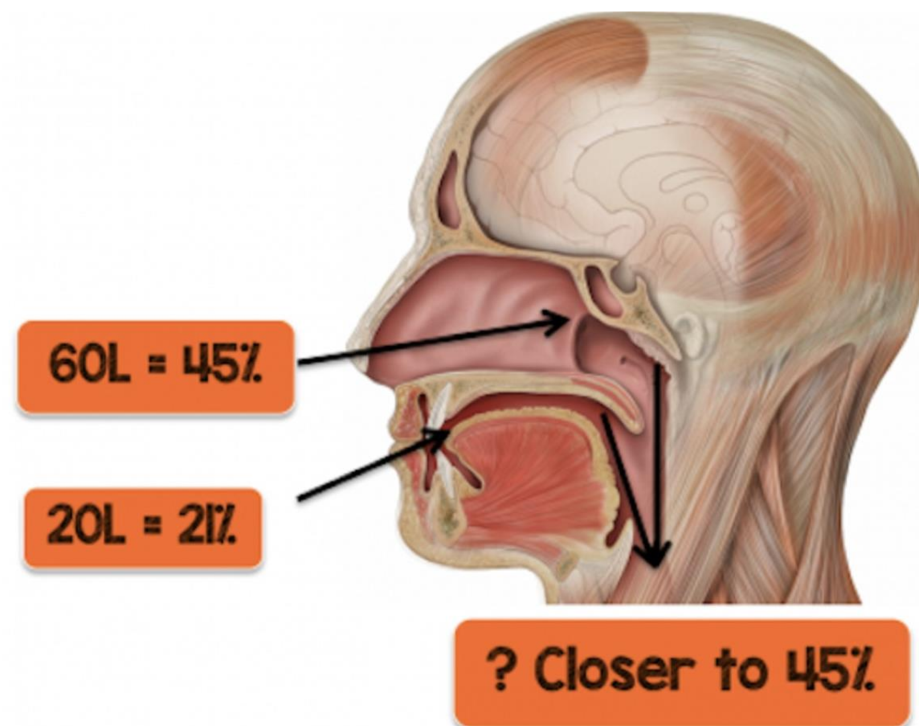
- Warm and wet airflow
- Delivered set FiO_2 and washout nasopharyngeal dead space
- Reduce inspiratory effort and provide positive airway pressure (4 cmH_2O)
- Setting
  - ✓ FiO_2: 0.21 – 1
  - ✓ Gas flow: 40 – 60 L/min
  - ✓ Temperature: 31 – 37°C

Grieco DL, et al., Intensive Care Med. 2021 Aug;47(8):851-866.

Physiologic effects of high-flow nasal cannula



Nasal Cannula



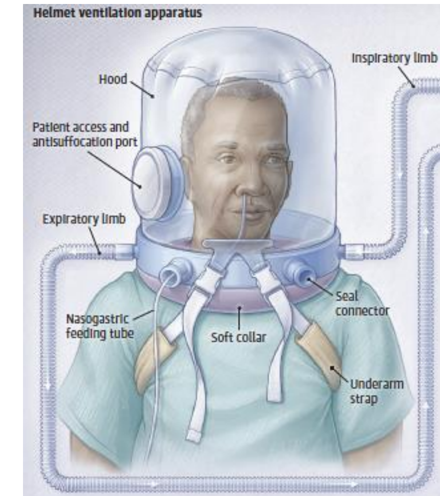
High-FlowNasal Cannula

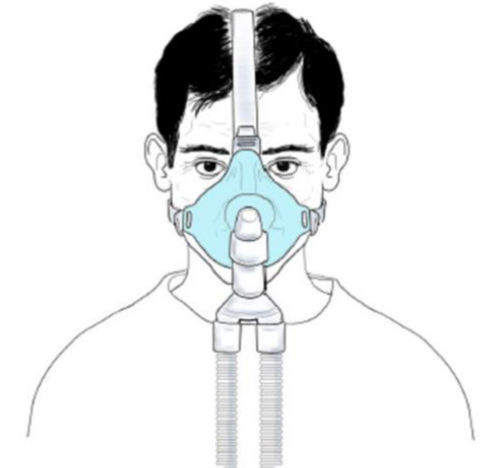
- Washout of anatomical deadspace
- Reduction of respiratory efforts
- Optimization in patients comforts

Lodeserto et al., Cureus. 2018 Nov 26;10(11):e3639; Maggiore et al., Intensive Care Med. 2023 Jun;49(6):673-676.

Non-invasive ventilation (NIV, NPPV)

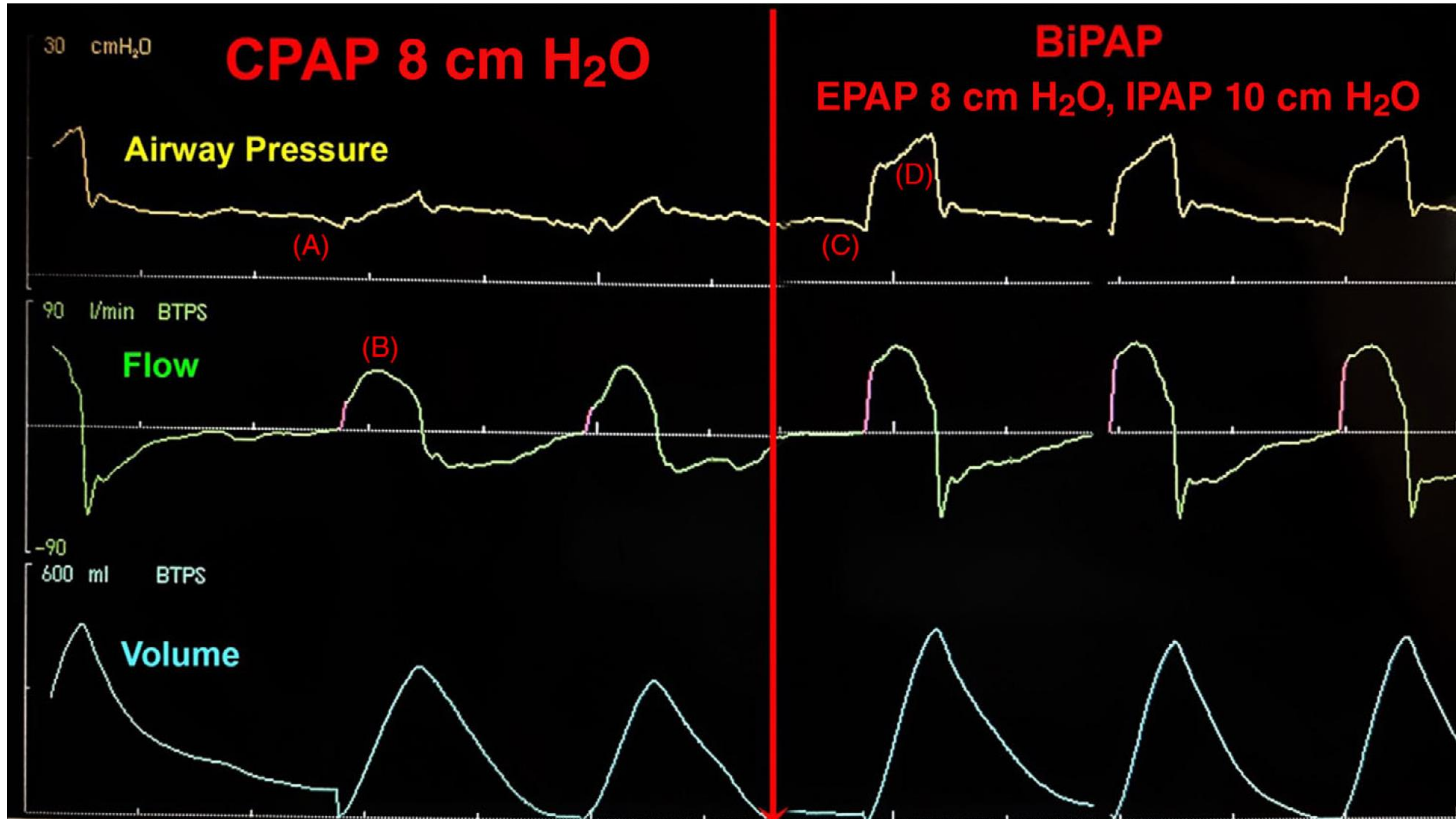
- CPAP or BIPAP
- Facemask (oronasal or full-face) or Helmet
- Setting
  - PEEP 5 – 8 (facemask) or 10 – 12(helmet) cmH_2O
  - PS: 7 – 10 (facemask) or 10 – 12 (helmet) cmH_2O
- Skin ulcer, air leaks (facemask); impossibility to measure tidal volume, asynchrony, upper limbs edema, dead space (helmet)
- Delayed intubation





Grieco DL, et al., Intensive Care Med. 2021 Aug;47(8):851-866.

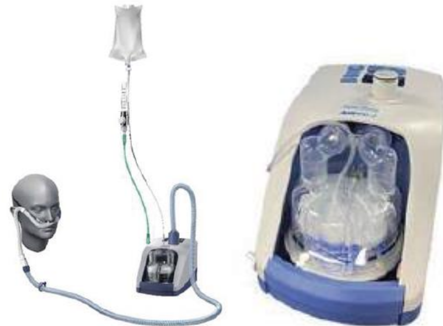
NIPPV provided PEEP and a driving pressure



Mosier et al., J Am Coll Emerg Physicians Open. 2024 Mar 7;5(2):e13118.

HFNC vs NIV

	HFNC	NIV
Interface	Nasal prone	Facemask or Helmet
O2 flow	Warm and wet (31 – 37°C)	Depends on machine
FiO_2	Constant (30 – 60 L/mins)	Depends on machine
PEEP (improve atelectasis)	3 – 4 cmH_2O	5 – 12 cmH_2O
Driving pressure (reduce muscle fatigue)	No	7 – 12 cmH_2O
Limitation	Hypercapnia, can not control V_T	Dealy intubation, can not control V_T
Adverse events	Nasal bleeding	Skin ulcer, air leaks, asynchrony, upper limbs edema, dead space
Prediction model	ROX index	HARCOR



Grieco DL, et al., Intensive Care Med. 2021 Aug;47(8):851-866.

Indications of non-invasive respiratory support

NIPPV	HFNC
• **Cardiogenic pulmonary edema** • **Hypercapnic respiratory failure** • **COPD exacerbation** • **Acute hypoxic respiratory failure** • **Immunocompromised patients** • Weaning from mechanical ventilation • Obesity hypoventilation • Post-operative • Asthma?	• **Acute hypoxic respiratory failure** • **Weaning from mechanical ventilation** • Acute hypercapnic respiratory failure?

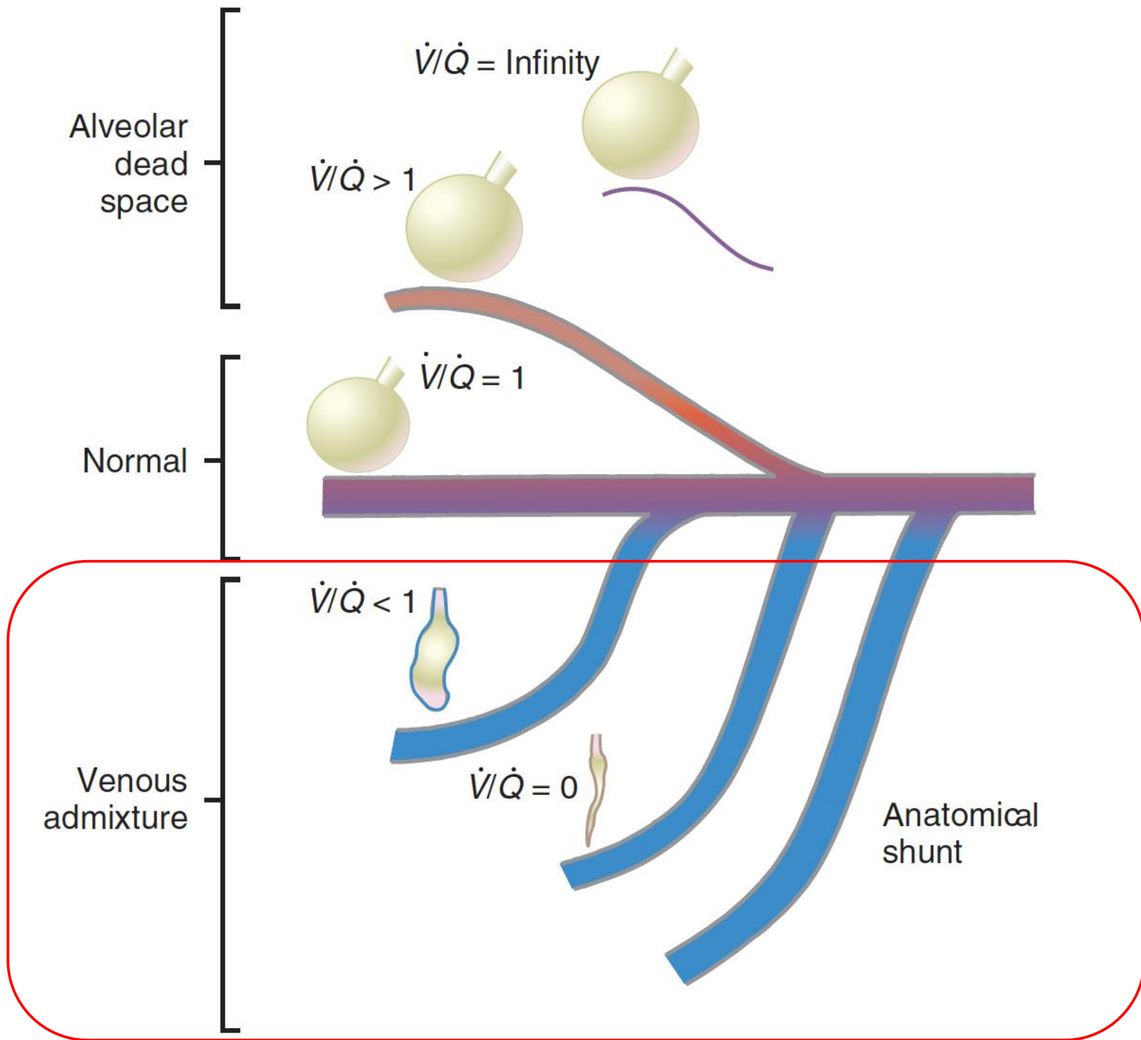
Munshi et al., N Engl J Med. 2022 Nov 3;387(18):1688-1698; Maggiore et al., Intensive Care Med. 2023 Jun;49(6):673-676.

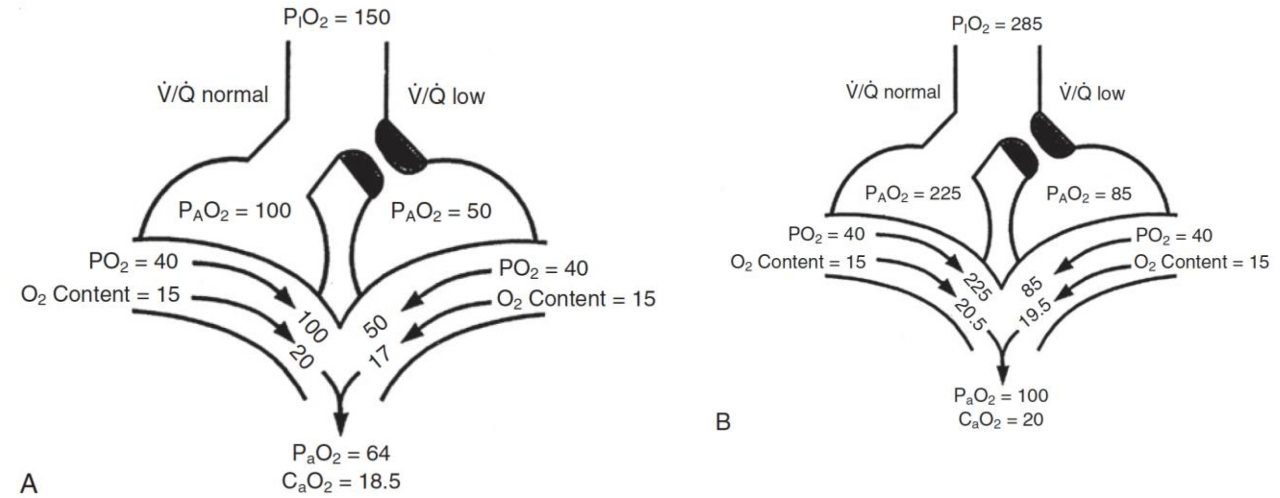
Why NIV or HFNC?

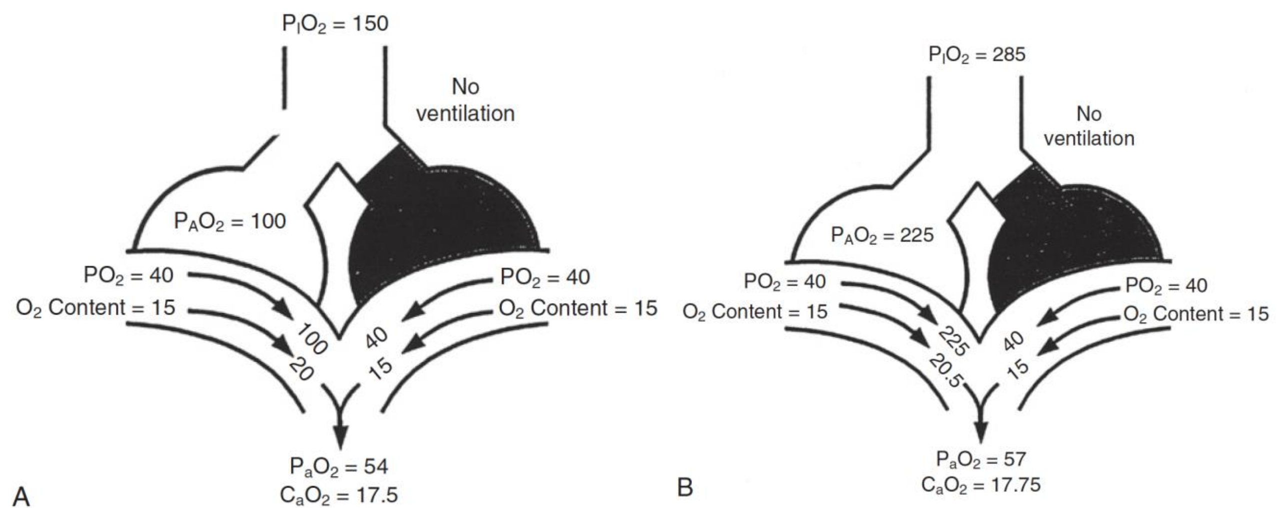
Respiratory failure

- Oxygenation failure
- Ventilation failure

Oxygenation failure (hypoxemia)

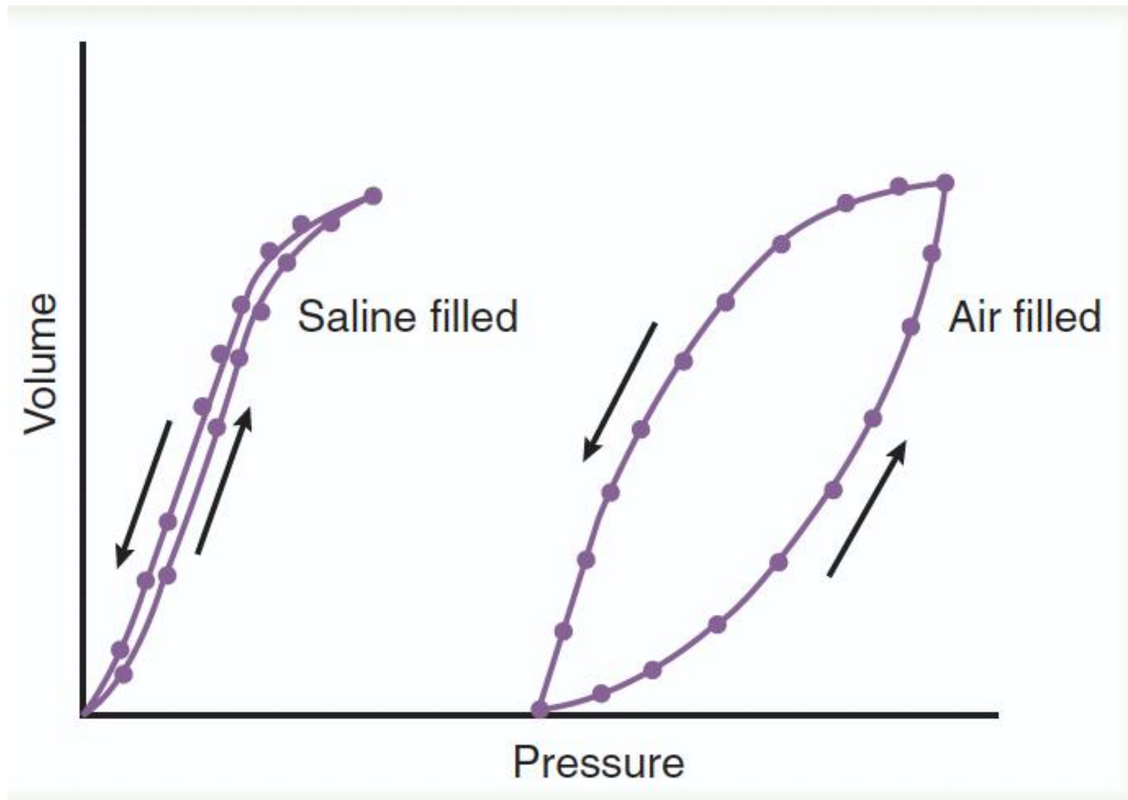


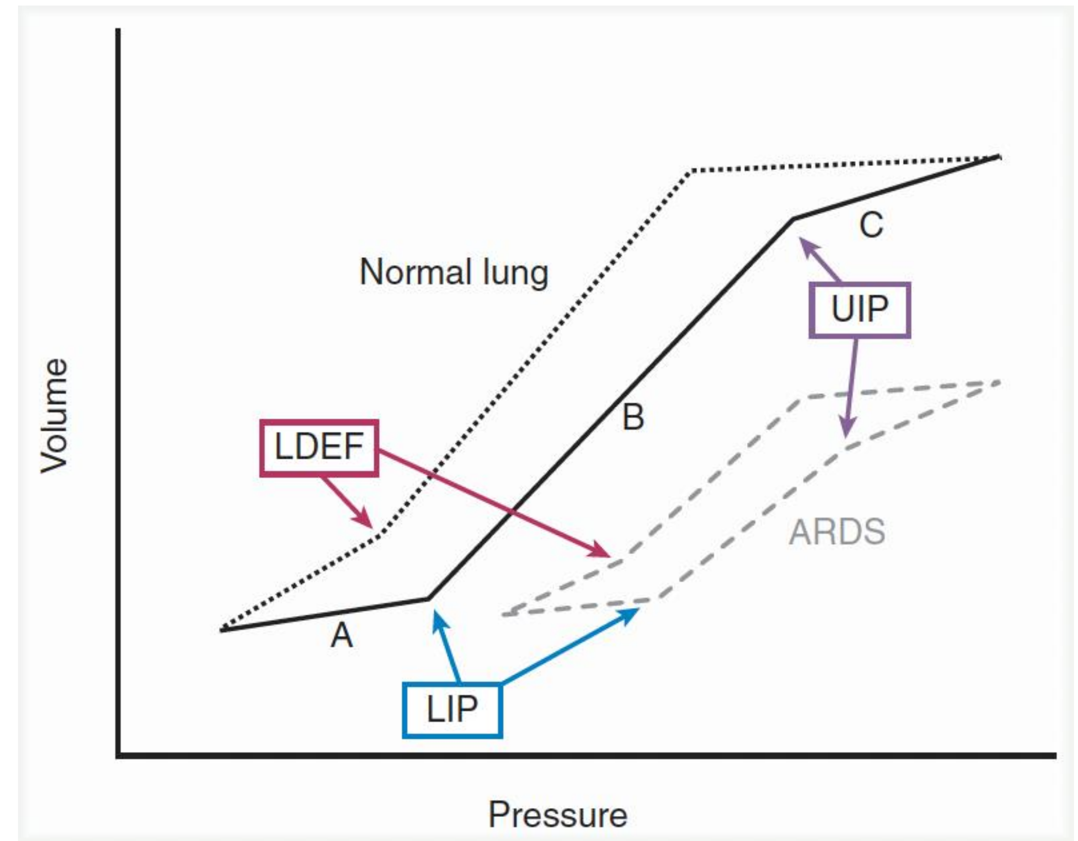




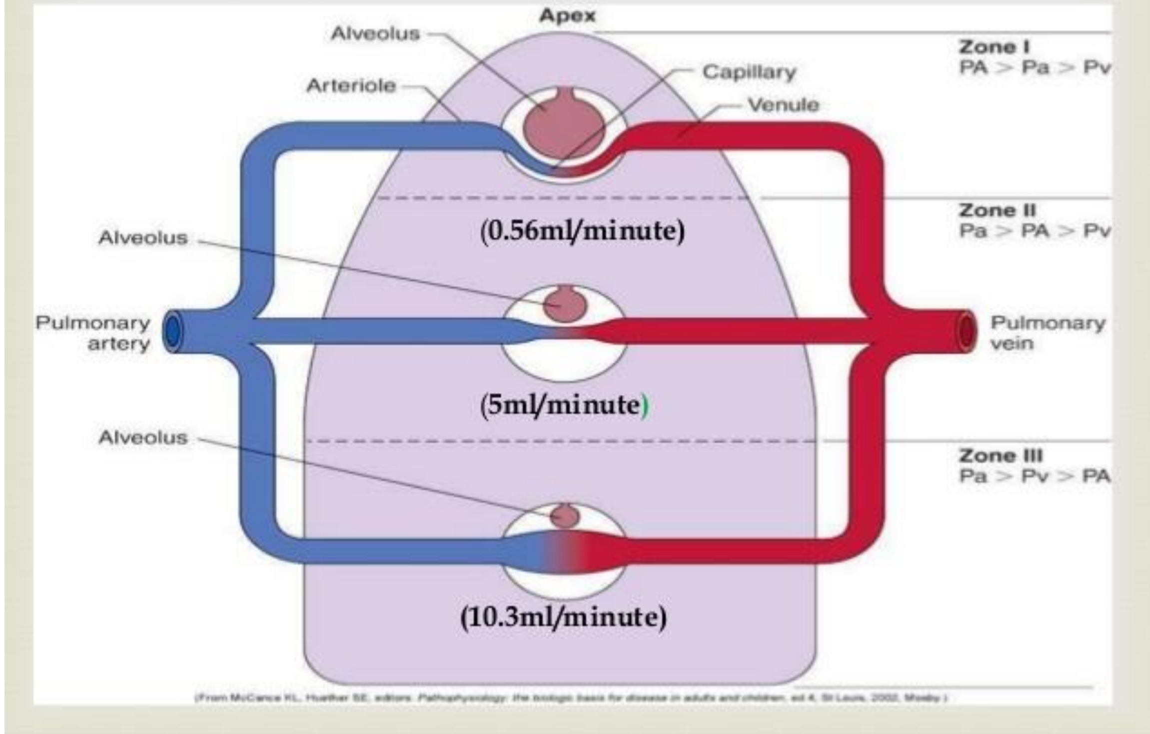
EGAN'S FUNDAMENTALS OF RESPIRATORY CARE, TWELFTH EDITION

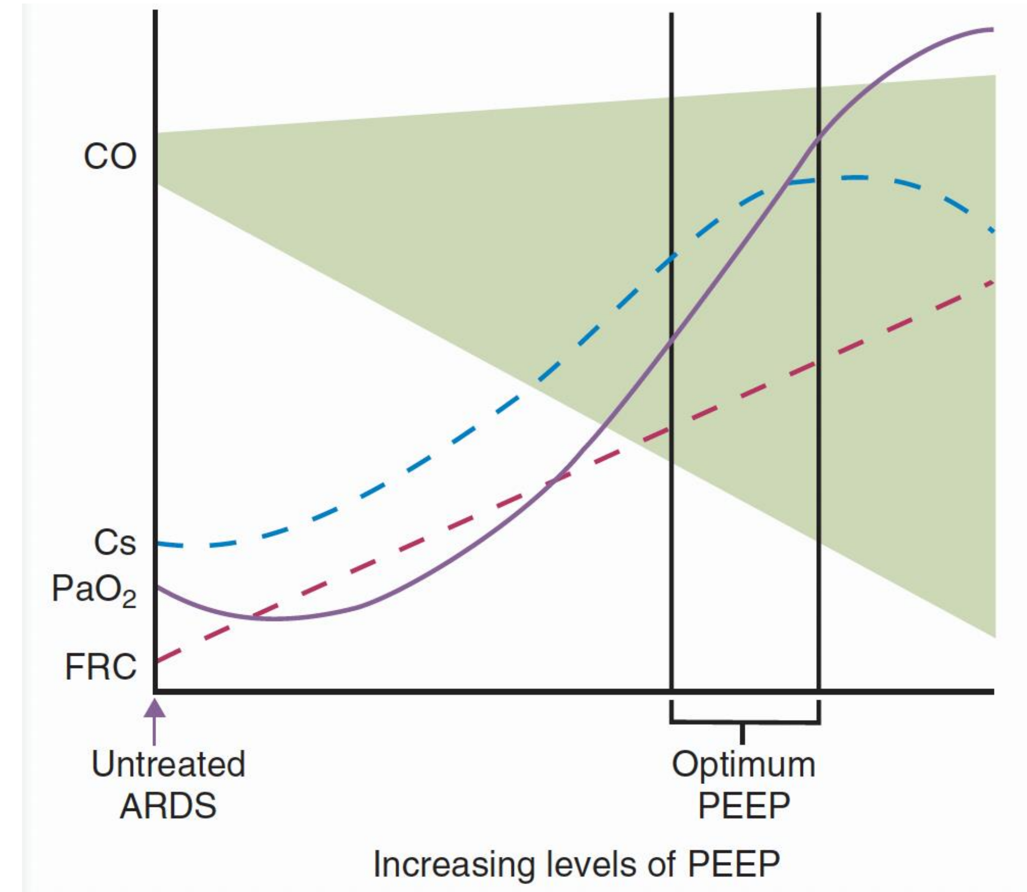
PEEP: keep the lung open





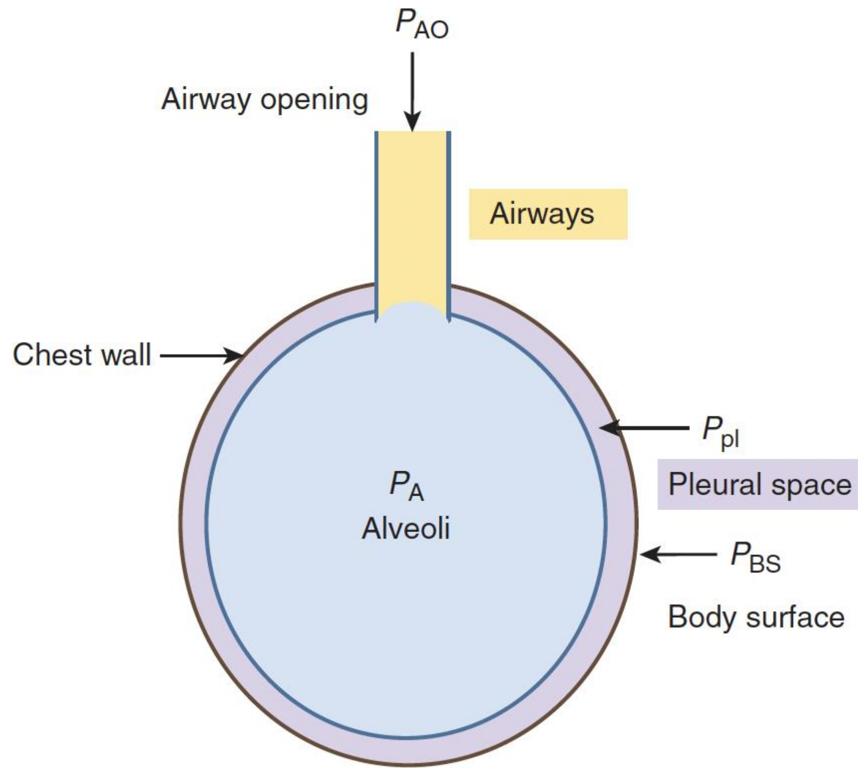
PEEP: keep the lung open





- Increasing functional residual capacity (FRC)
- Improving oxygenation

Ventilation



Definition	Name	Symbol
$P_{AO} - P_{BS}$	Transrespiratory pressure difference	ΔP_{TR}
$P_{AO} - P_A$	Transairway pressure difference	ΔP_{TAW}
$P_{AO} - P_{pl}$	Transpulmonary pressure difference	ΔP_{TP}
$P_A - P_{pl}$	Transalveolar pressure difference	ΔP_{TA}
$P_A - P_{BS}$	Transthoracic pressure difference	ΔP_{TT}
$P_{pl} - P_{BS}$	Trans–chest wall pressure difference	ΔP_{TCW}
	Global muscle pressure difference	ΔP_{mus}

Lung volume

450.00
400.00
350.00
300.00
250.00
200.00
150.00
100.00
50.00
0.00
−50.00
−100.00
−150.00
−200.00
−250.00

