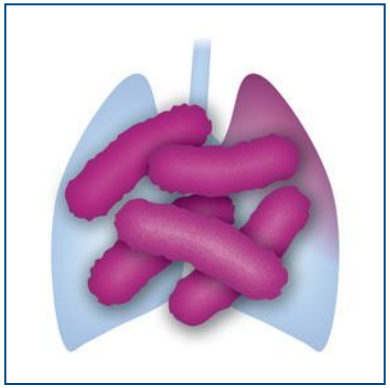
Pneumo Update Europe 2018

15 - 16 June, Budapest

Acute Respiratory Failure & Critical Care



Paolo Pelosi, Italy

Reclassifying Acute Respiratory Distress Syndrome

State of the Art

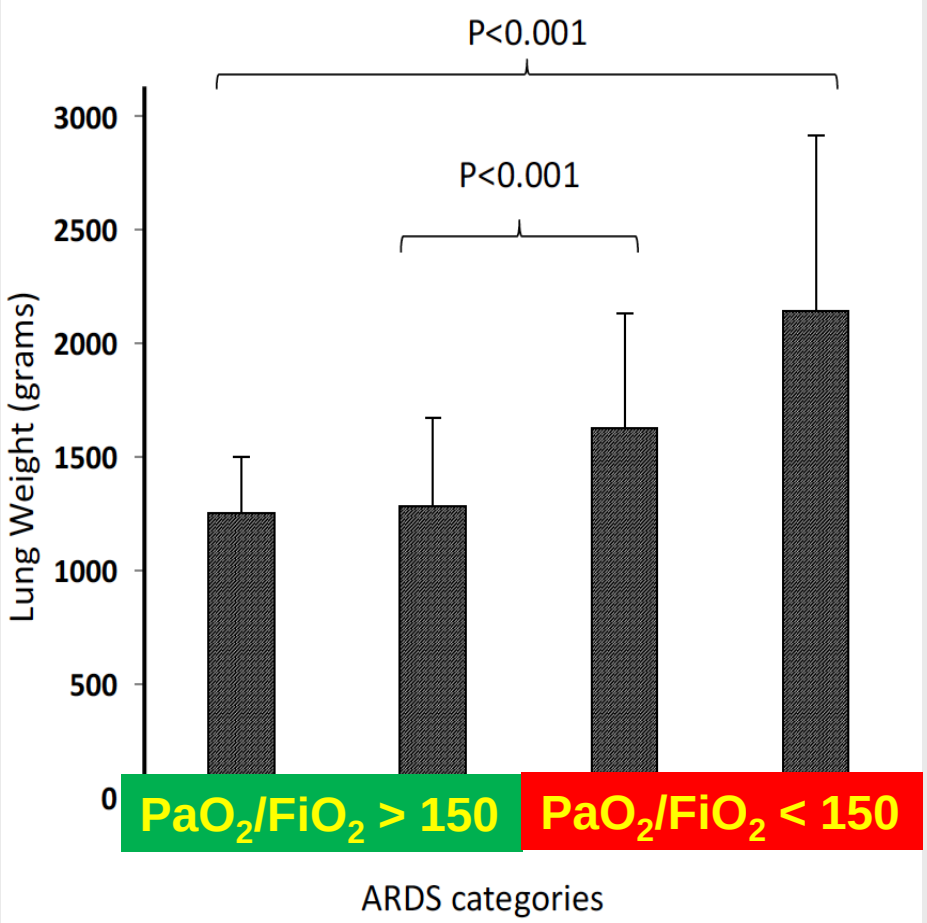
The Berlin Definition

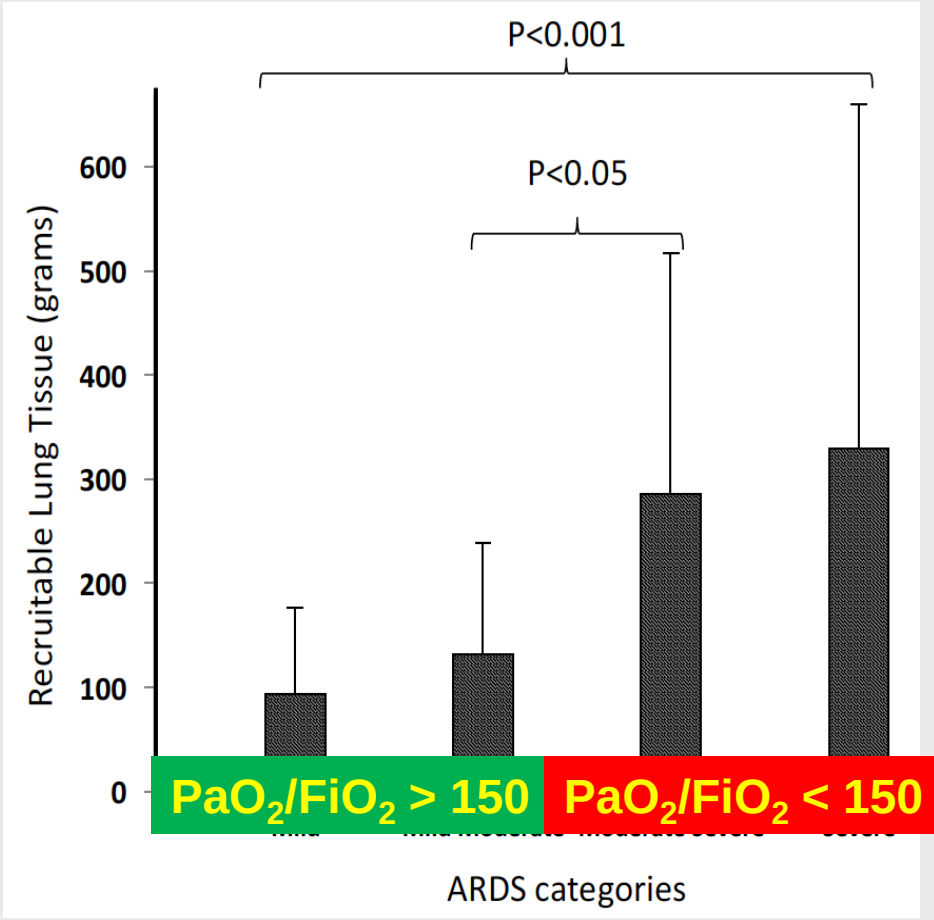
	Acute Respiratory Distress Syndrome		
Timing	Within 1 week of a known clinical insult or new/worsening respiratory symptoms		
Chest Imaging	Bilateral opacities – not fully explained by effusions, lobar/lung collapse, or nodules		
Origin of Edema	Respiratory failure not fully explained by cardiac failure or fluid overload; Need objective assessment (e.g., echocardiography) to exclude hydrostatic edema if no risk factor present		
	Mild	**Moderate**	**Severe**
Oxygenation	**$200 < PaO_2/FiO_2 \leq 300$** with PEEP/CPAP ≥ 5 cmH_2O	**$100 < PaO_2/FiO_2 \leq 200$** with PEEP ≥ 5 cmH_2O	**$PaO_2/FiO2 \leq 100$** with PEEP ≥ 5 cmH_2O

The moderate ARDS:
contains the majority of patients with shunt between 20 to 60%

The ARDS Definition Task Force JAMA. JAMA 2012; 307: 2526-2533.

Reclassifying Acute Respiratory Distress Syndrome





Maiolo G et al. AJRCCM Articles in Press. Published on 18-January-2018

Take-Home Message

- Using the 150 mmHg P/F threshold:

❖ Gave a more homogeneous distribution of ARDS patients across the severity subgroups

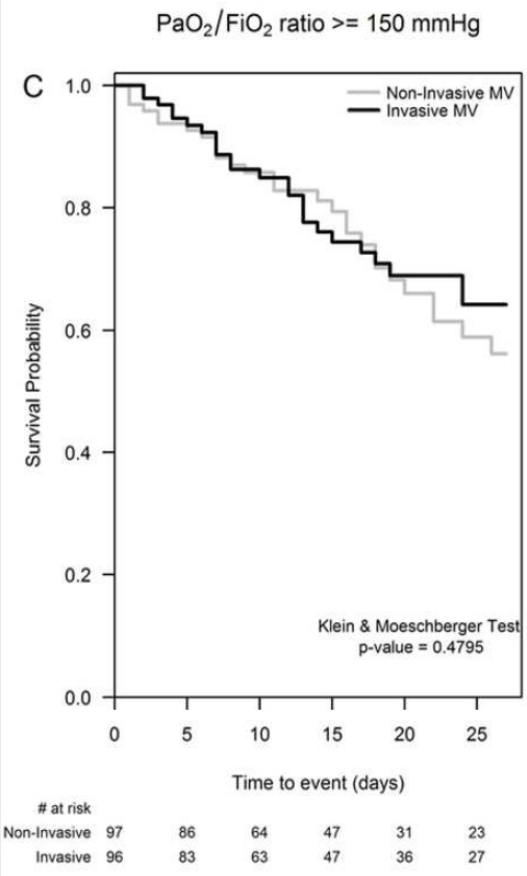
❖ Identified two populations that differed in their anatomical and physiological characteristics

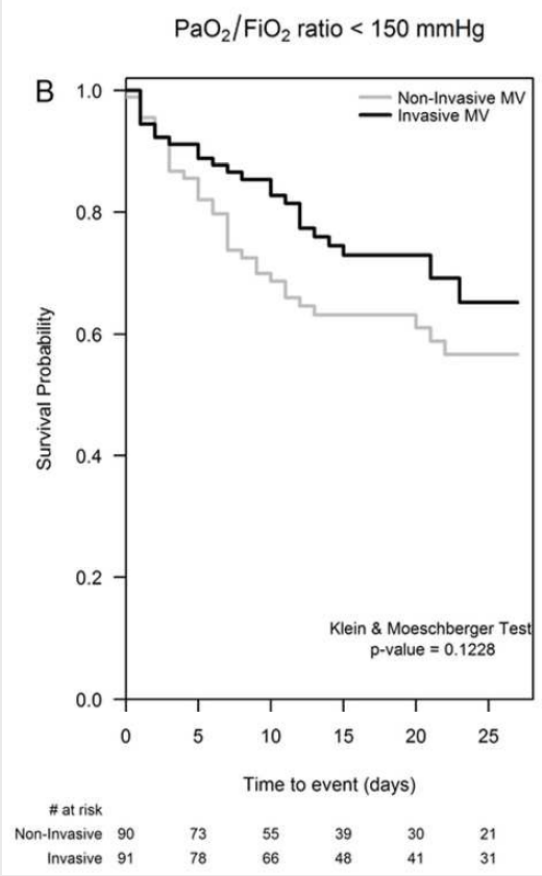
❖ Patients treated with Prone position and/or ECMO belonged to the severe ARDS group

Maiolo G et al. AJRCCM Articles in Press. Published on 18-January-2018

Non Invasive Ventilation in ARDS

NIV is associated with higher mortality in severe ARDS



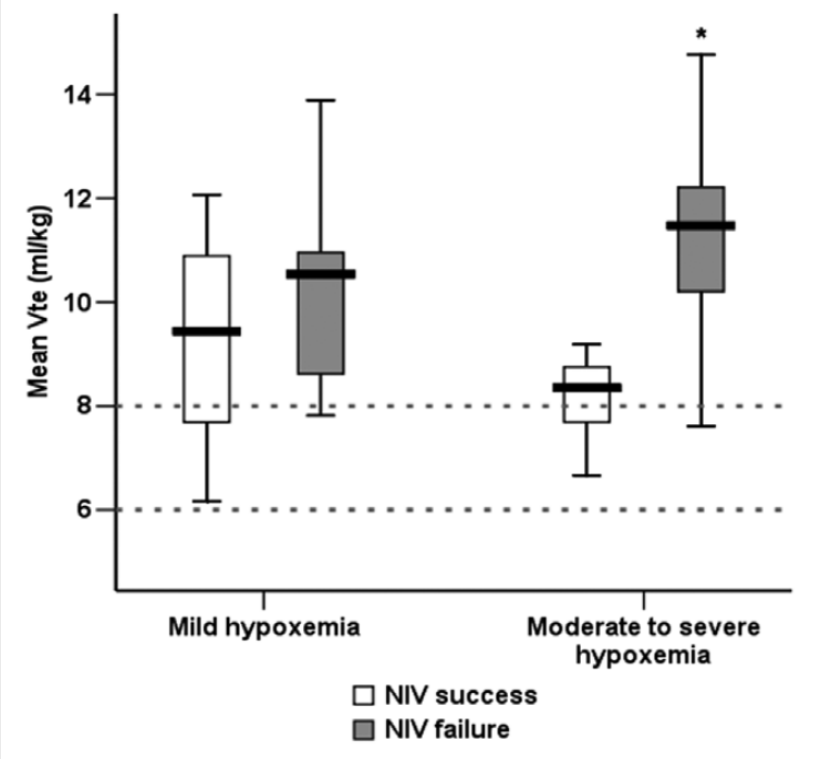


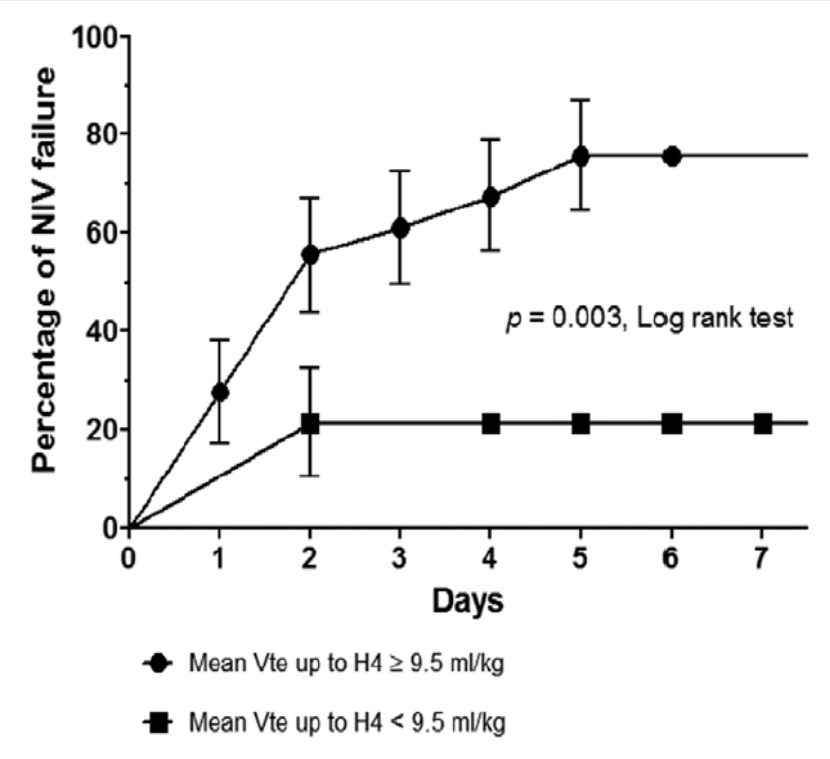
NIV is used in 15% of ARDS pts

	NIV	CMV
V_T (ml/Kg PBW)	8.4	7.6
PEEP (cmH_2O)	7.0	8.0
Respiratory Rate (b/min)	27	21
FiO_2(%)	60	65

