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Noninvasive ventilation vs. High flow nasal cannula to prevent extubation failure

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Ventilator related complications

- Ventilator associated pneumonia
- Ventilator associated lung injury
- Muscle weakness
- Reduced health related quality of life
- Post traumatic stress disorder
- Depression
- Delirium
- Cognitive impairment….

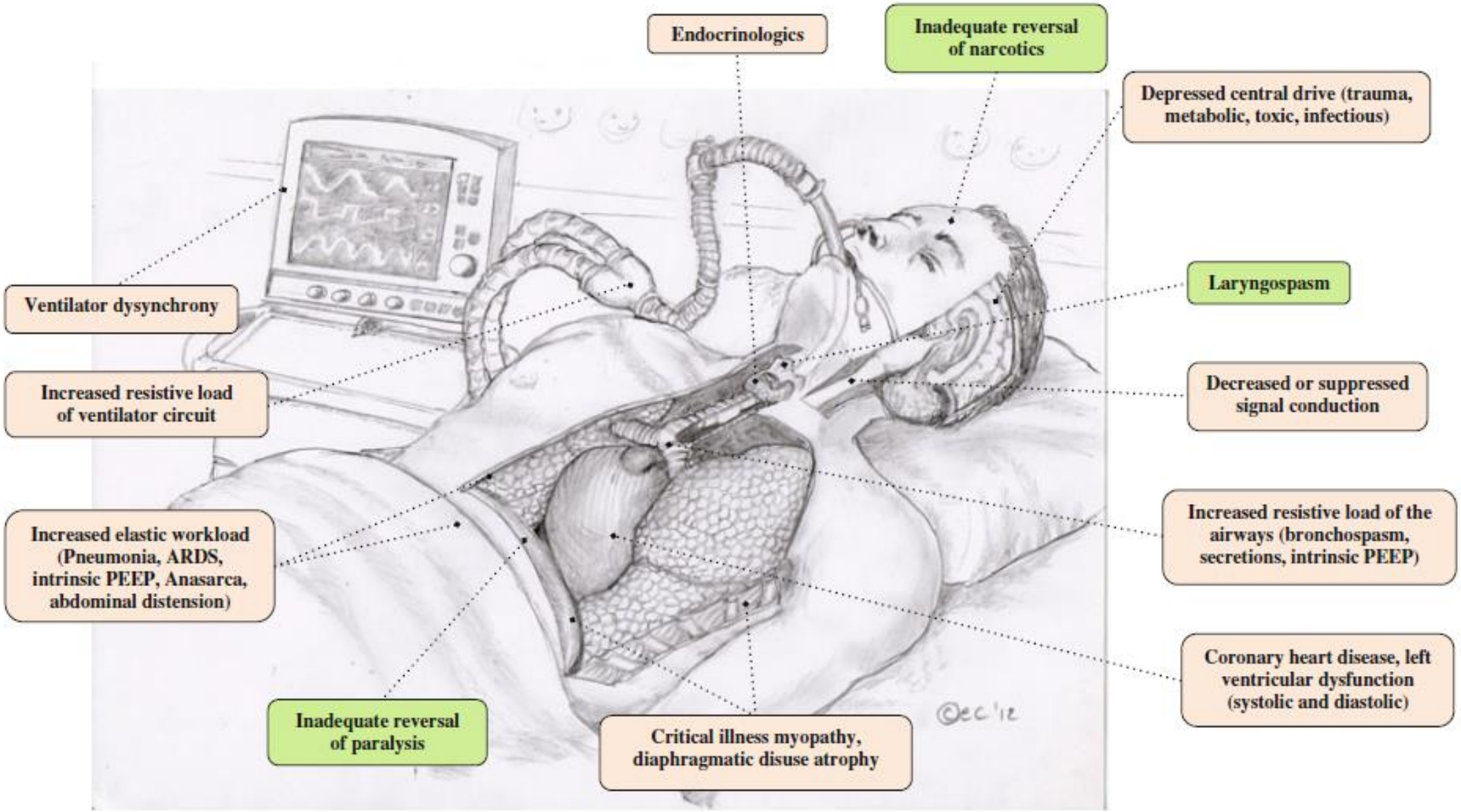


Fig. 1 Synoptic illustration of reasons contributing to weaning/extubation failure in anaesthetized and critically ill patients. anaesthetized, critically ill

Intensive Care Med (2013) 39:1885–1895

Increased respiratory workload

Elastic workload	
Lung parenchyma	Oedema (of whatever origin)
	Pneumonia, atelectasis, fibrosis, ARDS
	Extreme hyperinflation (asthma attack)
	High intrinsic PEEP (COPD)
Chest wall	Abdominal distension, ascites, obesity, anasarca
	Pleural effusion, pneumothorax
	Kyphoscoliosis, flail chest
Resistive load	
Airways	Bonchospasm, mucosal oedema, excessive secretions
	Intrinsic PEEP (asthma, COPD)
	Glottic oedema
Endotracheal tube resistance	Kinking, deposition of secretions, ventilator circuit
	Small tube diameter
Ventilator	Malfunctioning ventilator valves
	Inappropriate ventilator settings (see below)
	Imbibed heat and moisture exchangers
Ventilatory needs	
Higher minute ventilation	Fever, overfeeding, hyperventilation (agitation, pain)
	Ventilation/perfusion mismatch
	Intrapulmonary shunt, increased dead space (emphysema)
Ventilator dyssynchrony	Inappropriate ventilator settings
	Ineffective triggering (wasted inspiratory effort)
	Autotriggering (unwanted increase in respiratory rate)
	Inappropriate cycling off (expiratory effort, hyperinflation)

Intensive Care Med (2013) 39:1885–1895

Decreased respiratory capability

Signal generation	
Depressed central drive	Sedatives, narcotics
	Metabolic-toxic (urea↑, metabolic alkalosis)
	Infectious (encephalitis, meningitis)
	Stroke, trauma, oedema, central hypoventilation)
Signal conduction	
Decreased conduction	Spine lesion (para-/tetraplegia)
	Motoneuron (GBS, ALS, AIP)
	Phrenic nerve (traumatic/iatrogenic, poliomyelitis)
	Critical illness polyneuropathy (sepsis, MOF, hyperglycaemia, corticosteroids, aminoglycosides, prolonged use of neuromuscular blocking agents)
	Neuromuscular transmission (MG, neuromuscular blocking agents)
Muscular strength	
Reduced strength and/or endurance	Critical illness myopathy
	MV (disuse atrophy), muscular dystrophies
	Metabolic (decreased levels of PO_4, Mg, K, Ca), under nutrition
	Endocrinologic (thyroid disturbances, adrenal insufficiency)

Intensive Care Med (2013) 39:1885–1895

NIV

- Positive pressure is applied to the airway to inflate the lungs directly
- Negative pressure is applied externally to the abdomen and thorax to draw air into the lungs through the upper airway

- respiratory muscle loading, gas exchange improvement and augmentation of alveolar ventilation

- a decrease in venous return with subsequent preload reduction in both RV and LV

Eur Respir Rev 2018; 27: 180029

Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure

TABLE 2 Recommendations for actionable PICO questions

Clinical indication[#]	Certainty of evidence[¶]	Recommendation
Prevention of hypercapnia in COPD exacerbation	⊕⊕	Conditional recommendation against
Hypercapnia with COPD exacerbation	⊕⊕⊕⊕	Strong recommendation for
Cardiogenic pulmonary oedema	⊕⊕⊕	Strong recommendation for
Acute asthma exacerbation		No recommendation made
Immunocompromised	⊕⊕⊕	Conditional recommendation for
De novo respiratory failure		No recommendation made
Post-operative patients	⊕⊕⊕	Conditional recommendation for
Palliative care	⊕⊕⊕	Conditional recommendation for
Trauma	⊕⊕⊕	Conditional recommendation for
Pandemic viral illness		No recommendation made
Post-extubation in high-risk patients (prophylaxis)	⊕⊕	Conditional recommendation for
Post-extubation respiratory failure	⊕⊕	Conditional recommendation against
Weaning in hypercapnic patients	⊕⊕⊕	Conditional recommendation for

Eur Respir J 2017; 50: 1602426

Weaning

- Weaning process

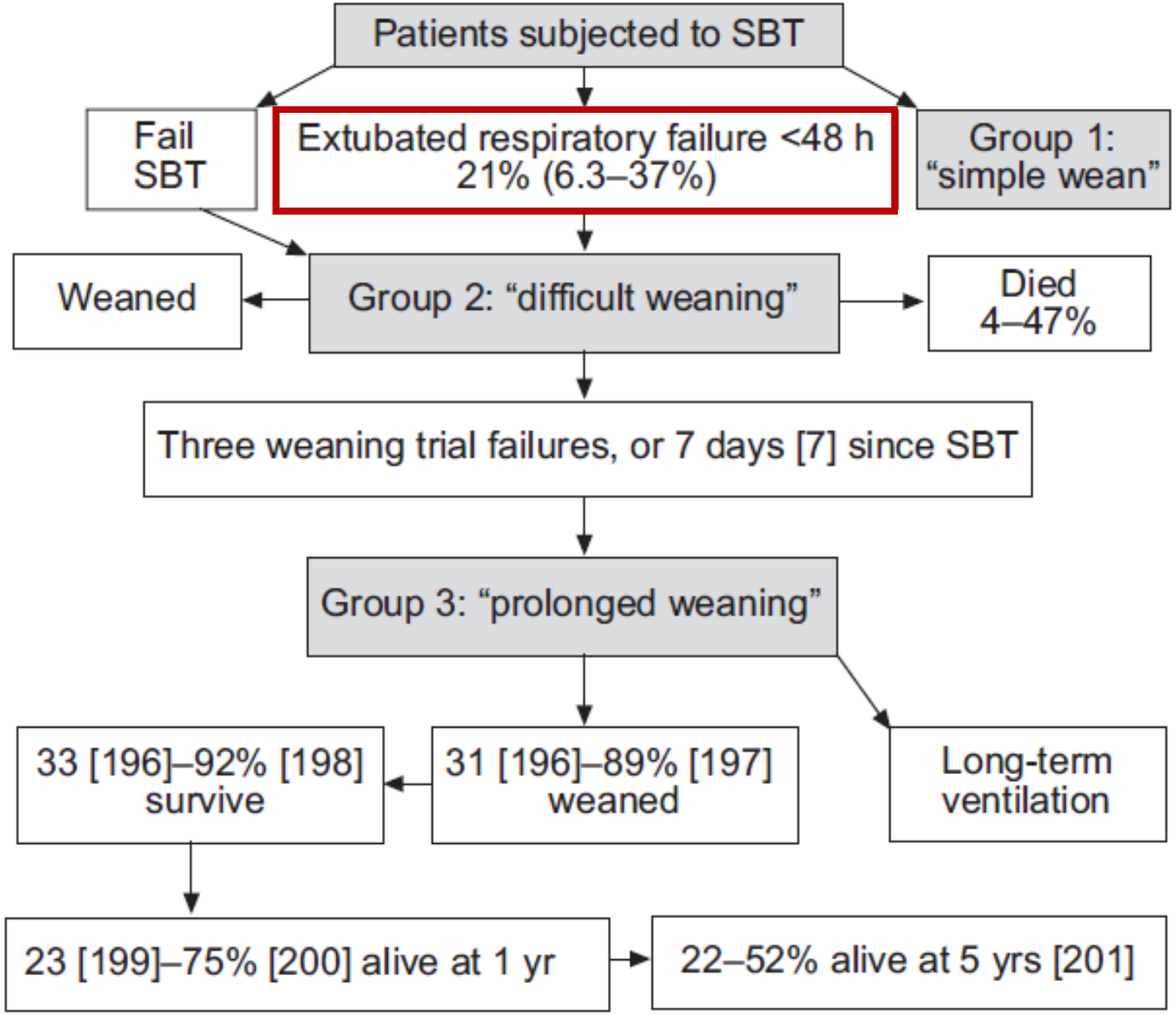
 - recognize that patients may no longer require mechanical ventilation

 - meet these “readiness to wean” criteria (SBT)

 - judge whether those patients will be able to sustain ventilation once the endotracheal tube has been removed (airway patency and clearance of secretions)

- The balance between the load imposed on the patient’s respiratory muscles and muscle’s capacity

 → Positive pressure to decrease the load and help restore balance



- Re-intubation is associated with a worse prognosis, even after controlling for level of severity (risk of death up to 50%)

- Facilitative NIV

Post-extubation after a failed SBT

- Prophylactic NIV

Passed SBT but high risk for re-intubation

- Curative NIV

Extubation failure, developing ARF

Eur Respir J 2007; 29: 1033–1056

Intensive Care Med (2013) 39:1885–1895

Use of non-invasive ventilation to wean critically ill adults off invasive ventilation: meta-analysis and systematic review

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BMJ 2009;338:b1574

Study	No of patients	Inclusion criteria (patients)	Inclusion criteria (weaning eligibility)	Experimental strategy	Control strategy
Nava,[w1] 1998	50	Exacerbation of COPD. Intubated for at least 36-48 hrs	Simple weaning criteria, 1 hr SBT failure	Non-invasive pressure support on conventional ventilator delivered with face mask	Invasive PS
Girault,[w2] 1999	33	Acute-on-chronic respiratory failure (COPD, restrictive, or mixed populations). Intubated for at least 48 hrs	Simple weaning criteria, 2 hr SBT failure	Flow or pressure mode with nasal or face mask	Flow or pressure mode (PS)
Hill,[w3] 2000	21	Acute respiratory failure	30 minute SBT failure	NIV using VPAP in ST-A mode	Invasive PS
Chen,[w4] 2001	24	Exacerbation of COPD. Intubated for at least 48-60 hrs. Saturations >88% on FiO_2 40%	Day 3 + weaning criteria	Bilevel NIV (pressure mode)	Invasive PS
Ferrer,[w5] 2003	43	Acute respiratory failure and persistent weaning failure. Intubated for at least 72 hrs	2 hr SBT failure on 3 consecutive days	Bilevel NIV in ST mode delivered with face or nasal mask	AC or invasive PS
Rabie,[w6] 2004	37	Exacerbation of COPD	2 hr SBT failure	NIV (proportional assist in timed mode) delivered by face or nasal mask	Invasive PS
Wang,[w7] 2004	28	COPD. Bronchopulmonary infection	PIC window	NIV (pressure mode) delivered by mask (unspecified)	SIMV+PS
Zheng,[w8] 2005	33	COPD. Severe pulmonary infection	PIC window	Bilevel NIV (pressure mode) delivered by face or nasal mask	Invasive PS
Zou,[w9] 2006	76	COPD with severe respiratory failure. Pulmonary infection	PIC window	Bilevel NIV (pressure, ST mode) delivered by nasal or oronasal mask	SIMV +PS
Wang,[w10] 2005	90	COPD with severe hypercapnic respiratory failure. Pneumonia or purulent bronchitis. Age ≤85. Capable of self care in past year	PIC window	Bilevel NIV (pressure mode)	SIMV+PS
Trevisan,[w11] 2008	65	Invasively ventilated >48 hours	30 min SBT failure	Bilevel NIV (pressure mode) delivered by facemask	Invasive mechanical ventilation
Shiva Prasad[w12]	30	COPD. Hypercapnic respiratory failure	2 hr SBT failure	Bilevel NIV (pressure mode) delivered by full face mask	Invasive PS

COPD=chronic obstructive pulmonary disease; SBT=spontaneous breathing trial; PS=pressure support; NIV=non-invasive ventilation; PIC=pulmonary infection control; AC=assist control; SIMV=synchronised intermittent mechanical ventilation; VPAP=ventilator positive airway pressure.

