

Protective ventilation for ALL patients

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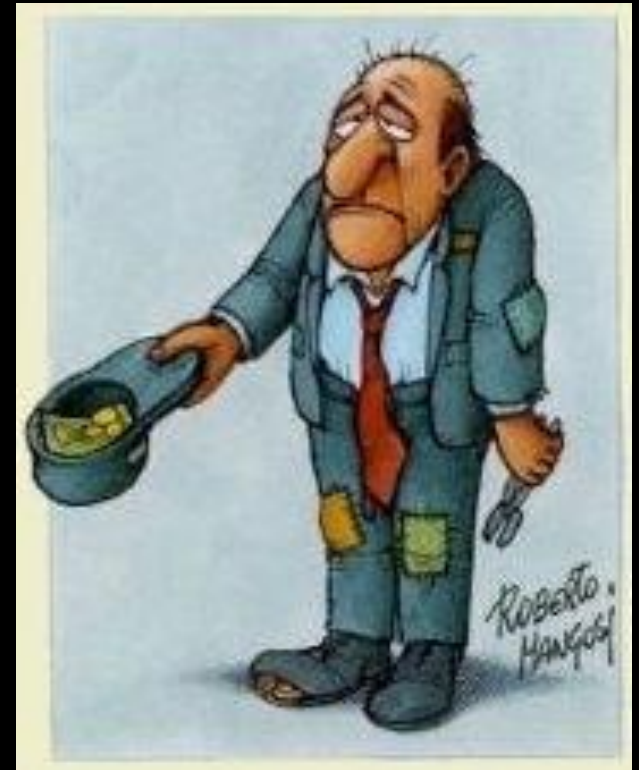


**2ND INTERNATIONAL INTER-CONGRESS CONFERENCE OF THE
POLISH SOCIETY OF ANAESTHESIOLOGY
AND INTENSIVE THERAPY (PTAIT)**

KARPACZ, 24–26 November 2016

Conflicts of interest

I declare
NO conflicts of interest



PROtective VEntilation NETWORK

PROTECTIVE
VENTILATION
NETWORK

ESA

To perform
Large multicenter
clinical studies,
randomized
controlled trials,
and meta-analyses