Bellani G et al. Am J Respir Crit Care Med. 2017 Jan 1;195(1):67-77

Higher V_T is associated with NIV failure in severe ARDS

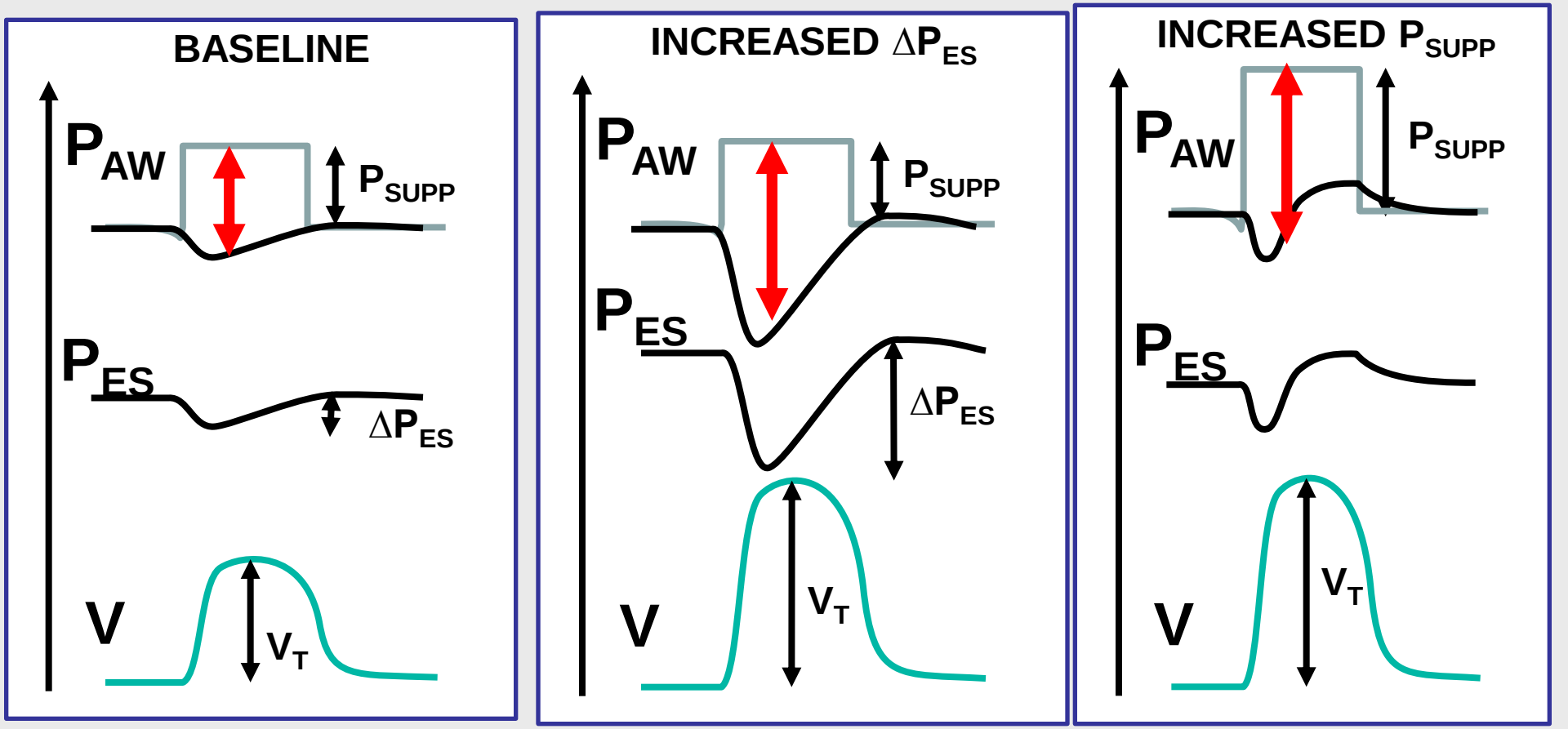




29% increased risk of failure
for each 1 mL/ kg PBW increase of mean V_T

Carteaux G et al Crit Care Med 2016; 44:282–290

Greater effort: higher V_T & VILI (Ptp)



V_T higher than 9 ml/Kg PBW is associated with worse outcome

Cruz FF et al. Expert Rev Respir Med. 2018 May;12(5):403-414

Take-Home Message

- NIV is used in about 15% patients with ARDS, irrespective of the severity of hypoxemia
- NIV is associated with worse outcome when $PaO_2/FiO_2<150$
- Higher (9ml/Kg PBW) V_T is associated with NIV failure

Bellani G et al. Am J Respir Crit Care Med. 2017 Jan 1;195(1):67-77

Carteaux G et al Crit Care Med 2016; 44:282–290

High Flow Oxygen Nasal Cannulas

State of the Art

Oxygenation

Ventilatory Support

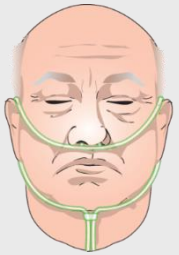
Ventilation
+/-Oxygenation

Oxygenation (Oxygen) Failure = Exchange (Lung) failure

Ventilation (Capnia) Failure = Pump (Muscles) failure

CPAP
(mask)

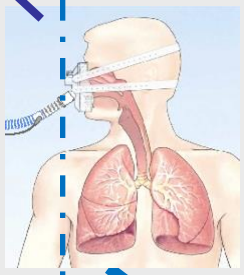
Intubation + Invasive Ventilation



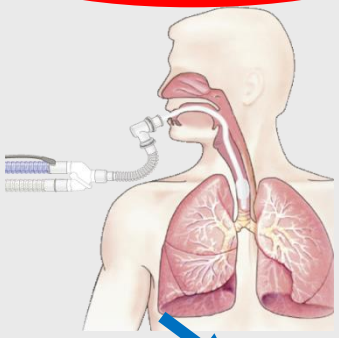
O2 canulae
(Low flow < 5 L/min)

O2
Mask high Concentration
(High flow > 10 L/min)

HFONC
(High Flow Oxygen)



NIV
(CPAP/Bi-PAP)

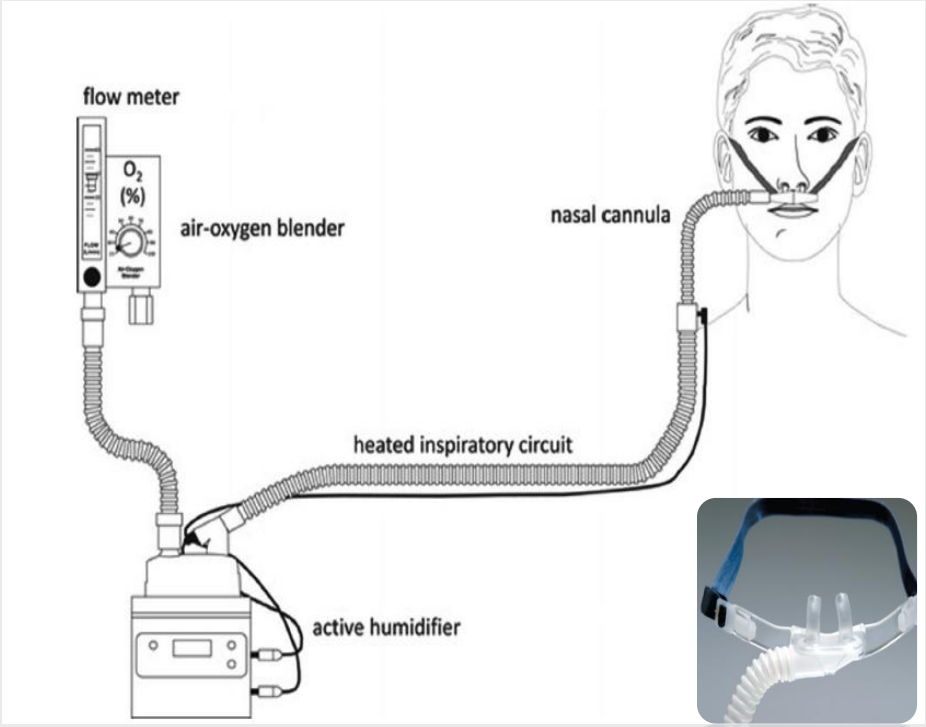


Invasive Ventilation
(Endotracheal tube)

Courtesy Prof. S Jaber

State of the Art

High Flow Oxygen Nasal Cannulas



High flows of inspired gas up to 60 L/min

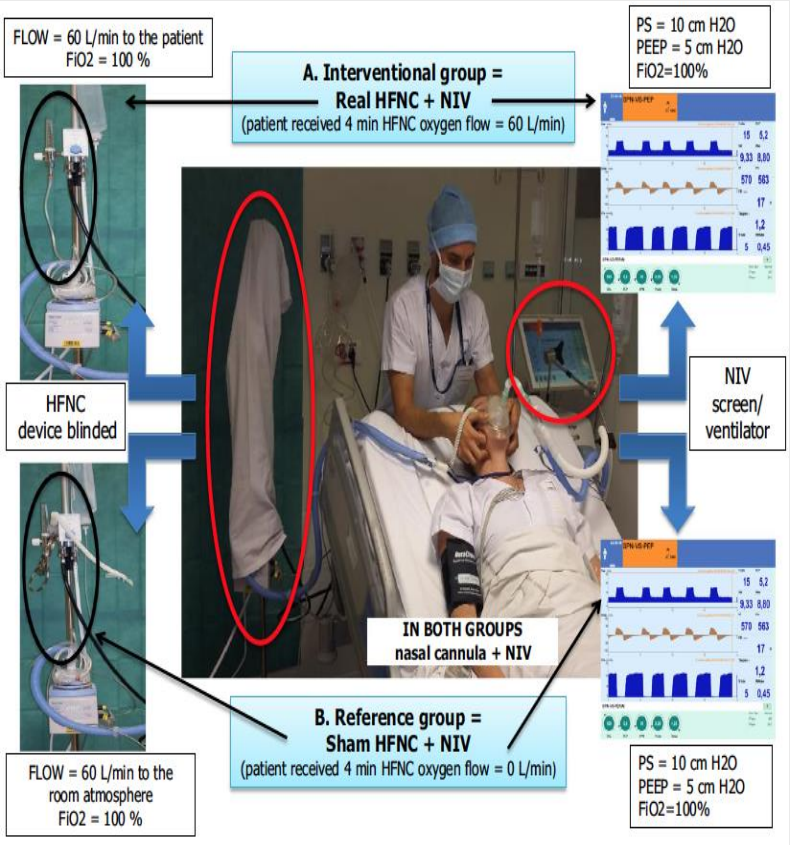
Full humidification (37 C, 100 RH, 44 mg H_2O/L)

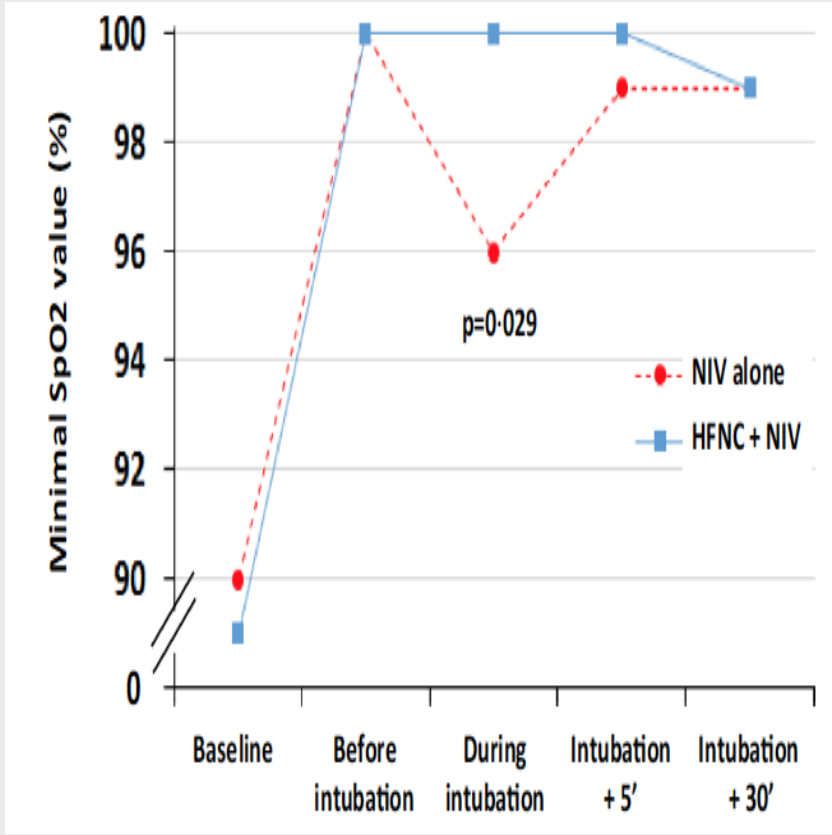
ARF features	NHF actions
Atelectasis/Derecruitment	Recruits the Lung (EPAP effect)
Alveolar Hypoventilation	Increases Alveolar Ventilation
Hypoxemia	Increases Oxygenation
Hypercapnia	Decreases PaCO2
Tachypnea	Decreases Respiratory Rate
Dyspnea	Reliefs Dyspnea
Discomfort	Improves Patient's Comfort
Increased Work Of Breathing	Decreases Respiratory Muscles' Effort

Papazian L et al. Intensive Care Med (2016) 42:1336–1349

Renda T et al. British Journal of Anaesthesia, 120(1): 18e27 (2018)

