

# High-Flow Nasal Oxygen Therapy: mechanisms of action, indications, and intervention protocols for acute and chronic patients

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*ERS Assembly 02.02 Noninvasive Ventilatory Support – Chair*

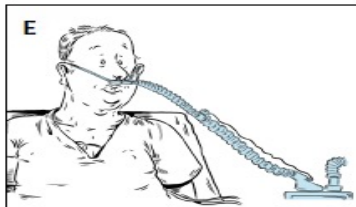


# Noninvasive oxygenation strategies

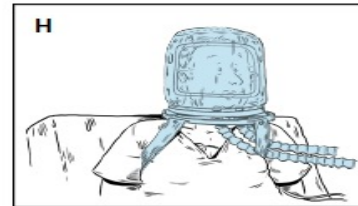
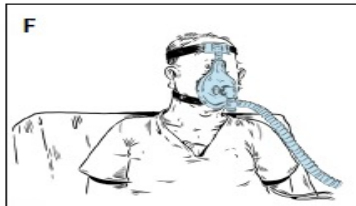
Low-flow  $O_2$



HFNC



NPPV



# Why is “High-Flow” Different?

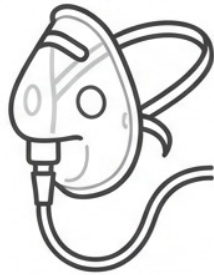


**Heated and humidified “high” gas flow  
can have major impact  
on physiological functions of  
upper & lower respiratory system**

# HFT: NOT JUST OXYGEN

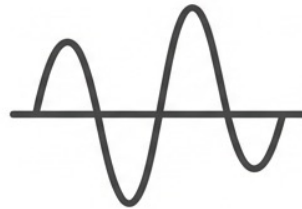
## Limitations of the Standard of Care (COT)

Defined as nasal prongs, simple facemasks, or venturi masks.



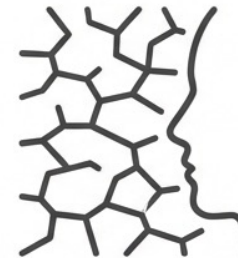
### Inadequate Support

Relies on passive gas delivery. Lacks positive pressure support.



### Instability

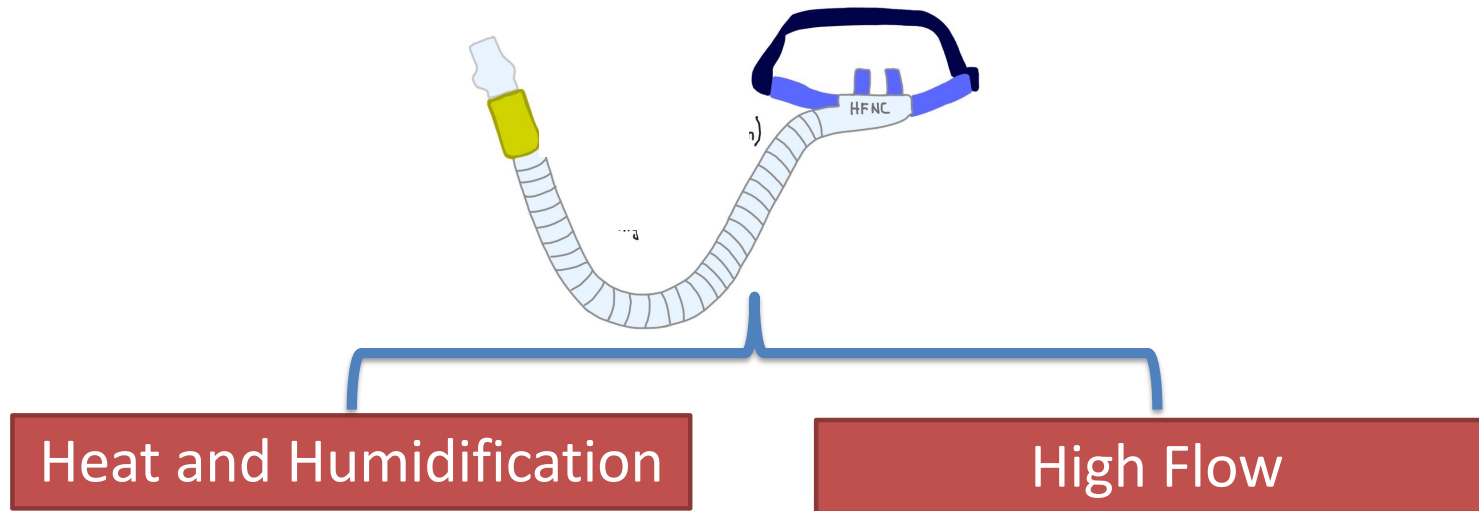
Delivers unstable FiO2 concentrations that fluctuate with patient breathing patterns.



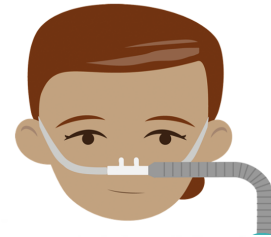
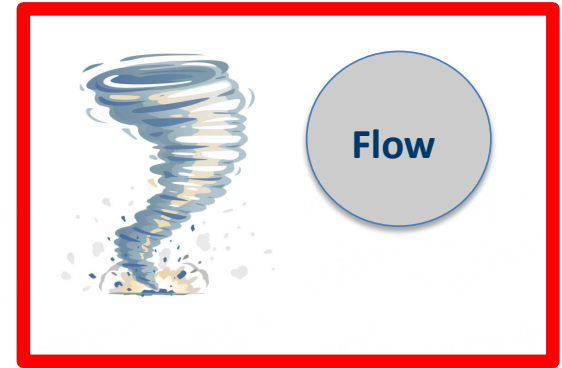
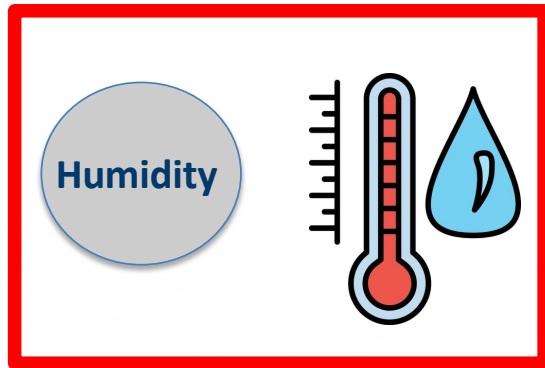
### Physiological Stress

Lack of heating and humidification leads to mucosal drying and discomfort.

# What is HFNT and why is different?



# WHY IT IS DIFFERENT?

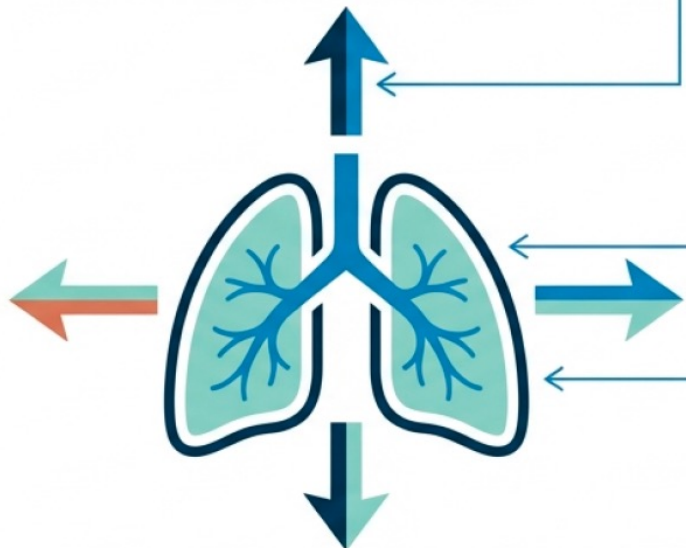


**Dead Space Wash-out**  
Increases CO<sub>2</sub> clearance

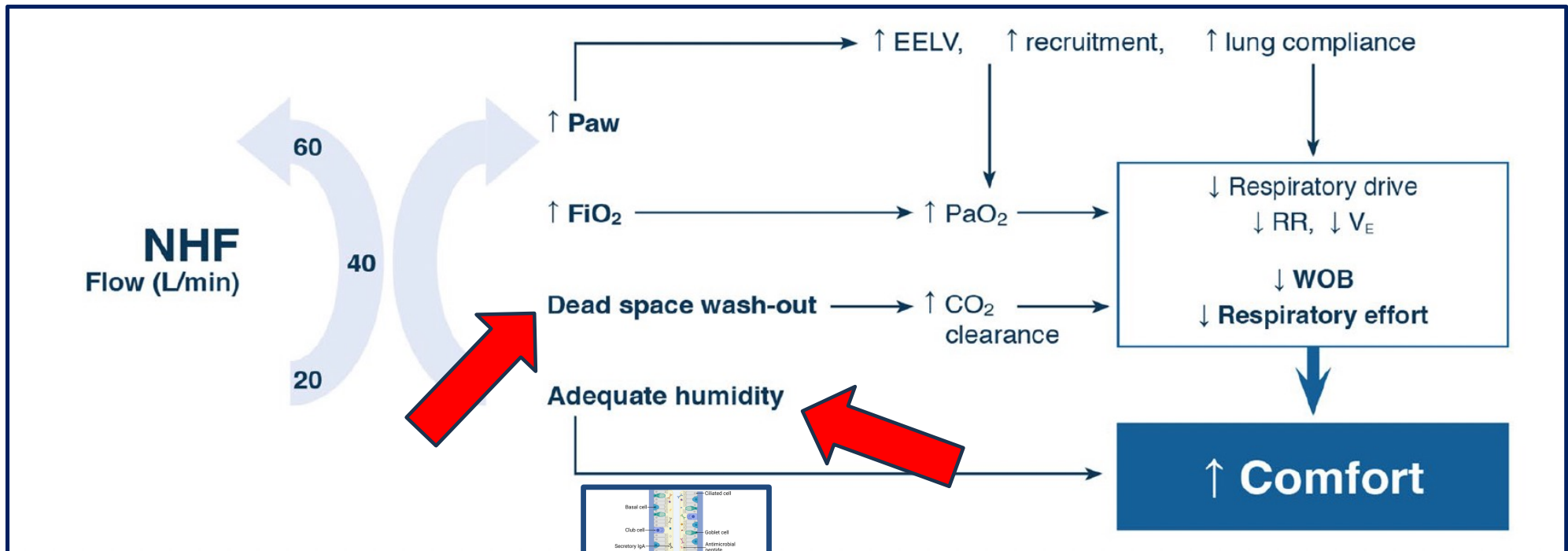
**Comfort**  
Adequate humidification  
& warming

**PEEP Effect**  
Increases EELV &  
alveolar recruitment  
Increase expiratory resistance

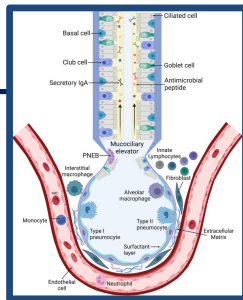
**Reduced Respiratory Drive**   
Lowers Respiratory Rate & Minute Ventilation  
Matches patient inspiratory demand



# Physiologic Effects of High Flow Therapy



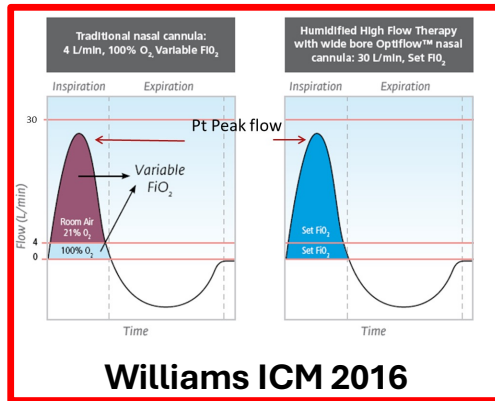
**Innate immune response in the lungs**



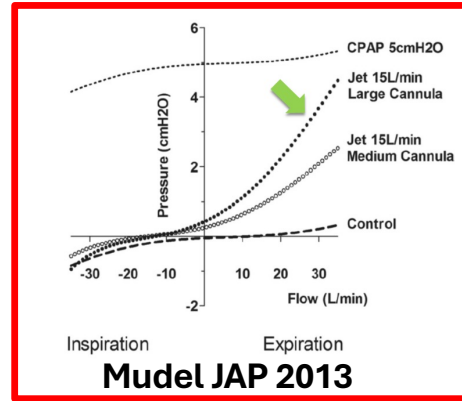
*Ricard JD et al Intensive Care Med 2020*

# HFT: mechanism of action

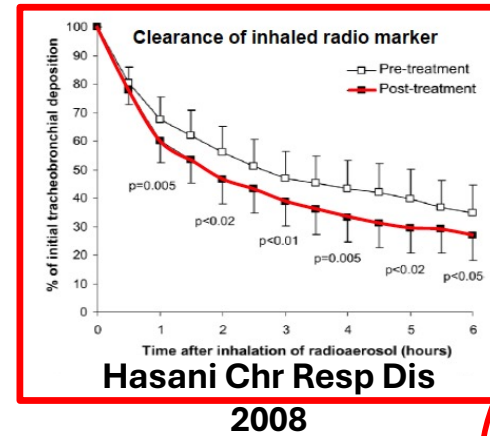
## Precise O2 delivery



## Expiratory resistance



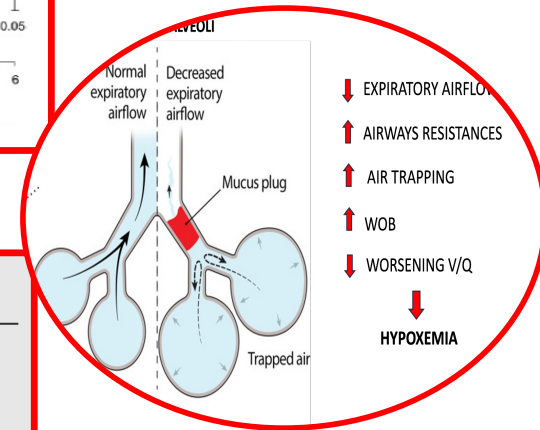
## Mucociliary clearance



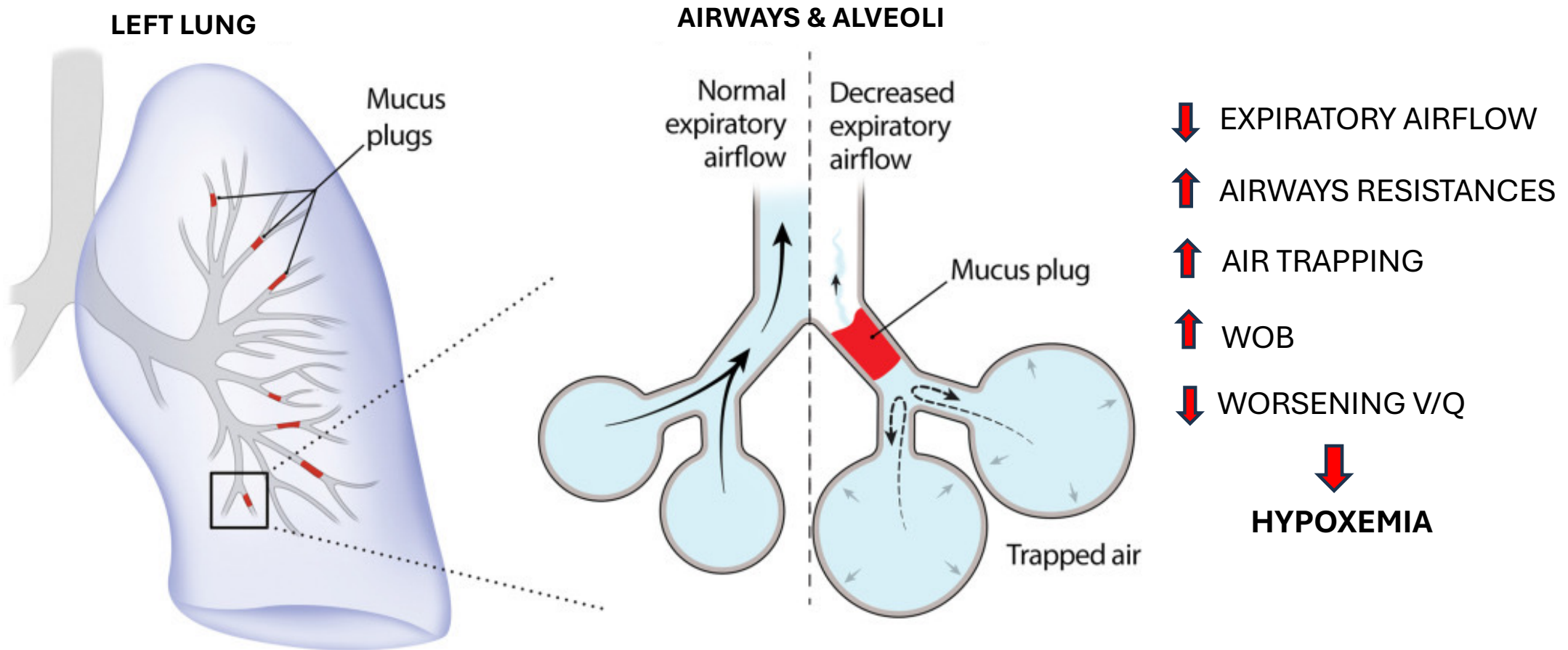
## WOB

	Baseline	HFOT 20 (closed)	HFOT 20 (open)	HFOT 30 (closed)	HFOT 30 (open)	NIV
TI,p (seconds)	0.95±0.2	0.85±0.4	0.96±0.2	0.94±0.3	0.92±0.3	1.00±0.2
TE,p (seconds)	1.94±0.4	2.35±0.4*	2.19±0.5*	2.30±0.5*	2.20±0.3*	2.61±1.0*
Breathing frequency (breaths/min)	24.8±2.3	19.01±5.2†	20.8±5.8	18.7±3.6†	19.64±2.8	17.8±3.8†
Tidal volume (mL)	314.50±84	391.22±106‡		364.22±66		456.20±100‡
Pdi swing (cmH <sub>2</sub> O)	13.5±6.7	8.7±4.1§	12±5.8	8.2±3.7§	10.2±5.2§	5.1±2.2§¶
PTPdi/min (cmH <sub>2</sub> Oxs/min)	238.3±82.1	164.2±51.3**	172.7±45.4**	143.2±48.9**	157.3±56.9**	101.7±42.9**††
PEEPi,dyn (cmH <sub>2</sub> O)	2.12±0.9	1.48±0.7‡‡		1.03±0.6‡‡		0.9±0.02‡‡

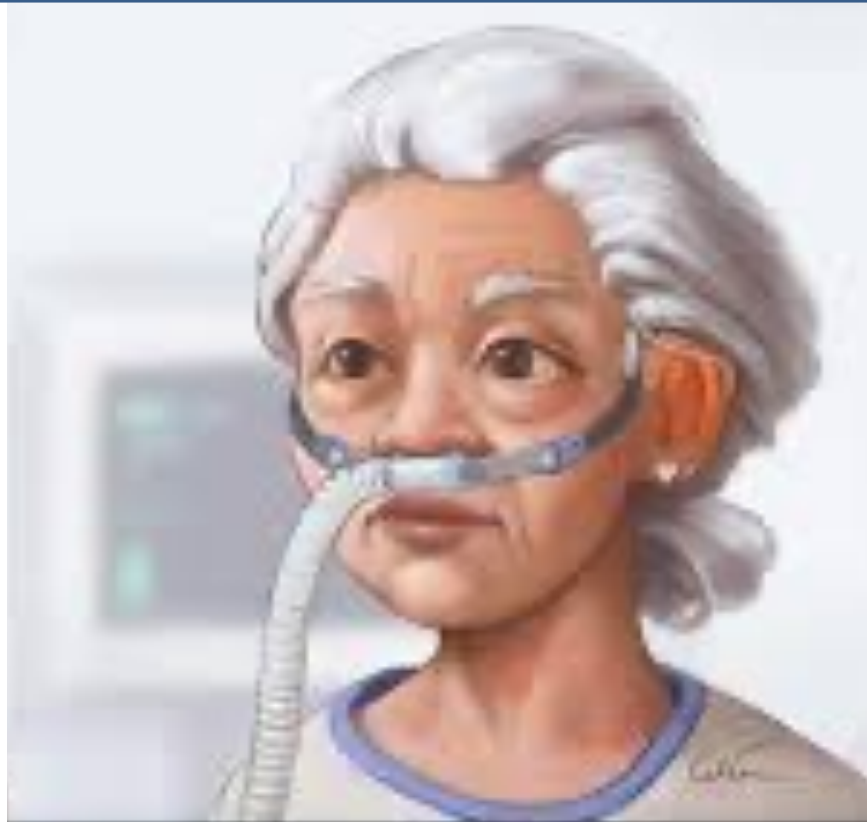
• Pisani Thorax 2017



# Pathophysiology



# ACUTE HYPOXEMIC RESPIRATORY FAILURE



**HIGH FLOW NASAL CANNULA**

# RCT HFNT vs. NIV vs. SO in *de novo* ARF

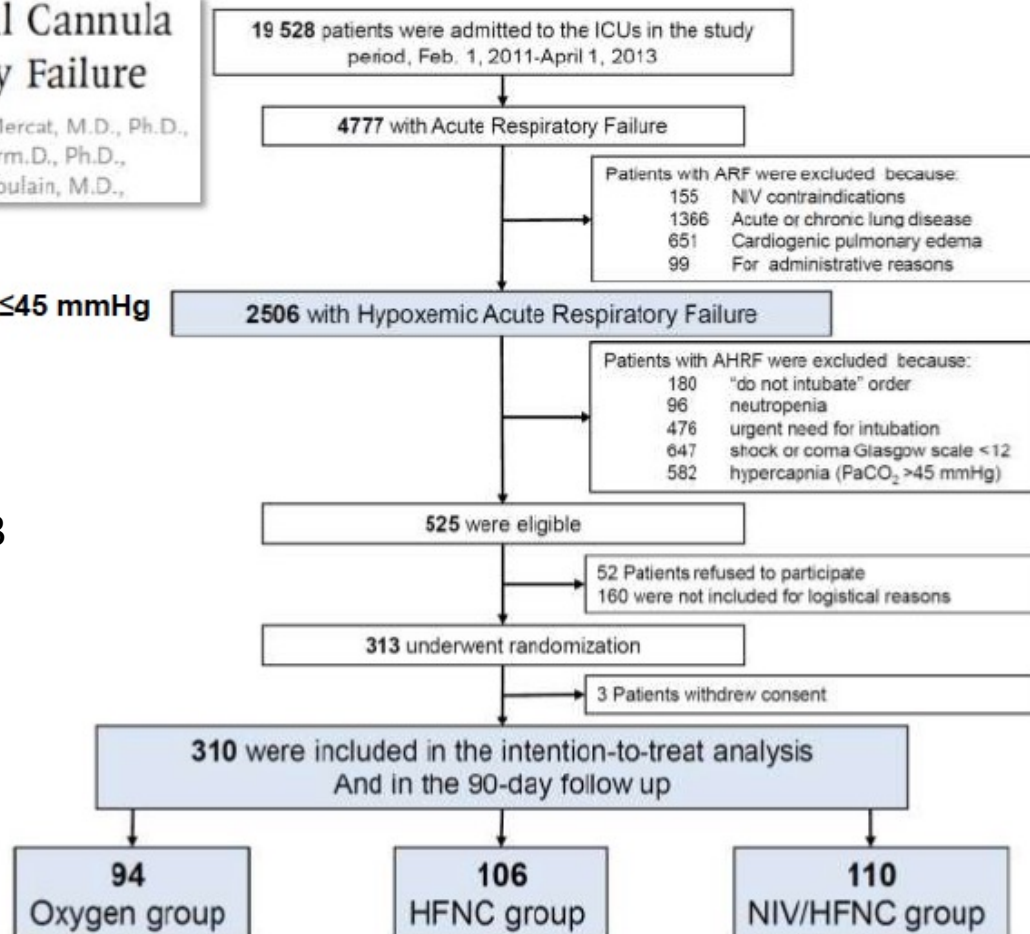
## High-Flow Oxygen through Nasal Cannula in Acute Hypoxemic Respiratory Failure

Jean-Pierre Frat, M.D., Arnaud W. Thille, M.D., Ph.D., Alain Mercat, M.D., Ph.D.,  
 Christophe Girault, M.D., Ph.D., Stéphanie Ragot, Pharm.D., Ph.D.,  
 Sébastien Perbet, M.D., Gwénael Prat, M.D., Thierry Boufain, M.D.,

RR >25 b/min; PaO<sub>2</sub>/FiO<sub>2</sub> ≤300, PaCO<sub>2</sub> ≤45 mmHg

SO ≥ 10 l/min,  
 HFO 50 l/min, FiO<sub>2</sub> 1.0 (82 %),  
 NIV VT 7-10 ml/kg (PS 8, PEEP 5, 67%, 9.3 ml/kg), 8 hrs daily X 2d

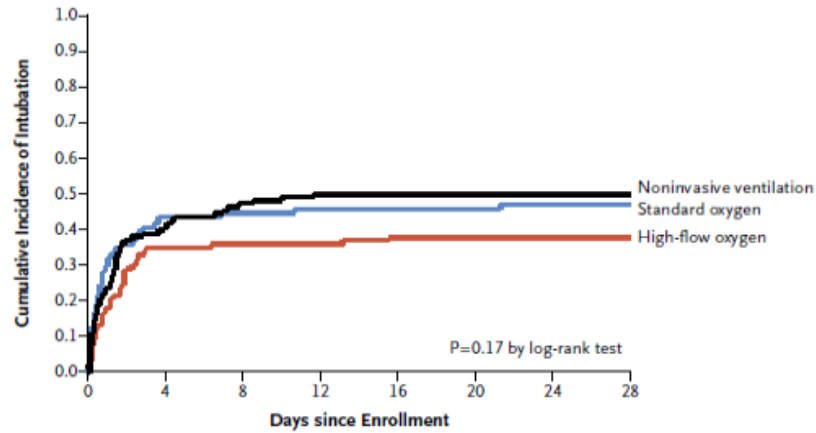
SpO<sub>2</sub> ≥92%, NIV ≥8 h/d



Frat J-P et al. NEJM 2015;372:2185-96

# PRIMARY END POINT - INTUBATION

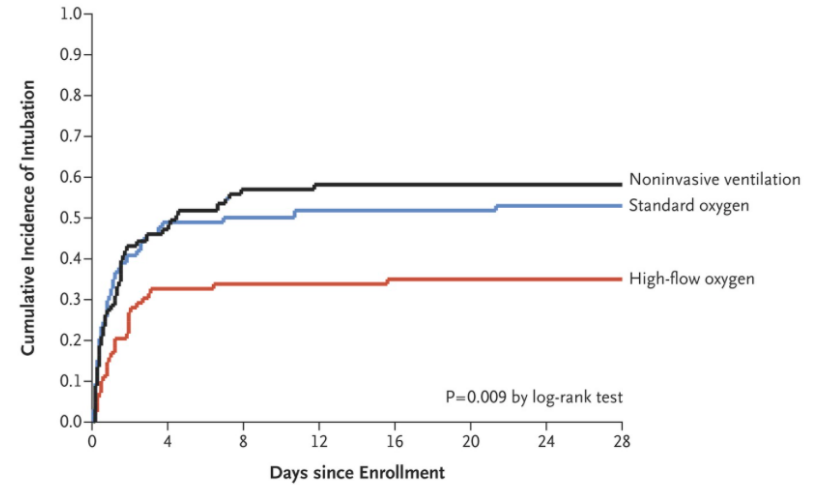
**A Overall Population**



**No. at Risk**

	0	4	8	12	16	20	24	28
High-flow oxygen	106	68	67	67	65	65	65	65
Standard oxygen	94	52	50	49	49	49	48	48
Noninvasive ventilation	110	64	57	53	53	53	53	52

**B Patients with a PaO<sub>2</sub>:FiO<sub>2</sub> ≤200 mm Hg**



**No. at Risk**

	0	4	8	12	16	20	24	28
High-flow oxygen	83	55	54	54	53	53	53	53
Standard oxygen	74	37	35	34	34	34	33	33
Noninvasive ventilation	81	41	34	32	32	32	32	32

Frat et al. NEJM 2015; 372: 2185-96

# Late HFNT Failure & ETI may cause harm

Byung Ju Kang  
Younsuck Koh  
Chae-Man Lim  
Jin Won Huh  
Seunghee Baek

## Failure of high-flow nasal cannula therapy may delay intubation and increase mortality

175 pts with NHF failure: 130 early ( $\leq 48$ h), 45 late ( $> 48$ h)


Early intubation associated with:

- ↓ ICU mortality (39.2 vs 66.7%)
- ↑ extubation success (37.7 vs 15.6%)
- ↑ ventilator weaning (55.4 vs 28.9%)
- ↑ ventilator-free days (8.6 vs 3.6)

*Conclusions:* Failure of HFNC might cause delayed intubation and worse clinical outcomes in patients with respiratory failure. Large prospective and randomized controlled studies on HFNC failure are needed to draw a definitive conclusion.



