Non-pharmacological treatment for COPD

Respiratory support: O_2, NIV, and HFNC

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Contents

- **Long-term Oxygen Therapy (LTOT)**
- Non-invasive ventilation (NIV)
- High-flow nasal cannula (HFNC)

Long-term oxygen therapy : terminology

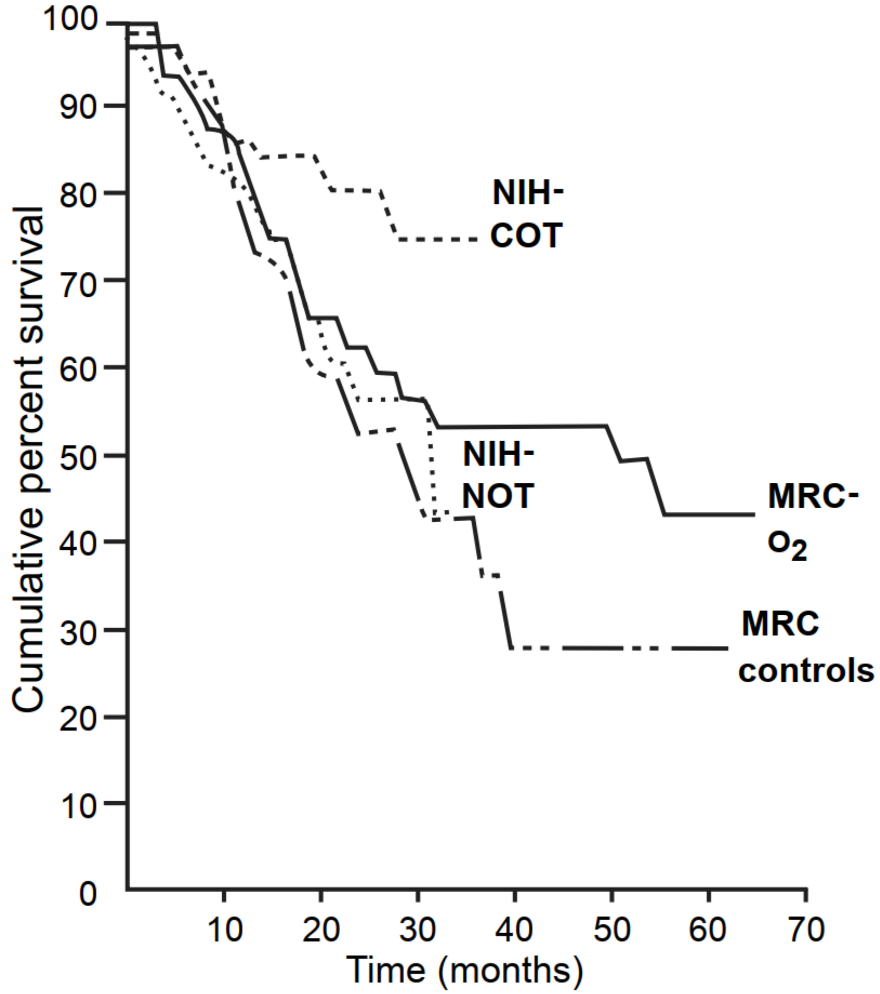
AMERICAN THORACIC SOCIETY DOCUMENTS

Home Oxygen Therapy for Adults with Chronic Lung Disease
An Official American Thoracic Society Clinical Practice Guideline

- Long-term oxygen (LTOT)
  - Oxygen that is delivered to patients with chronic hypoxemia, in most cases for the remainder of the patient's life. Long-term oxygen therapy is prescribed for at least 15 h/d
- Severe hypoxemia
  - PaO2 ≤ 55 mmHg **or** SaO2 (SpO2) ≤ 88%
  - PaO2 = 56 – 59 mmHg (**or** SpO2 = 89%) **plus** Right heart failure (edema or P pulmonale) or Erythrocytosis (Hct ≥ 55%)
- Moderate hypoxemia
  - SpO2 89 – 93%

AJRCCM 2021;203(8):1045-1046.

LTOT in severe hypoxemia



- Landmark studies : NOTT (1980) and MRC (1981)
- COT = continuous oxygen therapy > 19 hours /day

  → Clear survival benefit
- RR for death = 1.94 for NOT (12h/d) vs. COT (17.7h/d)

- Other benefits of LTOT in following studies

: Stabilization of PH, ↓arrhythmia, ↑exercise capacity, ↑HRQoL, ↑neuropsychiatric function, ↓ exacerbation, ↓ hospitalization

IJCOPD 2008:3(2) 231–237

LTOT in moderate hypoxemia : RCT

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 27, 2016 VOL. 375 NO. 17

A Randomized Trial of Long-Term Oxygen for COPD with Moderate Desaturation

The Long-Term Oxygen Treatment Trial Research Group*

- LOTT study (2016)
- Stable COPD with mod resting desat (SpO_2 89 – 93%) or mod exertional desat (6MWT, SpO_2 80 – 90%)
- N = 738 from 42 centers

- Primary outcome : time to death or first hospitalizaton
- Intervention : 24 hour O_2 (resting desat group) or ambulatory/nocturnal O_2 (exertional desat group) ***vs.*** No O_2 supplement

LTOT in moderate hypoxemia : patients characteristics

Table 1. Characteristics of the Patients at Enrollment.*

Characteristic	No Supplemental Oxygen (N=370)	Supplemental Oxygen (N=368)
Age — yr	69.3±7.4	68.3±7.5
Male sex — no. (%)	276 (75)	266 (72)
Race — no. (%)†		
Black	34 (9)	46 (12)
White	328 (89)	311 (85)
Other	11 (3)	17 (5)
Oxygen-desaturation type qualifying the patient for enrollment — no. (%)		
Resting only	60 (16)	73 (20)
Exercise only	171 (46)	148 (40)
Resting and exercise	139 (38)	147 (40)
Spo_2 at rest while breathing ambient air — %		
All patients	93.5±1.9	93.3±2.1
Resting only	92.3±0.8	92.4±0.9
Exercise only	95.2±1.2	95.4±1.4
Resting and exercise	91.9±1.2	91.7±1.1
Nadir Spo_2 during 6-min walk while breathing ambient air — no./total no. (%)¶		
<86%	85/290 (29)	86/292 (29)
86–88%	103/290 (36)	105/292 (36)
>88%	102/290 (35)	101/292 (35)

N Engl J Med 2016;375:1617-27.

LTOT in moderate hypoxemia : No benefit

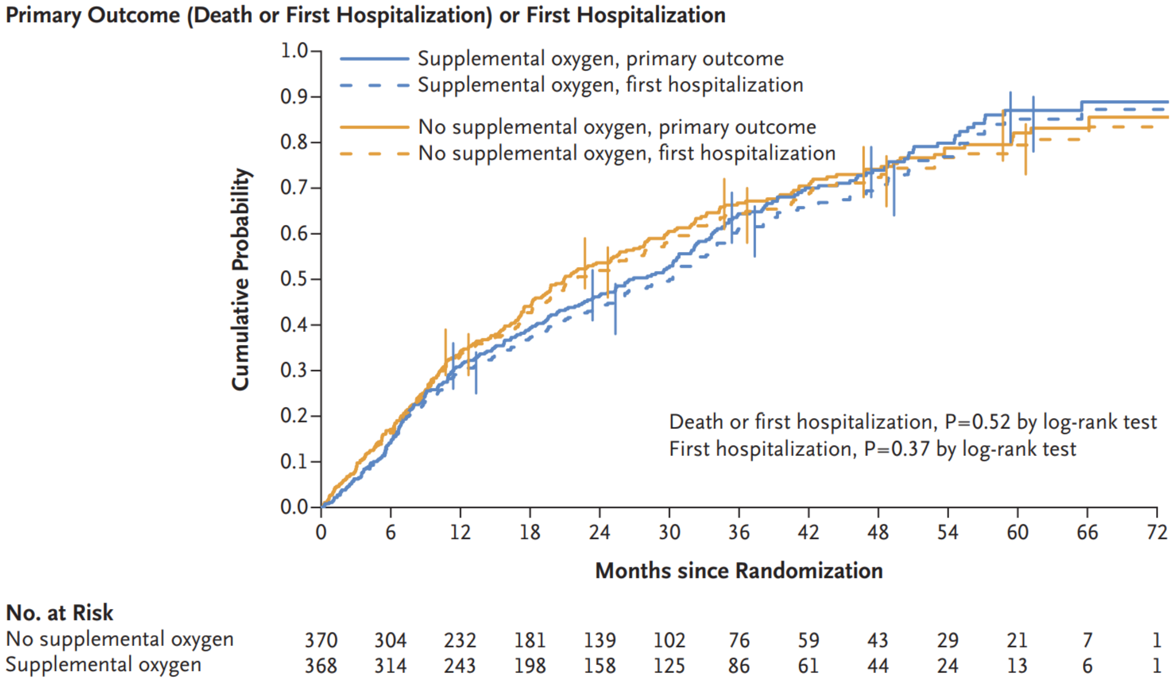


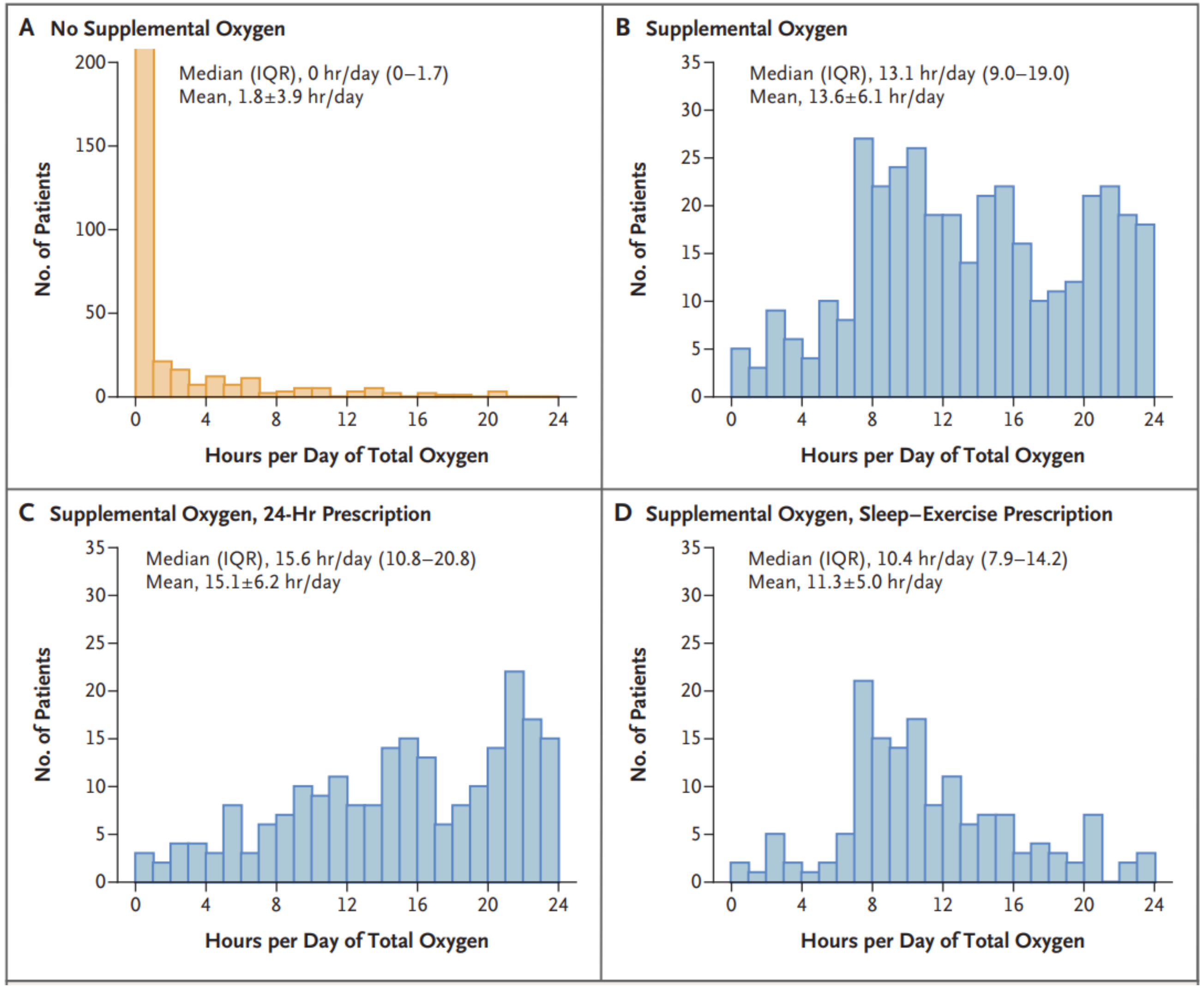
Table 2. Primary Composite Outcome of Death or First Hospitalization for Any Cause and Composite Events in the Intention-to-Treat Population.*

Outcome	No Supplemental Oxygen (N=370)	Supplemental Oxygen (N=368)	Hazard Ratio (95% CI)	P Value
Primary outcome				
Death or first hospitalization for any cause			0.94 (0.79–1.12)	0.52
No. of events	250	248		
Composite rate per 100 person-yr	36.4	34.2		
Primary-outcome component events				
Death			0.90 (0.64–1.25)	0.53
No. of deaths	73	66		
Rate per 100 person-yr	5.7	5.2		
First hospitalization for any cause			0.92 (0.77–1.10)	0.37
No. of first hospitalizations	237	229		
Rate per 100 person-yr	34.5	31.6		

No difference in primary outcomes (+ no effect in subgroups) and other outcomes (COPD AE, COPD hospitalization, QoL, anxiety/depression, lung function, 6MWD, or other functional status)

N Engl J Med 2016;375:1617-27.

LTOT in moderate hypoxemia : compliance



N Engl J Med 2016;375:1617-27.