Table 3 | Summary estimates of effect of non-invasive ventilation in critically ill adults

Outcome	No studies (No of patients)	Summary estimate (95% CI)	P value (summary estimate)	P value (heterogeneity)	I^2 (%)
Mortality	12 (530)	0.55* (0.38 to 0.79)	0.001	0.49	0
VAP	11 (509)	0.29* (0.19 to 0.45)	<0.001	0.51	0
Weaning failures	4 (141)	0.72* (0.37 to 1.42)	0.34	0.35	9.2
Length of stay:					
Intensive care	10 (485)	−6.27† (−8.77 to −3.78)	<0.001	<0.001	77.4
Hospital	8 (401)	−7.19† (−10.80 to −3.58)	<0.001	<0.001	76.8
Duration of mechanical ventilation:					
Total	7 (385)	−5.64† (−9.50 to −1.77)	0.004	<0.001	85.6
Related to weaning	6 (224)	−0.94† (−3.24 to 1.36)	0.42	<0.001	91.8
Endotracheal‡	9 (391)	−7.81† (−11.31 to −4.31)	<0.001	<0.001	89.9
Adverse events:					
Reintubation	6 (328)	0.73* (0.40 to 1.34)	0.31	0.19	32.4
Tracheostomy	3 (141)	0.16* (0.04 to 0.75)	0.02	0.30	17.2
Arrhythmia	2 (63)	1.05* (0.17 to 6.67)	0.96	0.35	0

VAP=ventilator associated pneumonia.
*Relative risk.
†Weighted mean difference.
‡Invasive ventilation.

BMJ 2009;338:b1574

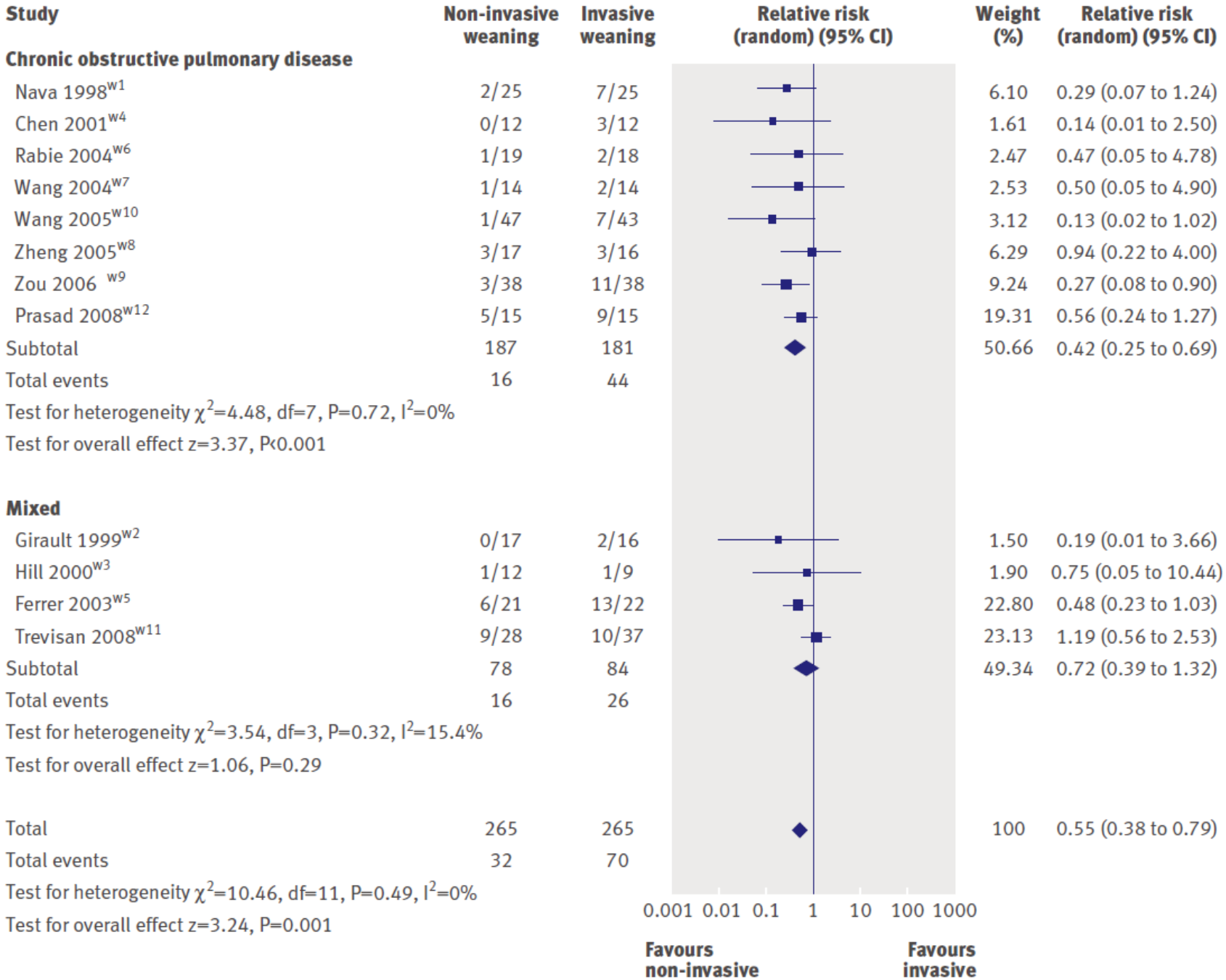


Fig 2 | Effect of non-invasive and invasive weaning on mortality in critically ill adults on invasive ventilation

Non-invasive ventilation versus invasive weaning in critically ill adults: a systematic review and meta-analysis

Burns KEA, *et al*. *Thorax* 2022;**77**:752–761.

Girault *et al*[37]	138	Chronic hypercapneic respiratory failure invasively ventilated for at least 48 hours	2 hours SBT failure	Non-invasive PS±PEEP or bilevel NIV with face mask (initial choice)	Invasive PS with once daily SBT with T-piece or PS±PEEP
Rabie Agmy *et al*[38]	264	Acute on chronic exacerbation of COPD	2 hours SBT failure	NIV (pressure, ST mode)	Invasive PS
Tawfeek and Ali-Elnabtity[39]	42	Invasively ventilated for >48 hours	2 hours SBT failure	Non-invasive PAV ventilation delivered by face mask	SIMV
Vaschetto *et al*[40]	20	Hypoxemic respiratory failure invasively ventilated for at least 48 hours	PS with PEEP +inspiratory support, <25 cmH_2O and PEEP 8–13 cmH_2O; PaO_2/FiO_2 200–300 mm Hg with $FiO_2 \leq 0.6$	Helmet NIV	Invasive PS with SBT when P/F ratio >250 mm Hg
Charra *et al*[41]	24	Invasively ventilated for greater than 48 hours in medical intensive care unit	T-piece SBT failure	Face mask bilevel NIV	Classic wean with invasive PS
Rong[42]	64	COPD with respiratory failure	PIC window	Bilevel positive airway pressure	SIMV+PS
Mohamed and Ibrahim[43]	30	COPD with infective exacerbation	Not reported	NIV	Invasive MV
Laiq *et al*[44]	60	Cardiac surgery patients invasively ventilated greater than 48 hours	30 min T-piece SBT failure	NIPPV	Invasive MV with daily SBT
El-Shimy *et al*[45]	40	COPD on MV	30 min–2 hours T-piece SBT failure	NIV (BiPAP)	SIMV+PS
Carron *et al*[46]	64	Intubated for ARF≥48 hours	30 min PSV SBT failure	Helmet NIV	PSV weaning
Mishra *et al*[47]	50	COPD exacerbation requiring invasive MV for at least 48 hours	T-piece SBT failure	Full face mask NIPPV (BiPAP)	PSV
Wang *et al*[48]	53	Surgical patients requiring invasive MV for acute respiratory distress syndrome	PaO_2/FiO_2 200–250 mm Hg with PEEP 8 and PS 12 cmH_2O, acute infiltrates resolved	NIV	Invasive MV with daily SBT
Guo *et al*[49]	96 (5 excluded)	Age≥75 years and community-acquired pneumonia requiring MV	Failed SBT	NIV	PSV weaning with SBT
Perkins *et al*[50]	364	Invasive MV for >48 hours	SBT failure	Face mask NIV	Invasive MV with daily SBT
Vaschetto *et al*[51]	130	Hypoxemic respiratory failure invasively ventilated for at least 48 hours	PS with PEEP +inspiratory support, <25 cmH_2O and PEEP 8–13 cmH_2O; PaO_2/FiO_2 200–300 mm Hg with $FiO_2 \leq 0.6$; $PaCO_2$ ≤50 mm Hg and pH ≥7.35, risk ratio≤30, Vt≤8 mL/kg IBW, T<38.5°C, GCS 10T, suction <2/hour	Oral-nasal or full face mask NIV	Invasive PS with 30 min PS 5/PEEP 5 SBT when P/F ratio >250 mm Hg
Chen *et al*[52]	106	COPD exacerbation requiring invasive MV	Criteria for moving to NIV in intervention group not clear	NIV	Invasive MV until successful SBT

28 RCTs

2066 patients, 44.6% COPD

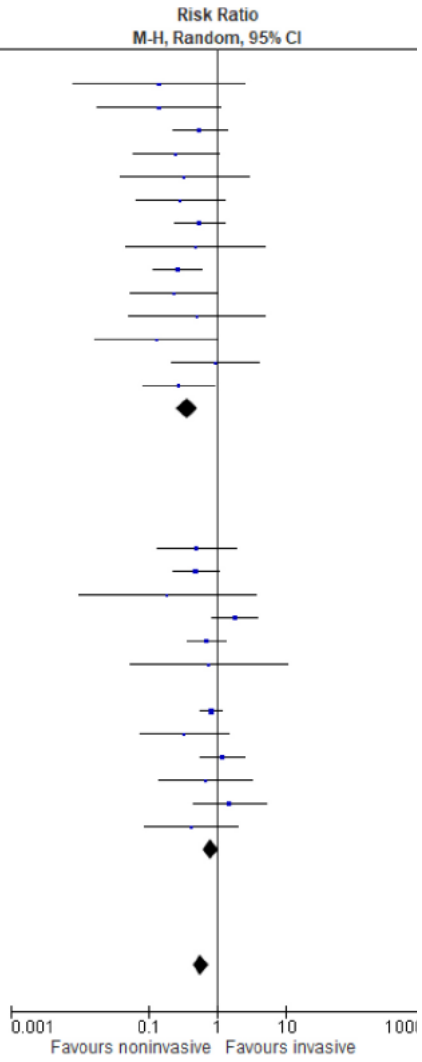
30min~2hrs T piece or PSV SBT failure

NIV (face, nasal, helmet)