**Hypoxemic respiratory failure**  
(*moderate certainty*)

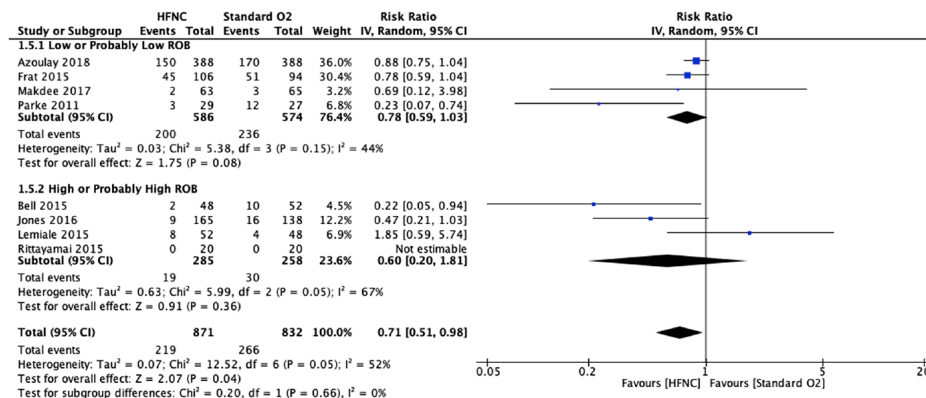
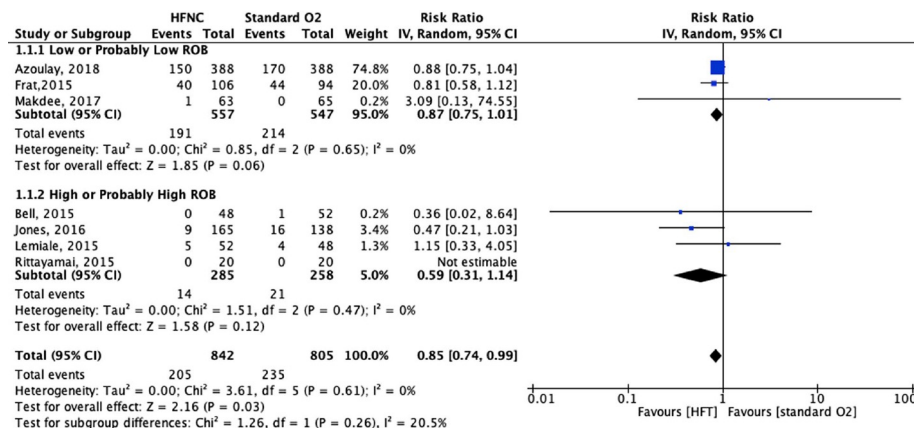


**Strong recommendation**

**PICO 1: Acute hypoxemic respiratory failure**

**Recommendation**

We recommend using HFNC compared to COT for patients with hypoxemic respiratory failure (strong recommendation, moderate certainty evidence).



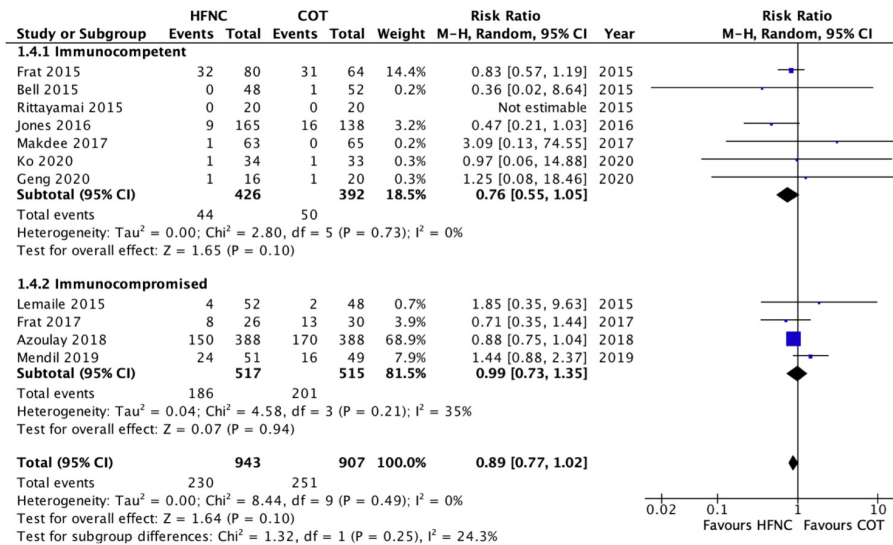
**Intubation: RR 0.85 [95% CI 0.74-0.99]**

**Escalation of respiratory support: RR 0.71 [0.51-0.98]**

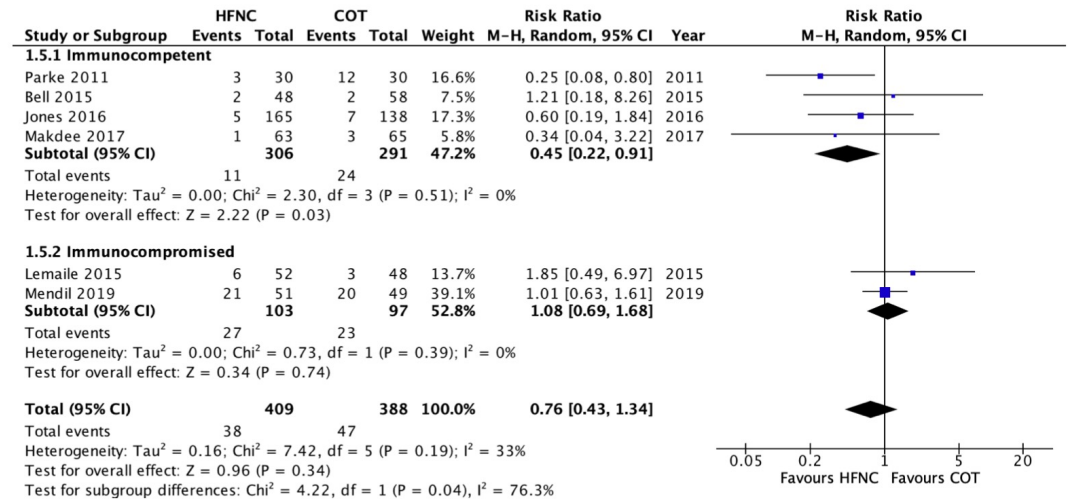
**Rochweg B et al. ICM 2020**

# ERS Task force

## 3. Intubation



## 4. Escalation to NIV



**PICO Question 1 : Should HFNC or COT be used in patients with acute hypoxemic respiratory failure?**

**Recommendation 1: We suggest the use of HFNC over COT in adults acute hypoxemic respiratory failure (conditional recommendation, moderate certainty of evidence)**



**Intubation: RR 0.89 [95% CI 0.77-1.02]**

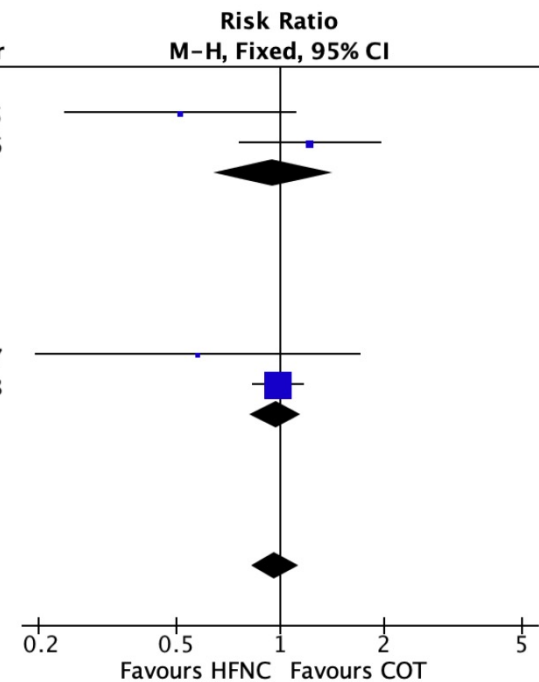
**Escalation to NIV: RR 0.76 [0.43-1.34]**

**Oczkowski S. et al ERJ 2021 ahead of print**

# ERS Task force

## 1. Mortality (90 day)

Study or Subgroup	HFNC		COT		Weight	Risk Ratio M-H, Fixed, 95% CI	Year
	Events	Total	Events	Total			
<b>1.1.1 Immunocompetent</b>							
Frat 2015	9	80	14	64	7.4%	0.51 [0.24, 1.11]	2015
Jones 2016	35	165	24	138	12.4%	1.22 [0.76, 1.95]	2016
<b>Subtotal (95% CI)</b>		<b>245</b>		<b>202</b>	<b>19.7%</b>	<b>0.96 [0.65, 1.42]</b>	
Total events	44		38				
Heterogeneity: $\text{Chi}^2 = 3.53$ , $\text{df} = 1$ ( $P = 0.06$ ); $I^2 = 72\%$							
Test for overall effect: $Z = 0.22$ ( $P = 0.82$ )							
<b>1.1.2 Immunocompromised</b>							
Frat 2017	4	26	8	30	3.5%	0.58 [0.20, 1.70]	2017
Azoulay 2018	160	388	162	388	76.7%	0.99 [0.84, 1.17]	2018
<b>Subtotal (95% CI)</b>		<b>414</b>		<b>418</b>	<b>80.3%</b>	<b>0.97 [0.82, 1.14]</b>	
Total events	164		170				
Heterogeneity: $\text{Chi}^2 = 0.94$ , $\text{df} = 1$ ( $P = 0.33$ ); $I^2 = 0\%$							
Test for overall effect: $Z = 0.37$ ( $P = 0.71$ )							
<b>Total (95% CI)</b>		<b>659</b>		<b>620</b>	<b>100.0%</b>	<b>0.97 [0.83, 1.13]</b>	
Total events	208		208				
Heterogeneity: $\text{Chi}^2 = 4.47$ , $\text{df} = 3$ ( $P = 0.22$ ); $I^2 = 33\%$							
Test for overall effect: $Z = 0.43$ ( $P = 0.67$ )							
Test for subaroup differences: $\text{Chi}^2 = 0.00$ , $\text{df} = 1$ ( $P = 0.95$ ). $I^2 = 0\%$							



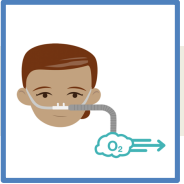
The impact on mortality is likely small

Oczkowski S. et al ERJ 2021 ahead of print

ACPE

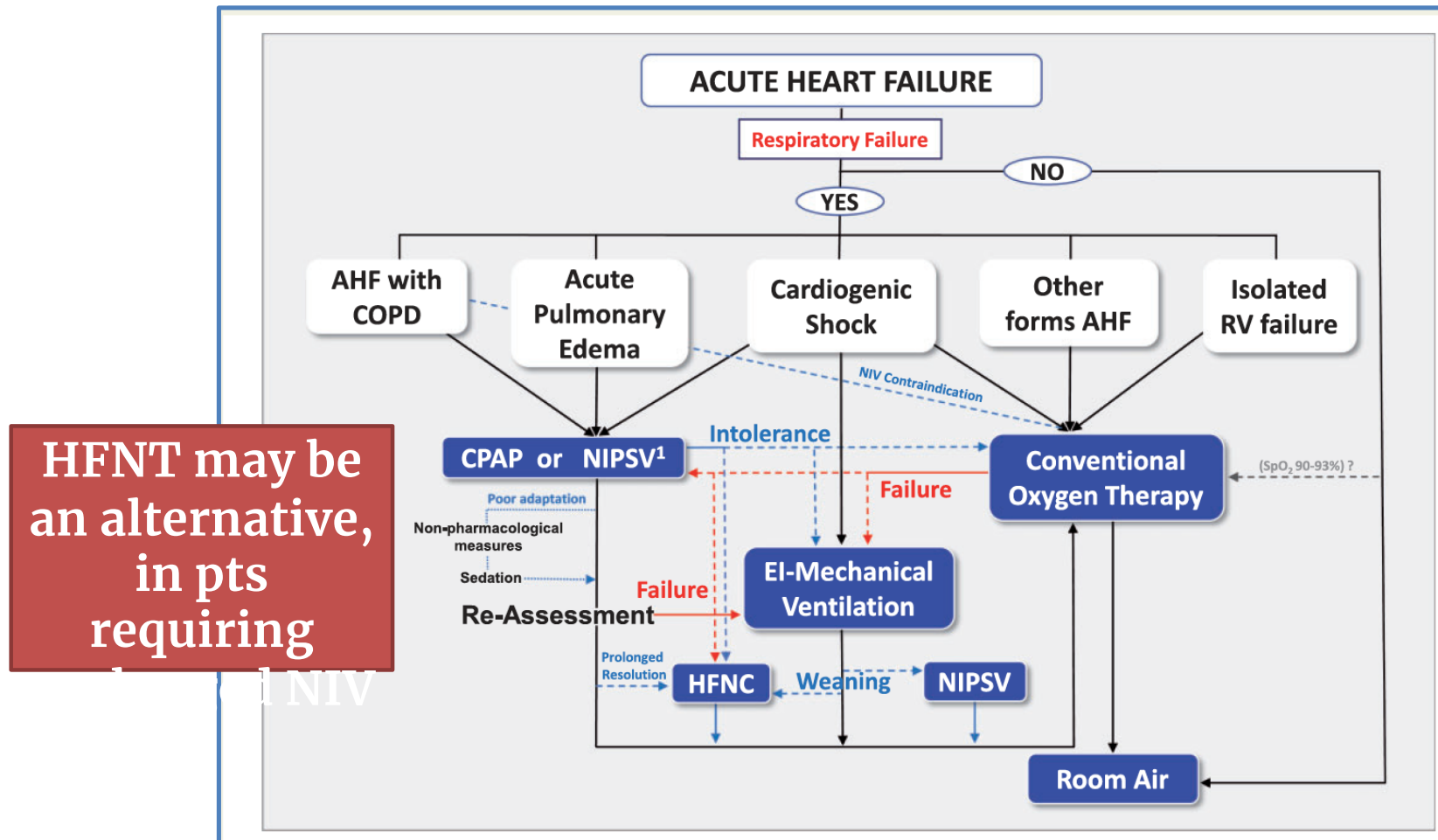


## Studies on HFNT in ACPE



Study	Study population	Intervention/Experimental group	Control group	Outcome
Ko et al. [36] (Randomized controlled trial)	Patient suspected of pulmonary edema due to heart failure	HFNC (n = 36)	COT (n = 33)	Significant difference in respiratory rate, SpO <sub>2</sub> at 30 and 60 minutes (improved in HFNC group) Significant difference in ABG parameters (PaO <sub>2</sub> and SpO <sub>2</sub> ) at 30 and 60 minutes (improved in HFNC group)
Makdee et al. [37] (Randomized controlled trial)	ED patients with cardiogenic pulmonary edema	HFNC (n = 63)	COT (n = 65)	60-minute respiratory rate significantly lower in HFNC group Lower respiratory rate at 15 and 30 minutes in HFNC group
Sener et al. [4] (Prospective observational study)	Patients with hypertensive pulmonary edema	HFNC (n = 62)	COT (n = 50)	HFNC shortens the length of stay in both emergency and intensive care unit HFNC shows better results in terms of heart rate, respiratory rate, and ABG parameters
Chang et al. [38] (Cohort study)	Post-extubated patients with heart failure with ejection fraction <50%	HFNC (n = 58)	NIPPV (n = 46)	No significant difference in treatment failure between two groups in 72 hours

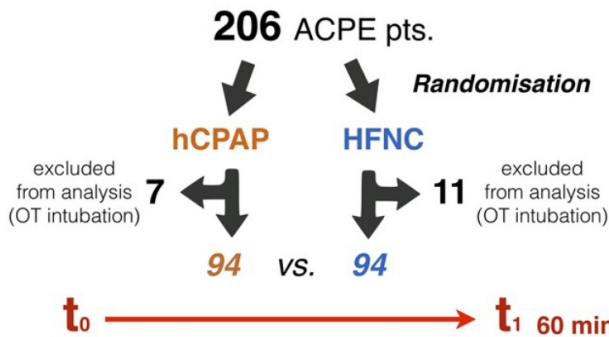
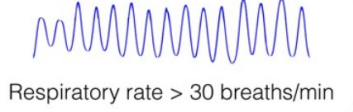
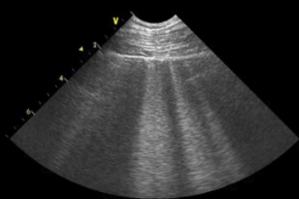
# Algorithm for noninvasive respiratory support in acute heart failure



HFNT may be an alternative, in pts requiring

# Helmet CPAP vs. High Flow Nasal Cannula O<sub>2</sub> in ACPE: A Randomized Controlled Trial

## Acute Cardiogenic Pulmonary Edema (ACPE) in the ER



hCPAP



VS.



HFNC

### PRIMARY OUTCOME, Absolute difference t<sub>0</sub>-t<sub>1</sub>

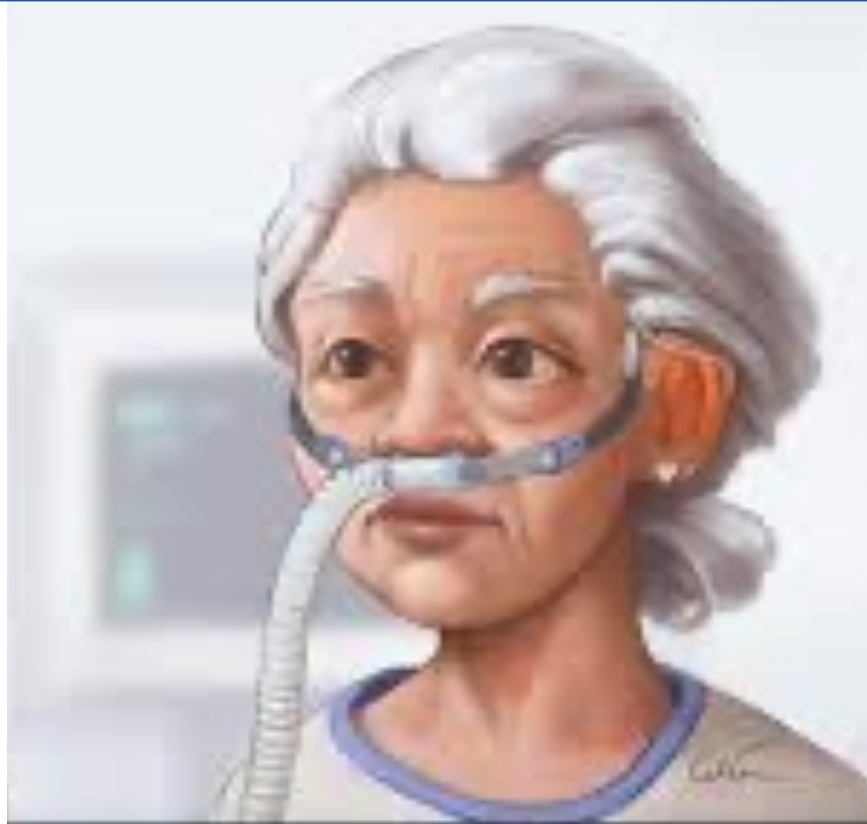
12 (11-13) **RESP RATE (breaths/min)** 9 (8-10) p < 0.001

### SECONDARY OUTCOMES, Absolute difference t<sub>0</sub>-t<sub>1</sub>

10 (8-12)	<b>MAP (mmHg)</b>	9 (7-12)	p < 0.001
20 (17-23)	<b>Heart rate (bpm)</b>	15 (12-18)	p = 0.04
149 (135-163)	<b>PaO<sub>2</sub>/FiO<sub>2</sub></b>	120 (107-132)	p = 0.03
6 (0-12)	<b>HACOR score</b>	4 (2-9)	p < 0.001
4 (1-7)	<b>Dyspnea scale</b>	3.5 (1-6)	p < 0.001

hCPAP in the very short term more effective than HFNC in improving dyspnea, hemodynamics and respiratory parameters

**ACUTE HYPERCAPNIC RESPIRATORY FAILURE:  
is there a clinical role for HFNC?**



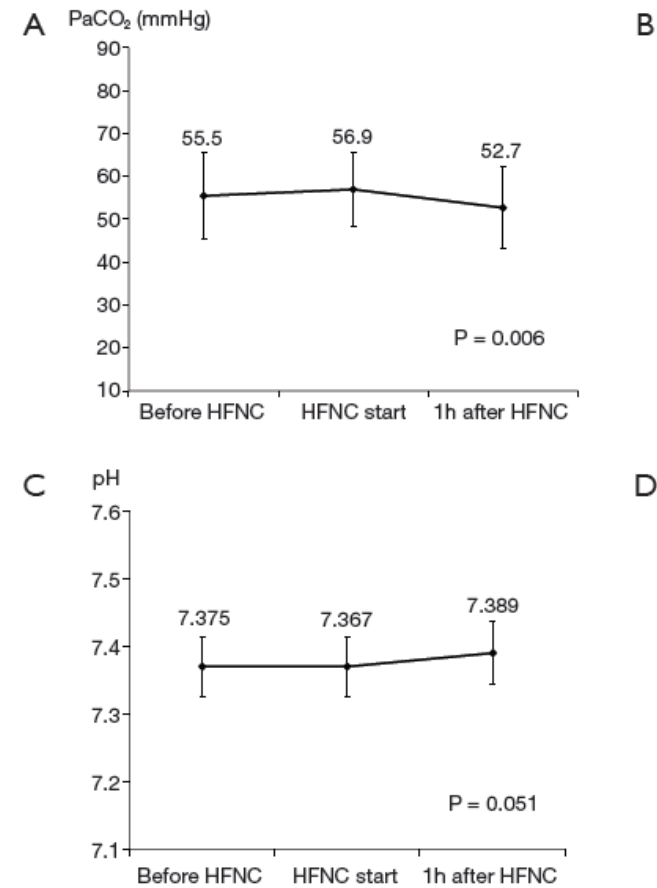
**HIGH FLOW NASAL CANNULA**

# Effectiveness of high-flow nasal cannula oxygen therapy for acute respiratory failure with hypercapnia

Eun Sun Kim, Hongyeul Lee, Se Joong Kim, Jisoo Park, Yeon Joo Lee, Jong Sun Park, Ho Il Yoon, Jae Ho Lee, Choon-Taek Lee, Young-Jae Cho

J Thorac Dis. 2018

Design: single retrospective  
33 pts AHRF PaCO<sub>2</sub> 56.3±10.7  
Setting: MICU



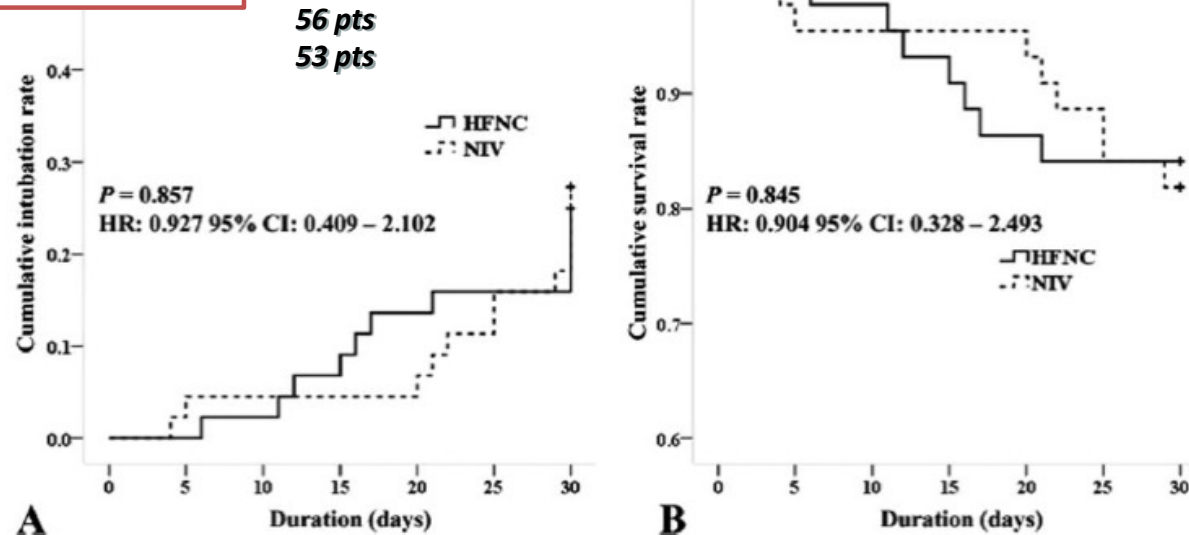
# High flow nasal cannulae oxygen therapy in acute-moderate hypercapnic respiratory failure

Myoung Kyu Lee<sup>1</sup> | Jaehwa Choi<sup>1</sup> | Bonil Park<sup>1</sup> | Bumjoon Kim<sup>1</sup> |

*Clin Respir J* 2018

**Design:** prospective observational  
**Settings:** 92 AECOPD- moderate hypercapnia pCO<sub>2</sub> > 45 pH 7.25-7.35  
**Intervention:** HFNC vs. NIV  
**Primary outcome:** intubation rate & mortality @ 30 days

pH= 7.31±0.02



HFNC is equivalent to NIV in avoiding intubation in AHRF

**RESEARCH**

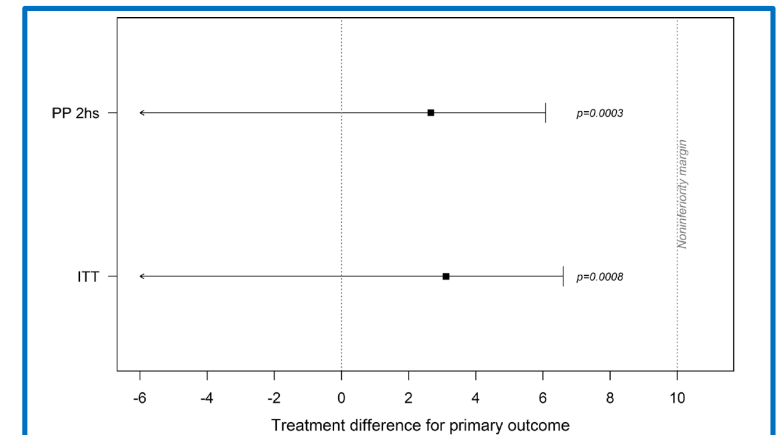
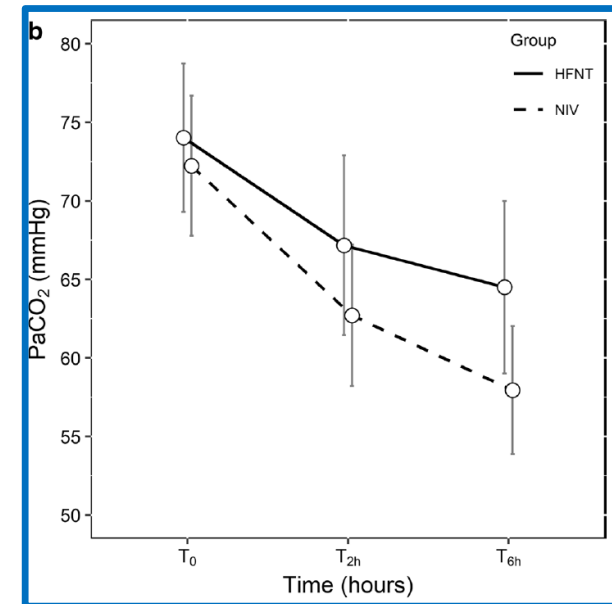
Open Access

High flow nasal therapy versus noninvasive ventilation as initial ventilatory strategy in COPD exacerbation: a multicenter non-inferiority randomized trial



- **79 pts** with mild-to-moderate **AECOPD** randoed to **HFNT** or **NIV**
- Primary endpoint: **mean difference in PaCO<sub>2</sub>** at 2 hours
- HFNT was **non-inferior** to NIV for the primary outcome
- **32% of HFNT switched to NIV within 6 hours**
- **57% of HFNT received NIV during hospitalization**
- Longer time on NIV in patients randomized to HFNTmize

