

Search strategy for MEDLINE

MEDLINE (Ovid) 1946 to August Week 4 2014

- 1 chronic obstructive pulmonary disease.mp. or exp Pulmonary Disease, Chronic Obstructive/
- 2 copd.mp.
- 3 chronic obstructive lung disease.mp.
- 4 chronic obstructive airway disease.mp.
- 5 chronic respiratory disorder\$.mp.
- 6 smoking-related lung disease\$.mp.
- 7 Pulmonary Emphysema/
- 8 exp Bronchitis/
- 9 emphysema.mp.
- 10 or/1-9
- 11 exp positive-pressure respiration/ or intermittent positive-pressure ventilation/
- 12 cpap.mp.
- 13 bipap.mp.
- 14 bi-level ventilation.mp.
- 15 niv.mp.
- 16 nippv.mp.
- 17 positive pressure ventilation.mp.
- 18 positive airway pressure.mp.
- 19 ((noninvasive or non-invasive) adj2 ventilation).mp.
- 20 nppv.mp.
- 21 or/11-20
- 22 10 and 21
- 23 limit 22 to yr="1980 - 2014"

Exacerbation results

Study	Design	Length of follow-up	Outcome	Results	Direction of effect	Indication of severity
<i>Stable population</i>						
Bhatt 2013 ¹	RCT	6 months	Number of exacerbations	NIV: 1/15, usual care 1/12 or 1/15 (unclear)	No difference. Not pre-defined outcome.	No details.
Casanova 2000 ²	RCT	3 and 12 months	Percentage patients affected by exacerbation	3 months: NIV: 52 %, usual care: 56% 12 months: NIV: 66%, usual care: 69%	Slight trend favoring NIV, but no significant differences Unclear if ITT analysis.	No details.
Duiverman 2011 ³	RCT	24 months	Number of exacerbations	Median of 3 exacerbations per year for both NIV and usual care	No significant difference. No other outcome statistics reported.	No details.
Zhou 2008 ⁴	RCT	12 months	Exacerbations/patient/year	NIV: 3.73(1.03) Usual care: 4.86(1.71)	Significant difference favoring NIV	No details on severity. Some may have led to hospitalizations, as these are also reported.
Tsolaki 2008 ⁵	Controlled	12 months	Exacerbations/patient/year	NIV: 1.4 (2.1) Usual care: 1.8 (1.4)	No significant difference.	All exacerbations, including those leading to hospitalizations.
			Exacerbations/patient/year leading to hospitalization	NIV: 1.0 (2.2) Usual care: 1.7 (1.3)	No significant difference.	Exacerbations assumed to be severe, as resulted in hospitalizations.
<i>Post-hospital population</i>						
Cheung 2010 ⁶	RCT	12 months	Exacerbation without AHFR	NIV: 5/23, usual care: 4/24	No details on statistical significance	Outcome listed as adverse event (not predefined outcome).
			Recurrent severe COPD exacerbation with AHFR	NIV: 7/23, usual care: 14/24 HR 0.39 (0.16, 0.98)	Statistically significant difference favoring NIV.	Severe (assumed to result in hospitalization and included in hospitalization outcome)
Struik 2014 ⁷	RCT	12 months	Annual number of exacerbations at home (median (range))	NIV: 1 (0-9) Usual care: 2 (0-14)	No statistically significant difference (p=0.26).	Exacerbation defined as an event in the natural course of the disease characterised by a change in the patient's baseline dyspnoea, cough, and/or sputum beyond day-to-day variations, is acute in onset, and treated with antibiotics and/or prednisolone.