5.010 6.000 7.000 8.000 9.000 10.000

Air flow

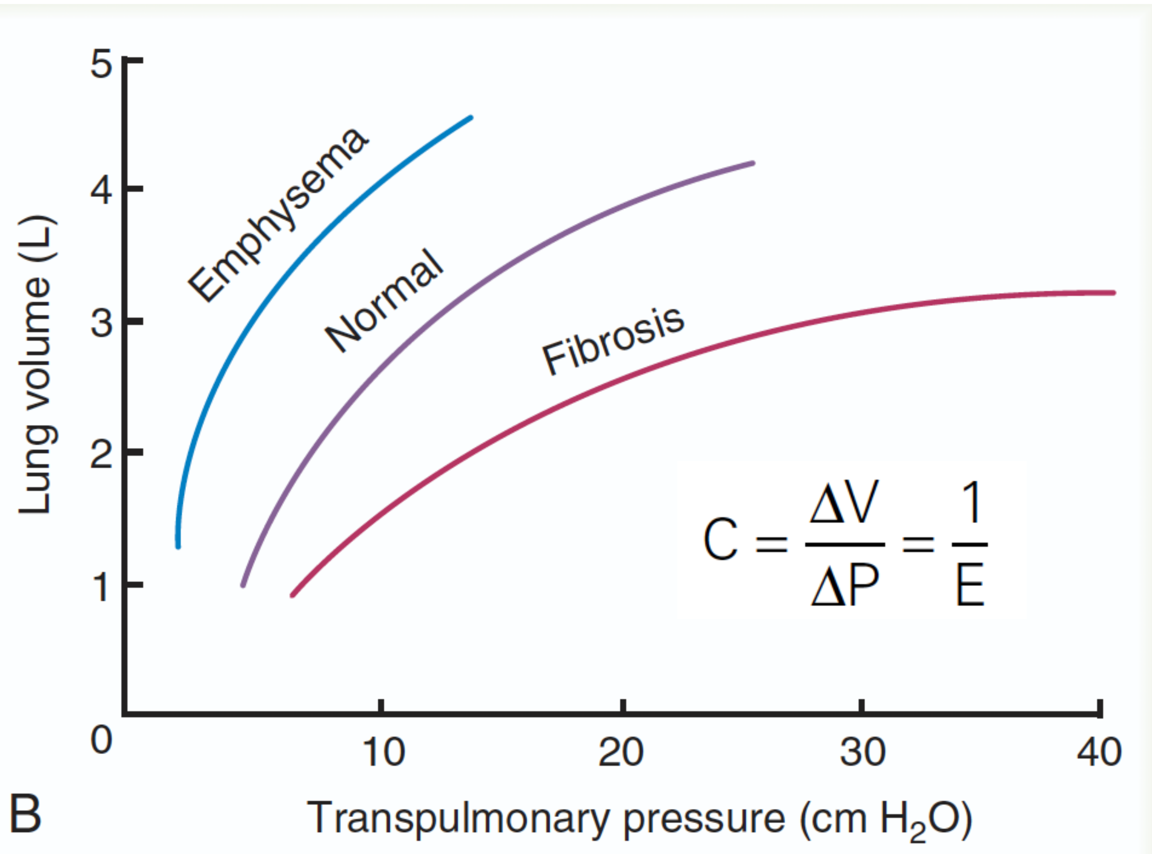
P_A

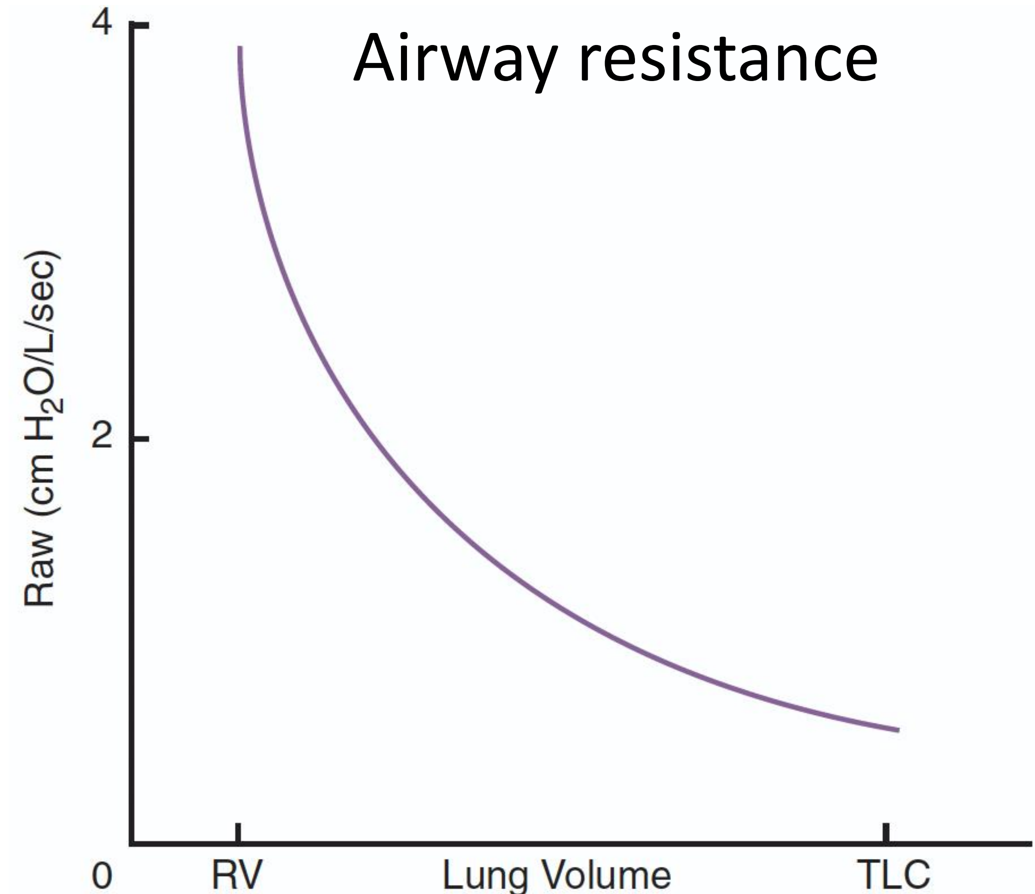
P_{pl}

EGAN'S FUNDAMENTALS OF RESPIRATORY CARE, TWELFTH EDITION

Opposing force during inspiration

Lung compliance





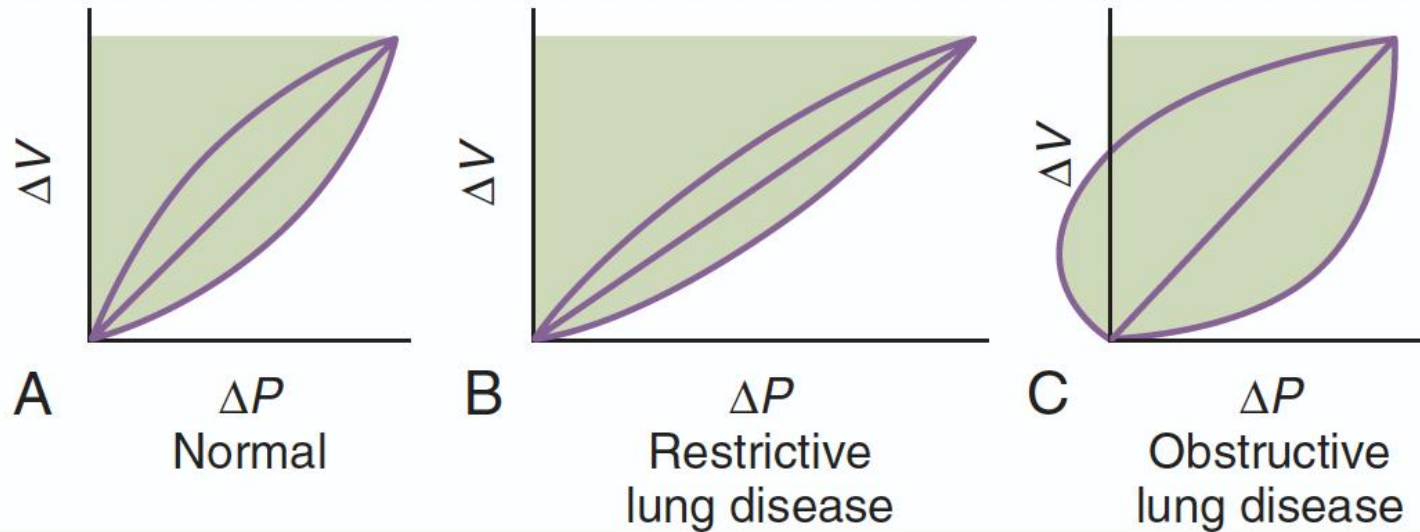
Location	Total Resistance (%)
Nose, mouth, upper airway	50
Trachea and bronchi	30
Small airways (<2 mm)	20

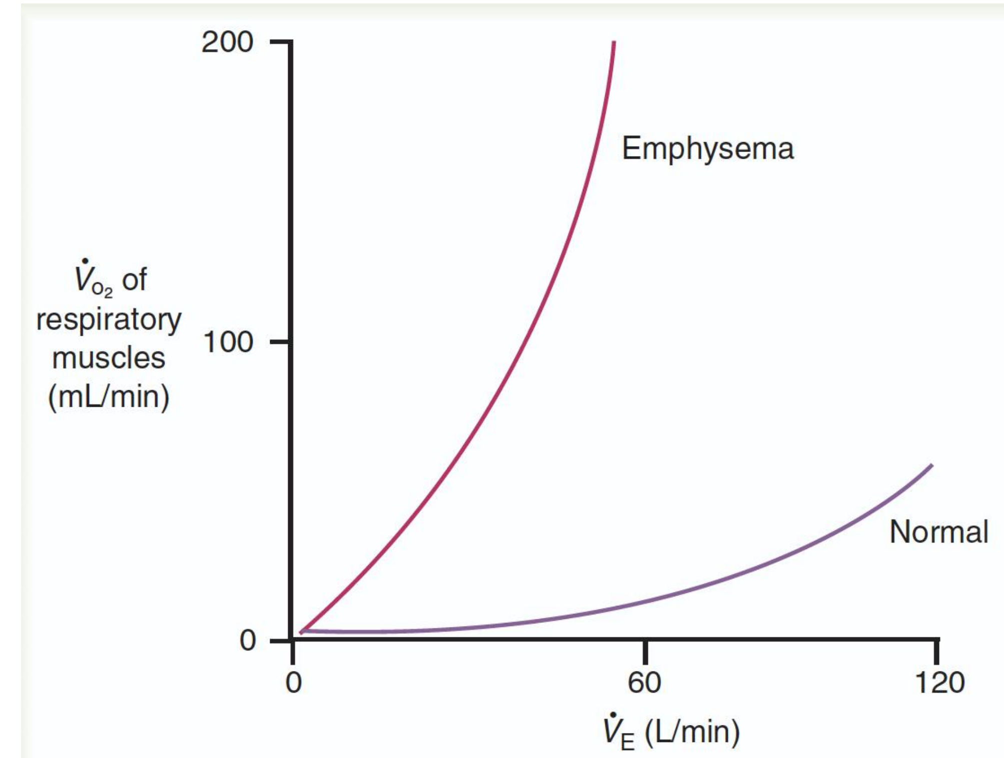
EGAN'S FUNDAMENTALS OF RESPIRATORY CARE, TWELFTH EDITION

Work of breath

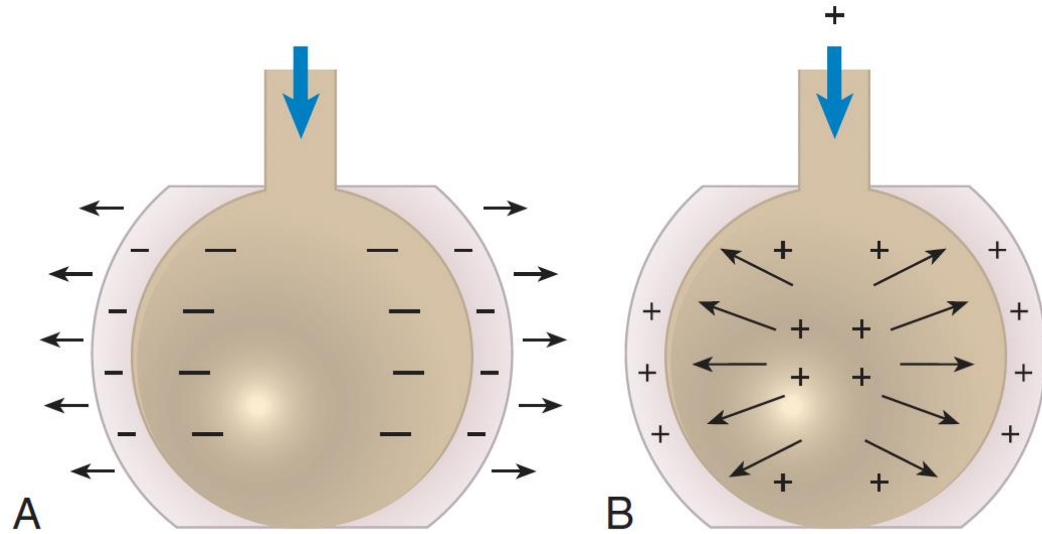
$$\text{Work} = \text{Force} \times \text{Distance}$$

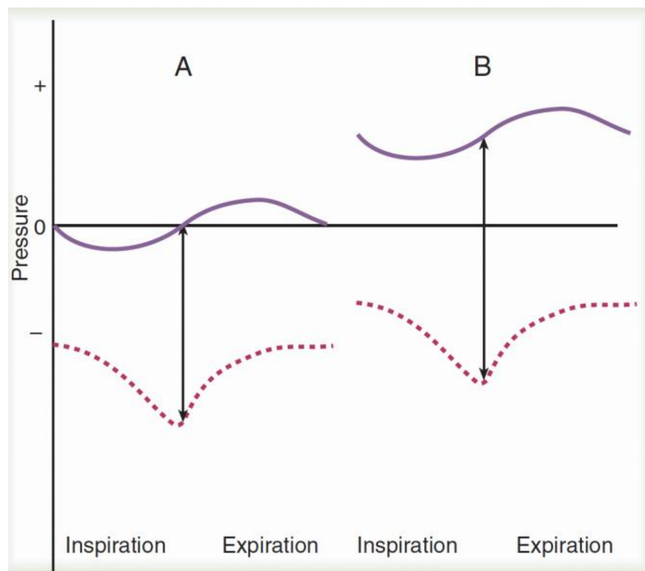
$$\text{Pressure} \times \text{Volume} = \frac{\text{Force}}{\text{Area}} \times (\text{Area} \times \text{Distance})$$
$$= \text{Force} \times \text{Distance}$$
$$= \text{Work}$$





A driving pressure helps to open the lung, and PEEP to keep the lung open





- Reducing end-expiratory atelectasis (lung recruitment)
- Unloading respiratory muscle
- Increasing functional residual capacity (FRC), improving oxygenation
- Decreasing inspiratory force, lung strain, and work of breath
- Increasing overdistension

Hypercapnic respiratory failure and COPD

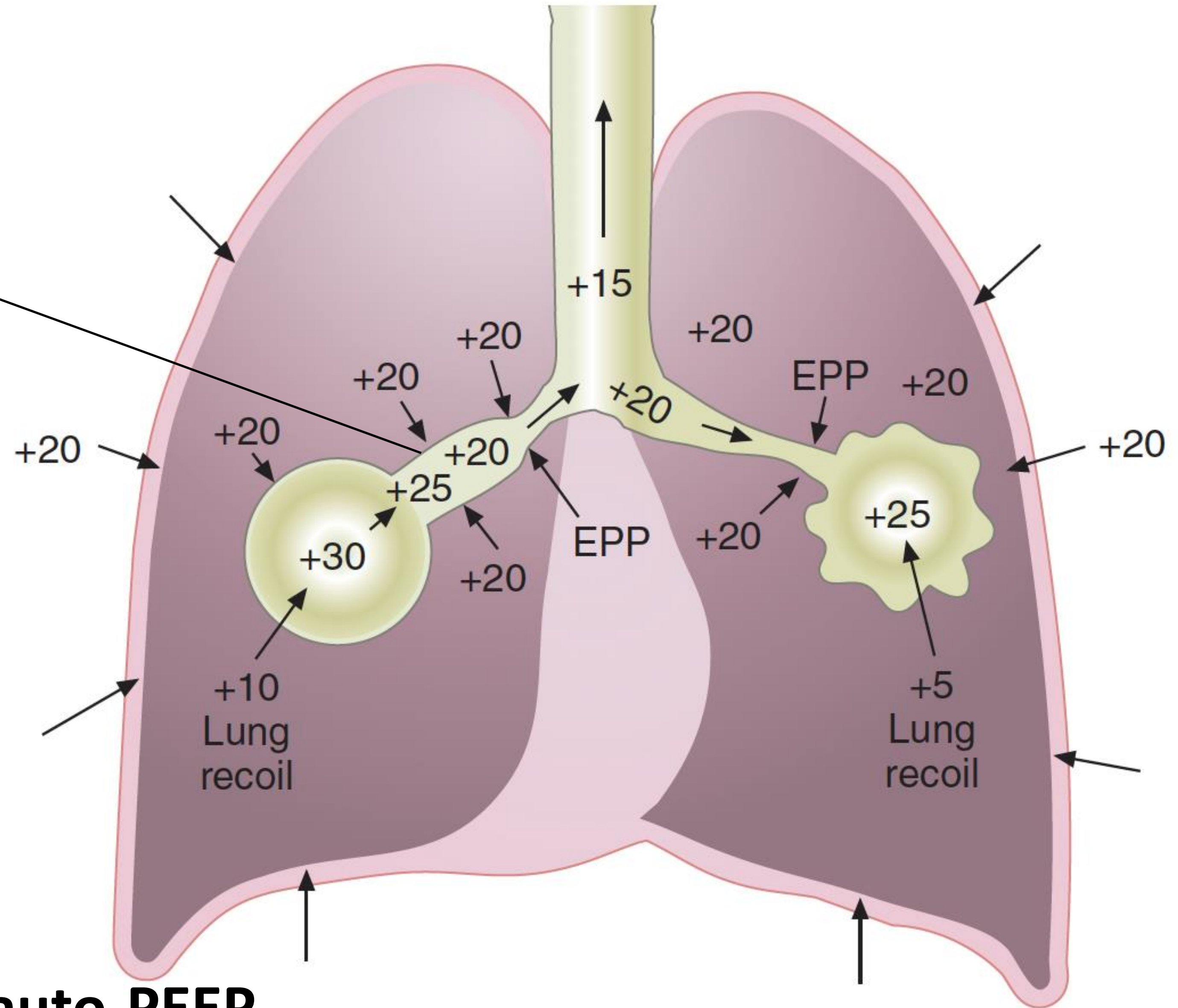
Pressure gradient during expiration

How to help patients with COPD with a PEEP

Transmural pressure

Equal pressure point (EPP)

Dynamic compression of airway

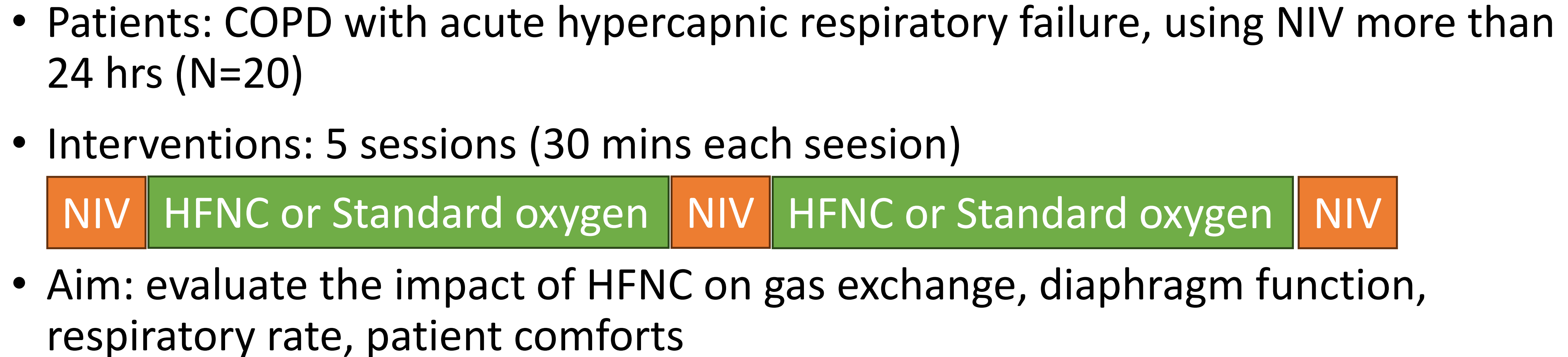


- **Prevent airway closing**
- **Help the patient to conquer auto-PEEP**

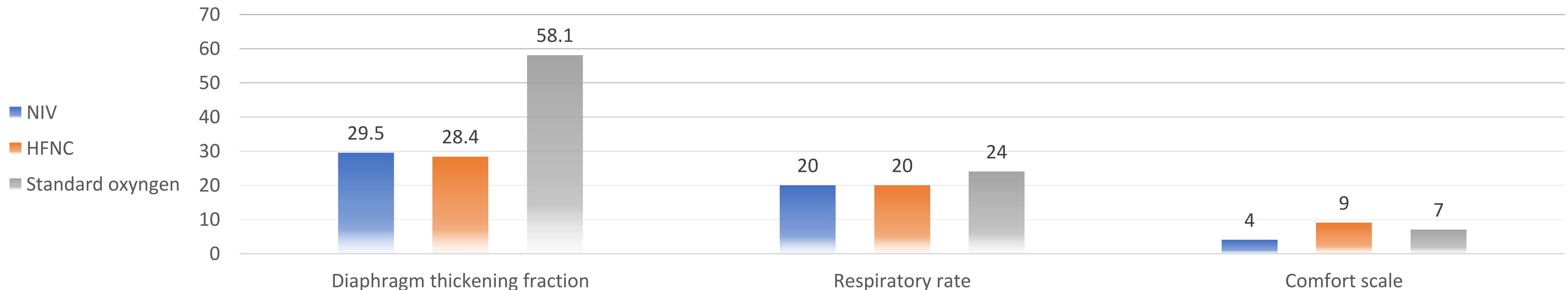
EGAN'S FUNDAMENTALS OF RESPIRATORY CARE, TWELFTH EDITION

HFNC after NIV interruption in patients recovering from hypercapnic respiratory failure

- Patients: COPD with acute hypercapnic respiratory failure, using NIV more than 24 hrs (N=20)
- Interventions: 5 sessions (30 mins each seesion)



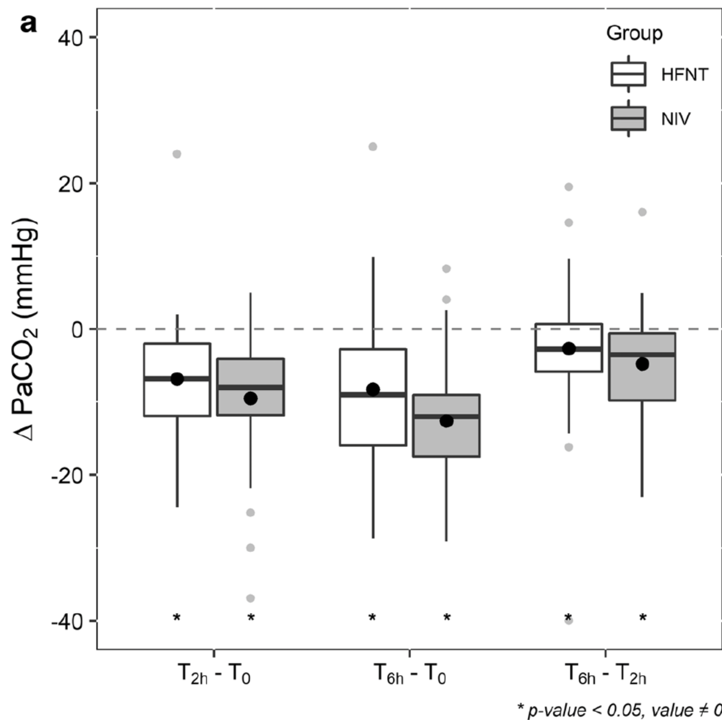
- Aim: evaluate the impact of HFNC on gas exchange, diaphragm function, respiratory rate, patient comforts

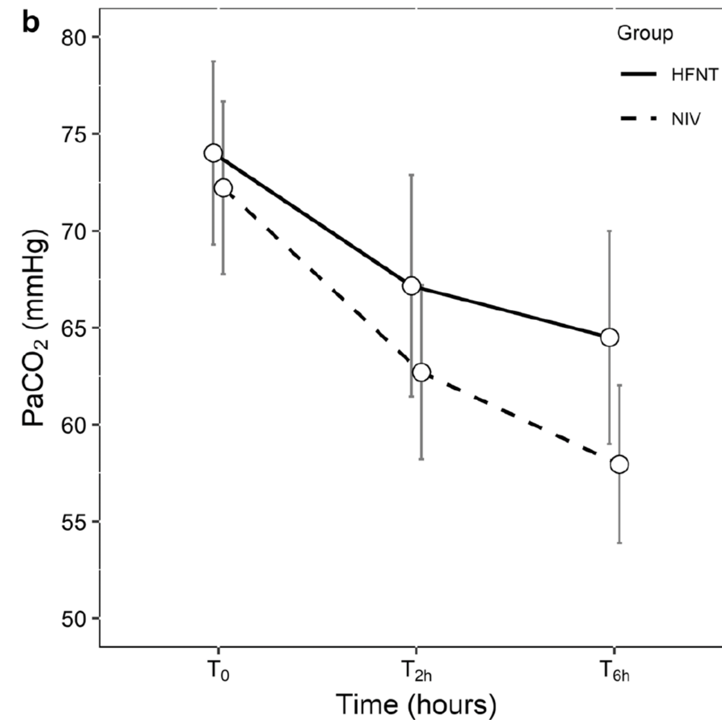


Longhini et al., Crit Care Med. 2019 Jun;47(6):e506-e511.

HFNC vs NIV in patients with COPD exacerbation

- Patients: COPD exacerbation with $PaCO_2$ ≥55 mmHg, pH 7.25 to 7.35
- Intervention: HFNC (n=40) vs BiPAP (n=39) for 2 to 6 hrs



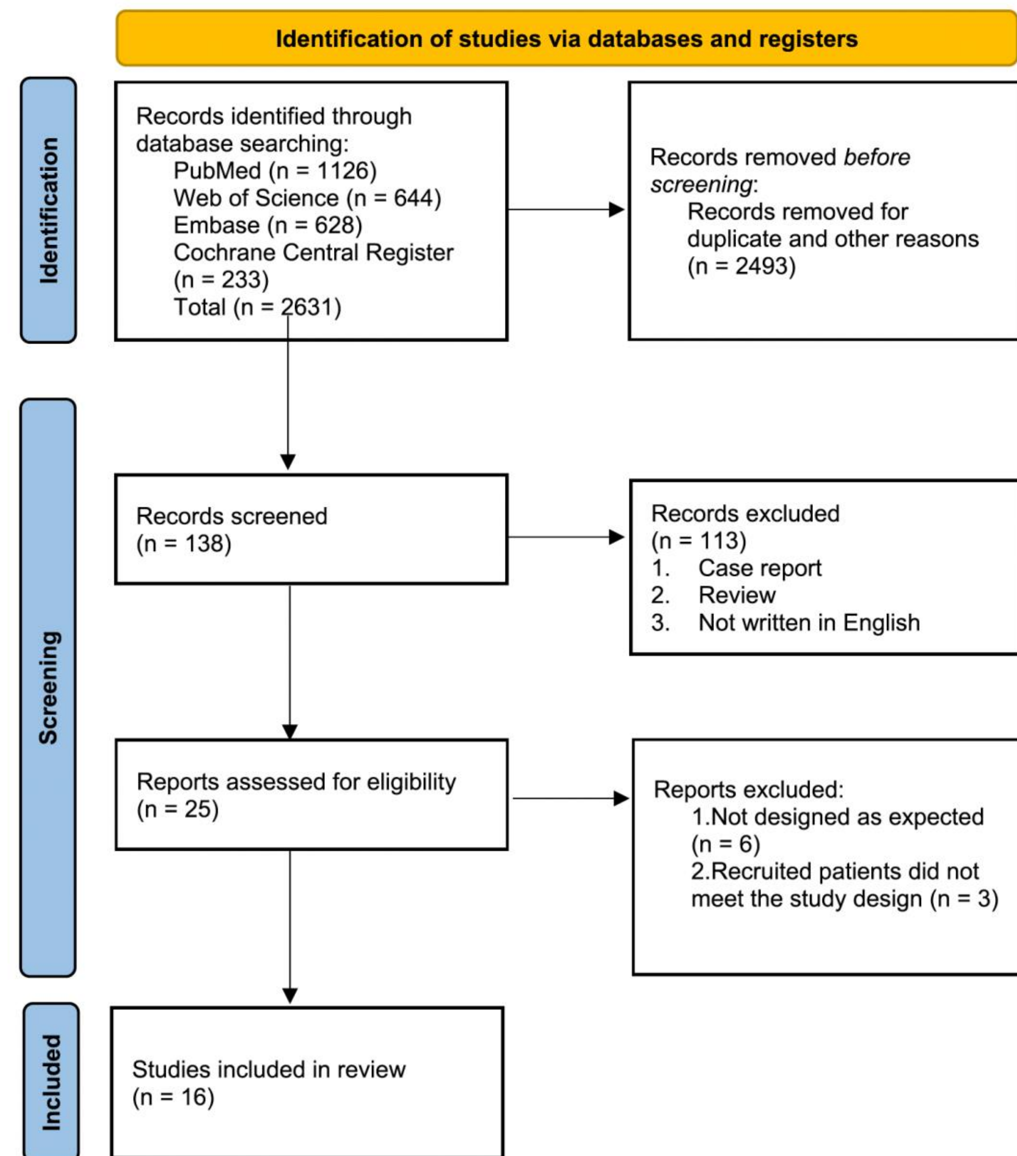


1. HFNC was non-inferior with NIV in CO2 reduction in first 2 hrs
2. 32% of patients receiving HFNC required NIV by 6 hrs

Cortegiani et al., Crit Care. 2020 Dec 14;24(1):692.

HFNC in patients with hypercapnic respiratory failure: a systemic review and meta-analysis

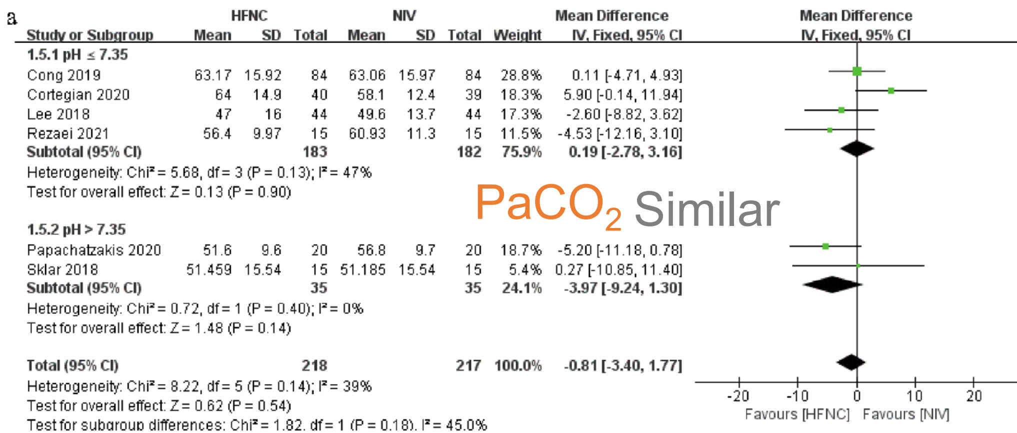
- HFNC vs NIV vs Conventional O_2 (COT)
- Acute hypercapnic respiratory failure (AHRF, 9 studies)
- Chronic hypercapnic respiratory failure (CHRF, 7 studies)
- Primary outcomes: $PaCO_2$

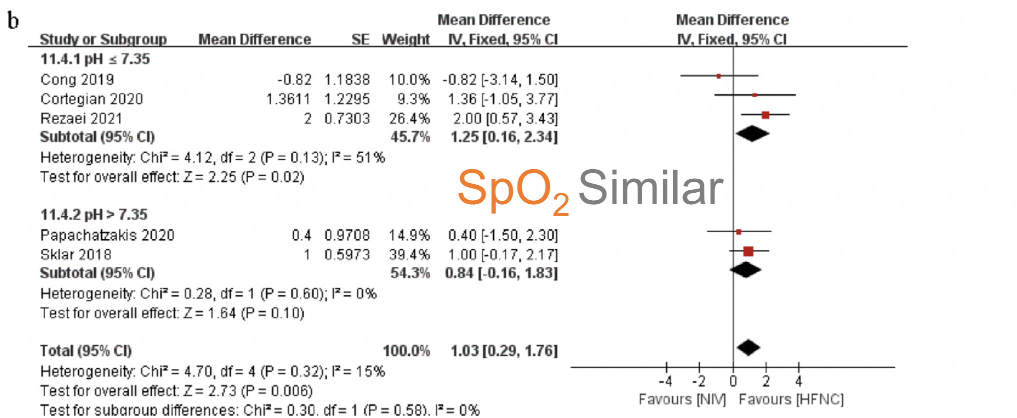


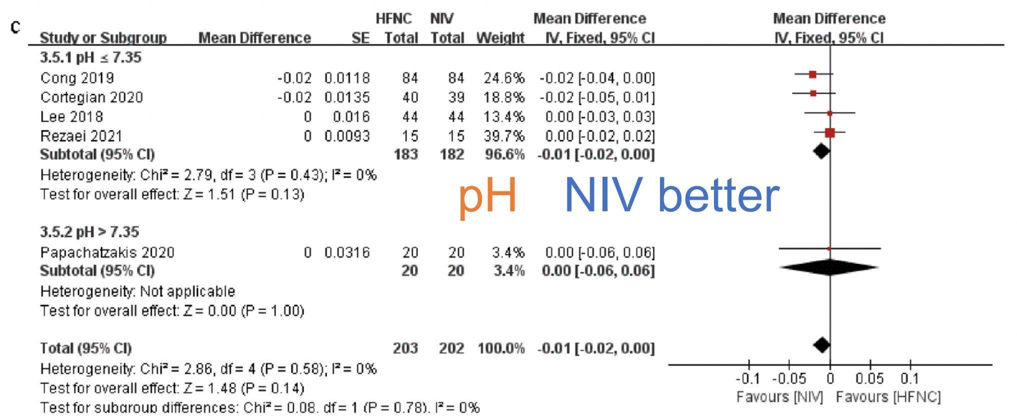
Guan L et al., Eur J Intern Med. 2025 Apr;134:119-129.