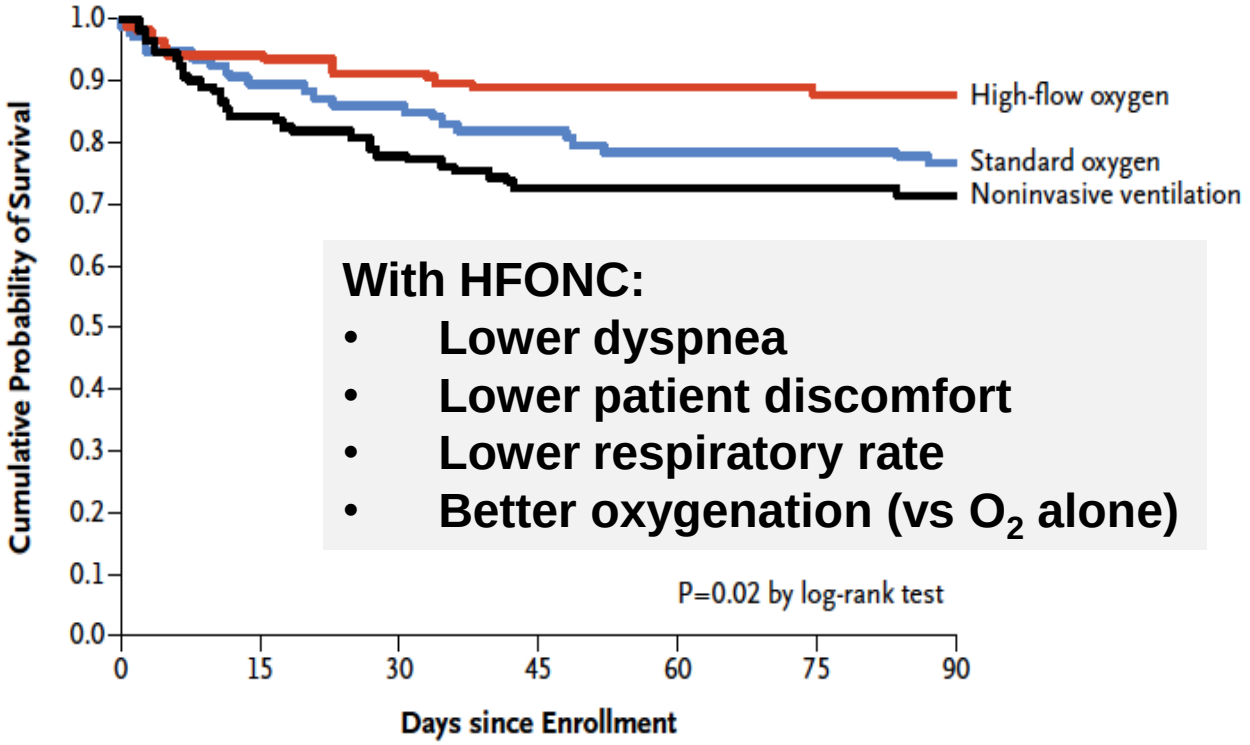
HFONC with NIV preoxygenation is better than NIV alone during intubation in hypoxaemic patients





Jaber S et al. Intensive Care Med (2016) 42:1877–1887

High Flow Oxygen Nasal Cannula is better than NIV or standard O_2 in ARDS



With HFONC:

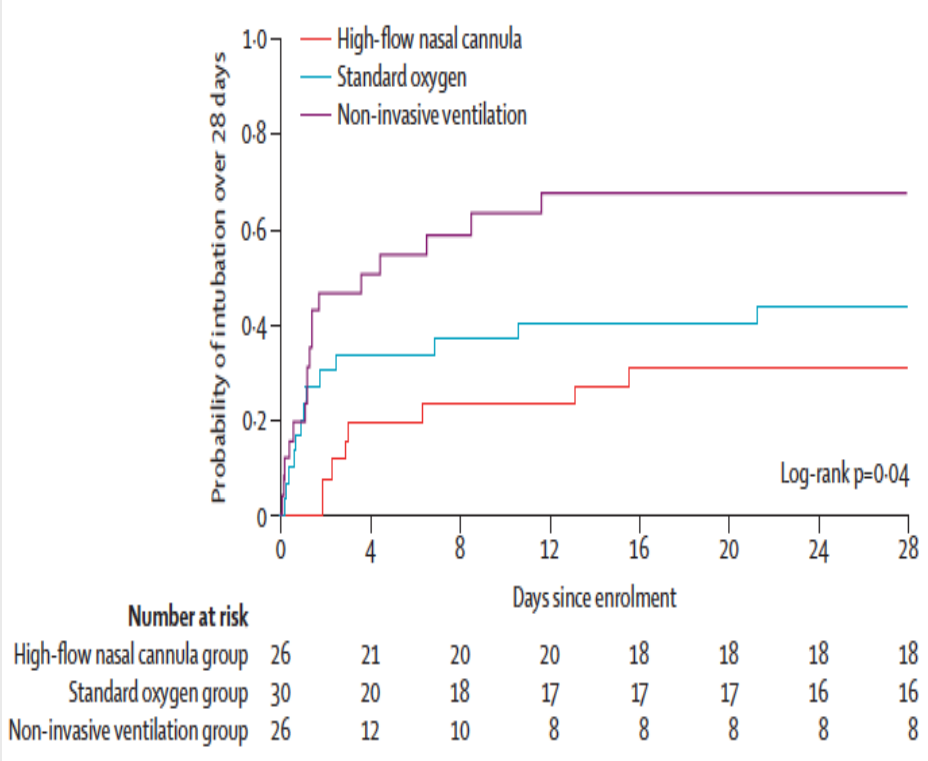
- **Lower dyspnea**
- **Lower patient discomfort**
- **Lower respiratory rate**
- **Better oxygenation (vs O_2 alone)**

No. at Risk

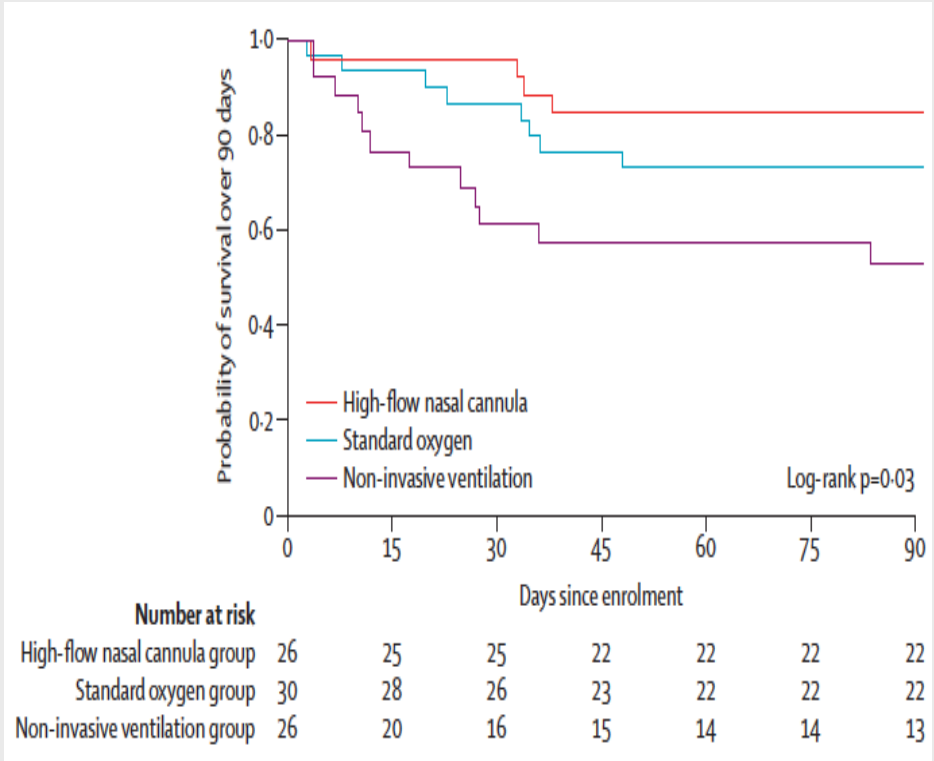
High-flow oxygen	106	100	97	94	94	93	93
Standard oxygen	94	84	81	77	74	73	72
Noninvasive ventilation	110	93	86	80	79	78	77

Frat J.P. et al. N Engl J Med. 2015 Jun 4;372(23):2185-96

High Flow Oxygen Nasal Cannula in immunocompromised ARDS pts



Number at risk								
High-flow nasal cannula group	26	21	20	20	18	18	18	18
Standard oxygen group	30	20	18	17	17	17	16	16
Non-invasive ventilation group	26	12	10	8	8	8	8	8



Number at risk							
High-flow nasal cannula group	26	25	25	22	22	22	22
Standard oxygen group	30	28	26	23	22	22	22
Non-invasive ventilation group	26	20	16	15	14	14	13

Nasal High-Flow Oxygen reduces the risk of intubation and improves survival in immunocompromised ARF patients

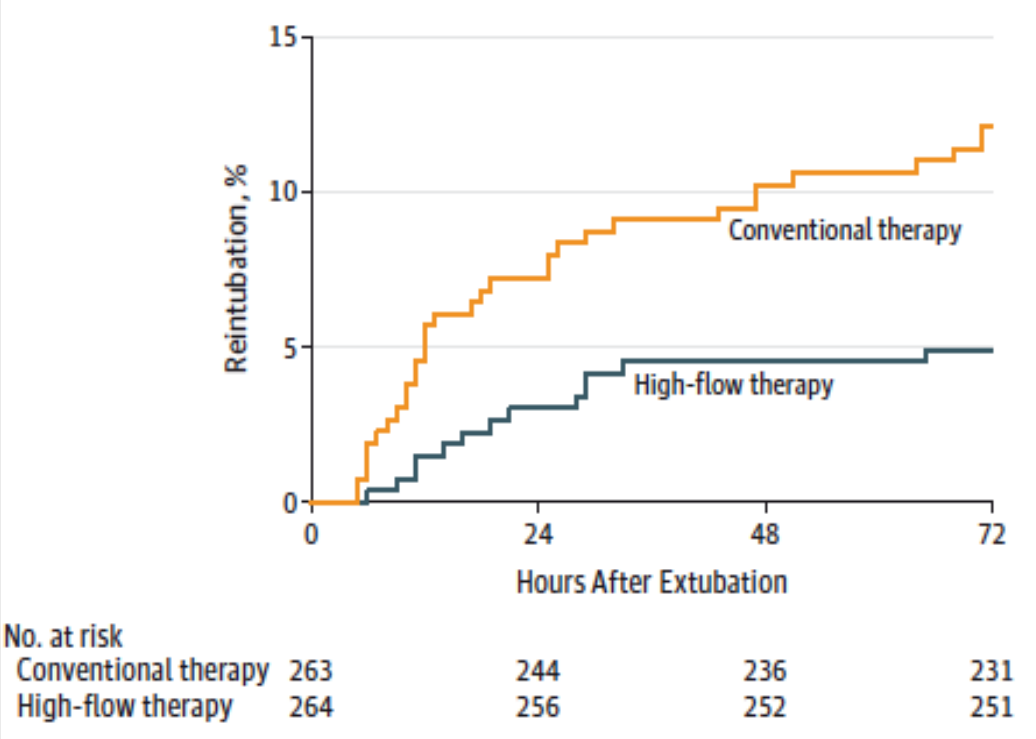
Frat JP et al. Lancet Respir Med. 2016 Aug;4(8):646-652

High-Flow Oxygen Nasal Cannula in pts at low risk of extubation failure

❖ **At least one of the following:**

✓ Younger than 65 years;
✓ APACHE II less than 12 on day of extubation;
✓ Body mass index less than 30;
✓ Adequate secretions management;
✓ Simple weaning;
✓ 0 or 1 comorbidity;
✓ Absence of heart failure;
✓ Moderate-to-severe COPD
✓ Airway patency problems
✓ Prolonged MV

➢ high-flow or conventional oxygen therapy for 24 hours after extubation.



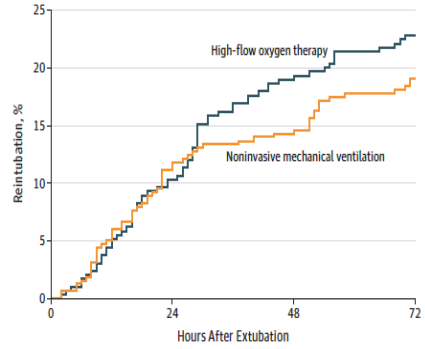
NHFO is superior to standard therapy to prevent reintubation

Hernandez G et al. JAMA. 2016 Apr 5;315(13):1354-61

High-Flow Oxygen Nasal Cannula in pts at high risk of extubation failure

- ❖ **At least 1 of the following**:
- ✓ Older than 65 years;
- ✓ APACHE II score higher than 12 points on extubation day;
- ✓ Body mass index higher than 30;
- ✓ Inadequate secretions management;
- ✓ Difficult or prolonged weaning;
- ✓ More than 1 comorbidity;
- ✓ Heart failure as primary indication for mechanical ventilation;
- ✓ Moderate to severe COPD;
- ✓ Airway patency problems;
- ✓ Prolonged mechanical ventilation

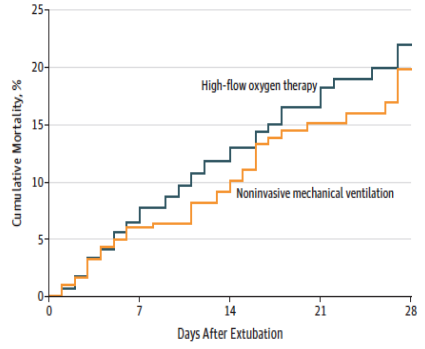
Figure 2. Kaplan-Meier Analysis of Time From Extubation to Reintubation



No. at risk

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

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



No. at risk

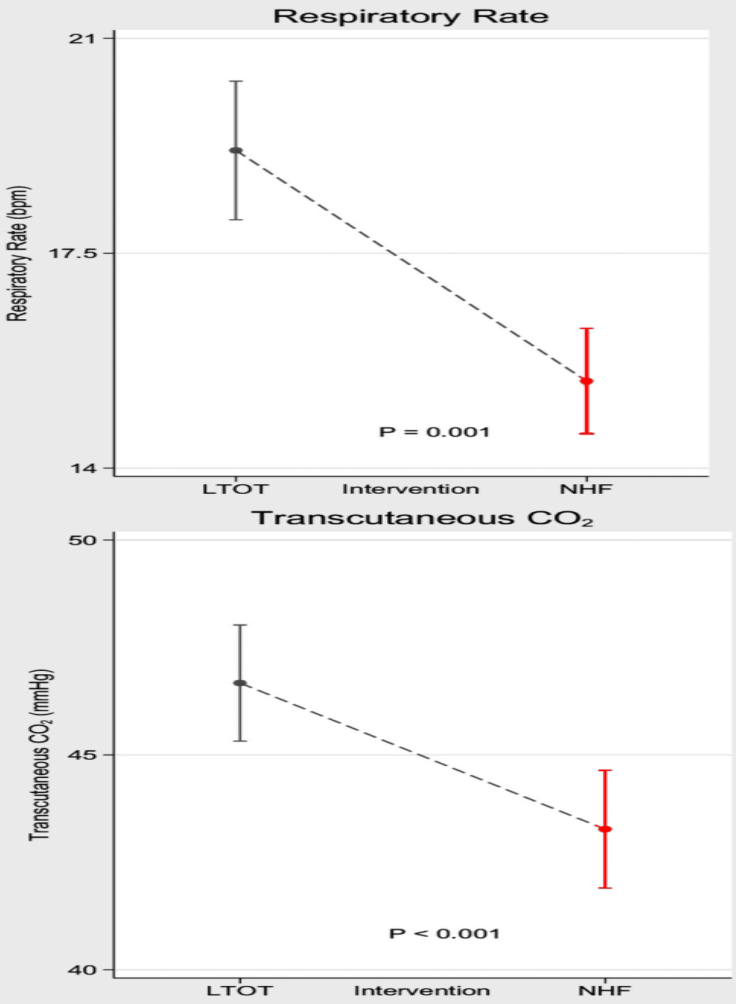
High-flow oxygen therapy	282	223	144	101	78
Noninvasive mechanical ventilation	309	261	187	112	79

NHFO is equivalent to NIV to prevent reintubation with less adverse events yielding treatment dicontinuation

Hernandez G et al. JAMA. 2016;316(15):1565-1574

High Flow Oxygen Nasal Cannula reduces RR and $PaCO_2$ in COPD

- RCT (2 x 20 min) in 30 patients ♂
- SpO_2 95.8 vs 95.7; **p=0.06**
- TcO_2 101.2 vs 97.1; **p=0.01**
- $TcCO_2$ 46.7 vs 43.3; **p<0.001**
- RR (b/m) 19.2 vs 15.4; **p=0.001**
- I:E 0.86 vs 0.75; **p=0.02**
- VT (ml) 0.40 vs 0.50; **p=0.003**
- Volume minute (L/m) 6.20 vs 6.18; **p=0.88**
- HR (b/m) 70.1 vs 69.8; **p=0.21**
- %ΔEELI 113 vs 174; **p<0.001**



Fraser et al; Thorax. 2016 pii: thoraxjnl-2015-207962

Take-Home Message

❖ High flow oxygen nasal cannula is a promising device in place of NIV

- *Better efficiency and tolerance*

- Intubation
- Treatment of AHRF
- Treatment acute exacerbation in COPD dead space wash-out (?)