Quality-of-Life results

Study	Design	Length of follow-up	Time-points for assessment	Results	Direction of effect
<i>Stable populations</i>					
<i>SF-36</i>					
Köhnlein 2014 ⁸	RCT	3, 6, 9 and 12 months	12 months	General health perception sub-score only: 8.6 (1.8 to 13.3) point greater improvement in NIV group	No significant difference for summary score (data not reported). Significant difference favoring NIV for general health perception sub-score (p=0.013). Results based on small sub-group only.
McEvoy 2009 ⁹	RCT	Median 28.5 (NIV) and 20.5 (usual care) months; up to 5 years	12 months	Results presented separately for the 8 sub-scales of SF-36. No summary scores.	Statistically significant difference for 2/8 sub-scales (general health and mental health) favoring usual care group. No significant differences for other sub-scales.
Tsolaki 2008 ⁵	Prospective controlled	12 months	1, 3, 6, 9 and 12 months	Results for mental and physical summary scores	Statistically significant difference favoring NIV for mental and physical scores at 6, 9 and 12 months
<i>SGRQ</i>					
Clini 2002 ¹⁰	RCT	24 months	24 months	Score changes: -5% in NIV group, -4% in usual care group (increase in QoL in both arms)	No significant difference
Köhnlein 2014 ⁸	RCT	3, 6, 9 and 12 months	12 months	6.2 (0.7 to 11.8) point greater improvement in NIV group.	Statistically significant difference favoring NIV (p=0.029), but results based on small sub-group only.
McEvoy 2009 ⁹	RCT	Median 28.5 (NIV) and 20.5 (usual care) months; up to 5 years	12 months	No data reported	No significant difference
Clini 2002 ¹⁰ & McEvoy 2009 ⁹	IPD data from both RCTs*	See above	12 months	Mean difference of 0.9 (95% CI -19.21 to 21.01)	No significant difference (small benefit favoring usual care arm)
Meecham-Jones 1995 ¹¹	RCT	3 months	3 months	Only individual results; no summary data	Significant difference for symptom, activity and total score favoring NIV; no significant difference for activity scale
<i>SRI</i>					
Duiverman 2008 ¹²	RCT	3 months	3 months	NIV: 60.1 (11), usual care 55.7 (15). Between group difference adjusted for baseline: 3.1 (-2, 8.2)	Trend for better QoL in NIV group; not statistically significant
Duiverman 2011 ³	RCT	24 months	6, 12, 18, 24 months	6 months: NIV: 59.5 (14.4); usual care: 55.6 (9.5.2) 12 months: NIV: 60.5 (10.9); usual care: 55.8 (13.4) 18 months: NIV: 56.8 (12.7); usual care: 54.4 (11.8) 24 months: adjusted difference in change 2.9 (-1.9, 7.8)	Trend for better QoL in NIV group at all time-points; not statistically significant
Köhnlein 2014 ⁸	RCT	3, 6, 9 and 12 months	12 months	5.6 (0.1 to 11.1) point greater improvement in NIV group.	Statistically significant difference favoring NIV (p=0.0445), but based on small sub-group only.
<i>CRDQ</i>					
Bhatt 2013 ¹	RCT	6 months	6 weeks, 3 months, 6 months	No total score given, only for sub-scales at 6 weeks, 3 months and 6 months.	Significant difference at 6 months for mastery sub-score favoring NIV, but no significant difference for other 3 sub-scales. No significant improvement in total score.
Duiverman 2008 ¹²	RCT	3 months	3 months	NIV: 96.8 (15), usual care 87.9 (20). Between group difference adjusted for baseline: 7.5 (-1, 16)	Trend for better QoL in NIV group but not statistically significant