Cortegiani A et al Critical Care 2020





RESEARCH

Open Access



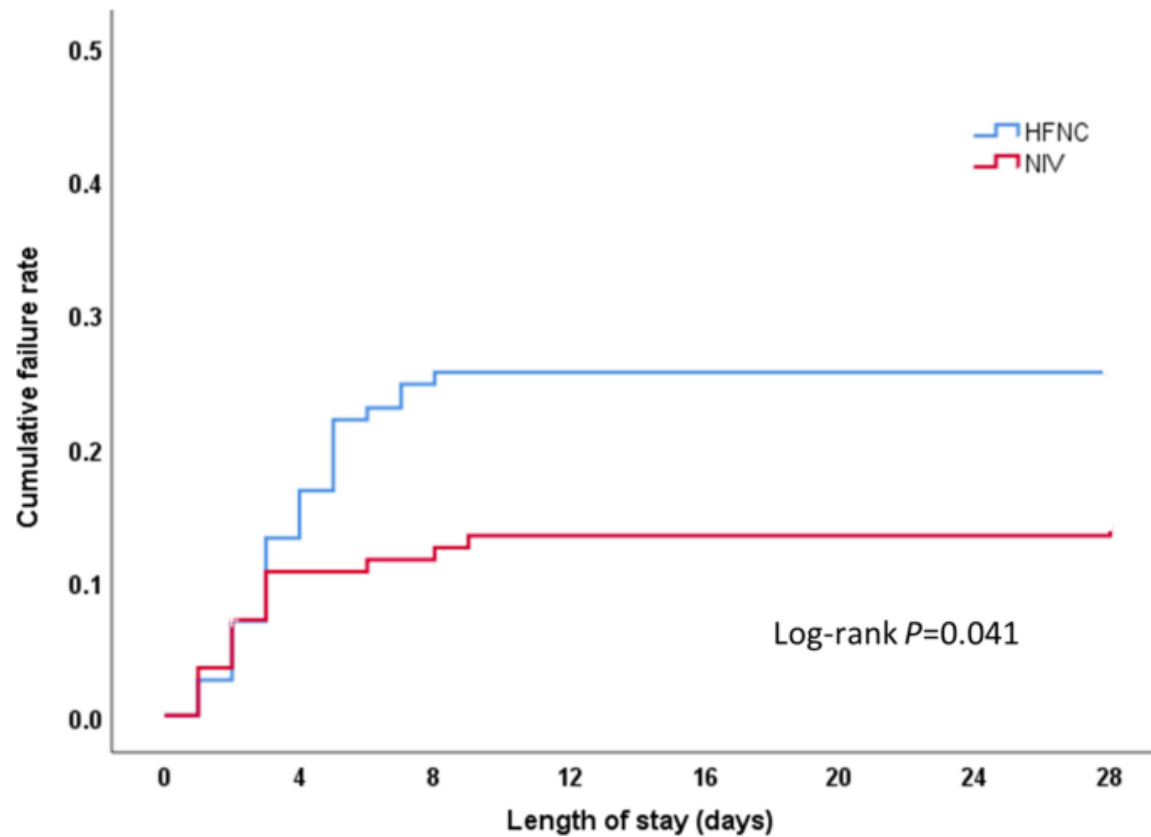
# High flow nasal cannula oxygen therapy versus non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease with acute-moderate hypercapnic respiratory failure: a randomized controlled non-inferiority trial

Dingyu Tan<sup>1†</sup>, Bingxia Wang<sup>1†</sup>, Peng Cao<sup>1</sup>, Yunyun Wang<sup>1\*</sup>, Jiayan Sun<sup>2\*</sup>, Ping Geng<sup>1</sup>, Joseph Harold Walline<sup>3</sup>, Yachao Wang<sup>1</sup> and Chenlong Wang<sup>1</sup>

**Design:** Randomized, controlled, non-inferiority trial (China, 2 ICUs)

**Patients:** AECOPD with pH 7.25–7.35, PaCO<sub>2</sub> ≥ 50 mmHg

**Primary Outcome:** Treatment failure (intubation or treatment switch)



- **Treatment failure:**
- HFNC: **25.7%**
- NIV: **14.3%**
- **Risk difference:** +11.4% (exceeded non-inferiority margin)
- **Intubation rates:**
- HFNC: **14.2%**
- NIV: **5.4%** (p = 0.026)
- **ICU/hospital stay and 28-day mortality:** No significant difference

# High-Flow Nasal Oxygen vs Noninvasive Ventilation in Patients With Acute Respiratory Failure

## The RENOVATE Randomized Clinical Trial

RENOVATE Investigators and the BRICNet Authors

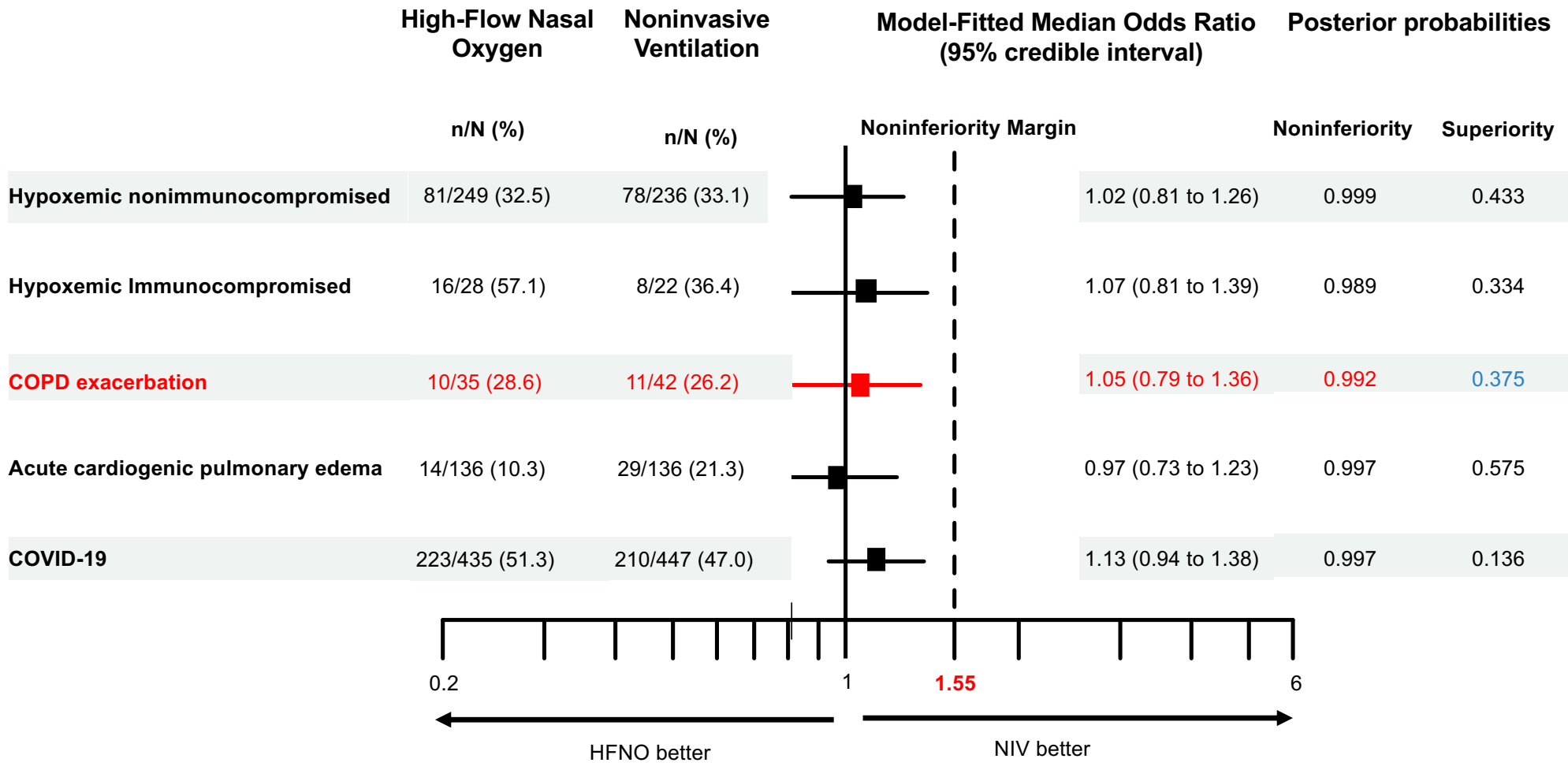
### Study Design (COPD Arm)

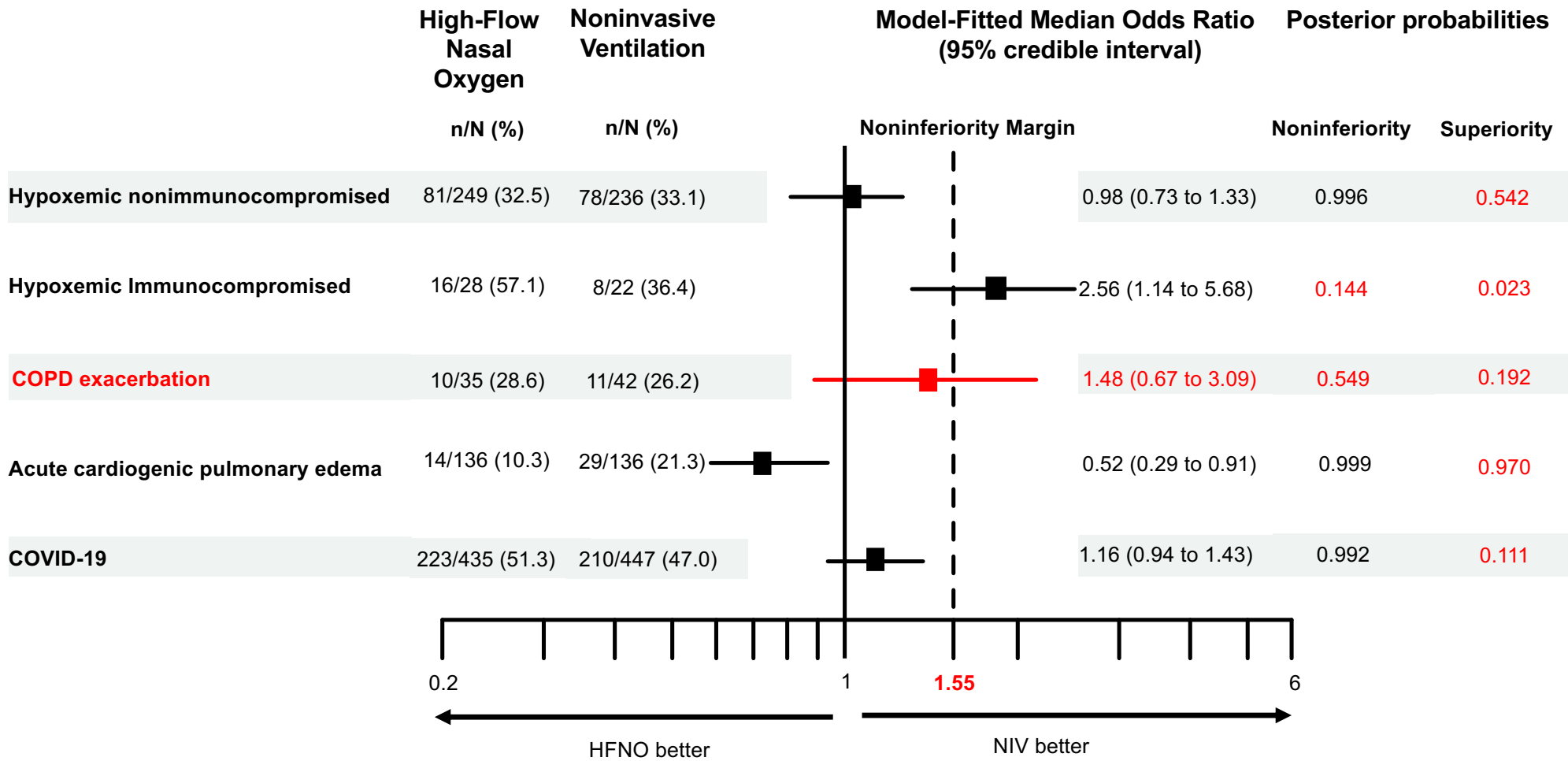
- Part of a large **multicenter bayesian RCT** comparing HFNC vs NIV across 5 respiratory failure phenotypes
- **Patients:** 273 patients with **AECOPD + respiratory acidosis**
- **Primary endpoint: Composite of intubation or death by Day 7**

### 📈 Key COPD Results

- **Treatment failure (intubation or death at Day 7):**
  - HFNC: **28.6%**
  - NIV: **26.2%**
  - **Odds ratio:** 1.05 (95% Credible Interval: 0.79–1.36)
- **HFNC was non-inferior to NIV** in AECOPD for preventing intubation or death at 7 days — offering a **viable alternative**, especially where NIV is not tolerated.  
(Posterior probability of non-inferiority = **0.992**)







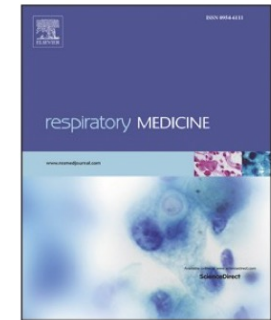
Original Research

## Nasal high flow or noninvasive ventilation? navigating hypercapnic COPD exacerbation treatment: A randomized noninferiority clinical trial

Ioannis Pantazopoulos<sup>a,b</sup>, Stylianos Boutlas<sup>b</sup>, Georgios Mavrovounis<sup>a,\*</sup>,  
Athanasia Papalampidou<sup>c</sup>, Nikolaos Papagiannakis<sup>d</sup>, Marina Kontou<sup>a</sup>, Eleni Bibaki<sup>e</sup>,  
Nikolaos Athanasiou<sup>f</sup>, Georgios Meletis<sup>e</sup>, Konstantinos Gourgoulianis<sup>b</sup>, Spyros Zakynthinos<sup>c</sup>,  
Eleni Ischaki<sup>c</sup>



2024



**Design:** Multicenter, randomized, **noninferiority trial** (Greece, 3 centers)

**Patients:** AECOPD with **pH 7.25–7.35** and **PaCO<sub>2</sub> > 45 mmHg**

**Primary Endpoint:** Treatment failure (IOT or treatment switch)

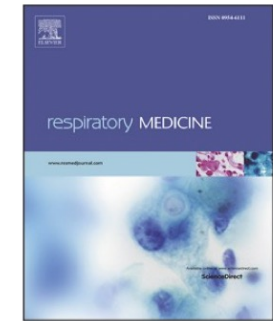
**Secondary Endpoints:** Comfort (dyspnea, VAS), respiratory parameters, complications



Original Research

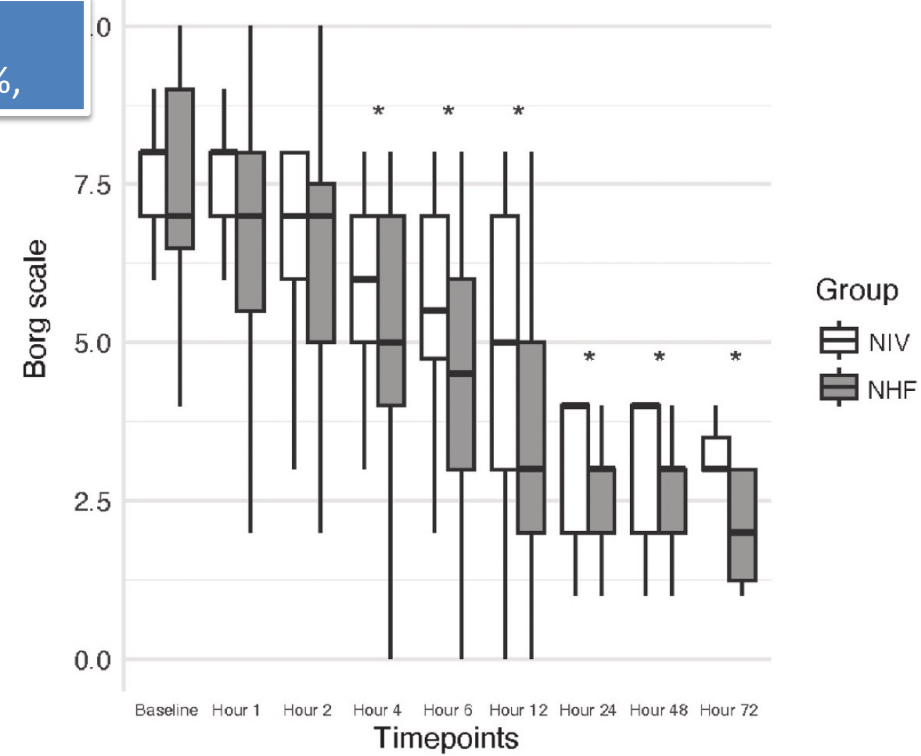
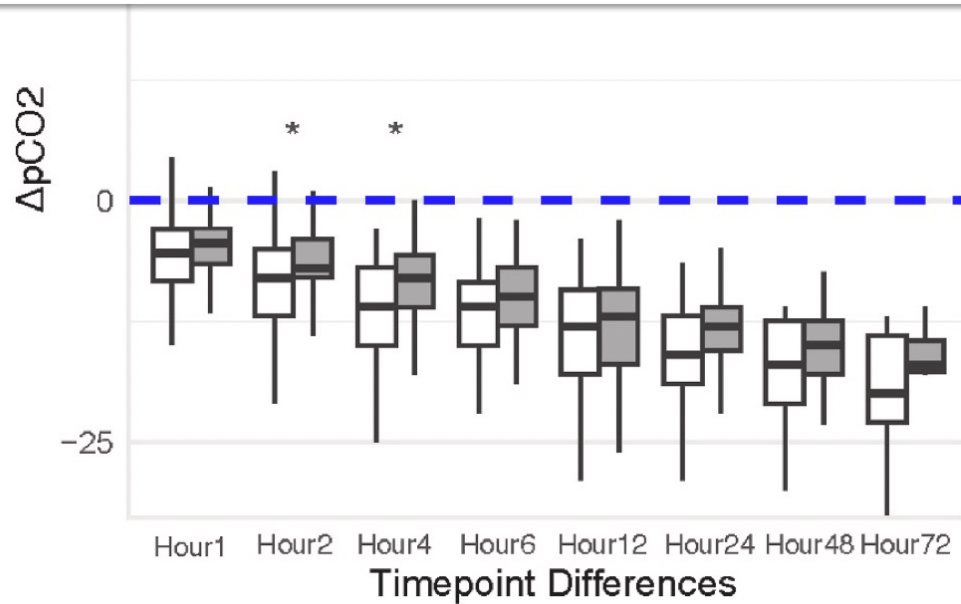
# Nasal high flow or noninvasive ventilation? navigating hypercapnic COPD exacerbation treatment: A randomized noninferiority clinical trial

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2024

Treatment failure: NIV 14.81 % (8/54) vs HFNT 19.61 % (10/51)  
Observed risk difference in treatment failure between groups was 4.80 %,





**Acute hypercapnic respiratory failure**

Trialling NIV prior to use of NHF in patients with COPD or acute hypercapnic respiratory failure.

**CONDITIONAL RECOMMENDATION**

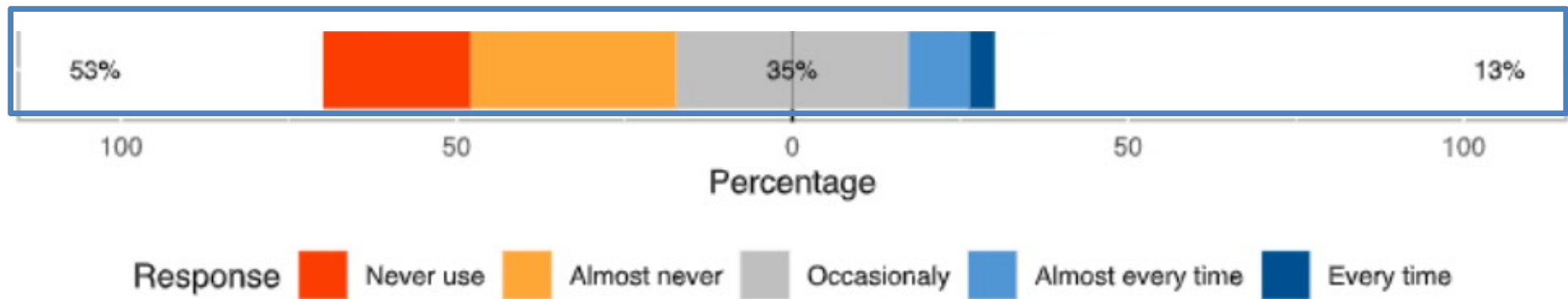
Low certainty of evidence

**PICO 8:** Should HFNC or NIV be used in patients with acute hypercapnic respiratory failure?

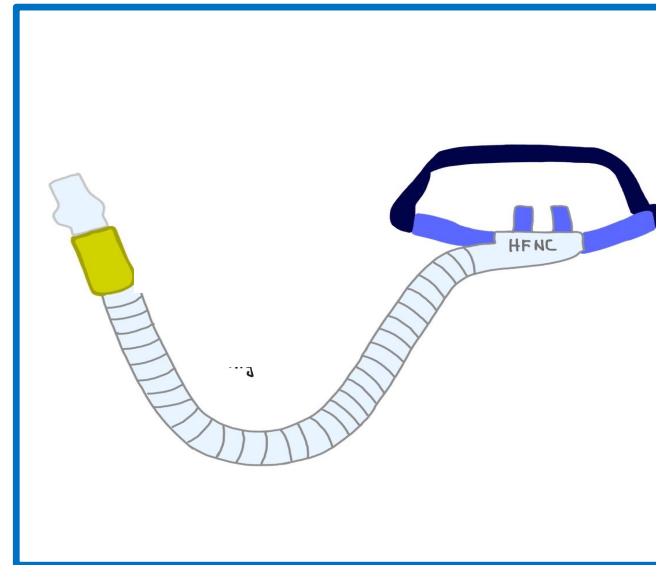


1176 respondents among ERS Assembly 2, 1 and 9

## How likely it occurs in your practice to use HFNT in COPD exacerbation with hypercapnia?



## In the NIV intervals



# High-Flow Oxygen Therapy After Noninvasive Ventilation Interruption in Patients Recovering From Hypercapnic Acute Respiratory Failure: A Physiological Crossover Trial

Critical Care Medicine

Federico Longhini, MD<sup>1</sup>; Lara Pisani, MD, PhD<sup>2</sup>; Ramona Lungu, MD<sup>3</sup>;  
Vittoria Comellini, MD<sup>2</sup>; Andrea Bruni, MD<sup>4</sup>; Eugenio Garofalo, MD<sup>4</sup>;  
Maria Laura Vega, MD<sup>2</sup>; Gianmaria Cammarota, MD, PhD<sup>3</sup>; Stefano Nava, MD, FERS<sup>2</sup>;  
Paolo Navalesi, MD, FERS<sup>4</sup>



At NIV stop:

Random Crossover



VS



**Conclusions:** At the time of noninvasive ventilation interruption,  $\text{Paco}_2$  and diaphragm displacement remained unchanged regardless of the modality of oxygen administration. However, although standard oxygen resulted in a remarkable increase in diaphragm thickening fraction, high-flow oxygen therapy allowed maintaining it unchanged, while improving patient comfort. (*Crit Care Med* 2019; 47:00–00)

# Home HFT in Chronic Respiratory Failure

PEEP effect

Generate a slight positive pressure

Dead Space Washout

Effectively washout CO<sub>2</sub>

Mucociliary Clearance

Humidification improves mucus clearance

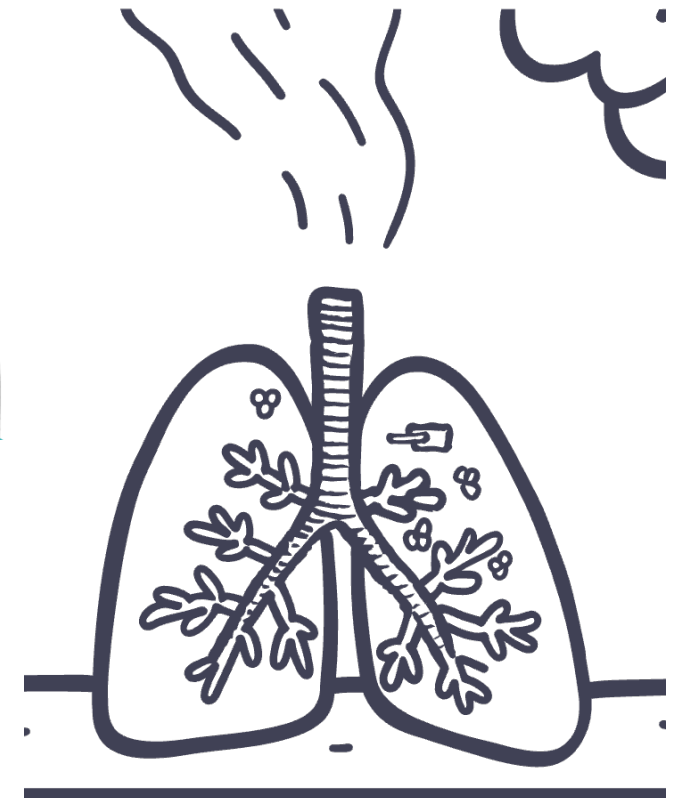
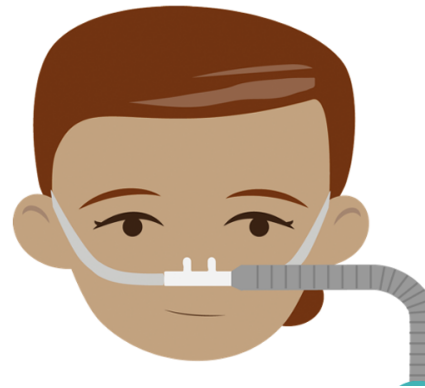
Reduces Work of breathing

Improvement in the breathing pattern

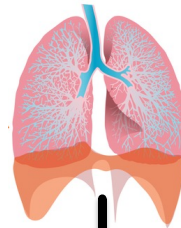
Improves Oxygenation

Accurate and stable oxygen delivery

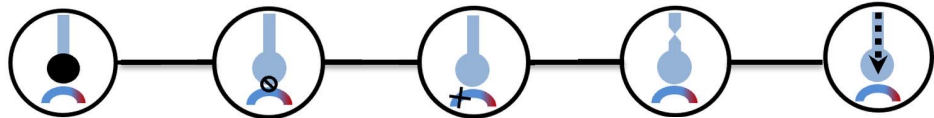
## HFT



# Pathophysiology of Chronic Respiratory Failure



## LUNG FAILURE



Focal Alveolar

Impaired Diffusion

Dead Space

Airway Disease

Hypoventilation

Pneumonia  
Mucus plugging  
Atelectasis

Emphysema  
CPFE  
ILD

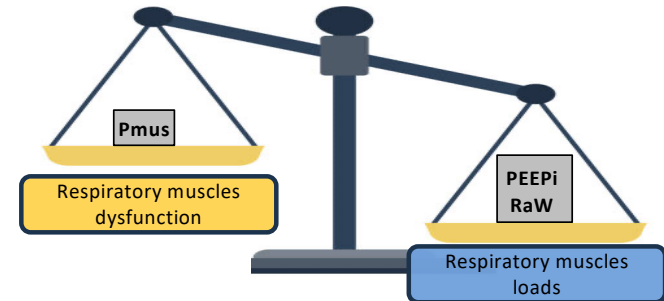
Emphysema

COPD  
Bronchiectasis

OHS

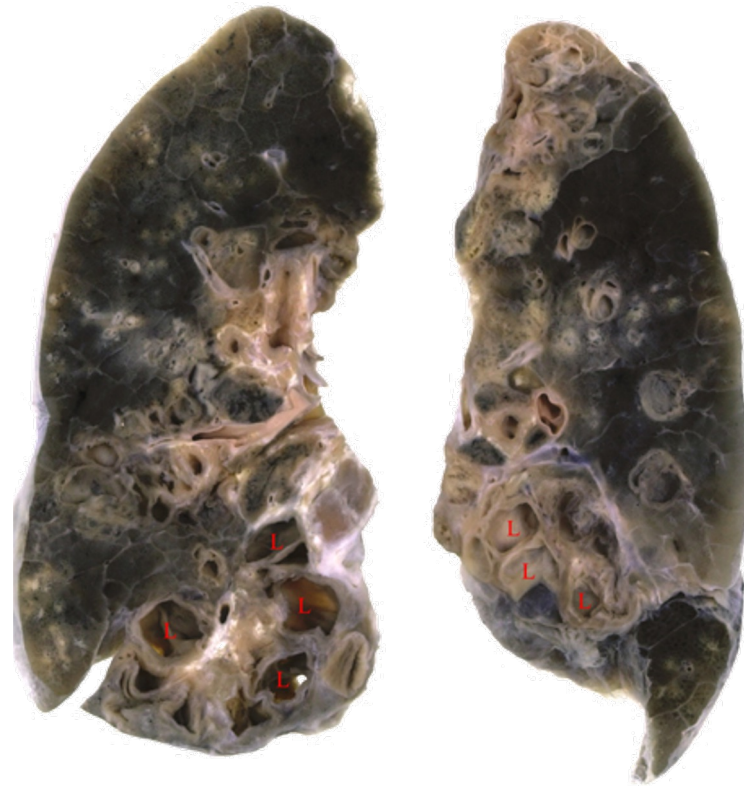
Chronic Respiratory Failure with Hypoxemia

## PUMP FAILURE



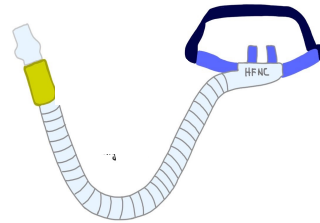
Chronic Respiratory Failure with Hypercapnia

# COPD



# What are the potential benefits of home HFNC in COPD?

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Improve  
secretions  
management