Liberal versus conservative oxygen therapy in critically ill patients

State of the Art

- Supplemental oxygen is administered to millions of acutely unwell patients around the world every day.
- 34% pts in ambulance
- 25% pts emergency rooms
- 15% pts admitted in hospital
- 50-85% pts are exposed to escess O_2 and hyperoxia

- Observational studies suggest that excessive oxygen exposure could have adverse consequences.

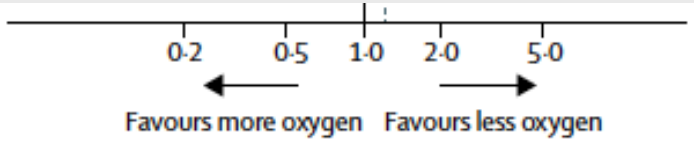
O'Driscoll BR et al. Thorax 2017; 72 (suppl 1): ii1–90.

Liberal versus conservative oxygen therapy in critically ill patients

Systematic review in 16000 patients

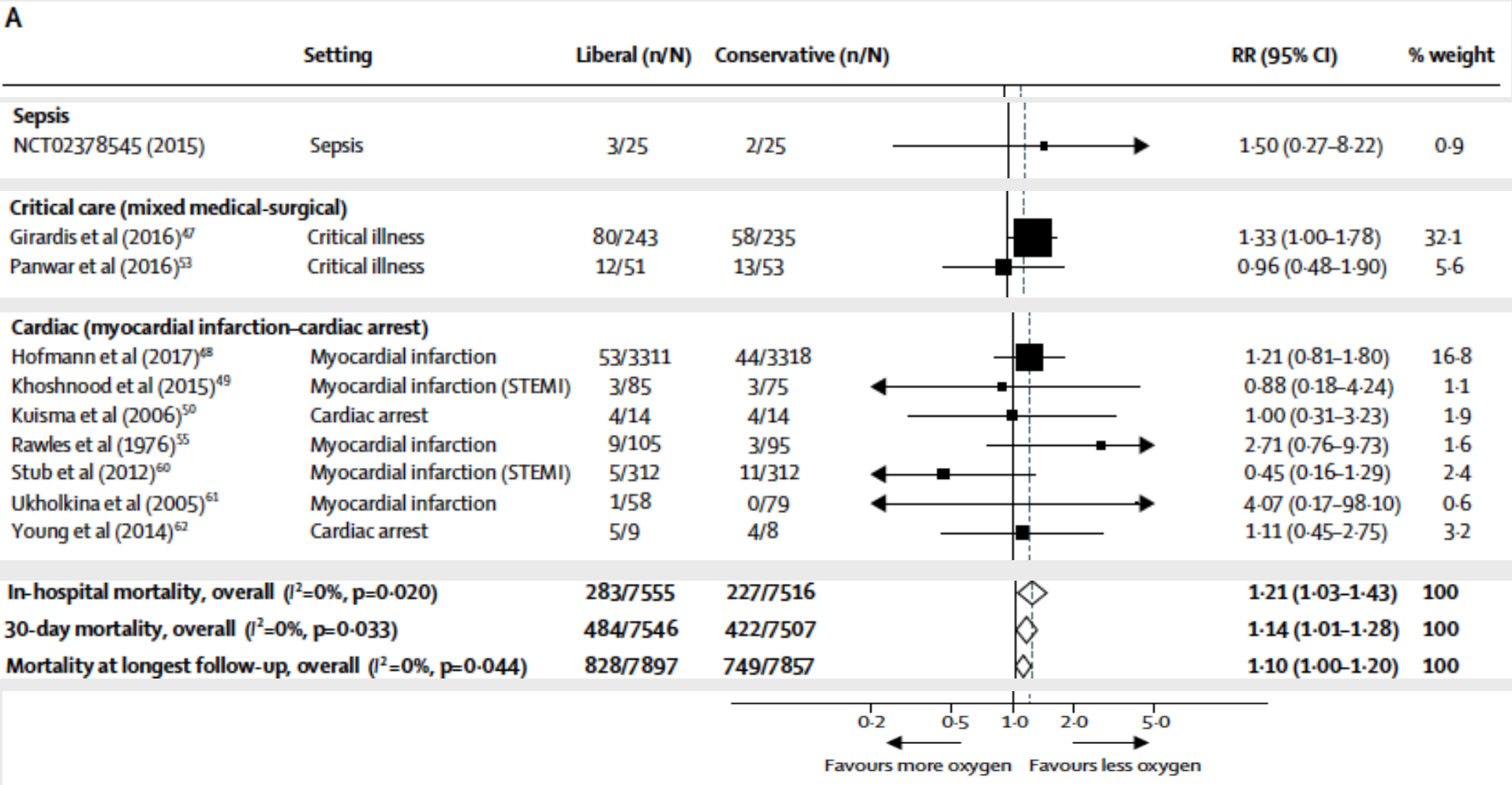
A

	Setting	Liberal (n/N)	Conservative (n/N)	RR (95% CI)	% weight
Neurological (stroke–traumatic brain injury)					
Ali et al (2014)[44,66]	Stroke	5/155	4/146	1·18 (0·32–4·30)	1·6
Roffe et al (2017)[59]	Stroke	50/2668	45/2668	1·11 (0·75–1·66)	16·6
Ronning et al (1999)[56]	Stroke	36/292	27/258	1·18 (0·74–1·89)	11·9
Singhal et al (2005)[58]	Stroke (ischaemic)	0/9	1/7	0·27 (0·01–5·70)	0·3
NCT00414726	Stroke (ischaemic)	14/43	4/42	3·42 (1·22–9·54)	2·5
Shi et al (2017)[65]	Stroke (ischaemic)	0/9	0/9	(Excluded)	0
Emergency surgery					
Butler et al (1987)[46]	Limb ischaemia	1/17	0/22	3·83 (0·17–88·62)	0·3
Schietroma et al (2016)[57]	Perforated peptic ulcer	2/119	4/120	0·50 (0·09–2·70)	0·9
NCT02687217	Acute appendicitis	0/30	0/30	(Excluded)	0



Chu DK et al. Lancet 2018; 391: 1693–705

Liberal versus conservative oxygen therapy in critically ill pattients



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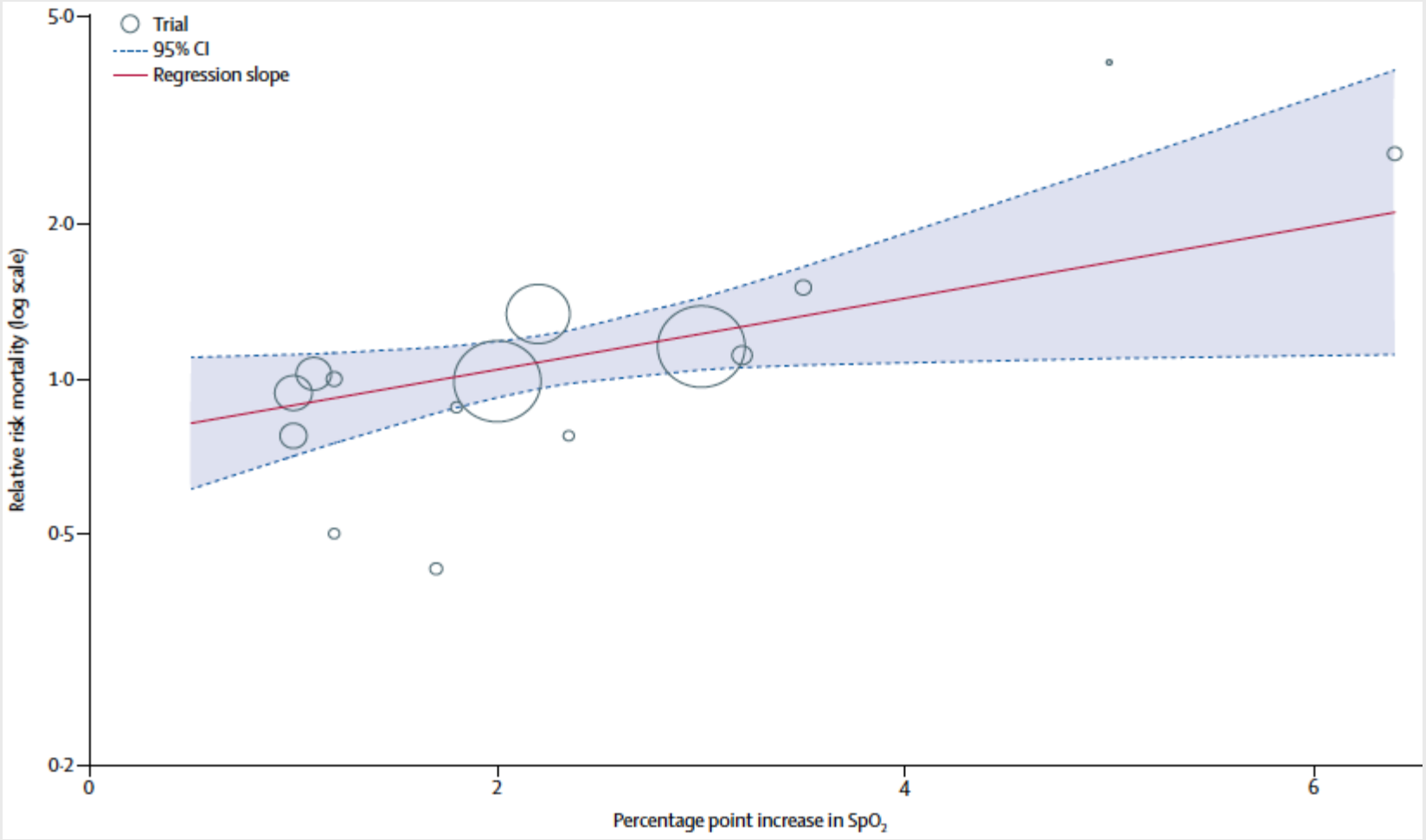

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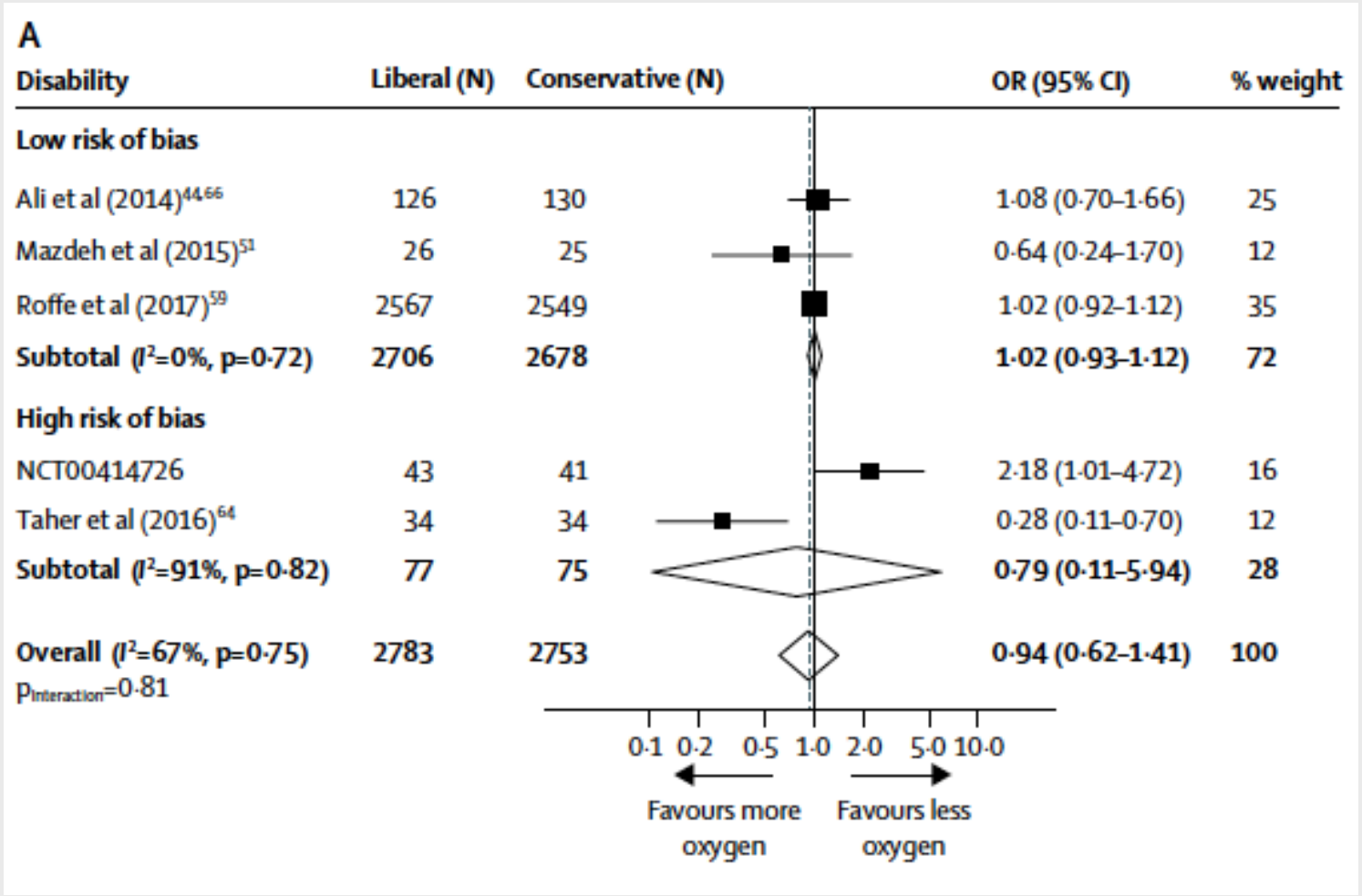