Study	Design	Length of follow-up	Time-points for assessment	Results	Direction of effect
Duiverman 2011 ³	RCT	24 months	6, 12, 18 and 24 months	6 months: NIV: 94.4 (20.3); usual care: 86.3 (18.4) 12 months: NIV: 93.5 (16.5); usual care: 87.7 (19.14) 18 months: NIV: 89.9 (17.3); usual care: 88.7 (21.5) 24 months: adjusted difference in change -1.3 (-9.7, 7.4)	Trend for better QoL in NIV group at all time-points; not statistically significant
Garrod 2000 ¹³	RCT	3 months	1,2 and 3 months	1 and 2 month data in graph only. 3 months: NIV: 92.2 (17); usual care: 85.1 (23.9). mean difference in change 12.3 (1.19, 23.4) , p=0.03	Statistically significant difference favoring NIV (3 months)
<i>MRF</i>					
Clini 2002 ¹⁰	RCT	24 months	24 months	Mean difference (adjusted for baseline) 7.1 (0.13-4.07), p=0.041	Statistically significant difference favoring NIV (24 months)
Duiverman 2008 ¹²	RCT	3 months	3 months	Mean difference (adjusted for baseline) -9.7 (-18 to -1), p<0.05	Statistically significant difference favoring NIV (3 months)
Duiverman 2011 ³	RCT	24 months	6, 12, 18 and 24 months	Mean difference (adjusted for baseline) 12 months: -13.4 (-22.7, -4.2) , p<0.05	Statistically significant difference favoring NIV (24 months)
<i>POMS</i>					
McEvoy 2009 ⁹	RCT	Median 28.5 (NIV) and 20.5 (usual care) months; up to 5 years	12 months	NIV Total mood score median 22 (IQR 48), usual care 5 (IQR 21); p=0.318	No statistically significant difference for total score; statistically significant difference favoring usual care for two sub-groups on POMS.
<i>Post-hospital population</i>					
<i>CCQ</i>					
Struik 2014 ⁷	RCT	12 months	12 months	Mean difference in change -0.04 (-0.5 to 0.4)	Not statistically significant between groups (completers only).
<i>MRF</i>					
Struik 2014 ⁷	RCT	12 months	12 months	Mean difference in change -1.5 (-8.6 to 5.7)	Not statistically significant between groups (completers only).
<i>CRDQ</i>					
Struik 2014 ⁷	RCT	12 months	12 months	Mean difference in change 0.01 (-0.4 to 0.4)	Not statistically significant between groups (completers only).
<i>SRI</i>					
Struik 2014 ⁷	RCT	12 months	12 months	Mean difference in change 4.8 (-0.1 to 9.7)	Not statistically significant between groups (completers only).

*From Struik (2013)¹⁴

Results of RCTs comparing different types of NIV

Adherence to NIV and adverse events associated with NIV (NIV versus NIV)

Study	Modes being compared	Period of adaptation/help in adapting to NIV	Recommended period of use	Adherence-how measured	Adherence –mean hours use	Adherence -% of patients or other	Adverse events associated with NIV
Dreher 2010 ¹⁵	High intensity	Number of days needed for initiation of NIV: 4.6 (1.0) high, period 2, 3.7 (1.0) high, period 2	'Nocturnal use'	Ventilator counter reading	Mean h/day period 1:10.8 (4.7), period 2: 8.9 (6.4)	2 drop-outs from low intensity treatment arm (first period). Two patients refused to swap to low intensity after first period with high intensity.	One patient refused low intensity NIV in hospital due to intolerance.
	Low intensity	Number of days needed for initiation of NIV: 1.7 (1.6) low, period 1, 1.6 (0.8) low, period 2			Mean h/day period 1: 7.7 (3.0), period 2: 4.6 (1.8)		
Murphy 2012 ¹⁶	High-intensity	No details	'Nocturnal use'	Ventilator download data	Mean nightly use (h:m) 6:33 (2:14)	1/12 withdrawal (acute exacerbation)	Appear to be none
	High-pressure				Mean nightly use (h:m): 6:37 (1:45) Mean difference 0:04 (-0:45 to 0:53)	4/12 withdrawals (1 claustrophobia, 2 intolerant of therapy, 1 prolonged central sleep apnoeas)	1 claustrophobia, 2 intolerant of therapy
Oscroft 2010 ¹⁷	Volume assured (va)	Patients already established on pp-NIV, mean use at study entry 7.8 (2.2) hours /day	'Nocturnal use'	Ventilator download data	8.2 (3.6) hours/day	1/25 withdrew due to exacerbation	Appear to be none
	Pressure preset (pp)				7.7 (2.4) hours/day		

Lung function, blood gases and 6MWD

FEV₁ (l or % predicted)		
<i>Study</i>	<i>Comparison</i>	<i>Main findings</i>
Dreher 2010 ¹⁵	High intensity (pressure) versus low intensity (pressure)	Significant increase from baseline to 6 weeks in high intensity group. No significant between group differences at 6 weeks for FEV ₁ (l).
Oscroft 2010 ¹⁷	Volume assured (higher pressure) versus pressure pre-set (lower pressure)	Slightly higher values with volume assured NIV. No significant between group differences at 6 weeks for FEV ₁ (l) or FEV ₁ (% predicted).
FVC (l or % predicted)		
Oscroft 2010 ¹⁷	Volume assured (higher pressure) versus pressure pre-set (lower pressure)	No significant between group differences at 8 weeks for FVC (l) or FVC (% predicted).
PaCO₂		
Dreher 2010 ¹⁵	High intensity (pressure) versus low intensity (pressure)	Statistically significant difference in reduction favoring high-intensity NIV (p=0.001).
Oscroft 2010 ¹⁷	Volume assured (higher pressure) versus pressure pre-set (lower pressure)	No significant between group differences (8 weeks).
Murphy 2012 ¹⁶	High intensity (high pressure + high back-up rate) versus high-pressure (high pressure + low back-up rate)	No significant between group differences (6 weeks).
6MWD		
Dreher 2010 ¹⁵	High intensity (pressure) versus low intensity (pressure)	No significant between group differences (6 weeks).