vs. invasive ventilation

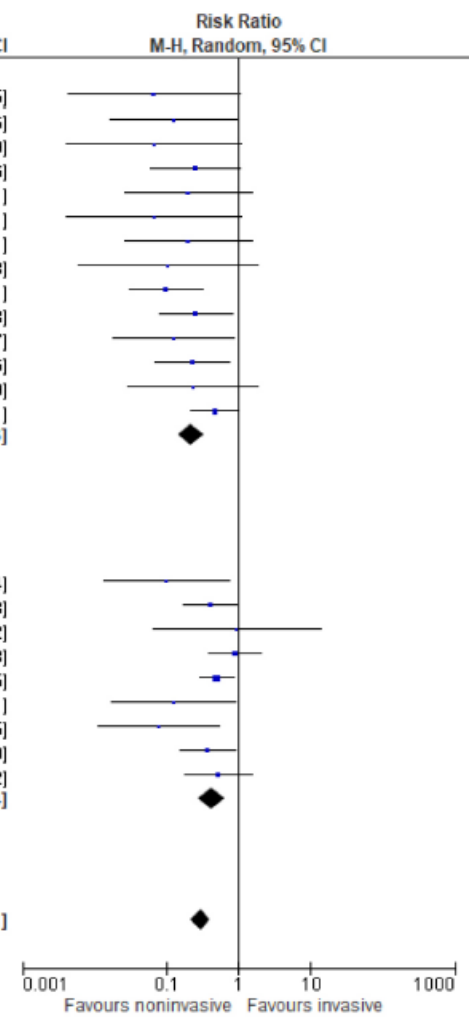
Mortality

Study or Subgroup	Noninvasive Weaning Events	Total	Invasive Weaning Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.1.1 COPD						
Chen 2001	0	12	3	12	0.8%	0.14 [0.01, 2.50]
Chen 2020	1	53	7	53	1.5%	0.14 [0.02, 1.12]
El-Shimy 2013	5	20	9	20	5.7%	0.56 [0.23, 1.37]
Mishra 2014	2	25	8	25	2.8%	0.25 [0.06, 1.06]
Mohamed 2012	1	15	3	15	1.4%	0.33 [0.04, 2.85]
Nava 1998a	2	25	7	25	2.7%	0.29 [0.07, 1.24]
Prasad 2009	5	15	9	15	6.4%	0.56 [0.24, 1.27]
Rabie 2004	1	19	2	18	1.2%	0.47 [0.05, 4.78]
Rabie Agmy 2012	7	134	26	130	6.7%	0.26 [0.12, 0.58]
Rong 2012	2	33	8	31	2.7%	0.23 [0.05, 1.02]
Wang 2004	1	14	2	14	1.2%	0.50 [0.05, 4.90]
Wang 2005	1	47	7	43	1.5%	0.13 [0.02, 1.02]
Zheng 2005	3	17	3	16	2.8%	0.94 [0.22, 4.00]
Zou 2006	3	38	11	38	3.8%	0.27 [0.08, 0.90]
Subtotal (95% CI)		**467**		**455**	**40.9%**	**0.36 [0.25, 0.51]**
Total events	34		105			
Heterogeneity: Tau² = 0.00; Chi² = 7.78, df = 13 (P = 0.86); I² = 0%						
Test for overall effect: Z = 5.69 (P < 0.00001)						
1.1.2 Mixed						
Carron 2014	3	32	6	32	3.3%	0.50 [0.14, 1.83]
Ferrer 2003	6	21	13	22	7.1%	0.48 [0.23, 1.03]
Girault 1999	0	17	2	16	0.7%	0.19 [0.01, 3.66]
Girault 2011	16	69	9	69	7.2%	1.78 [0.84, 3.75]
Guo 2015	11	44	17	47	8.6%	0.69 [0.37, 1.31]
Hill 2000	1	12	1	9	0.9%	0.75 [0.05, 10.44]
Laiq 2013	0	30	0	30		Not estimable
Perkins 2018	38	180	47	180	12.9%	0.81 [0.56, 1.18]
Tawfeek 2012	2	21	6	21	2.6%	0.33 [0.08, 1.47]
Trevisan 2008	9	28	10	37	7.1%	1.19 [0.56, 2.53]
Vaschetto 2012	2	10	3	10	2.4%	0.67 [0.14, 3.17]
Vaschetto 2019	6	65	4	65	3.7%	1.50 [0.44, 5.07]
Wang 2014	2	26	5	27	2.5%	0.42 [0.09, 1.95]
Subtotal (95% CI)		**555**		**565**	**59.1%**	**0.81 [0.62, 1.05]**
Total events	96		123			
Heterogeneity: Tau² = 0.02; Chi² = 11.87, df = 11 (P = 0.37); I² = 7%						
Test for overall effect: Z = 1.61 (P = 0.11)						
Total (95% CI)		**1022**		**1020**	**100.0%**	**0.57 [0.44, 0.74]**
Total events	130		228			
Heterogeneity: Tau² = 0.10; Chi² = 33.88, df = 25 (P = 0.11); I² = 26%						
Test for overall effect: Z = 4.26 (P < 0.0001)						
Test for subgroup differences: Chi² = 13.00, df = 1 (P = 0.0003), I² = 92.3%						



VAP

Study or Subgroup	Noninvasive Weaning Events	Total	Invasive Weaning Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
3.1.1 COPD						
Chen 2001	0	12	7	12	1.3%	0.07 [0.00, 1.05]
Chen 2020	1	53	8	53	2.2%	0.13 [0.02, 0.96]
El-Shimy 2013	0	20	7	20	1.2%	0.07 [0.00, 1.09]
Mishra 2014	2	25	8	25	4.0%	0.25 [0.06, 1.06]
Mohamed 2012	1	15	5	15	2.3%	0.20 [0.03, 1.51]
Nava 1998a	0	25	7	25	1.2%	0.07 [0.00, 1.11]
Prasad 2009	1	15	5	15	2.3%	0.20 [0.03, 1.51]
Rabie 2004	0	19	4	18	1.2%	0.11 [0.01, 1.83]
Rabie Agmy 2012	3	134	30	130	5.6%	0.10 [0.03, 0.31]
Rong 2012	3	33	11	31	5.5%	0.26 [0.08, 0.83]
Wang 2004	1	14	8	14	2.4%	0.13 [0.02, 0.87]
Wang 2005	3	47	12	43	5.4%	0.23 [0.07, 0.76]
Zheng 2005	1	17	4	16	2.2%	0.24 [0.03, 1.89]
Zou 2006	7	38	15	38	9.5%	0.47 [0.21, 1.01]
Subtotal (95% CI)		**467**		**455**	**46.4%**	**0.22 [0.15, 0.33]**
Total events	23		131			
Heterogeneity: Tau² = 0.00; Chi² = 9.34, df = 13 (P = 0.75); I² = 0%						
Test for overall effect: Z = 7.31 (P < 0.00001)						
3.1.2 Mixed						
Carron 2014	1	32	10	32	2.3%	0.10 [0.01, 0.74]
Ferrer 2003	5	21	13	22	8.7%	0.40 [0.17, 0.93]
Girault 1999	1	17	1	16	1.3%	0.94 [0.06, 13.82]
Girault 2011	9	69	10	69	8.7%	0.90 [0.39, 2.08]
Guo 2015	12	44	26	47	13.2%	0.49 [0.29, 0.85]
Tawfeek 2012	1	21	8	21	2.3%	0.13 [0.02, 0.91]
Trevisan 2008	1	28	17	37	2.4%	0.08 [0.01, 0.55]
Vaschetto 2019	6	65	16	65	8.3%	0.38 [0.16, 0.90]
Wang 2014	4	26	8	27	6.3%	0.52 [0.18, 1.52]
Subtotal (95% CI)		**323**		**336**	**53.6%**	**0.42 [0.28, 0.64]**
Total events	40		109			
Heterogeneity: Tau² = 0.11; Chi² = 11.00, df = 8 (P = 0.20); I² = 27%						
Test for overall effect: Z = 3.98 (P < 0.0001)						
Total (95% CI)		**790**		**791**	**100.0%**	**0.30 [0.22, 0.41]**
Total events	63		240			
Heterogeneity: Tau² = 0.13; Chi² = 28.77, df = 22 (P = 0.15); I² = 24%						
Test for overall effect: Z = 7.38 (P < 0.00001)						
Test for subgroup differences: Chi² = 4.75, df = 1 (P = 0.03), I² = 79.0%						



Burns KEA, *et al*. *Thorax* 2022;**77**:752–761.

Table 2 Summary estimates of effect of non-invasive ventilation in critically ill adults

Outcome	No. of studies (no. of patients)	Summary estimate (95% CI)	I^2 (%)
Mortality	26 (2042)	0.57 (0.44 to 0.74)	26
VAP	23 (1581)	0.30 (0.22 to 0.41)	24
Weaning failures	11 (829)	0.59 (0.43 to 0.81)	22
Length of stay			
Intensive care	22 (1804)	–4.6 (–5.9 to –3.3)	80
Hospital	13 (1061)	–6.3 (–8.9 to –3.7)	75
Duration of mechanical ventilation			
Total	12 (687)	–5.3 (–7.9 to –2.7)	83
Related to weaning	13 (1163)	–0.6 (–1.1 to –0.1)	88
Invasive ventilation	19 (1214)	–7.8 (–9.9 to –5.6)	94
Adverse events			
Reintubation	14 (1336)	0.69 (0.47 to 1.01)	59
Tracheostomy	10 (1130)	0.25 (0.10 to 0.61)	56
Arrhythmia	4 (565)	0.70 (0.41 to 1.20)	0

*Risk ratio.
†Mean difference.
‡Invasive ventilation.
VAP, ventilator-associated pneumonia.

Burns KEA, *et al*. *Thorax* 2022;**77**:752–761.

Table 3 Secondary analysis of summary estimates of effect of non-invasive ventilation by subgroup

Outcome	Subgroups	No. of trials	Effect estimate	Test for subgroup differences
Mortality	COPD	14	RR 0.36 (0.25, 0.51)	P=0.0003
	Mixed	12	RR 0.81 (0.62, 1.05)	
Weaning failure	COPD	4	RR 0.52 (0.37, 0.73)	P=0.56
	Mixed	7	RR 0.62 (0.37, 1.06)	
Ventilator-associated pneumonia	COPD	14	RR 0.22 (0.15, 0.33)	P=0.03
	Mixed	9	RR 0.42 (0.28, 0.64)	
ICU length of stay	COPD	12	MD –6.1 (–8.1, –4.0)	P=0.03
	Mixed	10	MD –3.1 (–5.0, –1.1)	
Hospital length of stay	COPD	7	MD –7.4 (–10.9, –4.0)	P=0.16
	Mixed	6	MD –4.0 (–7.4, –0.6)	
Total duration of mechanical ventilation	COPD	7	MD –6.4 (–10.4, –2.4)	P=0.15
	Mixed	5	MD –3.2 (–5.0, –1.4)	
Duration of ventilation related to weaning	COPD	6	MD –1.3 (–2.2, –0.4)	P=0.17
	Mixed	7	MD 0.3 (–1.8, 2.3)	
Duration of invasive ventilation	COPD	11	MD –8.0 (–11.0, –5.1)	P=0.81
	Mixed	8	MD –7.4 (–11.3, –3.6)	
Reintubation	COPD	4	RR 0.48 (0.34, 0.67)	P=0.02
	Mixed	10	RR 0.89 (0.59, 1.35)	
Tracheostomy	COPD	1	RR 0.04 (0.00, 0.60)	P=0.15
	Mixed	9	RR 0.31 (0.13, 0.71)	
Arrhythmia	COPD	1	RR 2.00 (0.20, 19.78)	P=0.36
	Mixed	3	RR 0.66 (0.38, 1.15)	

COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; MD, mean difference; RR, risk ratio.

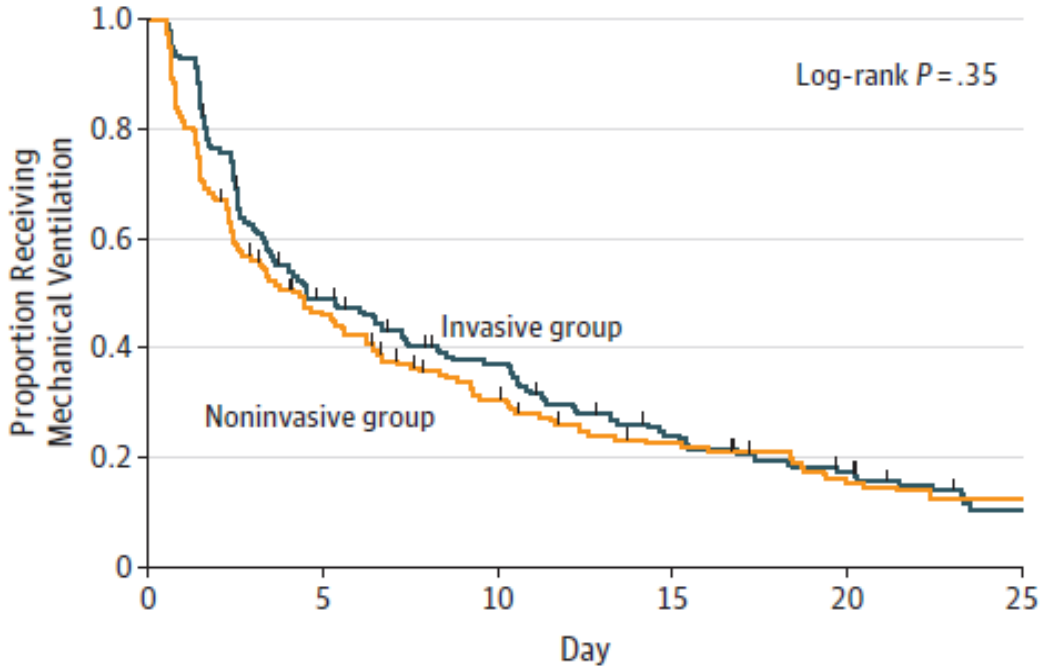
Burns KEA, *et al*. *Thorax* 2022;**77**:752–761.

ing With Early Extubation
s Invasive Weaning

Characteristics	Invasive Weaning (n = 182)	Noninvasive Weaning (n = 182)
Age, mean (SD), y	61.8 (15.8)	64.3 (13.6)
Male, No. (%)	94 (51.6)	90 (49.5)
Evidence of delirium (CAM-ICU positive), No. (%)[a]	17 (9.3)	23 (12.6)
Body mass index, mean (SD)[b]	27.7 (6.6)	28.2 (6.9)
Duration of ventilation prior to randomization, median (IQR), d	4.7 (3.0-7.4)	5.3 (3.3-8.1)
Antibiotics for respiratory infection, No. (%)	100 (55)	98 (54)
APACHE II score, mean (SD)[c]	18.8 (6.2)	18.9 (6.6)
Admission diagnosis, No. (%)		
Pneumonia/respiratory infection	73 (40.1)	57 (31.3)
Postsurgery respiratory failure	39 (21.4)	39 (21.4)
Cardiac	18 (9.9)	27 (14.8)
Nonrespiratory infection	21 (11.5)	16 (8.8)
Neuromuscular	8 (4.4)	7 (3.9)
COPD/asthma exacerbation	7 (3.9)	7 (3.9)
Traumatic injuries	5 (2.8)	3 (1.6)
Gastrointestinal bleeding	3 (1.7)	7 (3.9)
Pancreatitis	1 (0.5)	4 (2.2)
Stroke	1 (0.5)	0
Other[d]	6 (3.2)	15 (8.2)
Ventilation parameters prior to spontaneous breathing trial		
Exhaled minute volume, median (IQR), L/min	10.5 (8.2-13.1)	10.2 (8.4-12.6)
Total respiratory rate, median (IQR), /min	21 (17-27)	21 (16-27)
Positive end-expiratory pressure, median (IQR), cm H_2O	5 (5-8)	5 (5-8)
Pressure support, median (IQR), cm H_2O	11 (8-15)	11 (9-15)
P:F ratio, median (IQR), mm Hg[e]	242.2 (200.6-315)	227.5 (196.9-280.7)
Spontaneous tidal volume, median (IQR), mL/kg	8.2 (6.5-9.8)	7.9 (6.4-9.5)
Arterial blood gas measures prior to spontaneous breathing trial		
$Paco_2$, mean (SD), mm Hg	42.8 (10.2) (n=181)	42.6 (8.9) (n=180)
pH, mean (SD)	7.4 (0.06) (n=182)	7.4 (0.06) (n=181)
Hemoglobin, mean (SD), g/dL	9.7 (1.7) (n=182)	9.6 (1.6) (n=181)

JAMA. 2018;320(18):1881-1888.