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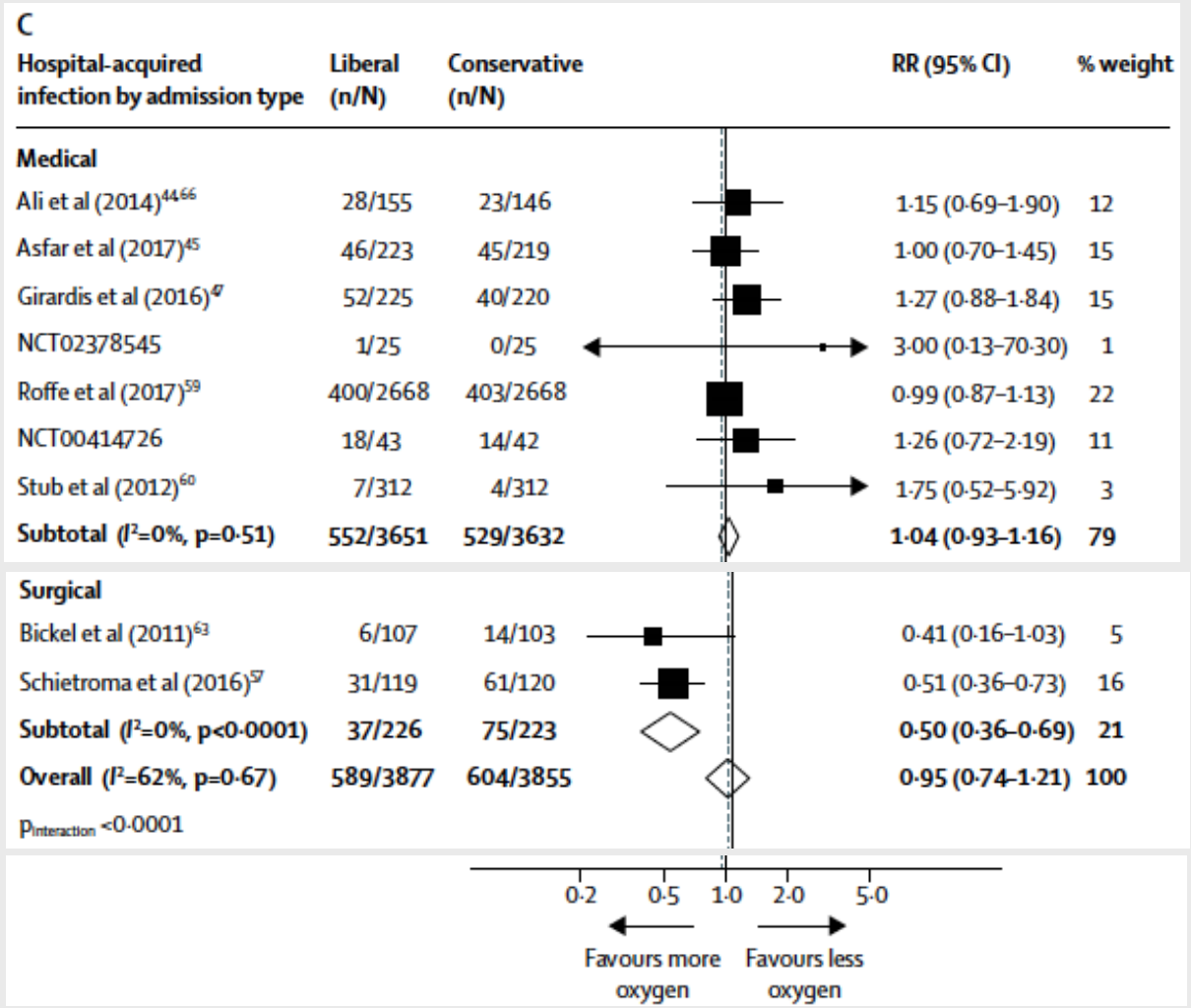


Chu DK et al. Lancet 2018; 391: 1693–705

Take-Home Message

- High-quality evidence that excessive supplemental oxygen in acute illnesses can be life-threatening

- Liberal oxygen therapy increased the relative risk of in-hospital mortality and mortality at 30 days and at longest follow-up

- No significant improvement in disability, risk of hospital-acquired pneumonia, risk of hospital-acquired infections, or length of hospital stay

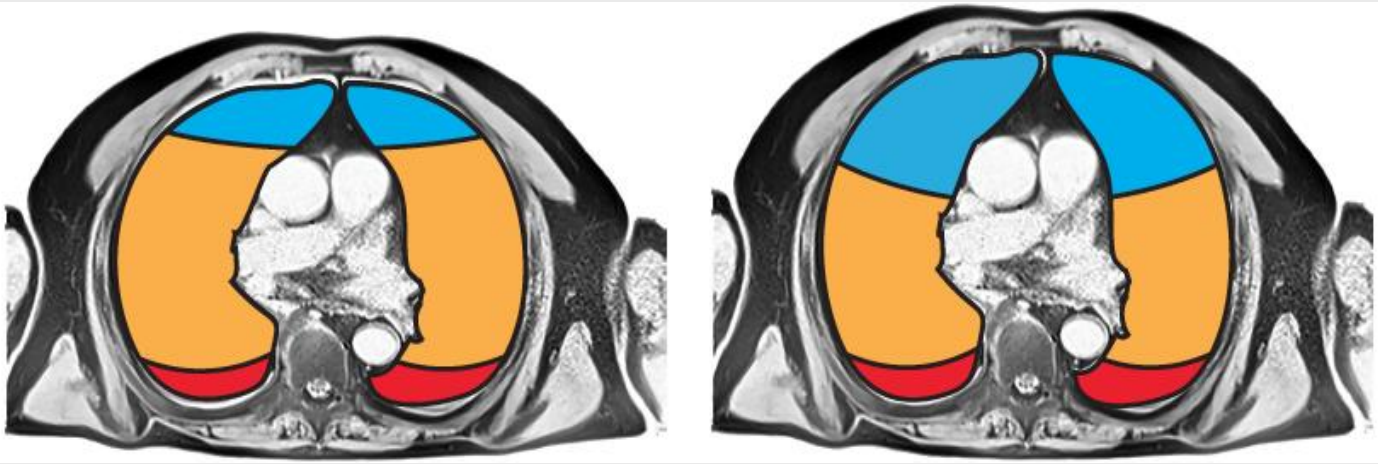
Chu DK et al. Lancet 2018; 391: 1693–705

Close the lungs and keep them closed!

Close the lungs and keep them rested !

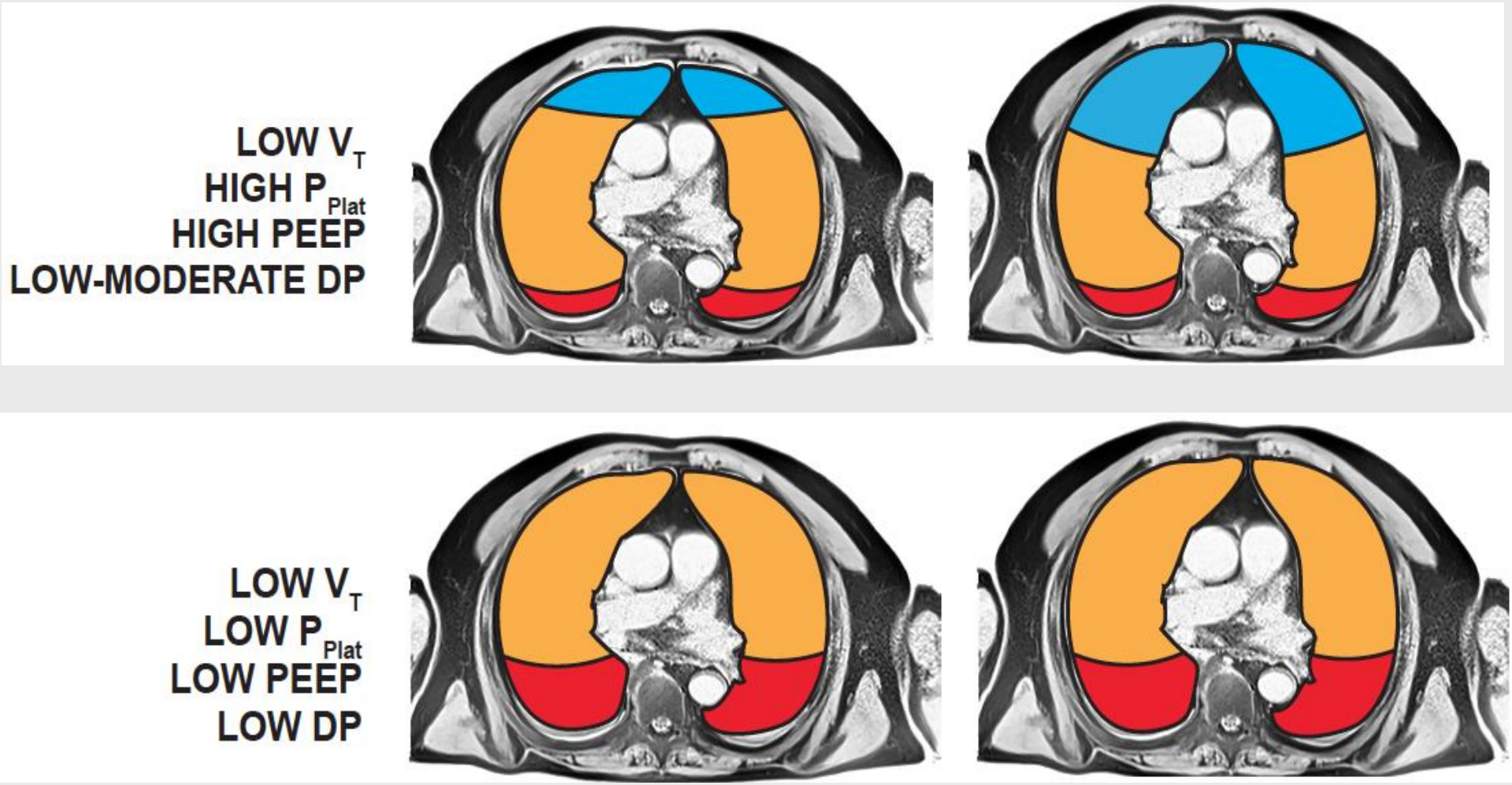
Expiration **Inspiration**

LOW V_T
HIGH P_{Plat}
HIGH PEEP
LOW-MODERATE DP



Pelosi P, et al. Crit Care. 2018 Mar 20;22(1):72

Close the lungs and keep them rested !



Pelosi P, et al. Crit Care. 2018 Mar 20;22(1):72

Close the lungs and keep them rested !

Expiration

Close the lungs and keep them rested!

Patients undergoing high-risk surgery frequently experience postoperative pulmonary complications (PPCs) which have a profound impact on mortality and morbidity. To combat this, a strategy that "closes the lungs and keeps them resting" could be key in minimizing ventilator-induced lung injury (VILI), reducing the incidence of PPCs, and improving clinical outcomes.

This will be the message of Paolo Pelosi (University of Genoa, San Martino Policlinico Hospital, IRCCS for Oncology, Genoa, Italy) who will present a detailed account of his perspectives during this afternoon's VILI session. He will speak on behalf of the PROtective VEntilation network (PROVEnet) and colleagues contributing to challenging dogmas on

which must be balanced with its alleged positive effects. While no doubt exists on the fact that PEEP can improve intraoperative oxygenation, all studies found that these advantages are rapidly lost in the postoperative period, and that clinical outcome is probably not affected.

A recent individual meta-analysis of randomized controlled trials suggested that during surgery the most important determinant for prevention of PPCs is lowering of VT, and not higher levels of PEEP (and recruitment). In general, a level of PEEP higher than 5 cmH_2O (without routine recruitment maneuver) should not be used in patients during surgery. However, higher PEEP might be used in patients in the Trendelenburg position, or for surgery lasting more

the fluid load to improve right ventricle function. However, when PEEP is reduced at the end of surgery, or when the patient is extubated, the fluid load previously adequate for that PEEP level could become excessive and impact negatively on respiratory function.

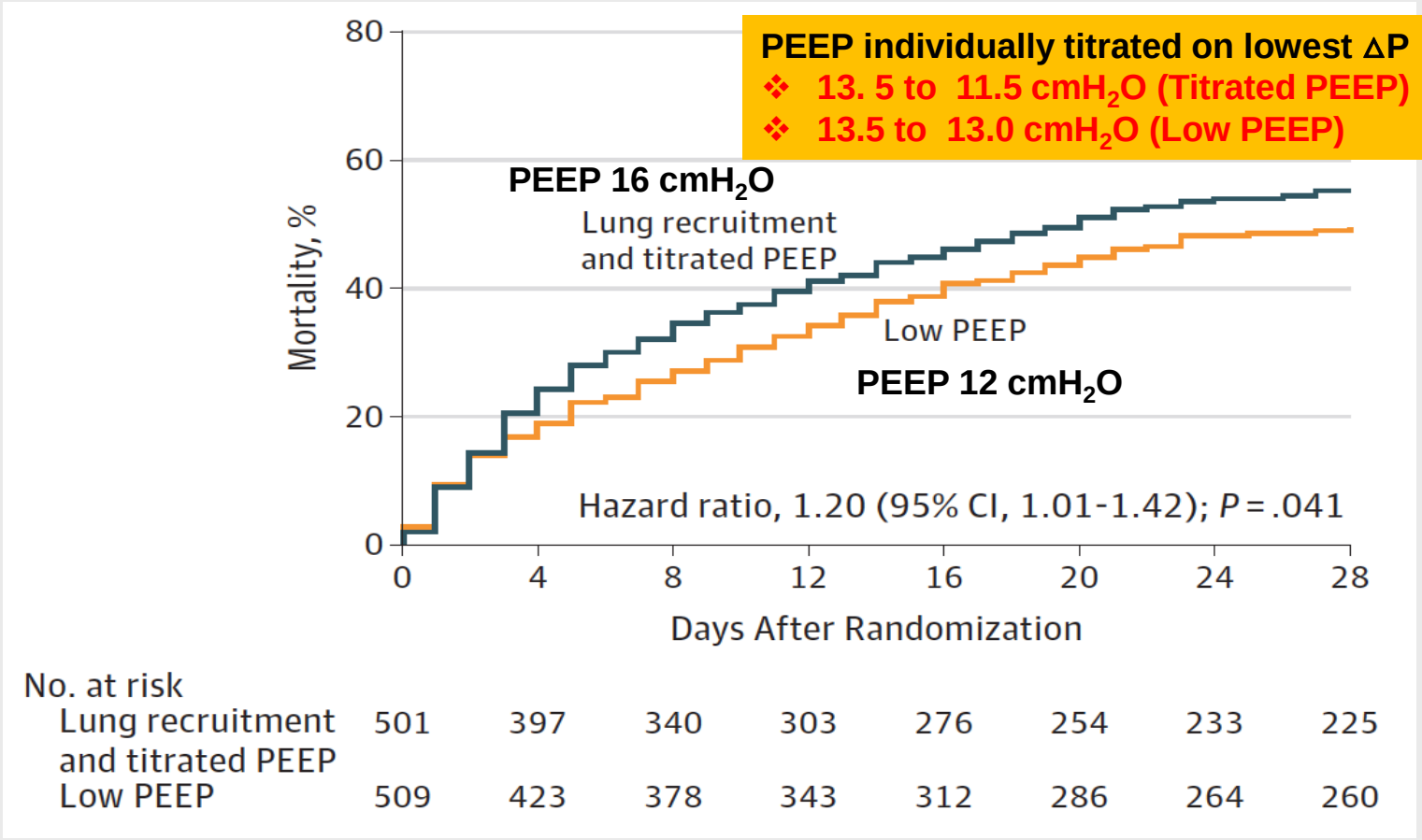
Is driving pressure more likely the key here, i.e. a higher ΔP is an independent risk factor for PPC?