HFNC vs NIV

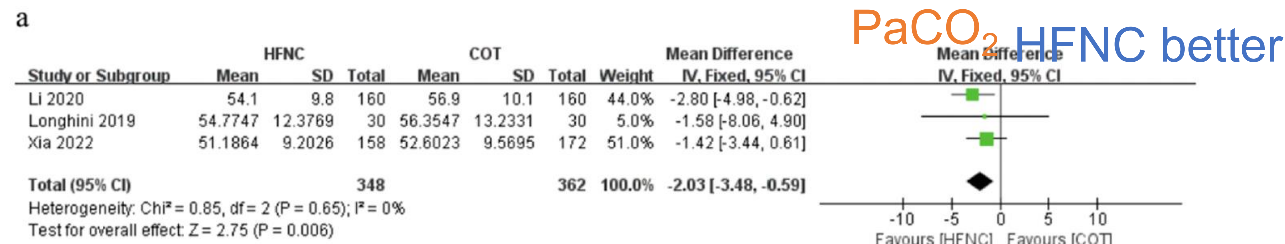
AHRF

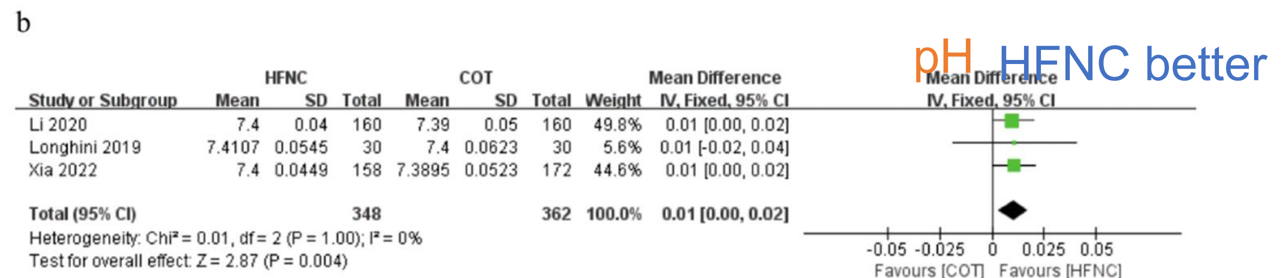


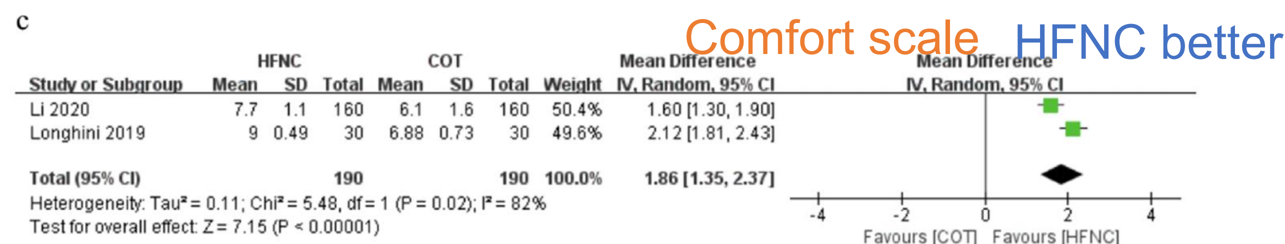


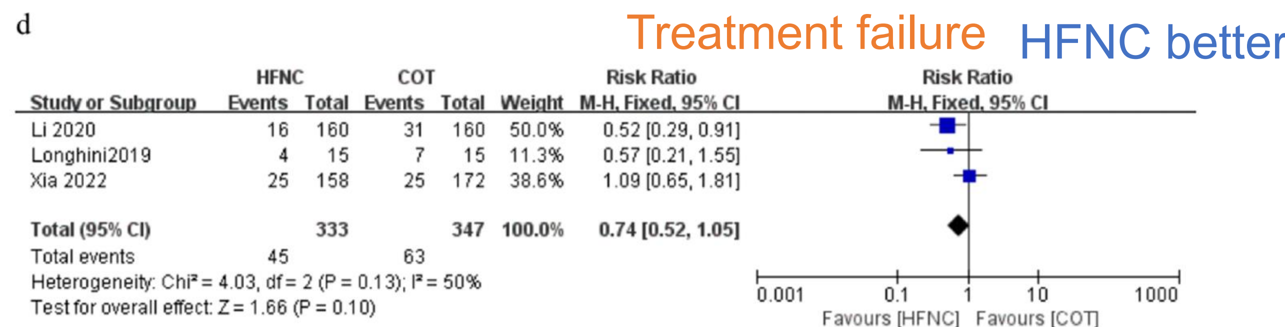


HFNC vs COT









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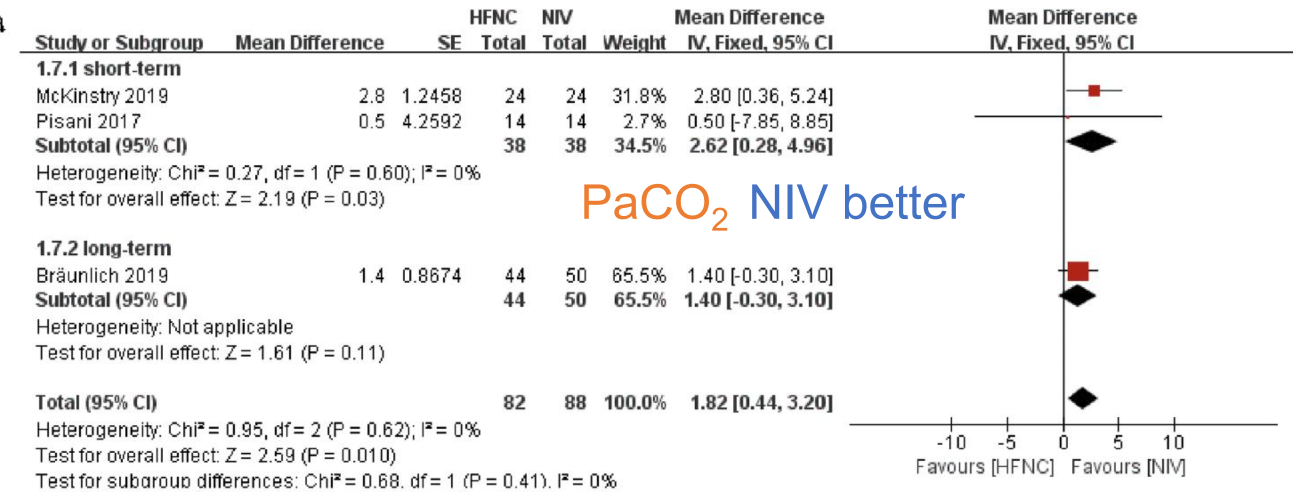
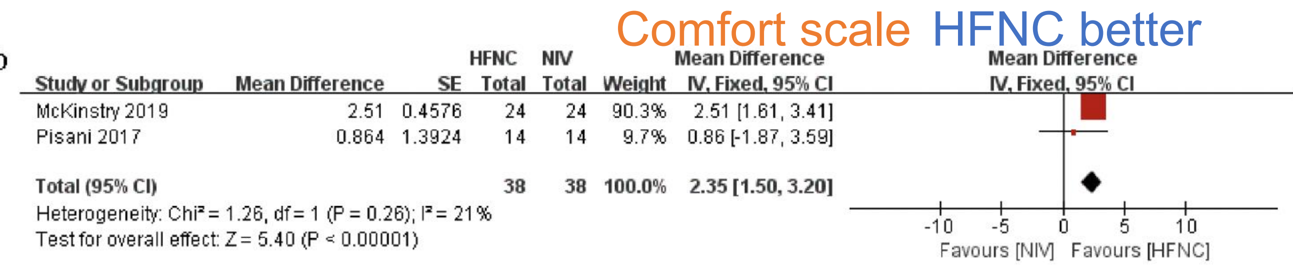
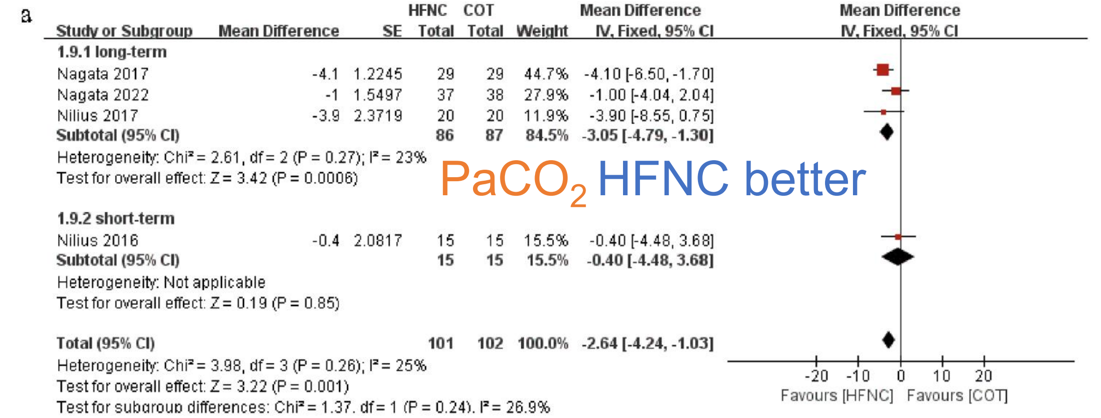
CHRF

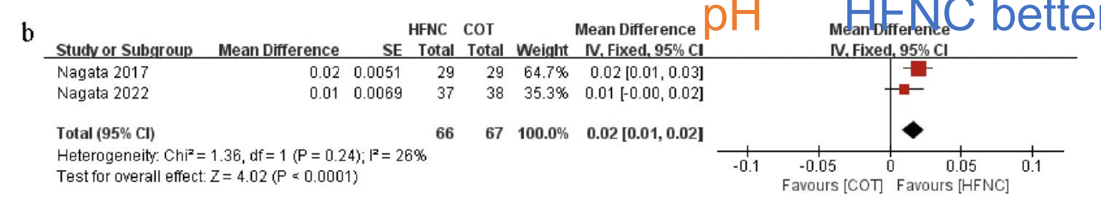
HFNC vs NIV

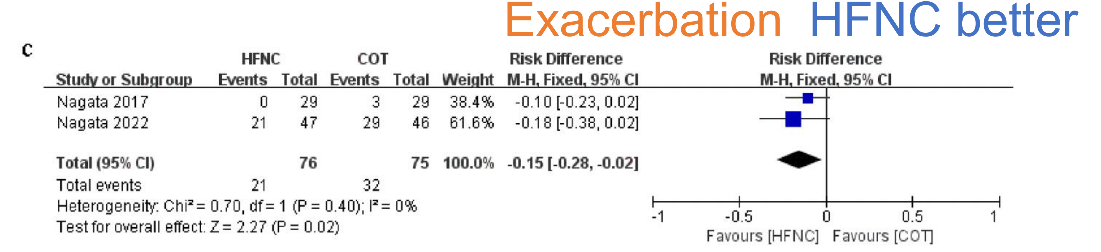


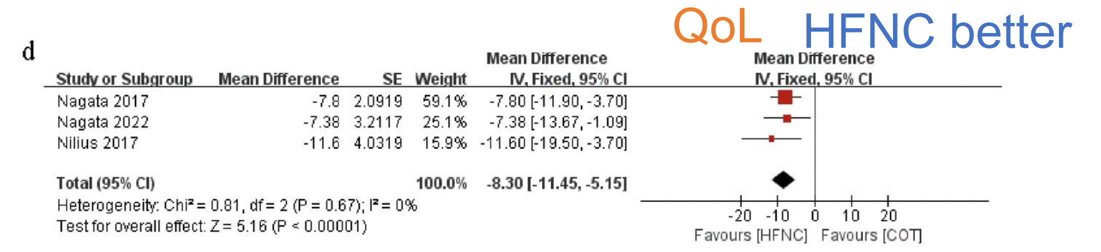


HFNC vs COT









For patients with **hypercapnic respiratory failure**

- Clinical efficacy of **HFNC vs NIV is inconclusive**
- Low-quality evidence shows that **HFNO vs COT** can **better** improve blood gases, comfort, health-related quality of life, and exacerbation in patients with AHRF or CHRF.

Guan L et al., Eur J Intern Med. 2025 Apr;134:119-129.

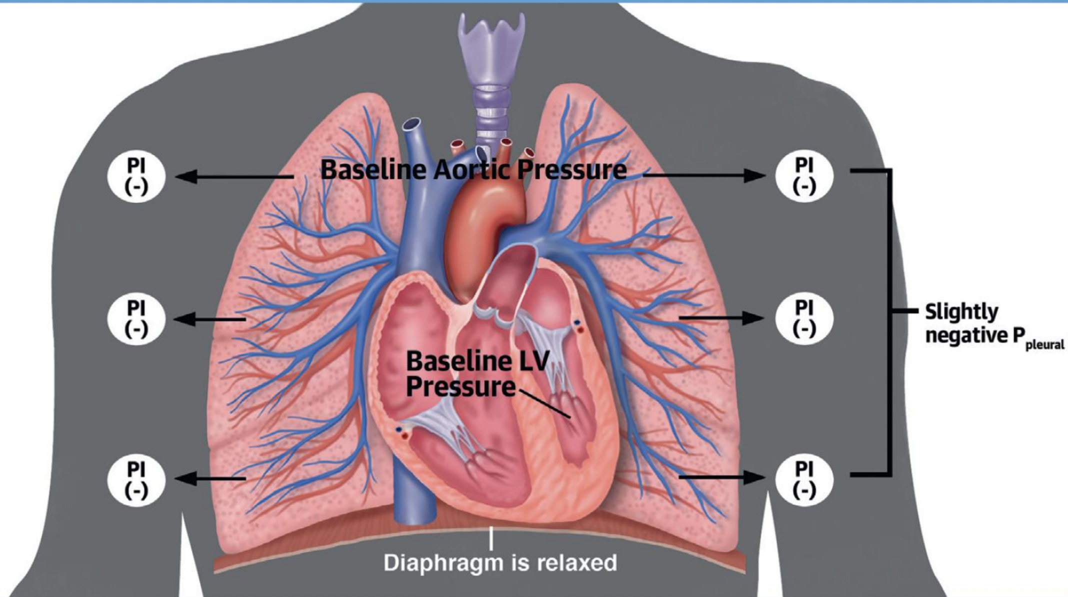
Acute hypoxic respiratory failure

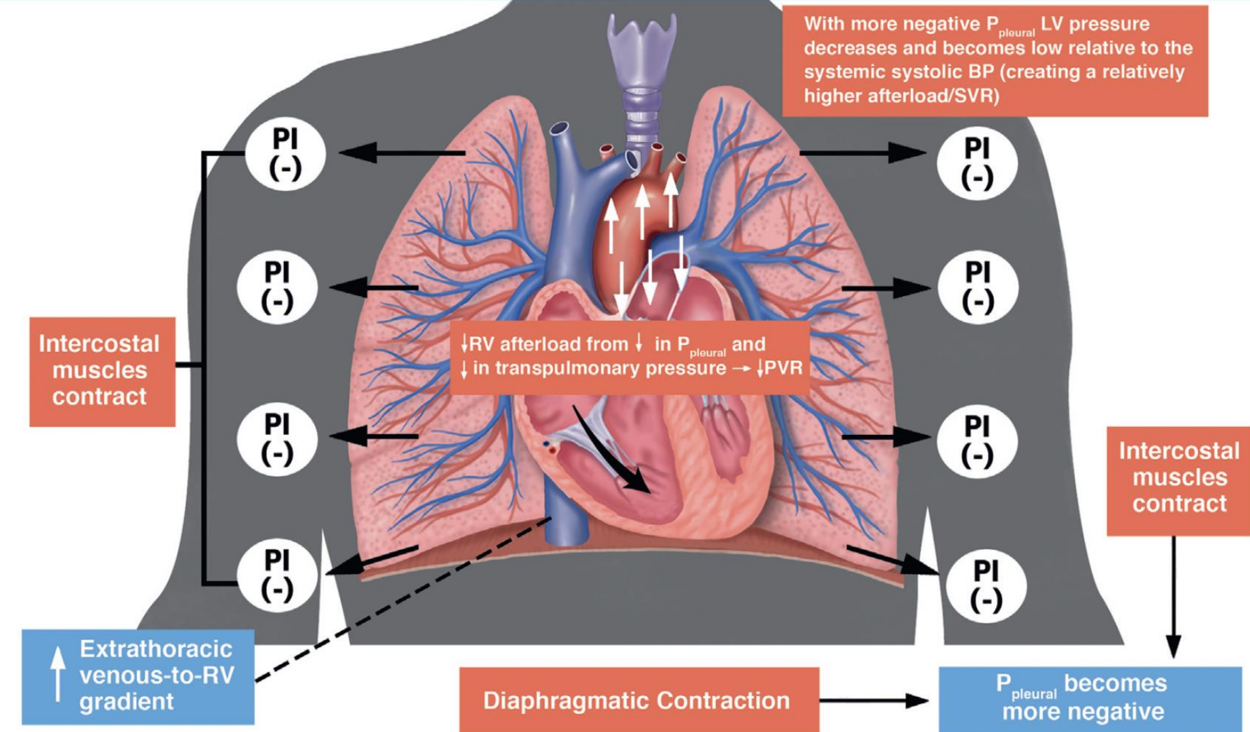
Acute hypoxic respiratory failure

- Acute cardiogenic pulmonary edema
- Acute respiratory distress syndrome
- Immunocompromised patients
- Preoxygenation

Cardiogenic pulmonary edema

Effects of intrathoracic pressure on cardiovascular system

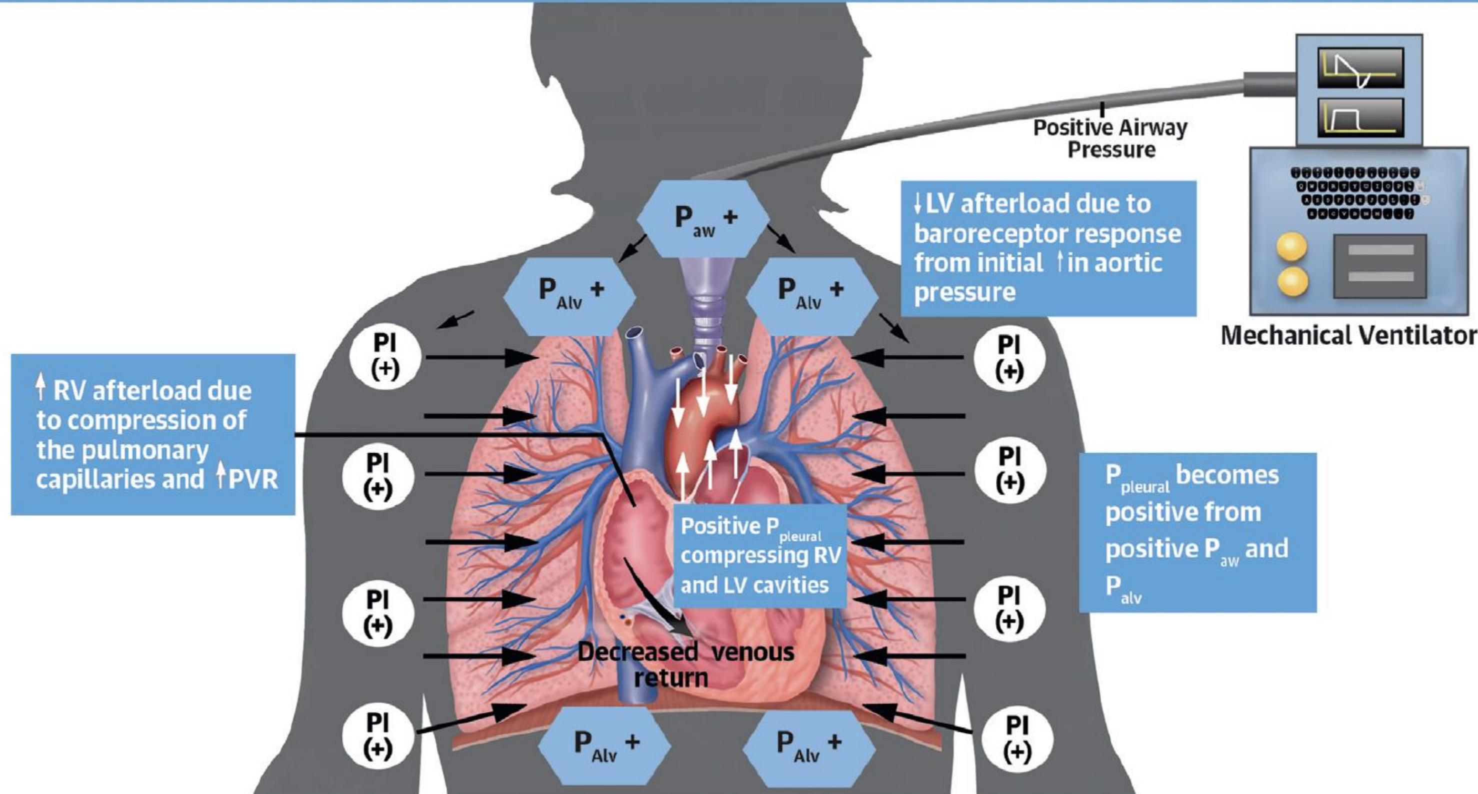




- Venous return ↑
- RV afterload ↓
- LV afterload ↑

Alviar et al., J Am Coll Cardiol. 2018 Sep 25;72(13):1532-1553.

Effects of intrathoracic pressure on cardiovascular system



- Venous return ↓
- RV afterload ↑
- LV afterload ↓

Alviar et al., J Am Coll Cardiol. 2018 Sep 25;72(13):1532-1553.

Updated definition of ARDS

	Criteria That Apply to All ARDS Categories
Risk factors and origin of edema	Precipitated by an acute predisposing risk factor, such as pneumonia, nonpulmonary infection, trauma, transfusion, aspiration, or shock. Pulmonary edema is not *exclusively or primarily* attributable to cardiogenic pulmonary edema/fluid overload, and hypoxemia/gas exchange abnormalities are not primarily attributable to atelectasis. However, ARDS can be diagnosed in the presence of these conditions if a predisposing risk factor for ARDS is also present.
Timing	Acute onset or worsening of hypoxemic respiratory failure within 1 week of the estimated onset of the predisposing risk factor or new or worsening respiratory symptoms.
Chest imaging	Bilateral opacities on chest radiography and computed tomography or bilateral B lines and/or consolidations on ultrasound* not fully explained by effusions, atelectasis, or nodules/masses.

	Criteria That Apply to Specific ARDS Categories		
	Nonintubated ARDS†	**Intubated ARDS**	**Modified Definition for Resource-Limited Settings**‡
Oxygenation§‖	$Pa_{O_2}:FI_{O_2} \leq 300$ mm Hg or $Sp_{O_2}:FI_{O_2} \leq 315$ (if $Sp_{O_2} \leq 97\%$) on HFNO with flow of ≥ 30 L/min or NIV/CPAP with at least 5 cm H_2O end-expiratory pressure	Mild¶: $200 < Pa_{O_2}:FI_{O_2} \leq 300$ mm Hg or $235 < Sp_{O_2}:FI_{O_2} \leq 315$ (if $Sp_{O_2} \leq 97\%$) Moderate: $100 < Pa_{O_2}:FI_{O_2} \leq 200$ mm Hg or $148 < Sp_{O_2}:FI_{O_2} \leq 235$ (if $Sp_{O_2} \leq 97\%$) Severe: $Pa_{O_2}:FI_{O_2} \leq 100$ mm Hg or $Sp_{O_2}:FI_{O_2} \leq 148$ (if $Sp_{O_2} \leq 97\%$)	$Sp_{O_2}:FI_{O_2} \leq 315$ (if $Sp_{O_2} \leq 97\%$)†. Neither positive end-expiratory pressure nor a minimum flow rate of oxygen is required for diagnosis in resource-limited settings.

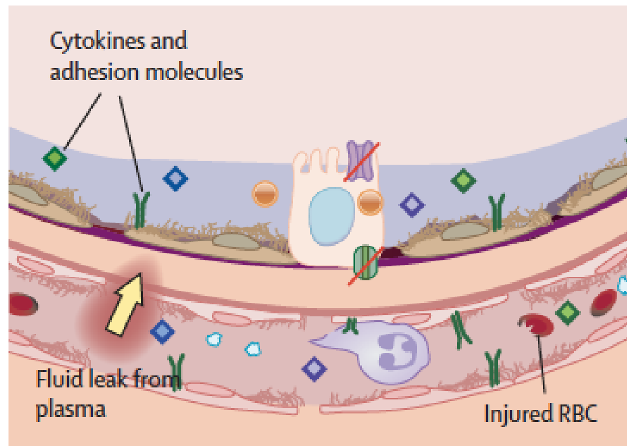
Matthay et al., Am J Respir Crit Care Med. 2024 Jan 1;209(1):37-47.

Pathophysiology during hypoxic respiratory failure (ARDS)

B Mild injury

Epithelial injury

- Mild oedema formation
- Disrupted tight junctions
- Decreased surfactant production
- Impaired sodium and chlorine transport
- Mild glycocalyx shedding
- Activated epithelial cells secrete chemokines and express adhesion molecules



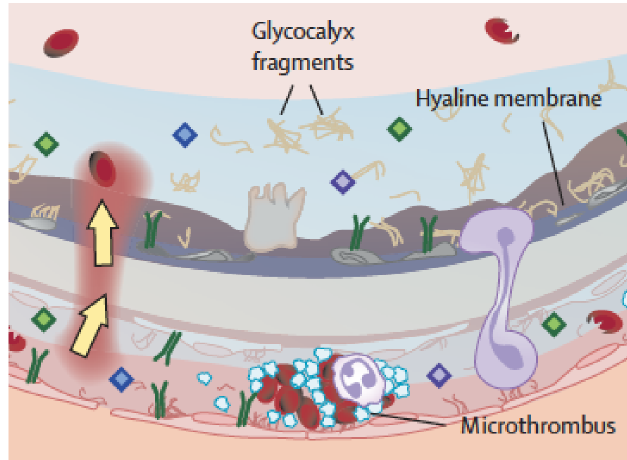
Endothelial injury

- Disrupted tight junctions
- Paracellular fluid leakage from plasma
- Injured endothelial glycocalyx
- Upregulated adhesion molecules
- RBCs might be injured transiting the capillary
- Adherent PMNs

C Severe injury

Epithelial injury

- Severe oedema formation
- Severe disruption of tight junctions
- Epithelial necrosis
- Hyaline membrane formation
- Absent sodium and chlorine transport
- Glycocalyx shedding
- Increased chemokines and adhesion molecules
- RBCs in airspace



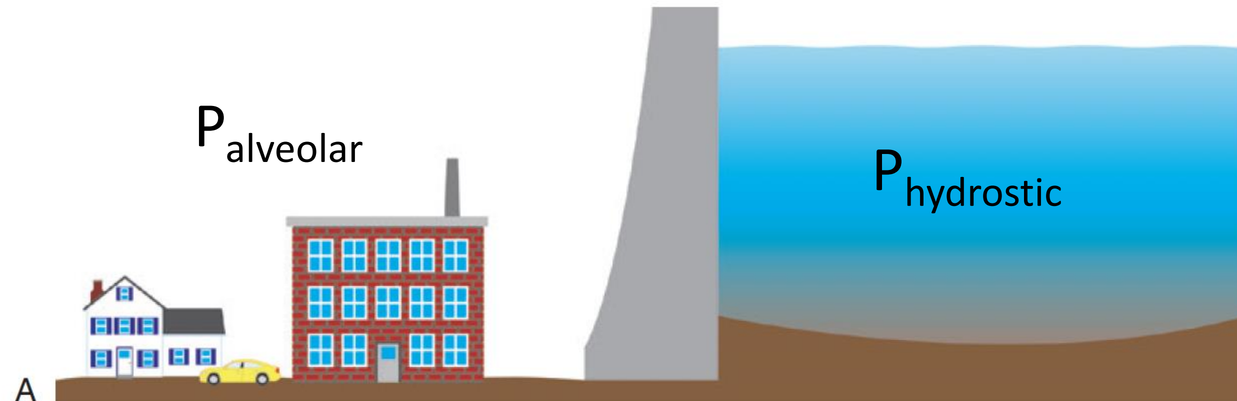
Endothelial injury

- More severe endothelial disruption with transit of fluid out of the capillary
- Loss of endothelial glycocalyx
- RBC injury
- PMN transmigration
- Platelet microthrombi

	Physiological	Clinical
Interstitial edema	Decreased lung compliance	Increased work of breath (WOB)
Diffuse alveolar filling	VQ mismatch and shunting	Hypoxemia, radiographic opacities
Decreased surfactant	Alveolar collapse	atelectasis
Microvascular thrombosis	Increased dead space and pulmonary hypertension	High minute ventilation, RV failure
Leak of inflammatory mediators	Systemic inflammation	Multi-organ failure

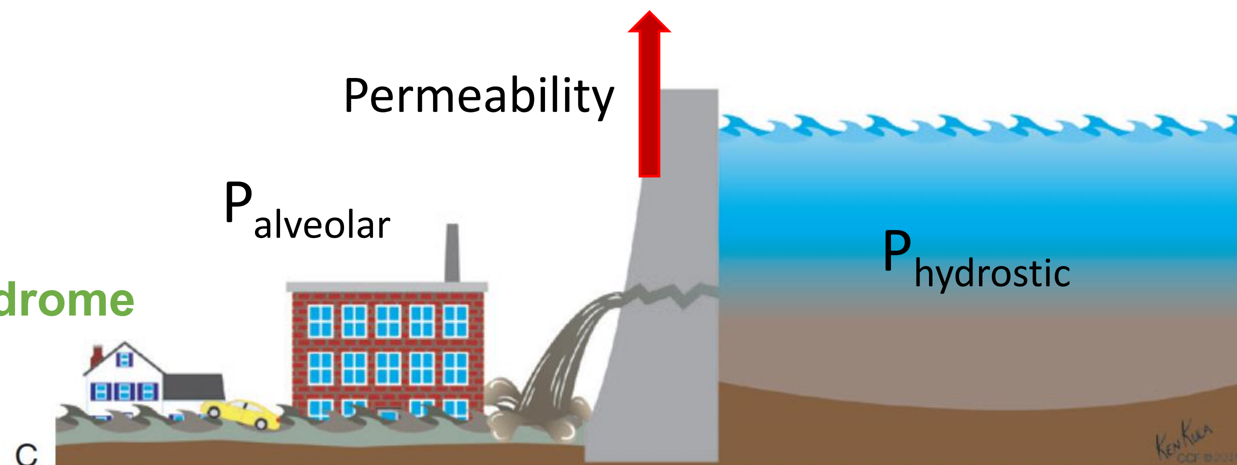
Bos LDJ, Ware LB.. Lancet. 2022 Oct 1;400(10358):1145-1156.

The balance of hydrostic pressure, osmotic pressure and alveolar pressure

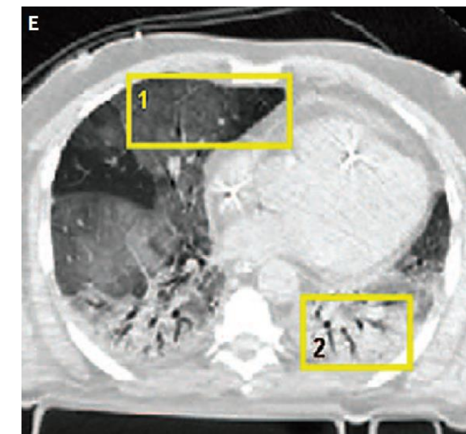


Cardiogenic pulmonary edema

Acute respiratory distress syndrome



Patient self-inflicted lung injury (PSILI)



Spontaneously breathing acute hypoxemic respiratory failure patient

$\uparrow$ respiratory drive
(hypoxia, lung edema, reduced compliance inflammation, agitation)

lung inhomogeneity
(gravitational forces, regional inflammation)

$\uparrow$ inspiratory effort

occult pendelluft
(Ventral to dorsal shift of gas at the beginning of inspiration)

solid-like behaviour of dorsal collapse

$\uparrow$ transpulmonary pressure swings

$\uparrow\uparrow$ dorsal tidal volume

$\uparrow\uparrow$ dorsal transpulmonary pressure swings

$\uparrow$ tidal volume

$\uparrow$ respiratory rate

Volutrauma
Barotrauma
Atelectrauma

Patient Self-inflicted lung injury

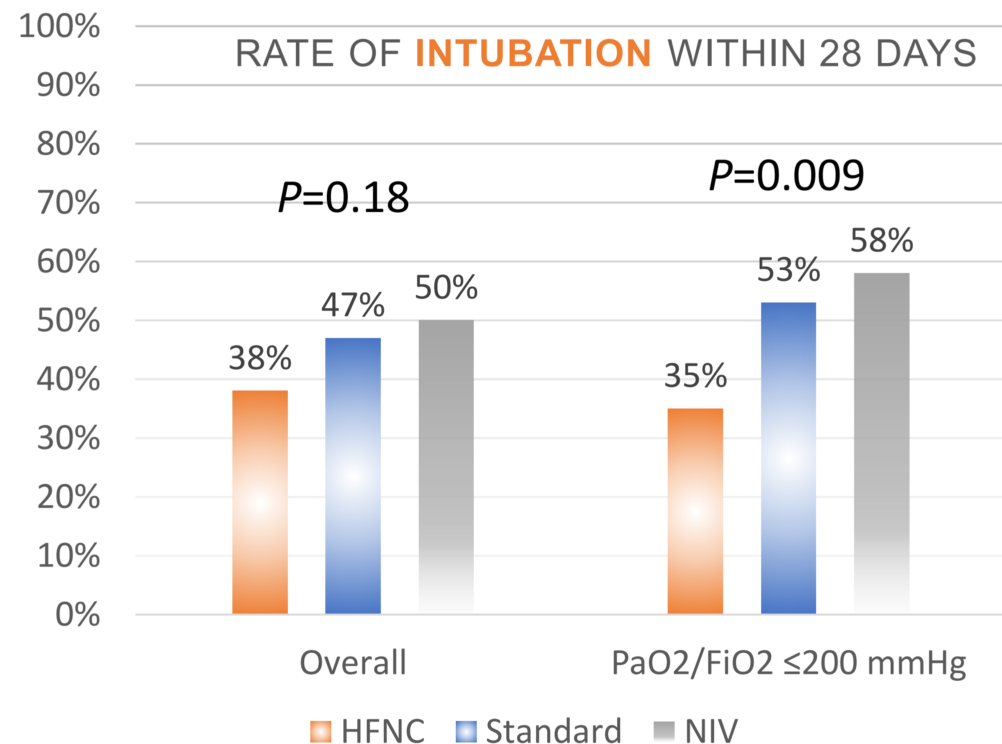
- Adequate O2 flow provide the demand
- A PEEP to recruit the lung (reducing atelectasis)
- A driving pressure to unloading respiratory muscle and open the lung
- Decreasing inspiratory force, lung strain, and work of breath
- Increasing overdistension

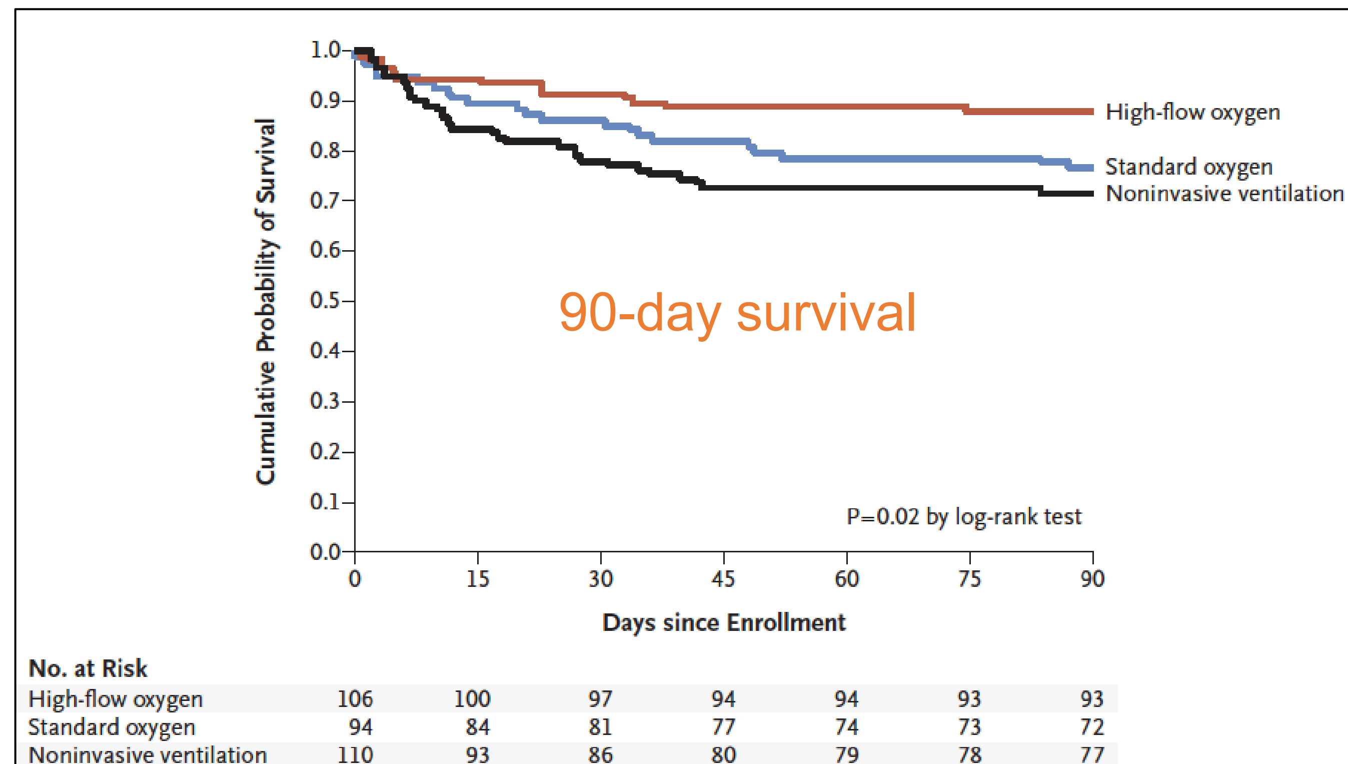
Reduce the drive

Thompson BT, et al., N Engl J Med. 2017 Aug 10;377(6):562-572; Grieco DL, et al., Intensive Care Med. 2021 Aug;47(8):851-866.

HFNC vs NIV vs COT in Acute Hypoxemic Respiratory Failure

- Prospective, RCT
- 23 ICUs in France and Belgium, N=310
- Adult patients with **acute hypoxic respiratory failure**
  - ✓ RR >25, **PaO_2:FiO_2 ≤300 mmHg**
  - ✓ Oxyngen therapy with O_2 flow ≥10L/min for 15 min
  - ✓ $PaCO_2$ ≤45 mmHg

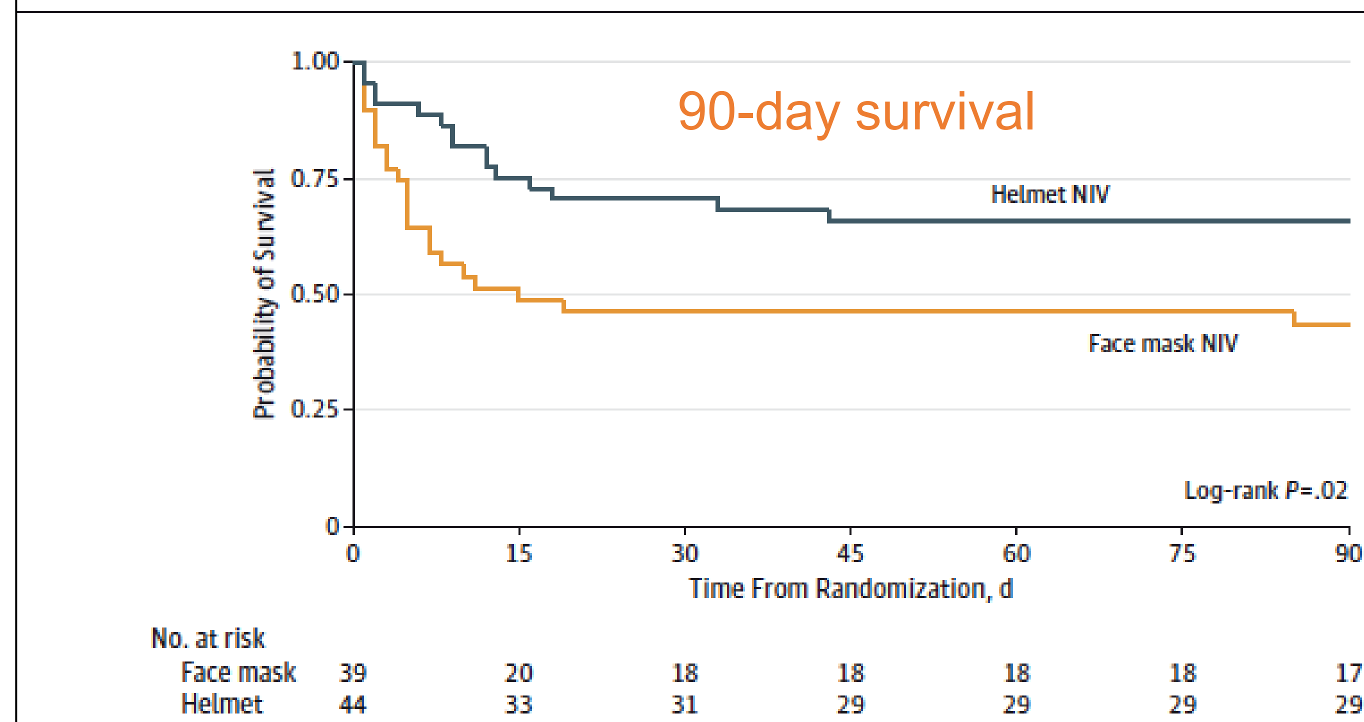




Frat et al. N Engl J Med. 2015 Jun 4;372(23):2185-96.