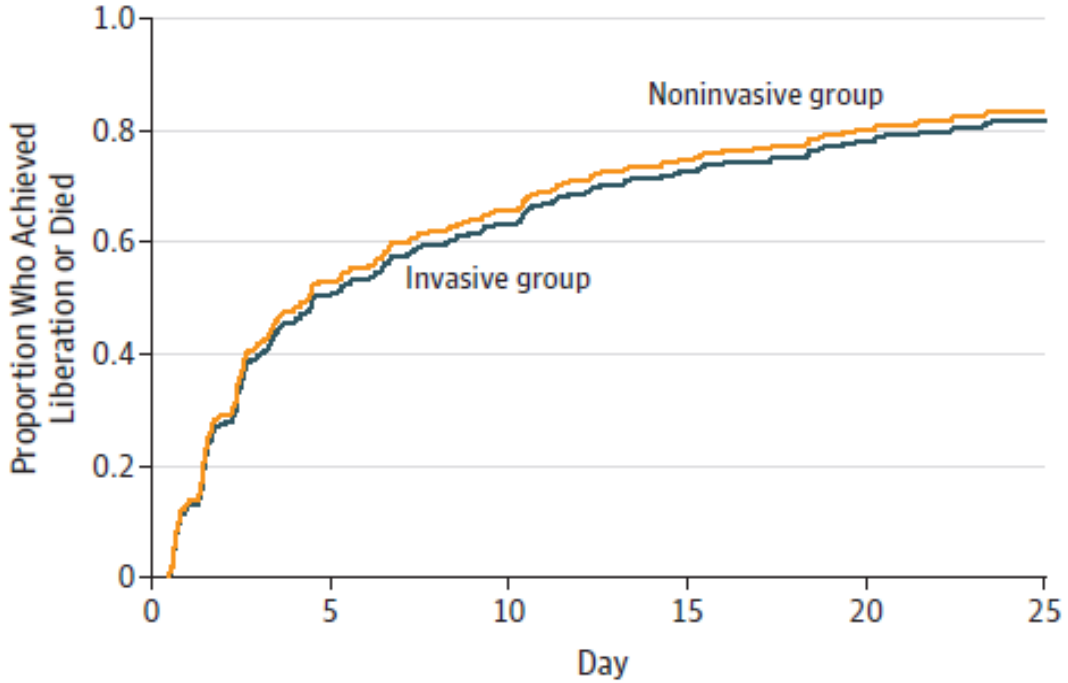
Figure 2. Time to Liberation From Mechanical Ventilation by Treatment Group



No. at risk						
Invasive group	182	86	61	37	24	12
Noninvasive group	182	79	48	32	21	17

Hash marks indicate each censoring time. Median time to liberation from ventilation was 4.5 days (95% CI, 3.46-7.25 days) in the invasive group and 4.3 days (95% CI, 2.63-5.58 days) in the noninvasive group.

Figure 3. Cumulative Incidence of Liberation From Ventilation or Death by Treatment Group



No. at risk						
Invasive group	182	86	61	37	24	12
Noninvasive group	182	79	48	32	21	17

HR 1.1 (0.86-1.34)

JAMA. 2018;320(18):1881-1888.

Table 2. Adverse Events

Adverse Events	No. (%) of Participants		Unadjusted Absolute Difference, % (95% CI)
	Invasive Weaning (n=182)	Noninvasive Weaning (n=182)	
Antibiotics for presumed respiratory infection	128 (70.3)	110 (60.4)	9.9 (0.2 to 19.6)
Reintubation	41 (28.7)(n=143)	67 (37.0)(n=181)	8.3 (−1.9 to 18.6)
Tracheostomy	55 (30.2)	43 (23.6)	6.6 (−2.5 to 15.7)
Death before intensive care unit discharge	25 (13.7)	22 (12.1)	1.6 (−5.2 to 8.5)
Dysrhythmias	22 (12.1)	14 (7.7)	4.4 (−1.7 to 10.5)
Nasal/skin/mouth sores or irritation	14 (7.7)	19 (10.4)	2.7 (−3.2 to 8.6)
Nonrespiratory infection	12 (6.6)	11 (6.0)	0.5 (−4.5 to 5.6)
Vomiting	8 (4.4)	14 (7.7)	3.3 (−1.6 to 8.2)
Gastric distension	6 (3.3)	7 (3.9)	0.5 (−3.3 to 4.4)
Barotrauma (eg, pneumothorax)	3 (1.7)	3 (1.7)	0 (−2.6 to 2.6)

JAMA. 2018;320(18):1881-1888.

Hypoxemic non-hypercapnic patients

6 studies, 459 participants (control 266 vs. intervention 233)
meta-analysis of RCTs

Table 2 Patient characteristics at ICU admission and ventilator settings and gas exchange at randomization

	Control (n = 226)	Intervention (n = 233)	*p* value
Characteristics at ICU admission			
Age, mean (SD)	60 (16)	63 (15)	0.037
Male, n (%)	134 (59%)	135 (58%)	0.769
Type of patient (medical vs. surgical)	116/110	140/93	0.059
Main causes of i-MV, n (%)			0.076
ARDS	64 (28%)	57 (25%)	
Pneumonia	19 (8%)	22 (9%)	
Septic Shock	13 (6%)	10 (4%)	
Polytrauma	23 (10%)	28 (12%)	
Post-operative ARF	69 (31%)	51(21%)	
Gastrointestinal Bleeding	7 (3%)	13 (6%)	
Cerebral Bleeding	4 (2%)	2 (1%)	
Pancreatitis	4 (2%)	4 (2%)	
Others	23 (10%)	46 (20%)	

Vaschetto *et al. Crit Care* *(2021) 25:189*

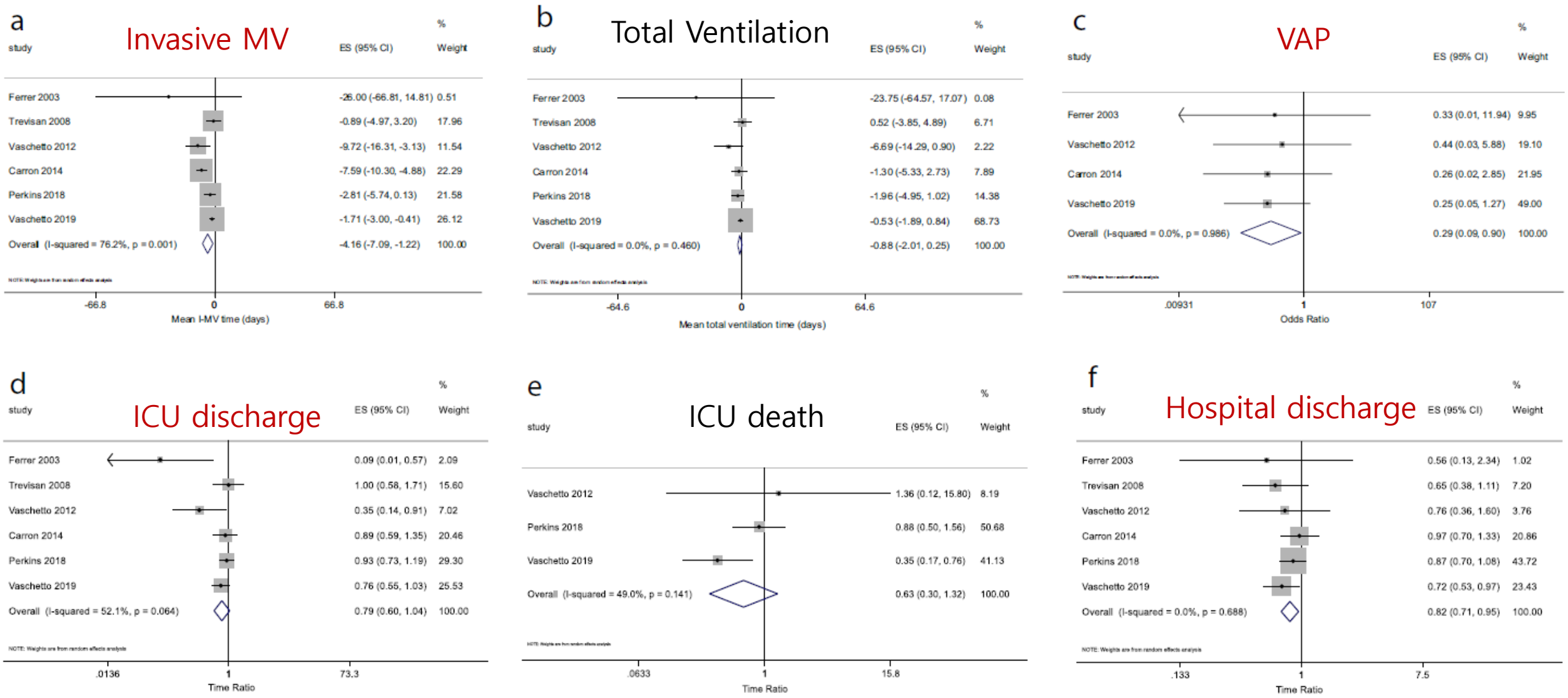


Fig. 2 Results of 2-stage IPD-MA. **a** Mean i-MV time (*p* value = 0.006); **b** mean total ventilation time (*p* value = 0.13); **c** occurrence of VAP (*p* value = 0.03); **d** time to ICU discharge (*p* value = 0.09); **e** time to ICU death (*p* value = 0.222), **f** time to hospital discharge (*p* value = 0.009). *CI* confidence interval, *ICU* intensive care unit, *i-MV* invasive mechanical ventilation, *IPD-MA* individual patient data meta-analysis, *VAP* ventilator associated pneumonia

Table 2 Patient characteristics at ICU admission and ventilator settings and gas exchange at randomization

	Control (n = 226)	Intervention (n = 233)	*p* value
Ventilator settings and gas exchange at randomization			
PEEP (cmH_2O), mean (SD)	7 (2)*	7 (2)**	0.451
Pressure Support (cmH_2O)§, mean (SD)	11 (5)*	11 (4)**	0.414
FiO_2 (%), mean (SD)	36 (8)	37 (8)	0.124
PaO_2 (cmH_2O), mean (SD)	91 (22)**	89 (21)++	0.287
PaO_2/FiO_2 (mmHg), mean (SD)	258 (77)**	242 (58)++	0.014
pH, mean (SD)	7.43 (0.06)^	7.44 (0.05) ++	0.748
$PaCO_2$ (mmHg), mean (SD)	39 (7)**	39 (6)++	0.741

Table 3 Results from 1-stage IPD-MA, according to different models

	Mean i-MV time (days)	Mean total ventilation time (days)	VAP (odds ratio)	Time to ICU discharge (time ratio)	Time to ICU death (time ratio)	Time to hospital discharge (time ratio)
Model 1*	−3.26 (−5.01 to −1.50)	−1.86 (−3.65 to −0.06)	0.23 (0.08 to 0.68)	0.82 (0.70 to 0.98)	0.77 (0.49 to 1.22)	0.80 (0.69 to 0.94)
	$p < 0.001$	$p = 0.042$	$p = 0.008$	$p = 0.027$	$p = 0.273$	$p = 0.006$
Model 2†	−3.43 (−5.19 to −1.68)	−2.04 (−3.84 to −0.25)	0.25 (0.08 to 0.75)	0.81 (0.69 to 0.96)	0.68 (0.41 to 1.15)	0.81 (0.69 to 0.95)
	$p < 0.001$	$p = 0.025$	$p = 0.014$	$p = 0.015$	$p = 0.152$	$p = 0.010$
Model 3‡	−3.43 (−5.17 to −1.69)	−2.04 (−3.82 to −0.27)	0.24 (0.08 to 0.71)	0.81 (0.68 to 0.96)	0.75 (0.45 to 1.23)	0.81 (0.69 to 0.95)
	$p < 0.001$	$p = 0.024$	$p = 0.014$	$p = 0.015$	$p = 0.251$	$p = 0.011$

*Model 1: adjusted by study (fixed-effect model)

† Model 2: adjusted by study, age, gender, PaO_2/FiO_2, risk score (fixed-effect model)

‡ Model 3: adjusted by study, age, gender, PaO_2/FiO_2, risk score (random effect model)

ICU Intensive Care Unit, *IPD-MA* Individual Patient Data Meta-Analysis, *i-MV* invasive Mechanical Ventilation, *PaO_2/FiO_2* arterial partial pressure of oxygen and oxygen inspired fraction ratio, *VAP* Ventilator Associated Pneumonia

Non-invasive ventilation after extubation in hypercapnic patients with chronic respiratory disorders: randomised controlled trial

Lancet 2009; 374: 1082–88

Miquel Ferrer, Jacobo Sellarés, Mauricio Valencia, Andres Carrillo, Gumersindo Gonzalez, Joan Ramon Badia, Josep Maria Nicolas, Antoni Torres

- NIV (n=54) vs. conventional oxygen therapy (n=52)

- Type of Chronic respiratory disease
- COPD or Chronic bronchitis
- Sequelae of pulmonary TB
- Bronchiectasis
- Obesity-hypoventilation syndrome
- Chest-wall deformity
- Chronic persistent asthma

	Non-invasive ventilation (n=54)	Control (n=52)	Odds ratio (95% CI)	p
Outcome variables				
Respiratory failure after extubation	8 (15%)	25 (48%)	5·32 (2·11–13·46)	<0·0001
Main causes of respiratory failure after extubation			..	0·3451
Respiratory failure	3	18		
Aspiration or excess respiratory secretions	3	3		
Cardiac failure	1	2		
Upper-airway obstruction	0	1		
Encephalopathy	1	1		
Time from extubation to respiratory failure (h)	29 (13)	17 (18)	..	0·0982
Criteria met for reintubation	6 (11%)	10 (19%)	1·90 (0·64–5·68)	0·3741
Mortality				
Intensive-care unit mortality	3 (6%)	4 (8%)	1·42 (0·30–6·67)	0·7132
Hospital mortality	6 (11%)	11 (22%)	2·15 (0·73–6·33)	0·2587
Mortality at 90 days	6 (11%)	16 (31%)	3·56 (1·27–10·0)	0·0244

Efficacy of noninvasive ventilation after planned extubation: A systematic review and meta-analysis of randomized controlled trials

Mixed (3)

High risk (2)

COPD (2)

Chronic respiratory disease (2)