Undoubtedly yes: independent of other ventilation parameters, patients with higher driving pressure develop more PPCs. However, whether this simply means that driving pressure is a marker of risk for PPCs, or if one can titrate ventilation aimed at reducing driving pressure is a much more debated topic.

In patients during surgery, higher driving pressure

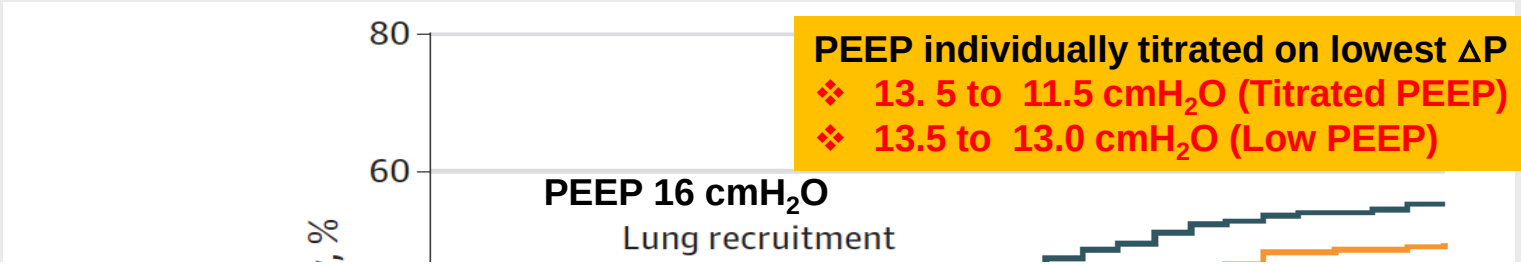
Pelosi P, et al. Crit Care. 2018 Mar 20;22(1):72

Lung recruitment and titrated PEEP vs low PEEP increase mortality in ARDS



Costa Leme A et al. JAMA. 2017 Apr 11;317(14):1422-1432

Lung recruitment and titrated PEEP vs low PEEP increase mortality in ARDS



PEEP individually titrated on lowest ΔP

- **13. 5 to 11.5 cmH_2O (Titrated PEEP)**
- **13.5 to 13.0 cmH_2O (Low PEEP)**

Lung Recruitment and Titrated PEEP in Moderate to Severe ARDS

Is the Door Closing on the Open Lung?

Sarina K. Sahetya, MD; Roy G. Brower, MD

	Days After Randomization							
No. at risk								
Lung recruitment and titrated PEEP	501	397	340	303	276	254	233	225
Low PEEP	509	423	378	343	312	286	264	260

Costa Leme A et al. JAMA. 2017 Apr 11;317(14):1422-1432

Mechanical Ventilation in ARDS

"Less is More"

- **Non invasive respiratory support: caution**
- **Low V_T (6 ml/Kg PBW)**
- **Low Plat (< 28 cmH_2O)**
- **PEEP based on lower PaO_2/FiO_2 Table**
- **ΔP < 13 cmH_2O (strain)**
- **RR to keep pHa > 7.25 (avoiding PEEPi)**

In severe-moderate, severe ARDS (P/F < 150):

- **Neuromuscular blockade – if needed**
- **PRONE POSITION !**

In very severe ARDS (P/F < 80)

- **Consider ECMO as a rescue therapy ($SatO_2$< 80%)**

Pelosi P, et al. Crit Care. 2018 Mar 20;22(1):72

Cruz F et al. Expert Rev Respir Med 2018 May;12(5):403-414

ECMO in patients with severe acute respiratory distress syndrome (ARDS)

State of the Art

- ARDS is associated with high mortality despite the use of low-volume, low-pressure ventilation strategies that are aimed at reducing VILI
- The most severe forms of ARDS may be associated with mortality exceeding 60%
- The efficacy of venovenous extracorporeal membrane oxygenation (ECMO) in patients with severe ARDS remains controversial

Combes A et al. N Engl J Med 2018;378:1965-75

ECMO in severe ARDS

Very severe ARDS, as indicated by 1 of 3 criteria:

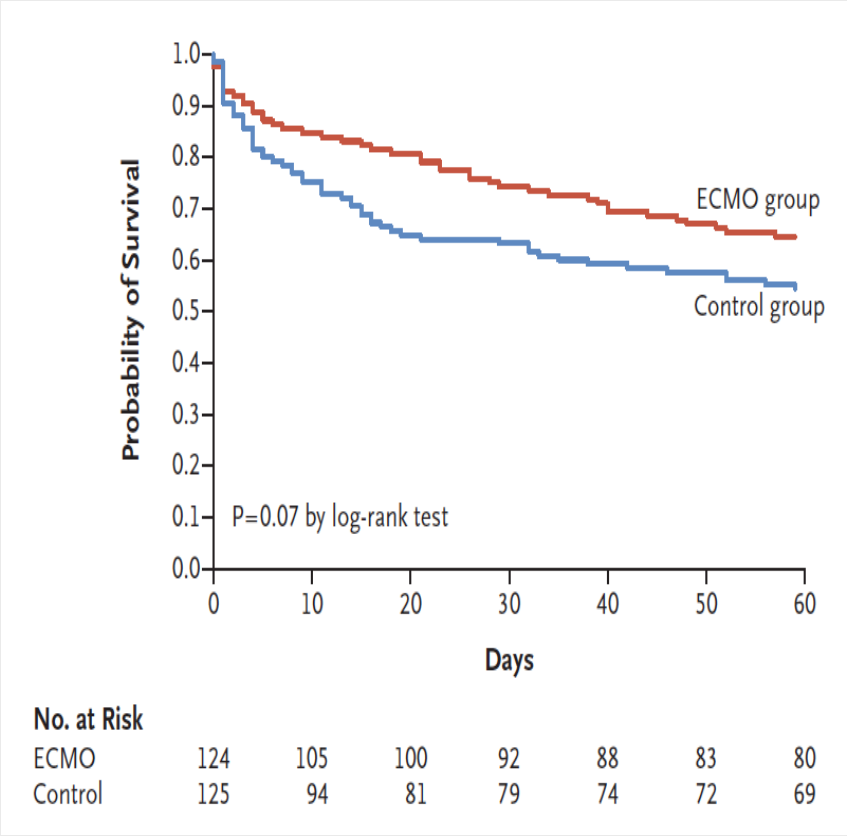
- a ratio of partial pressure of arterial oxygen (PaO_2) to the fraction of inspired oxygen (FiO_2) of less than 50 mm Hg for more than 3 hours
- PaO_2 : FiO_2 of less than 80 mm Hg for more than 6 hours;
- arterial blood pH of less than 7.25 with a partial pressure of arterial carbon dioxide of at least 60 mm Hg for more than 6 hours

- Immediate venovenous ECMO (ECMO group)
- Continued conventional treatment (control group)
- The primary end point was mortality at 60 days.

Combes A et al. N Engl J Med 2018;378:1965-75

ECMO in severe ARDS

- **Mortality at 60 days**
  - Control group 46% vs ECMO group 35%



- **In control group, 28% pts crossover to ECMO**

(SaO_2 of <80% for >6 hours, with RM, prone, NO or PG) .

- **Mortality at 60 days**
  - ECMO group 35%
  - Control (no cross over) 41%
  - All controls 46%
  - Cross over 57%

Combes A et al. N Engl J Med 2018;378:1965-75

Take-Home Message

- Among patients with very severe ARDS:

  - 60 day mortality not significantly lower with ECMO than conventional MV

- Rescue cross over to ECMO in 28% of control group

  - extremely sick before cross over

  - 57% died

- ECMO reserved as rescue therapy

Combes A et al. N Engl J Med 2018;378:1965-75

On-demand vs Routine nebulization in MV patients

State of the Art

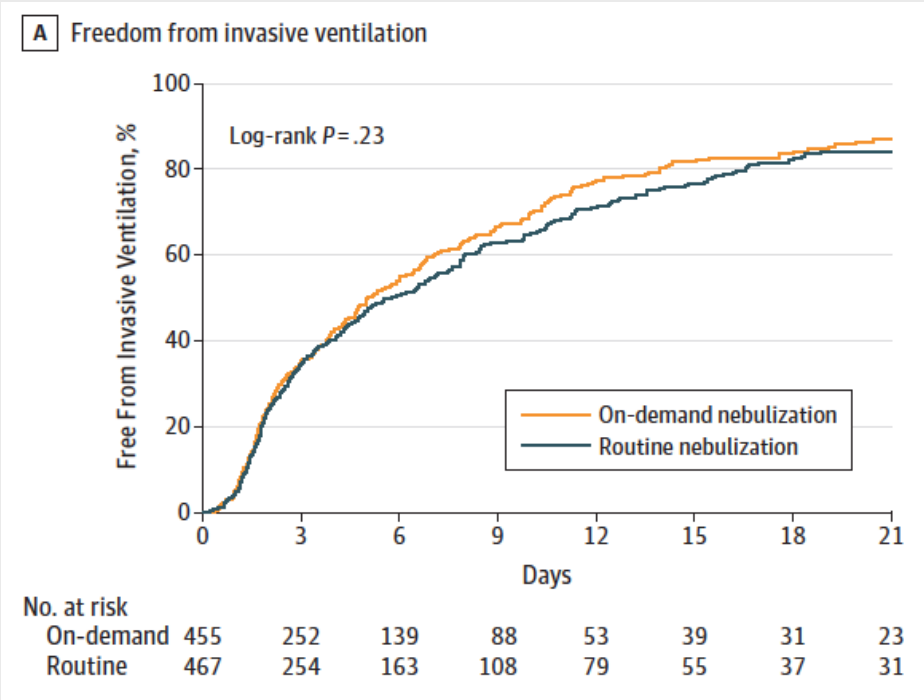
- Use of nebulized mucolytics may provide benefit in ICU patients receiving invasive ventilation, but evidence is limited.
- Acetylcysteine is one of the most commonly used mucolytics.
- Bronchodilators can further improve mucus clearance through an increase in small air- ways diameter.
- Preventive use of inhaled drugs in ICU patients receiving invasive ventilation

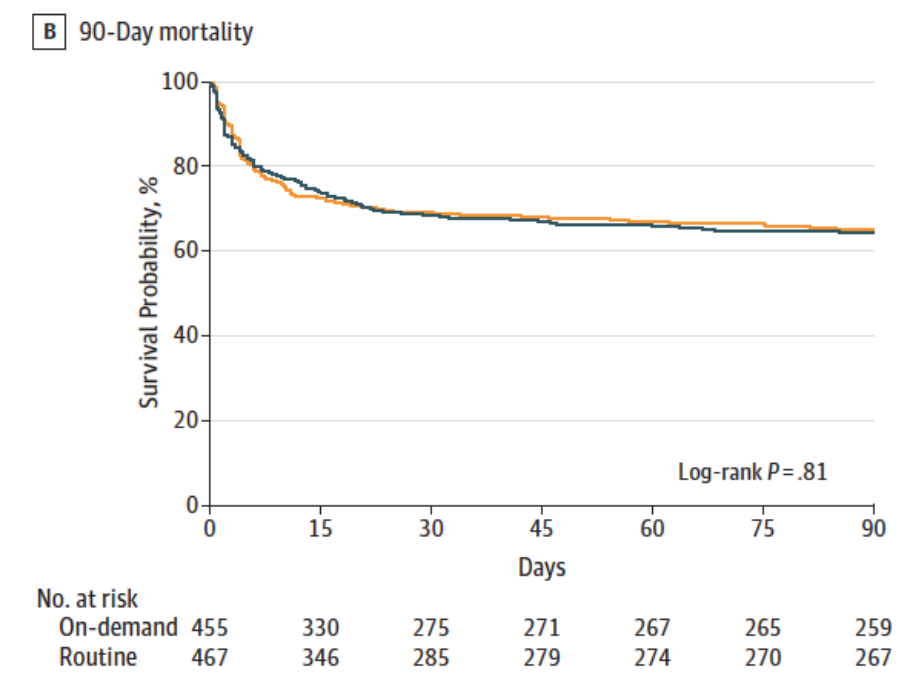
Icard BL et al. Expert Rev Respir Med. 2017;11(10): 807-814

On-demand vs Routine nebulization in MV patients

❖**On-demand** nebulization of acetylcysteine or salbutamol (based on strict clinical indications, n = 471)

❖**Routine** nebulization of acetylcysteine with salbutamol (every 6 hours until end of invasive ventilation, n = 473).





Van Meenen DMP et al. JAMA 2018 Mar 13;319(10):993-1001

On-demand vs Routine nebulization in MV patients

- **On-demand** nebulization of acetylcysteine or salbutamol (based on strict clinical indications, n = 471)
- **Routine** nebulization of acetylcysteine with salbutamol (every 6 hours until end of invasive ventilation, n = 473).