Helmet vs Face Mask NIV in ARDS

- Prospective, RCT
- Single ICU in Chicago, N=83
- Adult patients diagnosed **ARDS** according to Berlin criteria

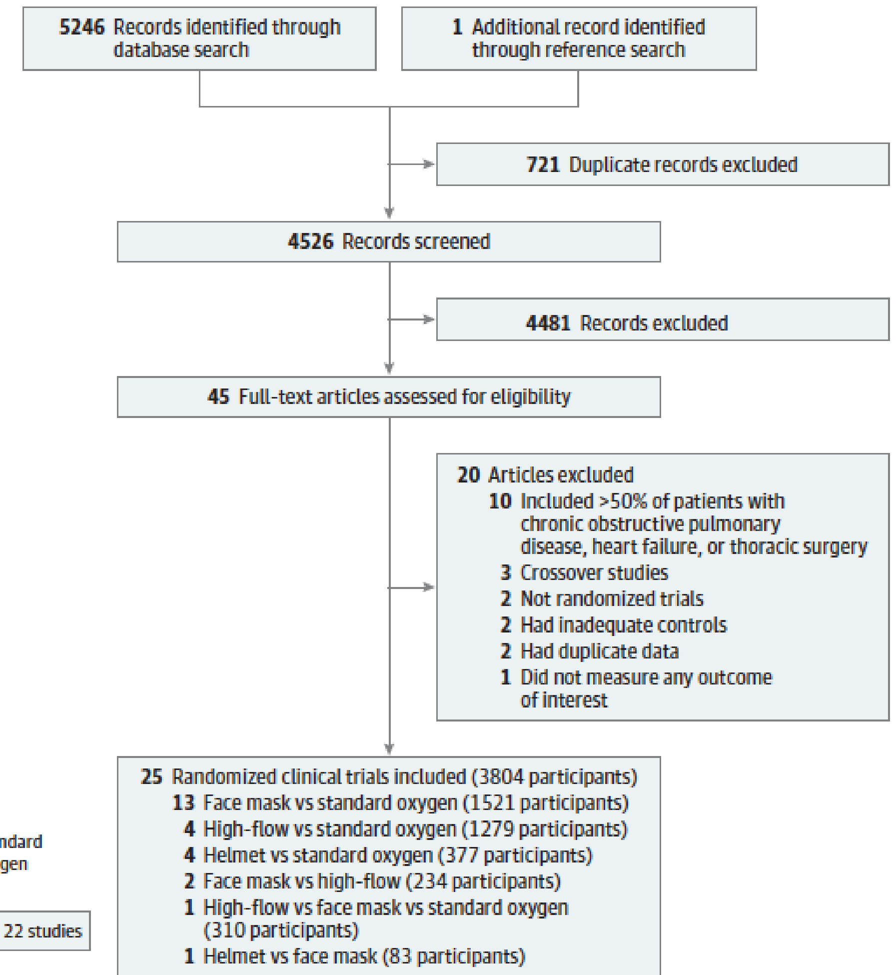


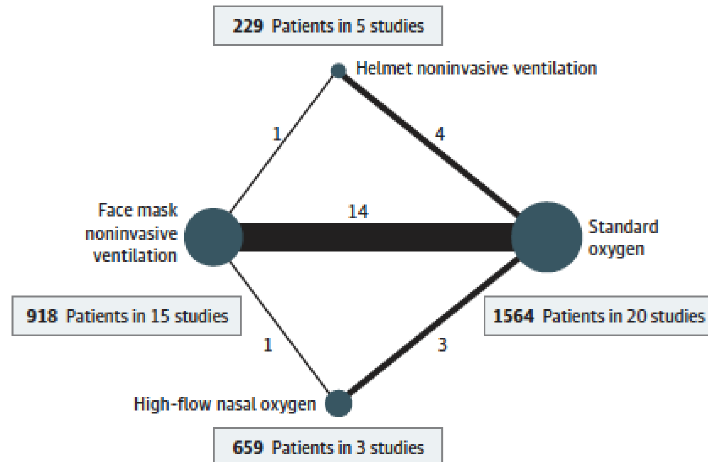
Patel et al. JAMA. 2016 Jun 14;315(22):2435-41

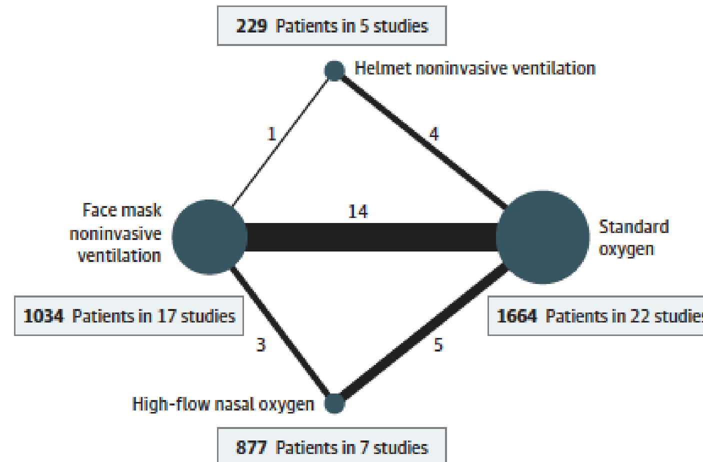
Association of Noninvasive Oxygenation Strategies With All-Cause Mortality in Adults With Acute Hypoxemic Respiratory Failure

A Systematic review and meta- analysis

- **Adult patients with acute hypoxic respiratory failure comparing HFNC, face mask NIV, helmet NIV, and standard oxygen therapy**
- **Excluding: COPE with AE, heart failure, and post-extubation.**
- **25 RCTs, 3,804 patients**





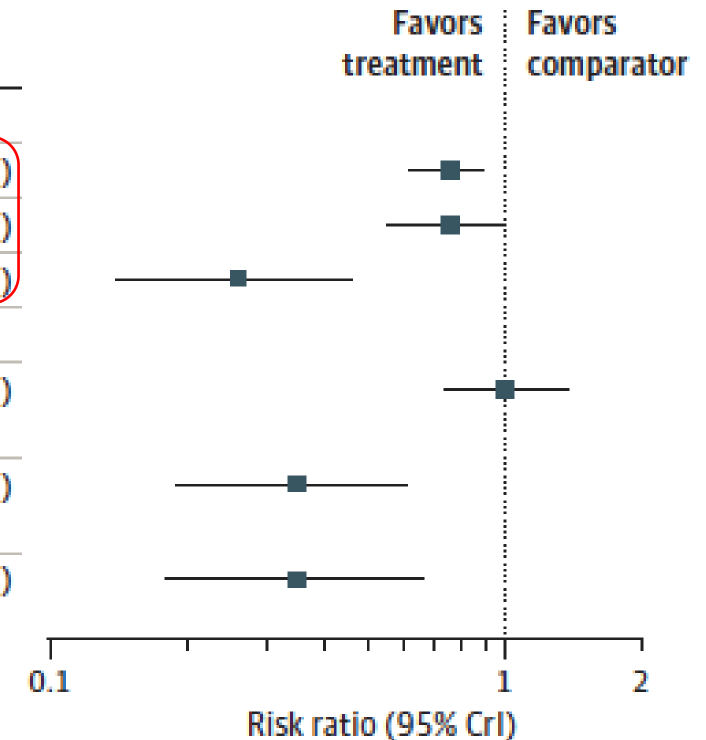


Ferreyro et al., JAMA. 2020 Jul 7;324(1):57-67.

Results

B Intubation

	No. of patients	No. of trials	Quality	Absolute risk difference (95% CrI)	Network risk ratio (95% CrI)
Compared with standard oxygen					
Face mask noninvasive ventilation	1725	14	Moderate	-0.12 (-0.25 to -0.05)	0.76 (0.62-0.90)
High-flow nasal oxygen	1479	5	Moderate	-0.11 (-0.27 to -0.01)	0.76 (0.55-0.99)
Helmet noninvasive ventilation	330	3	Low	-0.32 (-0.60 to -0.16)	0.26 (0.14-0.46)
Additional comparisons					
Face mask noninvasive ventilation vs high-flow nasal oxygen	450	3	Low	0.00 (-0.13 to 0.10)	1.01 (0.74-1.38)
Helmet noninvasive ventilation vs face mask noninvasive ventilation	83	1	Low	-0.20 (-0.40 to -0.09)	0.35 (0.19-0.61)
Helmet noninvasive ventilation vs high-flow nasal oxygen	0	0	Low	-0.20 (-0.43 to -0.08)	0.35 (0.18-0.66)

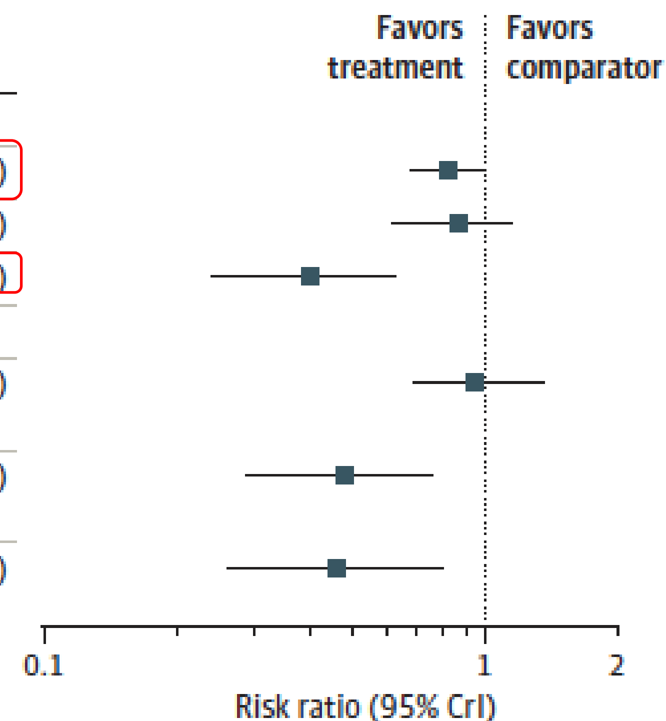


Ferreyro et al., JAMA. 2020 Jul 7;324(1):57-67.

Results

A All-cause mortality

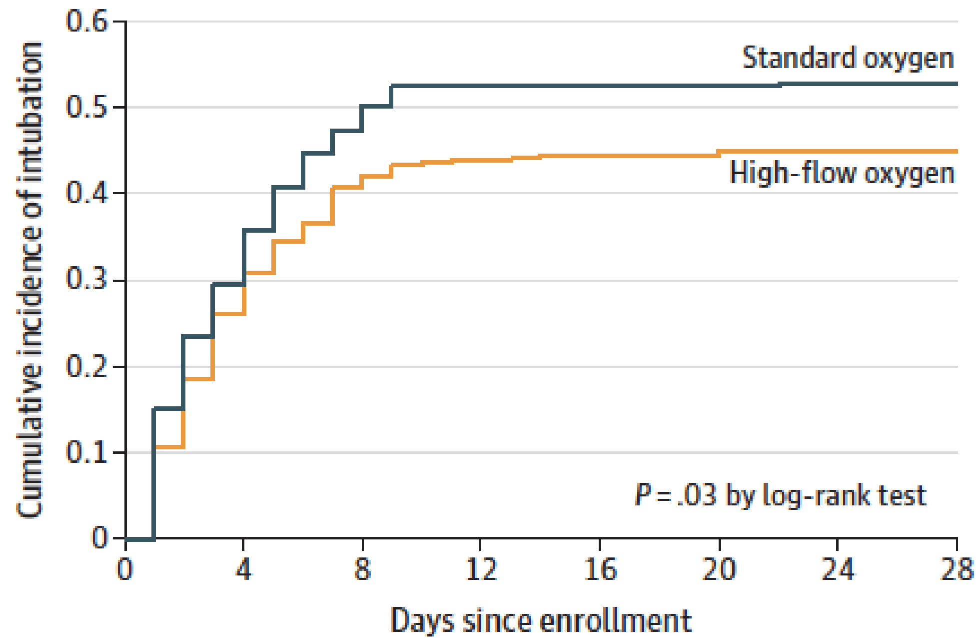
	No. of patients	No. of trials	Quality	Absolute risk difference (95% CrI)	Network risk ratio (95% CrI)
Compared with standard oxygen					
Face mask noninvasive ventilation	1725	14	Moderate	-0.06 (-0.15 to -0.01)	0.83 (0.68-0.99)
High-flow nasal oxygen	1279	3	Moderate	-0.04 (-0.15 to 0.04)	0.87 (0.62-1.15)
Helmet noninvasive ventilation	330	3	Low	-0.19 (-0.37 to -0.09)	0.40 (0.24-0.63)
Additional comparisons					
Face mask noninvasive ventilation vs high-flow nasal oxygen	216	1	Low	-0.02 (-0.14 to 0.07)	0.95 (0.69-1.37)
Helmet noninvasive ventilation vs face mask noninvasive ventilation	83	1	Low	-0.13 (-0.27 to -0.05)	0.48 (0.29-0.76)
Helmet noninvasive ventilation vs high-flow nasal oxygen	0	0	Low	-0.15 (-0.34 to -0.05)	0.46 (0.26-0.80)



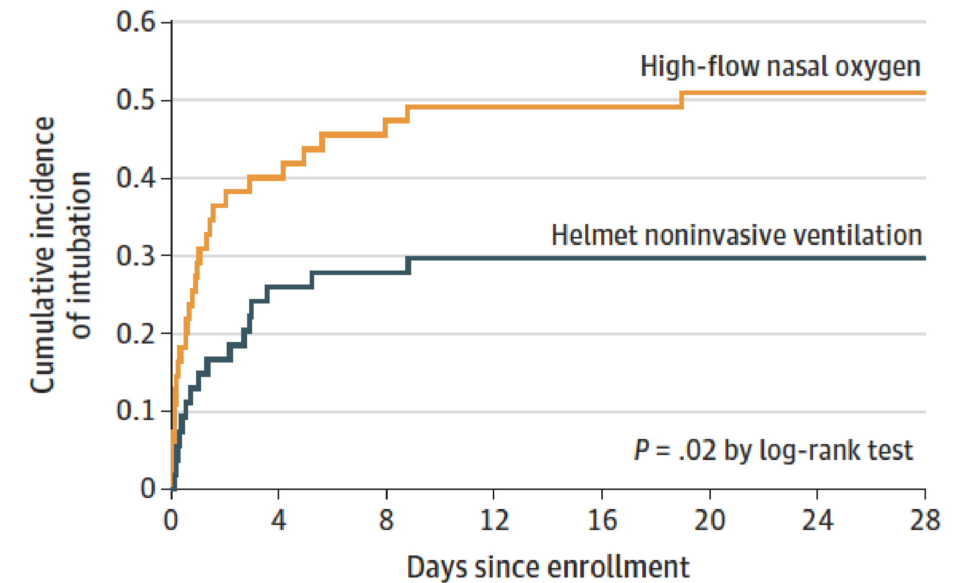
Ferreyro et al., JAMA. 2020 Jul 7;324(1):57-67.

Non-invasive supportin Patients With Respiratory Failure Due to COVID-19

SOHO-COVID

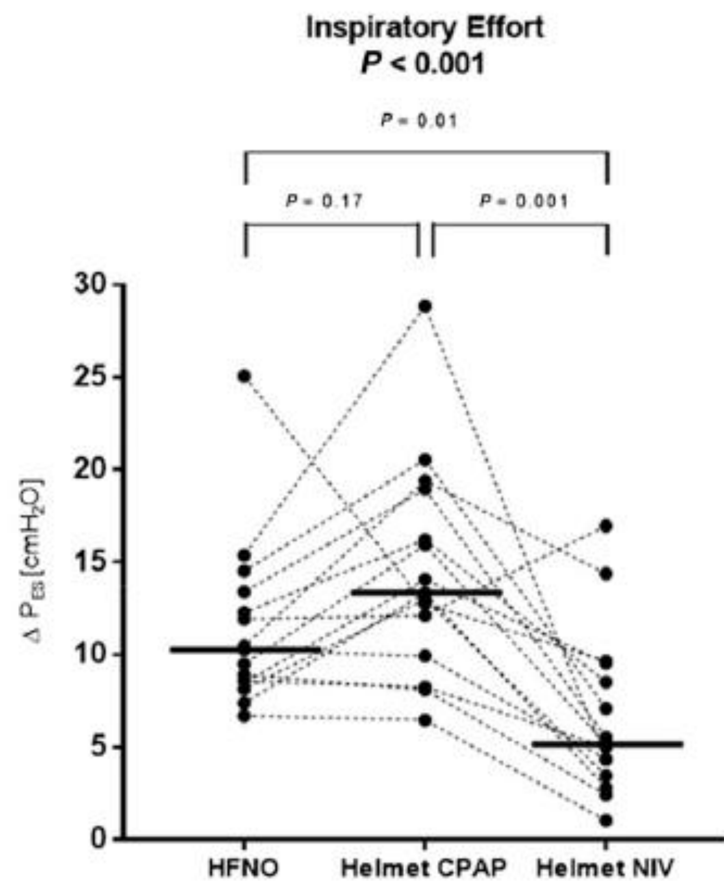


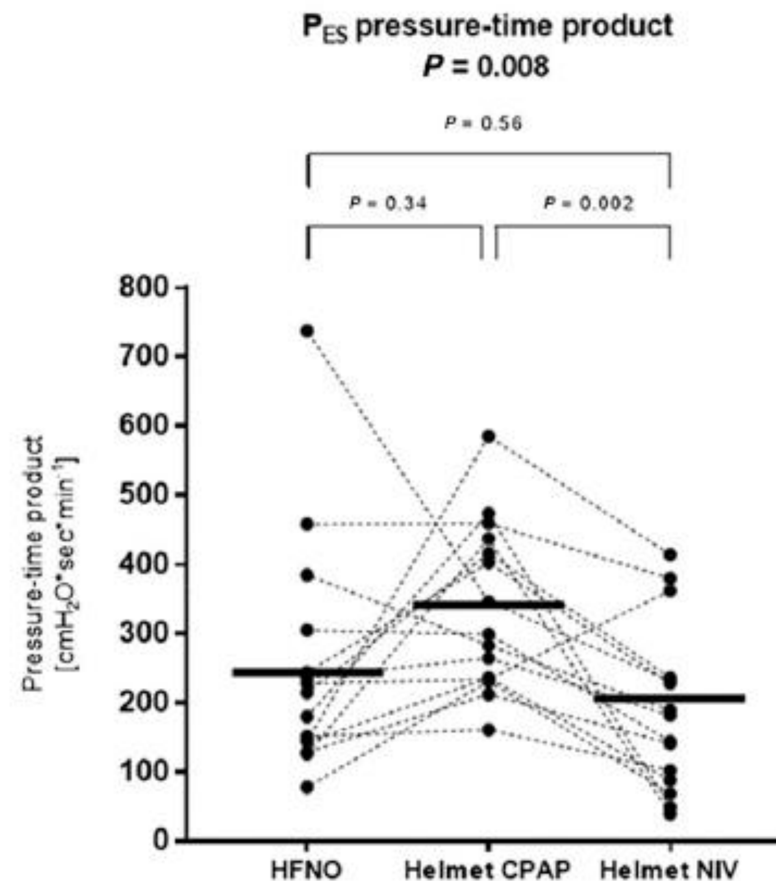
HENIVOT



Frat et., JAMA. 2022 Sep 27;328(12):1212-1222; Grieco et al., JAMA. 2021 May 4;325(17):1731-1743.

NIV reduced respiratory drive and dynamic lung strain more than HFNC in patients with high demand

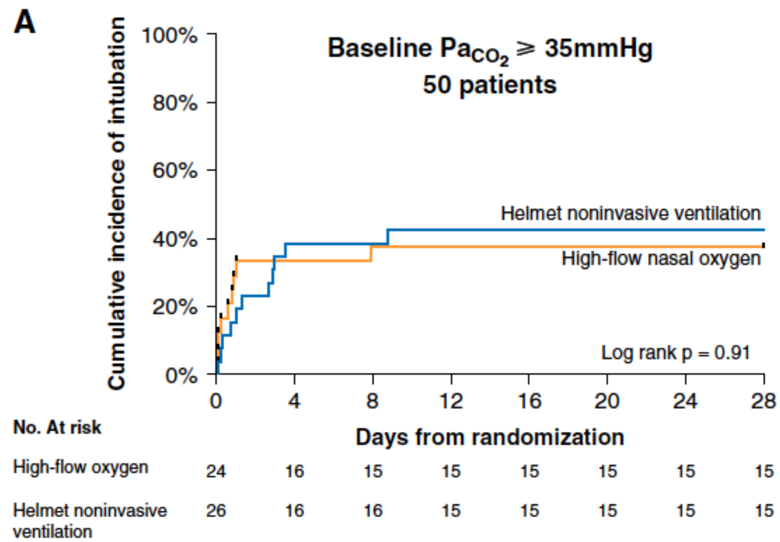


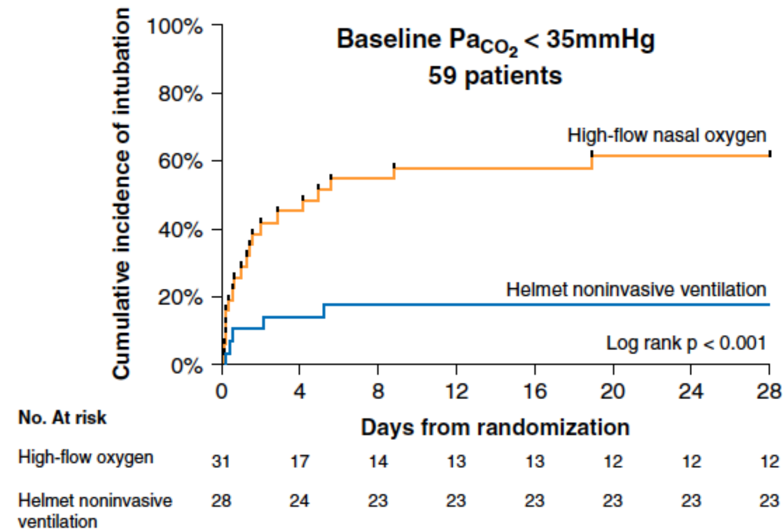


Menga et al., Am J Respir Crit Care Med. 2023 May 15;207(10):1310-1323.

HENIVOT Incidence of intubation

A





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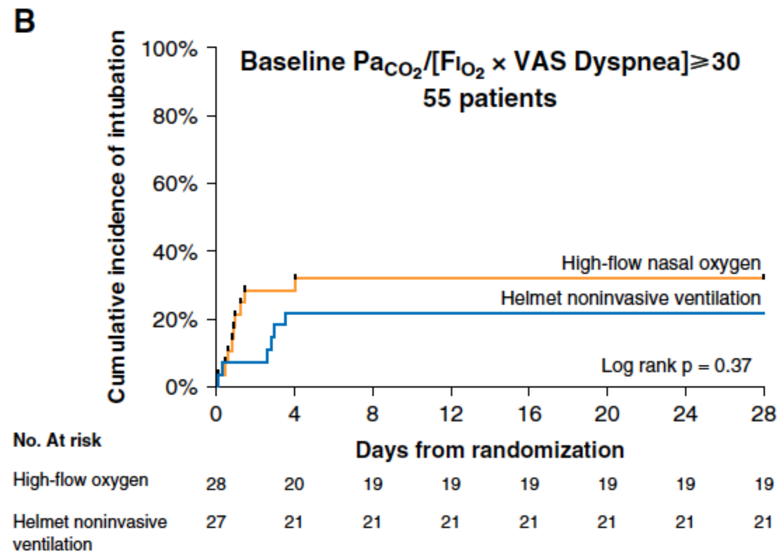
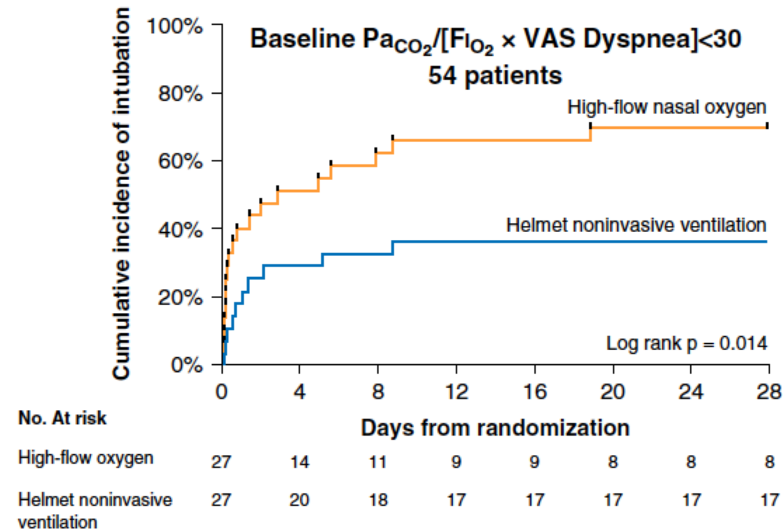




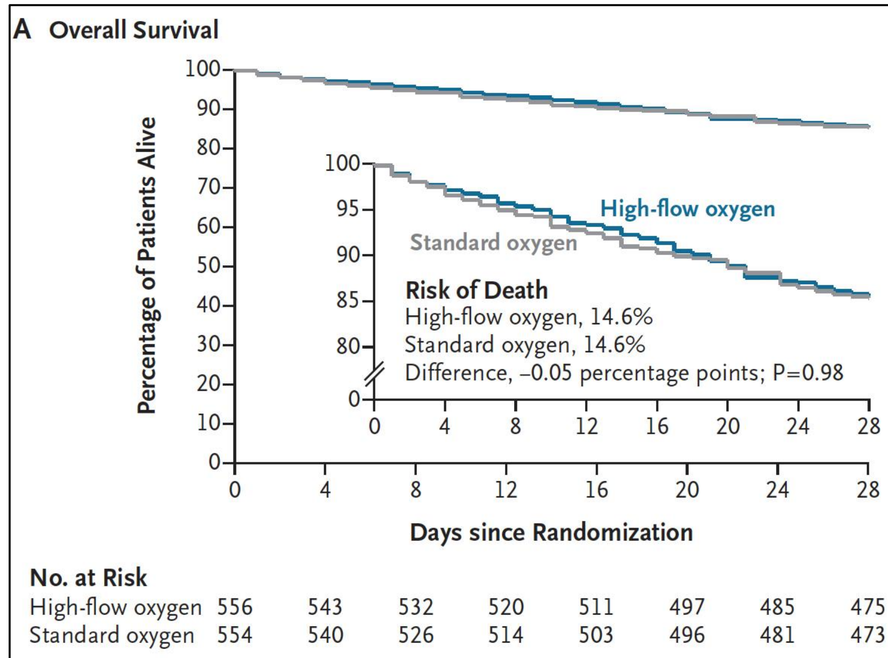
Helmet NIV may have a protective effect for patients at risk for PSILI

Grieco et al., Am J Respir Crit Care Med. 2022 Feb 1;205(3):360-364.

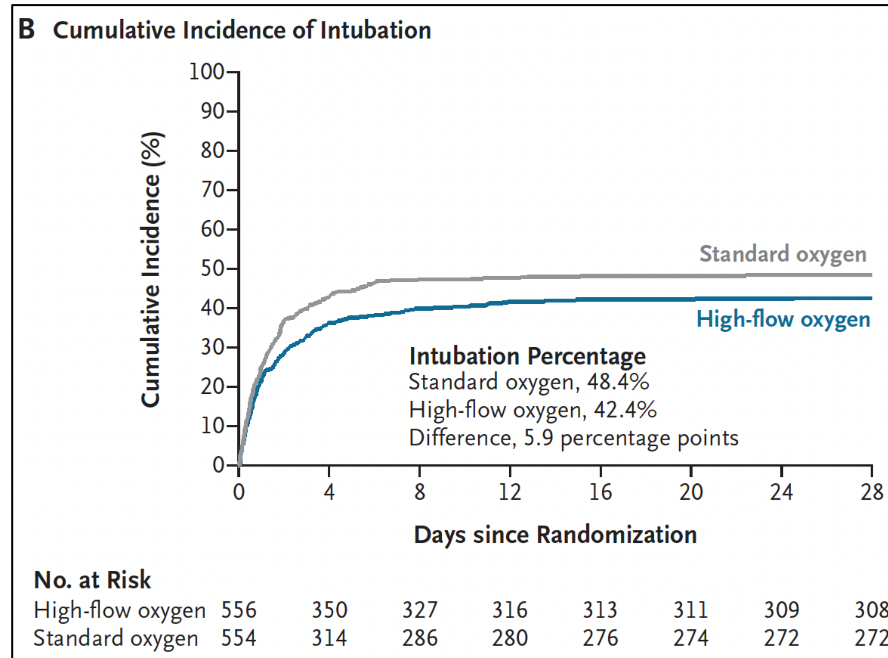
HFNC vs COT in Acute hypoxemic respiratory failure

- Open-lable, multicenter, RCT, France
- Patients with P/F ratio ≤200, N=1,110

Main reason for acute respiratory failure — no. (%)		
Viral pneumonia	300 (54.0)	292 (52.7)
Covid-19	258 (46.4)	259 (46.8)
Bacterial pneumonia	172 (30.9)	180 (32.5)
Fungal pneumonia	17 (3.1)	17 (3.1)
Other reason	67 (12.1)	65 (11.7)
Medication — no. (%)		
Glucocorticoid	343 (62.3)	338 (62.0)
Vasopressor	13 (2.3)	8 (1.4)



28-day OS: 14.6% vs 14.6%



Intubation: 42.4% vs 48.4%

HFNC did not significantly reduce 28-day mortality

Frat JP et al., N Engl J Med. 2026 Mar 17.

SSC sepsis guideline 2026

- **New recommendation**
  - ✓HFNC over COT
  - ✓HFNC over NIV
  - ✓Awakening prone

Conditional recommendation, with **very low or low certainty of evidence**

RESPIRATORY SUPPORT

No.	Strength	Certainty	Recommendation
65		⊕○○○	For adults with sepsis, we **suggest** measuring oxygenation by either pulse oximeter (SpO_2) or arterial blood gas (SaO_2) in conjunction with physical examination and clinical acumen. **Remark:** Arterial blood gas measurements are the gold standard for assessing oxygenation; include other important information such as pH, $PaCO_2$, lactate, and bicarbonate; and are preferable when available. SpO_2/FiO_2 by pulse oximeter may substitute for PaO_2/FiO_2 ratio, but is less accurate in patients in shock, with darker skin tones, and/or with oxygen saturations <90% or >97%.
66		⊕⊕○○	For adults with sepsis and acute hypoxemic respiratory failure, we **suggest** titrating FiO_2 to target either higher, more liberal oxygen levels or lower, conservative oxygen levels depending on patient factors and resource limitations. **Remark:** While there was variability across trials informing this recommendation, most used a lower target of approximately 90-93% SpO_2 and a higher target of $SpO_2 \geq 96$. **Remark:** ***In our practice***, panelists target SpO_2 between 90% (IQR 90-92%) to 96% (IQR 94-98%) for patients with sepsis and acute hypoxemic respiratory failure.
67	✓	⊕○○○	For adults with sepsis and acute hypoxemic respiratory failure, we **suggest** using high flow nasal cannula (HFNC) therapy over conventional oxygen therapy. **Remark:** This recommendation pertains to patients with a PaO_2/FiO_2 ratio <200 or SpO_2/FiO_2 ratio <235.
68	✓	⊕⊕○○	For adults with sepsis and acute hypoxemic respiratory failure, we **suggest** using HFNC as the initial therapy over non-invasive positive pressure ventilation.
69	✓	⊕○○○	For adults with sepsis and acute hypoxemic respiratory failure, we **suggest** using HFNC over high flow alternating with non-invasive positive pressure ventilation.
70	✓	⊕○○○	For adults with sepsis and acute hypoxemic respiratory failure who are not intubated, we **suggest** a trial of awake proning. **Remark:** The duration and frequency of proning will depend on patient tolerance. Sedation should not be used for the purposes of promoting tolerance of proning in non-intubated patients.
71	✓✓	⊕⊕⊕⊕	For adults with sepsis and ARDS, we **recommend** using a low tidal volume ventilation strategy (6 ml/kg) over a high tidal volume strategy (> 10 ml/kg).
72	✓	⊕⊕○○	For adults with sepsis acute hypoxemic respiratory failure without ARDS, we **suggest** using a tidal volume of 6 – 8 ml/kg IBW over a lower (4 to < 6 ml/kg IBW) tidal volume. **Remark:** Patients should be screened regularly for development of ARDS, as ARDS diagnosis is often missed or delayed in clinical practice.
73	✓✓	⊕⊕⊕⊕	For adults with sepsis and ARDS, we **recommend** using an upper limited goal for plateau pressure of 30 cm H_2O) over higher plateau pressures.
74	✓	⊕⊕⊕○	For adults with sepsis and moderate-severe ARDS, we **suggest** using higher PEEP over lower PEEP.
75	✗✗	⊕⊕⊕○	For adults with sepsis and moderate-severe ARDS, we **recommend against** using an incremental PEEP titration strategy
76	✓	⊕⊕⊕○	For adults with sepsis and moderate-severe ARDS, we **suggest** using prone ventilation for greater than 12 hours daily.
77	✓	⊕⊕⊕○	For adults with sepsis and moderate-severe ARDS, we **suggest** using intermittent NMBA boluses over continuous NMBA infusion.
78	✓	⊕⊕○○	For adults with severe ARDS due to sepsis, we **suggest** using veno-venous ECMO when conventional mechanical ventilation fails in experienced centers with infrastructure to support its use.