Meta-analysis

Home oxygen for moderate hypoxaemia in chronic obstructive pulmonary disease: a systematic review and meta-analysis

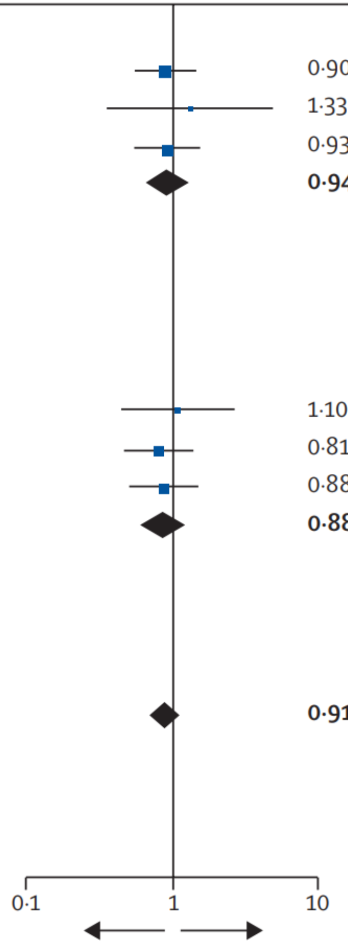
Yves Lacasse, Richard Casaburi, Pawel Sliwinski, Ari Chaouat, Eugene Fletcher, Peter Haidl, François Maltais

	Intervention and design	Definition of daytime or nocturnal hypoxaemia	Duration	Sample size
Fletcher et al (1992)[22]*	NOT; placebo controlled	SpO_2 <90% for ≥5 min with nadir of ≤85%	3 years	Treatment group n=19; control group n=19
Górecka et al (1997)[23]	LTOT; open label	PaO_2 56–65 mm Hg	At least 3 years	Treatment group n=68; control group n=67
Chaouat et al (1999)[24]	NOT; open label	≥30% recording time with SpO_2 <90%	Mean follow-up 35·1 months	Treatment group n=41; control group n=35
Haidl et al (2004)[25]	LTOT; open label	PaO_2 at rest of >55 mm Hg and reversible hypercapnia during exacerbation	3 years	Treatment group n=14; control group n=14
LOTT Research Group (2016; LOTT)[8]†	LTOT or NOT; open label	SpO_2 89–93% or moderate desaturation during exercise	1–6 years; median follow-up 18·4 months	Treatment group n=368; control group n=370
Lacasse et al (2020; INOX)[9]	NOT; placebo controlled	≥30% recording time with SpO_2 <90%	3–4 years	Treatment group n=123; control group n=120

Lancet Respir Med 2022;10: 1029–37

Meta-analysis : no survival benefit

	Oxygen therapy group		Control group			Relative risk (95% CI)
	Events	Total	Events	Total	Weight	
Long-term oxygen therapy						
Górecka et al (1997)[23]	22	68	24	67	26·1%	0·90 (0·56–1·45)
Haidl et al (2004)[25]	4	14	3	14	3·4%	1·33 (0·36–4·90)
LOTT Research Group (2016; LOTT)[8]	25	151	25	140	22·6%	0·93 (0·56–1·54)
Subtotal	··	**233**	··	**221**	**52·1%**	**0·94 (0·67–1·31)**
Total events	51	··	52	··	··	
Heterogeneity: χ^2=0·31, df=2 (p=0·86); τ^2=0·00						
Test for overall effect: Z=0·38 (p=0·70)						
Nocturnal oxygen therapy						
Chaouat et al (1999)[24]	9	41	7	35	7·5%	1·10 (0·46–2·64)
LOTT Research Group (2016; LOTT)[8]	19	109	26	121	20·3%	0·81 (0·48–1·38)
Lacasse et al (2020; INOX)[9]	21	123	23	119	20·1%	0·88 (0·52–1·51)
Subtotal	··	**273**	··	**275**	**47·9%**	**0·88 (0·62–1·25)**
Total events	49	··	56	··	··	
Heterogeneity: χ^2=0·33, df=2 (p=0·85); τ^2=0·00						
Test for overall effect: Z=0·71 (p=0·47)						
Total	··	**506**	··	**496**	**100·0%**	**0·91 (0·72–1·16)**
Total events	100	··	108	··	··	
Heterogeneity: χ^2=0·70, df=5 (p=0·98); τ^2=0·00						
Test for overall effect: Z=0·77 (p=0·44)						
Test for subgroup differences: χ^2=0·00, df=1 (p=0·80)						



Lancet Respir Med 2022;10: 1029–37

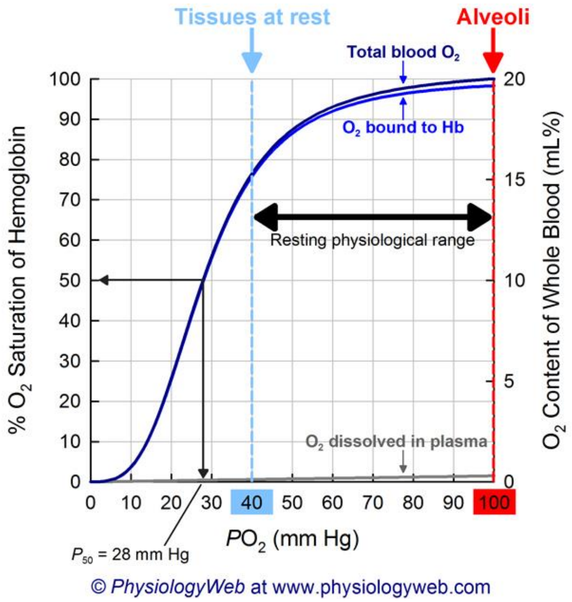
Meta-analysis : no other benefit

	Illustrative comparative risks (95% CI)*		Relative effect (95% CI)	Number of participants or extent of person-time (studies)	Quality of the evidence (GRADE)†	Comments
	Assumed risk; without oxygen (usual care or placebo)	Corresponding risk; supplemental oxygen (either LTOT or NOT)				
Mortality at 3-year follow-up	22%‡	20% (95% CI 16 to 23)	Relative risk 0·91 (0·72 to 1·16)	1002 patients (5 studies)	High§	Treatment effect excludes important benefit
Rate of acute exacerbations during follow-up	0·86 exacerbations per 1 person-year¶	0·94 exacerbations per 1 person-year (95% CI 0·81 to 1·10)	Rate ratio 1·09 (0·94 to 1·28)	3069 person-years (2 studies)	Moderate‖	··
Rate of respiratory hospitalisations during follow-up	0·24 hospitalisations per 1 person-year**	0·24 hospitalisations per 1 person-year (95% CI 0·19 to 0·29)	Rate ratio 0·99 (0·81 to 1·20)	3069 person-years (2 studies)	Moderate‖	··
Change in quality of life (SGRQ total score††)	Mean change in SGRQ total score in the control group ranged from 1·0 to 1·6 points‡‡	Change in SGRQ total score in the intervention group was 1·2 point lower than in the control group, in favour of intervention: mean difference –1·2 (95% CI –6·3 to 4·0)§§	··	480 patients (2 studies)	Low¶¶	SGRQ minimal clinically important difference of 4 points;‖‖ treatment effect overlaps important benefit

Lancet Respir Med 2022;10: 1029–37

Possible reasons for the negative result

- Non-linear threshold effects of oxygen saturation on pulmonary vasoconstriction, mediator release, and ventilatory drive
- Daily use of oxygen treatment might have been too low in moderate desaturation group
- Substantial developments in COPD management (compared to 1970s')

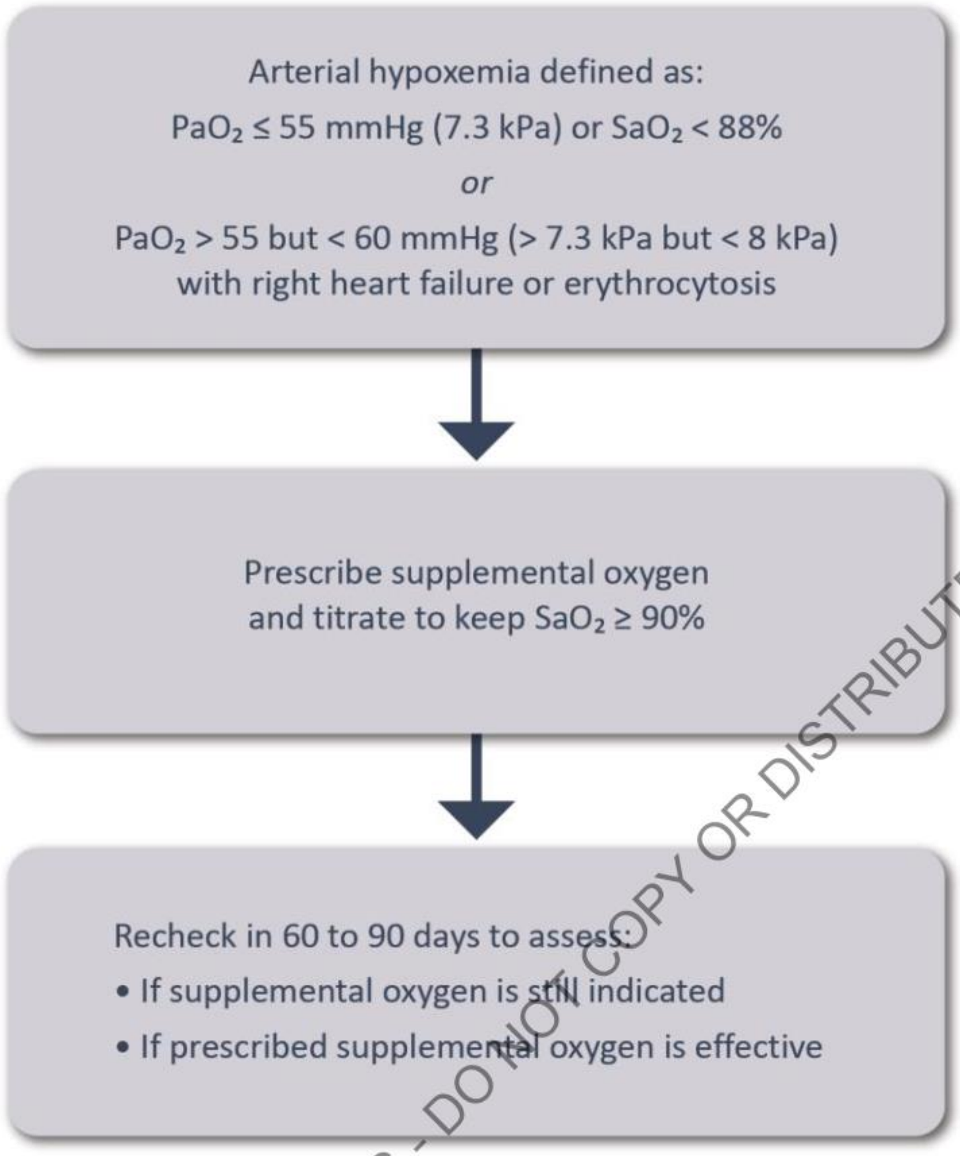


Lancet Respir Med 2022;10(11): 1010-1011

GOLD 2023 : LTOT in stable COPD

- The long-term administration of oxygen increases survival in patients with severe chronic resting arterial hypoxemia (Evidence A).
- In patients with stable COPD and moderate resting or exercise-induced arterial desaturation, prescription of lung-term oxygen does not lengthen time to death or first hospitalization or provide sustained benefit in health status, lung function and 6MWD (Evidence A).

- Resting oxygenation at sea level dose not exclude the development of severe hypoxemia when traveling by air (Evidence C).



GOLD 2023

Severe exertional hypoxemia? not mentioned in GOLD

Table 4. Summary of ATS Recommendations

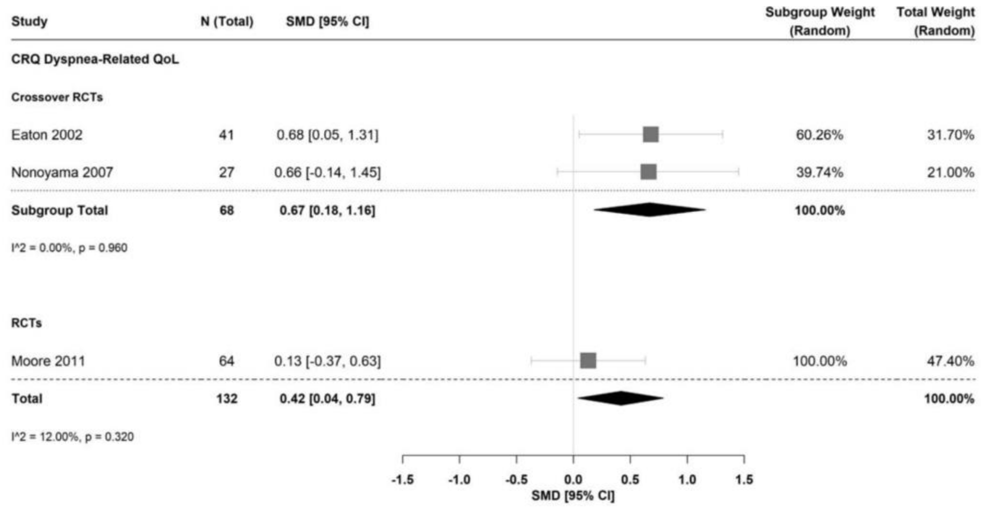
Question	ATS Recommendation	Strength of Recommendation and Level of Evidence
COPD		
Question 1: Should long-term oxygen be prescribed for adults with COPD who have severe* chronic resting room air hypoxemia?	In adults with COPD who have severe chronic resting room air hypoxemia, we recommend prescribing LTOT for at least 15 h/d.	Strong recommendation, moderate-quality evidence
Question 2: Should long-term oxygen be prescribed for adults with COPD who have moderate† chronic resting room air hypoxemia?	In adults with COPD who have moderate chronic resting room air hypoxemia, we suggest not prescribing LTOT.	Conditional recommendation, low-quality evidence
Question 3: Should ambulatory oxygen be prescribed for adults with COPD who have severe exertional room air hypoxemia?	In adults with COPD who have severe exertional room air hypoxemia, we suggest prescribing ambulatory oxygen.	Conditional recommendation, low-quality evidence

Term	Definition
Ambulatory oxygen	Oxygen delivered during exercise or activities of daily living.

AJRCCM 2021;203(8):1045-1046.