Hasani A, et al. 2008  
Rea H, et al. 2010

Reduce  
work of  
breathing

Fraser JF, et al. 2016  
Pisani L, et al. 2017

Improve  
nocturnal  
alveolar  
ventilation

Biselli PJ, et al. 2017

Improve  
quality of life

Storgaard LH, et al. 2018  
Nagata H, et al. 2017

Reduce acute  
exacerbation  
and  
hospitalisation  
rates

Storgaard LH, et al. 2018



Implications into everyday clinical practice

# HFT CHRONIC USE



**73%**

**DO NOT** prescribe  
home HFT

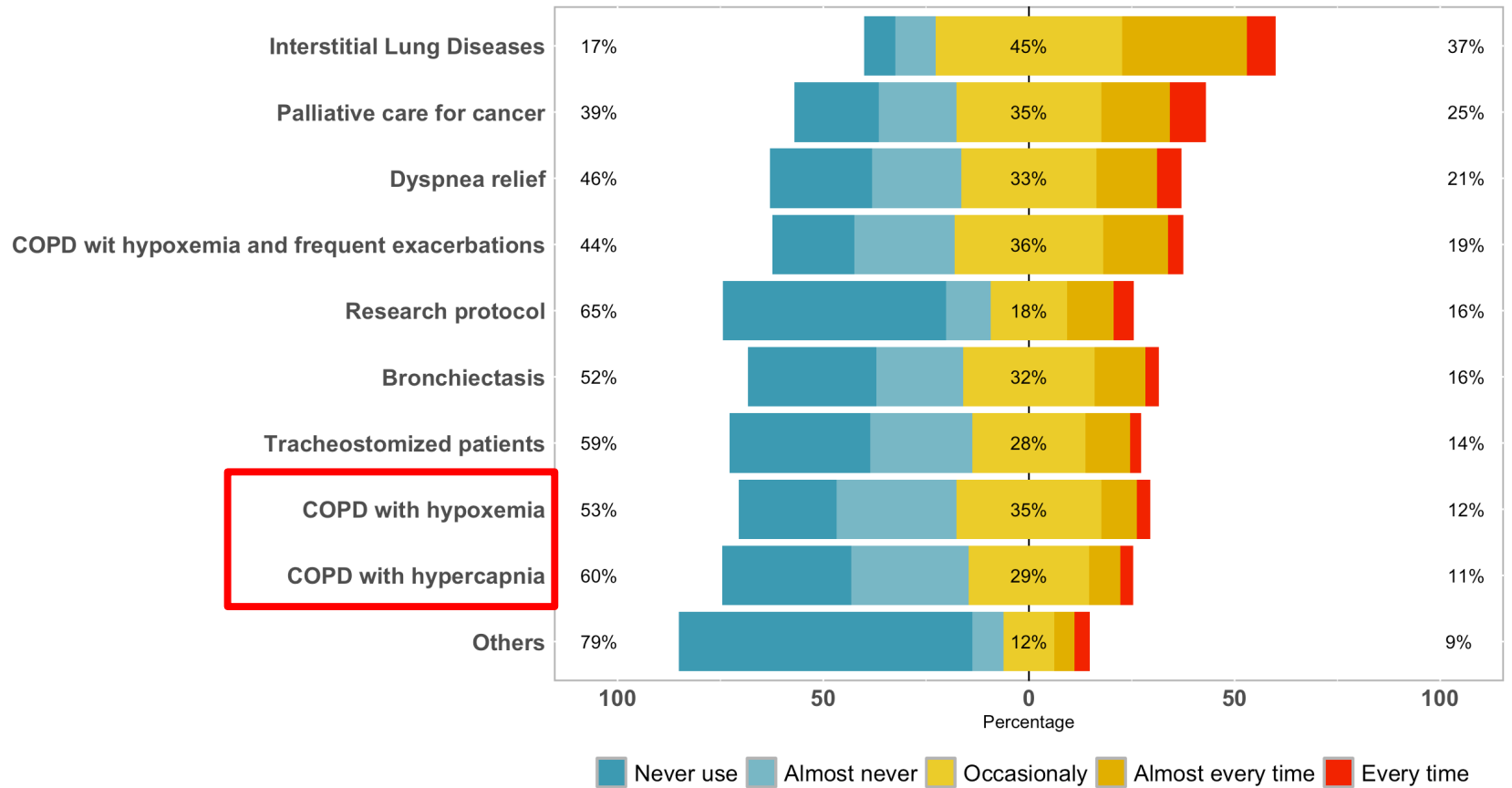
## **The primary Barrier**

Lack of **Funding/Reimbursement**  
(44%) #1 blocker

Estimated continuation after  
acute initiation: median **~13.5%**

# PATIENT PROFILE

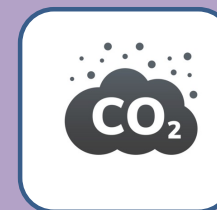
## Perceived Long-term use of HFT in Europe



# COPD: choosing the right patient

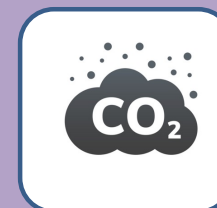


**Hypoxemic**



**Hypercapnic**

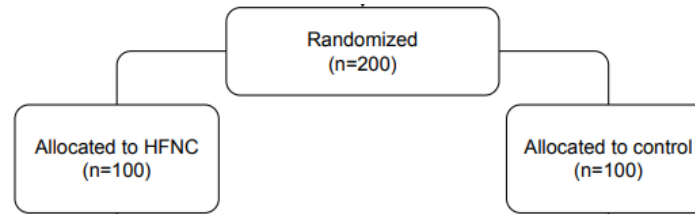
# COPD: choosing the right patient



**Hypoxemic**

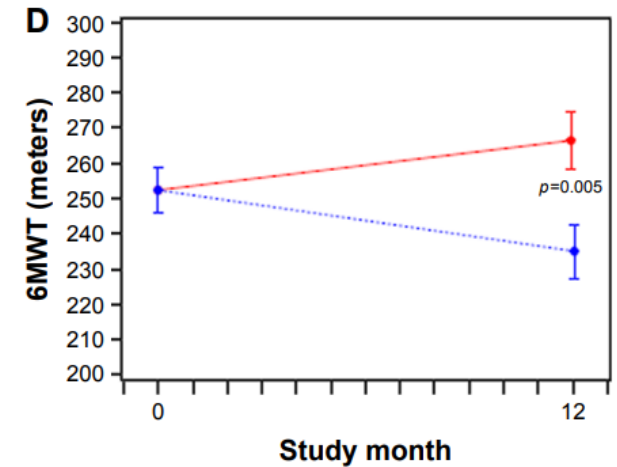
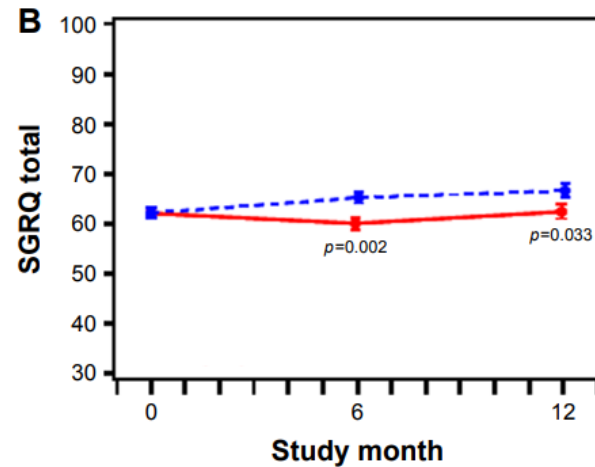
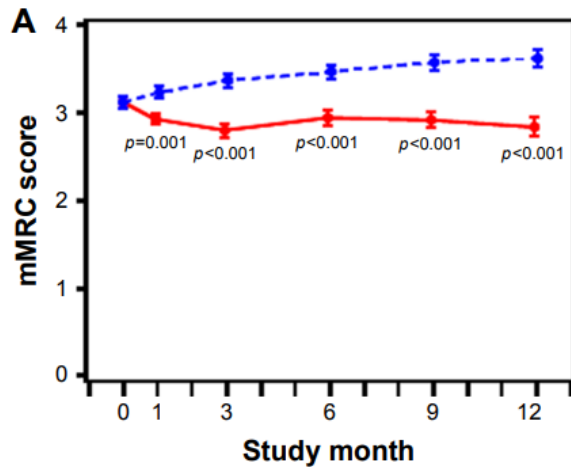
# Long-term effects of oxygen-enriched high-flow nasal cannula treatment in COPD patients with chronic hypoxemic respiratory failure

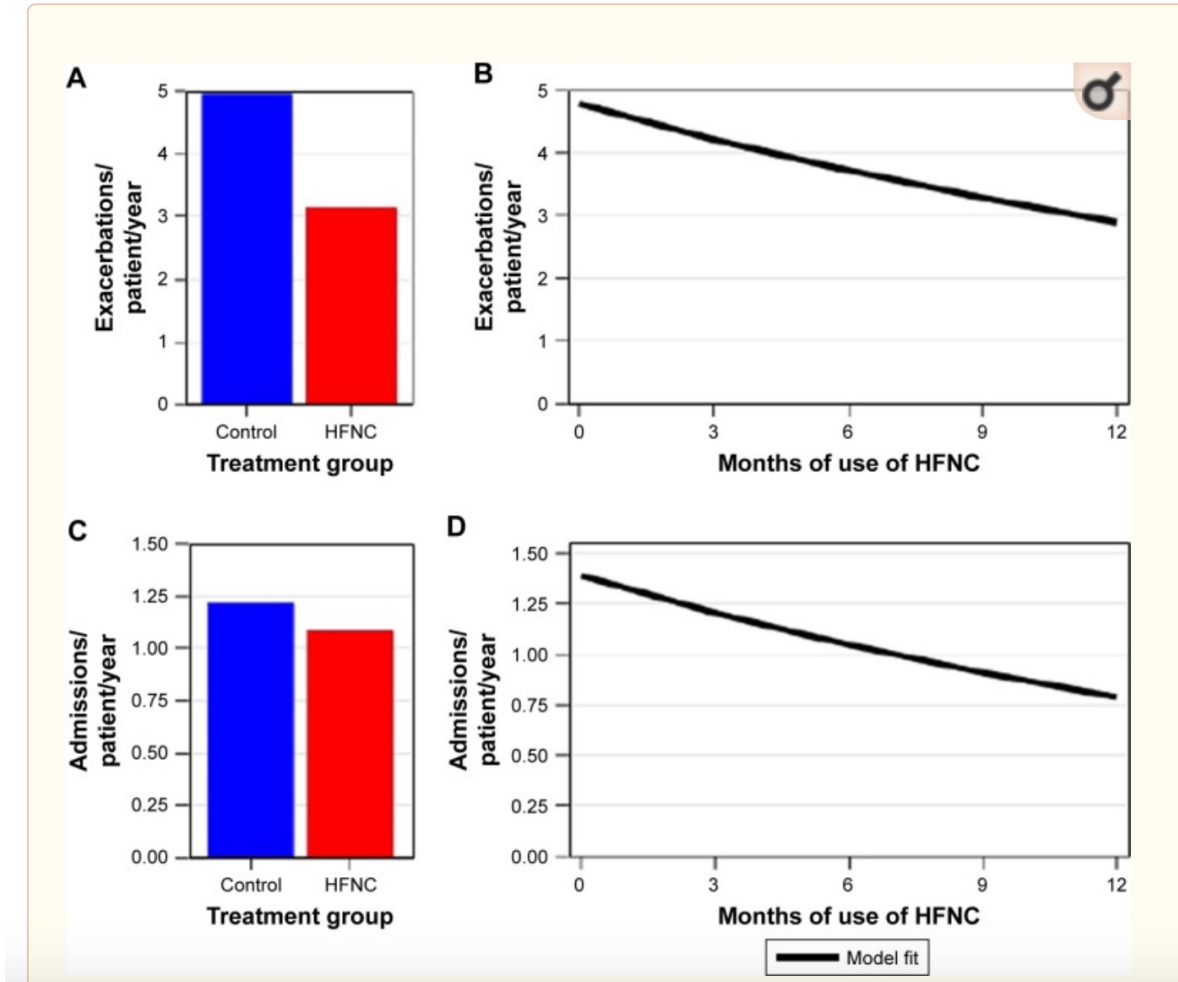
- RCT of 200 pts in Denmark between Dec 2013 & July 2015
- COPD with chronic hypoxemic respiratory failure on LTOT > 3 months prior to RCT inclusion.



average HFNT use of 6–7 hours/day

Primary outcome: rate of AECOPD





average HFNC use  
of 6–7 hours/day

# The Patient Perspective: Meaningful lifestyle Changes

Storgaard LH, et al. COPD 2020 (Qualitative thematic analysis)

**“I don’t have to think the same way about breathing. I’m more relaxed.”**



Reduced  
COPD  
symptoms

Perceived  
lower work of  
breathing

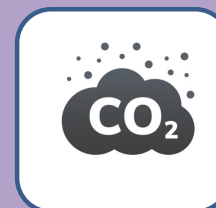
Technology  
use

Feeling safe

Increased  
activity of  
daily living

Improved  
quality of  
sleep

# COPD: choosing the right patient



**Hypercapnic**

# Domiciliary High-Flow Nasal Cannula Oxygen Therapy for Stable Hypercapnic COPD Patients: A Multicenter, Randomized Crossover Trial

HFNC 30-40 l/min  
At least 4h  
6 weeks  
29 pts

Primary Outcome: change in  
QOL as assessed by SGRQ  
and pCO<sub>2</sub>

	Adjusted Treatment Effect (95%CI)	P-values
<b>SGRQ-C</b>		
Total score	-7.8 (-11.9, -3.7) →	<0.01
Symptom score	-10.8 (-15.3, -6.3) →	<0.01
Activity score	-4.7 (-8.7, -0.6)	0.03
Impact score	-8.7 (-15, -2.5)	0.01
EQ-5D-5L score	0.05 (-0.01, 0.11)	0.08
EQ-5D-5L VAS	7.9 (2.9, 12.9)	<0.01
mMRC scale	-0.15 (-0.46, 0.15)	0.32
<b>Arterial blood gas</b>		
pH	0.02 (0.01, 0.02)	0.01
PaCO <sub>2</sub> , mmHg	-4.1 (-6.5, -1.7) →	<0.01
PaO <sub>2</sub> , mmHg	-3.4 (-9.5, 2.7)	0.27
SpO <sub>2</sub> , %	0.3 (-0.4, 1)	0.38
<b>Nocturnal PtcCO<sub>2</sub>, mmHg</b>		
95 <sup>th</sup> percentile	-4.8 (-8.1, -1.5) →	<0.01
Median	-5.1 (-8.4, -1.8) →	<0.01

	LTOT		HFNC/ LTOT	
	No.of events (No. of patient)		No.of events (No. of patient)	
	not related	related	related	not related
Severe	2 (2)	0	2 (2)	
Suicide	1*	0	0	
Ileus	0	0	1*(1)	
Right heart failure	1*	0	0	
Diverticulitis	0	0	1*(1)	
Moderate	3 (3)	0	2 (1)	
Fracture of upper limb	1	0	0	
Pseudogout	0	0	1	
Hypoxemia	0	0	1	
Pneumonia	1	0	0	
Bronchitis	1	0	0	
Mild	1 (1)	6 (4)	0 (0)	
Night sweat	0	4(4)	0	
Nasal discharge	0	1(1)	0	
Insomnia	0	1(1)	0	
Skin reaction				
Skin ulcer	1(1)	0	0	
Skin rash	0	1(1)	0	

Adverse  
Events

LTOT, long-term oxygen therapy; HFNC, high-flow nasal cannula oxygen therapy

\*serious adverse events

Nagata et al

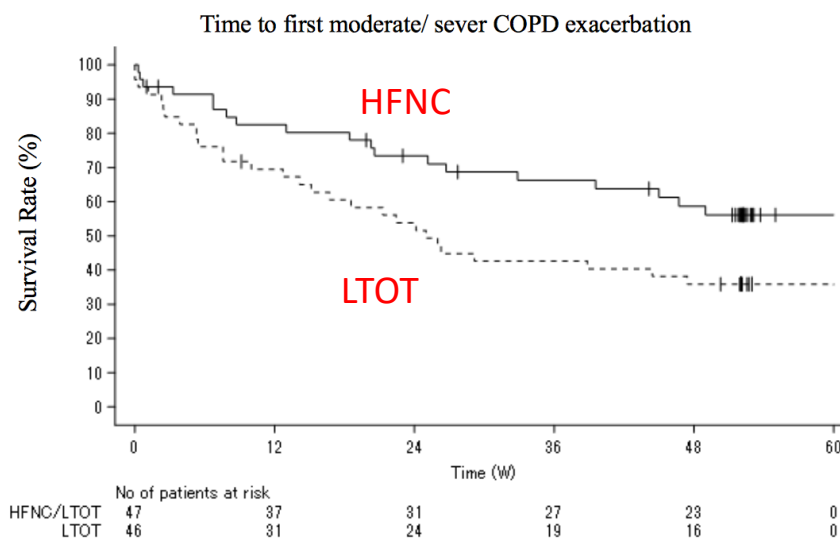
Ann Am Thorac Soc. 2017 Dec 28. doi: 10.1513

# Domiciliary high-flow nasal cannula oxygen therapy for stable hypercapnic COPD patients: a prospective, multicenter, open-label, randomized controlled trial

FLOCOP study

104 stable hypercapnic COPD  
52 weeks  
Aim: frequency of moderate/severe COPD exacerbations

Figure 1. Time to first moderate/severe COPD exacerbation and overall survival (OS).

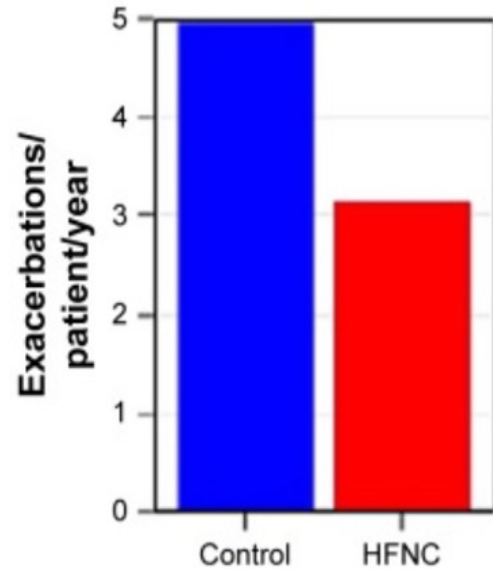


7 h/day

**HFNT prolonged the duration without moderate or severe COPD exacerbations over the 52-week study period**

# The COPD Paradox: *Perceptions vs RCT*

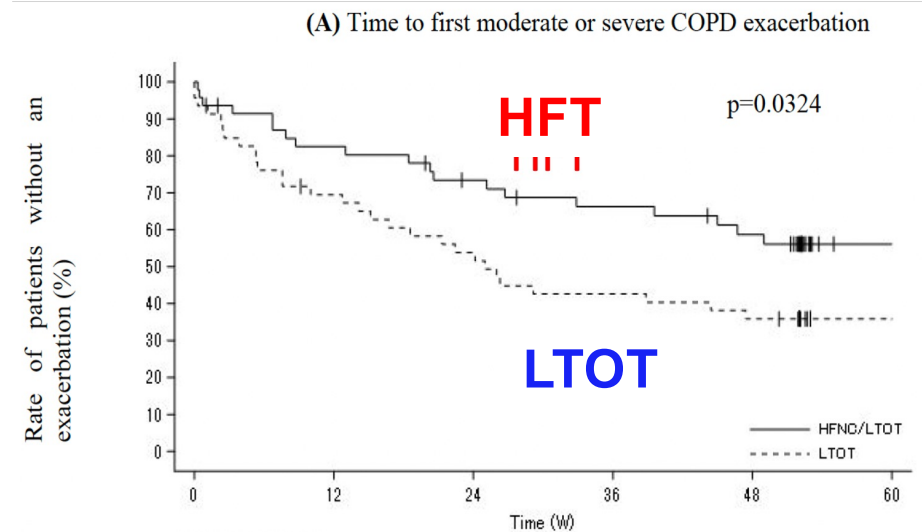
- RCT from Denmark
- n=200 COPD on LTOT > 3m
- Aim: exacerbations



Storgaard et al. International Journal of COPD 2018

**COPD with hypoxemia**

- RCT from Japan
- n=104 stable hypercapnic COPD (mean pCO<sub>2</sub> 52)
- Aim: moderate/severe COPD exacerbations

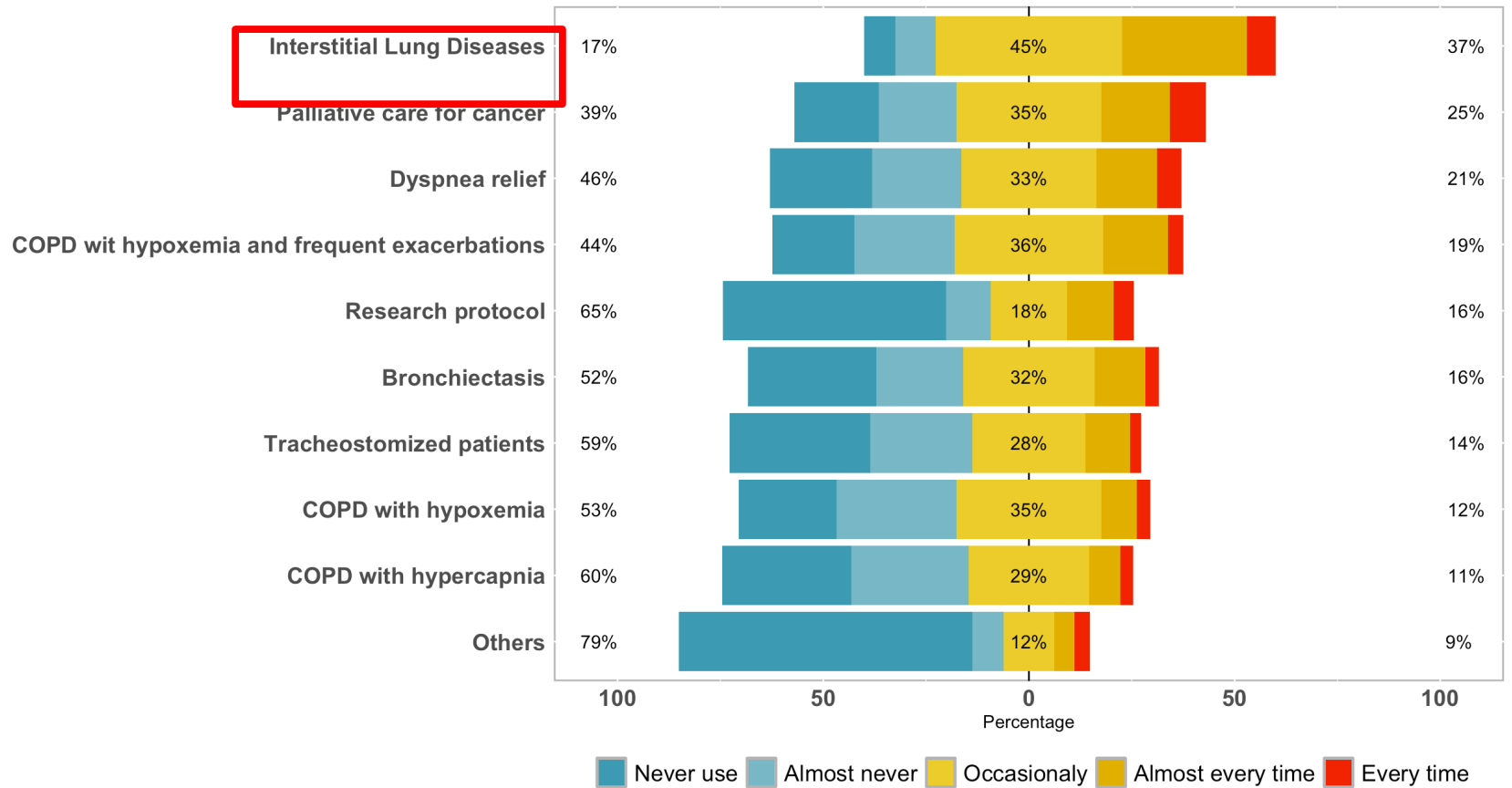


Nagata et al. American Journal Respiratory Critical Care 2022

**COPD with hypercapnia**

# PATIENT PROFILE

## Perceived Long-term use of HFT in Europe



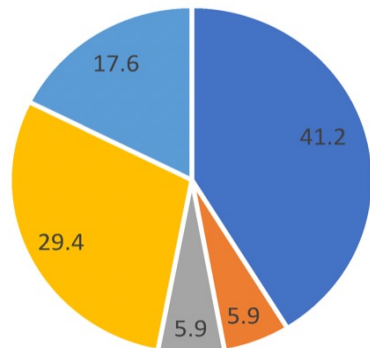
# The Palliative Paradox: *Comfort over RCT*



**Human empathy drives practices ahead of RCTs!**

# NIV intolerant Patients? Palliation?

- Retrospective from Denmark
- n=33 COPD with CRF
- Aim: Impact of LT-HFT & LT-NIV in end-stage COPD

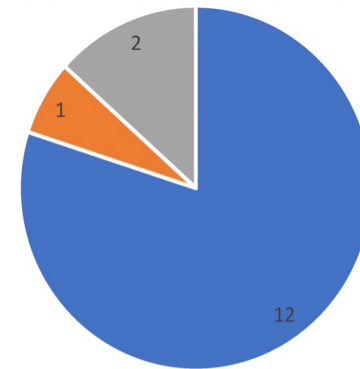


- 25% of LT-NIV switched to HFT due to NIV-intolerance

■ hypoxia ■ dyspnea ■ mucus clearance ■ unable to wean ■ intolerance of NIV  
*Weinreich et al. J. Clin. Med. 2023*

**NIV intolerant patients**

- Retrospective from Denmark
- n=33 COPD with CRF
- Aim: Impact of LT-HFT & LT-NIV in end-stage COPD
- 44% of LT-HFT PTS reinitiated HFT at end-of-life for symptom relief.