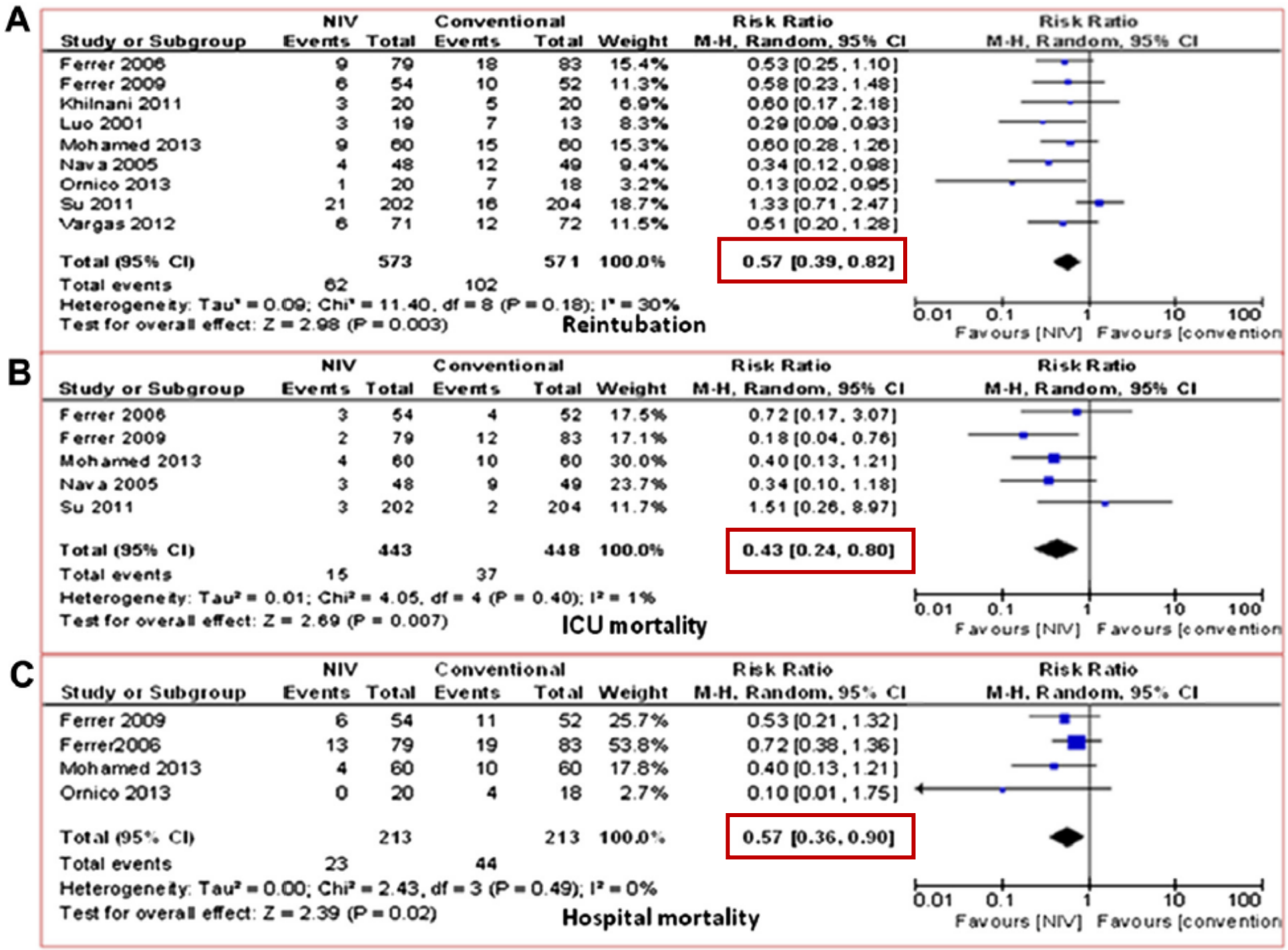
Study	Type of study	Population characteristics	Duration of NIV	Inclusion criteria	Exclusion criteria
Ornico[18]	RCT	Mixed ICU	Nasal mask for 24 h	ARF, on MV for >48 h with successful SBT	Age < 18 years, pregnancy, refusal to participate, contraindications for NIV
Su[19]	RCT	Mixed ICU	Facial mask for 12 h	ARF, on MV for >48 h with successful SBT	Refusal to participate, incompetence, ineligible diagnosis, physician refusal, contraindications for NIV
Mohamed[20]	RCT	Mixed ICU	Facial mask for 12 h	ARF, on MV for >48 h with successful SBT	Age < 18 years, refusal to participate, recent abdominal surgery, contra-indications for NIV
Ferrer (2006)[21]	RCT	High risk	Facial mask for 24 h	ARF, on MV for >48 h with one of the following: Age > 65 years, cardiac failure, APACHE > 12 with successful SBT	Contraindications for NIV, recent gastric or esophageal surgery
Ferrer (2009)[22]	RCT	CRDs	Facial mask for 24 h	ARF on CRD, on MV for>48 h with successful SBT and hypercapnia during SBT	Contraindications for NIV, recent gastric or esophageal surgery
Nava[23]	RCT	High risk	Facial mask for 48 h	ARF, on MV for>48 h and passed SBT and one of the following: 1. More than one failure of weaning trial 2. Chronic heart failure 3. $PaCO_2$ > 45 mm Hg after extubation 4. More than one comorbidity 5. Weak cough 6. Upper airways stridor at extubation	Neuromuscular disease, sleep apnea, uncontrolled cardiac ischemia and use of NIV at home, failure of >2 organs, obesity, arrhythmias
Khilnani[24]	RCT	COPD	Facial mask for 7 h/day	ARF due to COPD exacerbation, on MV for >48 h with successful SBT or able to extubate on SIMV with rate <6 and Ps < 7cm H_2O	Contraindications for NIV, myocardial ischemia or arrhythmias, prior reintubation
Luo[25]	RCT	COPD	Facial mask for 12 h	ARF due to exacerbation of COPD on MV with successful weaning	Contraindications for NIV
Vargas[26]	RCT	CRDs	Nasal mask for 48 h[a]	ARF on CRD, on MV with successful SBT or hypercapnia during SBT	

- 9 RCT studies, 1144 patients

Reintubation

ICU mortality

Hospital mortality



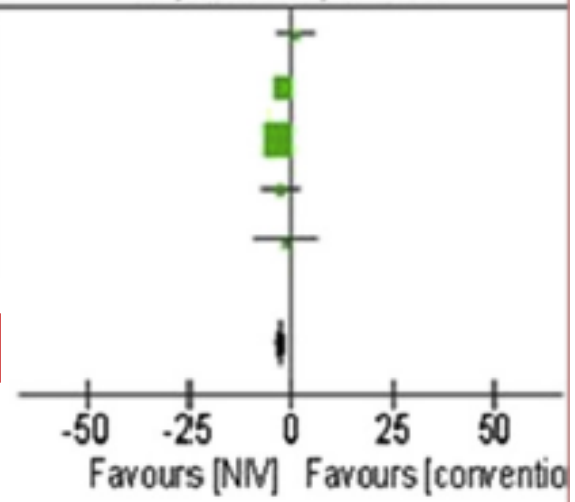
A

Study or Subgroup	NIV Mean	NIV SD	NIV Total	Conventional Mean	Conventional SD	Conventional Total	Weight	Mean Difference IV, Random, 95% CI
Ferrer 2009	11	13	54	10	9	52	6.8%	1.00 [-3.24, 5.24]
Ferrer2006	11	8	79	13	1	83	29.3%	-2.00 [-3.78, -0.22]
Mohamed 2013	8.3	3.1	60	11.6	2.6	60	55.5%	-3.30 [-4.32, -2.28]
Nava 2005	8.9	5.7	48	11.6	14.9	49	6.2%	-2.70 [-7.17, 1.77]
Ornico 2013	16.8	11.6	20	18.4	12.2	18	2.2%	-1.60 [-9.19, 5.99]
Total (95% CI)			**261**			**262**	**100.0%**	**-2.55 [-3.70, -1.41]**

Heterogeneity: Tau² = 0.34; Chi² = 4.87, df = 4 (P = 0.30); I² = 18%

Test for overall effect: Z = 4.37 (P < 0.0001)

ICU length of stay



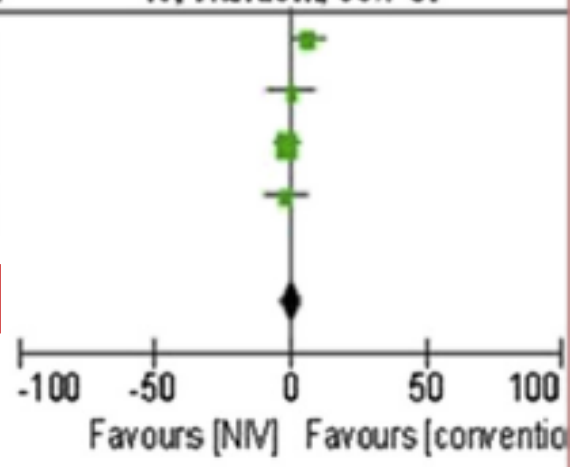
B

Study or Subgroup	NIV Mean	NIV SD	NIV Total	Conventional Mean	Conventional SD	Conventional Total	Weight	Mean Difference IV, Random, 95% CI
Ferrer 2006	30	23	79	24	18	83	25.3%	6.00 [-0.38, 12.38]
Ferrer 2009	29	27	54	29	17	52	16.6%	0.00 [-8.56, 8.56]
Khilnani 2011	16.1	6.29	20	18.25	7.91	20	38.2%	-2.15 [-6.58, 2.28]
Nava 2005	23.3	16.4	48	25.3	21.4	49	19.9%	-2.00 [-9.58, 5.58]
Total (95% CI)			**201**			**204**	**100.0%**	**0.30 [-3.68, 4.27]**

Heterogeneity: Tau² = 5.67; Chi² = 4.57, df = 3 (P = 0.21); I² = 34%

Test for overall effect: Z = 0.15 (P = 0.88)

Hospital length of stay

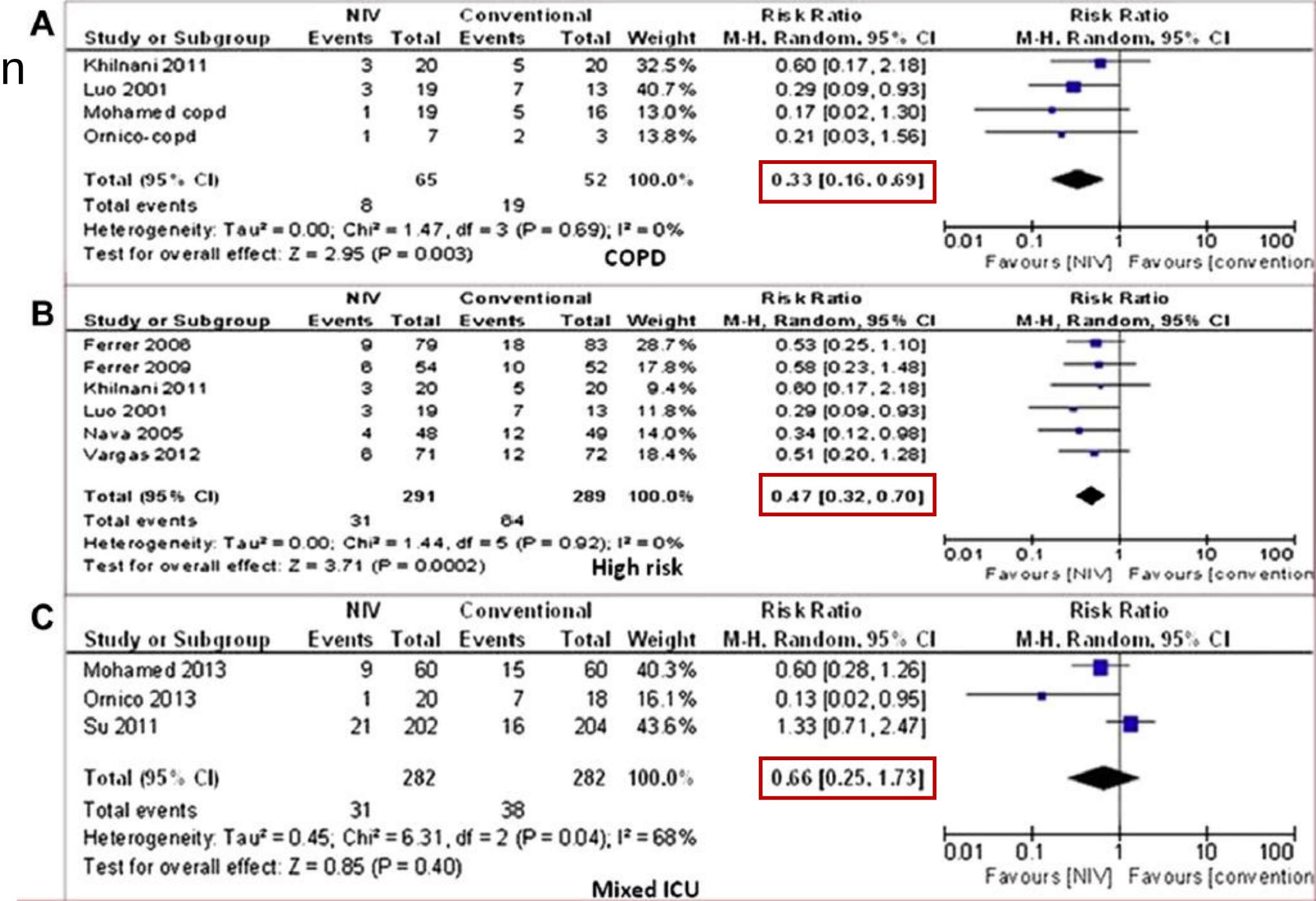


Reintubation

COPD

High risk

Mixed ICU



Noninvasive Positive-Pressure Ventilation for Respiratory Failure after Extubation

NIV (n=114) vs. standard (n=107)

- Reintubation

48% in both groups

- Death in ICU

NIV 25% vs. standard 14% (relative risk, 1.78;95% CI 1.03-3.20;p=0.048)

- Median time from respiratory failure to reintubation

NIV 12 hrs vs. standard 2 hrs 30min, p=0.02

Table 4. Reasons for Reintubation, as Defined in the Protocol Guidelines, According to Study Group.

Reason	Non-invasive Ventilation (N=55)	Standard Medical Therapy (N=51)	P Value
	no. (%)		
Lack of improvement in signs of muscle fatigue	25 (45)	23 (45)	0.97
Hypoxemia	9 (16)	15 (29)	0.11
Copious secretions	5 (9)	6 (12)	0.65
Lack of improvement in pH or partial pressure of carbon dioxide	8 (15)	3 (6)	0.13
Changes in mental status	4 (7)	2 (4)	0.45
Hypotension	4 (7)	2 (4)	0.45

N Engl J Med 2004;350:2452-60.