Severe exertional hypoxemia

- Isolated exertional hypoxemia (IEH)
  - Presents 40% in moderate to severe COPD
  - More rapid lung function decline,worse HRQoL, increased mortality (HR 2.63 in SpO_2<90% in 6MWT)
- Limited studies on O_2 during daily life
- No long-term studies on exercise capacity
- Meta-analysis for HRQoL (in ATS practice guideline) : Effect size < MCID (0.5)



Chest 2008; 134: 746-752
AJRCCM 2021;203(8):1045-1046

Severe exertional hypoxemia

Eur Respir J 2002; 20: 306–312
DOI: 10.1183/09031936.02.00301002

European Respiratory Journal
ISSN 0903-1936

ERJ 2002;20(2):306-12

Ambulatory oxygen improves quality of life of COPD patients: a randomised controlled study

Table 2. – Health-related quality of life (HRQL) measures for 41 patients

	Baseline	Δ cylinder oxygen-cylinder air	p-value
Disease specific HRQL			
CRQ#			
Dyspnoea (5–35)	16.6 (5.3)	2.0 (0.9)	0.02
Fatigue (4–28)	15.3 (4.9)	1.8 (0.7)	0.02
Emotional function (7–49)	34.3 (8.0)	3.3 (1.2)	0.006
Mastery (4–28)	19.5 (4.8)	1.8 (0.7)	0.008
Total (20–140)	85.8 (18.5)	8.8 (2.8)	0.002
HAD¶			
Anxiety (0–21)	5.6 (4.1)	-1.6 (0.6)	0.009
Depression (0–21)	4.3 (2.5)	-1.0 (0.5)	0.05
Generic HRQL			
SF-36#			
Physical functioning (0–100)	33.0 (18.8)	1.6 (3.5)	0.6
Role physical (0–100)	15.2 (27.3)	16.8 (5.5)	0.01
Bodily pain (0–100)	73.4 (26.3)	5.3 (5.0)	0.3
General health (0–100)	42.9 (22.8)	6.1 (2.9)	0.04
Vitality (0–100)	48.3 (20.5)	2.9 (3.0)	0.3
Social functioning (0–100)	67.1 (24.2)	10.5 (5.2)	0.05
Role emotional (0–100)	60.2 (44.2)	18.3 (7.7)	0.02
Mental health (0–100)	75.6 (14.7)	4.0 (2.7)	0.1

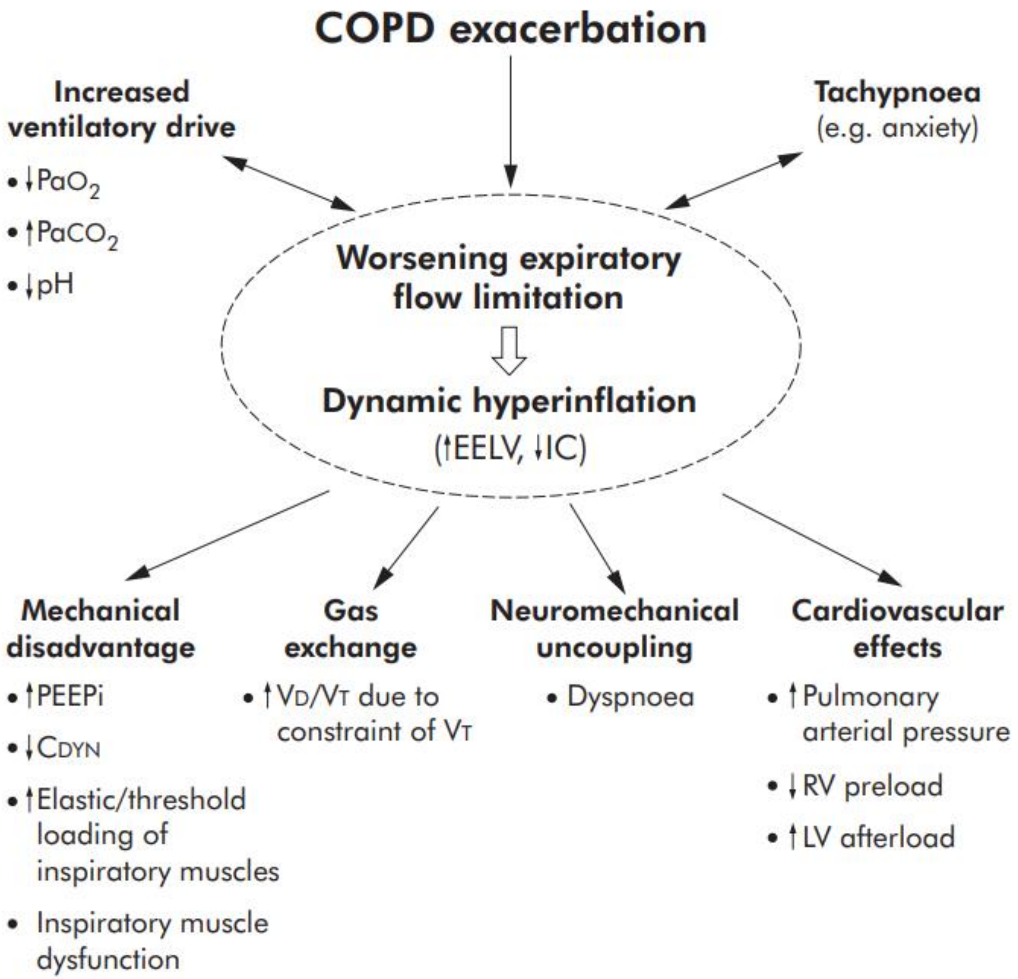
- Cross-over double blind RCT for 12 weeks (N = 41)
- Exertional desaturation ≤ 88%
- O_2 4L/min during exercise
- 41% of responders did not want to continue therapy

Significant improvement in physical role, general health, social functioning, and emotional role (exceed MCID except for social functioning)

Contents

- Long-term Oxygen Therapy (LTOT)
- **Non-invasive ventilation (NIV)**
- High-flow nasal cannula (HFNC)

Role of NIV in COPD AE



- Positive pressure open airways → Increase in alveolar ventilation
- EPAP adjusted to overcome intrinsic PEEP to decrease respiratory muscle load → Reduce in work of breathing
- Pressure support ventilation with backup rates reduced diaphragm effort → Resting diaphragm muscle

Thorax. 2006;61(4):354-61
Annals ATS 2019; 16(9): 1091-1098

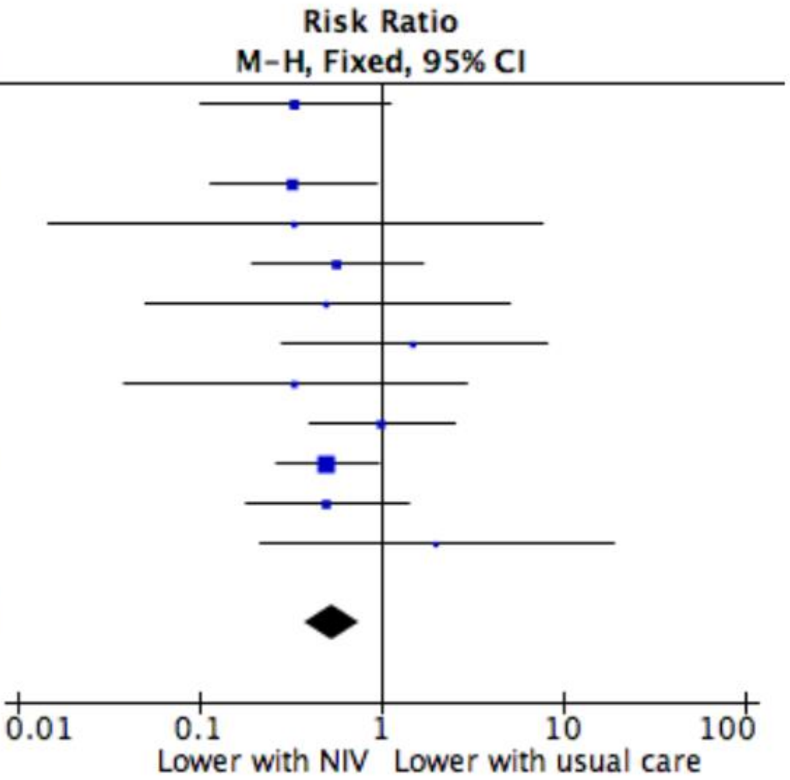
NIV in COPD AE : meta-analysis

Mortality

Study or Subgroup	NIV Events	NIV Total	Usual care Events	Usual care Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Avdeev 1998	3	29	9	29	11.5%	0.33 [0.10, 1.11]
Barbe 1996	0	14	0	10		Not estimable
Brochard 1995	4	43	12	42	15.6%	0.33 [0.11, 0.93]
Celikel 1998	0	15	1	15	1.9%	0.33 [0.01, 7.58]
Collaborative 2005	5	100	8	91	10.7%	0.57 [0.19, 1.68]
Dikensoy 2002	1	17	2	17	2.6%	0.50 [0.05, 5.01]
Khilnani 2010	3	20	2	20	2.6%	1.50 [0.28, 8.04]
Liu 2005	1	18	3	18	3.8%	0.33 [0.04, 2.91]
Matuska 2006	7	30	7	30	9.0%	1.00 [0.40, 2.50]
Plant 2001	12	118	24	118	30.8%	0.50 [0.26, 0.95]
Samaria 2009	4	20	8	20	10.3%	0.50 [0.18, 1.40]
Thys 2002	2	10	1	10	1.3%	2.00 [0.21, 18.69]
Total (95% CI)		**434**		**420**	**100.0%**	**0.54 [0.38, 0.76]**
Total events	42		77			

Heterogeneity: $Chi^2 = 6.36$, df = 10 (P = 0.78); $I^2 = 0\%$

Test for overall effect: Z = 3.49 (P = 0.0005)



Cochrane Database of Systematic Reviews 2017

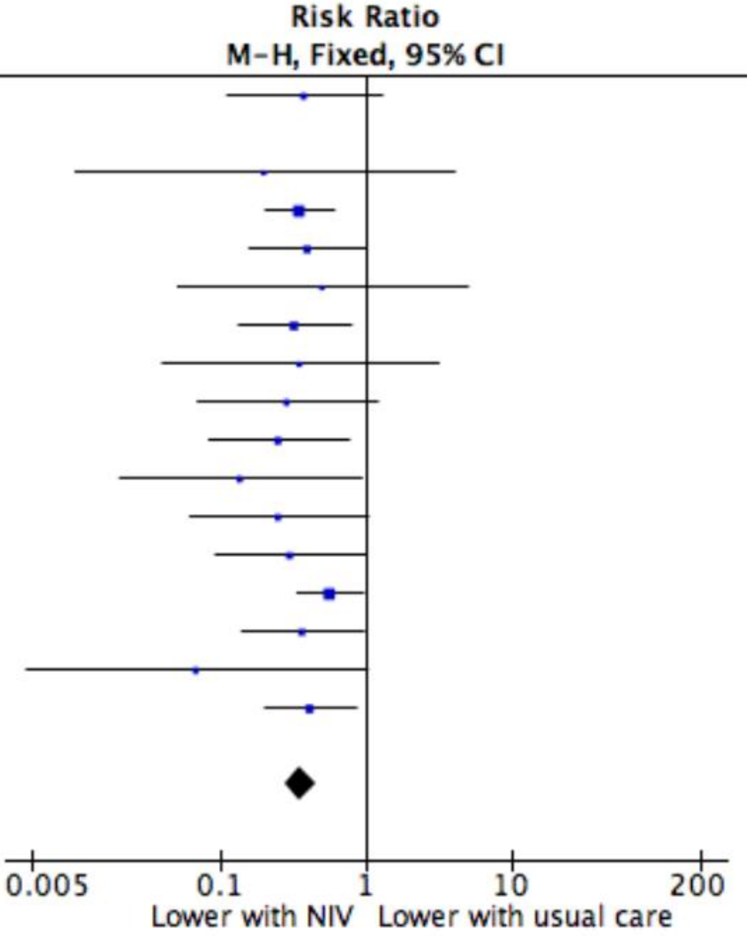
NIV in COPD AE : meta-analysis

Need for intubation

Study or Subgroup	NIV Events	NIV Total	Usual care Events	Usual care Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Avdeev 1998	3	29	8	29	4.2%	0.38 [0.11, 1.27]
Barbe 1996	0	14	0	10		Not estimable
Bott 1993	0	30	2	30	1.3%	0.20 [0.01, 4.00]
Brochard 1995	11	43	31	42	16.7%	0.35 [0.20, 0.60]
Carrera 2009	5	37	13	38	6.8%	0.40 [0.16, 1.00]
Celikel 1998	1	15	2	15	1.1%	0.50 [0.05, 4.94]
Collaborative 2005	6	100	17	91	9.5%	0.32 [0.13, 0.78]
del Castillo 2003	1	20	3	21	1.6%	0.35 [0.04, 3.09]
Dikensoy 2002	2	17	7	17	3.7%	0.29 [0.07, 1.18]
Khilnani 2010	3	20	12	20	6.4%	0.25 [0.08, 0.75]
Kramer 1995	1	11	8	12	4.1%	0.14 [0.02, 0.92]
Liu 2005	2	18	8	18	4.2%	0.25 [0.06, 1.02]
Matuska 2006	3	30	10	30	5.3%	0.30 [0.09, 0.98]
Plant 2001	18	118	32	118	17.0%	0.56 [0.34, 0.94]
Samaria 2009	4	20	11	20	5.8%	0.36 [0.14, 0.95]
Thys 2002	0	7	5	5	3.3%	0.07 [0.00, 1.01]
Zhou 2001	7	30	17	30	9.0%	0.41 [0.20, 0.85]
Total (95% CI)		**559**		**546**	**100.0%**	**0.36 [0.28, 0.46]**
Total events	67		186			

Heterogeneity: $Chi^2 = 6.68$, $df = 15$ ($P = 0.97$); $I^2 = 0\%$

Test for overall effect: $Z = 8.22$ ($P < 0.00001$)



Cochrane Database of Systematic Reviews 2017

NIV in COPD AE : meta-analysis

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)
	Risk with usual care - Overall	Risk with NIV			
Mortality	183 per 1000	99 per 1000 (70 to 139)	RR 0.54 (0.38 to 0.76)	854 (12 RCTs)	⊕⊕⊕⊝ MODERATE[a]
Need for endotracheal intubation	341 per 1000	123 per 1000 (95 to 157)	RR 0.36 (0.28 to 0.46)	1105 (17 RCTs)	⊕⊕⊕⊝ MODERATE[a]
Length of hospital stay (days)	Mean length of hospital stay (days) was 17.5	MD 3.39 lower (5.93 lower to 0.85 lower)	-	888 (10 RCTs)	⊕⊕⊕⊝ MODERATE[a,b]

Cochrane Database of Systematic Reviews 2017

NIV in COPD AE : Standard of care for RF

Indications for Noninvasive Mechanical Ventilation (NIV)

Table 5.7

At least one of the following:

- Respiratory acidosis ($PaCO_2 \geq 6.0$ kPa or 45 mmHg and arterial pH ≤ 7.35)
- Severe dyspnea with clinical signs suggestive of respiratory muscle fatigue, increased work of breathing, or both, such as use of respiratory accessory muscles, paradoxical motion of the abdomen, or retraction of the intercostal spaces
- Persistent hypoxemia despite supplemental oxygen therapy

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NIV in COPD AE : Technical issues

NIV SETUP

Mask
Full face mask (or own if home user of NIV)

Initial Pressure settings
EPAP: 3 (or higher if OSA known/expected)

IPAP in COPD/OHS/KS 15 (20 if pH <7.25)

Up titrate IPAP over 10-30 mins to IPAP 20—30 to achieve adequate augmentation of chest/abdo movement and slow RR

IPAP should not exceed 30 or EPAP 8* without expert review

IPAP in NM 10 (or 5 above usual setting)

Backup rate
Backup Rate of 16-20. Set appropriate inspiratory time

I:E ratio
COPD 1:2 to 1.3
OHS, NM & CWD 1:1

Inspiratory time
0.8-1.2s COPD
1.2-1.5s OHS, NM & CWD

Use NIV for as much time as possible in 1st 24hours.
Taper depending on tolerance & ABGs over next 48-72 hours

SEEK AND TREAT REVERSIBLE CAUSES OF AHRF

NIV Monitoring

Oxygenation

Aim 88-92% in all patients

Note: Home style ventilators CANNOT provide > 50% inspired oxygen.