Strength of Recommendation
- ✓✓ Strong Recommendation For
- ✓ Conditional Recommendation For
- ✗ Conditional Recommendation Against
- ✗✗ Strong Recommendation Against

Certainty of Evidence
- ⊕○○○ Very Low
- ⊕⊕○○ Low
- ⊕⊕⊕○ Moderate
- ⊕⊕⊕⊕ High

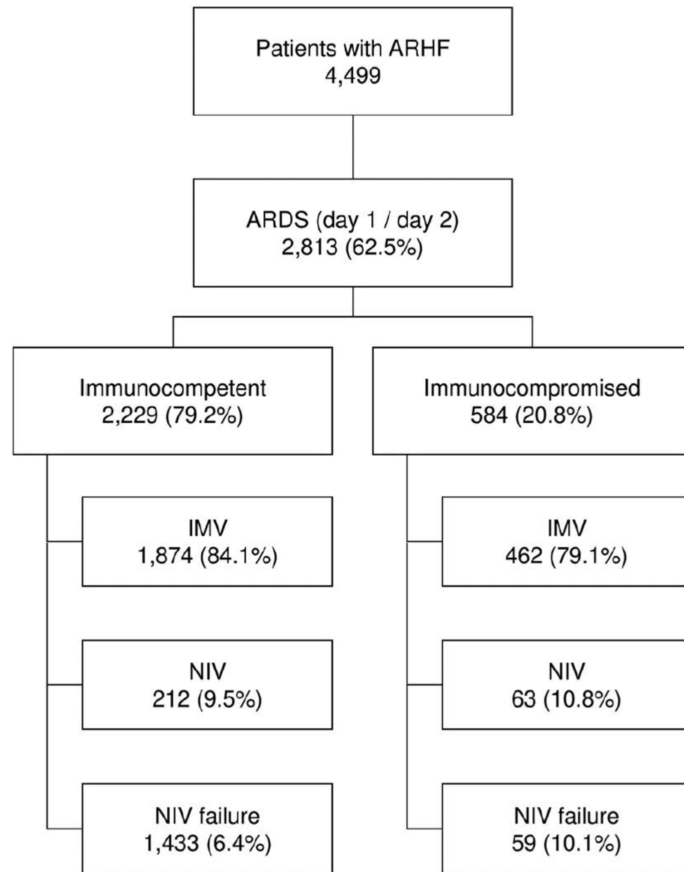
Type of Recommendation
- Carry Over
- New, Revised, or Revisited but Unchanged Statements

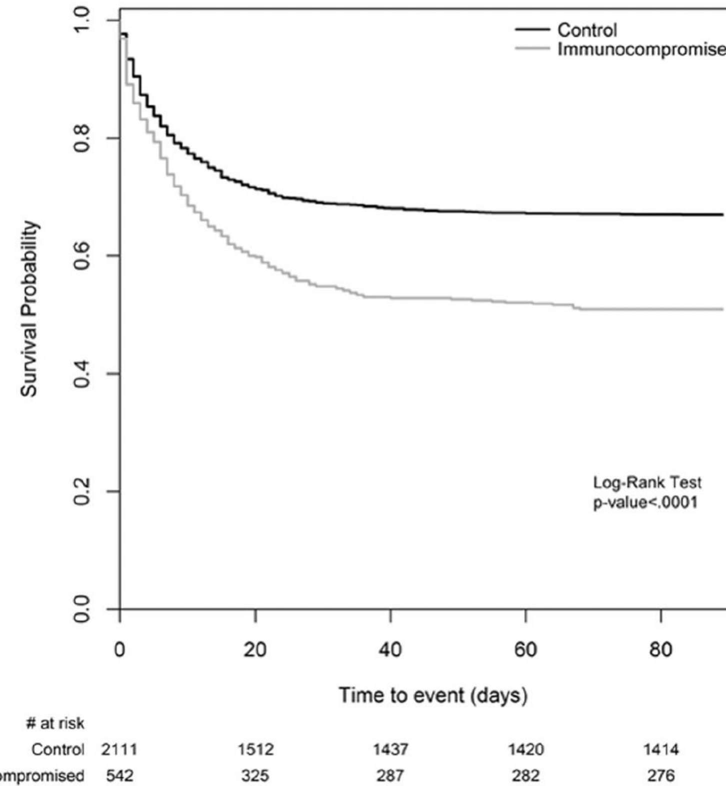
Change in Strength of Recommendation or Change in Certainty of Evidence
- ↖ Upgraded
- ↘ Downgraded

Prescott HC et al., Crit Care Med. 2026 Mar 23.

Immunocompromised patients

Immunocompromised patients with acute respiratory distress syndrome



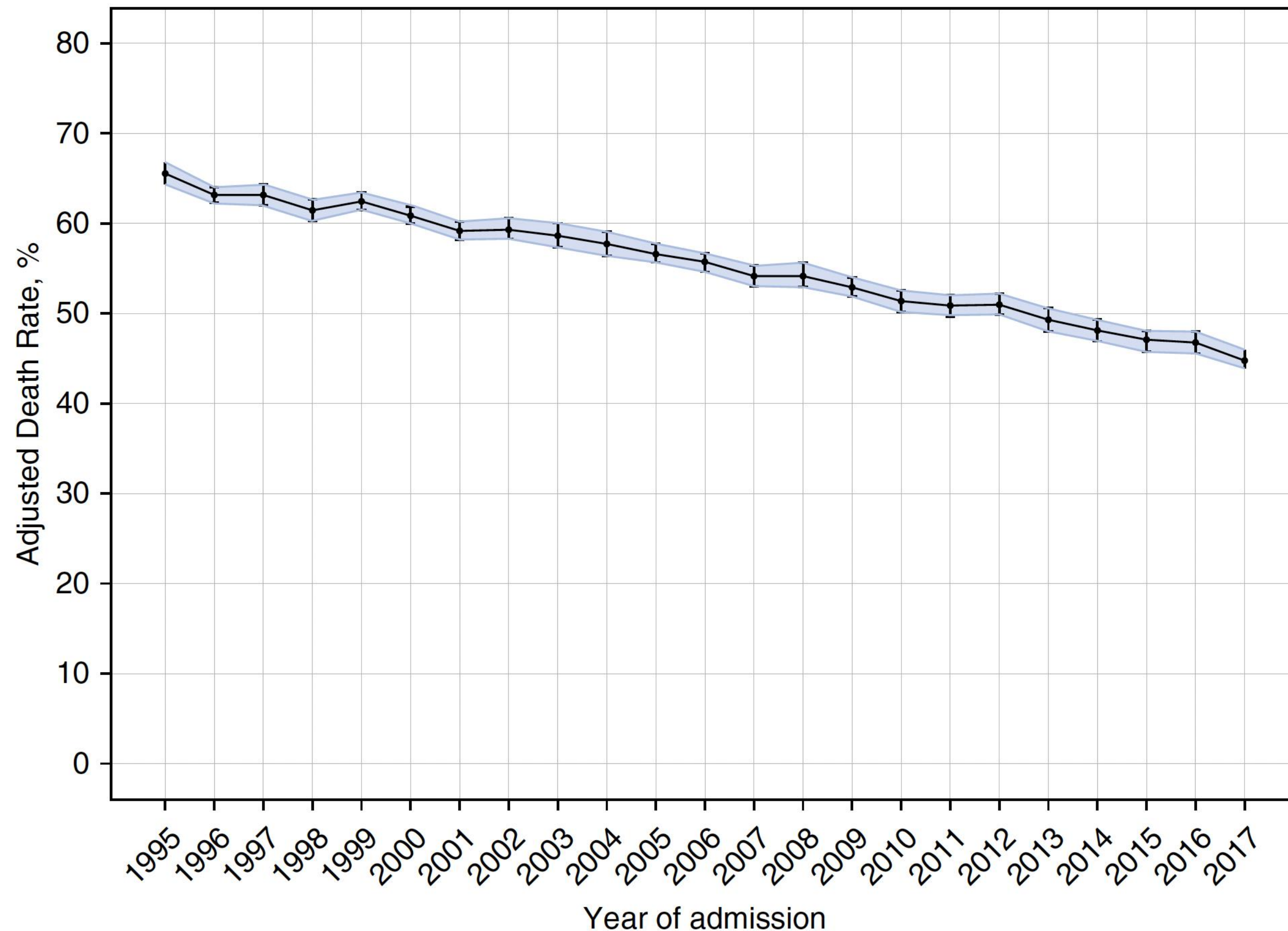


Hospital mortality
Immunocompromised 52.4% vs
control 36.2%

- Secondary analysis of the LUNG SAFE database
- More NIV as first-line treatment (20% vs 16%)
- Similar mortality of NIV-failure (62.7%) and IMV (52.8%)

Cortegiani et al., Crit Care. 2018 Jun 12;22(1):157.

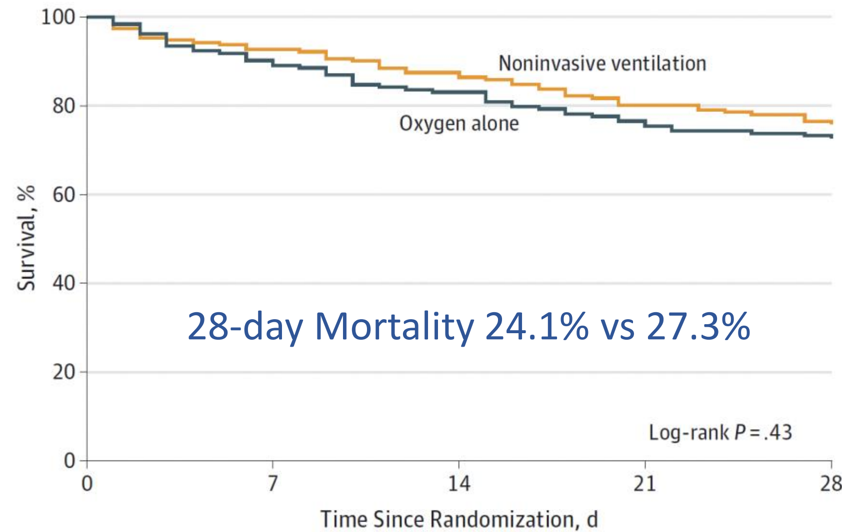
Survival in Immunocompromised Patients Requiring Invasive Mechanical Ventilation

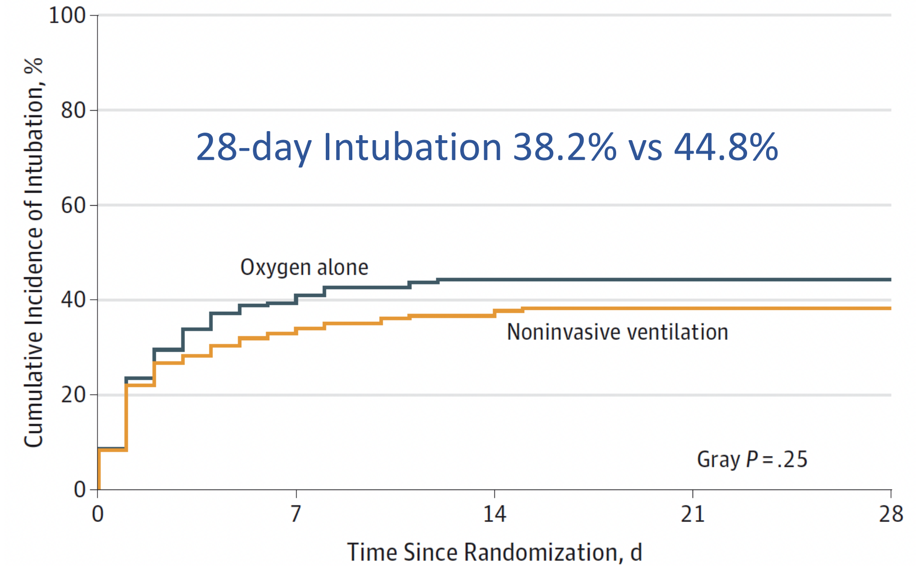


- Mortality 53.2% overall
- Survival improved over time
- Early intubation was associated with lower mortality (OR, 0.83 [0.72 – 0.79])

Dumas et al., Am J Respir Crit Care Med. 2021 Jul 15;204(2):187-196.

NIV vs Oxygenation Among Immunocompromised Patients With Acute Respiratory Failure





Mortality

Source	No. of Deaths/Total No. Oxygen Alone	No. of Deaths/Total No. Noninvasive Ventilation	Odds Ratio (95% CI)	*P* Value for Interaction[a]
Underlying Conditions				
Solid tumors or hematologic malignancies	43/150	41/161	0.85 (0.51-1.40)	.66
Immunosuppressive treatment or organ transplant	7/33	5/30	0.74 (0.2-2.63)	
Oxygen flow at randomization[b]				
>9 L/min	26/77	24/84	0.78 (0.4-1.53)	.64
≤9 L/min	24/106	22/107	0.88 (0.46-1.70)	
All patients	50/183	46/191	0.84 (0.53-1.34)	

Favors Noninvasive Ventilation | Favors Oxygen Alone

0.2 1.0 5.0

Odds Ratio (95% CI)

- HFNC was allowed in both groups (40% in control group)
- Limited study power (lower mortality than expected)

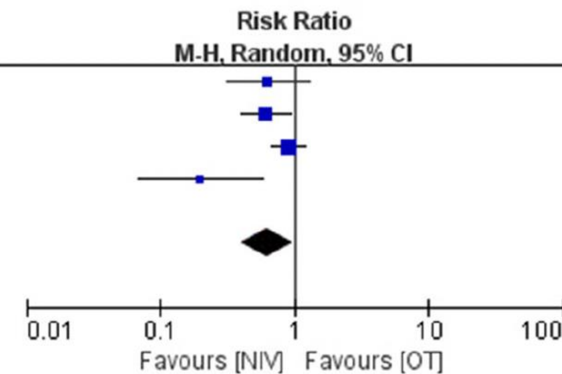
Lemiale et al., JAMA. 2015 Oct 27;314(16):1711-9.

Use of NIV in immunocompromised patients with acute respiratory failure

A Short-term mortality

Study or Subgroup	NIV Events	NIV Total	OT Events	OT Total	Weight	Risk Ratio M-H, Random, 95% CI
Antonelli 2000	7	20	11	20	20.4%	0.64 [0.31, 1.30]
Hilbert 2001	13	26	21	26	30.9%	0.62 [0.40, 0.95]
Lemiale 2015	59	191	63	183	36.5%	0.90 [0.67, 1.20]
Squadrone 2010	3	20	15	20	12.3%	0.20 [0.07, 0.59]
Total (95% CI)		**257**		**249**	**100.0%**	**0.62 [0.40, 0.97]**
Total events	82		110			

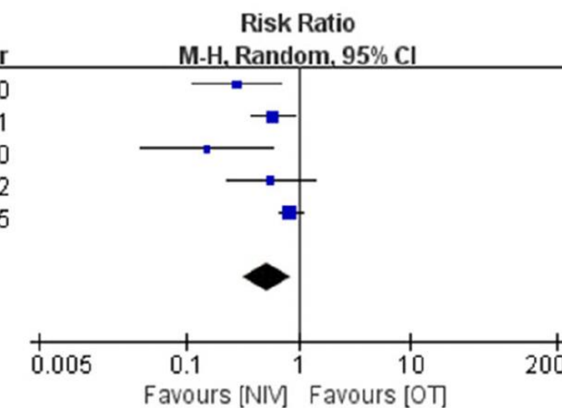
Heterogeneity: Tau² = 0.12; Chi² = 8.23, df = 3 (P = 0.04); I² = 64%
Test for overall effect: Z = 2.10 (P = 0.04)



B Incidence of intubation rate

Study or Subgroup	NIV Events	NIV Total	OT Events	OT Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Antonelli 2000	4	20	14	20	15.5%	0.29 [0.11, 0.72]	2000
Hilbert 2001	12	26	20	26	26.6%	0.60 [0.38, 0.96]	2001
Squadrone 2010	2	20	13	20	9.4%	0.15 [0.04, 0.60]	2010
Wermke 2012	6	42	11	44	15.9%	0.57 [0.23, 1.41]	2012
Lemiale 2015	73	191	82	183	32.5%	0.85 [0.67, 1.09]	2015
Total (95% CI)		**299**		**293**	**100.0%**	**0.52 [0.32, 0.85]**	
Total events	97		140				

Heterogeneity: Tau² = 0.17; Chi² = 11.90, df = 4 (P = 0.02); I² = 66%
Test for overall effect: Z = 2.62 (P = 0.009)

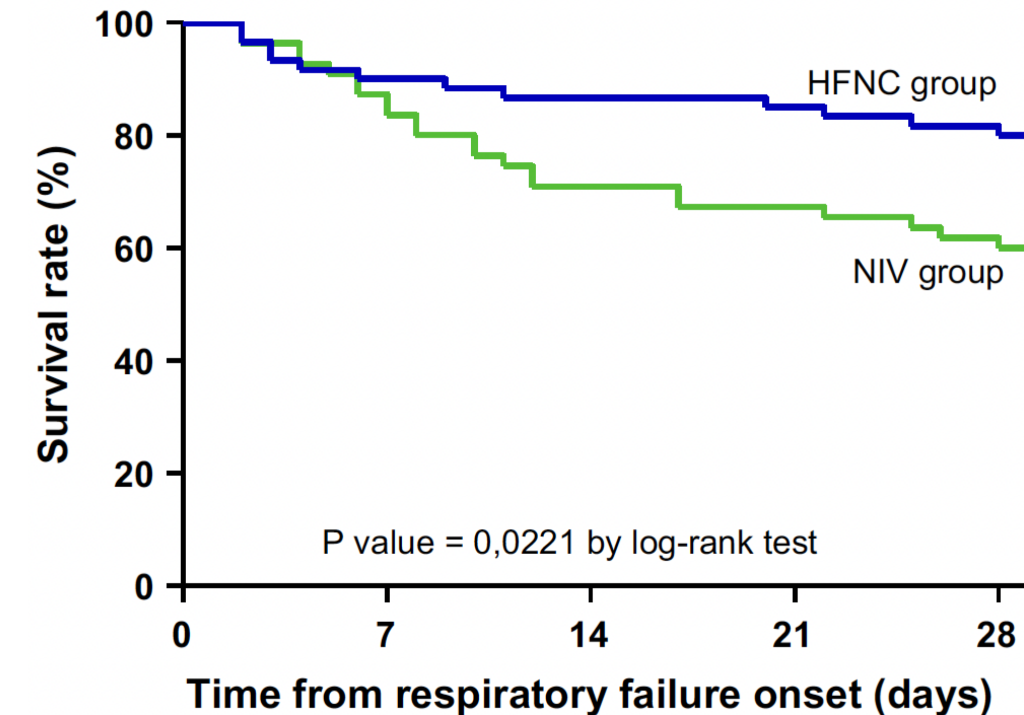


NIV better than O2 therapy alone

Huang et al., Crit Care. 2017 Jan 7;21(1):4.

HFNC versus NIV in immunocompromised patients with acute respiratory failure

	NIV (n=55)	HFNC (n=60)	*P* value
Intubation	55%	35%	0.04
Mortality	40%	20%	0.02



Multivariate analysis of factors associated with 28-day survival

	Adjusted odds ratio (95 % CI)	*p* value
Variables independently associated with intubation[a]		
Simplified Acute Physiology Score II, per point	1.04 (1.00–1.08)	0.04
Noninvasive ventilation as a first-line therapy	3.25 (1.39–7.60)	0.007
Use of vasopressors within 24 h after ICU admission	4.12 (1.32–12.84)	0.02
Variables independently associated with mortality at day 28[b]		
Age (per year)	1.03 (1.00–1.07)	0.04
Use of vasopressors within 24 h after ICU admission	2.83 (1.02–7.91)	0.047
Noninvasive ventilation as a first-line therapy	3.70 (1.49–9.19)	0.005

[a] Non-collinear variables included in the logistical regression model were Simplified Acute Physiology Score II, Noninvasive ventilation as a first-line therapy, use of vasopressors within 24 h after ICU admission, SpO_2 at ICU admission, cause of respiratory failure and $PaCO_2$ as a continuous variable. The year of ICU admission was forced in the model

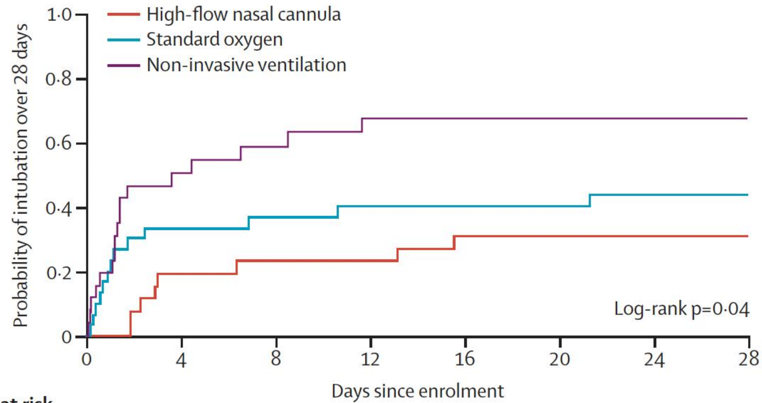
[b] Non-collinear variables included in the logistical regression model were age, PaO_2-to-FiO_2 ratio at ICU admission, use of noninvasive ventilation as a first-line therapy, type of immunosuppression, use of vasopressors in the 24 h after ICU admission, cause of respiratory failure and $PaCO_2$ > 45 mmHg. The year of ICU admission was forced in the model

- Retrospective observational cohort
- More hypercapnia and respiratory acidosis in NIV group

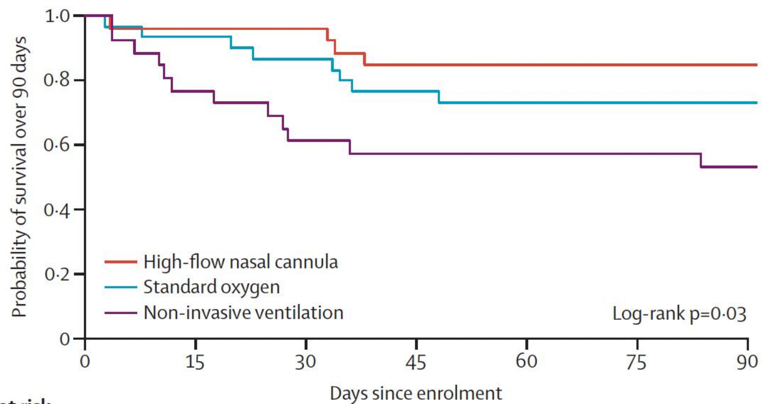
Coudroy et al., Ann Intensive Care. 2016 Dec;6(1):45

Non-invasive oxygenation in immunocompromised patients with severe acute respiratory failure

Intubation



Survival



	Adjusted OR for intubation	Adjusted OR for intensive care unit mortality	Adjusted HR for 90-day mortality
Age, per year	1·1 (1·0–1·1); p=0·008	1·1 (1·0–1·1); p=0·002	1·0 (1·0–1·1); p=0·003
Randomisation to non-invasive ventilation	4·4 (1·4–14); p=0·013	4·2 (1·3–13·5); p=0·016	3·3 (1·2–5·0); p=0·01

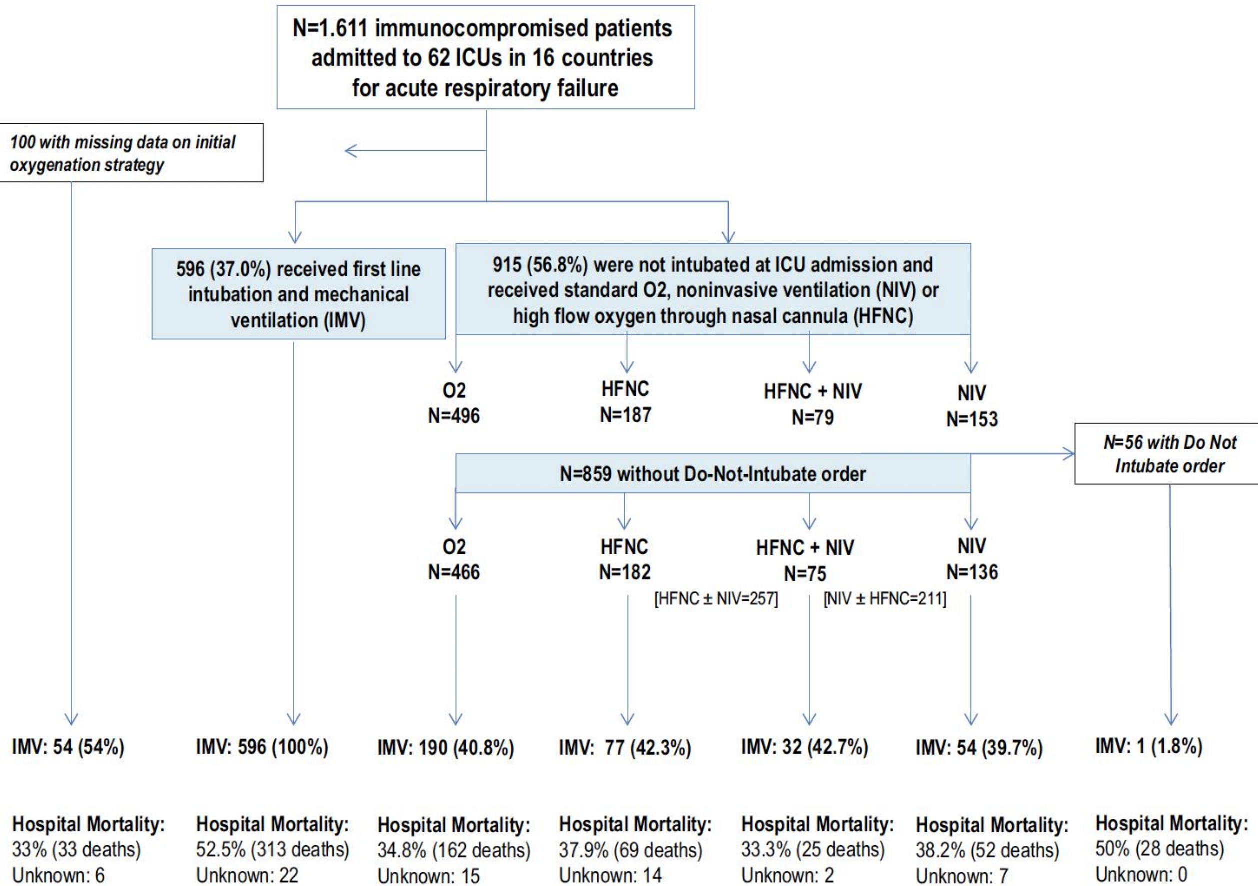
Data are OR (95% CI); p value or HR (95% CI); p value. For intubation, variables introduced in the maximal model were age, randomisation to non-invasive ventilation, SAPS II, and mean arterial pressure. For intensive care unit and 90-day mortality, variables introduced in the maximal model were age, randomisation to non-invasive ventilation, SAPS II, and PaO_2:FIO_2 ratio. OR=odds ratio. HR=hazard ratio. SAPS II=simplified acute physiology score. PaO_2:FIO_2=partial pressure of arterial oxygen to fraction of inspired oxygen ratio.

- Post-hoc analysis of a randomised trial
- Small patients number (n=82)

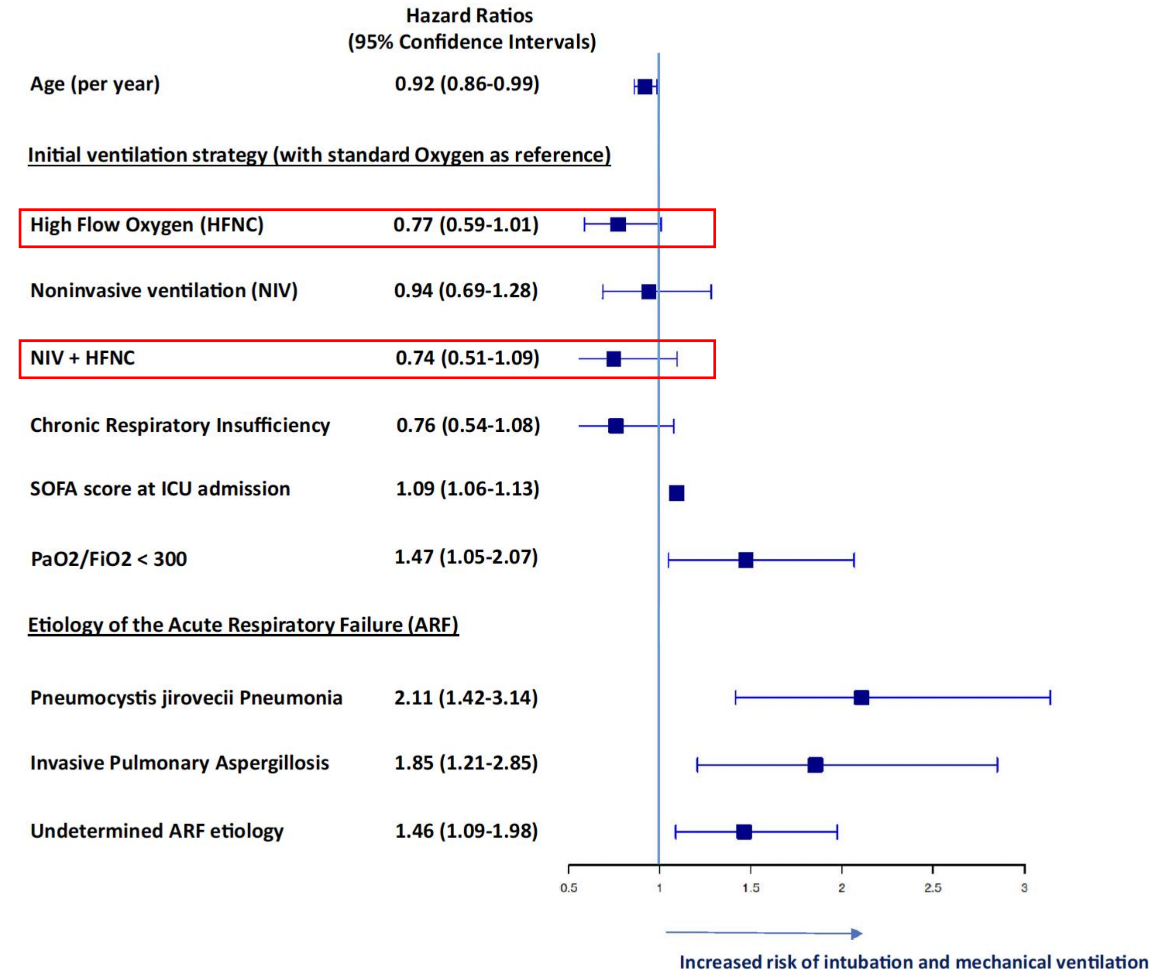
Frat et al., Lancet Respir Med. 2016 Aug;4(8):646-652.

Acute hypoxemic respiratory failure in immunocompromised patients

EFRAIM

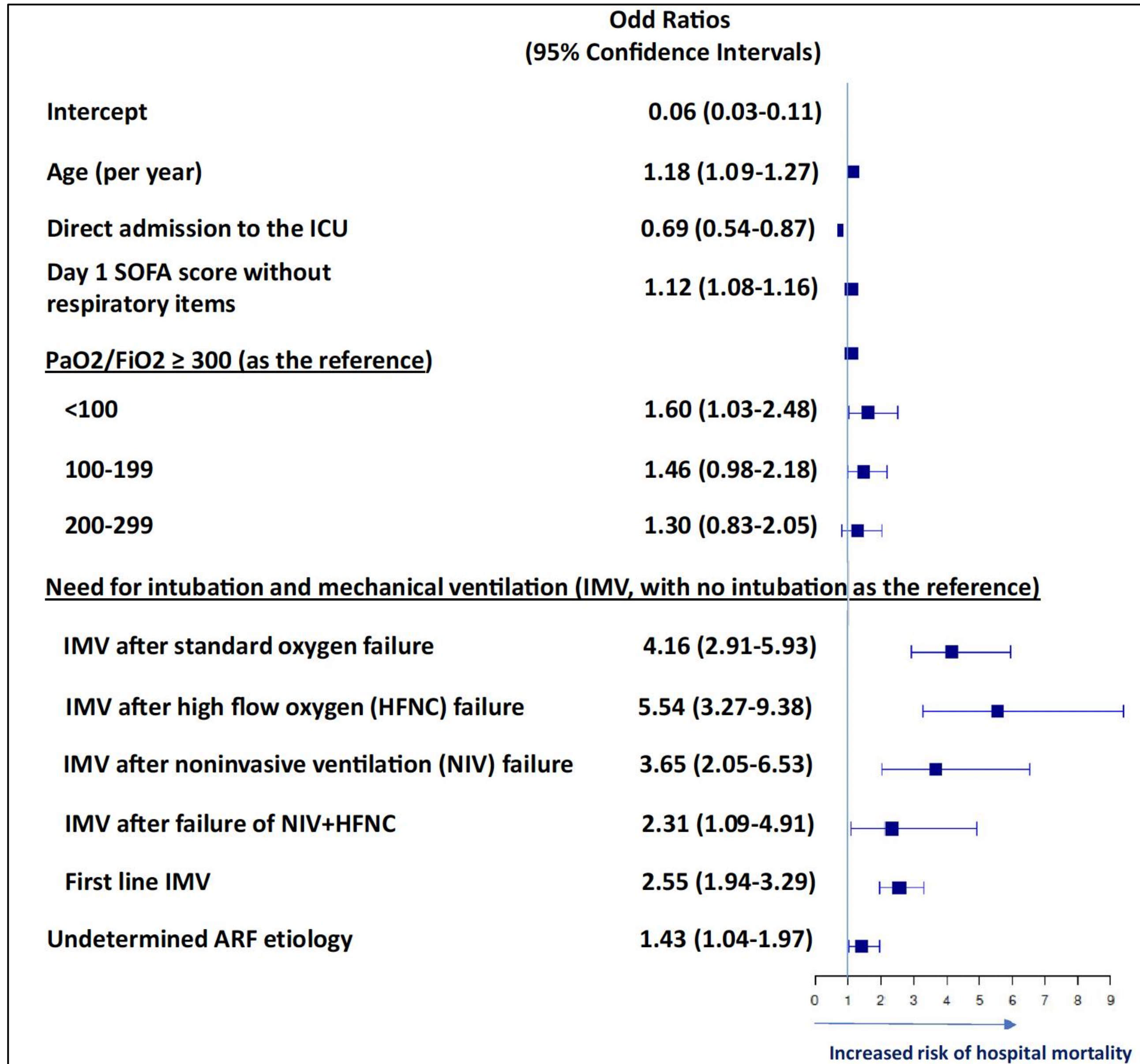


Multivariate analysis for factors associated with intubation



Azoulay et al., Intensive Care Med. 2017 Dec;43(12):1808-1819.

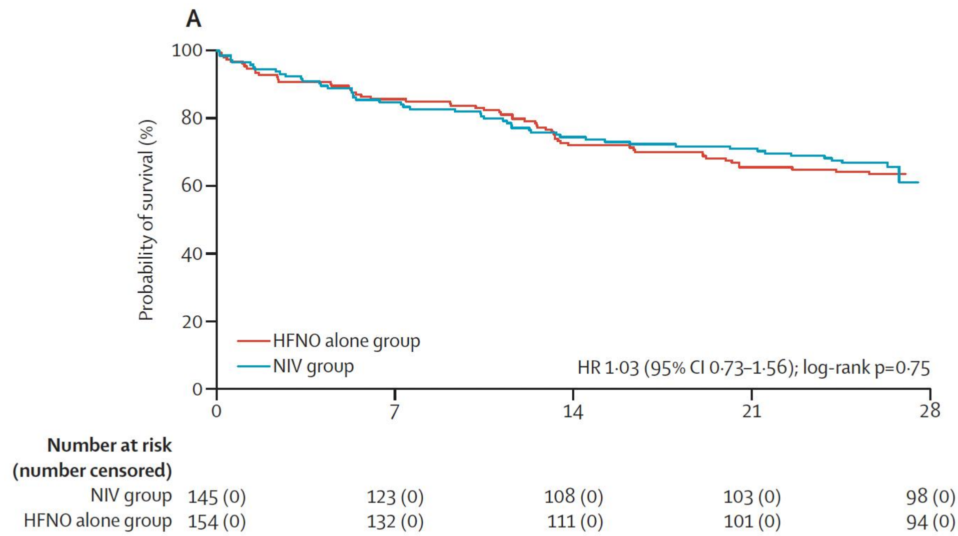
EFRAIM

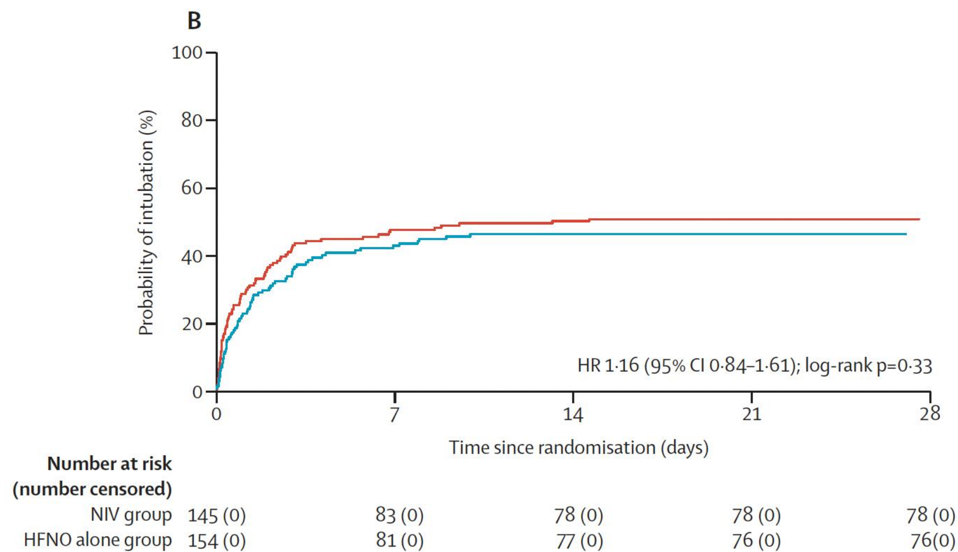


- HFNC was associated with lower rate of intubation (HR, 0.77[0.59 – 1.00])
- IMV was associated with mortality
- Undetermined etiology was associated with intubation and mortality

Azoulay et al., Intensive Care Med. 2017 Dec;43(12):1808-1819.