Outcome	On-Demand Nebulization (n = 455)	Routine Nebulization (n = 467)	Absolute Difference (95% CI)	*P* Value[a]
Adverse events, No. (%)[i]	63 (13.8)	137 (29.3)	-15.5 (-20.7 to -10.3)	<.001
Tachyarrhythmia	57 (12.5)	121 (25.9)	-13.4 (-18.4 to -8.4)	<.001
Agitation	1 (0.2)	20 (4.3)	-4.1 (-5.9 to -2.2)	<.001
Hypoxemia	9 (2.0)	20 (4.3)	-2.3 (-4.5 to -0.1)	.06
Dyspnea	1 (0.2)	5 (1.1)	-0.9 (-1.9 to 0.2)	.22
Bronchospasm	1 (0.2)	4 (0.9)	-0.6 (-1.6 to 0.3)	.37
Apnea	0	3 (0.6)	-0.6 (-1.4 to 0.1)	.25
Self-extubation	0	4 (0.9)	-0.9 (-1.7 to 0.0)	.06

Van Meenen DMP et al. JAMA 2018 Mar 13;319(10):993-1001

Take-Home Message

- Among ICU patients receiving invasive ventilation, on-demand compared with routine nebulization of acetylcysteine with salbutamol did not result in an inferior number of ventilator-free days.
- Routine nebulization may be promote adverse effects
- Nebulization only if required

Van Meenen DMP et al. JAMA 2018 Mar 13;319(10):993-1001

Procalcitonin-Guidance vs Usual Care for Antimicrobial Management in Critically Ill Patients

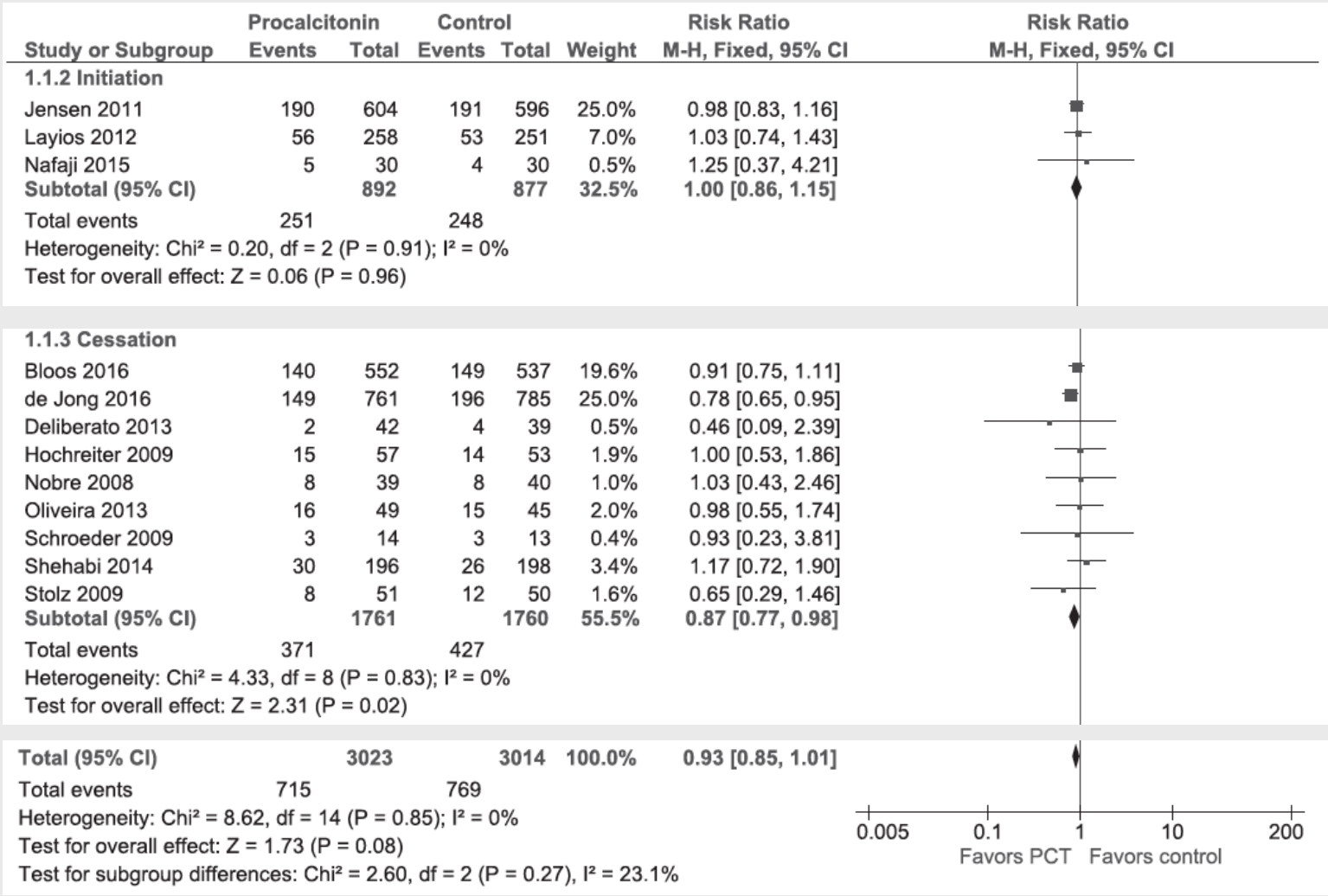
State of the Art

- Early adequate empiric antibiotics is associated with improved survival for patients with sepsis
- Unappropriate or unnecessary antibiotics are continued inmore than 50% of patients (no de-escalation).
- Surviving Sepsis Campaign (SSC) guidelines suggest that biomarkers such as procalcitonin to shorten the duration of antimicrobial use in patients with sepsis

Rhodes A et al. Crit Care Med 2017; 45:486–552

PCT- Guidance vs Usual Care for Antimicrobial Management in Critically Ill Patients

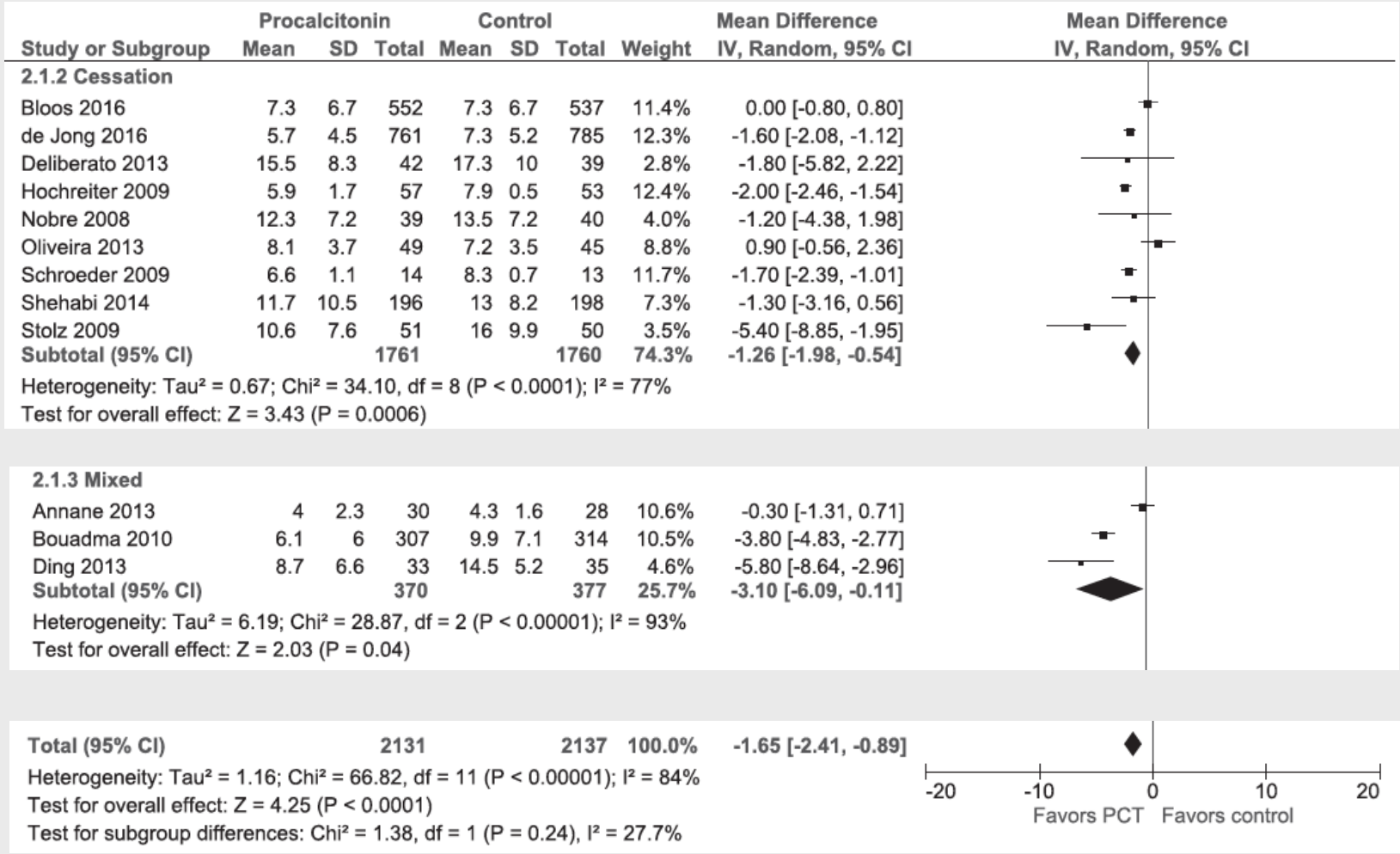
Mortality



Lam SV et al. Crit Care Med. 2018 May;46(5):684-690

PCT-Guidance vs Usual Care for Antimicrobial Management in Critically Ill Patients

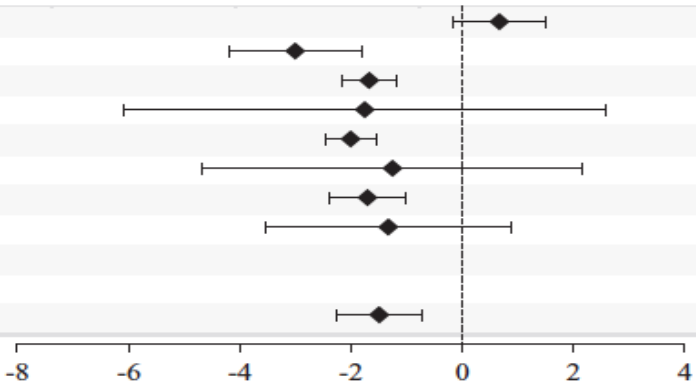
Antibiotic duration



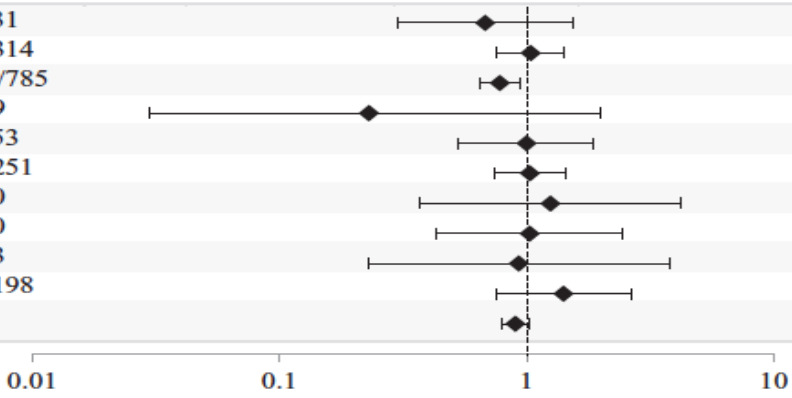
Lam SV et al. Crit Care Med. 2018 May;46(5):684-690

Efficacy and Safety of PCT Guidance in Patients With Suspected or Confirmed Sepsis

First author, year	AB duration (days), mean (SD) PCT	AB duration (days), mean (SD) Standard care	WMD (95% CI)	Weight %
Annane, 2013[24]	4.67 (0.7)	4.00 (2.2)	0.67 (-0.16, 1.49)	16.50
Bouadma, 2010[25]	10.30 (7.7)	13.30 (7.6)	-3.00 (-4.20, -1.80)	13.65
de Jong, 2016[26]	5.67 (4.4)	7.33 (5.2)	-1.67 (-2.15, -1.19)	18.79
Deliberato, 2013[27]	15.50 (9.0)	17.25 (10.8)	-1.75 (-6.08, 2.58)	2.79
Hochreiter, 2009[28]	5.90 (1.7)	7.90 (0.5)	-2.00 (-2.46, -1.54)	18.90
Nobre, 2008[31]	12.25 (7.8)	13.50 (7.8)	-1.25 (-4.67, 2.17)	4.14
Schroeder, 2009[32]	6.60 (1.1)	8.30 (0.7)	-1.70 (-2.39, -1.01)	17.47
Shehabi, 2014[33]	11.67 (10.4)	13.00 (11.9)	-1.33 (-3.53, 0.87)	7.76
Layios, 2012[29]			(Excluded)	
Najafi, 2015[30]			(Excluded)	
Overall (Heterogeneity: I^2=81.3%, p<0.001, T^2=0.782)			**-1.49 (-2.27, -0.71)**	**100.00**



First author, year	Deceased during follow-up, n/N PCT	Deceased during follow-up, n/N Standard care	RR (95% CI)	Weight %
Annane, 2013[24]	7/31	10/31	0.68 (0.30, 1.55)	2.57
Bouadma, 2010[25]	65/307	64/314	1.04 (0.76, 1.41)	18.57
de Jong, 2016[26]	149/761	196/785	0.78 (0.65, 0.95)	49.45
Deliberato, 2013[27]	1/42	4/39	0.23 (0.03, 1.99)	0.38
Hochreiter, 2009[28]	15/57	14/53	1.00 (0.53, 1.86)	4.49
Layios, 2012[29]	56/258	53/251	1.03 (0.74, 1.43)	15.80
Najafi, 2015[30]	5/30	4/30	1.25 (0.37, 4.21)	1.19
Nobre, 2008[31]	8/39	8/40	1.03 (0.43, 2.46)	2.29
Schroeder, 2009[32]	3/14	3/13	0.93 (0.23, 3.81)	0.88
Shehabi, 2014[33]	21/196	15/198	1.41 (0.75, 2.66)	4.38
Overall (Heterogeneity: I^2=0.0%, p=0.542, T^2=0.000)			**0.90 (0.79, 1.03)**	**100.00**



Iankova I et al. Crit Care Med 2018; 46:691–698

Take-Home Message

❖ In critically ill patients:

- PCT reduces antibiotic duration
- PCT guided cessation of antibiotics seems to be the most effective strategy
- Other studies are needed to define the role of PCT for guiding initiation therapy

Lam SV et al. Crit Care Med. 2018 May;46(5):684-690
Iankova I et al. Crit Care Med 2018; 46:691–698

Prevention of Ventilator Associated Pneumonia
The Multimodal Approach - “Pneumonia Zero”

State of the Art

- The prevalence rates of VAP is a common indicator for safety and quality of care in critically ill patients admitted to the ICU
- VAP increases morbidity and mortality
- Specific programmes for prevention have been proposed