If high oxygen need or rapid desaturation on disconnection from NIV consider IMV.

Red flags
pH <7.25 on optimal NIV
RR persisting > 25
New onset confusion or patient distress

Actions
Check synchronisation, mask fit, exhalation port : give physiotherapy/bronchodilators, consider anxiolytic

CONSIDER IMV

BTS/ICS guideline
Thorax. 2016;71 Suppl 2:ii1-35.

NIV in COPD AE : Standard of care

Indications for Invasive Mechanical Ventilation

Table 5.8

- Unable to tolerate NIV or NIV failure
- Status post-respiratory or cardiac arrest
- Diminished consciousness, psychomotor agitation inadequately controlled by sedation
- Massive aspiration or persistent vomiting
- Persistent inability to remove respiratory secretions
- Severe hemodynamic instability without response to fluids and vasoactive drugs
- Severe ventricular or supraventricular arrhythmias
- Life-threatening hypoxemia in patients unable to tolerate NIV

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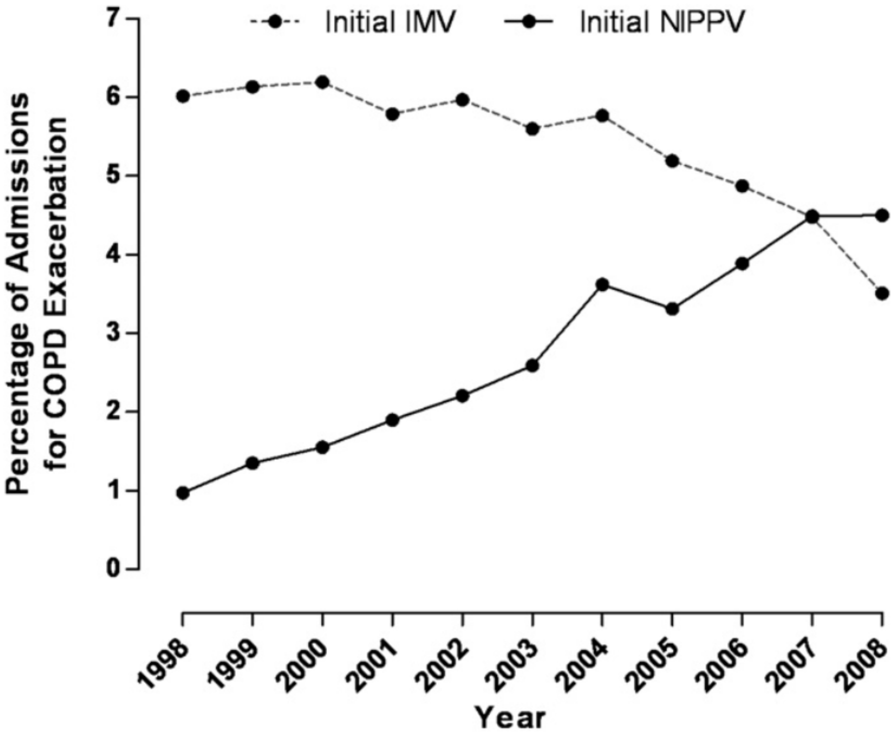
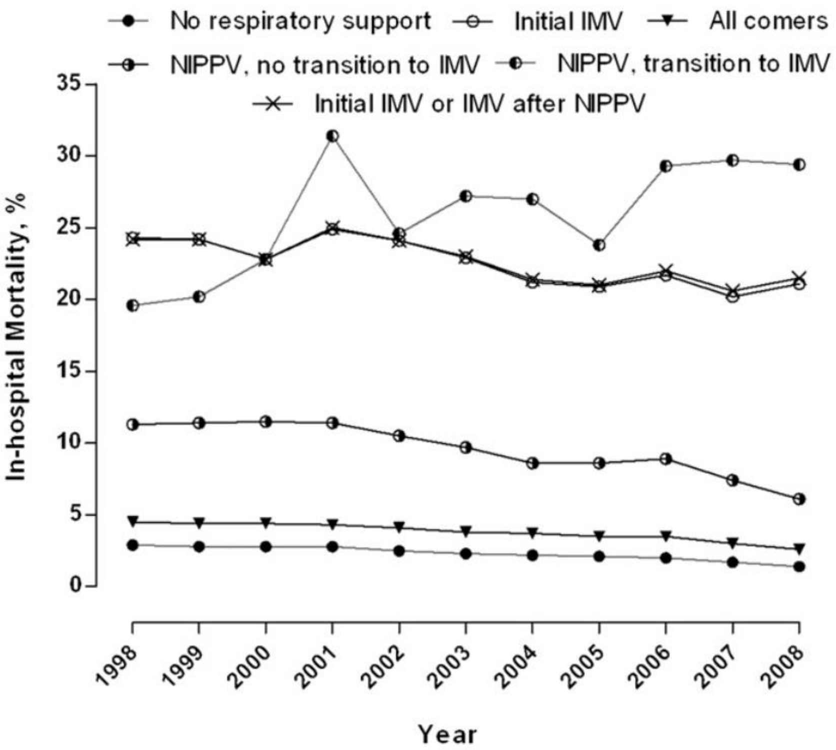
NIV failure in COPD AE : high mortality

Outcomes of Noninvasive Ventilation for Acute Exacerbations of Chronic Obstructive Pulmonary Disease in the United States, 1998–2008

Divay Chandra[1]*, Jason A. Stamm[1]*, Brian Taylor[2], Rose Mary Ramos[1], Lewis Satterwhite[2], Jerry A. Krishnan[3], David Mannino[4], Frank C. Sciurba[1], and Fernando Holguín[1]





NIV to IMV

NIV only

AJRCCM. 2012;185(2):152-9

NIV failure in COPD AE : Technical issues

Table 3 Technical issues: a guide for when NIV is failing

Problem	Cause(s)	Solution (s)
Ventilator cycling independently of patient effort	Inspiratory trigger sensitivity is too high Excessive mask leak	Adjust trigger Reduce mask leak
Ventilator not triggering despite visible patient effort	Excessive mask leak Inspiratory trigger sensitivity too low	Reduce mask leak Adjust trigger For NM patients consider switch to PCV
Inadequate chest expansion despite apparent triggering	Inadequate Tidal volume	Increase IPAP. In NM or chest wall disease consider longer Ti
Chest/abdominal paradox	Upper airway obstruction	Avoid neck flexion Increase EPAP
Premature expiratory effort by patient	Excessive Ti or IPAP	Adjust as necessary

BTS/ICS guideline
Thorax. 2016;71 Suppl 2:ii1-35.

Home NIV in post-AE COPD

JAMA | Original Investigation

Effect of Home Noninvasive Ventilation With Oxygen Therapy vs Oxygen Therapy Alone on Hospital Readmission or Death After an Acute COPD Exacerbation
A Randomized Clinical Trial

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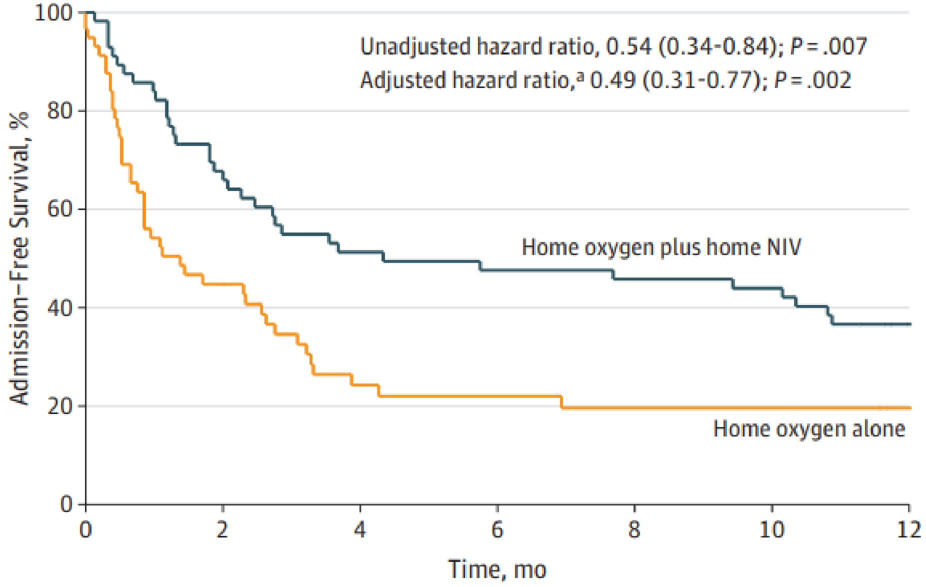
- N= 116, Persistent hypercapnia ($PaCO_2$ > 53mmHg) 2-4weeks after respiratory acidosis resolution
- O_2 + NIV (IPAP : EPAP 24:4, backup RR 14) vs. O_2 alone
- Mean $PaCO_2$ = 59mmHg
- NIV for at least 6 hours nightly → median 7.6 hours

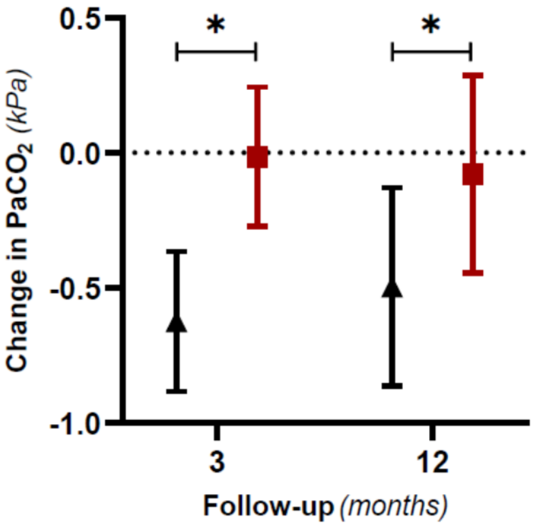
Time to Readmission or Death



No. at risk							
Home oxygen plus home NIV	57	37	28	26	25	24	16
Home oxygen alone	59	23	11	10	8	8	6

JAMA 2017;317(21): 2177-86

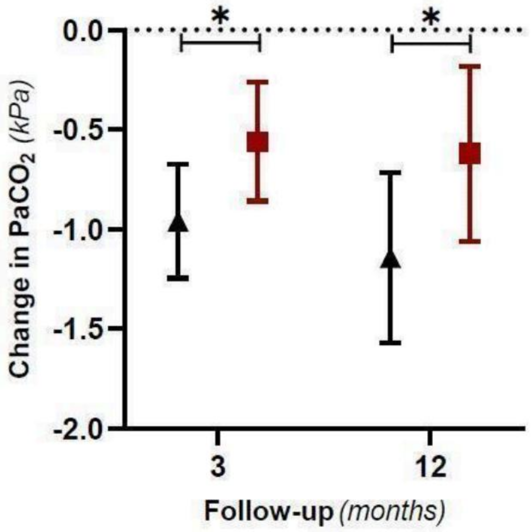
Home NIV in post-AE COPD



Chronic non-invasive ventilation compared to standard treatment following a severe exacerbation for people with severe COPD						
Patient or population: post-exacerbation COPD **Setting**: home treatment **Intervention**: NIV **Comparison**: Standard care						
Outcomes	**Anticipated absolute effects* (95% CI)**		**Relative effect (95% CI)**	**№ of participants (studies)**	**Certainty of the evidence (GRADE)**	**Comments**
	Risk with Standard care	**Risk with NIV**				
Admission-free survival follow up: 1 year	Study population		**HR 0.71** (0.54 to 0.94) [readmission or death] [h]	317 (2 RCTs)	⊕⊕⊝⊝ LOW [e, i, j]	The evidence suggests chronic NIV improves admission-free survival (number needed to treat for an additional beneficial outcome 12, 95% CI 7 to 61).
	333 per 1000	**458 per 1000** (356 to 552)				
All-cause mortality follow up: median 21 months	Study population		**HR 0.97** (0.74 to 1.28) [All-cause mortality] [h]	318 (2 RCTs)	⊕⊕⊝⊝ LOW [c, d]	The evidence suggests that chronic NIV does not improve all-cause mortality.
	642 per 1000	**631 per 1000** (532 to 731)				

Cochrane Database of Systematic Reviews 2021

Home NIV in stable COPD



Chronic non-invasive ventilation compared to standard treatment for people with stable COPD						
Patient or population: stable COPD **Setting**: home treatment **Intervention**: NIV **Comparison**: Standard care						
Outcomes	**Anticipated absolute effects*** **(95% CI)**		**Relative effect (95% CI)**	**№ of participants (studies)**	**Certainty of the evidence (GRADE)**	**Comments**
	Risk with Standard care	**Risk with NIV**				
All-cause mortality follow up: median 30 months	Study population		**HR 0.75** (0.58 to 0.97) [All-cause mortality] k	405 (3 RCTs)	⊕⊕⊕⊝ MODERATE c, d	Chronic NIV likely reduces all-cause mortality (number needed to treat for an additional beneficial outcome 14, 95% CI 8 to 120).
	655 per 1000	**550 per 1000** (461 to 644)				

Cochrane Database of Systematic Reviews 2021

Home NIV : mortality benefit in stable COPD

ORIGINAL ARTICLE
https://doi.org/10.4046/trd.2021.0062
ISSN: 1738-3536(Print)/2005-6184(Online) • Tuberc Respir Dis 2022;85:47-55