HFNC alone or alternating with NIV in critically ill immunocompromised patients





	HFNO alone group (n=154)	NIV group (n=145)	Hazard ratio (95% CI)	$p_{interaction}$
All patients	56/154	51/145	1·03 (0·73–1·56)	
Type of immunosuppression				
Haematological malignancy or leucopenia or neutropenia	31/81	22/75	1·37 (0·80–2·37)	0·18
Others	25/73	29/70	0·82 (0·48–1·41)	
PaO_2/FiO_2 at inclusion				
>200 mm Hg	6/25	7/21	0·81 (0·26–2·51)	0·50
≤200 mm Hg	50/129	44/124	1·11 (0·74–1·66)	
Cause of respiratory failure				
Confirmed diagnosis	48/132	40/118	1·09 (0·71–1·65)	0·87
No diagnosis	8/22	11/27	1·01 (0·40–2·56)	

0·0 0·5 1 1·5 2·0 2·5 3·0

Favours HFNO alone | Favours NIV

- RCT (2017 to 2019)
- 99% NIV delivered via face mask
- Limited study power

Coudroy et al., Lancet Respir Med. 2022 Jul;10(7):641-649.

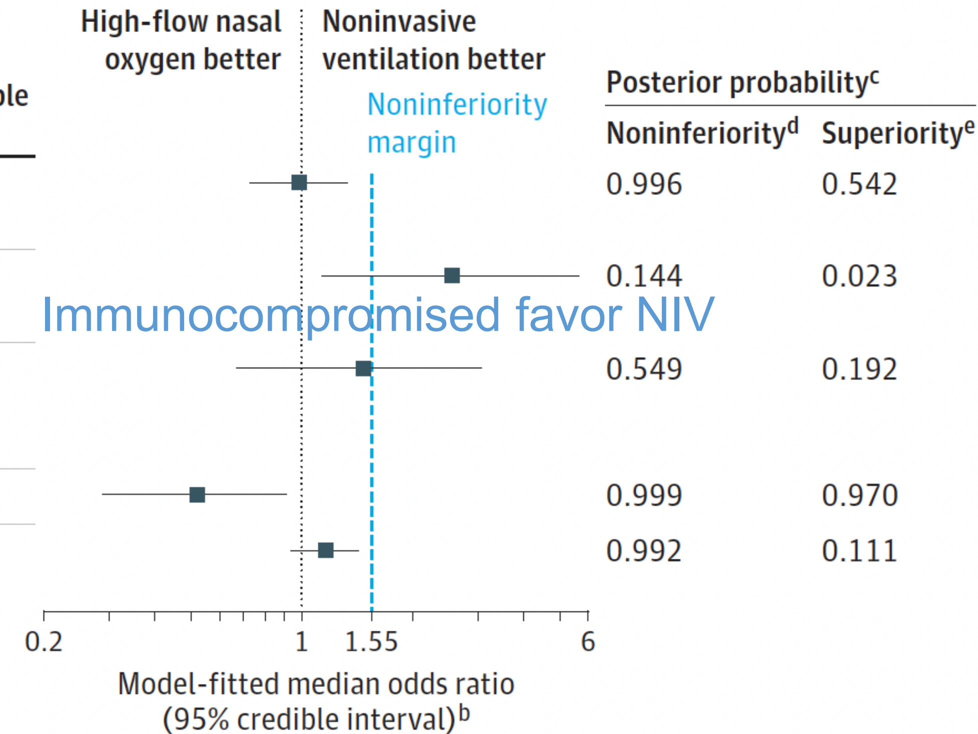
RENOVATE

HFNC vs NIV in patients with acute respiratory failure

- RCT, Brazil, 2019 to 2023
- Non-inferiority of HFNC vs NIV, N=1,766
- Primary outcomes: intubation or death

Intubation or death

Patients with acute respiratory failure	No./total (%) High-flow nasal oxygen	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)



HFNC failed to reach non-inferiority vs NIV in **immunocompromised patients**

The statistic power was limited in **COPD, immunocompromised, and cardiogenic edema** due to **small sample size**

Maia IS et al., JAMA. 2025 Mar 11;333(10):875-890.

Non-invasive respiratory support in respiratory failure

- **Reduced intubation most of the time**, **sometimes improve survival**
- **HFNC**
  - ✓Improved outcomes in **COVID-19 with AHF** compared with COT
  - ✓Preferentially over NIV in patients with **high sputum load** and may be preferred in **mild ARDS**
- **NIV**
  - ✓May be considered in **mild to moderate ARDS (P/F ≥150), higher respiratory drive**
  - ✓Helmet over face mask
  - ✓Titrating PEEP and monitor V_T as **lung protective strategy**
  - ✓Close monitor **hemodynamic, consciousness, arterial blood gas** and **never delay intubation**

Weaning from mechanical ventilation

High risk patients following extubation

High risk groups (mechanical ventilation more than 12 hours)
• Age ≥65 years • Heart failure • Moderate to severe COPD • APACHE II ≥12 on the day of extubation • BMI ≥30 • Airway patency problems • Respiratory secretions (inadequate cough, suction ≥2 times within 8 hrs) • Difficult weaning (re-intubated) • Mechanical ventilation for more than 7 days • ≥2 Comorbidities

Re-intubation

Comparison	Network odds ratio (95% CI)	Absolute risk difference (95% CI)	Number needed to treat
NIPPV vs conventional oxygen	0.65 (0.52–0.82)	− 5.18 (− 8.09 to − 2.26)	20 (13 to 45)
HFNC vs conventional oxygen	0.63 (0.45–0.87)	− 3.84 (− 6.7 to − 0.98)	26 (15 to 102)
NIPPV vs HFNC	1.04 (0.78–1.38)	− 1.34 (− 4.4 to 1.72)	N/A
HFNC + NIPPV vs conventional oxygen	0.38 (0.19–0.74)	− 10.25 (− 18.49 to − 2.01)	10 (6 to 50)
HFNC + NIPPV vs NIPPV	0.58 (0.3–1.11)	− 5.07 (− 13.38 to 3.24)	N/A
HFNC + NIPPV vs HFNC	0.6 (0.33–1.08)	− 6.41 (− 14.13 to 1.31)	N/A

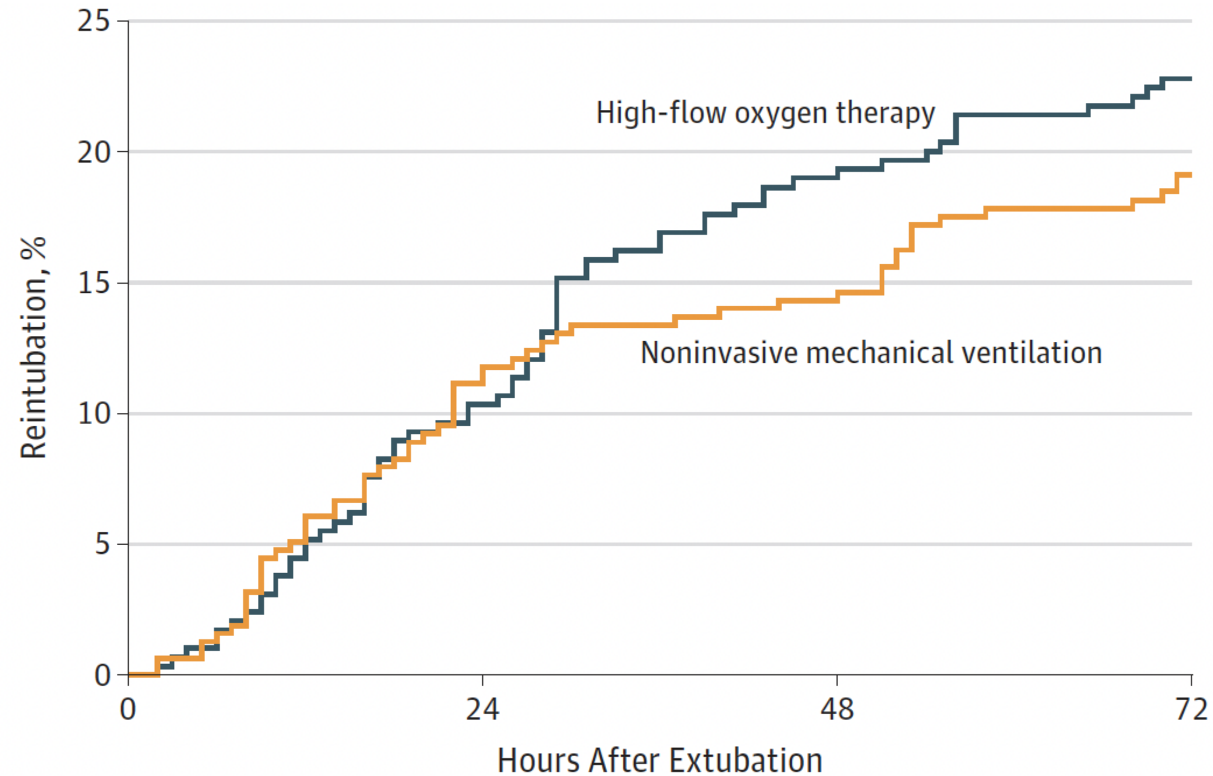
Fernando et al., Intensive Care Med. 2022 Feb;48(2):137-147.

HFNC for high risk patients following extubation

Non-inferior trial

Reintubation	
HFNC	22.8%
NIPPV	19.1%
Risk difference, -3.7% (-9.1% to ∞)	

Respiratory Failure	
HFNC	26.9%
NIPPV	39.8%
Risk difference, 12.9% (6.6% to ∞)	

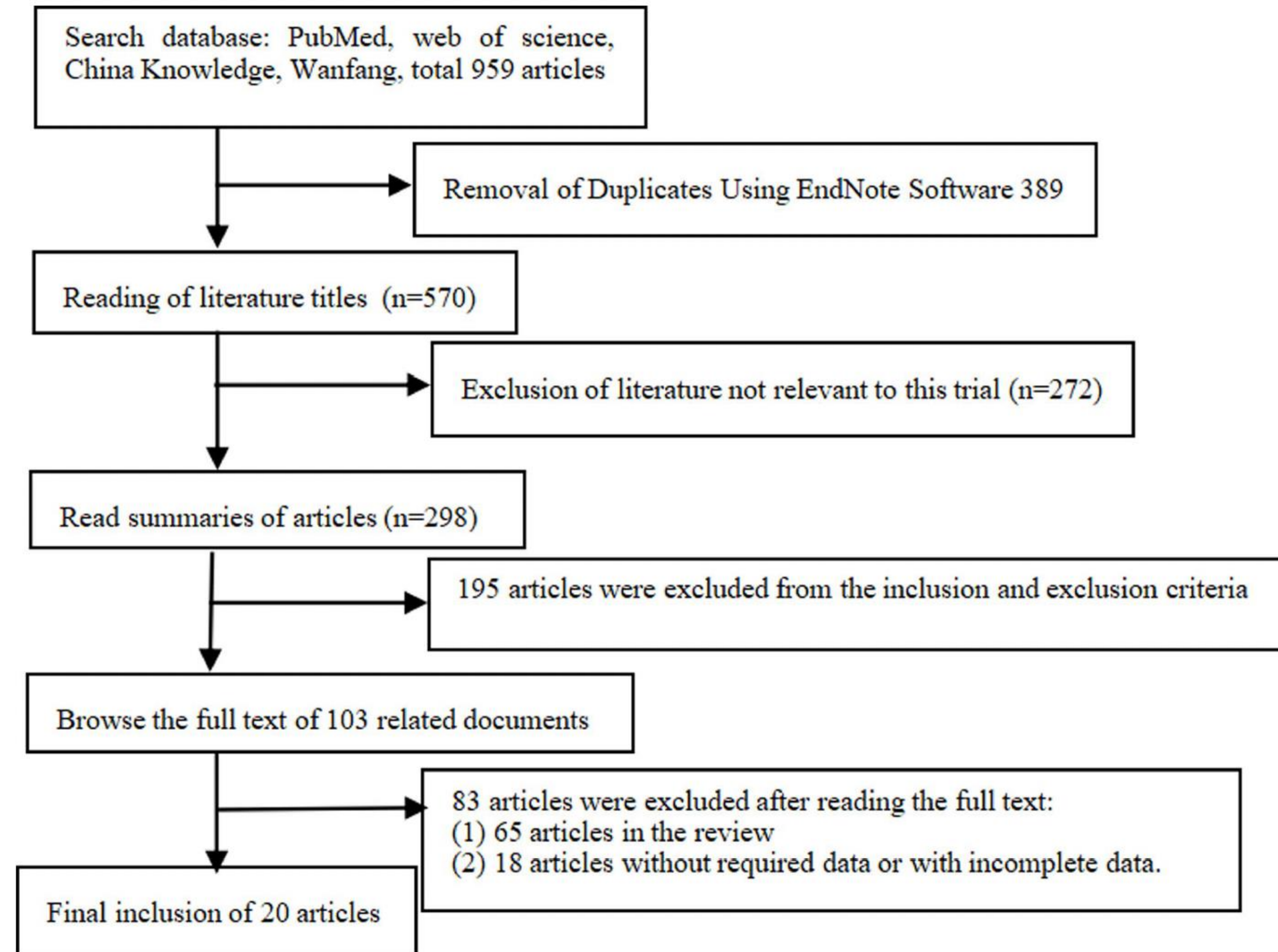


No. at risk	0	24	48	72
High-flow oxygen therapy	290	260	234	223
Noninvasive mechanical ventilation	314	279	269	253

Hernández et al., JAMA. 2016 Oct 18;316(15):1565-1574.; Erratum in: JAMA. 2016 Nov 15;316(19):2047-2048; Erratum in: JAMA. 2017 Feb 28;317(8):858

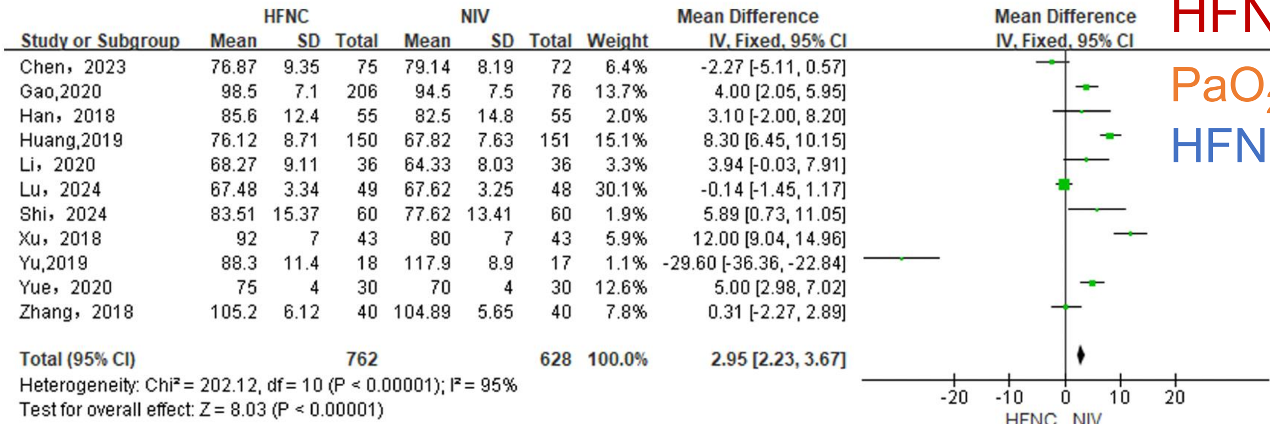
HFNC vs NIV after invasive mechanical ventilation: a systemic review and meta-analysis

- COPD, post-lung transplant, acute respiratory failure, post-operative hypoxemia, preterm infants
- 18 RCT and 2 non-RCT



Maimaitiniyazi M et al., Front Med (Lausanne). 2025 Sep 25;12:1594145.

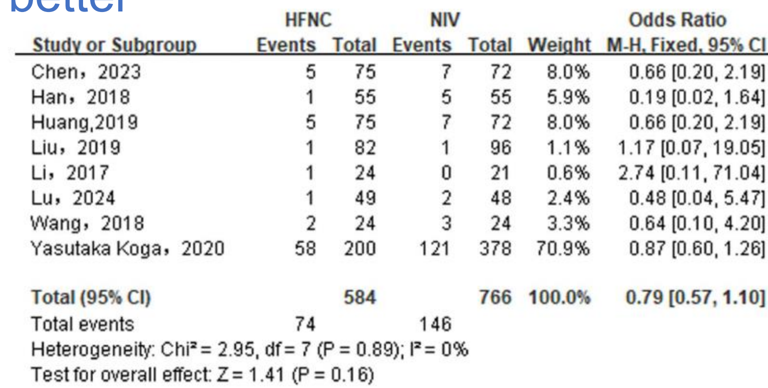
HFNC vs NIV



PaO$_2$
HFNC better

Study or Subgroup	HFNC Mean	HFNC SD	HFNC Total	NIV Mean	NIV SD	NIV Total	Weight	Mean Difference IV, Fixed, 95% CI
Chen，2023	76.87	9.35	75	79.14	8.19	72	6.4%	-2.27 [-5.11, 0.57]
Gao,2020	98.5	7.1	206	94.5	7.5	76	13.7%	4.00 [2.05, 5.95]
Han，2018	85.6	12.4	55	82.5	14.8	55	2.0%	3.10 [-2.00, 8.20]
Huang,2019	76.12	8.71	150	67.82	7.63	151	15.1%	8.30 [6.45, 10.15]
Li，2020	68.27	9.11	36	64.33	8.03	36	3.3%	3.94 [-0.03, 7.91]
Lu，2024	67.48	3.34	49	67.62	3.25	48	30.1%	-0.14 [-1.45, 1.17]
Shi，2024	83.51	15.37	60	77.62	13.41	60	1.9%	5.89 [0.73, 11.05]
Xu，2018	92	7	43	80	7	43	5.9%	12.00 [9.04, 14.96]
Yu,2019	88.3	11.4	18	117.9	8.9	17	1.1%	-29.60 [-36.36, -22.84]
Yue，2020	75	4	30	70	4	30	12.6%	5.00 [2.98, 7.02]
Zhang，2018	105.2	6.12	40	104.89	5.65	40	7.8%	0.31 [-2.27, 2.89]
Total (95% CI)			762			628	100.0%	2.95 [2.23, 3.67]

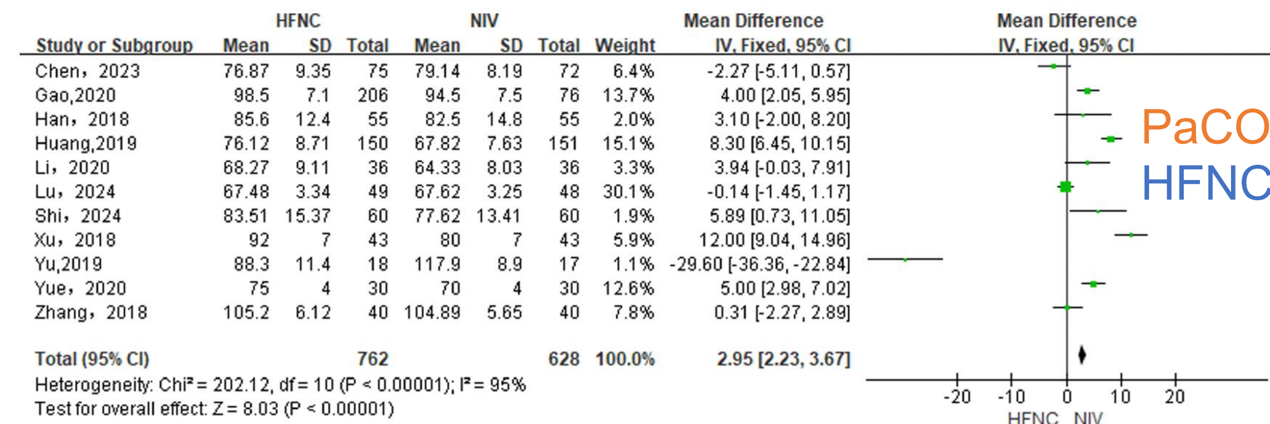
Heterogeneity: $Chi^2 = 202.12$, df = 10 (P < 0.00001); $I^2 = 95\%$
Test for overall effect: Z = 8.03 (P < 0.00001)



Mortality Similar

Study or Subgroup	HFNC Events	HFNC Total	NIV Events	NIV Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Chen，2023	5	75	7	72	8.0%	0.66 [0.20, 2.19]
Han，2018	1	55	5	55	5.9%	0.19 [0.02, 1.64]
Huang,2019	5	75	7	72	8.0%	0.66 [0.20, 2.19]
Liu，2019	1	82	1	96	1.1%	1.17 [0.07, 19.05]
Li，2017	1	24	0	21	0.6%	2.74 [0.11, 71.04]
Lu，2024	1	49	2	48	2.4%	0.48 [0.04, 5.47]
Wang，2018	2	24	3	24	3.3%	0.64 [0.10, 4.20]
Yasutaka Koga，2020	58	200	121	378	70.9%	0.87 [0.60, 1.26]
Total (95% CI)		584		766	100.0%	0.79 [0.57, 1.10]
Total events	74		146			

Heterogeneity: $Chi^2 = 2.95$, df = 7 (P = 0.89); $I^2 = 0\%$
Test for overall effect: Z = 1.41 (P = 0.16)



PaCO$_2$
HFNC better

Study or Subgroup	HFNC Mean	HFNC SD	HFNC Total	NIV Mean	NIV SD	NIV Total	Weight	Mean Difference IV, Fixed, 95% CI
Chen，2023	76.87	9.35	75	79.14	8.19	72	6.4%	-2.27 [-5.11, 0.57]
Gao,2020	98.5	7.1	206	94.5	7.5	76	13.7%	4.00 [2.05, 5.95]
Han，2018	85.6	12.4	55	82.5	14.8	55	2.0%	3.10 [-2.00, 8.20]
Huang,2019	76.12	8.71	150	67.82	7.63	151	15.1%	8.30 [6.45, 10.15]
Li，2020	68.27	9.11	36	64.33	8.03	36	3.3%	3.94 [-0.03, 7.91]
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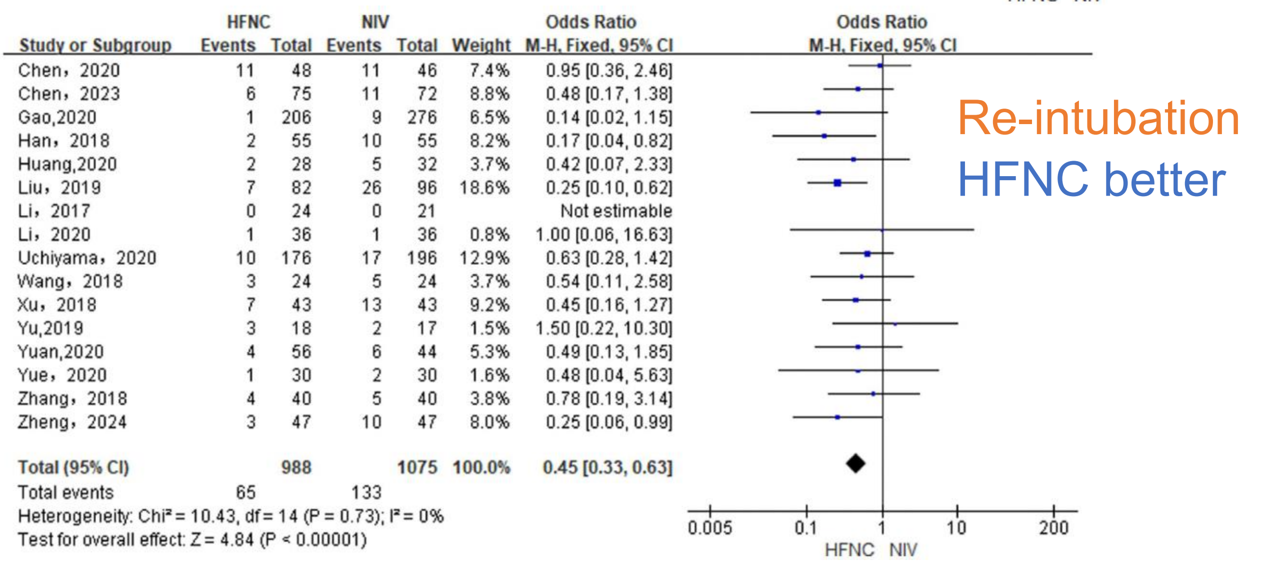
Yue，2020	75	4	30	70	4	30	12.6%	5.00 [2.98, 7.02]
Zhang，2018	105.2	6.12	40	104.89	5.65	40	7.8%	0.31 [-2.27, 2.89]
Total (95% CI)			762			628	100.0%	2.95 [2.23, 3.67]

Heterogeneity: $Chi^2 = 202.12$, df = 10 (P < 0.00001); $I^2 = 95\%$
Test for overall effect: Z = 8.03 (P < 0.00001)



Re-intubation
HFNC better

Study or Subgroup	HFNC Events	HFNC Total	NIV Events	NIV Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Chen，2020	11	48	11	46	7.4%	0.95 [0.36, 2.46]
Chen，2023	6	75	11	72	8.8%	0.48 [0.17, 1.38]
Gao,2020	1	206	9	276	6.5%	0.14 [0.02, 1.15]
Han，2018	2	55	10	55	8.2%	0.17 [0.04, 0.82]
Huang,2020	2	28	5	32	3.7%	0.42 [0.07, 2.33]
Liu，2019	7	82	26	96	18.6%	0.25 [0.10, 0.62]
Li，2017	0	24	0	21		Not estimable
Li，2020	1	36	1	36	0.8%	1.00 [0.06, 16.63]
Uchiyama，2020	10	176	17	196	12.9%	0.63 [0.28, 1.42]
Wang，2018	3	24	5	24	3.7%	0.54 [0.11, 2.58]
Xu，2018	7	43	13	43	9.2%	0.45 [0.16, 1.27]
Yu,2019	3	18	2	17	1.5%	1.50 [0.22, 10.30]
Yuan,2020	4	56	6	44	5.3%	0.49 [0.13, 1.85]
Yue，2020	1	30	2	30	1.6%	0.48 [0.04, 5.63]
Zhang，2018	4	40	5	40	3.8%	0.78 [0.19, 3.14]
Zheng，2024	3	47	10	47	8.0%	0.25 [0.06, 0.99]
Total (95% CI)		988		1075	100.0%	0.45 [0.33, 0.63]
Total events	65		133			

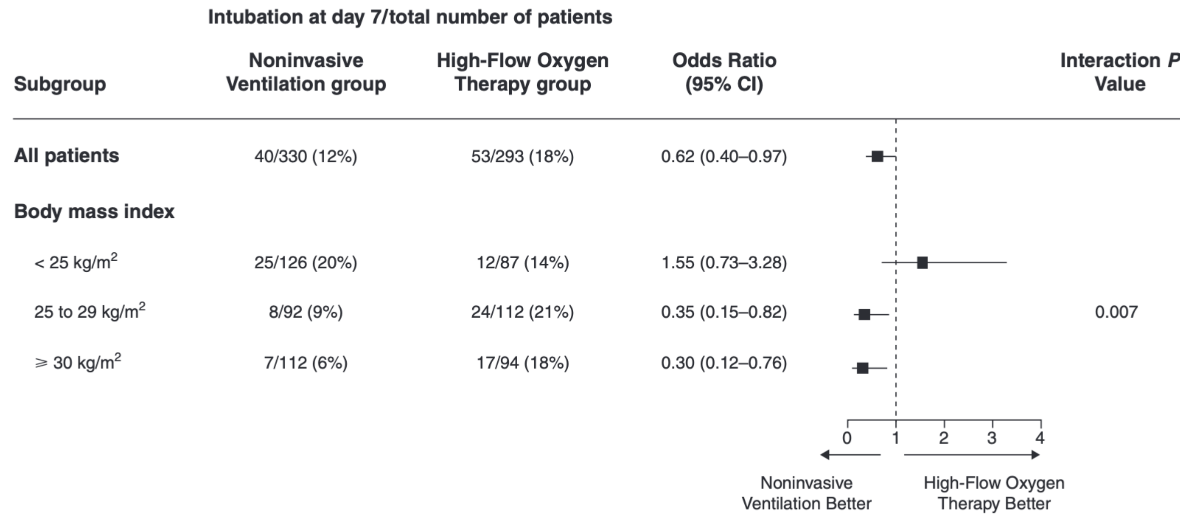
Heterogeneity: $Chi^2 = 10.43$, df = 14 (P = 0.73); $I^2 = 0\%$
Test for overall effect: Z = 4.84 (P < 0.00001)

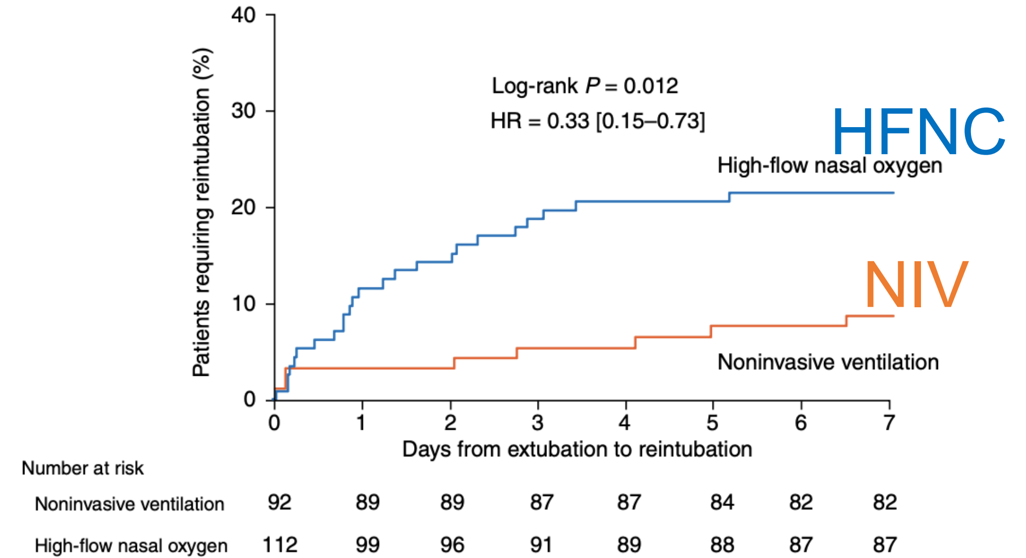
For patients with **extubated from invasive mechanical ventilation, HFNC**

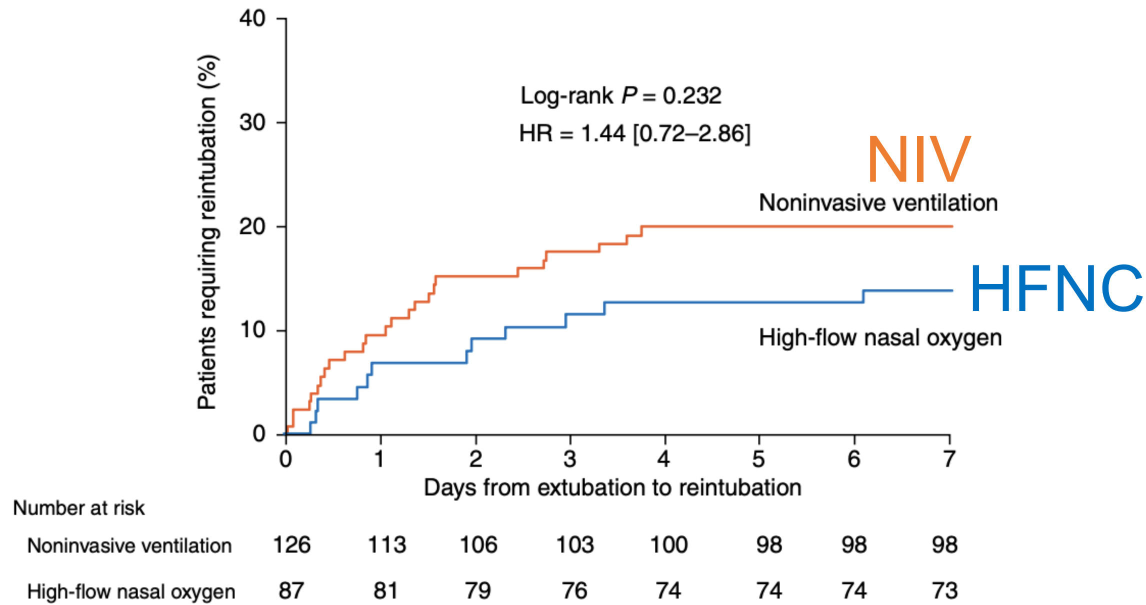
- **Improved PaO2**, reduced **PaCO2**, and lower **re-intubation rate**
- A viable **clinical alternative** for **post-extubation respiratory support**
- Only shorterm outcomes were evaluated
- Risk factor stratification?

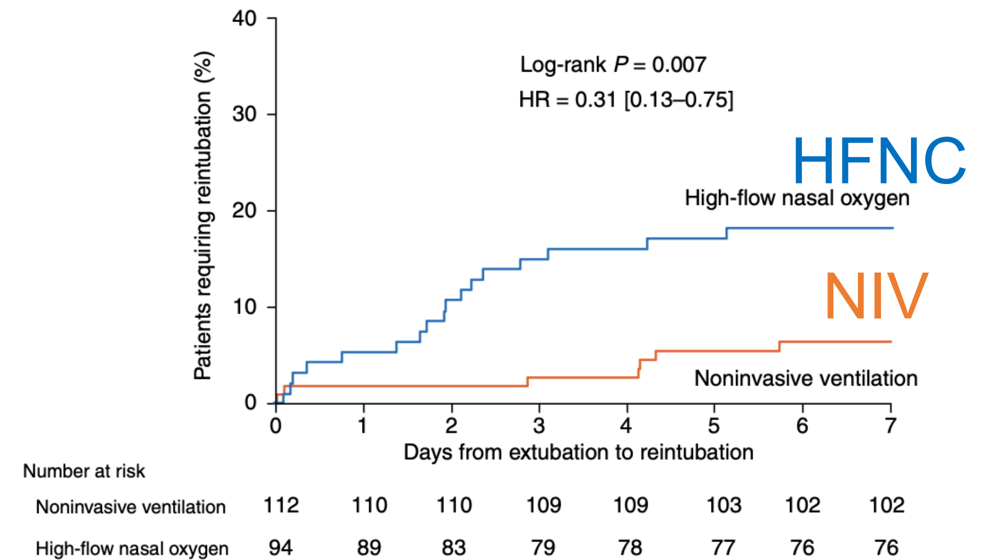
Maimaitiniyazi M et al., Front Med (Lausanne). 2025 Sep 25;12:1594145.