■ Difficulties speaking AND eating ■ Dry mouth ■ Cannot cooperate with the device  
*Weinreich et al. J. Clin. Med. 2023*

**Dyspnea palliation  
End-stage COPD**

**Transition Between Devices**

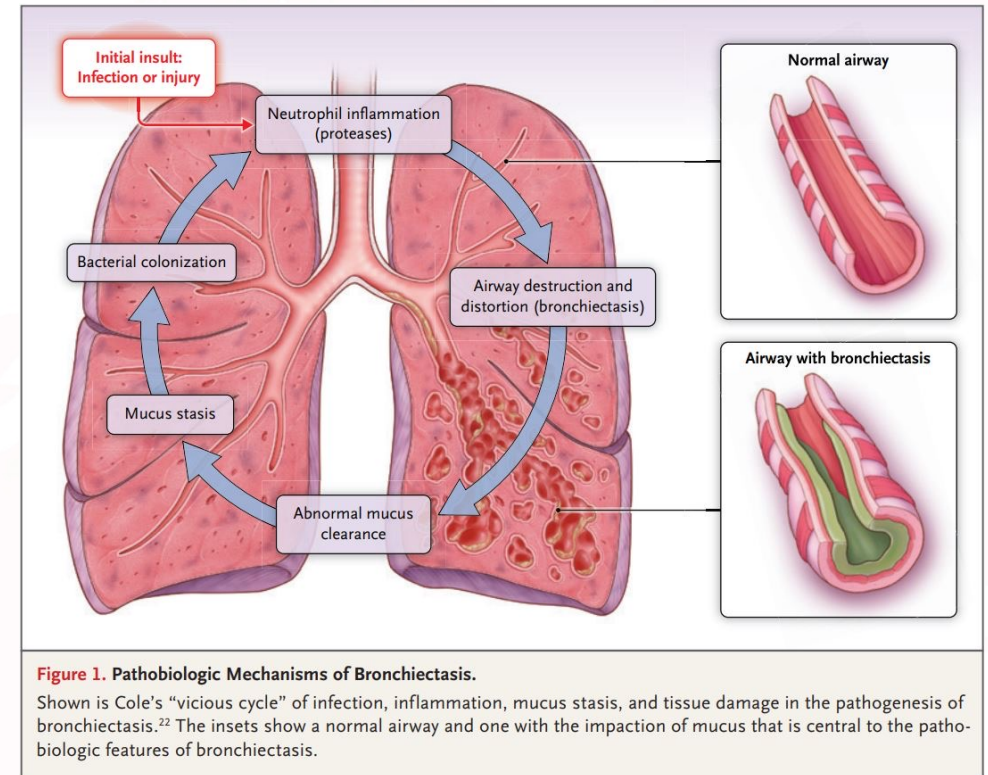
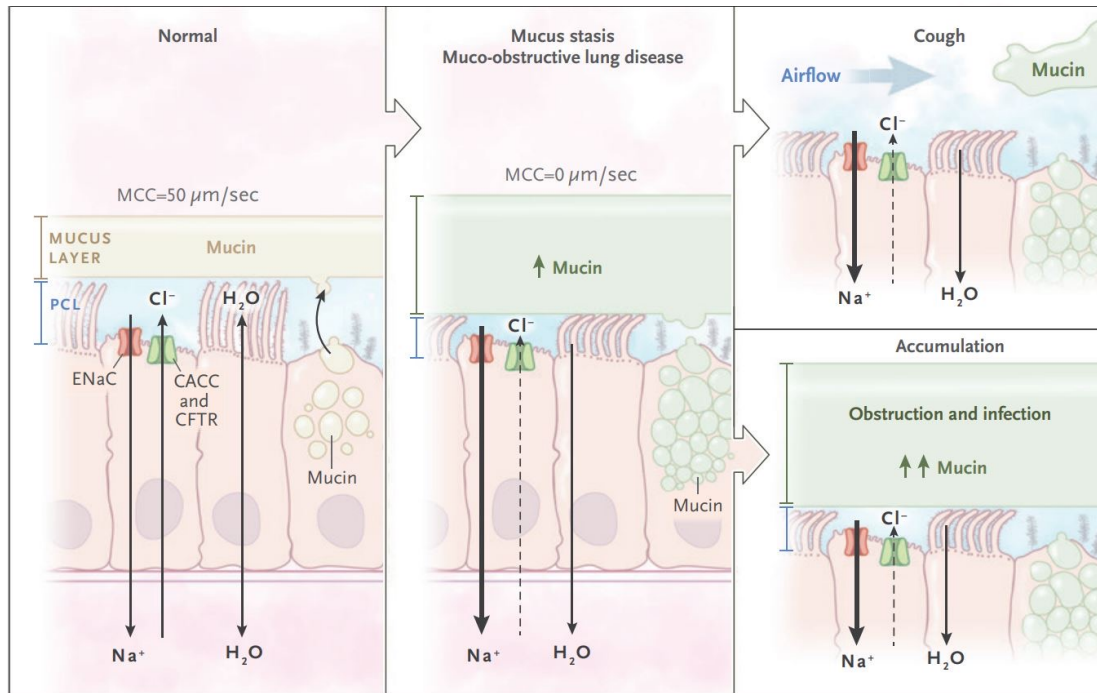
# Bronchiectasis

# Bronchiectasis

- Permanent airway dilation
- Inflamed, dilated, easily collapsible bronchi
- Airflow obstruction
- Impaired clearance of secretions



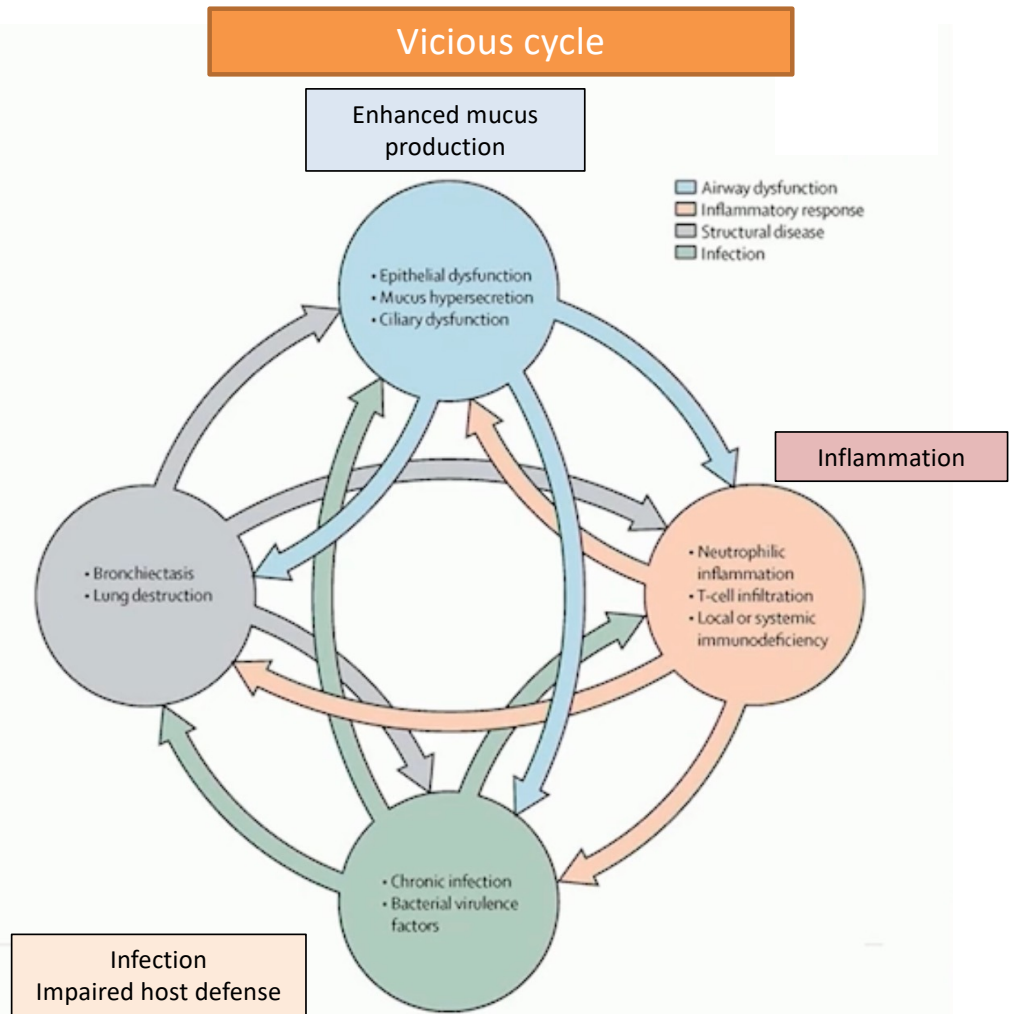
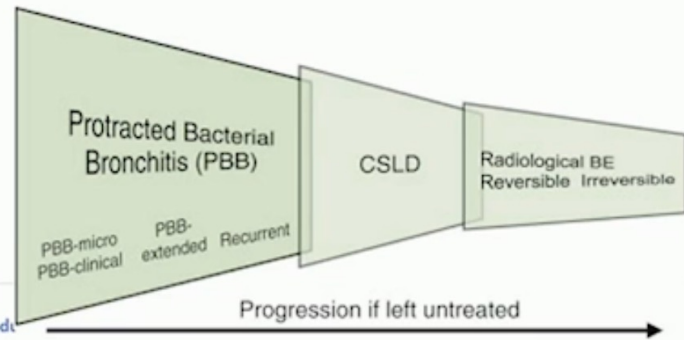
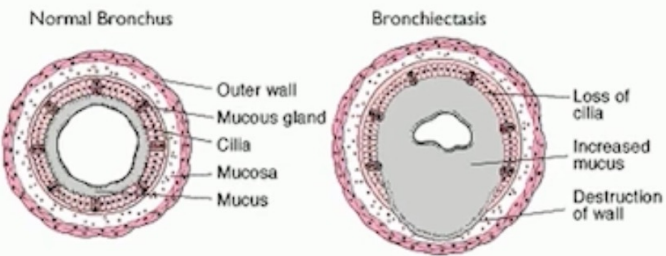
# Bronchiectasis and muco-obstructive lung diseases



Boucher RC. Muco-Obstructive Lung Diseases. N Engl J Med. 2019;380(20):1941-1953.

O'Donnell AE. Bronchiectasis - A Clinical Review. N Engl J Med. 2022;387(6):533-545.

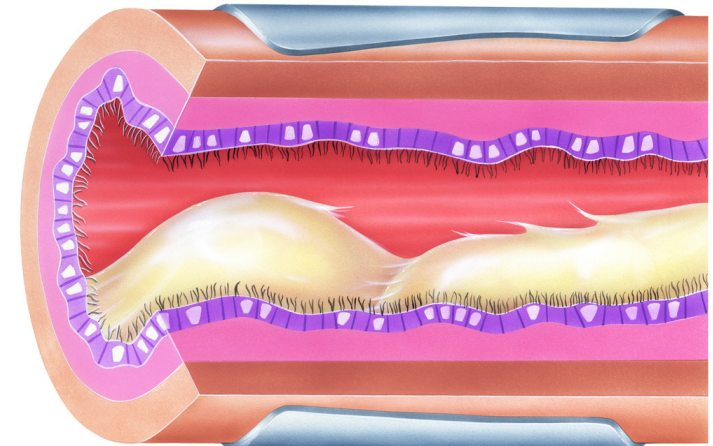
# Pathophysiology



# We have to fight against the monster “mucus”!

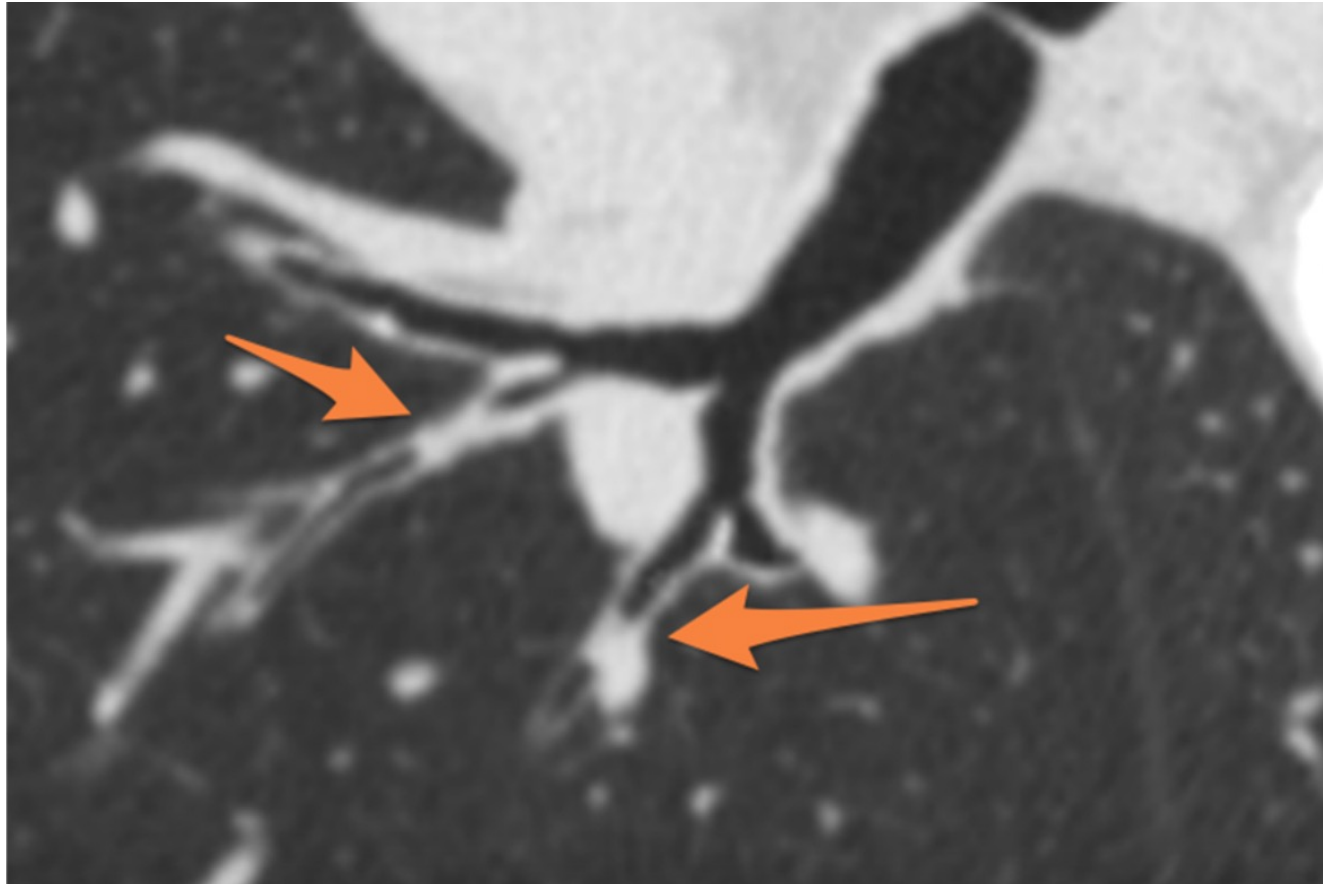
## CHRONIC HYPERSECRETION is associated with:

- More and faster lung function decline
- Worse QoL for patients
- Increased risk of exacerbation/hospitalization
- Increased risk of mortality



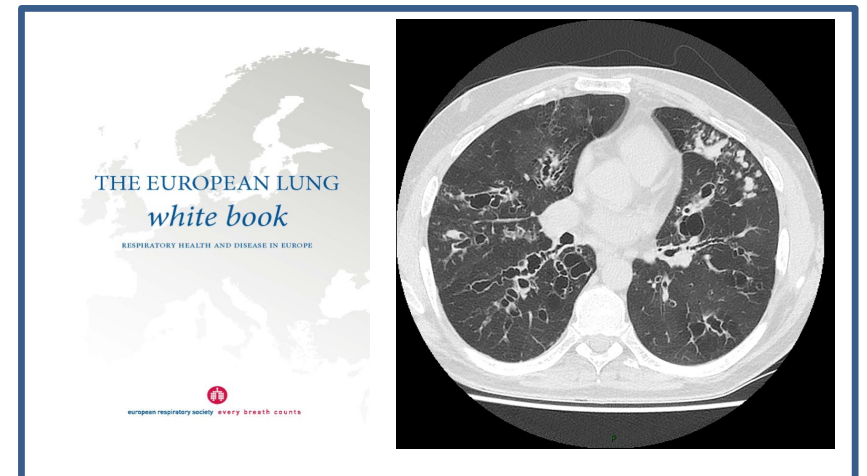
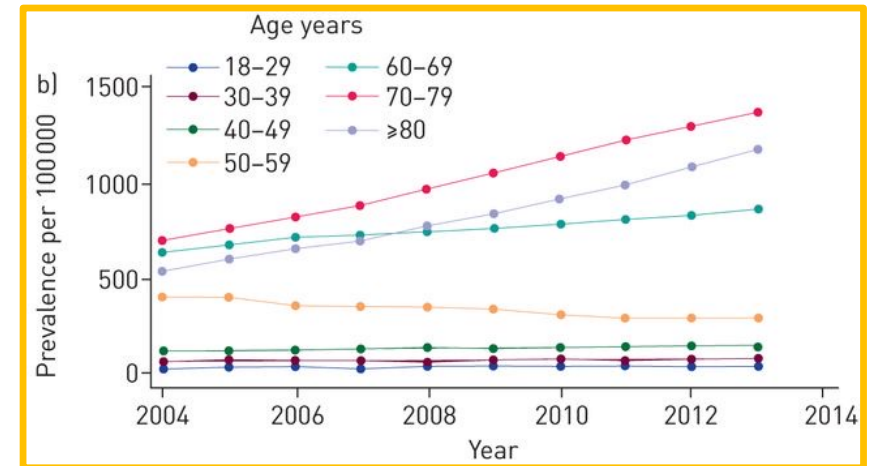
Ramos FL. et al. Int J Chron Obstruct Pulmon Dis 2014 ; 24;9:139-50  
Kim V. et al. Am J Respir Crit Care Med. 2013;187(3):228–237  
Finklea JD, et al. Respir Med. 2010  
Chalmers et al BSI index. AJRCCM 2014 Mar 1;189(5):576-85

# Mucus Plug



# Bronchiectasis - an orphan disease

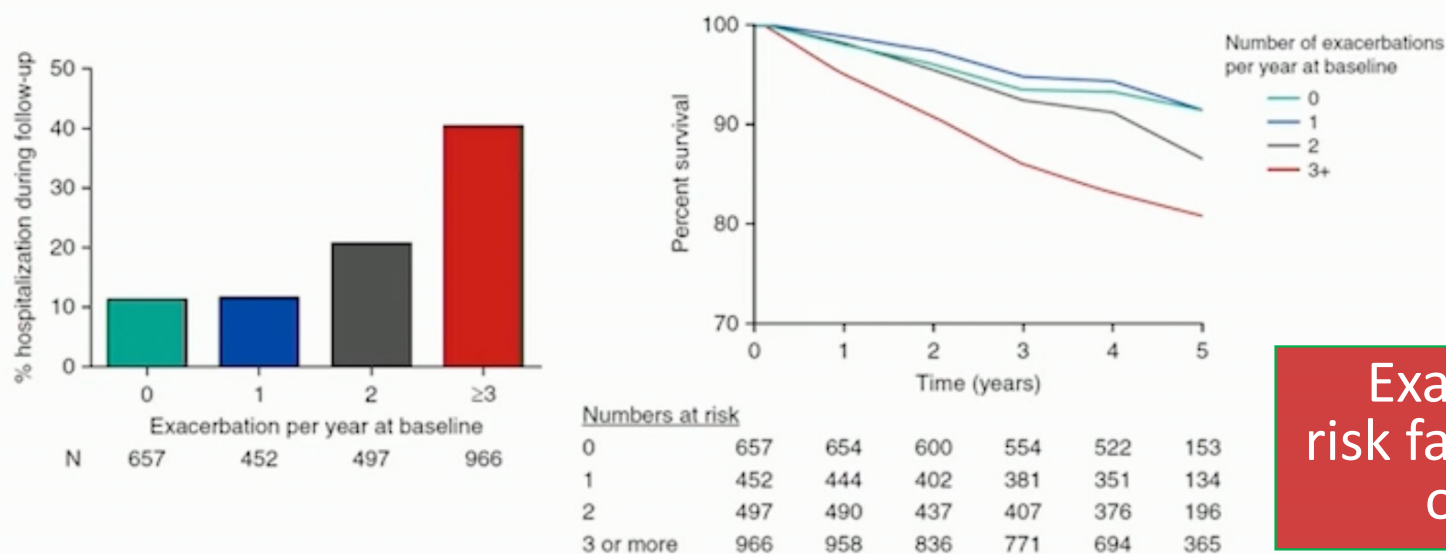
- A growing clinical problem
- 40% increase in prevalence over 10 years
- “The most neglected disease in respiratory medicine”
  - “Too complex disease”
  - “Too heterogeneous”
  - “Not a real disease”



# Surrogate markers of disease activity: exacerbations

## Characterization of the “Frequent Exacerbator Phenotype” in Bronchiectasis

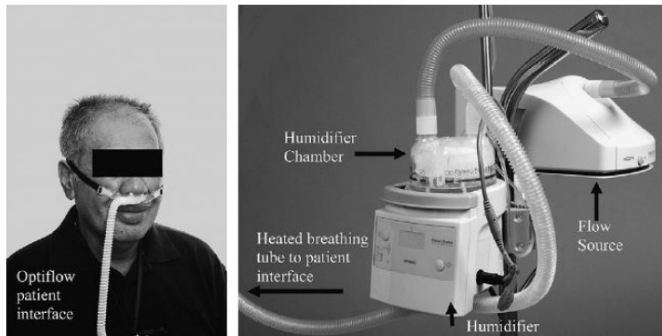
James D. Chalmers<sup>1</sup>, Stefano Aliberti<sup>2,3</sup>, Anna Filonenko<sup>4</sup>, Michal Shteinberg<sup>5</sup>, Pieter C. Goeminne<sup>6,7</sup>, Adam T. Hill<sup>8,9</sup>, Thomas C. Fardon<sup>1</sup>, Dusanka Obradovic<sup>10</sup>, Christoph Gerlinger<sup>4,11</sup>, Giovanni Sotgiu<sup>12</sup>, Elisabeth Operschall<sup>4</sup>, Robert M. Rutherford<sup>13</sup>, Katerina Dimakou<sup>14</sup>, Eva Polverino<sup>15</sup>, Anthony De Soyza<sup>16,17</sup>, and Melissa J. McDonnell<sup>13,17</sup>



**Exacerbations: risk factors for poor outcomes**

# The clinical utility of long-term humidification therapy in chronic airway disease

Harold Rea <sup>a</sup>, Sue McAuley <sup>b</sup>, Lata Jayaram <sup>c,\*</sup>, Jeffrey Garrett <sup>c</sup>, Hans Hockey <sup>d</sup>, Louanne Storey <sup>c</sup>, Glenis O'Donnell <sup>b</sup>, Lynne Haru <sup>b</sup>, Matthew Payton <sup>e</sup>, Kevin O'Donnell <sup>e</sup>

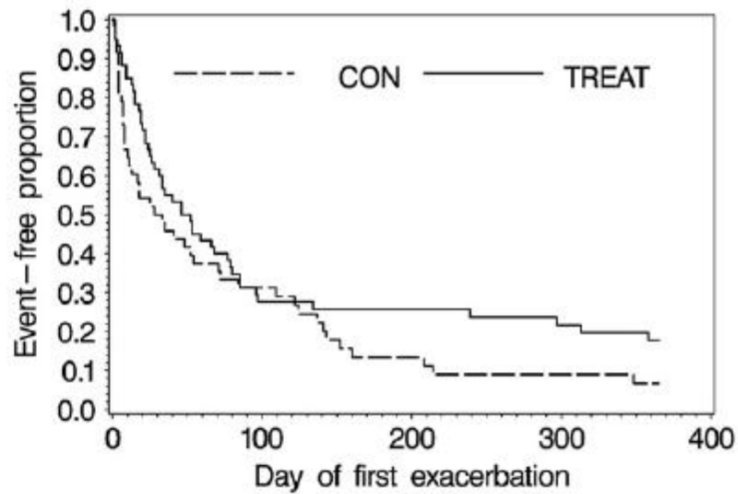


Study Design : 12-month prospective, single centre, open labelled, RCT, two parallel group, placebo-controlled trial

108 COPD or bronchiectasis (only enrollment criteria)

Humidified air, fully saturated at 37 ° C at a flow rate of 20-25 L/min was delivered via Optiflow nasal cannulae connected to a MR880 humidifier and HC210 flow source system (Fisher and Paykel Healthcare, New Zealand)

1° end points: frequency of exacerbations  
2° end points :QOL, lung function, exercise capacity



average HFNC use  
of 1–2 hours/day

Rea et al. Respiratory Medicine 2010

Figure 3 Kaplan–Meier plot for time to first exacerbation.

- Patients on HFNC had significantly fewer exacerbation days (18.2 vs 33.5 days;),
- Increased time to first exacerbation (median 52 vs 27 days;)
- Reduced exacerbation frequency (2.97/patient/year vs 3.63/ patient/year compared with usual care)

## HFT significantly reduced exacerbation rates and improved QoL compared with usual care in pts with bronchiectasis

45 pts with BE

TABLE 1 Bronchiectasis group trial end-points







Exacerbation end-points	HFNT	Control	Rate ratio (95% CI)	p-value
	Change from baseline			
	HFNT	Control		
→ Rate, number per patient per year	2.39	3.48	0.69 (0.49, 0.97)	0.034
Annual exacerbation days (geometric mean)	10.3	29.9	0.32 (0.14, 1.02)	0.056
Days to first exacerbation (predicted median)	84	54	0.70 <sup>#</sup> (0.35, 1.40)	0.316
Secondary end-points	Change from baseline		Difference (95% CI)	p-value
	HFNT	Control		
FEV <sub>1</sub> L	0.145	0.035	0.11 (-0.037, 0.257)	0.139
FVC L	0.115	-0.104	0.22 (-0.031, 0.468)	0.084
→ St George's respiratory questionnaire score <sup>††</sup>				
Total	-12.3	-1.2	-11.0 (-20.7, -1.3)	0.028
Symptoms	-16.9	-9.8	-7.1 (-21.0, 6.8)	0.308
Activity	-6.3	3.3	-9.6 (-20.7, 1.5)	0.087
Impacts	-14.7	-1.6	-13.1 (-23.7, -2.4)	0.018

31.3%



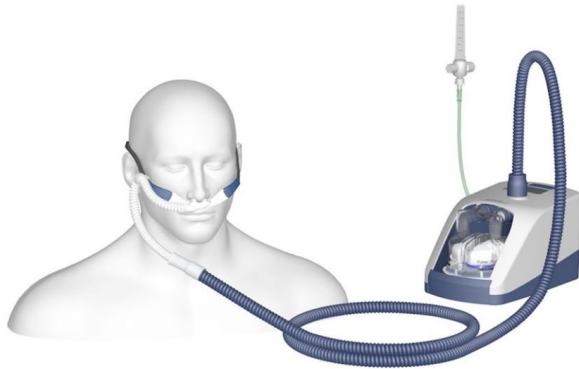
Article

# Long-Term Domiciliary High-Flow Nasal Therapy in Patients with Bronchiectasis: A Preliminary Retrospective Observational Case-Control Study

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Andrea Cortegiani <sup>5,6</sup> , Alberto Noto <sup>7</sup>, Andrea Gramegna <sup>8,9</sup>, Carlo Vancheri <sup>1,2</sup>, Francesco Blasi <sup>8,9</sup> ,  
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# High-flow nasal therapy settings and study outcomes

## F&P myAIRVO™ 2 settings



- Flow: 25 - 40 L/min
- Temperature: 34°C - 37°C
- Minimum of 6 h a day, preferably at night
- If necessary, FiO<sub>2</sub> was adjusted to maintain SpO<sub>2</sub> ≥ 92%

## Primary outcome

1. Annual exacerbation rate

## Secondary outcomes

2. Annual hospitalization rate
3. mMRC dyspnea scale
4. Difficulty of mucus expectoration (VAS)
5. Quality of life (SGRQ)
6. Pulmonary function (FEV<sub>1</sub>, FVC, FEF<sub>25-75</sub>)

## Baseline patients characteristics

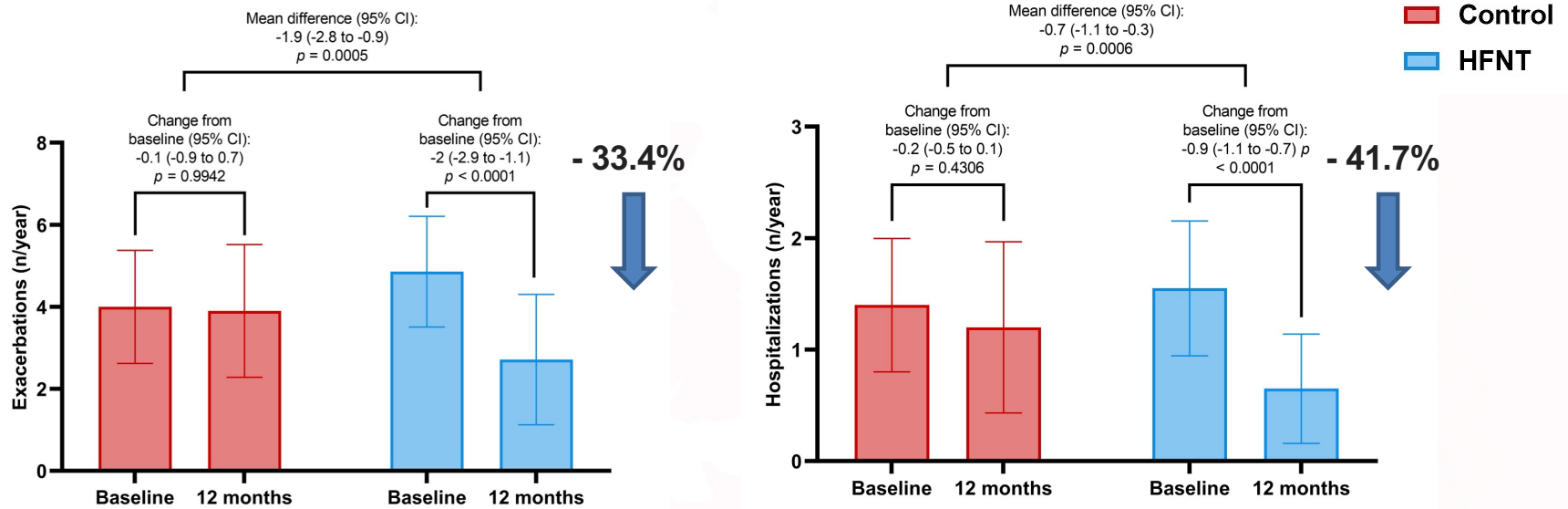
Table 1. Baseline patients' characteristics.

	HFNT (n = 20)	Control (n = 20)	p-Value
Age, years, mean (SD)	70.7 (9.4)	68.6 (8.9)	0.4835
Female, n (%)	14 (70)	14 (70)	0.9999
BMI, Kg/m <sup>2</sup> , mean (SD)	24.8 (7.6)	25.6 (7.9)	0.7542
Smoking history, n (%)			
Current	1 (5)	1 (5)	0.9999
Ex-smoker	4 (20)	6 (30)	0.7164
Cardiovascular disease, n (%)	12 (60)	11 (55)	0.9999
GERD, n (%)	13 (65)	11 (55)	0.7475
Depression and/or anxiety, n (%)	7 (35)	5 (25)	0.7311
<b>Bronchiectasis aetiology, n (%)</b>			
Idiopathic	4 (20)	6 (30)	0.7164
Post-infective	7 (35)	4 (20)	0.4801
Chronic obstructive pulmonary disease	5 (25)	5 (25)	0.9999
Immunodeficiency	1 (5)	4 (20)	0.3416
Primary ciliary dyskinesia	1 (5)	1 (5)	0.9999
Inflammatory bowel disease	1 (5)	n/a	n/a
Severe asthma	2 (10)	2 (10)	0.9999
ICS-LABA, n (%)	5 (25)	5 (25)	0.9999
ICS-LABA and/or LAMA, n (%)	10 (50)	10 (50)	0.9999
LAMA + LABA, n (%)	5 (25)	5 (25)	0.9999
Long-term macrolide therapy, n (%)	10 (50)	7 (32.5)	0.5231
Airway clearance and/or pulmonary rehabilitation, n (%)	20 (100)	20 (100)	0.9999

Table 2. Bronchiectasis severity assessment and microbial sputum cultures.

