

GRADE Evidence Profile- Section 1

PICO 1a) Does long-term NIV as compared to best practice without NIV in *stable severe* COPD patients result in improved:

Quality assessment							Summary of findings					Importance
No of studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other considerations (eg, publication bias)	No of patients		Effect		Quality	
							Intervention	Control	Relative (95% CI)	Absolute		
Outcome #1 Dyspnea												
7	RCT	Serious ¹	Serious	No	Serious	No	2 studies negative (Zhou, Marquez) , 5 positive (at least some timepoints - Casanova, Clini, Bhatt, Garrod, Duiverman MRC)				Very Low	6
Outcome #2 Health-related QoL:												
10	RCT	Serious ¹	Serious	No	Serious ²	No	SF-36 no diff except subscales (Kohnlein); subscales worse in McEvoy; CAT trend toward improved(Zhou); SGRQ (MCID 4) better in Kohnlein (delta 5.8), Meecham Jones, Oscroft – deterioration in NPPV- c/w NPPV+, unchanged in Clini or McEvoy; SRI (MCID 0.5) better in Kohnlein (delta 5.6), not better in Zhou shown as % ; CRQ more improved in NIV in (Garrod) not different in Marquez and Bhatt; MRF-28 better in Clini, Duiverman				Very Low	9
Outcome #3 pCO₂												
12	RCT	No	Serious ³	No	No	No	Improved pCO ₂ in 5 studies (Meecham Jones, Duiverman, Kohnlein, Zhou, Marquez) but no change in 7. All studies where improvement occurred had a mean IPAP no less than 17.8 (except Marquez – not provided). Those with no improvement had mean or median IPAP of 16 or less.				Mod	6
Outcome #4 Hospitalization												
4	RCT	Serious ⁴	No	No	Very Serious ⁵	No	No difference				Very Low	9
Outcome #5 Survival												
4	RCT	No	Serious	No	Serious ⁶	No	Kohnlein: one-year survival: p=0.0004; HR 0.24, 95% CI 0.11–0.49; 2 positive studies, largest SS (McEvoy, Kohnlein). 2 neg not powered for mort. (Casanova, Clini)				Low	9

Footnotes:

¹Unblinded, subjective outcomes

²Wide CIs when reported; “trend” p values; positive subscales of QOL tools. Small sample sizes.

³Heterogeneity (which may be due to study population differences)

⁴criteria for hospitalization not described.

GRADE Evidence Profile- Section 1

PICO b) Does long-term NIV as compared to best practice without NIV in COPD patients *post severe exacerbation* result in improved:

Quality assessment							Summary of findings					Importance
No of studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other considerations (eg, publication bias)	No of patients		Effect		Quality	
							Intervention	Control	Relative (95% CI)	Absolute		
Outcome #1 Dyspnea												
1	RCT	Serious ¹	Serious	No	Very Serious	No					Very Low	6
Outcome #2 Health-related QoL:												
3	RCT	Serious ¹	Serious	No	Serious ²	No	CRQ no diff (Struik); SGRQ (MCID 4) better (Murphy delta 4.9 at 3 m but not sig at 6 wks or 6 mo. SRI (MCID 0.5) better but inconsistent (, Murphy delta 4.5 at 6 wks but not sig at 3 or 6 mo. [crossed over to active tx 18/59 and withdrew 13 – imprecision], Struik delta 4.8 p=.054				Very Low	9
Outcome #3 pCO₂												
4	RCT	No	Serious ³	No	Serious	No	Blood gases: PaO ₂ not diff (Cheung, , Murphy,); pCO ₂ not diff (Cheung, , Struik when done in same conditions) or better (DeBacker, Murphy up to 3 m but not at 6 or 12 m but cross-overs) other for discussion: Lung function: no diff , Struik. Nocturnal gas exchange: mean and max TCO ₂ better at 1d, 6m and 12 m except mean at 6m (Murphy); Murphy – overnight oximetry not shown??				Low	6
Outcome #4 Hospitalization												
3	RCT	Serious ⁴	Serious ³	No	(Large effect in Murphy +1)	No	No diff (Cheung, Struik) except in Murphy : reduced time to readmission adj HR 0.49 (0.31-0.77), absolute RR 17%; post-hoc 28d readmit adj HR 0.26 (0.11-0.61)				Low	9
Outcome #5 Survival												
3	RCT	No	No	No	Very Serious ⁴	No	Murphy: all-cause mortality no different: unadj HR, 0.68 [95% CI, 0.35-1.32], P=.26; adj HR, 0.67 [95% CI, 0.34-1.30], P=.23) most causes of death respiratory [wide CI, cross-overs/withdrawals in controls] ; Cheung & Struik (died 30/29) no sig diff				Low	9

Footnotes:

¹Unblinded, subjective outcomes

²Wide CIs when reported; “trend” p values; positive subscales of QOL tools. Small sample sizes.

³Heterogeneity (which may be due to study population differences)

⁴criteria for hospitalization not described.

GRADE Evidence Profile- Section 2

PICO 2a) When applying long-term NIV to COPD patients, does high intensity NIV compared to low intensity NIV improve:

Quality assessment							Summary of findings					Importance
No of studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other considerations (eg, publication bias)	No of patients		Effect		Quality	
							Intervention	Control	Relative (95% CI)	Absolute		
Outcome #1 Dyspnea												
2	Cross-over, one study: short term (30 min intervention)	High	Yes	No	Yes		One study positive, one negative					difficult to conclude, different measures across studies
Outcome #2 Health-Related QoL:												
2	Cross-over, 6-week intervention	high	No	No	Yes		SRI and CAT improved with both intervention					No added benefit of Hi-NIPPV
Outcome #3 pCO₂												
3	See above	High	Yes	No	Yes		Inconsistent improvement in daytime and nighttime PaCO ₂ with Hi_NPPV,					Hi-NiPPV appears to improve physiological variables. However, higher leaks and more duction in cardiac output with Hi-NIPPV

GRADE Evidence Profile- Section 2

PICO 2b) When applying long-term NIV to COPD patients, does volume-assured pressure ventilation compared to S/T mode improve:

Quality assessment							Summary of findings					Importance
No of studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other considerations (eg, publication bias)	No of patients		Effect		Quality	
							Intervention	Control	Relative (95% CI)	Absolute		
Outcome #1 Dyspnea (length of follow up: mean/media/range)												
0												
Outcome #2 Health-Related QoL:												
2	Cross-over	High	No	No	Yes		VT-assured Ni-NPPV vs Pressure preset					No added benefit of VT-assured ventilation
Outcome #3 pCO₂												
4	Cross-over	High	Yes	No	No		VT-assured Ni-NPPV vs Pressure preset. No change in daytime PaCO ₂ in two studies, reduction in PtCO ₂ at night in one study, no reduction in 3 studies.					No added benefit of VT-assured ventilation on blood gases.