NIV vs HFNC in obesity after extubation







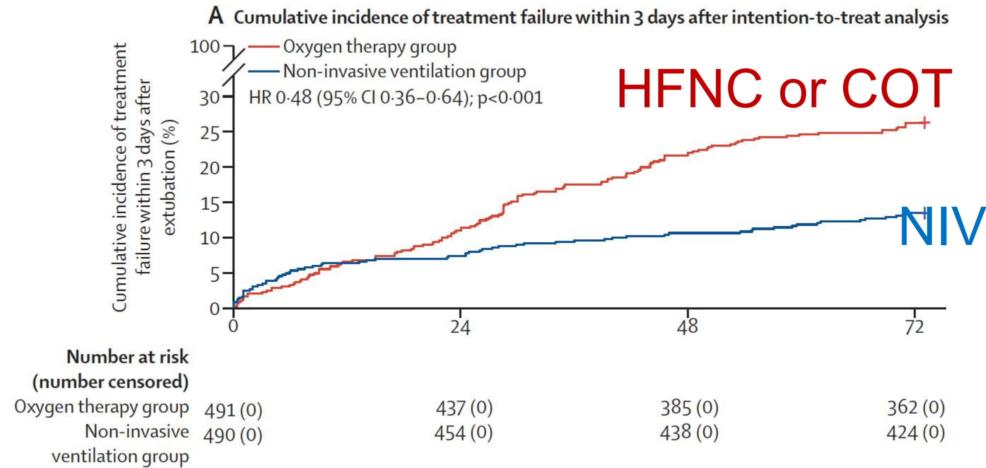


Thille et al., Am J Respir Crit Care Med. 2022 Feb 15;205(4):440-449.

NIV in obesity patients following extubation

- Adult patients have mechanical ventilation ≥6 hrs and admitted to ICU
- BMI ≥30

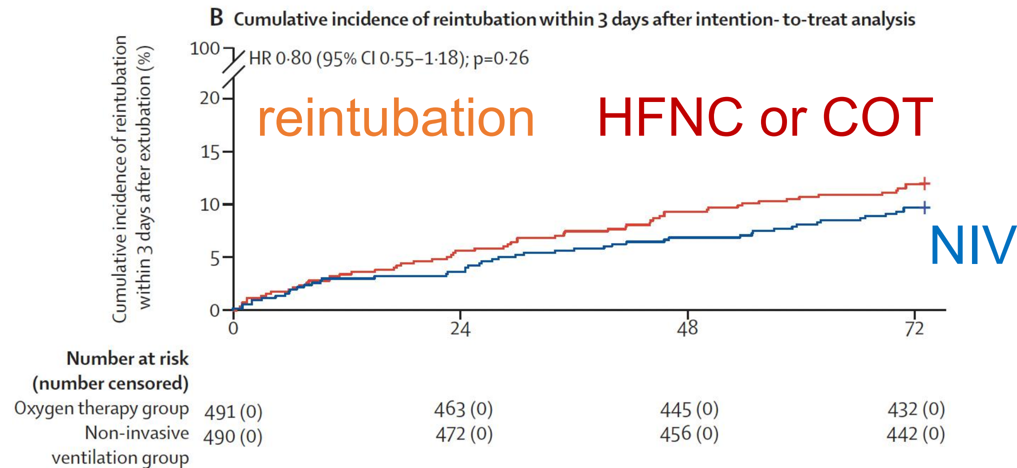
Treatment failure

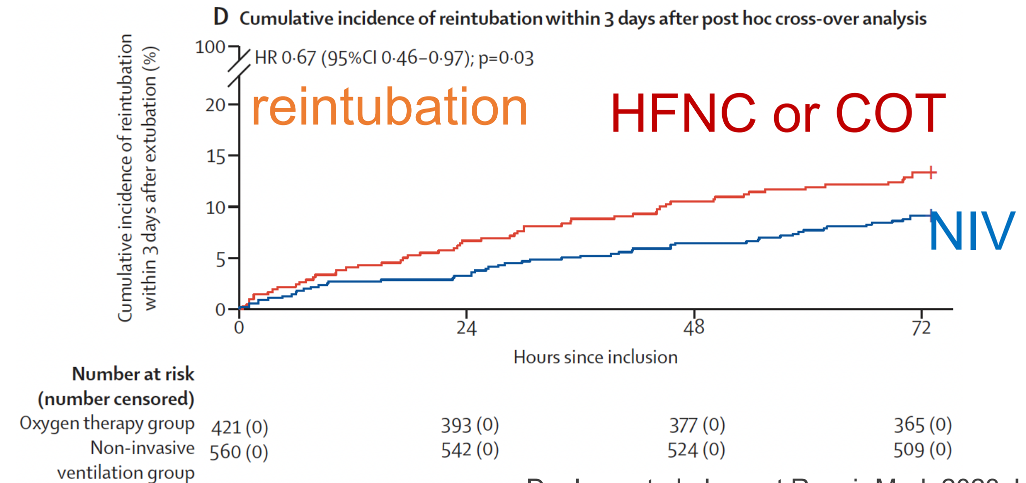


	Treatment failure		Relative risk for treatment failure (95% CI)	p value for interaction
	NIV	Oxygen therapy		
Randomisation variable				
Type of oxygen therapy administered				0·50
Standard oxygen	31/245 (12·7%)	67/245 (27·4%)	0·29 (0·17–0·49)	
High-flow nasal oxygen	35/245 (14·3%)	63/246 (25·6%)	0·44 (0·27–0·73)	
Stratification variables				
Type of admission				0·38
Surgical	39/292 (13·4%)	70/293 (23·9%)	0·49 (0·32–0·76)	
Medical	27/198 (13·6%)	60/198 (30·3%)	0·37 (0·22–0·61)	
Length of ventilation				0·34
<48 h	30/239 (12·6%)	51/235 (21·7%)	0·52 (0·32–0·85)	
≥48 h	36/251 (14·3%)	79/256 (30·9%)	0·38 (0·24–0·59)	
Subgroup variable				
COVID-19 disease				0·16
Yes	8/60 (13·3%)	24/60 (40·0%)	0·24 (0·10–0·59)	
No	57/425 (13·4%)	105/427 (24·6%)	0·48 (0·33–0·68)	
Overall	**66/490 (13·5%)**	**130/491 (26·5%)**	**0·43 (0·31–0·60)**	

0 1 2

Favours NIV ← → Favours oxygen therapy

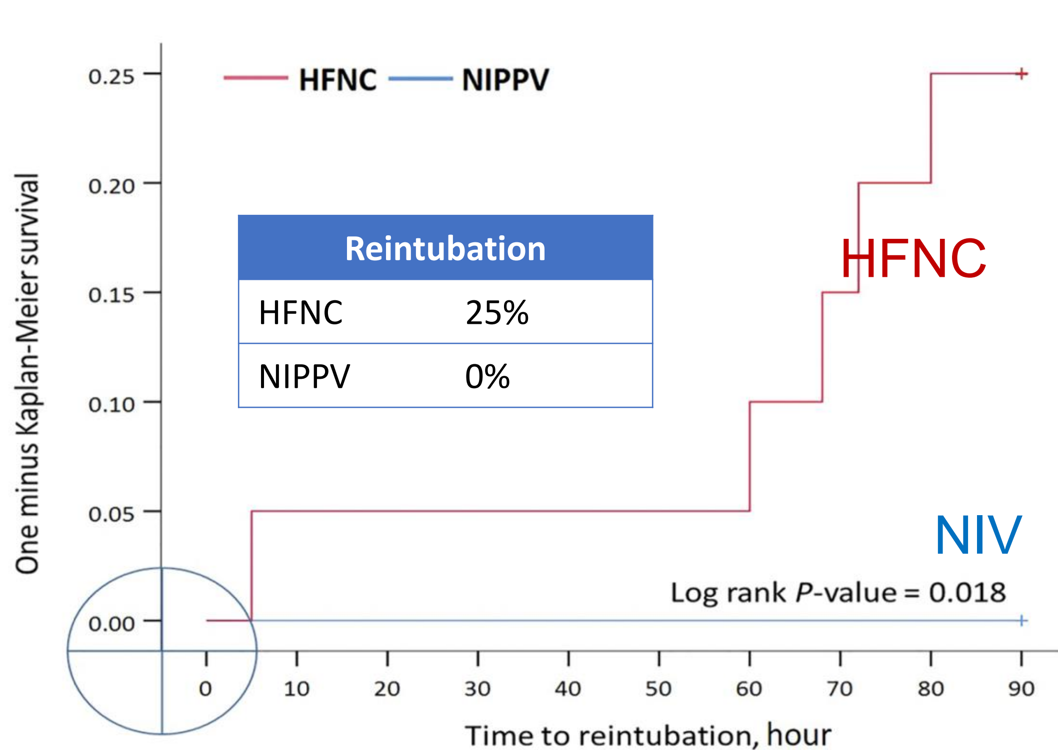


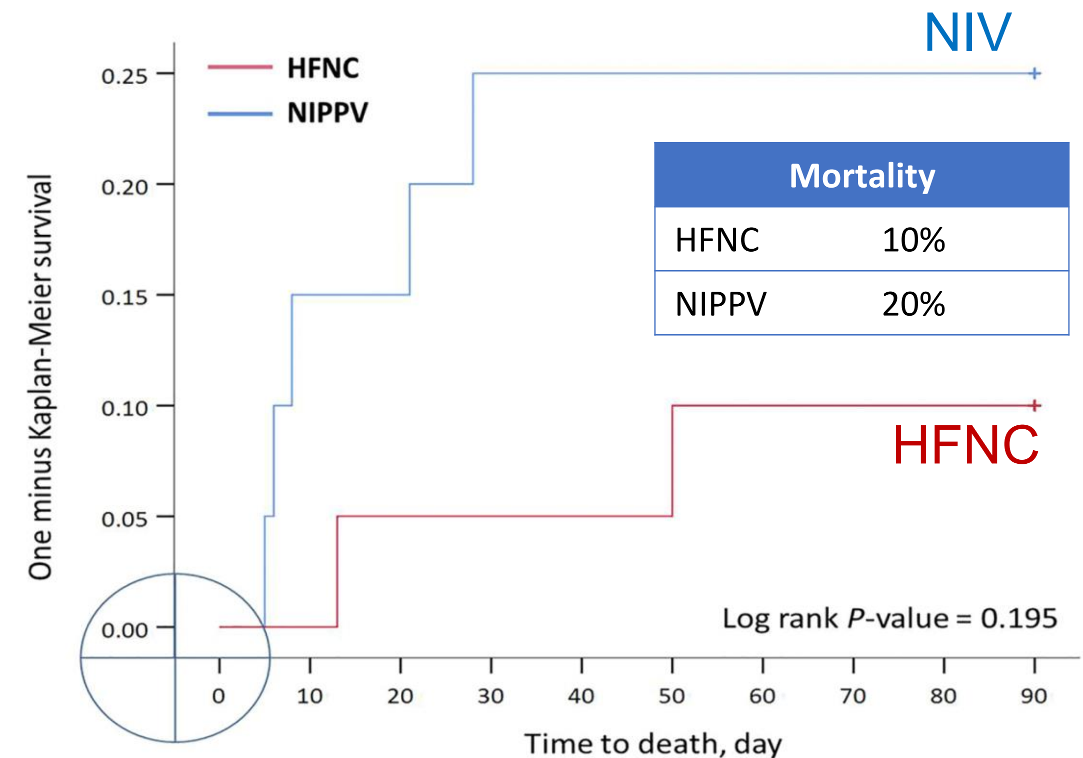


De Jong et al., Lancet Respir Med. 2023 Jun;11(6):530-539.

HFNC and NIV for patients with prolonged mechanical ventilation following extubation

- Adult patients transferred from ICU to RCC
- Mechanical ventilation ≥14 days



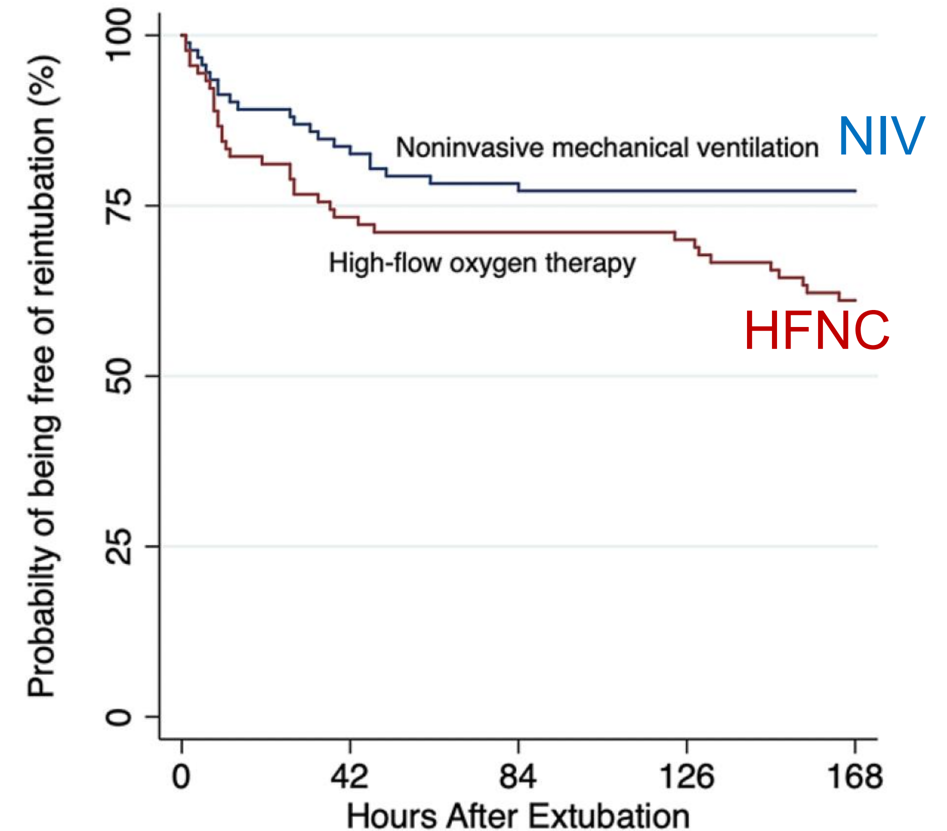


Tseng et al., Sci Rep. 2023 Mar 22;13(1):4689.

Very high risk patients following extubation

- Adult patients received mechanical ventilation ≥24 hrs
- ≥4 risk factors for post-extubation respiratory failure

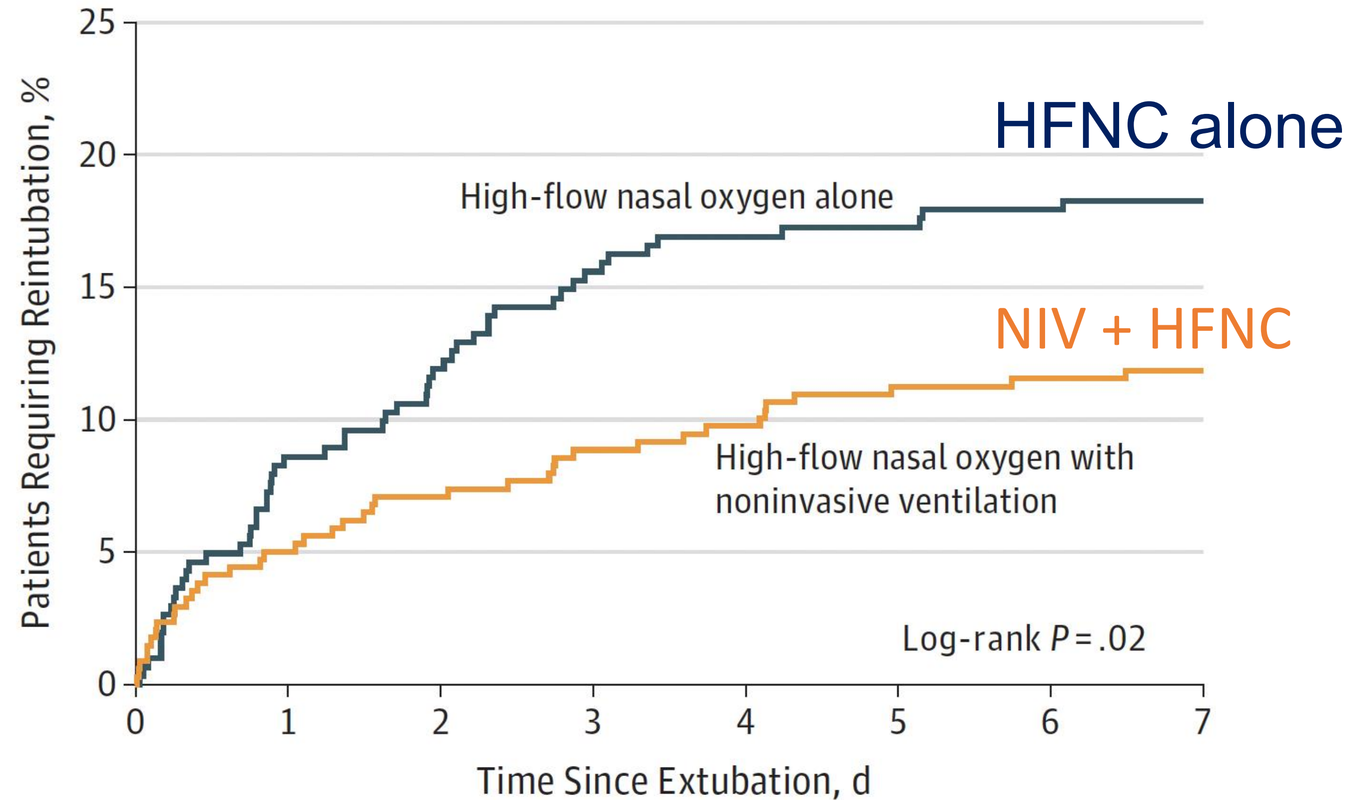
	NIV (n=92)	HFNC (n=90)	*P* value
Re-intubation	22.8%	38.9%	0.019
ICU LOS (days)	9.5	12.5	0.047
Hospital mortality	15.2%	6.7%	0.475



Hernández et al., Intensive Care Med. 2022 Dec;48(12):1751-1759; Erratum in: Intensive Care Med. 2023 Mar;49(3):385.

Combination with NIV and HFNC following extubation

HFNC or HFNC + NIPPV for at least 48 hours following extubation for high risk patients

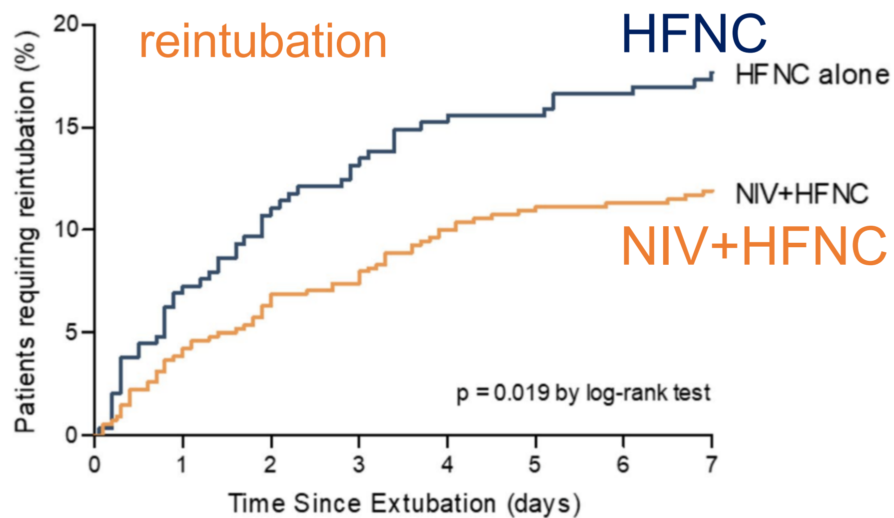


No. at risk								
High-flow nasal oxygen								
Alone	302	276	265	253	248	246	244	243
With noninvasive ventilation	339	321	314	308	305	294	292	291

Thille et al., JAMA. 2019 Oct 15;322(15):1465-1475

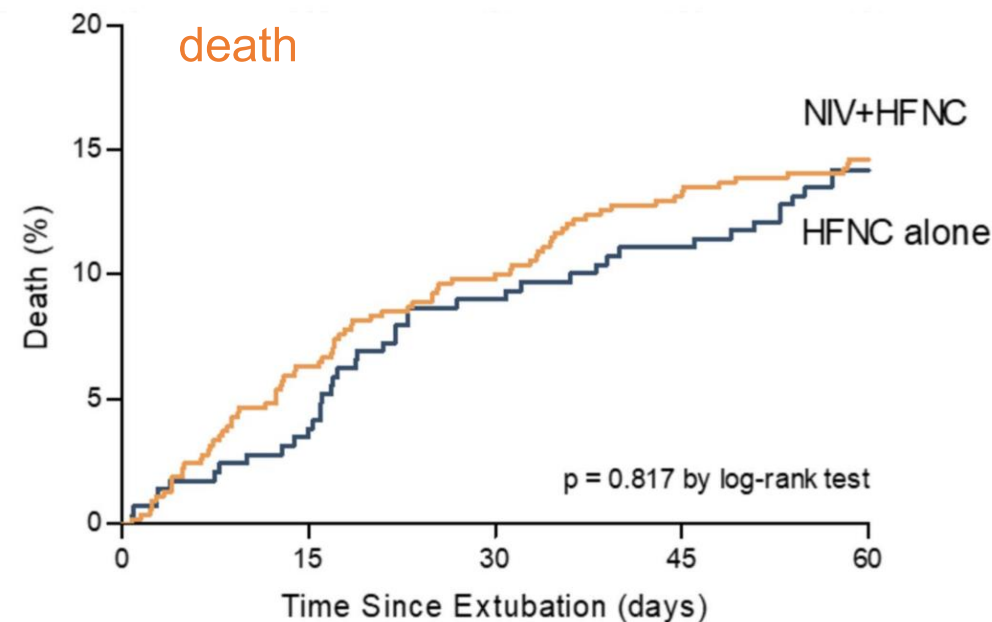
HFNC vs HFNC + NIV after extubation

- Post-hoc analysis combining 2 RCT
- Patients without hypercapnia before extubation, N=829



Number at risk.

HFNC alone	289	269	258	250	244	243	240	237
NIV +HFNC	540	519	505	498	484	473	471	467



Number at risk.

HFNC alone	289	278	263	257	248
NIV +HFNC	540	506	487	469	461

	Reintubation by day 7
NIV + HFNC	11.8%
HFNC alone	17.6%
Absolute difference	−5.8% (p=0.021)
Adjusted analysis (G-computation)	Risk difference −5.6% (95% CI −11.0 to −0.5)

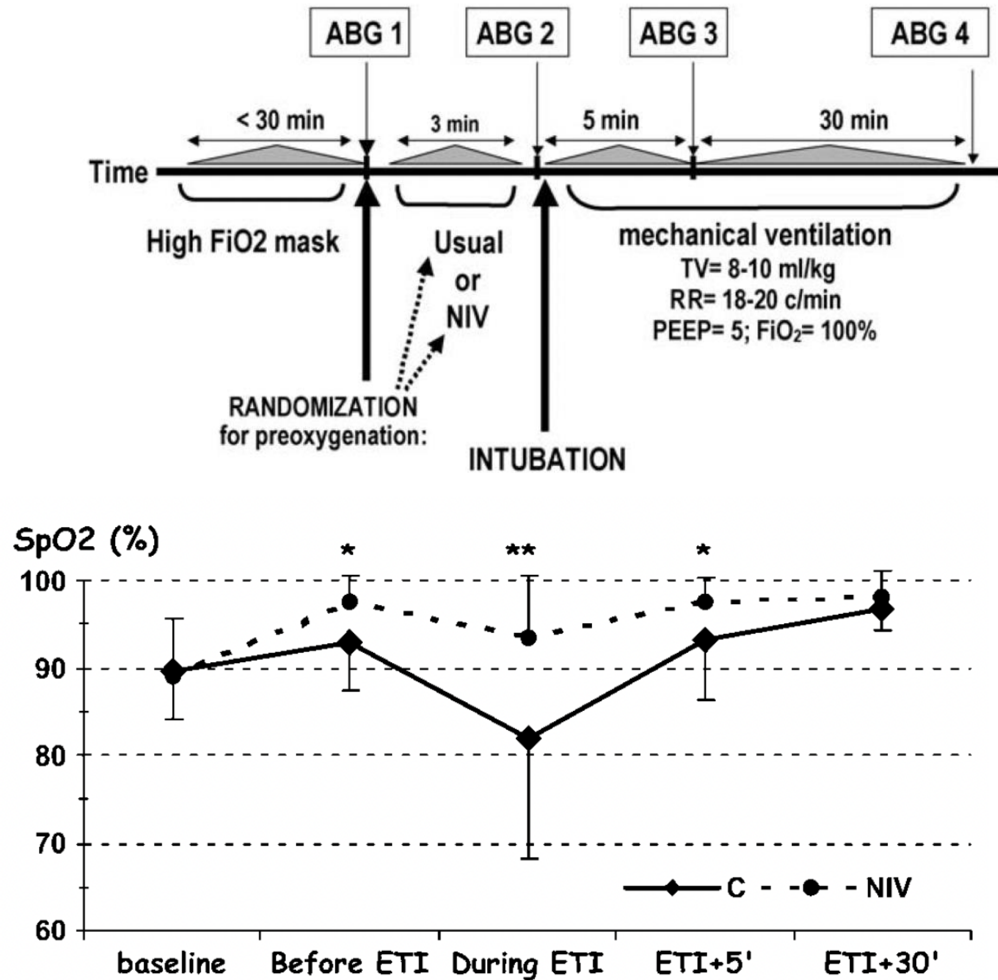
Thille AW et al., Intensive Care Med. 2026 Apr 13.

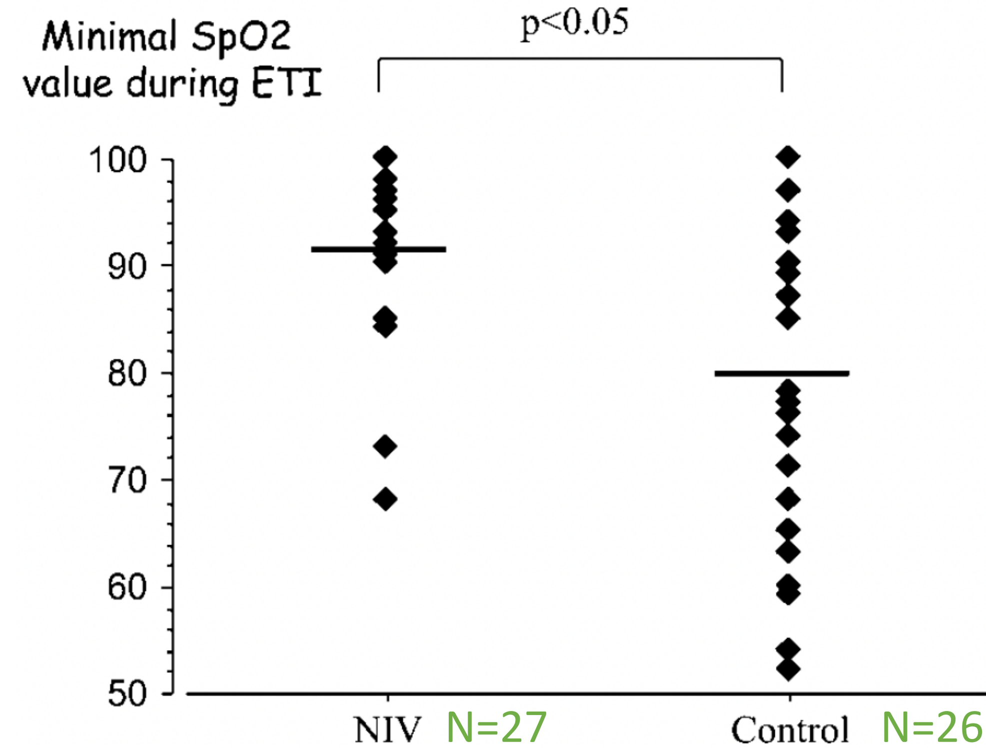
Respiratory support after mechanical ventilation

- HFNC or NIV reduced intubation in high-risk patients than COT
- NIV better than HFNC in obesity, prolong mechanical ventilation, very high risk
- NIV+HFNC reduce re-intubation even more than HFNC alone

Preoxygenation before intubation

Noninvasive ventilation improves preoxygenation before intubation of hypoxic patients





For the intubation of hypoxemic patients, preoxygenation using NIV reduces desaturation than the usual method

Usual method: ≥3 min of normal tidal volume ventilation with bag and mask with 100% O_2

Baillard et al., Am J Respir Crit Care Med. 2006 Jul 15;174(2):171-7.

Effect of preoxygenation using non-invasive ventilation before intubation in hypoxaemic patients

Table 2 Characteristics of patients before preoxygenation. Data are presented as *n* (%) or median (interquartile). NIV, non-invasive ventilation

Variables	Preoxygenation NIV *n*=99	Preoxygenation face mask *n*=102
NIV before preoxygenation	45 (46%)	46 (45%)
Systolic arterial pressure (mm Hg)	131 (110–149)	130 (113–150)
Heart rate (beats min^{-1})	109 (92–120)	110 (98–129)
Pulse oximetry (SpO_2), %	93 (88–98)	93 (90–98)
FiO_2 (%)	70 (48–90)	70 (48–70)
Blood gases		
PaO_2 (pKa)	9.7 (7.9–14)	10.9 (8.1–13.2)
$PaCO_2$ (pKa)	5.5 (4.4–6.8)	4.8 (3.9–6.3)
pH	7.4 (7.3–7.4)	7.4 (7.3–7.5)
BE (mmol $litre^{-1}$)	24 (21–27)	22 (18–25)
SaO_2 (%)	94 (90–97)	95 (91–98)
PaO_2/FiO_2	132 (80–175)	126 (95–207)

Table 4 Outcome. Data are presented as *n* (%) or median (interquartile). NIV, non-invasive ventilation, SOFA, sequential organ failure assessment score

Variables	Preoxygenation NIV *n*=99	Preoxygenation face mask *n*=102	P
Maximal SOFA value*	9 (6–12)	10 (6–12)	0.65
Number of organ failures:			
0	8 (8.2%)	3 (3.1%)	0.34
1	23 (23.5%)	27 (27.6%)	
2	34 (34.7%)	26 (26.5%)	
3	20 (20.4%)	26 (26.5%)	
4	9 (9.2%)	11 (11.2%)	
5	4 (4.1%)	5 (5.1%)	
Death†	31 (31.3%)	38 (37.3%)	0.76
Duration of stay in ICU‡	4 (0–17)	3 (0–12)	0.14
Duration of ventilation¶	9 (1–21)	5.5 (1–21)	0.37
Duration of invasive ventilation¶	13 (1–23)	9 (1–21)	0.40
Duration of non-invasive ventilation¶	27 (18–28)	26 (14.5–28)	0.85

NIV as a preoxygenation method **did not reduce organ dysfunction (SOFA score during 7 days)** compared with usual preoxygenation in hypoxaemic, critically ill patients requiring tracheal intubation for invasive ventilation.

Baillard et al., Br J Anaesth. 2018 Feb;120(2):361-367

Table 5 Adverse events in patients with non-invasive, NIV, respiratory support at the time of randomisation (prior to intervention), n=91. Data are presented as n (%) or median (interquartile). NIV, non-invasive ventilation; SOFA, sequential organ failure assessment score

Variables	Preoxygenation NIV n=45	Preoxygenation face mask n=46	OR	P
Patients with at least one adverse event during preoxygenation or intubation	8 (17.8%)	19 (41.3%)	5.2 (1.6–17)	0.006
SpO_2<80%	7 (16.6%)	19 (41.3%)		0.002
Arrhythmia with haemodynamic failure	0 (0%)	2 (4.3%)		
Regurgitation	0 (0%)	1 (2.2%)		
Myocardial ischaemia	1 (2.2%)	0 (0%)		
Preoxygenation failure	0 (0%)	5 (10.8%)		
Total number of adverse events	8	27		
Maximal SOFA value*	9.5 (6–13)	9.5 (7–12)		0.59
Number of organ failures:	2 (2–3)	2 (1–4)		0.68
0	1 (2.2%)	2 (4.3%)		
1	10 (22.2%)	10 (21.7%)		
2	15 (33.3%)	13 (28.3%)		
3	9 (20.0%)	8 (17.4%)		
4	6 (13.3%)	10 (21.7%)		
5	4 (8.9%)	3 (6.5%)		
Death†	15 (33%)	16 (35%)	1.2 (0.46–3.14)	0.70

- NIV should not be discontinued for preoxygenation in the cases of patients treated by NIV before the decision to intubate.

Adverse events: occurrence of arrhythmia with haemodynamic failure, occurrence of regurgitation (presence of gastric content seen during laryngoscoy), severe O2 desaturation (SpO2<80%), de novo myocardial ischemia (myocardial repolarization and/or elevated serum troponin sampled between 4 and 8 hr after intubation)

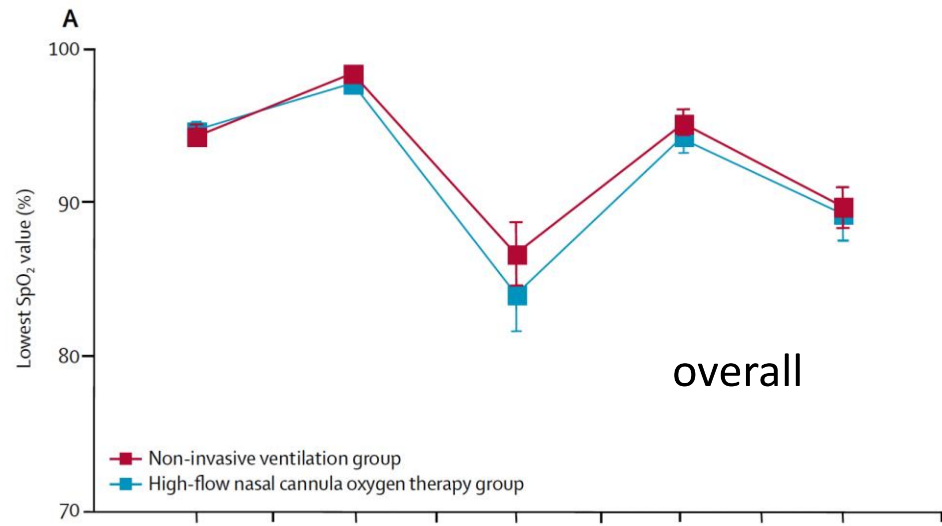
Baillard et al., Br J Anaesth. 2018 Feb;120(2):361-367

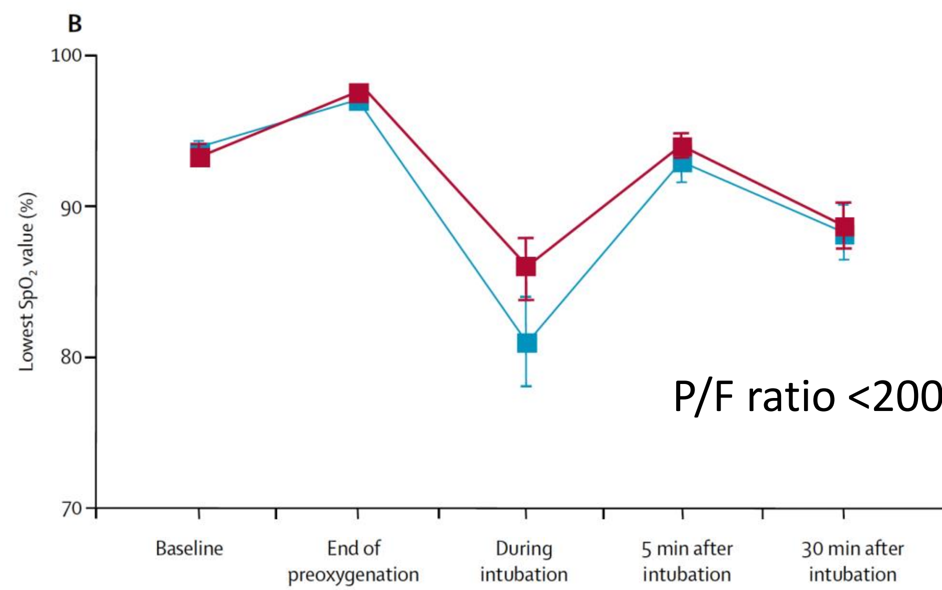
Non-invasive ventilation versus high-flow nasal cannula oxygen therapy with apnoeic oxygenation for preoxygenation before intubation

- Acute hypoxic respiratory failure
  - RR ≥25 or signs of respiratory distress
  - P/F ratio ≤300mmHg regardless of oxygenation strategy
- Preoxygenation ≥3 mins with NIV vs HFNC (no valve-bag-facemask)

	Non-invasive ventilation (n=142)	**High-flow nasal cannula oxygen therapy (n=171)**	**p value**
Oxygen device the last hour before inclusion	..	..	0·90
Standard oxygen	63 (44%)	73 (43%)	..
High-flow nasal cannula oxygen therapy	48 (34%)	57 (33%)	..
Non-invasive ventilation	31 (22%)	41 (24%)	..
Vasopressor support at inclusion	27 (19%)	35 (20%)	0·75
Bilateral pulmonary infiltrates	88 (62%)	106 (62%)	0·98
Respiratory rate, breaths per min	30 (8)	31 (8)	0·35
PaO_2:FiO_2 ratio, mm Hg	142 (65)	148 (70)	0·40
Stratification sub-groups	..	..	0·06
PaO_2:FiO_2 ratio >200 mm Hg	25 (18%)	46 (27%)	..
PaO_2:FiO_2 ratio ≤200 mm Hg	117 (82%)	125 (73%)	..