	HFNT (n = 20)	Control (n = 20)	p-Value
Bhalla score, mean (SD)	10.1 (3.5)	13.3 (3.7)	0.0344
Bhalla, n (%)			
Mild (16–25)	1 (5)	3 (27.3)	0.1154
Moderate (9–15)	13 (65)	7 (63.6)	0.9999
Severe (0–8)	6 (30)	1 (9.1)	0.3717
BSI, mean (SD)	12.4 (3.6)	12.3 (3.5)	0.8950
BSI, n (%)			
Mild (0–4)	0 (0)	0 (0)	0.9999
Moderate (5–8)	2 (10)	2 (10)	0.9999
Severe (≥9)	18 (90)	18 (90)	0.9999
Sputum cultures, n (%)			
Negative	6 (30)	5 (25)	0.9999
<i>Pseudomonas aeruginosa</i>	8 (40)	9 (45)	0.9999
Other bacteria	3 (7.5)	3 (7.5)	0.9999
<i>Aspergillus fumigatus</i>	1 (5)	1 (5)	0.9999

# Exacerbation and hospitalization rate

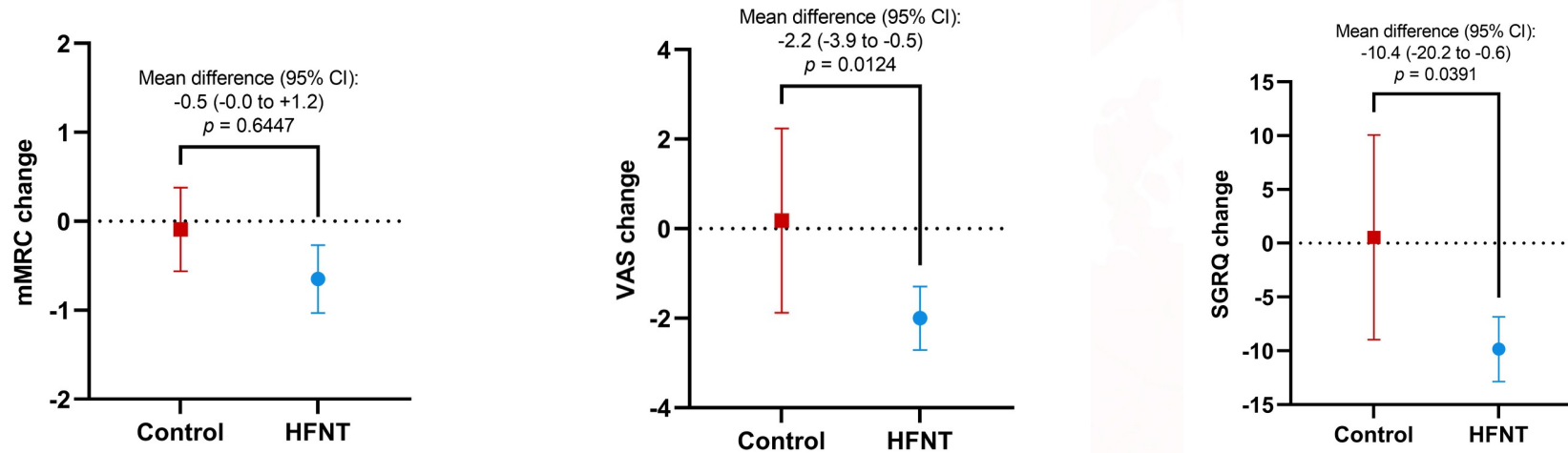


	HFNT		Control		Difference * and Relative Risk	p-Value
	12 Months	Change from Baseline *	12 Months	Change from Baseline *		
Annual exacerbations, mean (SD)	2.6 (1.4)	-2 (-2.9 to -1.1)	3.9 (1.6)	-0.1 (-0.9 to 0.7)	-1.9 (-2.8 to -0.9)	0.0005
Patients with ≥ 3 annual exacerbations, n (%)	12 (60)	-7 (-35)	17 (85)	-0 (-0)	0.6 (0.4 to 0.0)	0.0084
Annual severe exacerbations requiring hospitalizations, mean (SD)	0.7 (0.5)	-0.9 (-1.1 to -0.7)	1.2 (0.8)	-0.2 (-0.5 to 0.1)	-0.7 (-1.1 to -0.3)	0.0006
Patients with ≥ 1 annual hospitalization, n (%)	13 (65)	-7 (-35)	16 (80)	-4 (-20)	0.8 (0.5 to 1.2)	0.4801

Crimi C. et al. Long-Term Domiciliary High-Flow Nasal Therapy in Patients with Bronchiectasis: A Preliminary Retrospective Observational Case-Control Study. *J Clin Med.* 2022;11(24):7323

# Dyspnea, mucus expectoration and quality of life

■ Control  
● HFNT

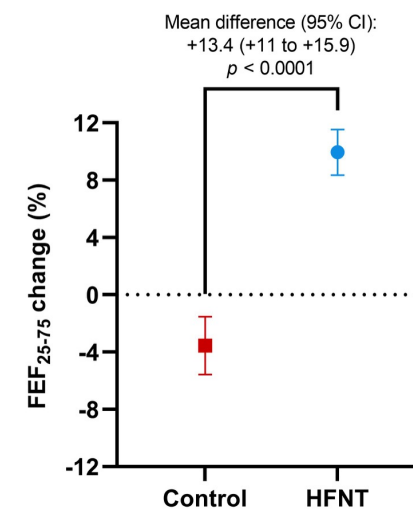
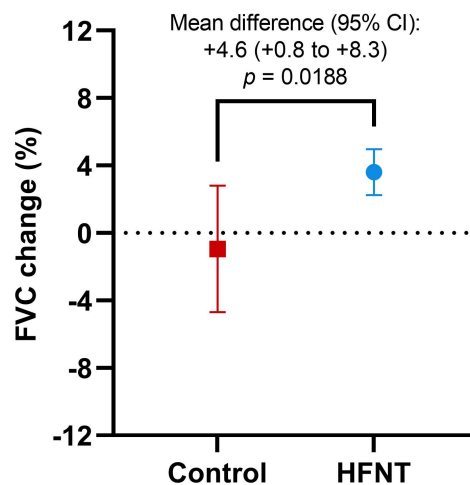
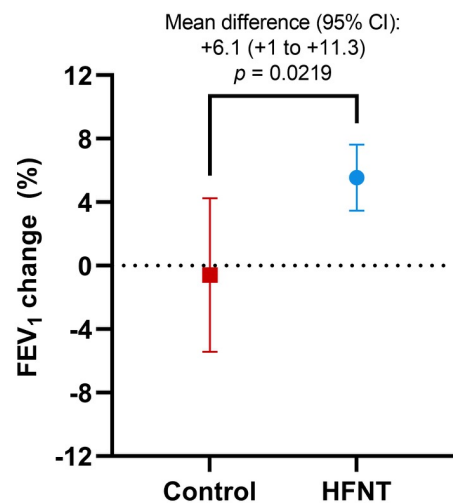


	HFNT		Control		Difference * and Relative Risk	p-Value
	12 Months	Change from Baseline *	12 Months	Change from Baseline *		
mMRC dyspnea scale, mean (SD)	2 (0.7)	-0.6 (-1.0 to -0.3)	2.3 (0.5)	-0.1 (-0.6 to +0.4) †	-0.5 (-0.0 to +1.2)	0.6447
Difficulty of mucus expectoration VAS, mean (SD)	4.9 (2.2)	-2 (-2.7 to -1.3)	7.3 (2.1)	+0.2 (-1.9 to +2.2) †	-2.2 (-3.9 to -0.5)	<b>0.0124</b>
SGRQ, mean (SD)	55.2 (11.3)	-9.9 (-12.9 to -6.8)	70 (10.5)	+0.5 (-9.0 to +10.6) †	-10.4 (-20.2 to -0.6)	<b>0.0391</b>

Crimi C, Nolasco S, Campisi R, et al. Long-Term Domiciliary High-Flow Nasal Therapy in Patients with Bronchiectasis: A Preliminary Retrospective Observational Case-Control Study. *J Clin Med.* 2022;11(24):7323

# Pulmonary function

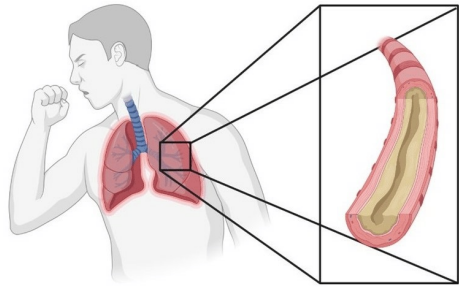
■ Control  
● HFNT



	HFNT		Control		Difference * and Relative Risk	p-Value
	12 Months	Change from Baseline *	12 Months	Change from Baseline *		
FEV <sub>1</sub> , % predicted, mean (SD)	64.3 (18.7)	+5.6 (+3.5 to +7.6)	62.7 (17.8)	-0.6 (-5.4 to +4.2) †	+6.1 (+1 to +11.3)	<b>0.0219</b>
FVC, % predicted, mean (SD)	72.8 (11.6)	+3.6 (+2.3 to +5.0)	75.8 (18.9)	-1 (-4.7 to +2.8) †	+4.6 (+0.8 to +8.3)	<b>0.0188</b>
FEF <sub>25-75</sub> , % predicted, mean (SD)	55.1 (12.2)	+9.9 (+8.3 to +11.5)	42.9 (11.5)	-3.5 (-5.6 to -1.5) †	+13.4 (+11 to +15.9)	<b>&lt;0.0001</b>

Crimi C, et al. Long-Term Domiciliary High-Flow Nasal Therapy in Patients with Bronchiectasis: A Preliminary Retrospective Observational Case-Control Study. *J Clin Med.* 2022;11(24):7323

## Patients



Patients with non-cystic fibrosis bronchiectasis and  $\geq 1$  severe exacerbation in the previous year ( $n = 86$ )

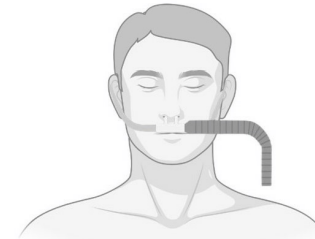


Bronchiectasis Severity Index (BSI)  $\geq 9$   
(Severe  $n = 50$ )



Bronchiectasis Severity Index (BSI)  $< 9$   
(Mild-moderate  $n = 36$ )

## Treatment



Baseline  $\xrightarrow{\text{High-Flow Nasal Therapy} + \text{Standard of Care}}$  12 months

## Results

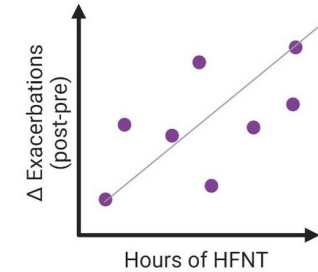
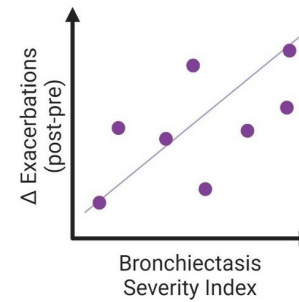


• Exacerbations

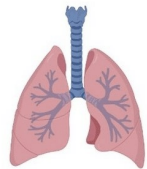
BSI  $\geq 9$   
(Severe  $n = 50$ )



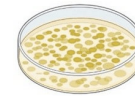
BSI  $< 9$   
(Mild-moderate  $n = 36$ )



• Symptoms



• Lung function



Baseline

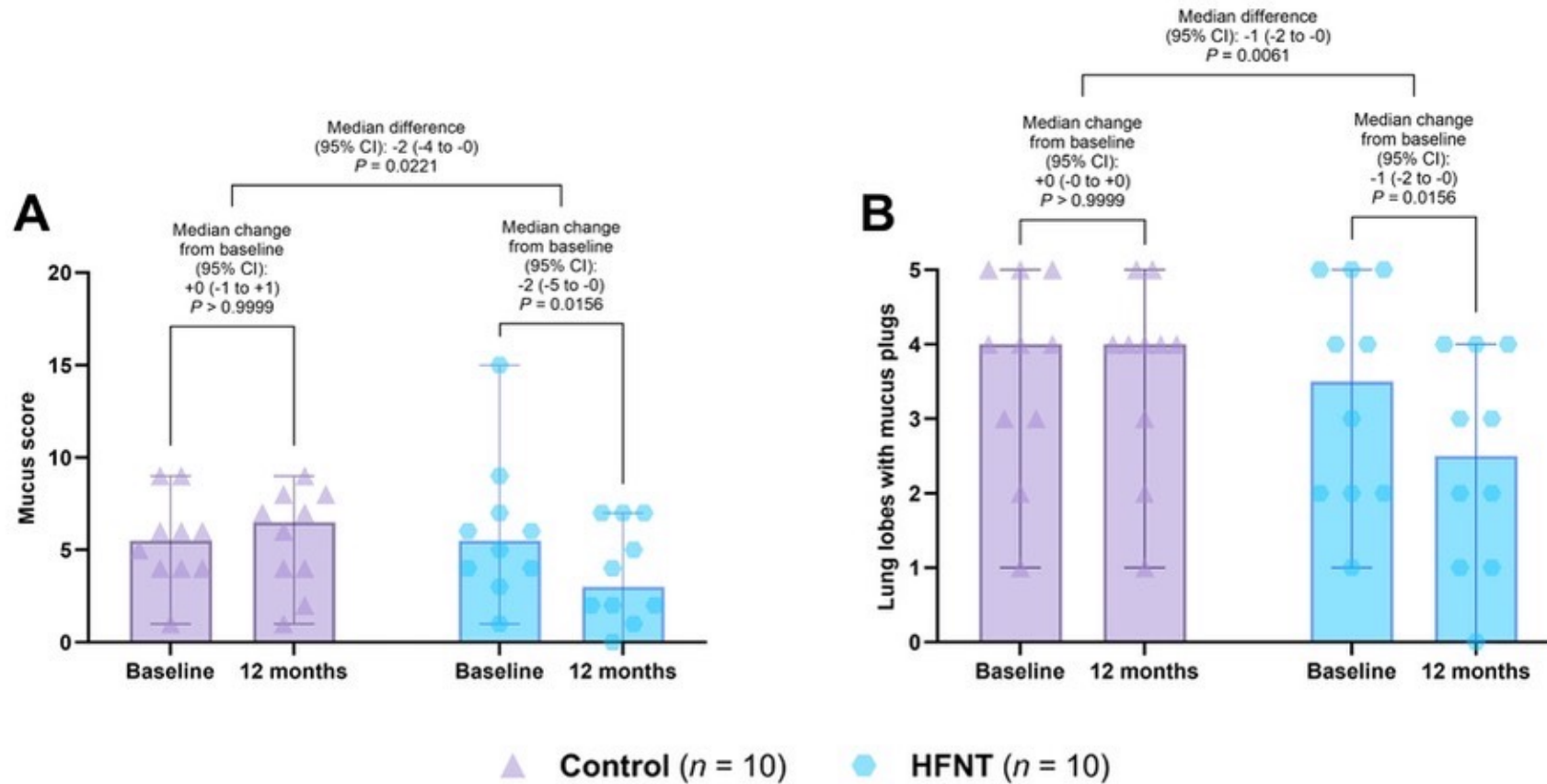
Positive sputum cultures  $\downarrow$



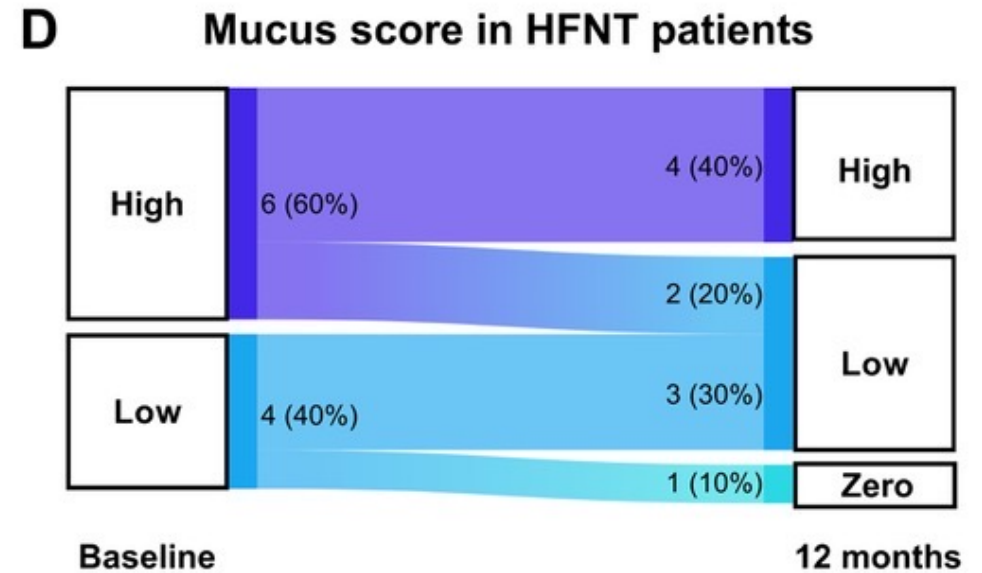
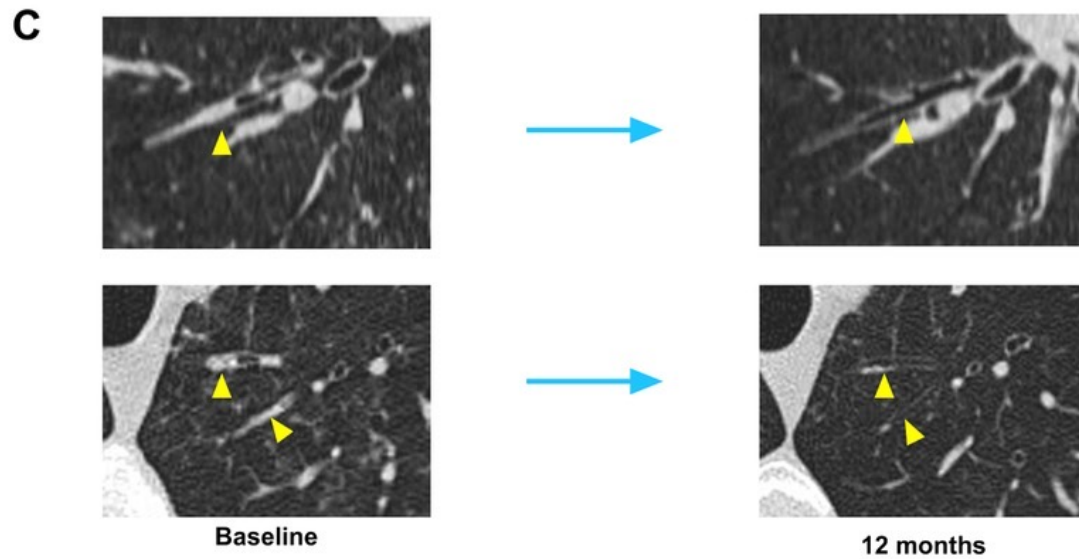
12 months

Calabrese, Crimi et al JCM 2024

# HFT & MUCUS PLUGS



# HFT & MUCUS PLUGS



**Increased  
mucus production**

Inflammatory infiltrates  
Oxidative stress  
Viral infections  
Bacterial infections

**Decreased  
mucus clearance**

Poor ciliary clearance  
Airway occlusion  
Reduced peak expiratory flow  
Respiratory muscle weakness

**Excessive  
airway mucus**

**Occluding mucus plugs in  
patients with obstructive  
lung diseases:  
a new treatable trait?**

# Mucus Plugs & Mortality

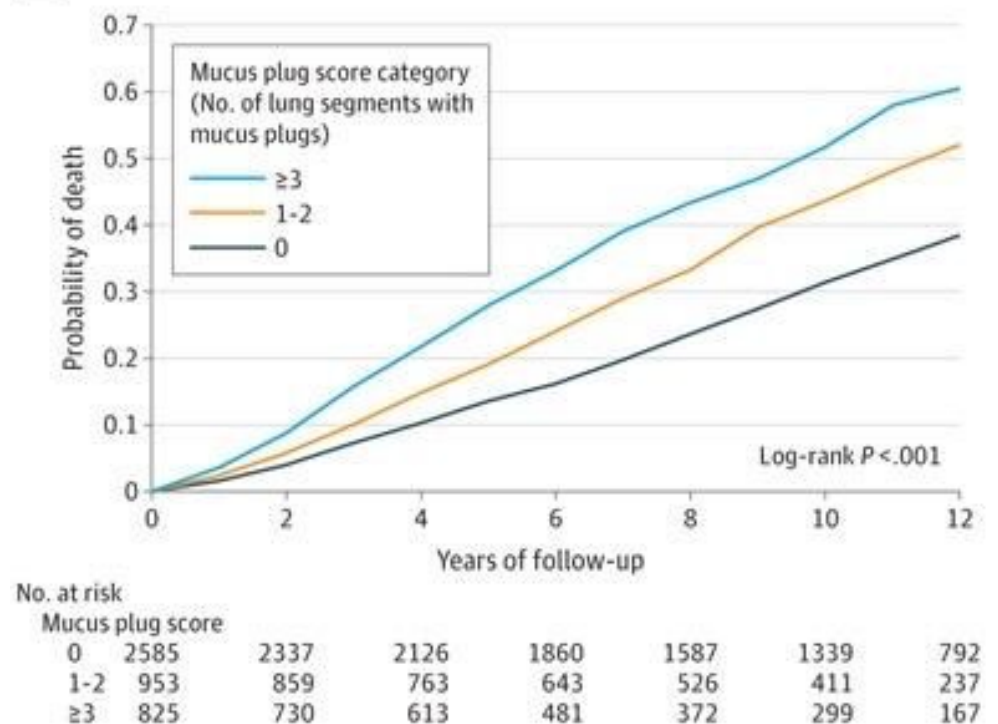
**4363 active smoker COPD pts**  
**Median FU 9.5 yrs**

*Diaz A. et al JAMA 2023*

Table 1. Characteristics of Participants With COPD by Mucus Plug Score Category

Characteristic	Mucus plug score category (No. of lung segments with mucus plugs), No. (%)		
	0 (n = 2585)	1-2 (n = 953)	≥3 (n = 825)
Age, median (IQR), y	62.4 (55.9-68.7)	63.9 (57.6-70.6)	65.3 (57.9-71.1)
Sex			
Female	1072 (41.5)	448 (47.0)	400 (48.5)
Male	1513 (58.5)	505 (53.0)	425 (51.5)
Race and ethnicity <sup>a</sup>			
Non-Hispanic Black	636 (24.6)	199 (20.9)	142 (17.2)
Non-Hispanic White	1949 (75.4)	754 (79.1)	683 (82.8)
BMI, median (IQR)	27.6 (24.2-31.9)	26.8 (23.4-31.0)	25.5 (22.1-30.1)
Current smoker, No. (%) [No.]	1155 (44.7) [2584]	383 (40.2)	347 (42.1) [824]
Pack-years of smoking, median (IQR)	44.3 (33.2-64)	46.1 (35.0-65.7)	47.6 (35.0-67.6)
Medical history			
Chronic bronchitis	584 (22.6)	248 (26.0)	293 (35.5)
Coronary artery disease	417 (16.1)	154 (16.2)	113 (13.7)
Asthma <sup>b</sup>	406 (15.7)	168 (17.6)	187 (22.7)
COPD GOLD stage of severity <sup>c</sup>			
1 (Mild)	597 (23.1)	116 (12.2)	53 (6.4)
2 (Moderate)	1250 (48.4)	389 (40.8)	248 (30.1)
3 (Severe)	523 (20.2)	297 (31.2)	307 (37.2)
4 (Very severe)	215 (8.3)	151 (15.8)	217 (26.3)
BODE index, median (IQR) [No.] <sup>d</sup>	2 (0-4) [2525]	3 (1-5) [924]	4 (2-6) [803]
FEV <sub>1</sub> , L	1.8 (1.3-2.4)	1.4 (0.9-1.9)	1.1 (0.8-1.6)
FEV <sub>1</sub> , % predicted	65.0 (47.1-78.4)	51.9 (36.4-69.7)	42.1 (29.1-59.4)
Emphysema on CT, median (IQR) [No.], % <sup>e</sup>	5.6 (1.8-14.9) [2466]	9.2 (2.8-22.1) [916]	12.4 (3.4-24.2) [787]
Airway wall thickness, median (IQR) [No.], mm <sup>f</sup>	2.5 (2.1-2.9) [2466]	2.7 (2.3-3.1) [916]	2.9 (2.5-3.3) [787]

A Unadjusted probability of death by mucus plug score



# HOME HFT USE: RATIONALE

# Rationale for Home HFNT use

## Target Population

- COPD
- Bronchiectasis
- Palliative care

## Overall Advantages



Reduced  
exacerbations



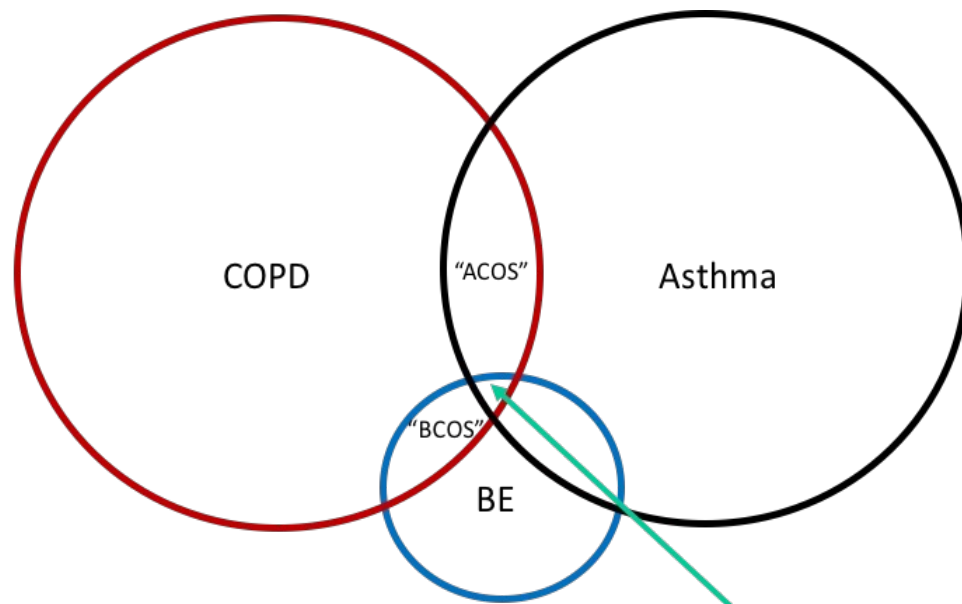
Improved QoL



Decreased  
healthcare  
utilization

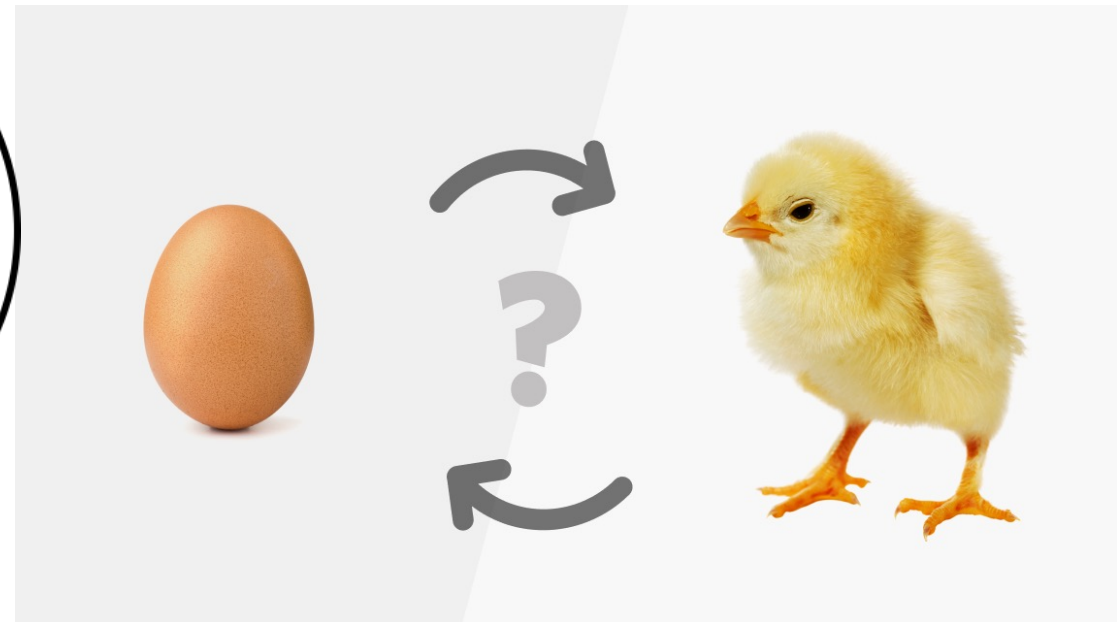
# Do we really need this?! Is Respiratory failure Phenotype enough?

Treat patients independent of diagnostic labels!



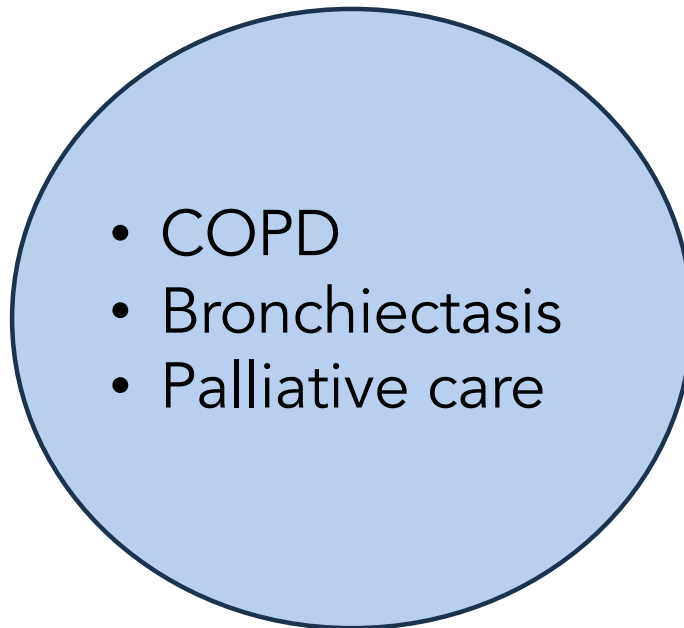
ACOS= Asthma COPD overlap syndrome  
BCOS= Bronchiectasis COPD overlap syndrome

ABCos?