The Long-term Efficacy of Domiciliary Noninvasive Positive-Pressure Ventilation in Chronic Obstructive Pulmonary Disease: A Meta-Analysis of Randomized Controlled Trials

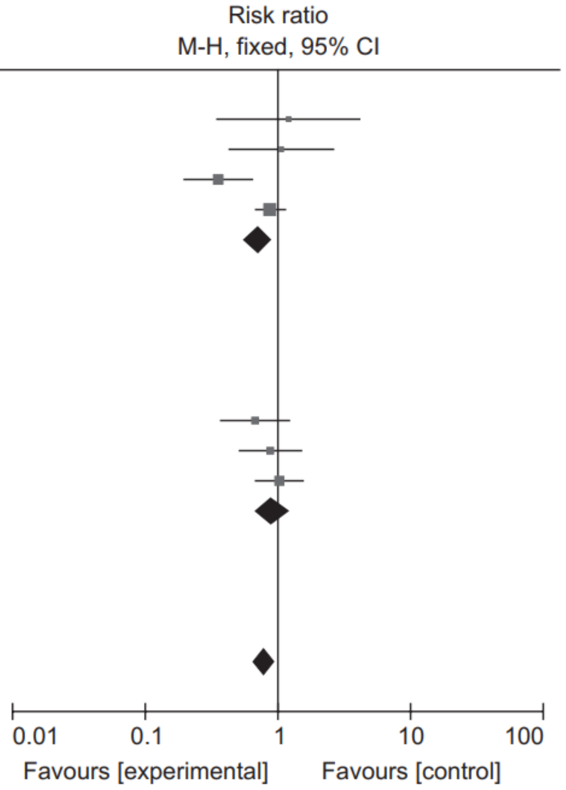
trd Tuberculosis & Respiratory Diseases

Stable COPD
↓ 29% death

Post AE COPD
= death

Total COPD
↓ 21% death

Study or subgroup	NIPPV Events	NIPPV Total	Control Events	Control Total	Weight (%)	Risk ratio M-H, fixed, 95% CI
1.3.1 Stable COPD						
Casanova (2000)	4	20	4	24	2.4	1.20 [0.34, 4.20]
Clini (2002)	7	39	8	47	4.8	1.05 [0.42, 2.65]
Kohnlein (2014)	12	102	31	93	21.5	0.35 [0.19, 0.65]
McEvoy (2009)	40	72	46	72	30.5	0.87 [0.66, 1.14]
Subtotal (95% CI)		233		236	59.2	0.71 [0.56, 0.91]
Total events	63		89			
Heterogeneity: Chi^2=8.68, df=3 (p=0.03); I^2=65%						
Test for overall effect: Z=2.73 (p=0.006)						
1.3.2 Post hopital COPD						
Cheung (2010)	9	23	14	24	9.1	0.67 [0.36, 1.24]
Murphy (2017)	16	57	19	59	12.4	0.87 [0.50, 1.52]
Struik (2014)	30	101	29	100	19.3	1.02 [0.67, 1.57]
Subtotal (95% CI)		181		183	40.8	0.90 [0.67, 1.21]
Total events	55		62			
Heterogeneity: Chi^2=1.25, df=2 (p=0.54); I^2=0%						
Test for overall effect: Z=0.70 (p=0.48)						
Total (95% CI)		414		419	100.0	0.79 [0.65, 0.95]
Total events	118		151			
Heterogeneity: Chi^2=9.95, df=6 (p=0.13); I^2=40%						
Test for overall effect: Z=2.47 (p=0.01)						
Test for subgroup differences: Chi^2=1.43, df=1 (p=0.23); I^2=30.2%						



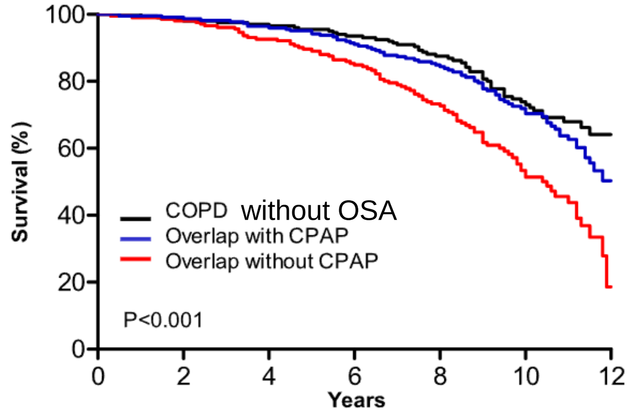
TRD (Seoul) 2022; **85**(1): 47-55.

NIV in stable COPD + OSA

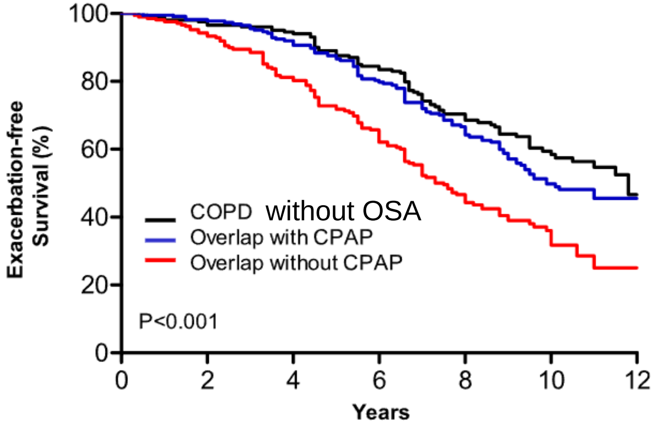
Outcomes in Patients with Chronic Obstructive Pulmonary Disease and Obstructive Sleep Apnea

The Overlap Syndrome

Jose M. Marin[1,2]*, Joan B. Soriano[2,3]*, Santiago J. Carrizo[1]*, Ana Boldova[1]*, and Bartolome R. Celli[4]*



No at risk							
COPD	210	203	196	184	144	89	10
Overlap with CPAP	228	223	215	201	167	97	8
Overlap without CPAP	213	204	186	161	121	57	3



No at risk							
COPD	210	199	189	158	107	47	6
Overlap with CPAP	228	222	202	168	114	41	5
Overlap without CPAP	213	197	165	124	66	24	2

AJRCCM 2010; 182(3): 325-31.

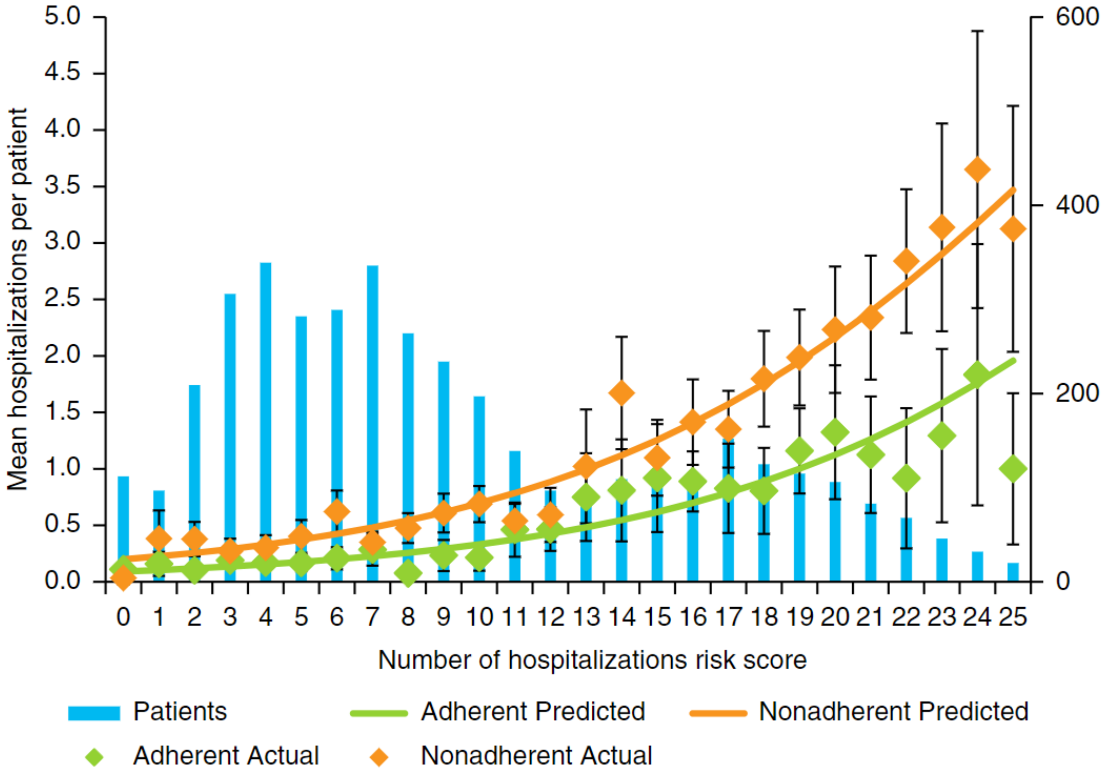
NIV in stable COPD + OSA

ORIGINAL ARTICLE

Impact of Positive Airway Pressure Therapy Adherence on Outcomes in Patients with Obstructive Sleep Apnea and Chronic Obstructive Pulmonary Disease

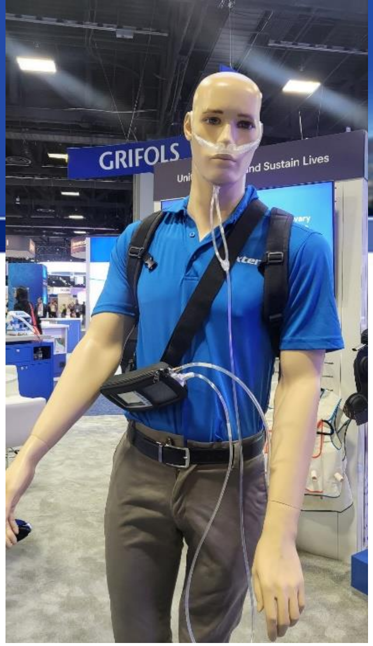
Kimberly L. Sterling[1], Jean-Louis Pépin[2], Walter Linde-Zwirble[3], Jiaming Chen[1], Adam V. Benjafield[4], Peter A. Cistulli[5], Kate V. Cole[1], Hussein Emami[1], Caleb Woodford[6], Jeff P. Armitstead[4], Carlos M. Nunez[1], Jadwiga A. Wedzicha[7], and Atul Malhotra[8]; on behalf of the medXcloud group

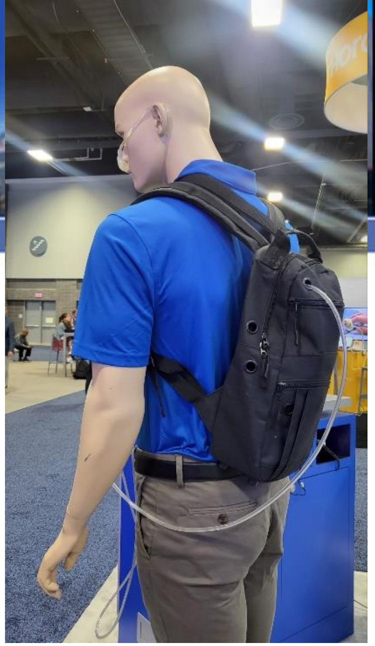
Resource Usage (Mean Number per Patient)	**Matched**		
	Adherent (*n* = 712)	**Nonadherent (*n* = 712)**	***P* Value**
Year before PAP			
Doctor visits	15.80	17.65	0.01
Emergency room visits	1.75	1.89	0.59
Inpatient hospitalizations	0.51	0.50	0.67
PAP Year 1			
Doctor visits	16.71	17.37	0.33
Emergency room visits	1.25	1.83	<0.001
Inpatient hospitalization	0.24	0.46	<0.001
PAP Year 2			
Doctor visits	15.43	15.71	0.37
Emergency room visits	1.16	1.70	<0.001
Inpatient hospitalizations	0.21	0.42	<0.001



AJRCCM 2022;206(2): 197-205

NIV in stable COPD : Ambulatory NIV





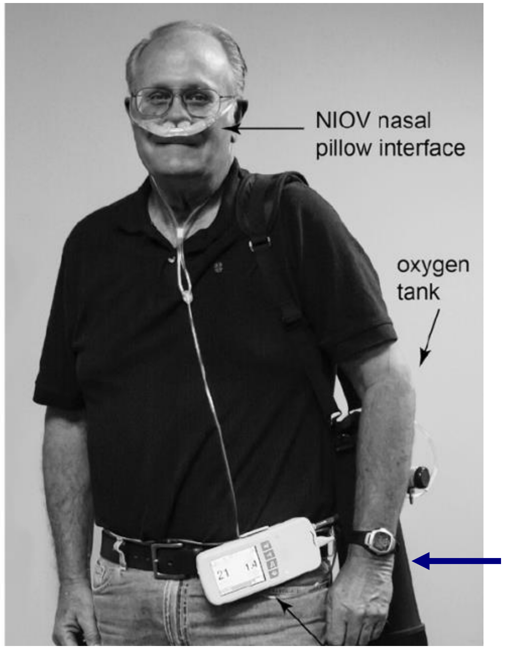
Physiologic Effects of an Ambulatory Ventilation System in Chronic Obstructive Pulmonary Disease

Janos Porszasz[1], Robert Cao[1], Richard Morishige[2], Leo A. van Eykern[3], Alex Stenzler[4], and Richard Casaburi[1]

- N= 15, mean FEV_1 32.2%, exertional SpO_2 86.5%
- Constant work rate (CWR) cycle ergometer exercise