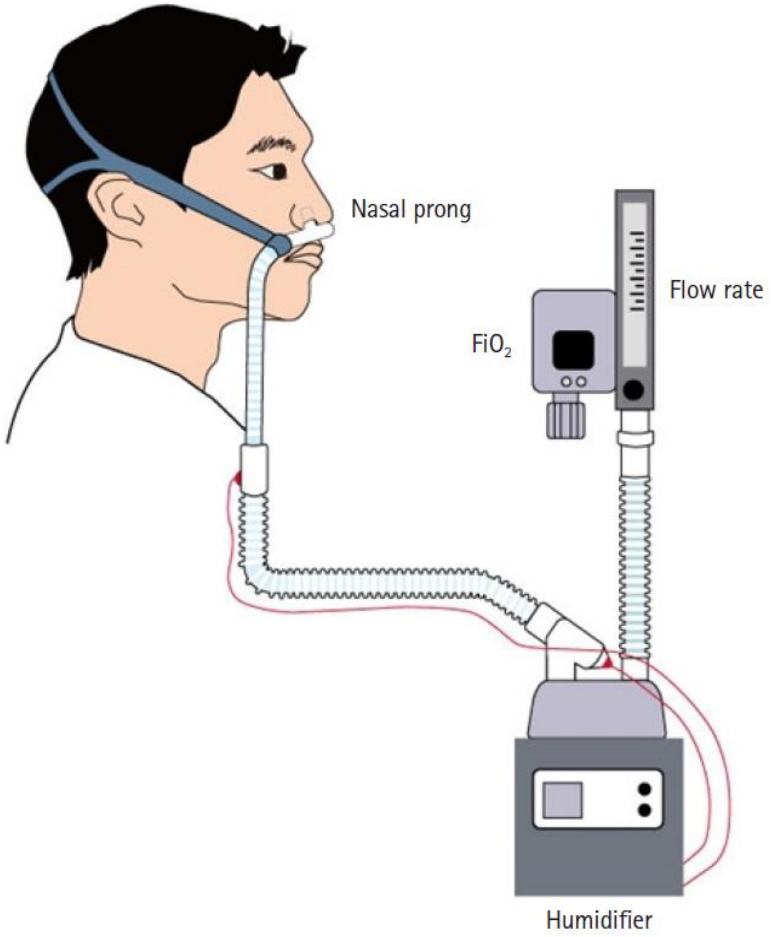
Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure

TABLE 2 Recommendations for actionable PICO questions

Clinical indication[#]	Certainty of evidence[¶]	Recommendation
Prevention of hypercapnia in COPD exacerbation	⊕⊕	Conditional recommendation against
Hypercapnia with COPD exacerbation	⊕⊕⊕⊕	Strong recommendation for
Cardiogenic pulmonary oedema	⊕⊕⊕	Strong recommendation for
Acute asthma exacerbation		No recommendation made
Immunocompromised	⊕⊕⊕	Conditional recommendation for
De novo respiratory failure		No recommendation made
Post-operative patients	⊕⊕⊕	Conditional recommendation for
Palliative care	⊕⊕⊕	Conditional recommendation for
Trauma	⊕⊕⊕	Conditional recommendation for
Pandemic viral illness		No recommendation made
Post-extubation in high-risk patients (prophylaxis)	⊕⊕	Conditional recommendation for
Post-extubation respiratory failure	⊕⊕	Conditional recommendation against
Weaning in hypercapnic patients	⊕⊕⊕	Conditional recommendation for

Eur Respir J 2017; 50: 1602426

HFNC



- Anatomical dead space washout
- PEEP effect
- Fraction of inspired oxygen
- Humidification
- Comfortable interface

SeungYong Park Acute and Critical Care 2021 November 36(4):275-285

HFNC

- Improve oxygenation
- Reduce other causes of respiratory failure such as increased work of breathing and respiratory muscle fatigue
- Conditioning the inspired gas
    - management of respiratory secretions
    - alleviates inflammation of the tracheal mucosa after transglottic intubation

JAMA 2016;315(13):1354-1361

Nasal High-Flow versus Venturi Mask Oxygen Therapy after Extubation

Effects on Oxygenation, Comfort, and Clinical Outcome

RCT

Salvatore Maurizio Maggiore[1], Francesco Antonio Idone[1], Rosanna Vaschetto[2], Rossano Festa[1], Andrea Cataldo[1], Federica Antonicelli[1], Luca Montini[1], Andrea De Gaetano[3], Paolo Navalesi[4,5,6], and Massimo Antonelli[1]

- 105 patients mechanically ventilated for more than 24 hrs
- passed SBT
- PF ratio ≤300

Table 2. Need for Ventilatory Support during the 48-Hour Study Period

	Control Group (*n* = 52)	NHF (*n* = 53)	*P* Value
Noninvasive ventilation, n (%)	8 (15.4)	2 (3.8)	0.042
Endotracheal intubation, n (%)	11 (21.2)	2 (3.8)	0.005
Cause of endotracheal intubation			
Hypercapnia with respiratory acidosis, n (%)	0	0	N/A
Changes in mental status, n (%)	1 (1.9)	1 (1.9)	0.989
Oxygen desaturation or hypoxia, n (%)	6 (11.5)	1 (1.9)	0.047
Unbearable dyspnea with respiratory muscle failure, n (%)	4 (7.7)	1 (1.9)	0.162
Persistent hypotension, n (%)	2 (3.8)	0	0.149
Inability to clear secretions, n (%)	6 (11.5)	1 (1.9)	0.047

Definition of abbreviation: NHF = nasal high-flow oxygen therapy.

Am J Respir Crit Care Med Vol 190, Iss 3, pp 282–288, Aug 1, 2014

Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Postextubation High-Flow Nasal Cannula vs Conventional Oxygen Therapy on Reintubation in Low-Risk Patients

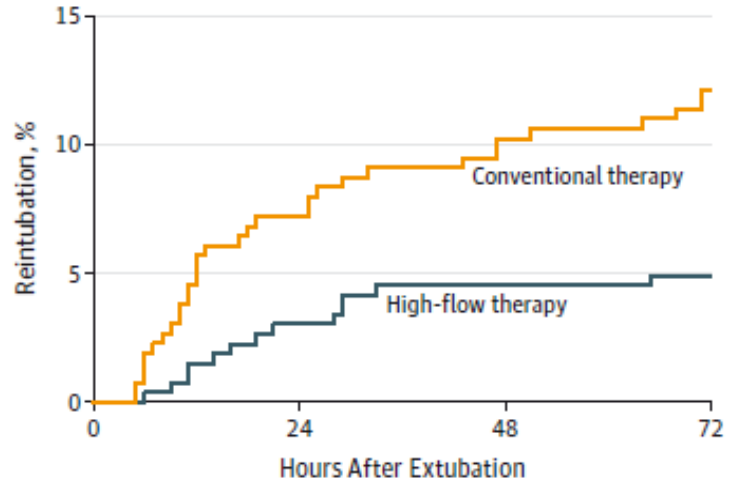
A Randomized Clinical Trial

JAMA 2016;315(13):1354-1361

- 527 patients for longer than 12hrs
- Ready for scheduled extubation after tolerating SBT
- Low risk of reintubation
    - younger than 65 years, absence of heart failure
    - absence of moderate to severe COPD
    - APACHEII score <12, BMI < 30
    - absence of patency problems
        - laryngeal edema
        - ability to manage respiratory secretion (< 2 times within 8hrs)
    - no prolonged mechanical ventilation (as longer than 7 days)

High flow (n=264) vs. conventional (n=263)

Figure 2. Kaplan-Meier Analysis of Time From Extubation to Reintubation



No. at risk

Conventional therapy	263	244	236	231
High-flow therapy	264	256	252	251

4.9% vs. 12.2%, p = 0.004

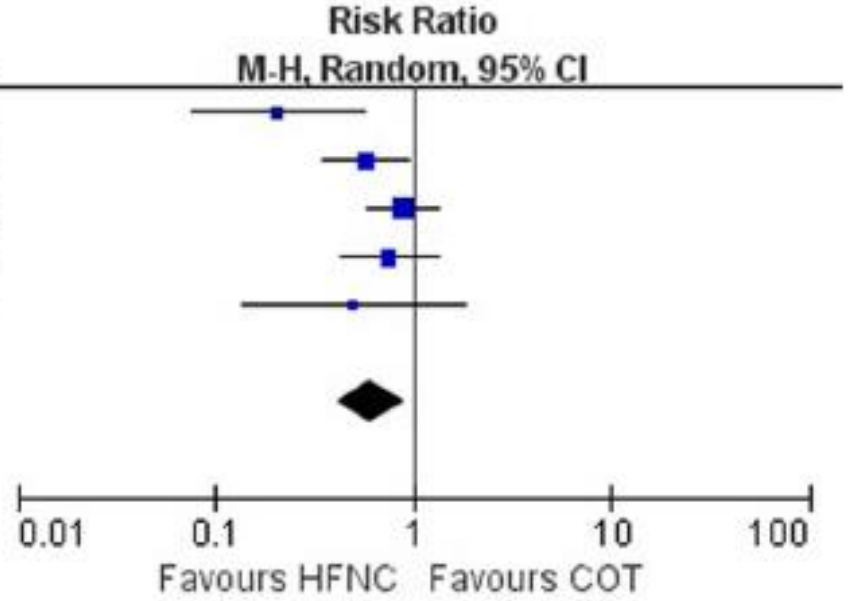
Variable	Oxygen Therapy: High-Flow (n = 264)	Oxygen Therapy: Conventional (n = 263)	Difference Between Groups (95% CI)	*P* Value
Secondary Outcomes				
Postextubation respiratory failure, No. (%)	22 (8.3)	38 (14.4)	6.1 (0.7 to 11.6)	.03[a]
Respiratory infection, No. (%)	6 (2.3)	13 (4.9)	2.7 (−0.6 to 6.2)	.07[a]
Ventilator-associated tracheobronchitis	3 (1.1)	7 (2.6)	1.5 (−1.0 to 4.4)	.22[a]
Ventilator-associated pneumonia	3 (1.1)	6 (2.3)	1.2 (−1.3 to 3.9)	.31[a]
Time to reintubation, median (IQR), h	19 (12 to 28)	15 (9 to 31)	−4 (−54 to 46)	.66[f]
ICU length of stay, median (IQR), d	6 (2 to 8)	6 (2 to 9)	0 (−10 to 24)	.29[f]
Hospital length of stay, median (IQR), d	11 (6 to 15)	12 (6 to 16)	4 (−28 to 32)	.76[f]
ICU mortality	3 (1.1)	3 (1.1)	0 (−2.3 to 2.3)	.99[a]
Hospital mortality	10 (3.8)	13 (5)	1.2 (−2.5 to 4.9)	.94[a]
Inability to clear secretions	3 (13.6)	14 (36.8)		
Reasons for reintubation, No. (%)				
Respiratory causes for reintubation				
Cardiorespiratory arrest	0	1 (0.4)		
Agitation	1 (0.4)	0		
Inability to clear secretions	0	5 (1.9)		
Hemodynamic impairment[d]	1 (0.4)	1 (0.4)		
Persistent postextubation respiratory failure	2 (0.8)	16 (6)		.02[b]
Nonrespiratory causes for reintubation				
Surgery	4 (1.5)	6 (2.3)		
Low level of consciousness[e]	5 (1.9)	3 (1.1)		

HFNC vs. conventional oxygen therapy in patients after planned extubation

7 RCT and 3 crossover studies
HFNC (n=856) vs. conventional oxygen (n=852)

Study or Subgroup	HFNC group Events	Total	COT group Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Maggiore 2014	4	53	19	52	11.8%	0.21 [0.08, 0.57]	2014
Hernández 2016	22	264	38	263	26.5%	0.58 [0.35, 0.95]	2016
Futier 2016	29	108	34	112	30.0%	0.88 [0.58, 1.34]	2016
Fernandez 2017	16	78	21	77	23.6%	0.75 [0.43, 1.33]	2017
Song 2017	3	30	6	30	8.1%	0.50 [0.14, 1.82]	2017
Total (95% CI)		**533**		**534**	**100.0%**	**0.61 [0.41, 0.92]**	
Total events	74		118				

Heterogeneity: $Tau^2 = 0.10$; $Chi^2 = 7.82$, $df = 4$ ($P = 0.10$); $I^2 = 49\%$
Test for overall effect: $Z = 2.38$ ($P = 0.02$)



Postextubation respiratory failure

Table 4 Summary of findings

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with COT	Risk with HFNC				
Postextubation respiratory failure	219 per 1000	136 per 1000 (92 to 202)	RR 0.62 (0.42 to 0.92)	1067 (5 RCTs)	⊕⊕⊕⊕ High	
PaO_2 (mmHg)	The mean paO_2 was 83.63 mmHg	The mean paO2 in the intervention group was 89.39 mmHg (75.91 to 102.86 mmHg)	–	497 (5 RCTs)	⊕⊕⊕⊕ High	
Respiratory rates (breaths per minute)	The mean respiratory rates was 23.24 breaths per minute	The mean respiratory rates in the intervention group was 20.4 breaths per minute (18.84 to 21.95 breaths per minute)	–	311 (5 RCTs)	⊕⊕⊕⊕ High	Respiratory rates obtained from the study by Maggiore and colleague was reported with cartograms, and we extracted data with DigitizeIt software (Braunschweig, Germany).
Reintubation	82 per 1000	48 per 1000 (25 to 91)	RR 0.58 (0.30 to 1.11)	1562 (7 RCTs)	⊕⊕⊕⊕ High	

No significant differences

reintubation rate, length of ICU and hospital stay, comfort score, $PaCO_2$, mortality in ICU and hospital, and severe adverse events

Effect of Postextubation High-Flow Nasal Cannula vs Noninvasive Ventilation on Reintubation and Postextubation Respiratory Failure in High-Risk Patients

A Randomized Clinical Trial

- Patients who tolerated the SBT
- High risk patients
- HFNC (**n=290)** for 24 hrs. if necessary, conventional oxygen
  initially set at 10L/min and titrated upwards in 5L/min
  target SpO_2 92%

  vs. Full face mask NIV (**n=314**) for 24hrs. Venturi mask
  PEEP and inspiratory pressure support
  target a respiratory rate of 25/min,
  SaO_2 92%, with pH of 7.35

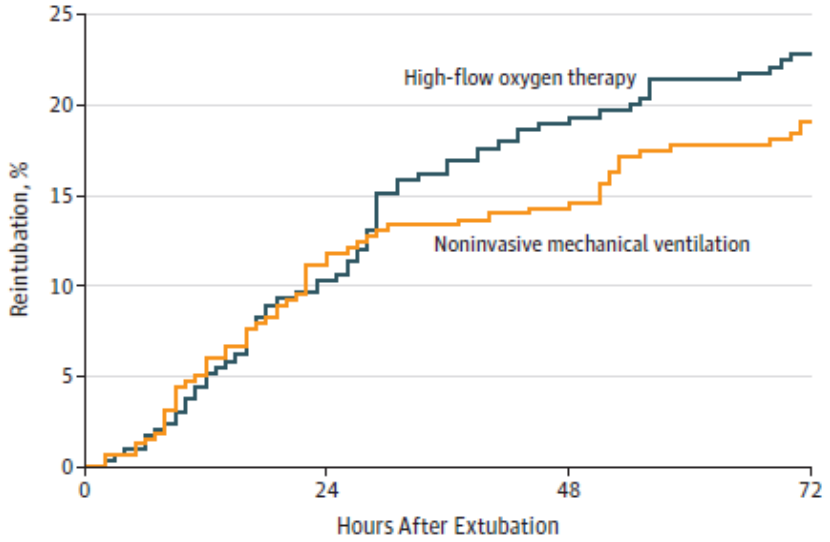
JAMA. 2016;316(15):1565-1574.