# Rationale for Home HFNT use

## Target Population



**HYPOXIC?**

## Overall Advantages



Reduced exacerbations



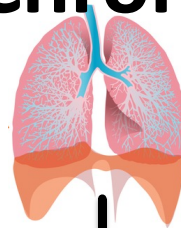
Improved QoL



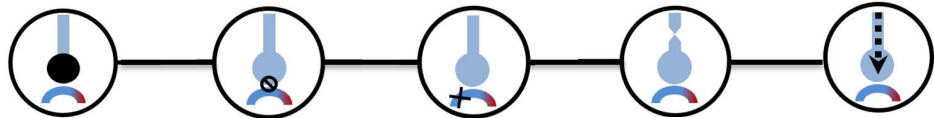
Decreased healthcare utilization

**HYPERCAPNIC?**

# Pathophysiology of Chronic Respiratory Failure



## LUNG FAILURE



Focal Alveolar    Impaired Diffusion    Dead Space    Airway Disease    Hypoventilation

Pneumonia  
Mucus plugging  
Atelectasis

Emphysema  
CPFE  
ILD

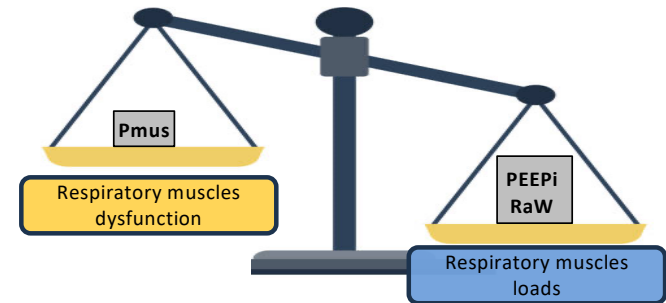
Emphysema

COPD  
Bronchiectasis

OHS

Chronic Respiratory Failure with Hypoxemia

## PUMP FAILURE



Chronic Respiratory Failure with Hypercapnia

# COPD is an heterogeneous disease

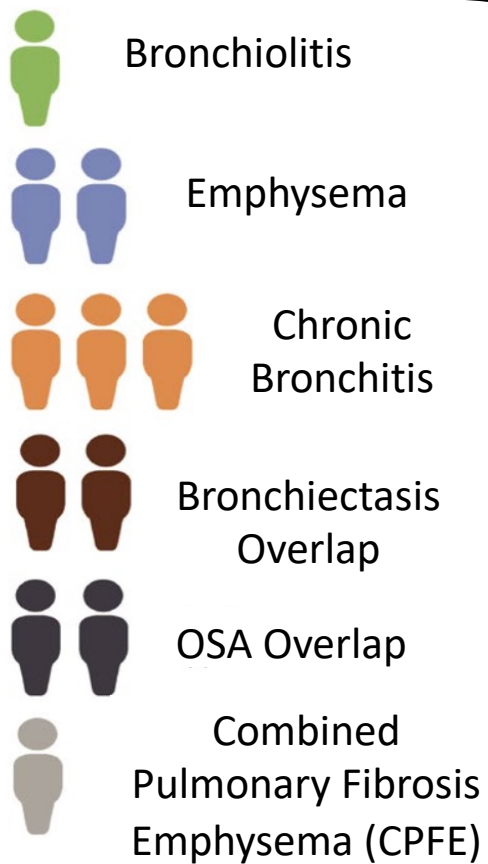
## Clinical Presentation

Coughing + shortness of breath

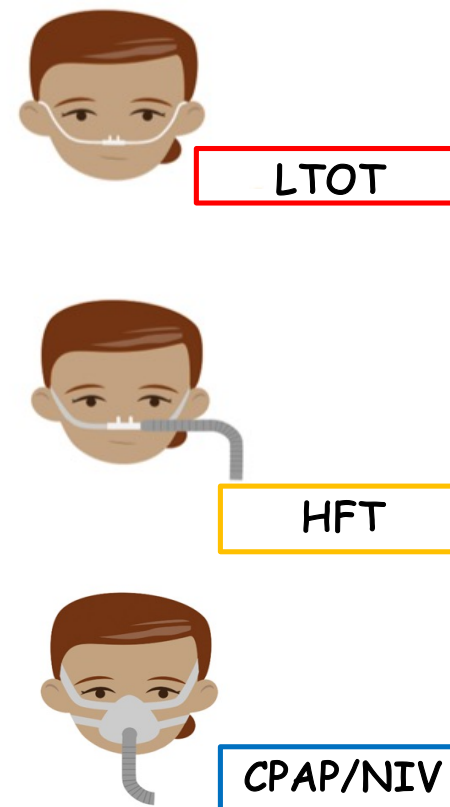


Chronic Respiratory Failure

## Phenotyping

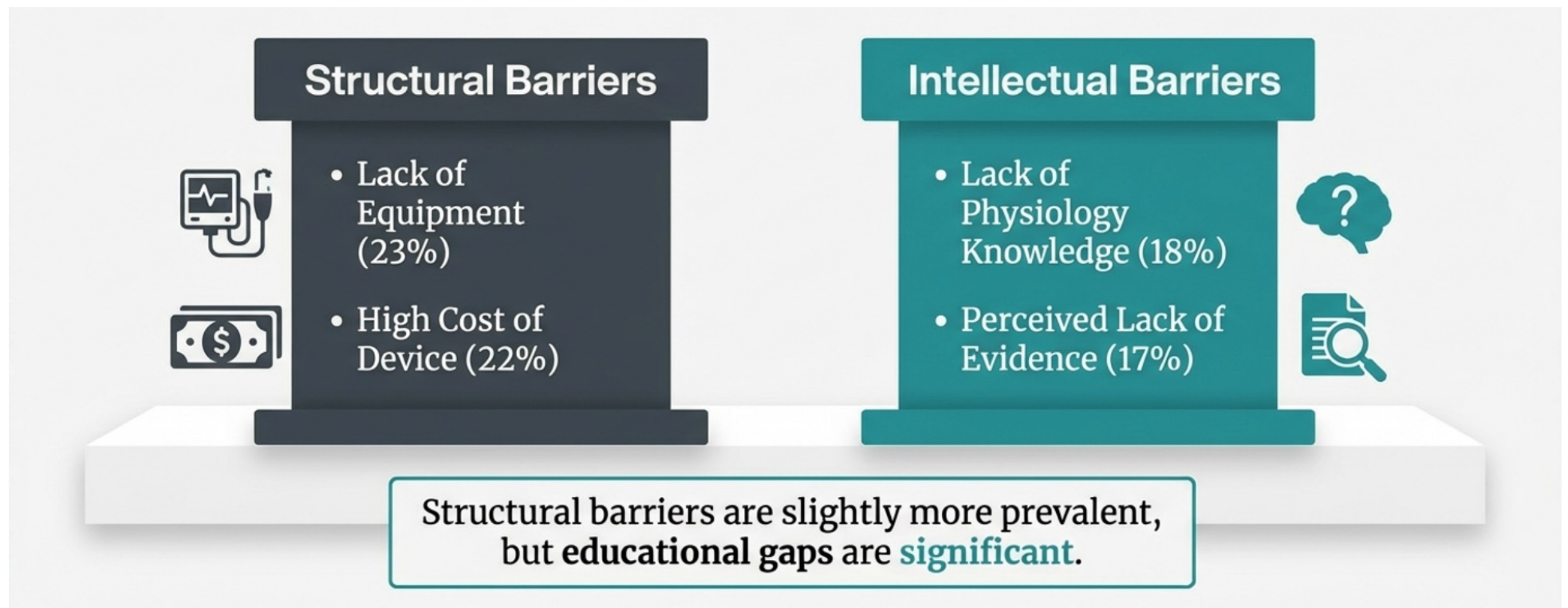


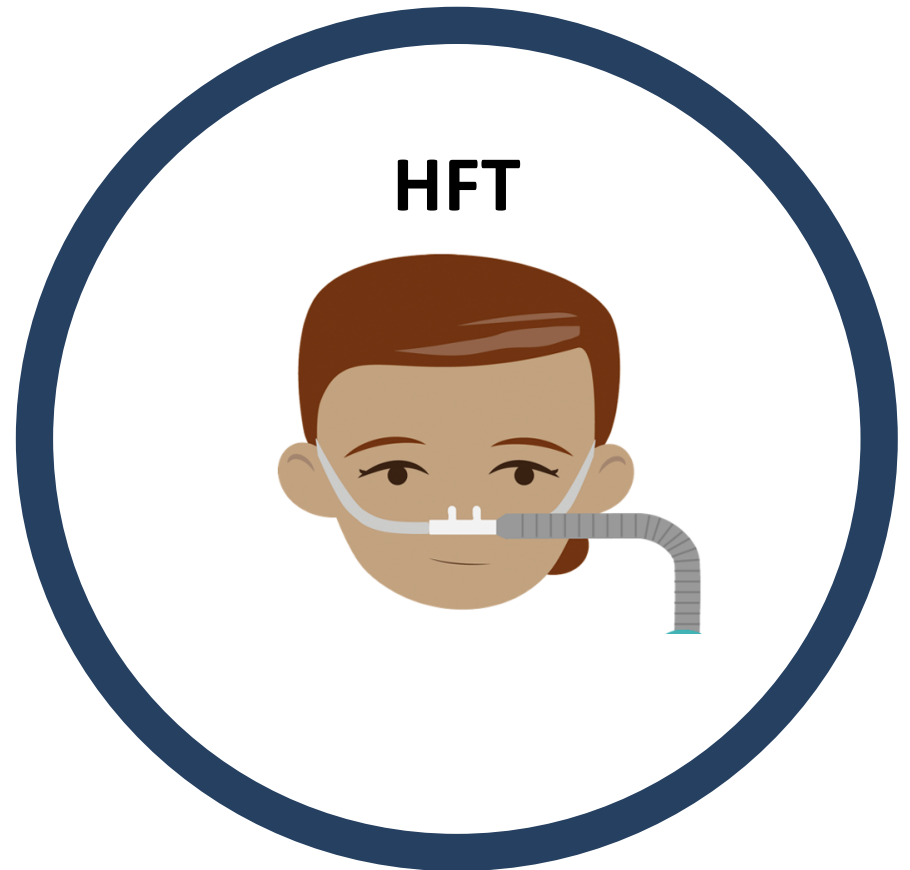
## Targeted Non-Pharmacological Therapy



# BARRIERS TO ADOPTION

The main barrier is not physiology. It's organisation.





# How to implement HFT

1

## Cannula selection

Appropriate size for the patient's nostrils

2

## Initial Settings

Flow 20-30 L/min,  $FiO_2$  to achieve  $SpO_2$  88-92%, T adjustment for pt comfort

3

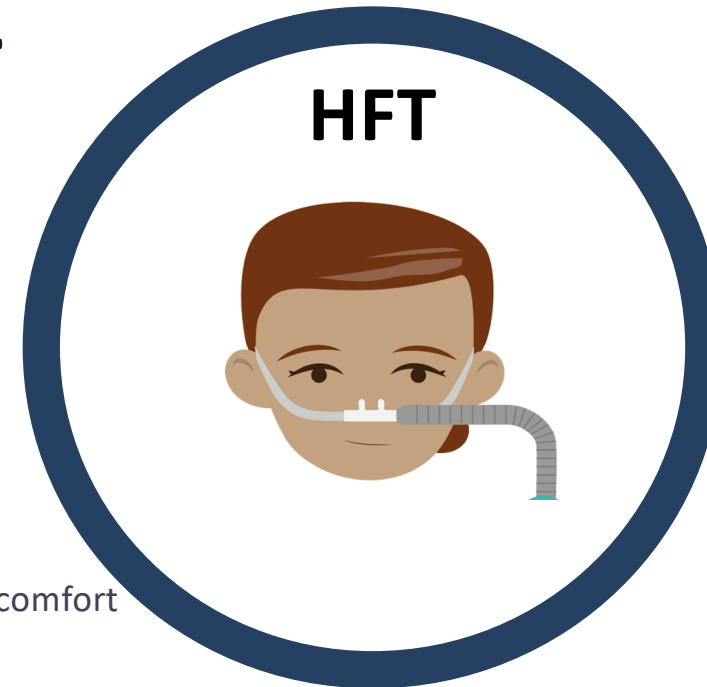
## Titration

Adjust based on comfort and parameters

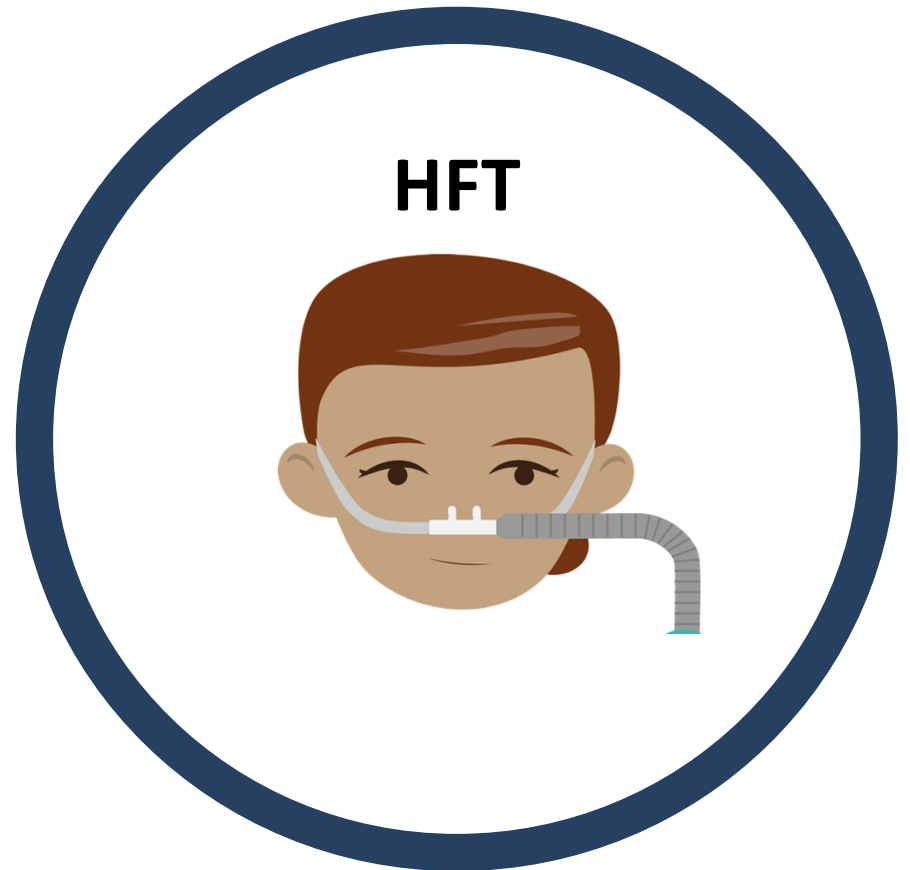
4

## Monitoring

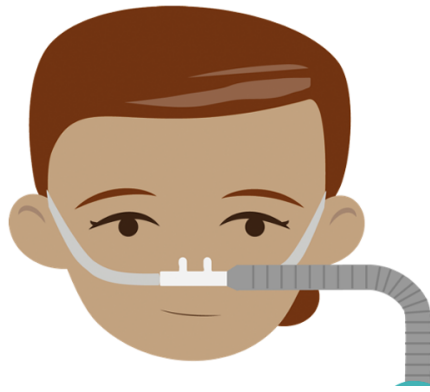
Assess  $SpO_2$ , RR, dyspnea, pH,  $PaCO_2$ ,  $PaO_2$



Individualized  
approach in  
settings, titration,  
and monitoring



# HFT



# DEVICE



**MyAirvo™  
(Fisher and Paykel)**



**Lumis™ HFT  
(ResMed)**



**H-FLOW™  
(Medical Products Research  
S.r.l.)**

	MyAirvo™ (Fisher and Paykel)	Lumis™ HFT (ResMed)	H-FLOW™ (Medical Products Research S.r.l.)
<b>Flow range</b>	10–60 L/min.	15–40 L/min.	10–60 L/min.
<b>Concentrator oxygen flow rate</b>	Up to 15 L/m.	Up to 15 L/m.	Up to 15 L/m.
<b>Humidification and temperature settings</b>	Pass-over system. Reusable or auto-fill water chamber. Heated breathing tube T° target setting = 31 °C, 34 °C, 37 °C. Humidity performance of 33 mg/L at 37 °C, and of 12 mg/L at 31 °C and 34 °C.	Pass-over system. Reusable water chamber. Heated breathing tube (ClimateLineAir™ + tube cover) T° target setting of 31 °C, 34 °C, 37 °C). Humidity level from 1 to 5 (from the lowest to the highest humidity).	Pass-over system. Reusable or auto-fill water chamber. Heated breathing tube T° target setting = 31 °C, 34 °C, 37 °C. Humidity performance of 33 mg/L at 37 °C, and of 12 mg/L at 31 °C and 34 °C.
<b>Interface</b>	Optiflow +™ nasal cannula (3 sizes). Optiflow Tracheostomy™ interface.	AcuCare™ nasal cannula or generic high-flow nasal cannula (note: tracheostomy use is contraindicated for Lumis HFT).	Generic high-flow nasal cannula. Generic high-flow tracheostomy interface.
<b>Alarms</b>	Yes.	Messages and warnings.	Yes.
<b>Patient compliance monitoring</b>	USB port for data download therapy, Infosmart™.	SD card for data download therapy (ResScan™ and Airview™- telemonitoring). Soon, the ability to remotely edit settings will be available.	SD card.
<b>Possibility of connecting a built-in oximeter</b>	No.	Yes, Air10 oximeter adapter (Nonin-XPod®, Global Headquarters, Plymouth, UK).	Yes.
<b>Weight</b>	2.2 kg.	1.29 kg.	3 kg.

# How to implement HFT

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Appropriate size for the patient's nostrils

2

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Flow 20-30 L/min,  $FiO_2$  to achieve  $SpO_2$  88-92%, T adjustment for pt comfort

3

## Titration

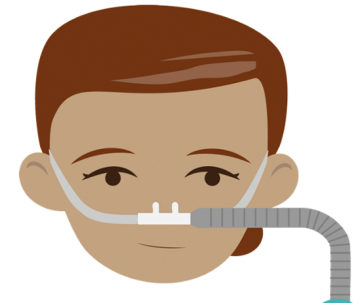
Adjust based on comfort and parameters

4

## Monitoring

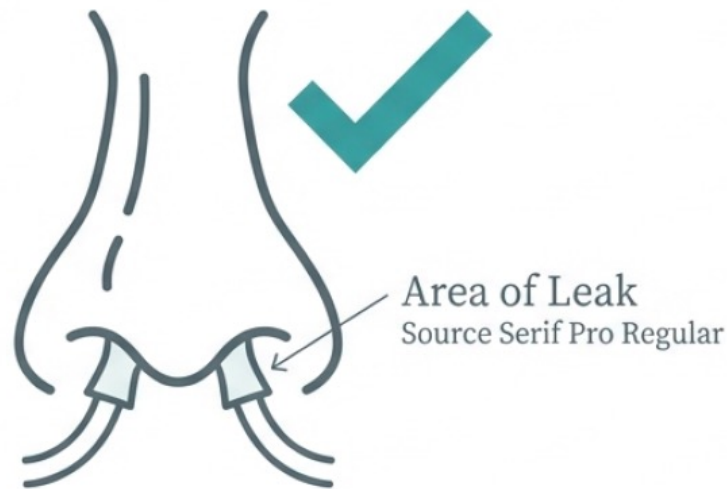
Assess  $SpO_2$ , RR, dyspnea, pH,  $PaCO_2$ ,  $PaO_2$

HFT

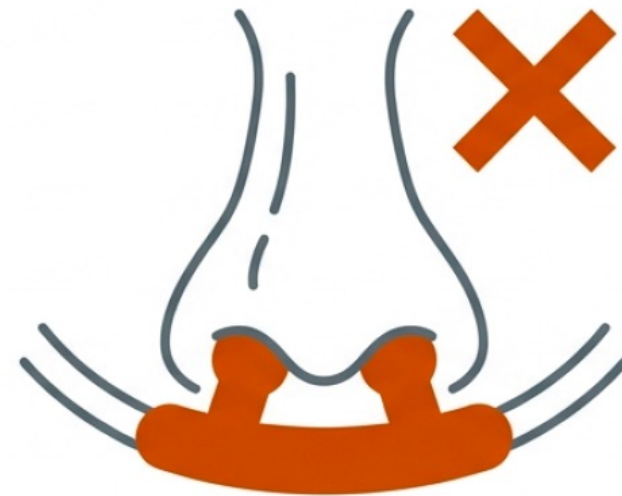


Individualized  
approach in  
settings, titration,  
and monitoring

# Interface Selection: The Golden Rule of Leak

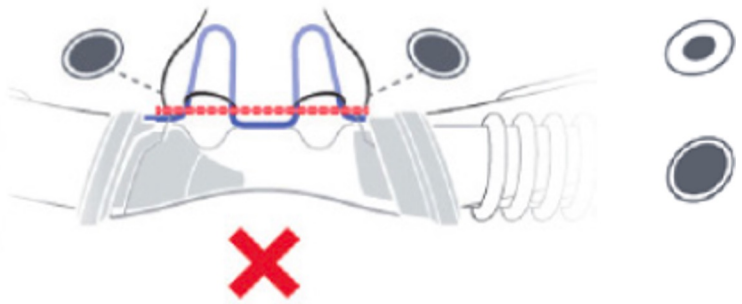
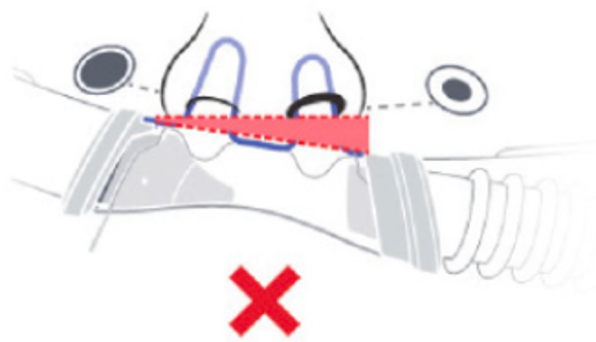
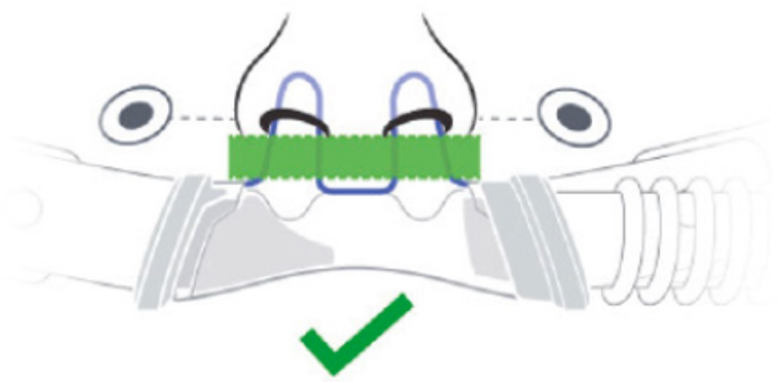
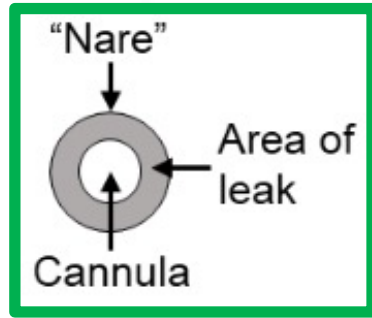


Correct Sizing: 50% occlusion.



Dangerous: Sealed Nares.

Prongs must not seal the nares. A leak is required to prevent excessive airway pressure.



**Prongs must not seal the nares**

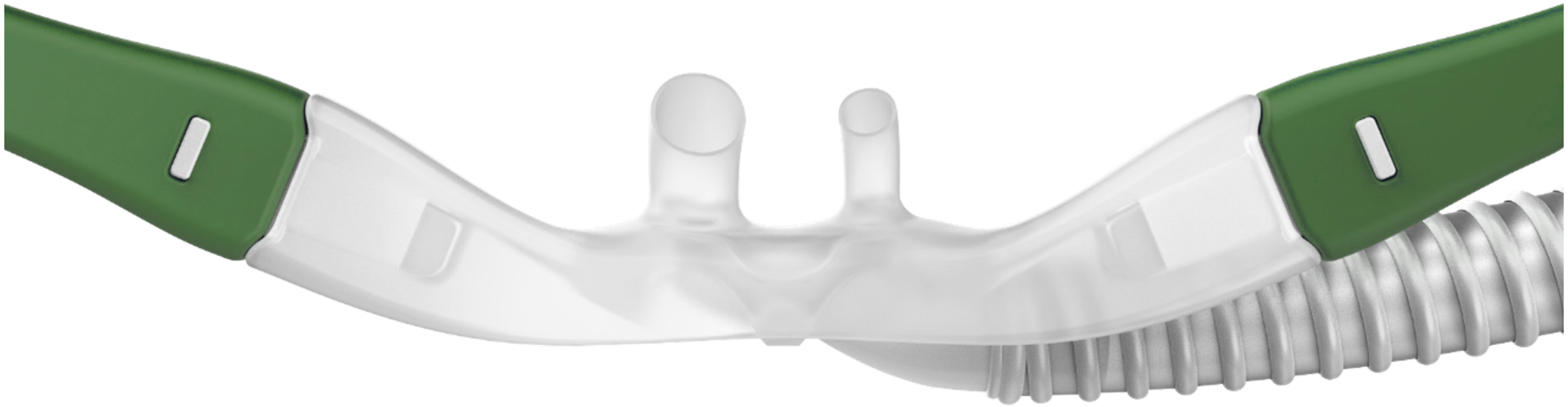


Note: Airway pressure increases progressively with both increasing flow rate and nasal prong-to-nares ratio.