Quality-of-Life

The studies by Dreher (2010)¹⁵ and Oscroft (2010)¹⁷ comparing different pressures found no differences in total SRI score¹⁵ or SF-36 and SGRQ scores¹⁷ respectively, though there was a trend for better quality-of-life on the SGRQ with volume assured NIV. The first¹⁵ of these two studies was rated as having a high risk of bias regarding incomplete outcome data. Neither of these studies was designed to look at quality-of-life as a primary outcome.

Murphy (2012)¹⁶, which compared different breathing frequencies, also found no significant differences in total SRI scores, though there was a statistically significant difference for the respiratory symptom domain favoring high pressure ventilation (pressure support ventilation).

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- (2) Casanova C, Celli BR, Tost L, Soriano E, Abreu J, Velasco V et al. Long-term controlled trial of nocturnal nasal positive pressure ventilation in patients with severe COPD. *Chest* 2000; 118(6):1582-1590.
- (3) Duiverman ML, Wempe JB, Bladder G, Vonk JM, Zijlstra JG, Kerstjens HA et al. Two-year home-based nocturnal noninvasive ventilation added to rehabilitation in chronic obstructive pulmonary disease patients: a randomized controlled trial. *Respiratory Research* 2011; 12:112.
- (4) Zhou X. Effect of Non-Invasive Positive Pressure Ventilation and Long-term Oxygen Therapy in Patients with Stable COPD. *Clinical Medical Journal of China* 2008; 15(4):486-488.
- (5) Tsolaki V, Pastaka C, Karetsi E, Zygoulis P, Koutsokera A, Gourgoulisanis KI et al. One-year non-invasive ventilation in chronic hypercapnic COPD: effect on quality of life. *Respiratory Medicine* 2008; 102(6):904-911.
- (6) Cheung AP, Chan VL, Liong JT, Lam JY, Leung WS, Lin A et al. A pilot trial of non-invasive home ventilation after acidotic respiratory failure in chronic obstructive pulmonary disease. *International Journal of Tuberculosis & Lung Disease* 2010; 14(5):642-649.
- (7) Struik FM, Sprooten RT, Kerstjens HA, Bladder G, Zijnen M, Asin J et al. Nocturnal non-invasive ventilation in COPD patients with prolonged hypercapnia after ventilatory support for acute respiratory failure: a randomised, controlled, parallel-group study. *Thorax* 2014; 69(9):826-834.
- (8) Kohnlein T, Windisch W, Kohler D, Drabik A, Geiseler J, Hartl S et al. Non-invasive positive pressure ventilation for the treatment of severe stable chronic obstructive pulmonary disease: a prospective, multicentre, randomised, controlled clinical trial. *Lancet Respir Med* 2014; 2(9):698-705.
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- (15) Dreher M, Storre JH, Schmoor C, Windisch W. High-intensity versus low-intensity non-invasive ventilation in patients with stable hypercapnic COPD: a randomised crossover trial. *Thorax* 2010; 65(4):303-308.
- (16) Murphy PB, Brignall K, Moxham J, Polkey MI, Davidson AC, Hart N. High pressure versus high intensity noninvasive ventilation in stable hypercapnic chronic obstructive pulmonary disease: a randomized crossover trial. *Int J Chron Obstruct Pulmon Dis* 2012; 7:811-818.
- (17) Oscroft NS, Ali M, Gulati A, Davies MG, Quinnell TG, Shneerson JM et al. A randomised crossover trial comparing volume assured and pressure preset noninvasive ventilation in stable hypercapnic COPD. *Copd: Journal of Chronic Obstructive Pulmonary Disease* 2010; 7(6):398-403.