	No. (%)	
	Noninvasive Mechanical Ventilation (n = 314)	High-Flow Conditioned Oxygen Therapy (n = 290)
High-risk factors for reintubation		
>65 y	182 (58)	166 (57.2)
Heart failure as the primary indication for MV	31 (9.9)	16 (5.5)
COPD	65 (20.7)	51 (17.6)
APACHE II >12 on extubation day[a]	128 (40.8)	131 (45.2)
Body mass index >30[c]	62 (19.7)	63 (21.7)
Airway patency problems	10 (3.2)	7 (2.4)
Inability to deal with respiratory secretions	66 (21)	66 (22.8)
Difficult or prolonged weaning[d]	87 (27.7)	73 (25.2)
≥2 Comorbidities	218 (69.4)	204 (70.3)
Prolonged mechanical ventilation	120 (38.2)	101 (34.8)
Diagnosis at admission[e]		
Medical	186 (59.2)	154 (53.1)
Respiratory primary failure	121 (38.5)	98 (33.8)
ARDS[f]	26 (8.3)	27 (9.3)
Respiratory infection	48 (15.3)	37 (12.8)
Exacerbated COPD	33 (10.5)	15 (5.2)
Airway patency problem	6 (1.9)	7 (2.4)
Other	8 (2.5)	12 (4.1)
Nonrespiratory primary failure	65 (20.7)	56 (19.3)
Cardiologic	51 (16.2)	39 (13.4)
Neurologic	6 (1.9)	11 (3.8)
Other	8 (2.5)	6 (2.1)

JAMA. 2016;316(15):1565-1574.

All cause reintubation

Figure 2. Kaplan-Meier Analysis of Time From Extubation to Reintubation



No. at risk

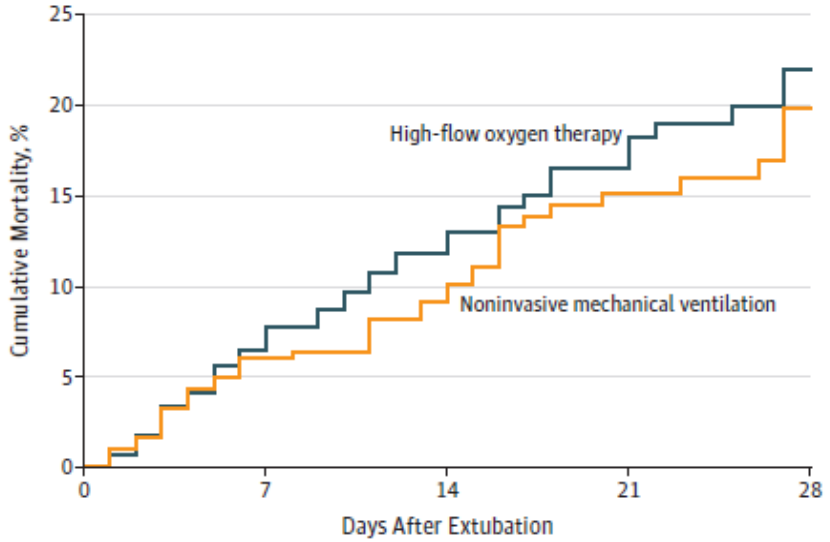
High-flow oxygen therapy	290	260	234	223
Noninvasive mechanical ventilation	314	279	269	253

NIV 19.1% vs. HFNC 22.8%. Noninferior to NIV

Respiratory related intubations
NIV 15.9% vs. HFNC 16.9% (95% CI -4.9 to 6.9)

Mortality

Figure 3. Kaplan-Meier Analysis of Time From Extubation to Death



No. at risk

High-flow oxygen therapy	282	223	144	101	78
Noninvasive mechanical ventilation	309	261	187	112	79

Mortality
ICU: NIV 5.7% vs. HFNC 6.6%
Hospital: NIV 17.8% vs. HFNC 20.3%

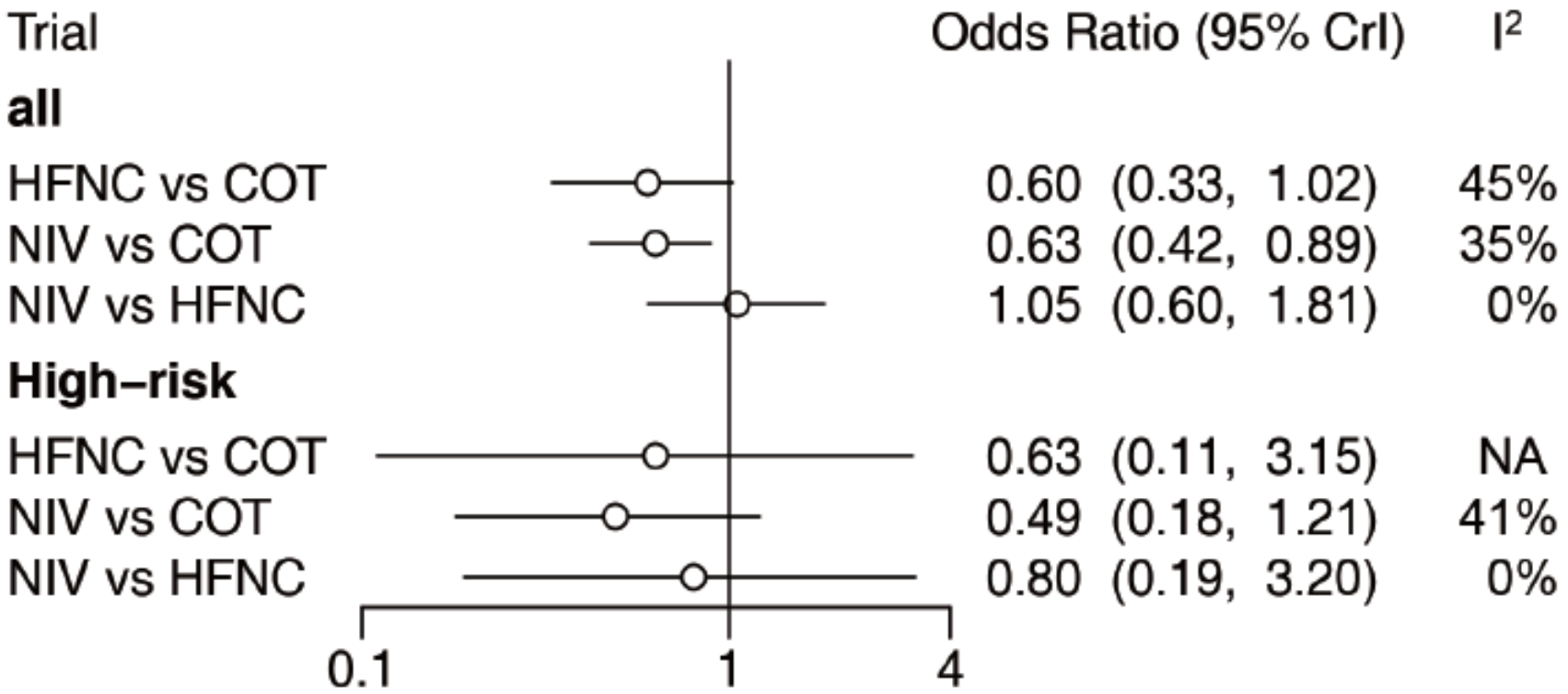
JAMA. 2016;316(15):1565-1574.

	No. (%)		
	Noninvasive Mechanical Ventilation (n = 314)	High-Flow Conditioned Oxygen Therapy (n = 290)	Difference Between Groups (95% CI)[a]
Primary outcome			
All-cause reintubation[b]	60 (19.1)	66 (22.8)	−3.7 (−9.1 to ∞)[c]
Postextubation respiratory failure[b]	125 (39.8)	78 (26.9)	12.9 (6.6 to ∞)[c]
Secondary Outcomes			
Causes of postextubation respiratory failure			*P* = .89[d]
Respiratory acidosis[e]	21 (6.7)	11 (3.8)	
Hypoxia[f]	19 (6.1)	12 (4.1)	
Unbearable dyspnea	26 (8.3)	21 (7.2)	
Decreased level of consciousness	7 (2.2)	4 (1.4)	
Inability to clear secretions	52 (16.6)	30 (10.3)	
Causes for reintubation			*P* = .28[d]
Cardiorespiratory arrest	3 (1)	3 (1)	
Agitation	1 (0.3)	3 (1)	
Inability to clear secretions	20 (6.4)	13 (4.5)	
Hemodynamic impairment[g]	10 (3.2)	14 (4.8)	
Persistent postextubation respiratory failure[f]	16 (5.1)	16 (5.5)	
Nonrespiratory causes for reintubation			
Surgery	4 (1.3)	2 (0.7)	
Low level of consciousness[h]	6 (1.9)	15 (5.2)	

JAMA. 2016;316(15):1565-1574.

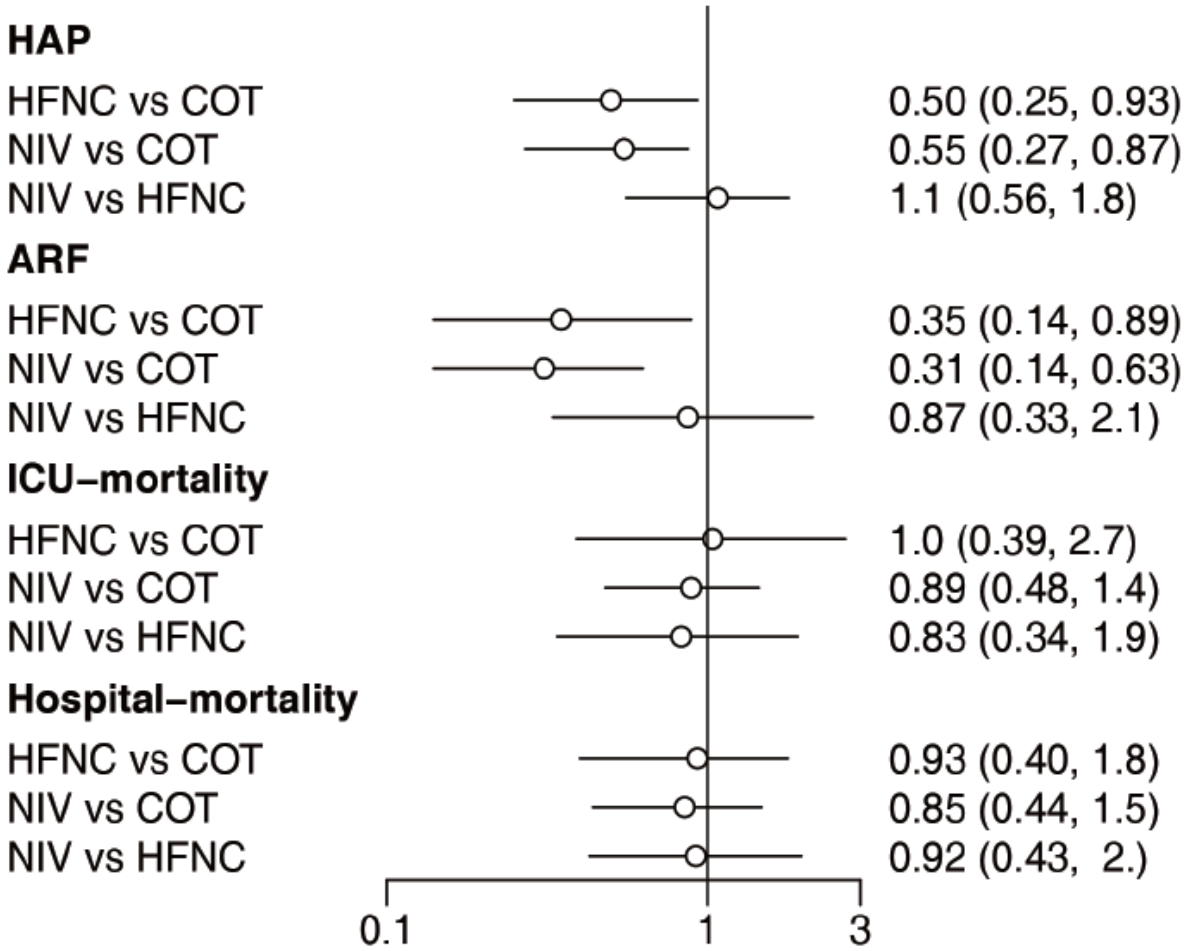
Effect of high-flow nasal cannula versus conventional oxygen therapy and non-invasive ventilation for preventing reintubation: a Bayesian network meta-analysis and systematic review

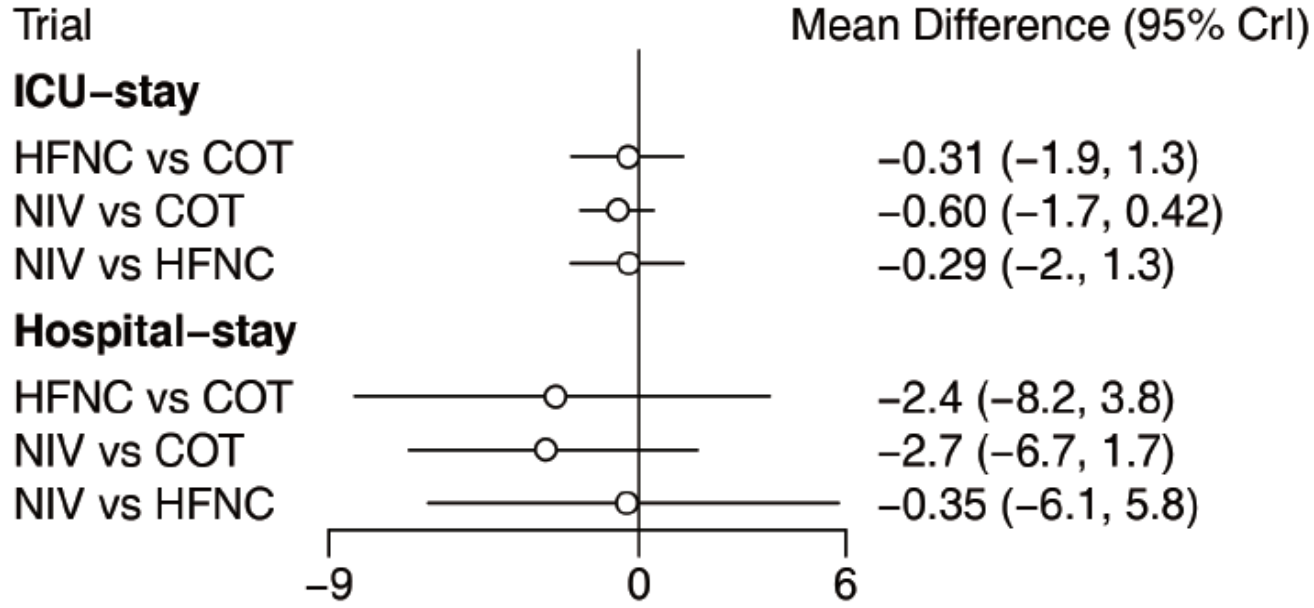
21 studies (4,218 patients)