TABLE 5. PHYSIOLOGIC RESPONSES TO CONSTANT WORK RATE EXERCISE AT LIMIT OF TOLERANCE

	CWR (V1)	Room Air (V2 and V3)	NIOV+Air (V2 and V3)	O_2 Cannula (V4)	NIOV + O_2 (V2, V3, and V4)
Scalene EMG, μV·s	n/a	9.7 ± 6.8	9.5 ± 7.0	7.7 ± 6.5	6.8 ± 5.1*†
Intercostal EMG, μV·s	n/a	3.8 ± 3.1	3.3 ± 2.3	3.7 ± 3.3	2.8 ± 2.3*
Diaphragmatic EMG, μV·s	n/a	5.1 ± 2.3	5.3 ± 2.2	4.1 ± 2.3*†	4.0 ± 2.2*†
Fb, breaths/min	33.8 ± 9.8	28.8 ± 7.8‡	26.7 ± 7.3‡	27.1 ± 7.8‡	26.6 ± 6.7‡
Heart rate, beats/min	125 ± 17	118 ± 14‡	120 ± 13‡	120 ± 17	119 ± 13
Sp_{O_2}, %	85.1 ± 3.4	86.0 ± 2.9	85.9 ± 4.1	91.2 ± 4.2*†‡	97.4 ± 1.8*†‡§
TcP_{CO_2}, mm Hg	47.3 ± 6.7	46.3 ± 7.6	44.8 ± 7.0	43.5 ± 4.5	47.5 ± 7.4
Borg CR10 score	6.7 ± 2.3	6.6 ± 2.5	6.3 ± 2.5	6.3 ± 3.6	6.1 ± 2.9
T_{lim}, min	5.1 ± 1.1	5.6 ± 1.9	6.3 ± 4.1	11.4 ± 6.8*†‡	17.6 ± 5.7*†‡§



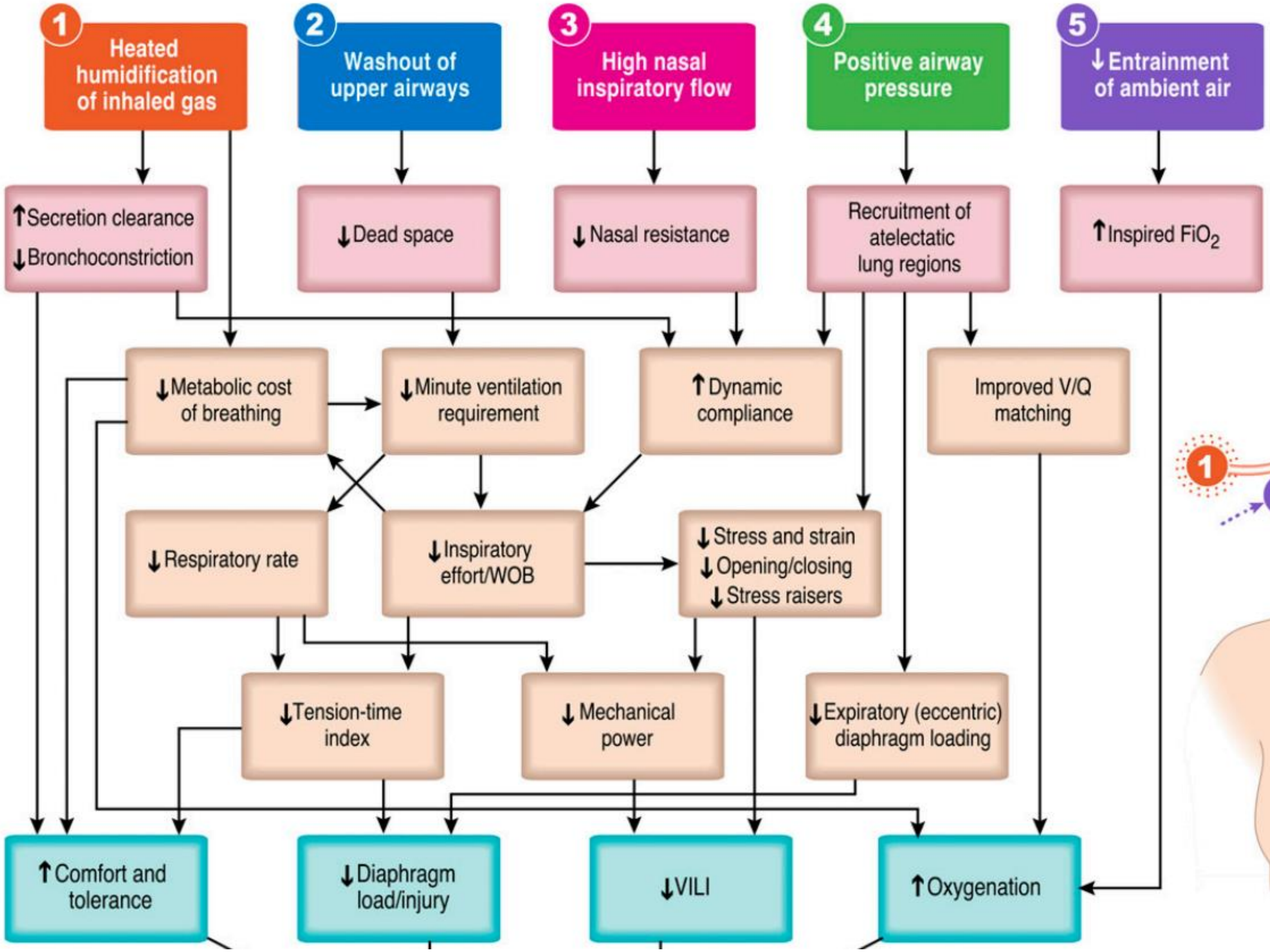
0.45kg

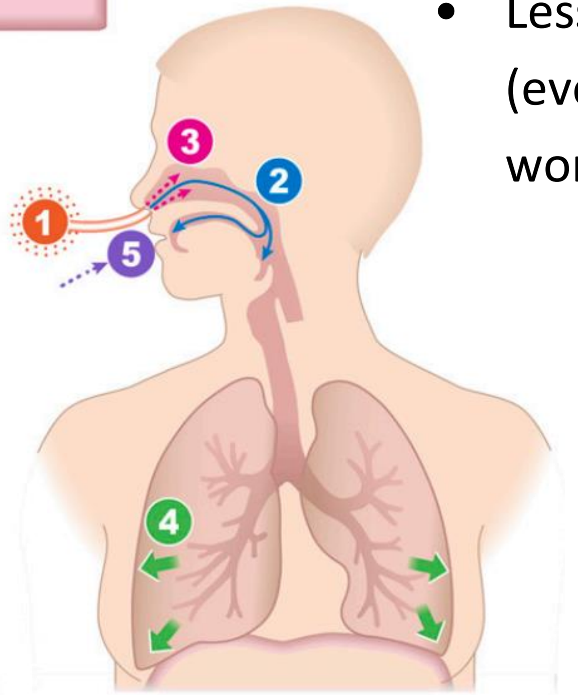
AJRCCM 2013;188(3):334–342.

Contents

- Long-term Oxygen Therapy (LTOT)
- Non-invasive ventilation (NIV)
- **High-flow nasal cannula (HFNC)**

HFNC





- Physiologic benefits
- Avoid adverse event of IMV
- Patients' comfort
- Less resource required (even in terms of healthcare workload)

AJRCCM 2017;195(9):1128-1131.

HFNC (vs. NIV) in COPD AE

ORIGINAL ARTICLE

WILEY

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

Myoung Kyu Lee[1] | Jaehwa Choi[1] | Bonil Park[1] | Bumjoon Kim[1] | Seok Jeong Lee[1] | Sang-Ha Kim[1] | Suk Joong Yong[1] | Eun Hee Choi[2] | Won-Yeon Lee[1]

- Single center prospective observational study (not RCT) in Korea
- N = 88 (NIV:HFNC = 1:1)
- COPD AE with PF ratio < 200, $PaCO_2$ > 45 mm Hg, pH 7.25 – 7.35

Clin Respir J. 2018;12(6):2046-2056

HFNC (vs. NIV) in COPD AE

Variables	Total (n = 88)	HFNC (n = 44)	NIV (n = 44)	P value
Clinical, median (IQR)				
Mean BP (mm Hg)	92.3 (79.5–108.7)	90.5 (79.2–101.0)	99.5 (81.7–113.7)	.242
PR (beats/minute)	106.5 (93.25–120)	106 (89.5–119.5)	106.5 (94.5–120)	.277
RR (1/minute)	24 (20.5–28)	24 (20–28)	24 (22–29)	.235
Laboratory, mean ± SD[a]				
Oxygen saturation (%)	89.1 ± 3.1	88.9 ± 3.0	88.2 ± 3.2	.660
pH	7.32 ± 0.03	7.32 ± 0.28	7.31 ± 0.29	.595
PaO_2/FiO_2 (mm Hg)	134.6 ± 7.4	134.8 ± 7.3	134.5 ± 7.5	.877
$paCO_2$ (mm Hg)	54.5 ± 9.6	56.4 ± 10.1	52.6 ± 8.8	.067
Hb (g/dL)	12.7 ± 2.2	12.5 ± 2.5	12.9 ± 1.7	.342
Albumin (g/dL)	3.4 ± 0.5	3.4 ± 0.5	3.4 ± 0.5	.983
hs-CRP (mg/dL)	8.6 ± 8.5	8.9 ± 8.0	8.2 ± 9.0	.678
Functional (before an admission)				
FEV_1 (%)	51.0 ± 18.9	52.8 ± 21.2	49.1 ± 16.3	.364
FVC (%)	72.0 ± 20.4	73.8 ± 21.1	70.3 ± 19.7	.418
FEV_1/FVC (%)	49.9 ± 13.2	49.1 ± 13.4	50.6 ± 13.1	.591
$FEF_{25\%-75\%}$	28.4 ± 21.6	26.8 ± 22.3	29.9 ± 21.0	.508