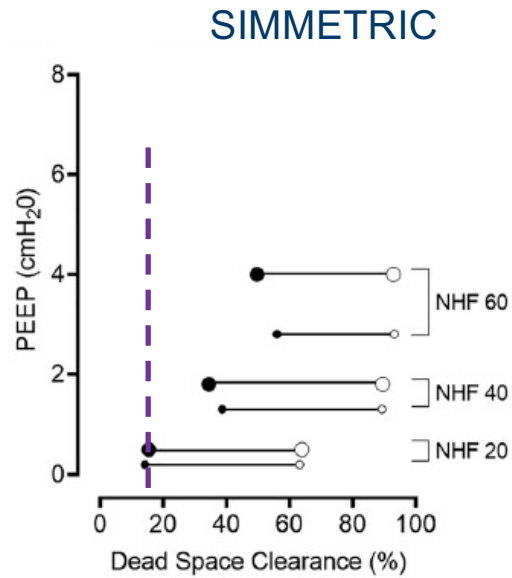
# Asymmetrical cannula

The large prong optimizes pressure

The small prong optimizes CO2 Clearance



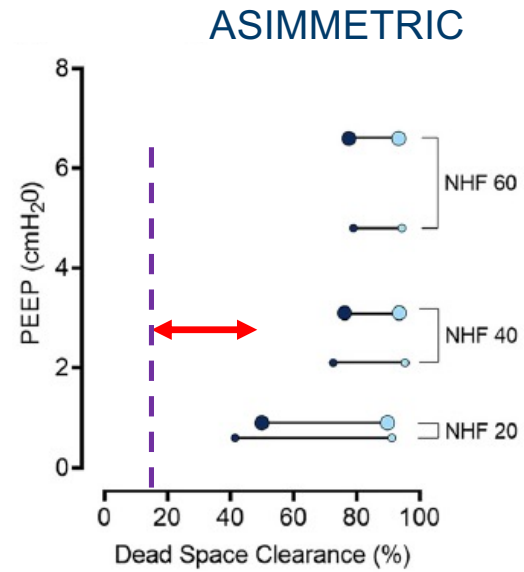
# Dead space clearance



Breaths/min<sup>-1</sup> 45

Larger   

Smaller   



Breaths/min<sup>-1</sup> 45

Larger   

Smaller   

# How to implement HFT

1

## Cannula selection

Appropriate size for the patient's nostrils

2

## Initial Settings

Flow 20-30 L/min,  $FiO_2$  to achieve  $SpO_2$  88-92%, T adjustment for pt comfort

3

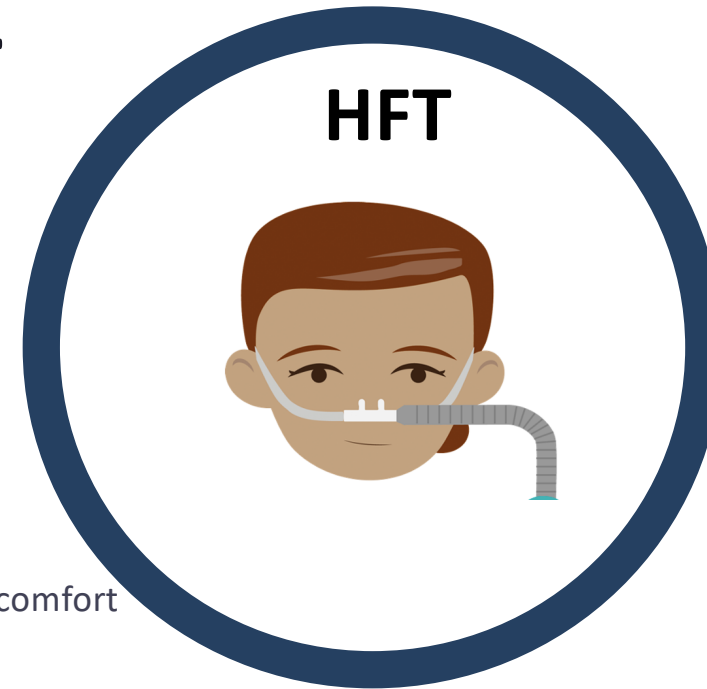
## Titration

Adjust based on comfort and parameters

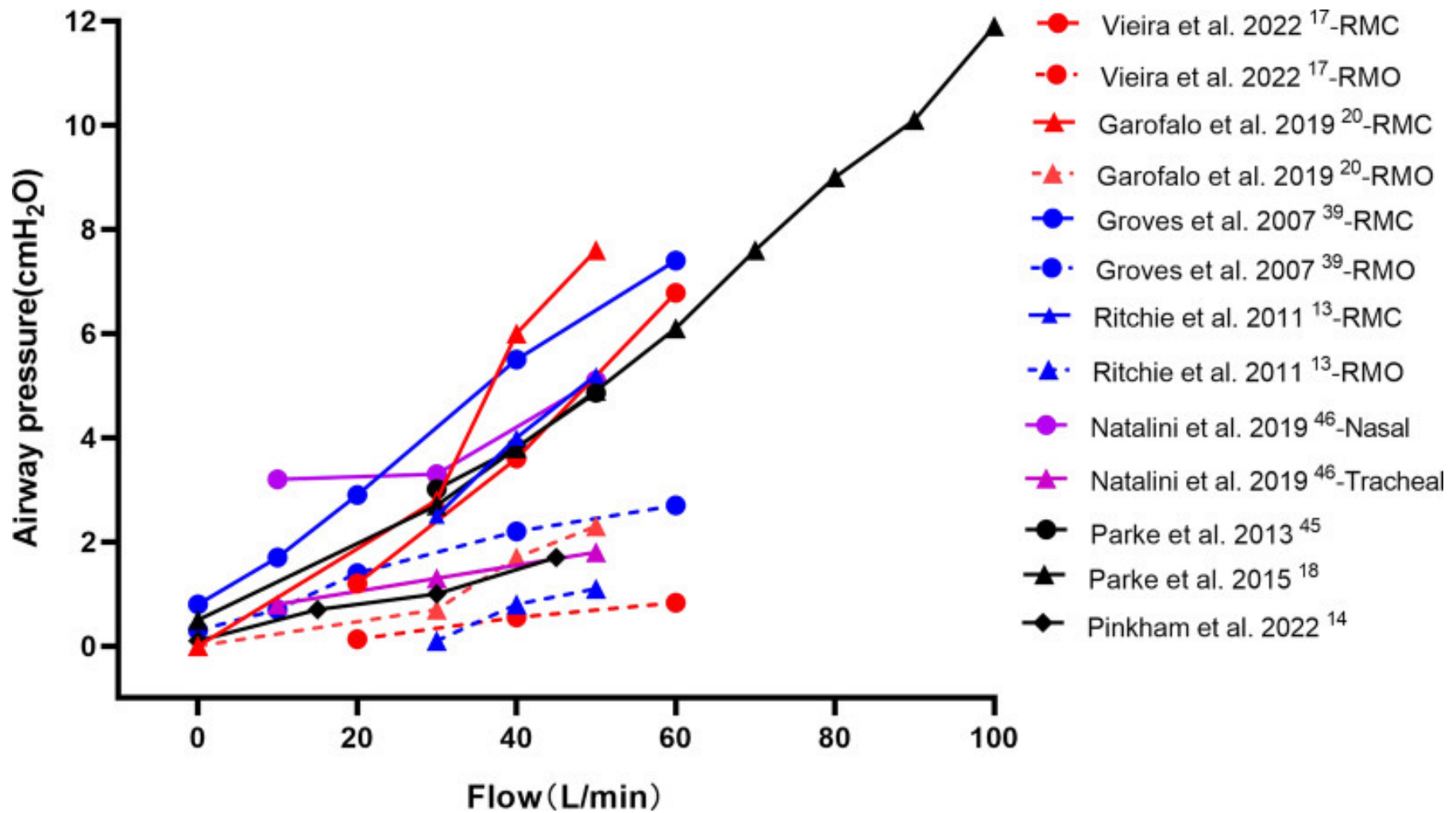
4

## Monitoring

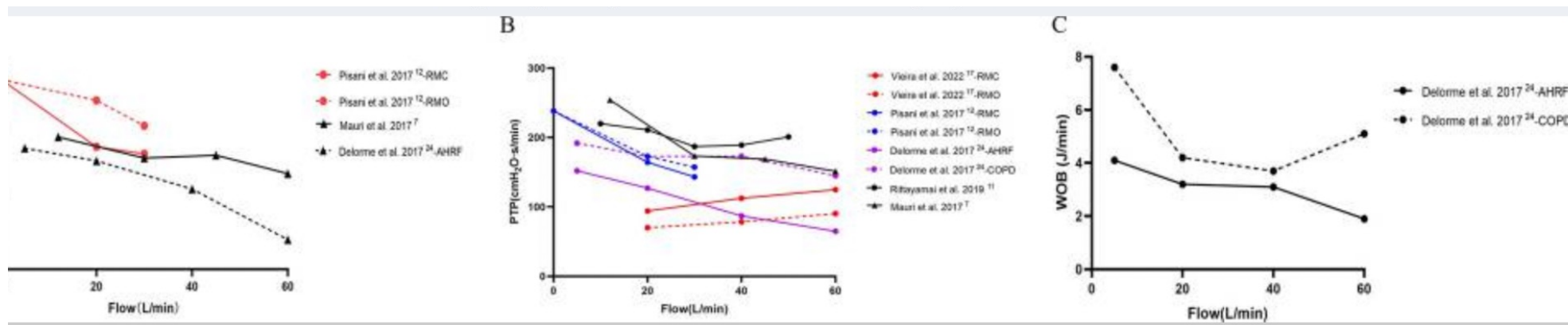
Assess  $SpO_2$ , RR, dyspnea, pH,  $PaCO_2$ ,  $PaO_2$



Individualized  
approach in  
settings, titration,  
and monitoring



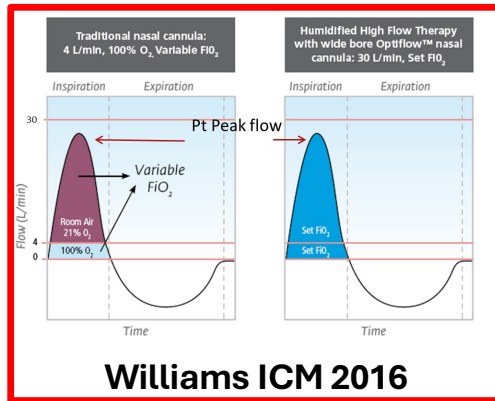
Li J, Crit Care. 2023



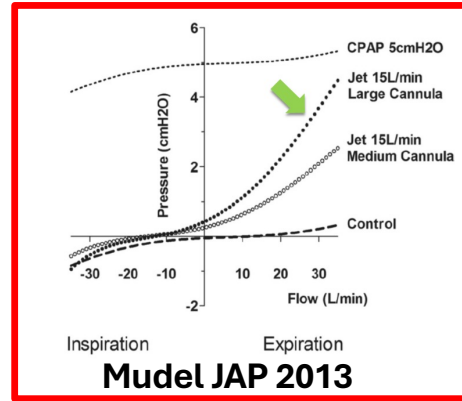
Effects of flow settings on  $\Delta$  Pes (A), PTP (B), and WOB (C). HFNC, high-flow nasal cannula;  $\Delta$  Pes: esophageal pressure swings (cmH<sub>2</sub>O); PTP: esophageal pressure–time product per minute (cmH<sub>2</sub>O·s/min); WOB, work of breathing (J/min)

# HFT: mechanism of action

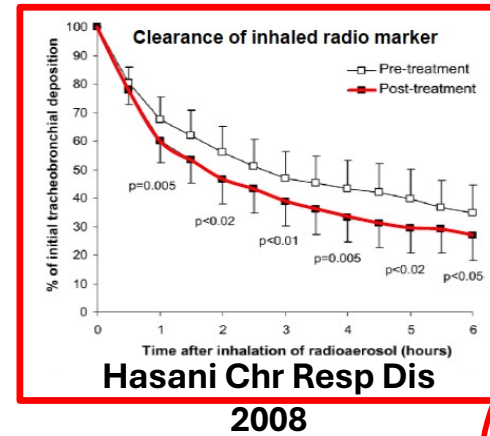
## Precise O2 delivery



## Expiratory resistance



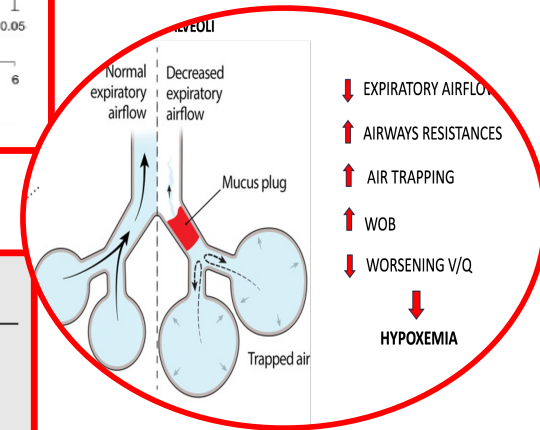
## Mucociliary clearance



## WOB

	Baseline	HFOT 20 (closed)	HFOT 20 (open)	HFOT 30 (closed)	HFOT 30 (open)	NIV
TI,p (seconds)	0.95±0.2	0.85±0.4	0.96±0.2	0.94±0.3	0.92±0.3	1.00±0.2
TE,p (seconds)	1.94±0.4	2.35±0.4*	2.19±0.5*	2.30±0.5*	2.20±0.3*	2.61±1.0*
Breathing frequency (breaths/min)	24.8±2.3	19.01±5.2†	20.8±5.8	18.7±3.6†	19.64±2.8	17.8±3.8†
Tidal volume (mL)	314.50±84	391.22±106‡		364.22±66		456.20±100‡
Pdi swing (cmH <sub>2</sub> O)	13.5±6.7	8.7±4.1§	12±5.8	8.2±3.7§	10.2±5.2§	5.1±2.2§¶
PTPdi/min (cmH <sub>2</sub> Oxs/min)	238.3±82.1	164.2±51.3**	172.7±45.4**	143.2±48.9**	157.3±56.9**	101.7±42.9**††
PEEPi,dyn (cmH <sub>2</sub> O)	2.12±0.9	1.48±0.7‡‡		1.03±0.6‡‡		0.9±0.02‡‡

• Pisani Thorax 2017





# How to set the oxygen?



## Target SpO2

- 92–96% (General Population)
- 88–92% (Chronic Respiratory Disease)

	Flow (L/m)						
	35	40	45	50	55	60	
23	23	23	23	23	22	22	
24	24	24	24	24	24	24	
25	25	25	25	24	25	25	
26	26	26	26	26	27	26	
27	27	27	27	27	27	28	
28	28	28	28	28	28	29	
29	29	29	29	29	29	30	
30	30	30	30	30	30	31	
31	31	31	31	31	31	32	
32	32	32	32	32	32	33	
33	33	33	33	33	33	34	
34	34	34	34	34	34	35	
35	35	35	35	35	35	36	



↓ Dilutes Mixture, Reducing FiO<sub>2</sub>

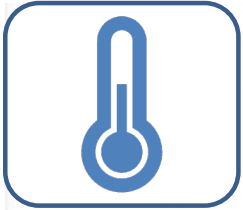
FiO<sub>2</sub> is flow-dependent. Increasing flow dilutes the mixture, reducing delivered FiO<sub>2</sub> unless the source is adjusted.

# Estimated FiO2 according to flow setting

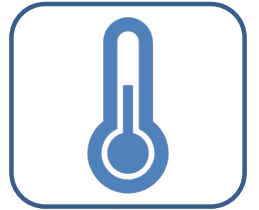
FiO <sub>2</sub> *		Flow (L/m)									
		15	20	25	30	35	40	45	50	55	60
Concentrator oxygen flow rate in L/m	1	26	25	24	24	23	23	23	23	22	22
	2	32	29	27	26	26	25	25	24	24	24
	3	37	33	31	29	28	27	26	26	25	25
	4	42	37	34	32	30	29	28	27	27	26
	5	47	41	37	34	32	31	30	29	28	28
	6	53	45	40	37	35	33	32	31	30	29
	7	58	49	43	40	37	35	33	32	31	30
	8	63	53	46	42	39	37	35	34	33	32
	9	68	56	50	45	42	39	37	35	34	33
	10	73	60	53	47	44	41	39	37	36	34
	11	78	64	56	50	46	43	41	39	37	36
	12	82	68	59	53	48	45	42	40	38	37
	13	87	71	62	55	50	47	44	42	40	38
	14	92	75	65	58	53	49	46	43	41	40
	15	93	79	68	60	55	51	47	45	43	41

(Note: It is always recommended to monitor the efficiency of oxygen therapy (i.e., in terms of SaO<sub>2</sub>) and not prescribe without particular control). \* Actual data calculated using a medical oxygen cylinder with a purity of 99.5%. FiO<sub>2</sub> may vary ±1-2% regarding the devices.

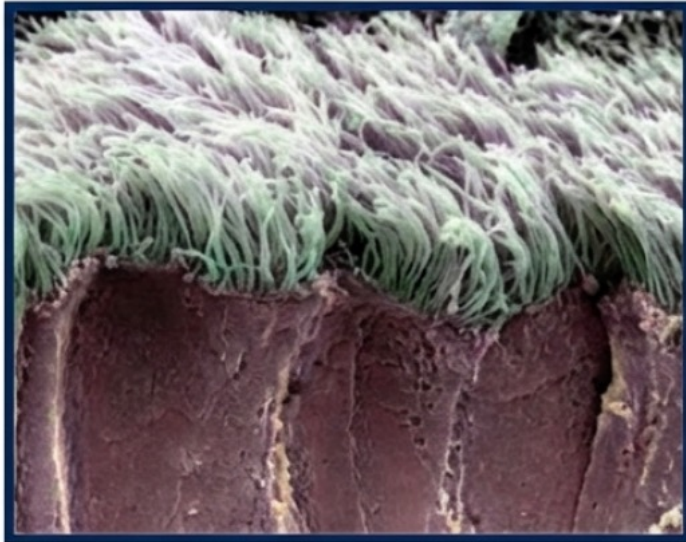
FiO<sub>2</sub> is a “**flow-dependent**” parameter  
(any increase in flow will reduce FiO<sub>2</sub>, and vice versa)



# Temperature & Humidification Strategy

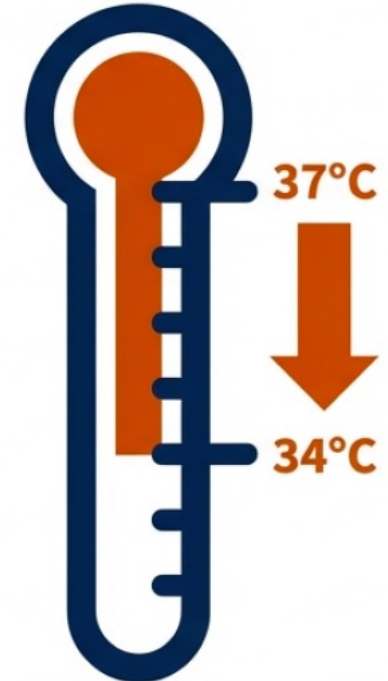


## The Physiology



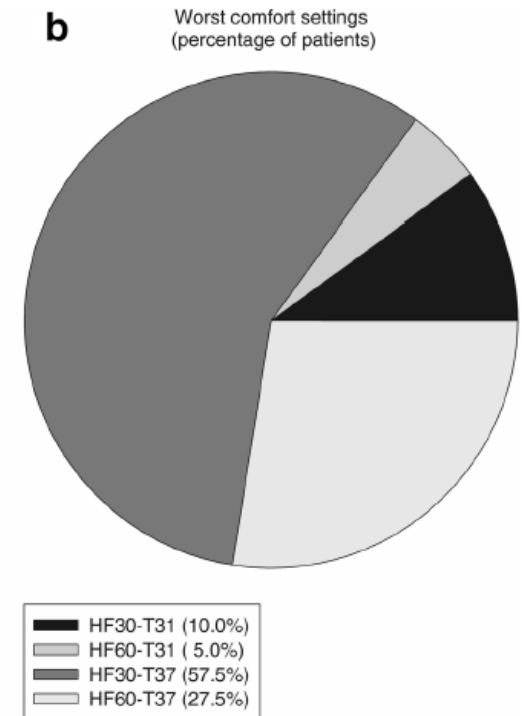
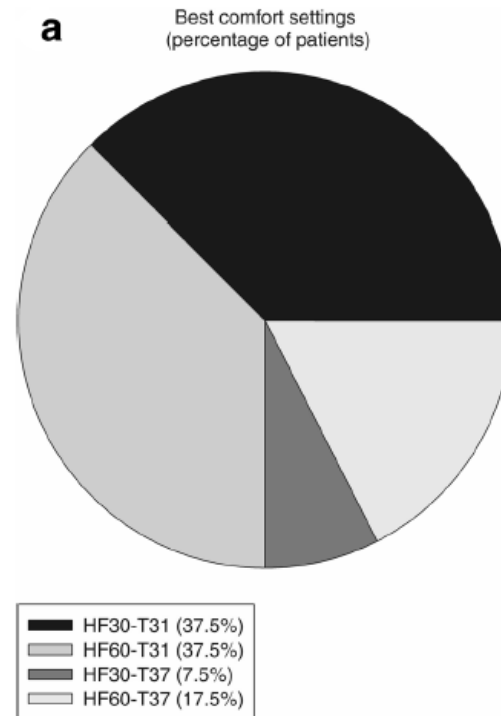
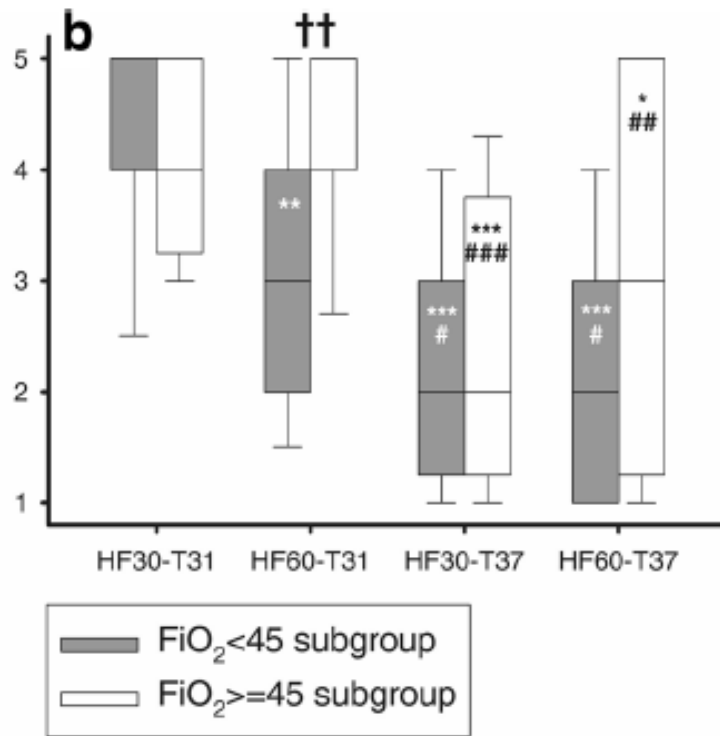
Goal: 37°C = 100% Relative Humidity.  
Optimizes mucociliary clearance.

## The Strategy



# Impact of **flow** and **temperature** on patients' **comfort** during HFNT

*Mauri T et al. Crit Care 2020*



# Chronic Management & Home Settings



**Usage:** Recommended at night (6-8 hours).



**Noise:** Use larger prongs to reduce gas velocity noise.



**Dryness:** Adjust temperature/humidity. Avoid placement near cold windows (**condensation risk**).



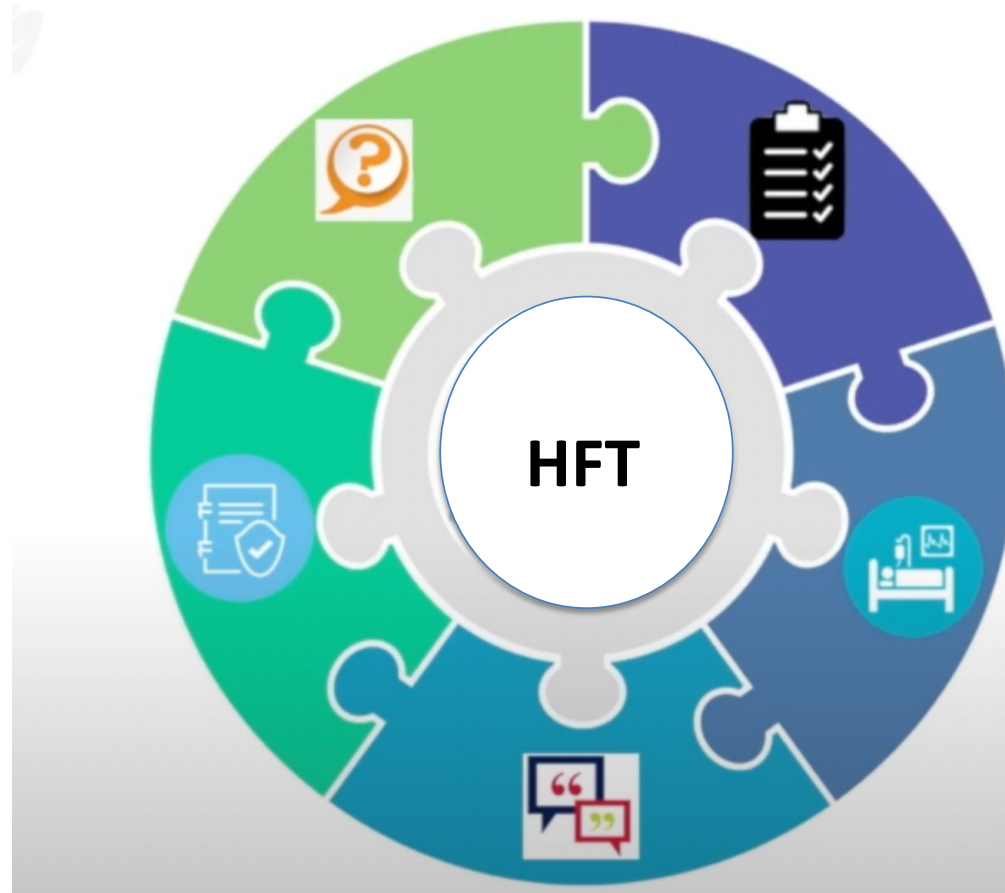
**Follow-up:** Every 6 months. Check Flow, FiO<sub>2</sub>, Cannula fit, and adherence.

# HFT bundle

Is HFT indicated?

Explain  
treatment to  
the patient

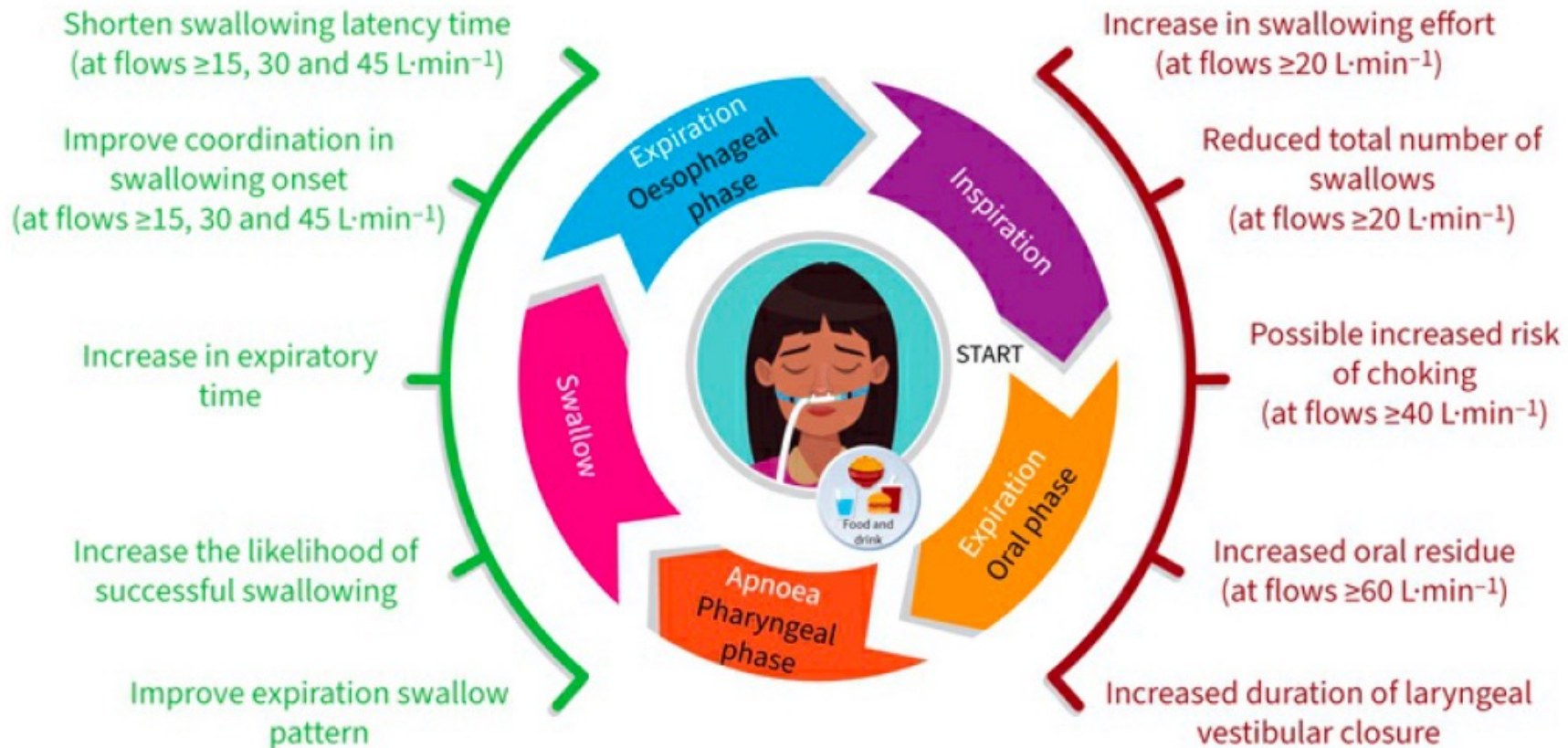
Appropriate  
settings



Treatment of  
underlying medical  
problem

Schedule  
Follow-up

# Swallowing during High-flow Nasal Therapy



# Troubleshooting

Problem (patient says...)	Most likely cause	Practical fix
Too noisy	Flow too high / poor cannula fit	↓ Flow stepwise; check cannula size; secure tubing
Dry nose	Inadequate humidification / low temperature / empty chamber	↑ Temperature; check humidifier + water chamber; nasal hygiene
Can't tolerate flow	Air jetting / discomfort / dryness	Start lower flow and titrate; consider split sessions; nasal gel/spray
SpO <sub>2</sub> still low	Mouth breathing / insufficient FiO <sub>2</sub> / oxygen source issue	Check O <sub>2</sub> source; ↑ FiO <sub>2</sub> ; encourage nasal breathing; reassess
CO <sub>2</sub> rising / persistent distress	Chronic hypoventilation / HFNC failure	Reassess clinically; <b>trial NIV</b> (do not delay escalation)

# Limitations & Future outlook

## Current Limitations

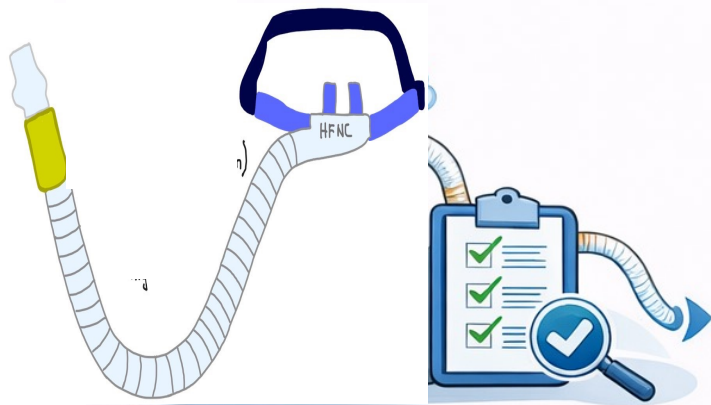
- Lack of cost-benefit analysis
- Few multicenter RCTs
- Observational study heterogeneity

## Future Evidence

Awaiting EPiC-HFT & HIFAE trials



# HOME HFT: 5 Takeaways



**More than oxygen**  
airway conditioning  
+ ventilatory demand  
modulation

**COPD:  
Exacerbation  
reduction**  
evidence supports  
in selected populations



**Bronchiectasis:  
Emerging evidence**  
best fit sputum/  
exacerbation-driven disease



**Success Factors**  
patient selection +  
comfort-first titration +  
early follow-up



**Future Directions**  
integrated home  
pathways + monitoring  
+ phenotypetargeted trials



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