Frat et al., Lancet Respir Med. 2019 Apr;7(4):303-312.





	Severe-to-moderate hypoxaemia (PaO_2/FiO_2 ≤200 mm Hg)				Mild hypoxaemia (PaO_2/FiO_2 >200 mm Hg)			
	Non-invasive ventilation (n=117)	High-flow nasal cannula oxygen therapy (n=125)	Absolute difference estimate (95% CI)	p value	Non-invasive ventilation (n=25)	High-flow nasal cannula therapy (n=46)	Absolute difference estimate (95% CI)	p value
Primary outcome								
SpO_2 <80% during intubation procedure	28 (24%)	44 (35%)	−11·3 (−22·3 to 0·3)	0·0553	5 (20%)	3 (7%)	13·4 (−2·2 to 33·1)	0·1197
95% CI	16–32	27–44	..	..	4–36	0–14	..	..
Adjusted on PaO_2	..	..	..	0·0459	..	..	..	0·1003
Secondary outcomes								
SpO_2 at the beginning of preoxygenation	94% (5)	94% (4)	0·0 (−1·1 to 1·1)	0·75	97% (3)	97% (4)	0·0 (−1·8 to 1·8)	0·36
SpO_2 at the end of preoxygenation	97% (4)	96% (6)	1·0 (−0·0 to 2·0)	0·02	99% (3)	98% (4)	1·0 (−0·8 to 2·8)	0·31
Lowest SpO_2 during intubation procedure	86% (12)	81% (17)	5·0 (1·2 to 8·7)	0·02	90% (15)	93% (8)	−3·0 (−8·4 to 2·4)	0·31

Data are n (%) or mean % (SD), unless otherwise indicated. SpO_2=pulse oximetry.

Table 3: **Outcomes in the intention-to-treat population, by subgroup of stratification and treatment group**

- Preoxygenation with **valve-bag facemasks should be replaced by HFNC therapy or NIV** in ICUs before the intubation
- **Further studies are needed** in a larger population to investigate whether **NIV** should be used for all patients regardless of their **level of hypoxaemia**.

Frat et al., Lancet Respir Med. 2019 Apr;7(4):303-312.

Noninvasive Ventilation for Preoxygenation during Emergency Intubation

- Inclusion criteria
  - ✓ Planed tracheal intubation using a laryngoscope and sedation
  - ✓ Operator is a clinician routinely perform tracheal intubation in participant units

Preoxygenation ≥3 mins with NIV vs NRM or BVM (with or without manual ventilation)

Table 1. Characteristics of the Patients at Baseline.*

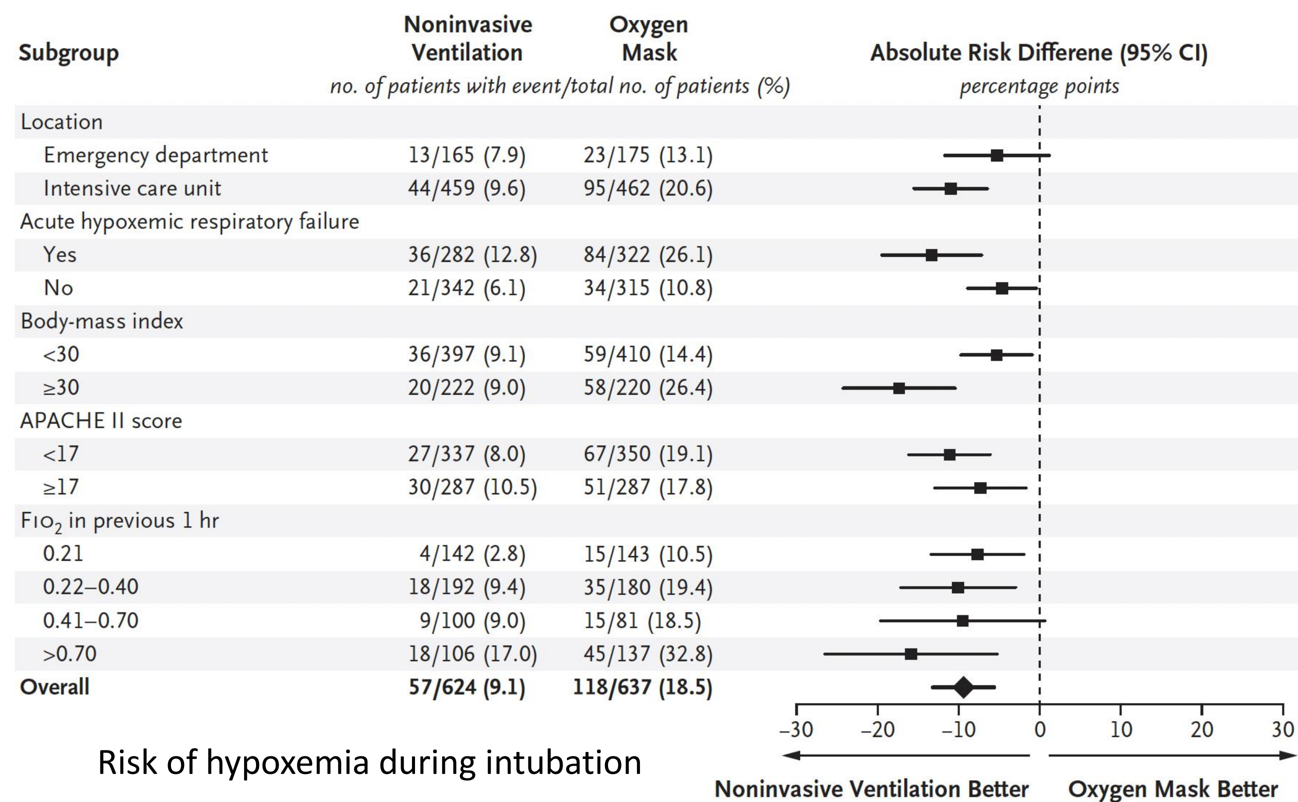
Characteristic	Noninvasive Ventilation (N = 645)	Oxygen Mask (N = 656)
Acute conditions — no. (%)§		
Altered mental status	402 (62.3)	390 (59.5)
Sepsis or septic shock	301 (46.7)	312 (47.6)
Pneumonia	107 (16.6)	102 (15.5)
Gastrointestinal bleeding	107 (16.6)	102 (15.5)
Traumatic injury	40 (6.2)	36 (5.5)
Median APACHE II score (IQR)¶	17 (12–23)	17 (12–23)
Median Glasgow Coma Scale score (IQR)‖	12 (8–15)	12 (8–15)
Treatment or measurement within the hour before enrollment		
Receipt of vasopressors — no. (%)	178 (27.6)	178 (27.1)
Receipt of high-flow nasal cannula — no. (%)**	150 (23.3)	165 (25.2)
Median lowest oxygen saturation (IQR) — %††	95 (92–98)	95 (92–98)
Median highest F_{IO_2} (IQR)‡‡	0.33 (0.21–0.66)	0.36 (0.21–0.70)
Ratio of oxygen saturation to F_{IO_2}§§		
Median (IQR)	271 (145–426)	268 (124–423)
≤315 — no. (%)	328 (58.9)	331 (59.7)

Gibbs et al., N Engl J Med. 2024 Jun 20;390(23):2165-2177.

Table 3. Outcomes of Tracheal Intubation.

Outcome	Noninvasive Ventilation (N=645)	Oxygen Mask (N=656)	Difference (95% CI)*
Primary outcome			
Hypoxemia during intubation — no./total no. (%)†‡	57/624 (9.1)	118/637 (18.5)	−9.4 (−13.2 to −5.6)§
Secondary outcome			
Median lowest oxygen saturation (IQR) — %‡	99 (95 to 100)	97 (89 to 100)	2 (1 to 3)
Exploratory procedural outcomes			
Lowest oxygen saturation <80% — no./total no. (%)‡	39/624 (6.2)	84/637 (13.2)	−6.9 (−10.2 to −3.7)
Lowest oxygen saturation <70% — no./total no. (%)‡	15/624 (2.4)	36/637 (5.7)	−3.2 (−5.4 to −1.1)
Cardiovascular collapse — no./total no. (%)¶	113/645 (17.5)	127/656 (19.4)	−1.8 (−6.1 to 2.4)
Systolic blood pressure <65 mm Hg — no./total no. (%)	18/621 (2.9)	28/633 (4.4)	−1.5 (−3.6 to 0.6)
New or increased use of vasopressors — no./total no. (%)	111/645 (17.2)	117/656 (17.8)	−0.6 (−4.8 to 3.5)
Cardiac arrest — no./total no. (%)‖	1/645 (0.2)	7/656 (1.1)	−0.9 (−1.8 to −0.1)
Successful intubation on the first attempt — no./total no. (%)	534/645 (82.8)	535/656 (81.6)	1.2 (−2.9 to 5.4)
Median time from induction to intubation (IQR) — seconds	115 (89 to 150)	113 (85 to 152)	2 (−5 to 9)
Exploratory safety outcomes			
Operator-reported aspiration — no./total no. (%)**	6/645 (0.9)	9/656 (1.4)	−0.4 (−1.6 to 0.7)
New infiltrate on chest imaging — no./total no. (%)††	144/509 (28.3)	148/497 (29.8)	−1.5 (−7.1 to 4.1)
New pneumothorax — no./total no. (%)‡‡	7/509 (1.4)	7/497 (1.4)	0.0 (−1.5 to 1.4)
Median oxygen saturation at 24 hr (IQR)§§	97 (95 to 100)	97 (95 to 100)	0 (−1 to 1)
Median F_{IO_2} at 24 hr (IQR)¶¶	0.40 (0.30 to 0.40)	0.40 (0.30 to 0.40)	0.01 (−0.05 to 0.05)
Exploratory clinical outcomes‖‖			
Median ventilator-free days (IQR)	21 (0 to 26)	17 (0 to 25)	4 (−1 to 9)
Median ICU-free days (IQR)	16 (0 to 23)	14 (0 to 23)	2 (−1 to 8)
In-hospital death — no./total no. (%)	209/645 (32.4)	217/656 (33.1)	−0.7 (−5.8 to 4.4)

Risk of hypoxemia during intubation
NIV 9.1% vs Oxygen mask 18.5% (P <0.001)
Cardiac arrest
NIV 0.2% vs Oxygen mask 1.1%



Risk of hypoxemia during intubation

- **Critically ill adults** undergoing **tracheal intubation** in an emergency department or an ICU, the incidence of **hypoxemia was lower** with **preoxygenation with noninvasive ventilation** than with an oxygen mask
- The use of high-flow nasal cannula during tracheal intubation was not evaluated

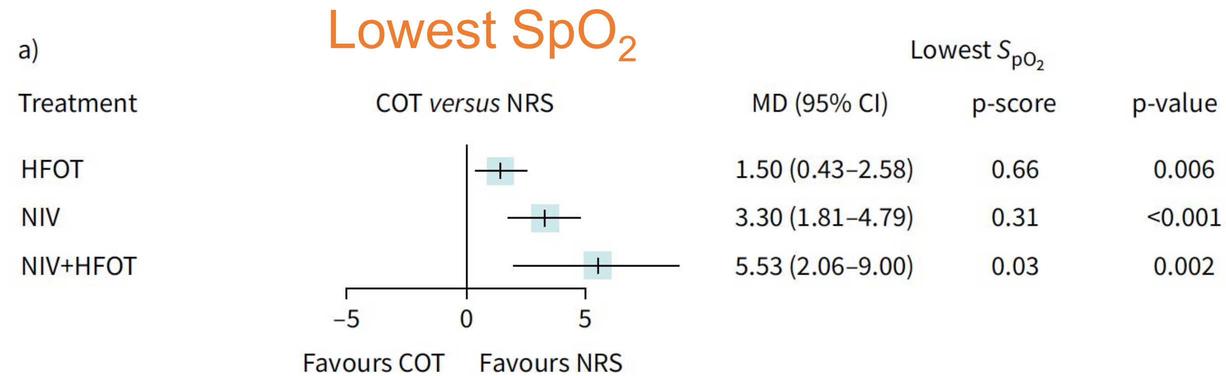
Gibbs et al., N Engl J Med. 2024 Jun 20;390(23):2165-2177.

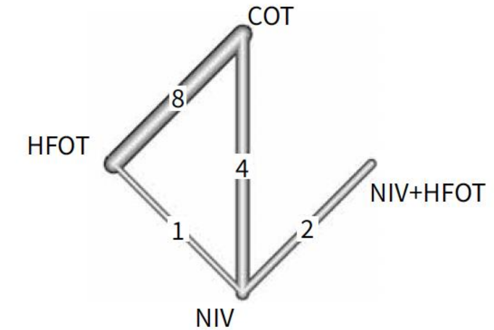
NIV for preoxygenation

Meta-analysis

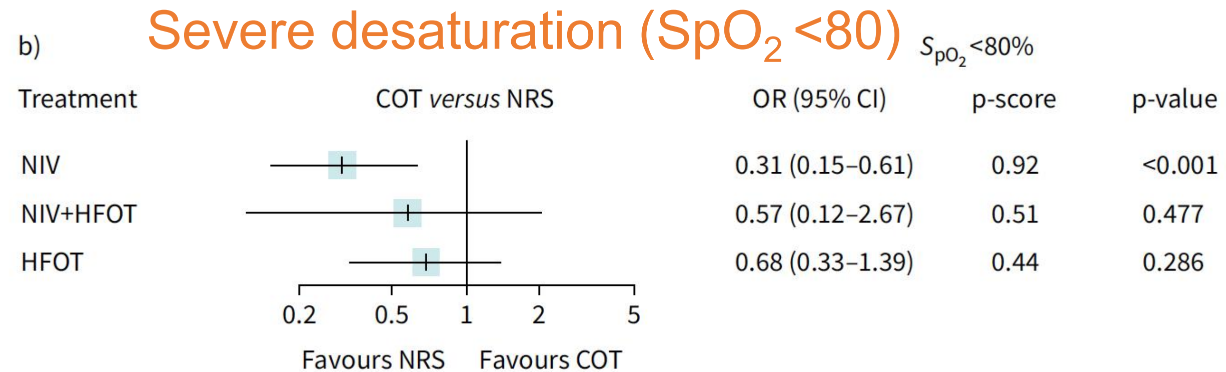
- 15 RCT, n=2,939
- NIV vs HFOT vs COT
- ICU, ED, OR

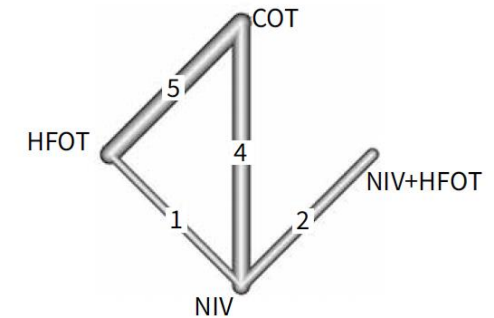
Lowest SpO_2





Severe desaturation (SpO_2 <80)





- ➢ During emergent endotracheal intubation in critical care areas, **preoxygenation** with **NIV or HFOT** **overperformed** COT in **maintaining SpO_2**.
- ➢ Only **NIV** **reduced** the incidence of **severe desaturation**

Boscolo A et al., ERJ Open Res. 2025 Dec 15;11(6):00329-2025.

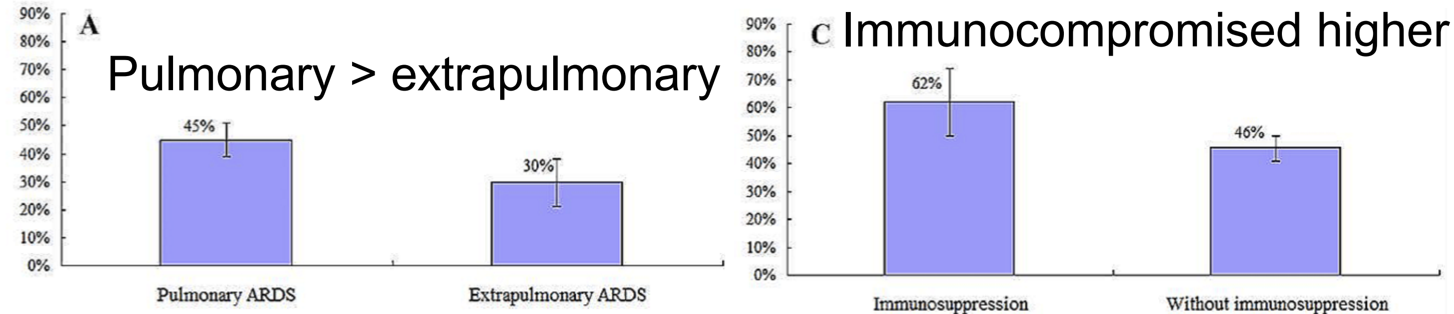
Monitor parameters during the non-invasive respiratory support

Incidence of NIV failure and mortality in patients with ARDS

Systematic review and meta-analysis

- Patients with ARDS
- 90 studies, 98 arms

NIV failure rate

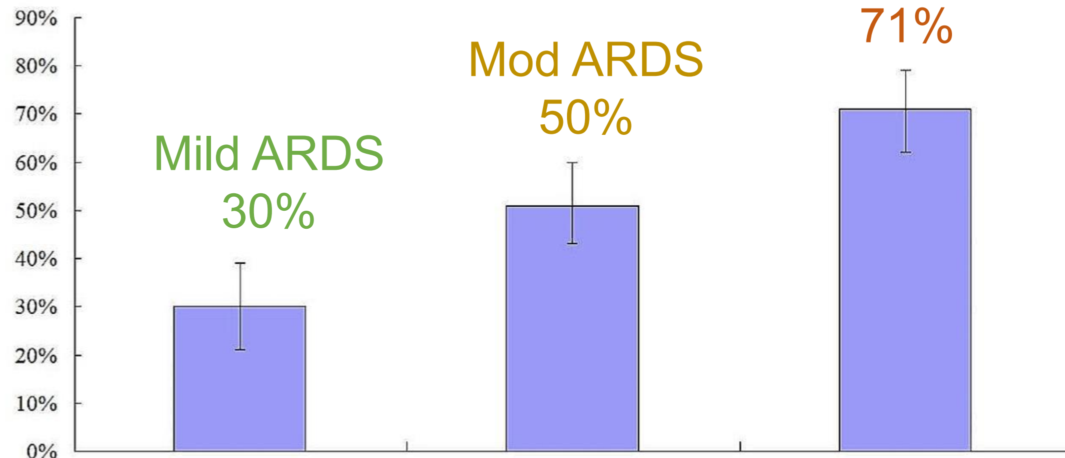


NIV failure rate

Sev ARDS
71%

Mod ARDS
50%

Mild ARDS
30%



	Mild ARDS	Moderate ARDS	Severe ARDS
Study arms	24	20	17
Total patients	819	1332	525
NIV failure (95%CI)	30% (21-39%)	51% (43-60%)	71% (62-79%)

ICU **mortality 29%**

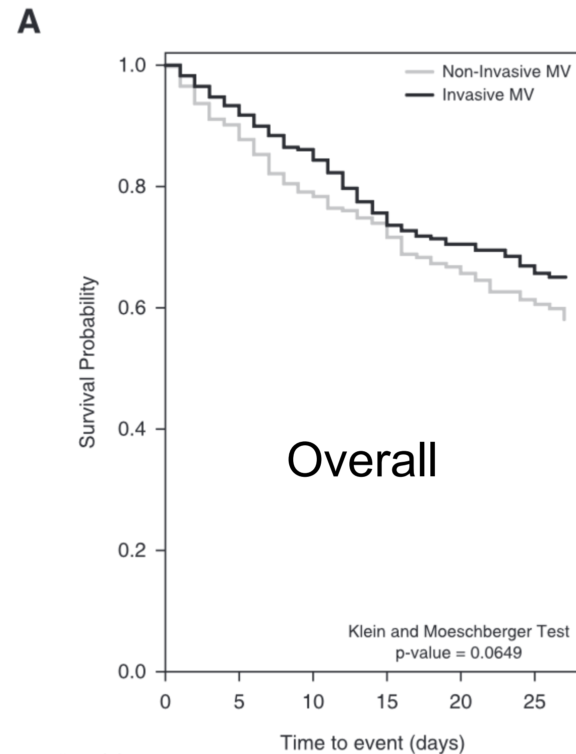
NIV failure rate 45%

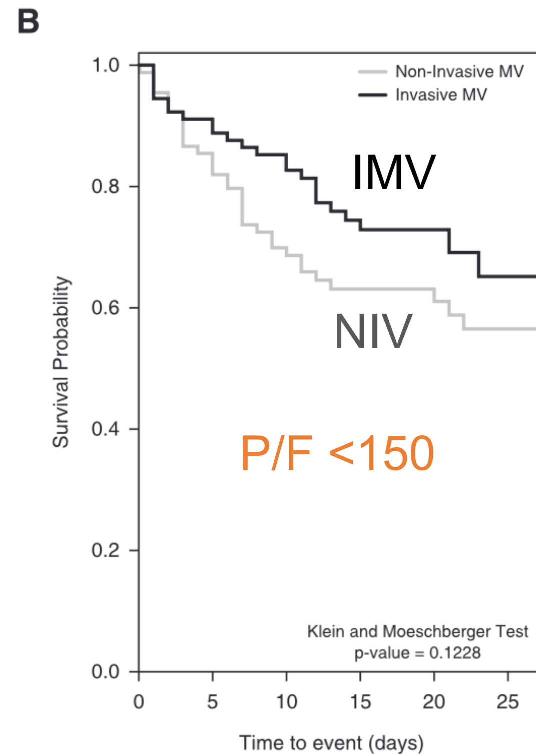
- **Severe** > Moderate > Mild ARDS
- Pulmonary > extrapulmonary
- Immunosuppression > without immunesuppresion

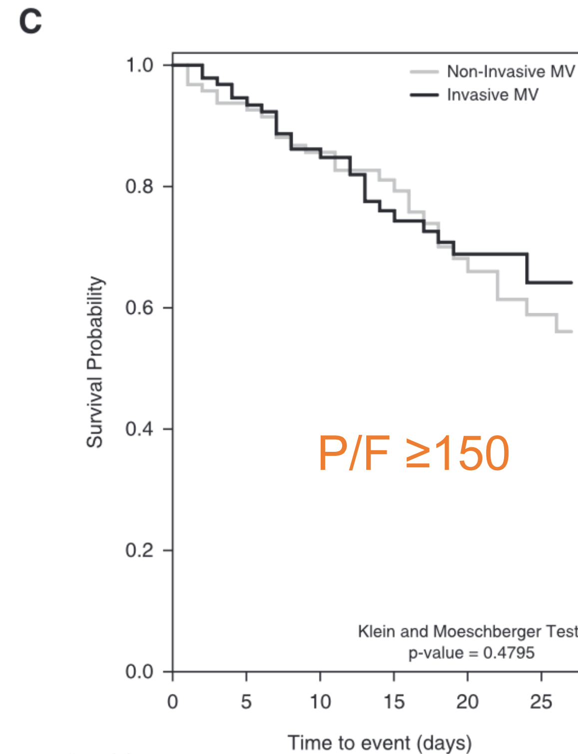
Wang J et al., BMC Pulm Med. 2024 Jan 22;24(1):48.

NIV of Patients with ARDS: LUNGSAFE

- N=2,813; with 436 (15%) managed with NIV
- Propensity score matching comparing NIV vs IMV







NIV failure rate **37.5%**

- **Severe (47%)** > Moderate(43) > Mild (22%)

Hospital **mortality**

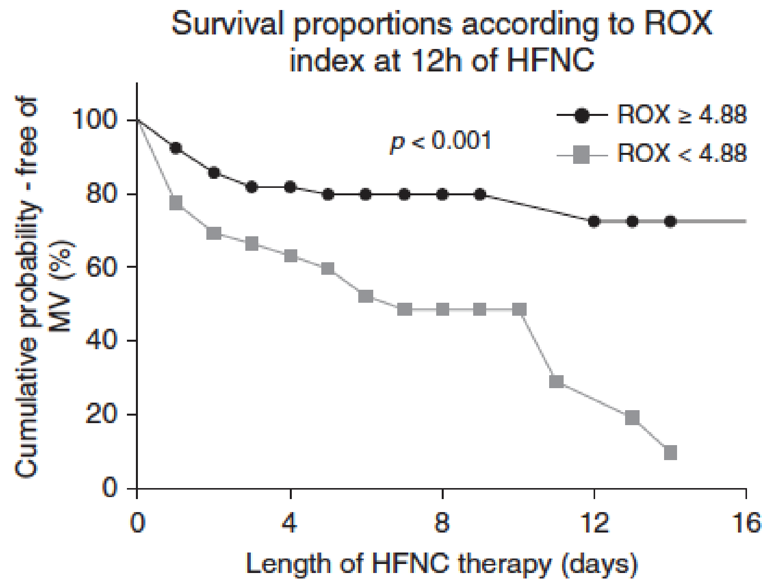
- **NIV failure (45%)** > success (16%)

NIV seems associated with **higher mortality** in **P/F < 150** mmHg

Bellani G et al., Am J Respir Crit Care Med. 2017 Jan 1;195(1):67-77.

ROX index

$$\frac{SpO_2/FiO_2}{RR}$$



2hrs	6hrs	12hrs	All times
< 2.85	< 3.47	< 3.85	≥ 4.88
Intubation			Observe

Roca et al., Am J Respir Crit Care Med. 2019 Jun 1;199(11):1368-1376.

HARCO

(Hear rate, acidosis, consciousness, oxygenation, and respiratory rate)

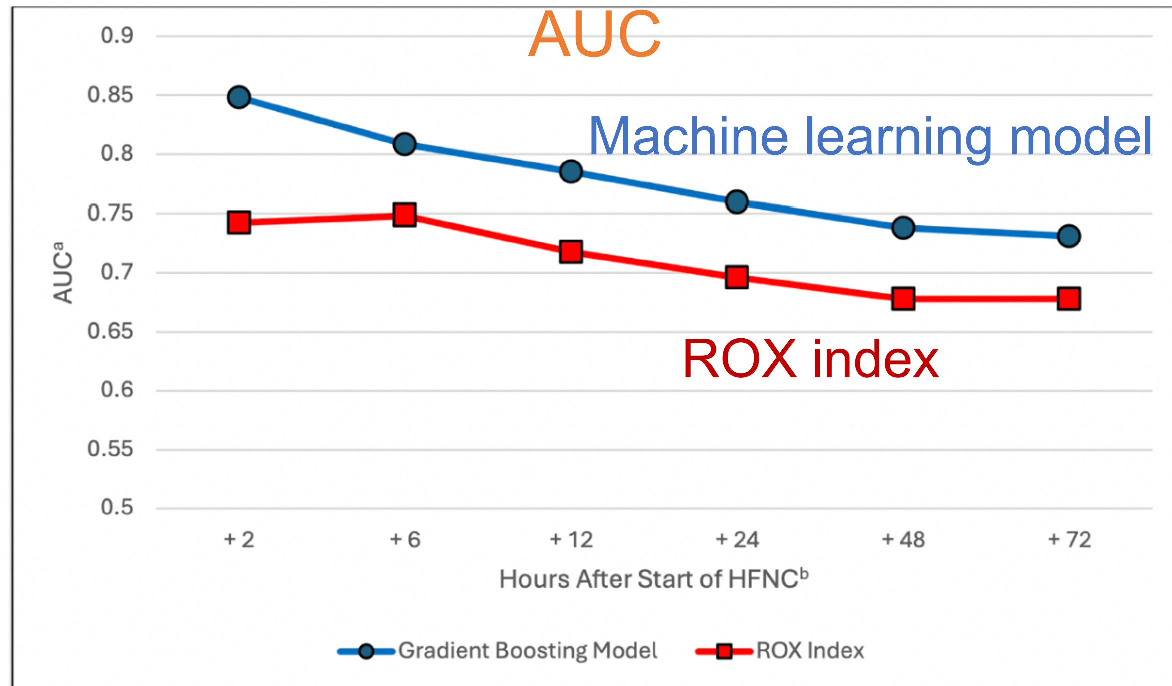
HACOR score >5 at 1hour of NIV with a >80% risk of NIV failure.

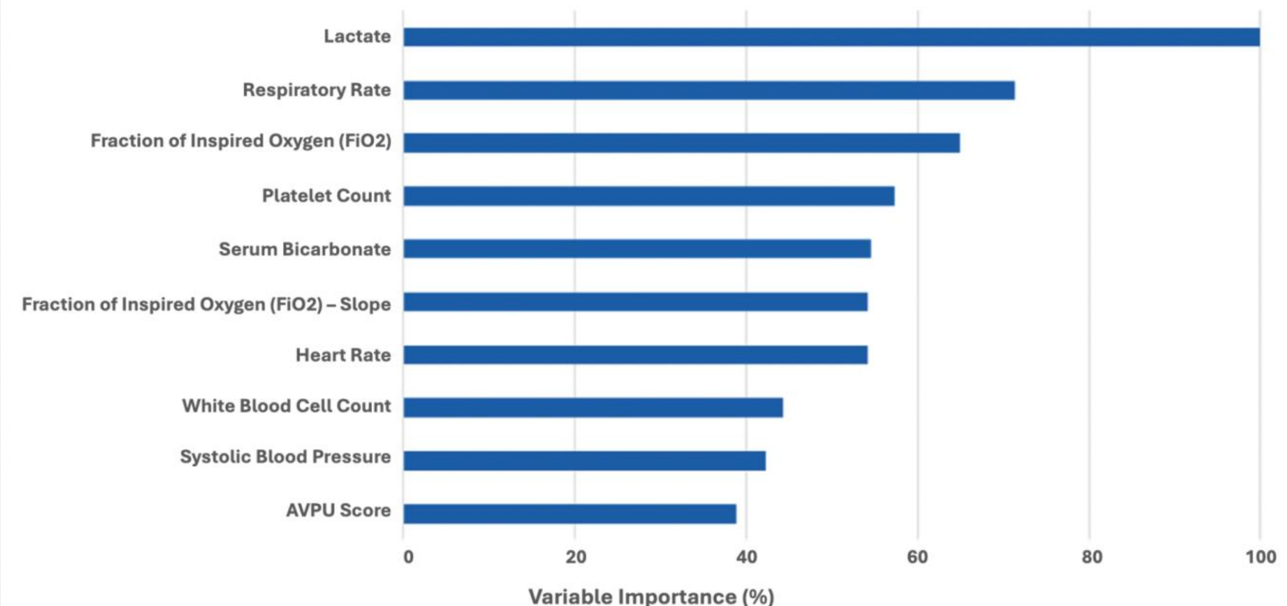
Variables	Category (j)	Assigned points
Heart rate, beats/min	≤120	0
	≥121	1
pH	≥7.35	0
	7.30–7.34	2
	7.25–7.29	3
	<7.25	4
GCS	15	0
	13–14	2
	11–12	5
	≤10	10
PaO_2/FiO_2	≥201	0
	176–200	2
	151–175	3
	126–150	4
	101–125	5
	≤100	6
Respiratory rate, breaths/min	≤30	0
	31–35	1
	36–40	2
	41–45	3
	≥46	4

Duan et al., Intensive Care Med. 2017 Feb;43(2):192-199.

Machine learning model to predict HFNC failure

- Retrospective, multicenter, USA
- 2009 to 2022, N=11,618 (6,787 training; 4,831 validation)





Temte B et al., BMJ Open Respir Res. 2025 Nov 18;12(1):e003355.

Parameters to predict respiratory failure

- $PaCO_2$
- Consciousness
- Hemodynamics

Parameter	Monitoring technique/score calculation	Clinical thresholds associated with risk of failure	Limitations
SpO_2/FiO_2	Pulse oximetry	< 120 and/or worsening trend	Underestimation of severity with low $PaCO_2$
PaO_2/FiO_2	Arterial blood gas analysis	< 150–200 mmHg and/or worsening trend	Intermittent
Respiratory Rate	Clinical examination	> 25–30 and/or not decreasing with support	Poorly correlated with effort
Expired tidal volume	Ventilator	> 9–9.5 ml/kg PBW	Not feasible during HFNO, standard helmet NIV
ΔP_{ES}	Esophageal balloon catheter	> 15 cmH_2O and/or reduction < 10 cmH_2O during NIV	Needs some expertise
ROX	(SpO_2/FiO_2)/Respiratory Rate	< 2.85 at 2 h of HFNO initiation < 3.47 at 6 h of HFNO initiation < 3.85 at 12 h of HFNO initiation	Validated only for HFNO
HACOR scale[a]	Heart rate, acidosis, consciousness, oxygenation and respiratory rate[a]	> 5 at 1 h of NIV initiation	Intermittent, time consuming, validated only for NIV

PBW predicted body weight, *NIV* noninvasive ventilation, *HFNO* high-flow nasal oxygen, *DeltaPes* inspiratory effort

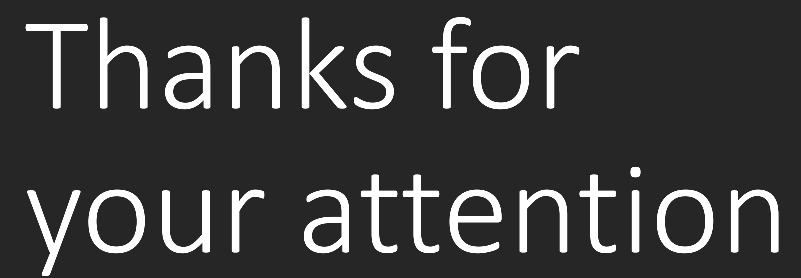
[a] The HACOR score is calculated as the sum of the scores for each individual variable, assigned as follows. Heart rate: ≤ 120 beats/min = 0, ≥ 121 beats/min = 1; pH: ≥ 7.35 = 0, 7.30–7.34 = 2, 7.25–7.29 = 3, < 7.25 = 4; Glasgow Coma Scale score: 15 = 0, 13–14 = 2, 11–12 = 5, ≤ 10 = 10; PaO_2/FiO_2 ratio: ≥ 201 mmHg = 0, 176–200 mmHg = 2, 151–175 mmHg = 3, 126–150 mmHg = 4, 101–125 mmHg = 5, ≤ 100 mmHg = 6; Respiratory rate: ≤ 30 breaths/min = 0, 31–35 breaths/min = 1, 36–40 breaths/min = 2, 41–45 breaths/min = 3, ≥ 46 = 4

We Shall Never Delay Intubation

Grieco DL, et al., Intensive Care Med. 2021 Aug;47(8):851-866.

Take home message

- Physiologic effects of non-invasive respiratory support
  - ✓**PEEP** to **reduced atelectasis**, **increased FRC**, driving pressure to **unloading respiratory muscle**
  - ✓Improving oxygenation, **reduced respiratory drive** and work of breath
- For patients with **acute respiratory failure**
  - ✓NIV and HFNC **reduced intubation** than COT
  - ✓**NIV** provide **more respiratory support** than HFNC in patients with **higher respiratory drive**
- NIV and HFNC **reduce re-intubation** than COT in high-risk patients
- NIV and HFNC prevent severe hypoxemia during **emergent endotracheal intubation**
- **Never delay intubation** when using NIV or HFNC


Thanks for
your attention