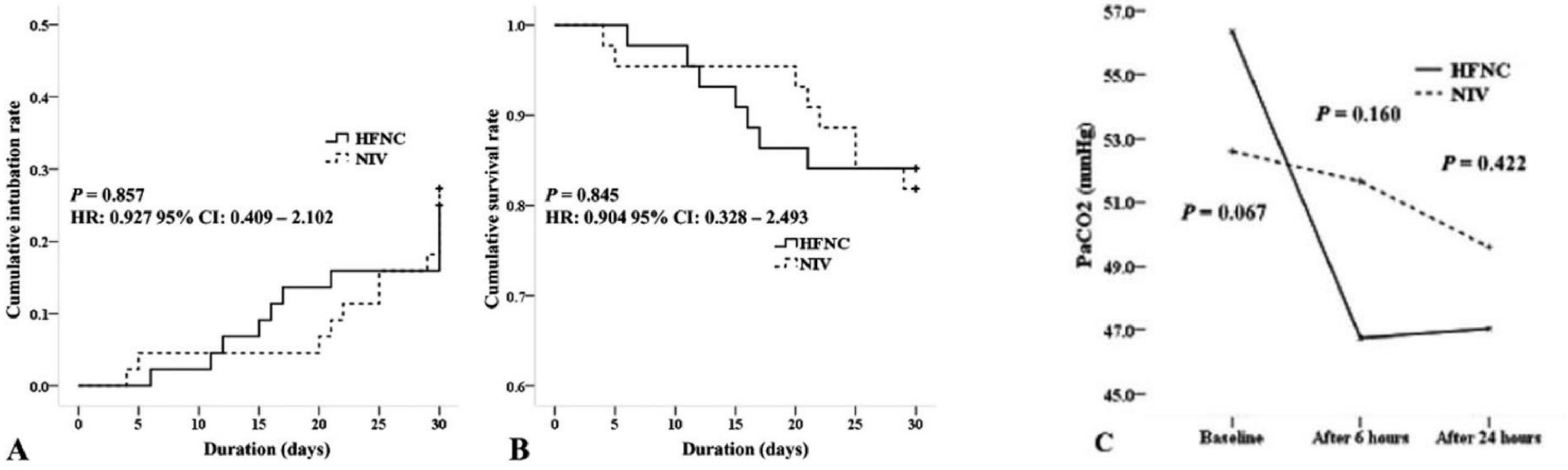
Clin Respir J. 2018;12(6):2046-2056

HFNC (vs. NIV) in COPD AE

Intubation

Mortality

$PaCO_2$

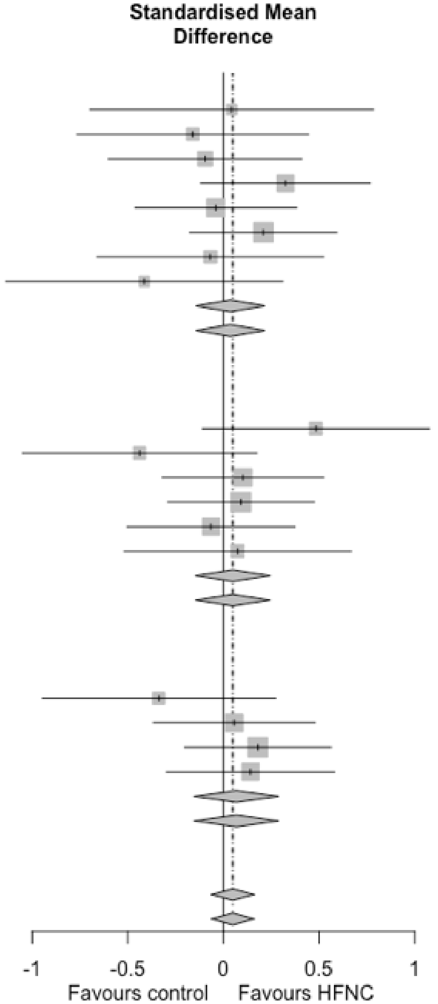


Clin Respir J. 2018;12(6):2046-2056

HFNC (vs. NIV) in COPD AE : $PaCO_2$ removal

Study	HFNC Total	HFNC Mean	HFNC SD	NIV Total	NIV Mean	NIV SD	SMD	95%-CI	Weight (fixed)	Weight (random)
≤3h										
Pisani(2017)	14	55.70	10.6000	14	55.20	11.9000	0.04	[-0.70; 0.78]	2.4%	2.4%
Jing, G(2019)	22	54.20	9.4000	20	55.90	11.4000	-0.16	[-0.77; 0.45]	3.5%	3.5%
Longhini(2019)	30	54.67	12.1434	30	55.99	15.0235	-0.10	[-0.60; 0.41]	5.1%	5.1%
Cortegiani(2020)	40	68.20	15.6000	39	63.40	13.6000	0.32	[-0.12; 0.77]	6.6%	6.6%
Tan(2020)	44	54.69	7.4338	42	55.04	9.5948	-0.04	[-0.46; 0.38]	7.3%	7.3%
Cao(2021)	53	59.50	10.6000	52	57.20	11.3000	0.21	[-0.18; 0.59]	8.8%	8.8%
Fang, G(2021)	20	38.20	4.8000	24	38.50	3.8000	-0.07	[-0.66; 0.52]	3.7%	3.7%
Rezaee(2021)	15	56.40	9.9700	15	60.93	11.3000	-0.41	[-1.14; 0.31]	2.5%	2.5%
Fixed effects model	238			236			0.04	[-0.14; 0.22]	39.9%	--
Random effects model							0.04	[-0.14; 0.22]	--	39.9%
Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.69$										
24h										
Zhang(2018)	21	51.70	5.0000	24	48.30	8.2000	0.48	[-0.11; 1.08]	3.7%	3.7%
Jing, G(2019)	22	54.70	4.7000	20	58.90	12.7000	-0.44	[-1.05; 0.17]	3.5%	3.5%
Tan(2020)	44	53.65	6.8973	42	52.96	6.3710	0.10	[-0.32; 0.53]	7.3%	7.3%
Cao(2021)	53	57.80	13.7000	52	56.50	14.4000	0.09	[-0.29; 0.47]	8.9%	8.9%
Ding(2021)	40	45.96	3.1600	40	46.17	3.2200	-0.07	[-0.50; 0.37]	6.8%	6.8%
Fang, G(2021)	20	38.00	9.7000	24	37.20	11.3000	0.07	[-0.52; 0.67]	3.7%	3.7%
Fixed effects model	200			202			0.05	[-0.15; 0.25]	33.7%	--
Random effects model							0.05	[-0.15; 0.25]	--	33.7%
Heterogeneity: $I^2 = 0\%$, $\tau^2 = < 0.0001$, $p = 0.43$										
48h										
Jing, G(2019)	22	56.90	10.0000	20	61.50	16.3000	-0.34	[-0.95; 0.27]	3.5%	3.5%
Tan(2020)	44	52.70	6.7440	42	52.35	5.3731	0.06	[-0.37; 0.48]	7.3%	7.3%
Cao(2021)	53	56.30	11.2000	52	54.30	10.8000	0.18	[-0.20; 0.56]	8.9%	8.9%
Ding(2021)	40	42.54	2.4800	40	42.18	2.5600	0.14	[-0.30; 0.58]	6.8%	6.8%
Fixed effects model	159			154			0.07	[-0.15; 0.29]	26.4%	--
Random effects model							0.07	[-0.15; 0.29]	--	26.4%
Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.54$										
Fixed effects model	**597**			**592**			**0.05**	**[-0.07; 0.16]**	**100.0%**	**--**
Random effects model							**0.05**	**[-0.07; 0.16]**	**--**	**100.0%**

Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.81$
Test for subgroup differences (fixed effect): $\chi^2_2 = 0.04$, df = 2 ($p = 0.98$)
Test for subgroup differences (random effects): $\chi^2_2 = 0.04$, df = 2 ($p = 0.98$)



Heart & Lung 2023; 60:116-126

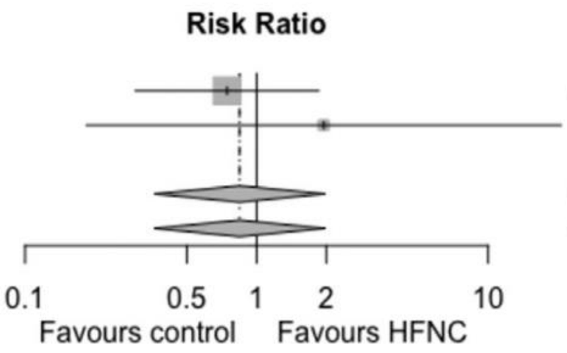
HFNC (vs. NIV) in COPD AE : intubation risk

Risk of intubation (COPD AE)

b

Study	HFNC Events	HFNC Total	NIV Events	NIV Total	RR	95%-CI	Weight (fixed)	Weight (random)
Wang, J(2019)	6	23	7	20	0.75	[0.30; 1.85]	87.0%	87.0%
Cortegiani(2020)	2	40	1	39	1.95	[0.18; 20.64]	13.0%	13.0%
Fixed effects model		**63**		**59**	**0.84**	**[0.36; 1.98]**	**100.0%**	**--**
Random effects model					**0.84**	**[0.36; 1.98]**	**--**	**100.0%**

Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.46$

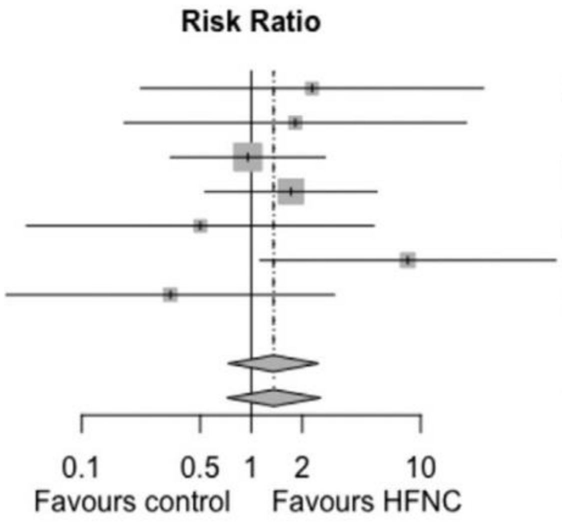


Risk of reintubation (Post intubation)

c

Study	HFNC Events	HFNC Total	NIV Events	NIV Total	RR	95%-CI	Weight (fixed)	Weight (random)
Zhang(2018)	2	21	1	24	2.29	[0.22; 23.44]	7.0%	7.3%
Jing, G(2019)	2	22	1	20	1.82	[0.18; 18.55]	7.0%	7.4%
Tan(2020)	6	44	6	42	0.95	[0.33; 2.73]	34.4%	33.1%
Cao(2021)	7	53	4	52	1.72	[0.53; 5.52]	27.8%	27.3%
Ding(2021)	1	40	2	40	0.50	[0.05; 5.30]	6.8%	7.1%
Fang, G(2021)	7	20	1	24	8.40	[1.13; 62.66]	9.4%	9.8%
Xu(2021)	1	50	3	50	0.33	[0.04; 3.10]	7.6%	8.0%
Fixed effects model		**250**		**252**	**1.35**	**[0.73; 2.50]**	**100.0%**	**--**
Random effects model					**1.36**	**[0.72; 2.57]**	**--**	**100.0%**

Heterogeneity: $I^2 = 3\%$, $\tau^2 = 0.0331$, $p = 0.40$



Heart & Lung 2023; 60:116-126

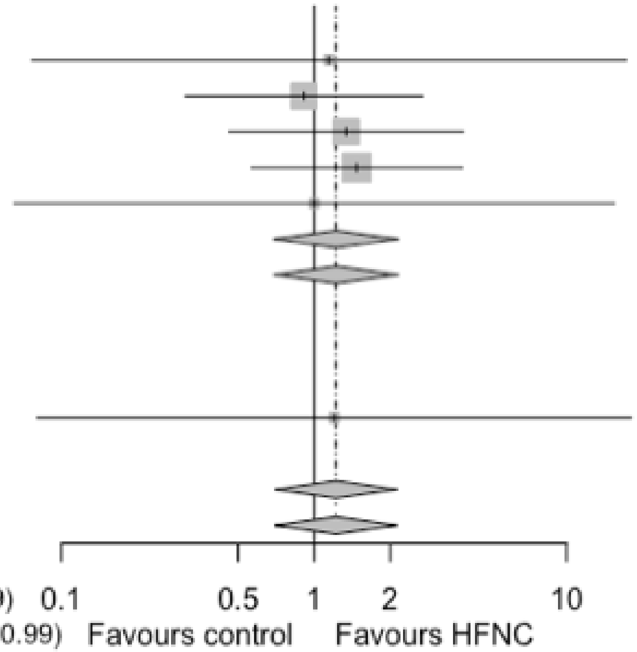
HFNC (vs. NIV) in COPD AE : mortality

Study	HFNC Events	HFNC Total	NIV Events	NIV Total	RR	95%-CI	Weight (fixed)	Weight (random)
28-day mortality								
Zhang(2018)	1	21	1	24	1.14	[0.08; 17.16]	4.2%	4.2%
Jing, G(2019)	5	22	5	20	0.91	[0.31; 2.68]	26.5%	26.5%
Tan(2020)	7	44	5	42	1.34	[0.46; 3.88]	27.2%	27.2%
Cao(2021)	9	53	6	52	1.47	[0.56; 3.84]	33.7%	33.7%
Ding(2021)	1	40	1	40	1.00	[0.06; 15.44]	4.1%	4.1%
Fixed effects model		180		178	1.22	[0.69; 2.15]	95.8%	--
Random effects model					1.22	[0.69; 2.15]	--	95.8%
Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.98$								
In-hospital mortality								
Fang, G(2021)	1	20	1	24	1.20	[0.08; 17.99]	4.2%	4.2%
Fixed effects model		**200**		**202**	**1.22**	**[0.70; 2.13]**	**100.0%**	**--**
Random effects model					**1.22**	**[0.70; 2.13]**	**--**	**100.0%**

Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.99$

Test for subgroup differences (fixed effect): $\chi^2_1 = 0.00$, df = 1 ($p = 0.99$)

Test for subgroup differences (random effects): $\chi^2_1 = 0.00$, df = 1 ($p = 0.99$)



28-day

In-hospital

Heart & Lung 2023; 60:116-126

HFNC (vs. NIV) in COPD AE : Recommendation

EUROPEAN RESPIRATORY JOURNAL
ERS OFFICIAL DOCUMENTS
S. OCZKOWSKI ET AL.

ERS clinical practice guidelines: high-flow nasal cannula in acute respiratory failure

HFNC in hypercapnic respiratory failure

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

Recommendation 8

We suggest a trial of NIV prior to use of HFNC in patients with COPD and acute hypercapnic respiratory failure (conditional recommendation, low certainty of evidence).

This is insufficient to make a recommendation in favour of HFNC, given the high-certainty evidence for the use of NIV in COPD, and that more evidence would be required before HFNC could be considered equivalent or superior to NIV.

Eur Respir J 2022; 59(4): 2101574

HFNC (vs. O_2) in COPD AE

Xia *et al. Critical Care* (2022) 26:109
https://doi.org/10.1186/s13054-022-03973-7

Critical Care

RESEARCH Open Access

High-flow nasal cannula versus conventional oxygen therapy in acute COPD exacerbation with mild hypercapnia: a multicenter randomized controlled trial

- Multi-center (17 tertiary hospitals) RCT in China
- N =337, COPD AE with mild hypercapnia ($PaCO_2$ > 45 mm Hg and pH ≥ 7.35)
- Primary outcome : Intubation during hospitalization
- Secondary outcome : Intolerance and need for NIV or IMV, LOS, hospital cost, mortality, readmission

Crit Care. 2022;26(1):109.

HFNC (vs. O_2) in COPD AE

Characteristic	No. (%)		Absolute difference, % (95%CI)	*P*
	High-flow nasal cannula group (*n* = 158)	Conventional oxygen therapy group (*n* = 172)		
Primary outcome				
Criteria for intubation, No. (%)	4 (2.5%)	1 (0.6%)	1.95 (− 0.8–4.7)	0.198*
Secondary outcome				
Treatment failure, No. (%)	25 (15.8%)	25 (14.5%)	1.29 (− 6.5–9.0)	0.745*
Intubation, No. (%)	3 (1.9%)	1 (0.6%)	1.95 (− 0.8–4.7)	0.353*
NPPV, No. (%)	15 (9.5%)	22 (12.8%)	− 3.3 (− 10.1–3.5)	0.343*
Duration of NPPV, median (IQR), days	6.0 (2.0–10.0)	5.5 (4.0–8.0)	1.0 (− 2.7–4.7)	0.780†
Mortality in hospital, No. (%)	0 (0%)	1 (0.6%)		> 0.999*
Mortality at day 90, No. (%)	5/153 (3.3%)	5/171 (2.9%)	0.34 (− 3.4–4.1)	> 0.999*
Length of hospital stay, median (IQR), days	9.0 (7.0–13.0)	8.0 (7.0–11.0)	1.0 (0.0–2.0)	0.021†
Hospital cost, median (IQR), $	2298 (1613–3782)	2005 (1439–2968)	265 (− 104–632)	0.006†
Readmission rate at day 90, No. (%)	25/153 (16.3%)	23/170 (13.5%)	2.8 (− 5.0–10.6)	0.478*

Crit Care. 2022;26(1):109.

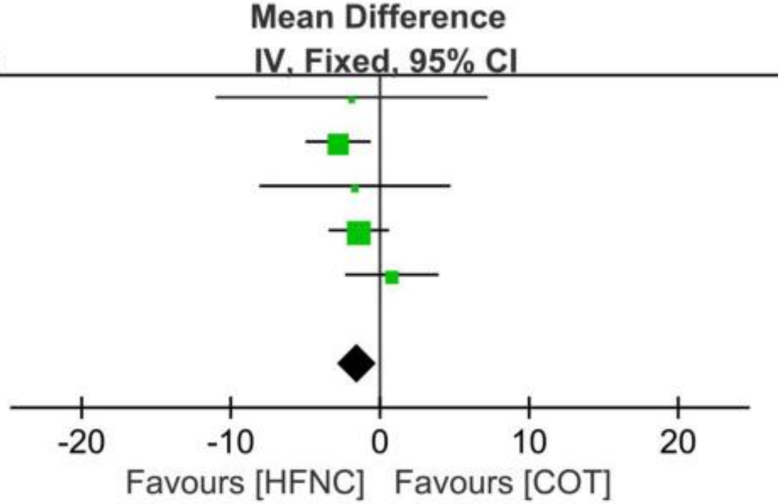
HFNC (vs. O_2) in COPD AE : $PaCO_2$ removal

(A) acute

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
Di Mussi 2018 [20]	49.9	11.9	14	51.8	12.7	14	2.0%	-1.90 [-11.02, 7.22]
Li 2020 [4]	54.1	9.8	160	56.9	10.1	160	35.5%	-2.80 [-4.98, -0.62]
Longhini 2019 [13]	54.67	12.1	30	56.35	13.2	30	4.1%	-1.68 [-8.09, 4.73]
Xia 2022 [14]	51.18	9.2	158	52.6	9.57	172	41.2%	-1.42 [-3.45, 0.61]
Yang 2019 [23]	47	7.3	35	46.2	6.2	37	17.2%	0.80 [-2.34, 3.94]
Total (95% CI)			**397**			**413**	**100.0%**	**-1.55 [-2.85, -0.25]**

Heterogeneity: $Chi^2 = 3.44$, df = 4 (P = 0.49); $I^2 = 0\%$

Test for overall effect: Z = 2.34 (P = 0.02)