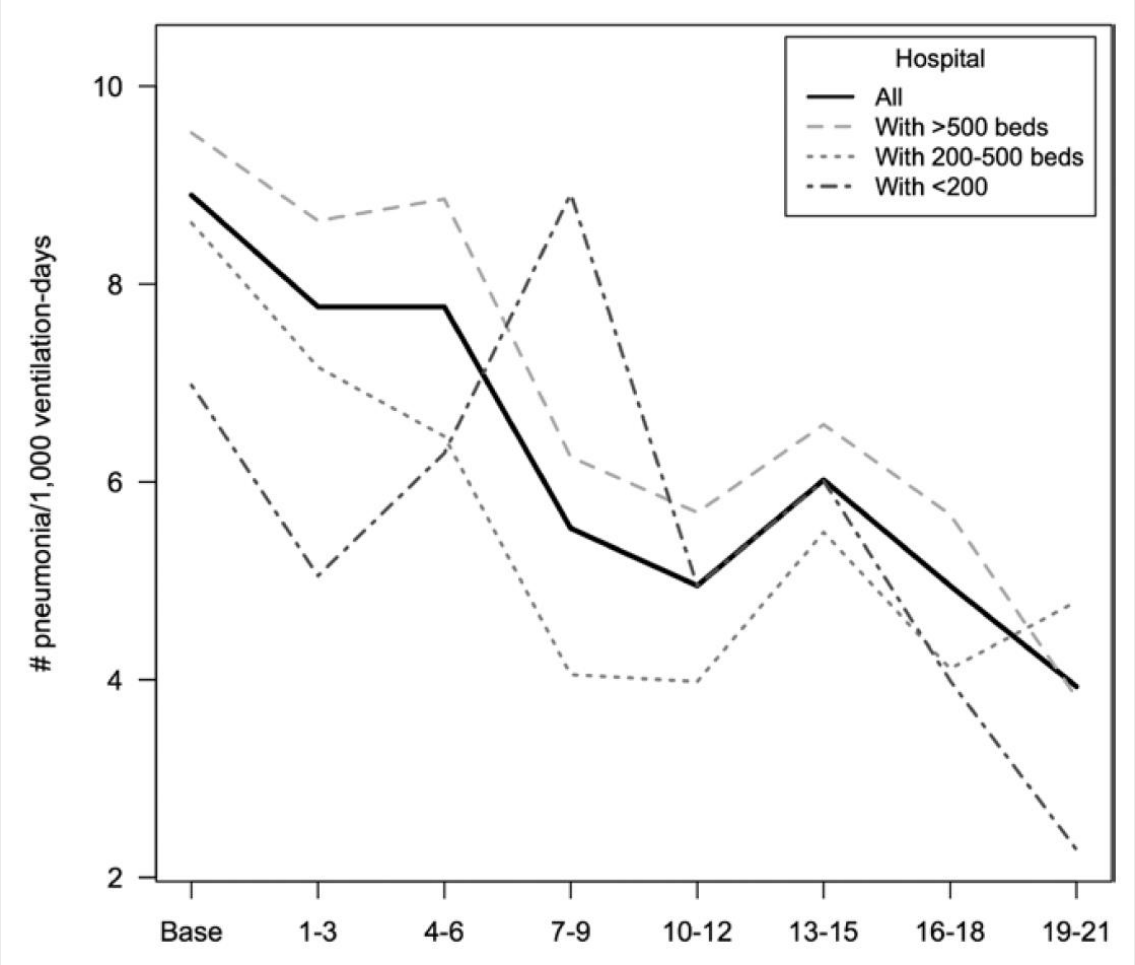
Berwick DM et al JAMA 2006; 295:324–327

Prevention of VAP: The Multimodal Approach - “Pneumonia Zero”

Seven Basic Mandatory Measures	Three Highly Recommended Measures
1. Education and training in appropriate airway management.[a]	1. Selective decontamination of the digestive tract or selective oropharyngeal decontamination.
2. Strict hand hygiene with alcohol solutions before airway management.	2. Continuous aspiration of subglottic secretions.
3. Control and maintenance of cuff pressure.	3. Short course (2-3 doses) of systemic antibiotics during intubation of patients with previous decreased consciousness.
4. Oral hygiene with chlorhexidine.	
5. Semirecumbent positioning. Avoidance of 0° supine positioning if possible.	
6. Promoting procedures and protocols that safely avoid or reduce duration of mechanical ventilation.[b]	
7. Avoidance of elective changes of ventilator circuits, humidifiers, and endotracheal tubes.	

Alvarez-Lerma F et al. Crit Care Med 2018; 46:181–188

Prevention of VAP: The Multimodal Approach - “Pneumonia Zero”



Alvarez-Lerma F et al. Crit Care Med 2018; 46:181–188

Take-Home Message

- A nationwide implementation of a VAP prevention bundle was associated with a significant reduction of VAP rates of more than 50%
- These findings confirm the hypothesis that implementation of a comprehensive evidencebased bundle is effective in reducing VAP rates

Alvarez-Lerma F et al. Crit Care Med 2018; 46:181–188

Corticosteroids in septic shock and CAP

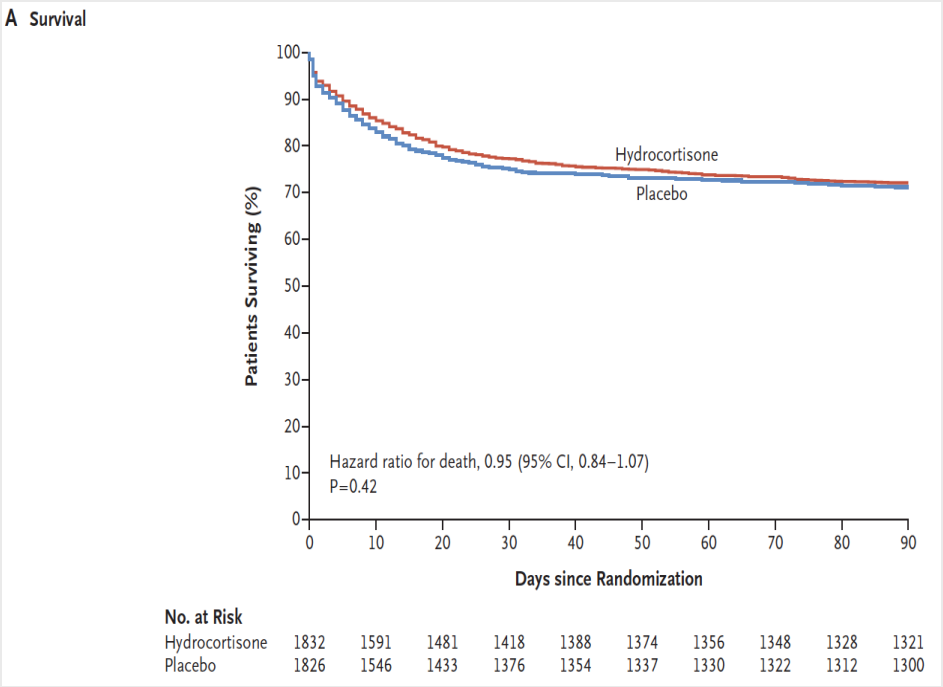
State of the Art

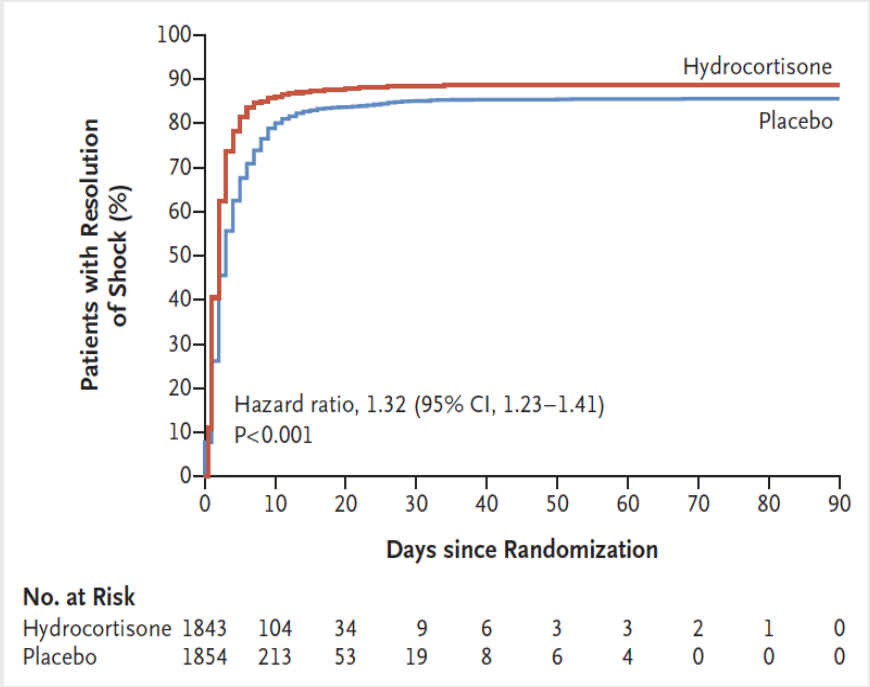
- Sepsis has been identified by the World Health Organization as a global health priority
- Death rates among hospitalized patients range between 30% and 45%.
- Glucocorticoids have been used as an adjuvant therapy but uncertainty about their safety and efficacy

Reinhart K et al. N Engl J Med 2017; 377: 414-7.

Adjunctive Glucocorticoid Therapy in pts with Septic Shock“Adrenal trial”

- hydrocortisone (at a dose of 200 mg per day) or placebo for 7 days or until death or discharge from the intensive care unit (ICU),



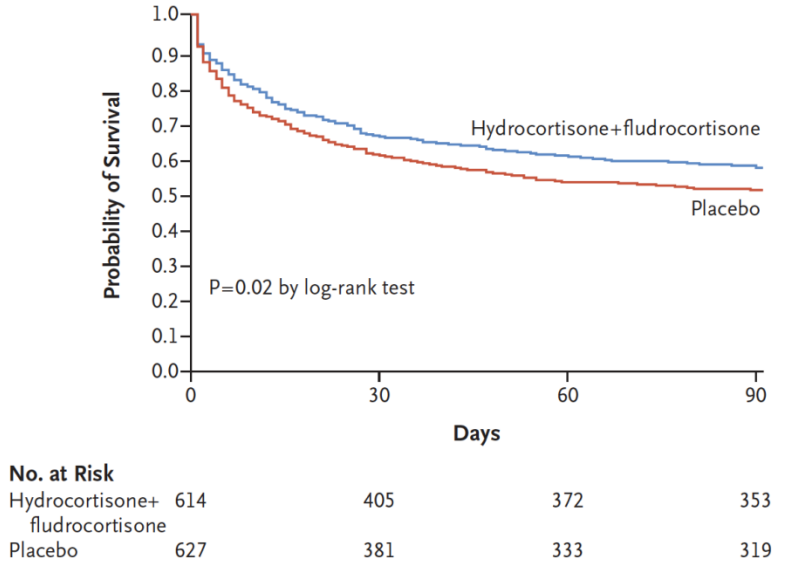


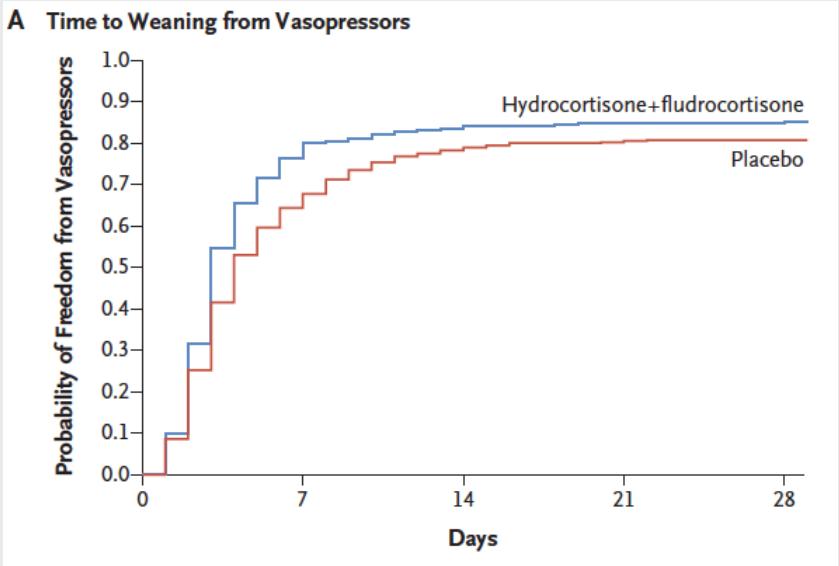
Hydrocortisone (at a dose of 200 mg per day) did not improved survival but reduced the time to resolution of shock

Venkatesh B et al N Engl J Med. 2018 Mar 1;378(9):797-808.

Hydrocortisone plus Fludrocortisone for Adults with Septic Shock

- Hydrocortisone was administered as a 50-mg intravenous bolus every 6 hours, and fludrocortisone was given as a 50-µg tablet through a nasogastric tube once daily in the morning.
- Trial agents were administered for 7 days without tapering





Hydrocortisone (at a dose of 200 mg per day) + Fludrocortisone improved outcome in septic shock

Annane D et al N Engl J Med. 2018 Mar 1;378(9):809-818

Corticosteroids in Patients Hospitalized With Community-Acquired Pneumonia

Outcome	Corticosteroid (n = 748)	Placebo (n = 758)	Intention-to-Treat Regression analysis, OR or Coefficient (95% Confidence Interval), *P* Value
Primary			
All-cause mortality, no. (%)	37 (5.0)	45 (5.9)	OR 0.75 (0.46 to 1.21), *P* = .24
Secondary			
Length of hospital stay, days	7.0 (5.0–11.0)	8.0 (5.0–12.0)	–1.15 days (–1.75 to –0.55), *P* < .001
Time to clinical stability, days[b]	3.0 (2.0–5.4)	4.0 (2.5–7.0)	–1.03 days (–1.62 to –0.43), *P* = .001
Intravenous antibiotic treatment, days[c]	4.0 (3.0–6.0)	5.0 (3.0–7.0)	–0.62 days (–1.07 to –0.16), *P* = .01
Community-acquired pneumonia–related rehospitalization, no. (%)[e]	33 (5.0)	18 (2.7)	OR 1.85 (1.03 to 3.32), *P* = .04
Hyperglycaemia requiring insulin, no. (%)[f]	160 (22.1)	88 (12.0)	OR 2.15 (1.60 to 2.90), *P* < .001
Nosocomial infections, no. (%)	33 (4.4)	25 (3.3)	OR 1.31 (0.77 to 2.24), *P* = .32
Empyema/complicated parapneumonic effusion, no. (%)	12 (1.6)	14 (1.9)	OR 0.90 (0.41 to 1.96), *P* = .79
Gastrointestinal bleeding, no. (%)	5 (0.7)	5 (0.7)	OR 0.95 (0.27 to 3.33), *P* = .93

Briel M et al. Clin Infect Dis. 2018 Jan 18;66(3):346-354

Take-Home Message

- Hydrocortisone may be safely used in patients with septic shock
- Uncertain to imporve survival
- Faster resolution of shock
- No collateral effects
- Just do it ?

Venkatesh B et al N Engl J Med. 2018 Mar 1;378(9):797-808.

*Annane D et al N Engl J Med. 2018 Mar 1;378(9):809-81***8**

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List of Abbreviations

- ARDS: Acute Respiratory Distress Syndrome
- ECMO: Extracorporeal Membrane Oxygenation
- NIV: Non invasive ventilation
- CMV: Controlled Mechanical Ventilation
- VILI: Ventilator Induced Lung Injury
- PEEP: Positive end-expiratory pressure
- COPD : Chronic Obstructive Pulmonary Disease
- PCT: Procalcitonin
- ICU: Intensive Care Unit