Reintubation

J Thorac Dis 2020;12(7):3725-3736


HAP
HFNC vs COT
NIV vs COT
NIV vs HFNC
0.50 (0.25, 0.93)
0.55 (0.27, 0.87)
1.1 (0.56, 1.8)
ARF
HFNC vs COT
NIV vs COT
NIV vs HFNC
0.35 (0.14, 0.89)
0.31 (0.14, 0.63)
0.87 (0.33, 2.1)
ICU−mortality
HFNC vs COT
NIV vs COT
NIV vs HFNC
1.0 (0.39, 2.7)
0.89 (0.48, 1.4)
0.83 (0.34, 1.9)
Hospital−mortality
HFNC vs COT
NIV vs COT
NIV vs HFNC
0.93 (0.40, 1.8)
0.85 (0.44, 1.5)
0.92 (0.43, 2.)
0.1
1
3


Trial
Mean Difference (95% CrI)
ICU−stay
HFNC vs COT
NIV vs COT
NIV vs HFNC
−0.31 (−1.9, 1.3)
−0.60 (−1.7, 0.42)
−0.29 (−2., 1.3)
Hospital−stay
HFNC vs COT
NIV vs COT
NIV vs HFNC
−2.4 (−8.2, 3.8)
−2.7 (−6.7, 1.7)
−0.35 (−6.1, 5.8)
−9
0
6

Effect of Postextubation High-Flow Nasal Oxygen With Noninvasive Ventilation vs High-Flow Nasal Oxygen Alone on Reintubation Among Patients at High Risk of Extubation Failure

A Randomized Clinical Trial

JAMA. 2019;322(15):1465-1475.

- 648 patients intubated more than 24hrs after a successful SBT
- HFNC alone (n=302)

  at least 48 hours with a flow of 50L/min

  set FiO2 to target by SpO2 at least 92%
- NIV+HFNC (n=339)

  NIV was initiated immediately after extubation within a first session of at least 4 hours and minimal duration of at least 12 hours a day during the 48 hours

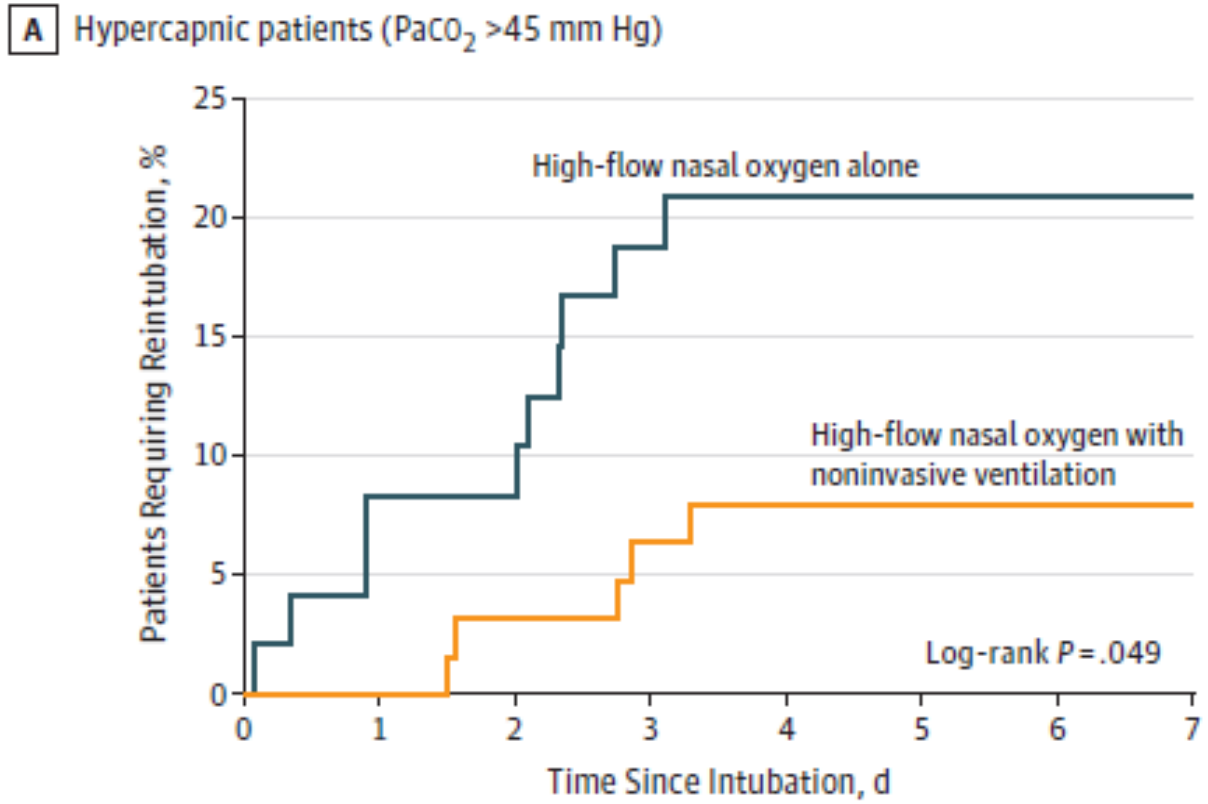
  PS mode with a minimal pressure support level of 5 cmH_2O targeting a tidal volume around 6 to 8 mL/kg, PEEP between 5 and $10H_2O$

Characteristic	No. (%)	
	High-Flow Nasal Oxygen Alone (n = 302)	High-Flow Nasal Oxygen With NIV (n = 339)
Main reason for intubation		
Acute respiratory failure	158 (52)	167 (49)
Coma	55 (18)	57 (17)
Shock	30 (10)	37 (11)
Cardiac arrest	26 (9)	35 (10)
Surgery	28 (9)	35 (10)
Other reason	5 (2)	8 (2)
Risk factors of extubation failure		
Age >65 y	223 (74)	237 (70)
Underlying chronic cardiac disease[d]	145 (48)	161 (47)
Ischemic heart disease	78 (26)	88 (26)
Atrial fibrillation	58 (19)	45 (13)
Left ventricular dysfunction	39 (13)	52 (15)
History of cardiogenic pulmonary edema	21 (7)	25 (7)
Underlying chronic lung disease[d]	87 (29)	126 (37)
Chronic obstructive pulmonary disease	64 (21)	86 (25)
Obesity-hypoventilation syndrome	16 (5)	20 (6)
Chronic restrictive pulmonary disease	12 (4)	24 (7)

Table 2. Primary, Secondary, and Exploratory Outcomes

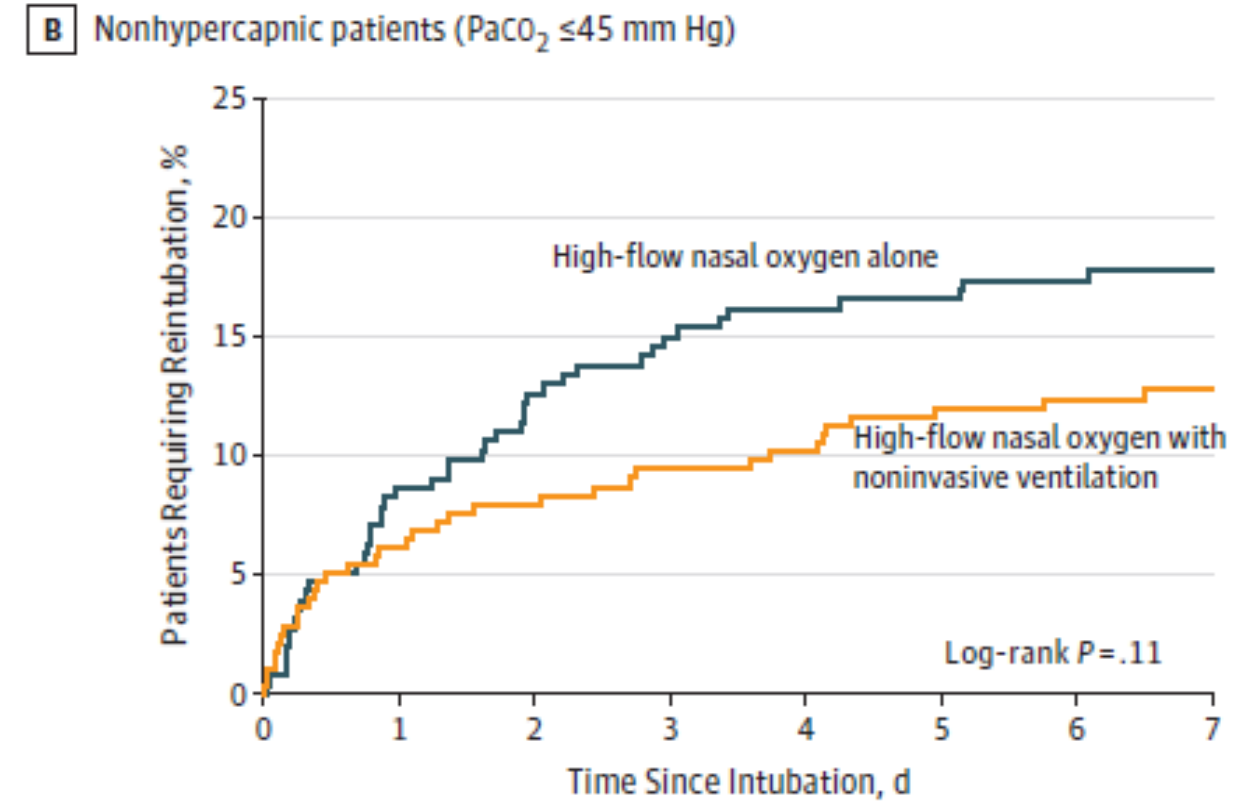
	No. (%)			
	High-Flow Nasal Oxygen Alone (n = 302)	High-Flow Nasal Oxygen With NIV (n = 339)	Absolute Difference, % (95% CI)	*P* Value
Primary Outcome				
Reintubation at day 7	55 (18)	40 (12)	−6.4 (−12.0 to −0.9)	.02
Secondary Outcomes				
Postextubation respiratory failure at day 7	88 (29)	70 (21)	−8.5 (−15.2 to −1.8)	.01
Reintubation				
At 48 h	36 (12)	24 (7)	−4.8 (−9.6 to −0.3)	.04
At 72 h	47 (16)	30 (9)	−6.7 (−11.9 to −1.7)	.009
Up until ICU discharge	59 (20)	41 (12)	−7.4 (−13.2 to −1.8)	.009
Length of stay, median (IQR), days				
In ICU	11 (7 to 19)	12 (7 to 19)	0.5 (−1.6 to 2.6)	.55
In hospital	23 (15 to 39)	25 (15 to 42)	2.3 (−1.4 to 6.1)	.31
Mortality				
In ICU	26 (9)	21 (6)	−2.4 (−6.7 to 1.7)	.25
In hospital	46 (15)	54 (16)	0.7 (−5.0 to 6.3)	.80
At day 28	33 (11)	39 (12)	0.6 (−4.4 to 5.5)	.82
At day 90	65 (21)	62 (18)	−3.2 (−9.5 to 2.9)	.30
Exploratory Outcomes				
Patients meeting reintubation criteria during ICU stay	65 (22)	49 (14)	−7.1 (−13.1 to −1.1)	.02
Mortality or reintubation in ICU	64 (21)	51 (15)	−6.2 (−12.2 to −0.2)	.04
Mortality of reintubated patients	21/59 (36)	11/41 (27)	−8.8 (−25.7 to 9.9)	.35

Figure 3. Kaplan-Meier Analysis of Time From Extubation to Reintubation According to Predefined Strata



No. at risk								
High-flow nasal oxygen								
Alone	48	44	44	39	38	37	37	37
With noninvasive ventilation	63	63	61	59	58	58	58	58

8% vs. 21% p=0.049



No. at risk								
High-flow nasal oxygen								
Alone	254	232	221	214	210	209	207	206
With noninvasive ventilation	276	258	253	249	247	236	234	233

13% vs. 18% p=0.10

ORIGINAL ARTICLE

Spontaneous-Breathing Trials with Pressure-Support Ventilation or a T-Piece

All the patients were followed until day 28 after the initial spontaneous-breathing trial. After extubation, the prophylactic use of noninvasive ventilation (oxygen administered through a face mask) for at least 48 hours, as well as oxygen administered through a high-flow nasal cannula between sessions of noninvasive ventilation, was strongly encouraged in all patients.[10,15]

Prophylactic respiratory support after extubation

At least one extubation attempt in ICU	N=477	N=481
High-flow nasal oxygen – no. (%)	191 (40%)	197 (41%)
- Treatment duration within the first 24 hours – hours	13 ± 7	12 ± 7
Noninvasive ventilation – no. (%)	367 (77%)	383 (80%)
- Treatment duration within the first 24 hours – hours	10 ± 6	10 ± 6
NIV interspaced with standard oxygen – no. (%)	208 (44%)	211 (44%)
NIV interspaced with high-flow oxygen – no. (%)	159 (33%)	172 (36%)

N Engl J Med 2022;387:1843-54.

Take home messages

- NIV

  - Facilitative weaning from MV can be used in patients with COPD or chronic hypercapnic respiratory failure

  - Prophylactic weaning can be used in high risk hypercapnic patients

  - Curative weaning is not recommended

  - Further studies are needed in other patients populations (hypoxemic ARF)

Take home messages

• HFNC for post-extubation respiratory failure (prophylactic)

- Compared to COT, HFNC reduced post-extubation respiratory failure

→ HFNC can be used in patients who are intubated more than 24hr and have any high-risk feature

- Compared to NIV, HFNC is not superior to NIV

- HFNC with NIV can be considered in high risk patients