IJCOPD 2023:18 895–906

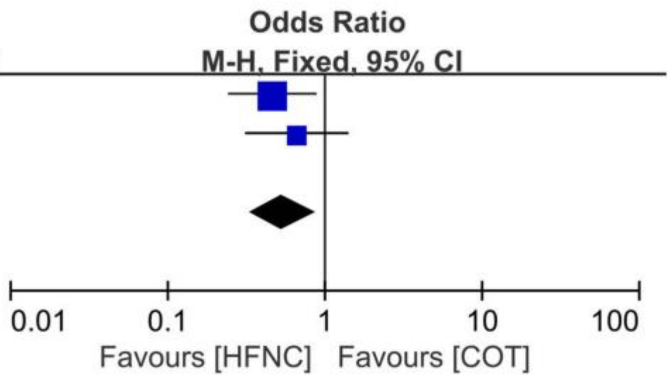
HFNC (vs. O_2) in COPD AE : treatment failure

Treatment failure

(A) treatment failure

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Li 2020[4]	16	160	31	160	62.4%	0.46 [0.24, 0.88]
Xia 2022[14]	12	158	19	172	37.6%	0.66 [0.31, 1.41]
Total (95% CI)		**318**		**332**	**100.0%**	**0.54 [0.33, 0.88]**
Total events	28		50			

Heterogeneity: $Chi^2 = 0.50$, df = 1 (P = 0.48); $I^2 = 0\%$
Test for overall effect: Z = 2.48 (P = 0.01)

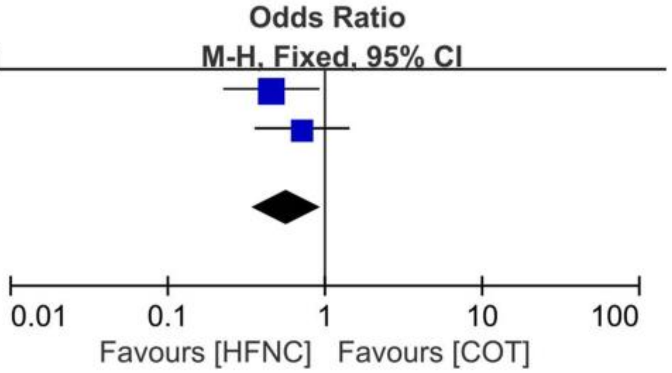


Escalation to NIV

(B) actual upgraded to noninvasive ventilation

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Li 2020[4]	13	160	26	160	55.6%	0.46 [0.23, 0.92]
Xia 2022[14]	15	158	22	172	44.4%	0.72 [0.36, 1.43]
Total (95% CI)		**318**		**332**	**100.0%**	**0.57 [0.35, 0.94]**
Total events	28		48			

Heterogeneity: $Chi^2 = 0.79$, df = 1 (P = 0.37); $I^2 = 0\%$
Test for overall effect: Z = 2.23 (P = 0.03)



IJCOPD 2023:18 895–906

Home HFNC (vs. O_2) in stable COPD

ORIGINAL ARTICLE

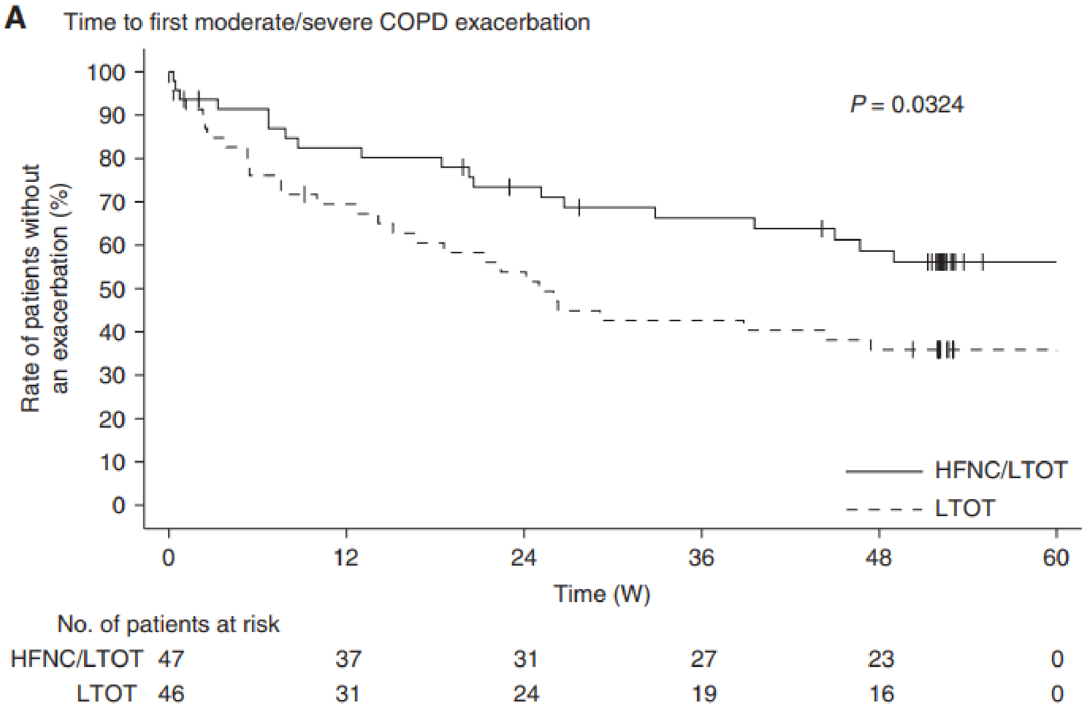
Home High-Flow Nasal Cannula Oxygen Therapy for Stable Hypercapnic COPD
A Randomized Clinical Trial

- Multi-center (42 hospitals) RCT in Japan
- N =104, Stable COPD with daytime hypercapnia ($PaCO_2$ ≥ 45 mm Hg and pH ≥ 7.35) receiving LTOT (≥ 16hours/day) for at least 1 month + History of AE within 1 year
- LTOT vs. LTOT/HFNC (HFNC for ≥ 4 h/night during sleep at flow rates of 30–40 L/min → mean 7.3 h)
- Primary outcome : Moderate or severe exacerbation rate.
- Secondary outcome : ABGA, lung function, HRQoL, 6MWT, Intubation during hospitalization

AJRCCM 2022;206(11):1326-1335

Home HFNC (vs. O_2) in stable COPD

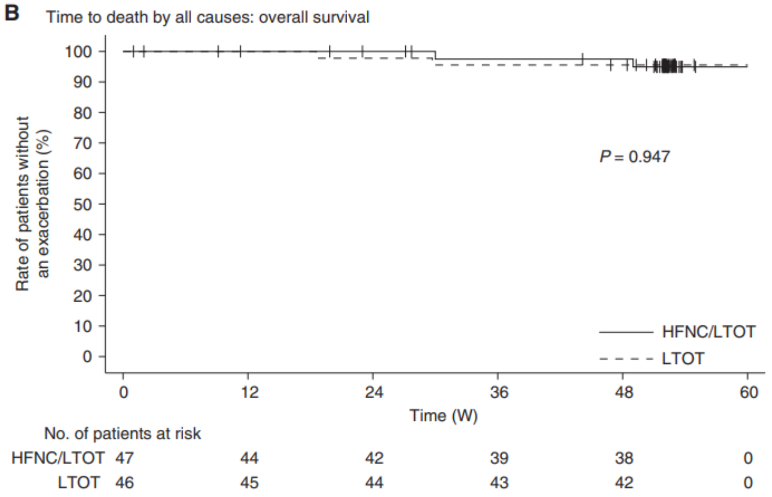
Endpoints	Items	Statistics	HFNC/LTOT (*n* = 47)	*n*	LTOT (*n* = 46)	*n*	*P* Values
Primary	COPD exacerbation rate (moderate/ severe)	Ratio of the mean count (95% CI)	Reference level		2.85 (1.48–5.47)		0.002
		Unadjusted mean count (SD)	1.0 (1.8)		2.5 (3.8)		



Median time to first mod or severe AE
= 25 weeks in LTOT << Not met in HFNC/LTOT group

AJRCCM 2022;206(11):1326-1335

Home HFNC (vs. O_2) in stable COPD



Endpoints	Items	Statistics	HFNC/LTOT ($n = 47$)	n	LTOT ($n = 46$)	n	P Values
Primary	COPD exacerbation rate (moderate/severe)	Ratio of the mean count (95% CI)	Reference level		2.85 (1.48–5.47)		0.002
		Unadjusted mean count (SD)	1.0 (1.8)		2.5 (3.8)		
Secondary	COPD exacerbation rate (severe)	Ratio of the mean count (95% CI)	Reference level		1.54 (0.74–3.22)		0.250
		Unadjusted mean count (SD)	0.3 (0.5)		0.5 (0.9)		
	COPD exacerbation rate (all)	Ratio of the mean count (95% CI)	Reference level		1.40 (0.91–2.16)		0.126
		Unadjusted mean count (SD)	3.8 (4.0)		5.3 (4.4)		
	Modified MRC scale score at 52 wk	Count	Grade 0	0	Grade 0	0	0.922
			Grade 1	2	Grade 1	3	
			Grade 2	10	Grade 2	9	
			Grade 3	17	Grade 3	21	
			Grade 4	7	Grade 4	7	
	Sp_{O_2}, %*	LSM (SE)	1.01 ± 0.33%	37	−0.20 ± 0.32%	40	0.010
	pH†	Sample mean (SD)	7.38 (0.03)	37	7.38 (0.04)	38	0.118
		Difference‡	0.00 (0.03)	37	−0.01 (0.03)	38	
	Pa_{CO_2}†	Sample mean (SD)	50.87 (8.28)	37	51.65 (8.57)	38	0.520
		Difference‡	0.54 (7.23)	37	1.54 (6.13)	38	
	Pa_{O_2}†	Sample mean (SD)	84.82 (23.36)	37	77.37 (14.53)	38	0.063
		Difference‡	4.21 (26.51)	37	−7.04 (24.94)	38	
	VC†	Sample mean (SD)	2.24 (0.50)	36	2.27 (0.61)	39	0.351
		Difference‡	−0.04 (0.27)	35	0.03 (0.33)	36	
	FVC†	Sample mean (SD)	2.05 (0.56)	36	2.07 (0.63)	39	0.888
		Difference‡	−0.02 (0.31)	35	−0.03 (0.33)	38	
	FEV_1†	Sample mean (SD)	0.66 (0.25)	36	0.65 (0.21)	39	0.265
		Difference‡	0.00 (0.07)	35	−0.02 (0.08)	39	
	D_{LCO}†	Samplex mean (SD)	6.90 (2.21)	30	6.18 (3.32)	28	0.850
		Difference‡	−0.35 (1.68)	21	−0.46 (2.04)	15	
	6-min-walk distance†	Sample mean (SD)	238.5 (88.62)	32	222.25 (109.96)	36	0.177
		Difference‡	8.80 (72.17)	31	−12.85 (55.34)	34	
	Time to NIV†	Sample mean (SD)	188.0 ± 8.9	3	234.7 ± 178.3	3	NA

AJRCCM 2022;206(11):1326-1335

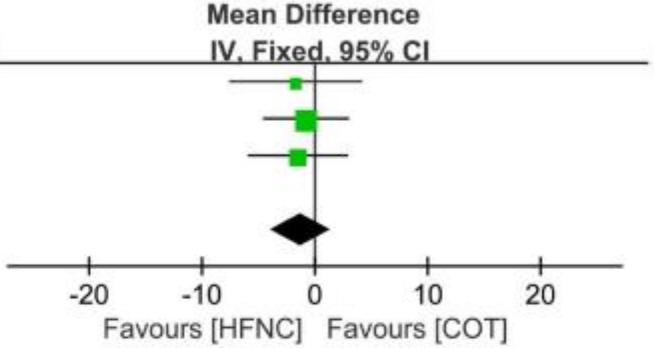
Home HFNC (vs. O_2) in stable COPD

$PaCO_2$

(B) chronic

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
Nagata 2018[21]	50.9	8.4	13	52.6	7.6	16	19.5%	-1.70 [-7.59, 4.19]
Nagata 2022[2]	50.87	8.28	37	51.65	8.6	38	46.3%	-0.78 [-4.60, 3.04]
Storgaard 2020[22]	54	10.5	31	55.5	8.25	43	34.2%	-1.50 [-5.94, 2.94]
Total (95% CI)			**81**			**97**	**100.0%**	**-1.21 [-3.81, 1.39]**

Heterogeneity: Chi² = 0.09, df = 2 (P = 0.96); I² = 0%
Test for overall effect: Z = 0.91 (P = 0.36)

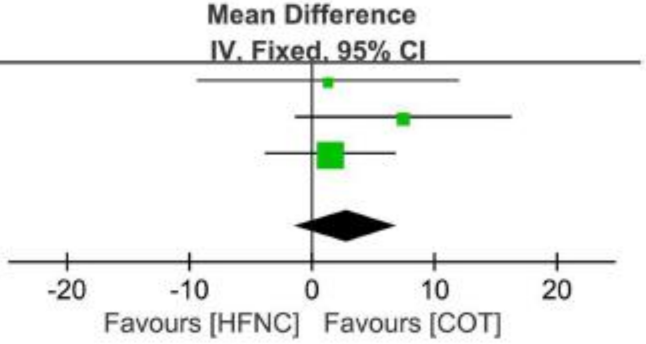


PaO_2

(B) chronic

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
Nagata 2018[21]	80.9	12.7	13	79.6	16.7	16	15.4%	1.30 [-9.41, 12.01]
Nagata 2022[2]	84.82	23.4	37	77.37	14.53	38	22.6%	7.45 [-1.39, 16.29]
Storgaard 2020[22]	72.75	11.25	31	71.25	12	43	62.0%	1.50 [-3.84, 6.84]
Total (95% CI)			**81**			**97**	**100.0%**	**2.81 [-1.39, 7.02]**

Heterogeneity: Chi² = 1.37, df = 2 (P = 0.51); I² = 0%
Test for overall effect: Z = 1.31 (P = 0.19)



Heart & Lung 2023; 60:116-126

Summary

- Long-term Oxygen Therapy (LTOT)
  - Survival benefit in patients with severe resting hypoxemia (not with moderate hypoxemia)
  - Isolated severe exertional hypoxemia
- Non-invasive ventilation (NIV)
  - 1st recommended treatment for respiratory support in AE COPD with hypercapnia
  - Mortality benefit in stable COPD
  - Ambulatory NIV
- High-flow nasal cannula (HFNC)
  - Possible alternative to NIV in AE COPD (currently, insufficient evidence)
  - Superior to conventional O2 in AE COPD and stable COPD

경청해 주셔서 감사합니다.

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