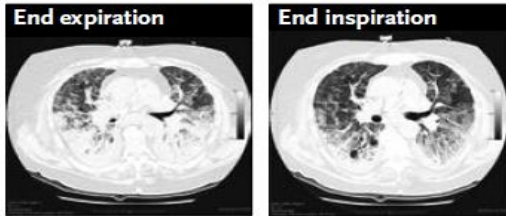


<http://www.provenet.eu/>

Ventilator-Induced Lung Injury

Slutsky AS & Ranieri VM N Engl J Med 2013;369:2126-36

A Ventilation at low lung volume

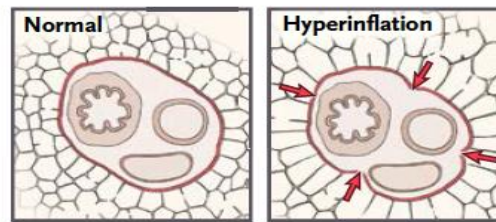


Atelectrauma

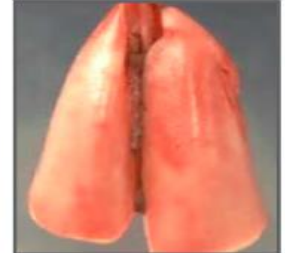


Lung inhomogeneity

B Ventilation at high lung volume

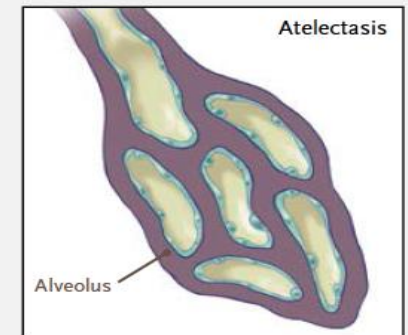
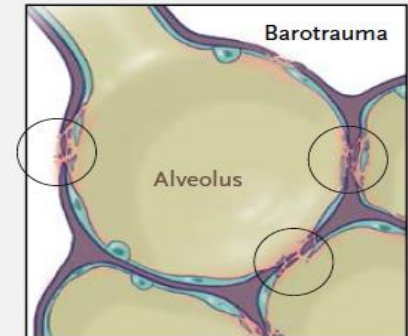
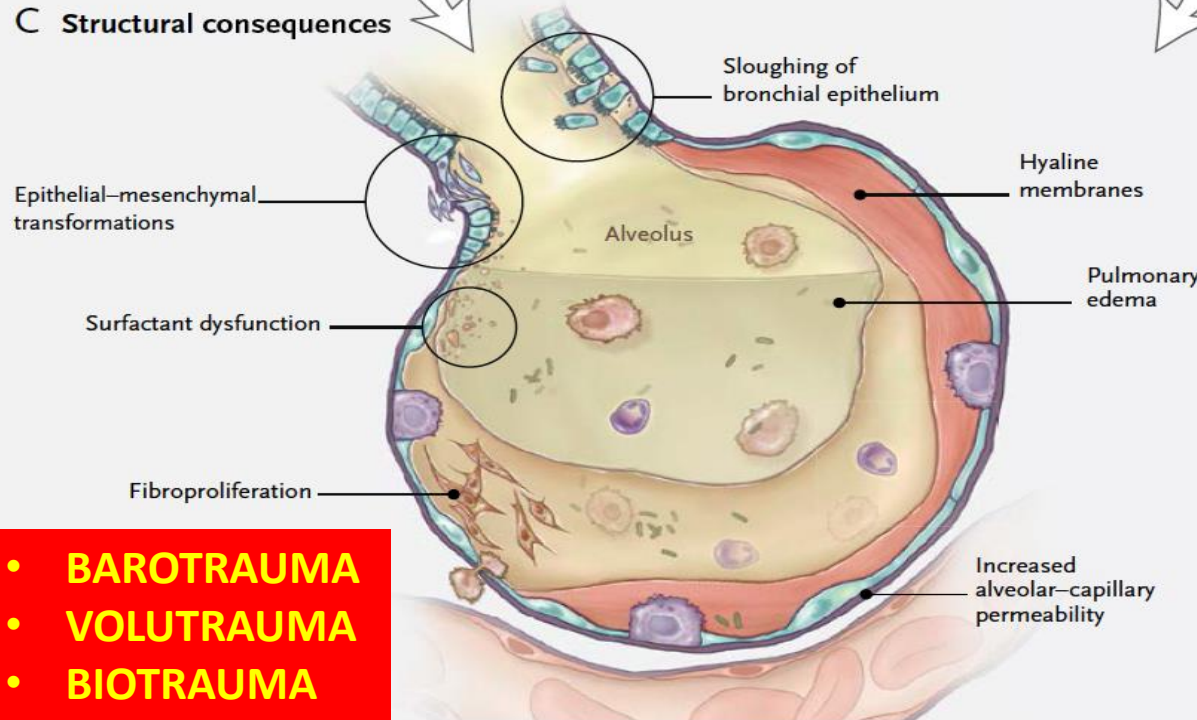


Air leaks



Overdistention

C Structural consequences

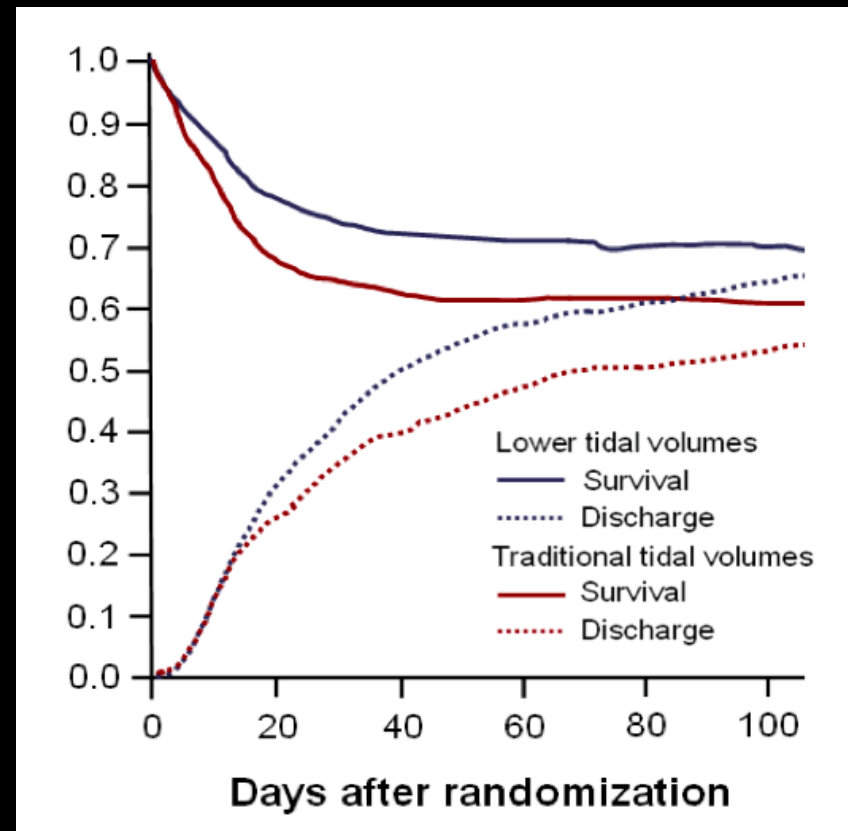


- **BAROTRAUMA**
- **VOLUTRAUMA**
- **BIOTRAUMA**

Use of Lower Tidal Volumes Benefits Patients *with* ARDS

ARDS Network. *N Engl J Med.* 2000; 342:1301

- RCT, USA
- 821 ARDS patients
- 6 vs. 12 ml/kg
- stopped early



Use of Lower Tidal Volumes Benefits Patients *with* ARDS

Putensen C. *Ann Internal Med.* 2009; 151:566

- 1,297 patients with ARDS from 6 RCTs
- outcome: hospital death

	No	Low V_T at similar PEEP	High V_T at similar PEEP	Odds ratio
Brochard	116	–	–	
Brower	52	13/26	12/26	1.17 [0.39 – 3.47]
Brower	861	134/342	171/429	0.68 [0.51 – 0.90]
Stewart	120	30/60	28/60	1.14 [0.56 – 2.34]
				0.75 [0.58 – 0.96]

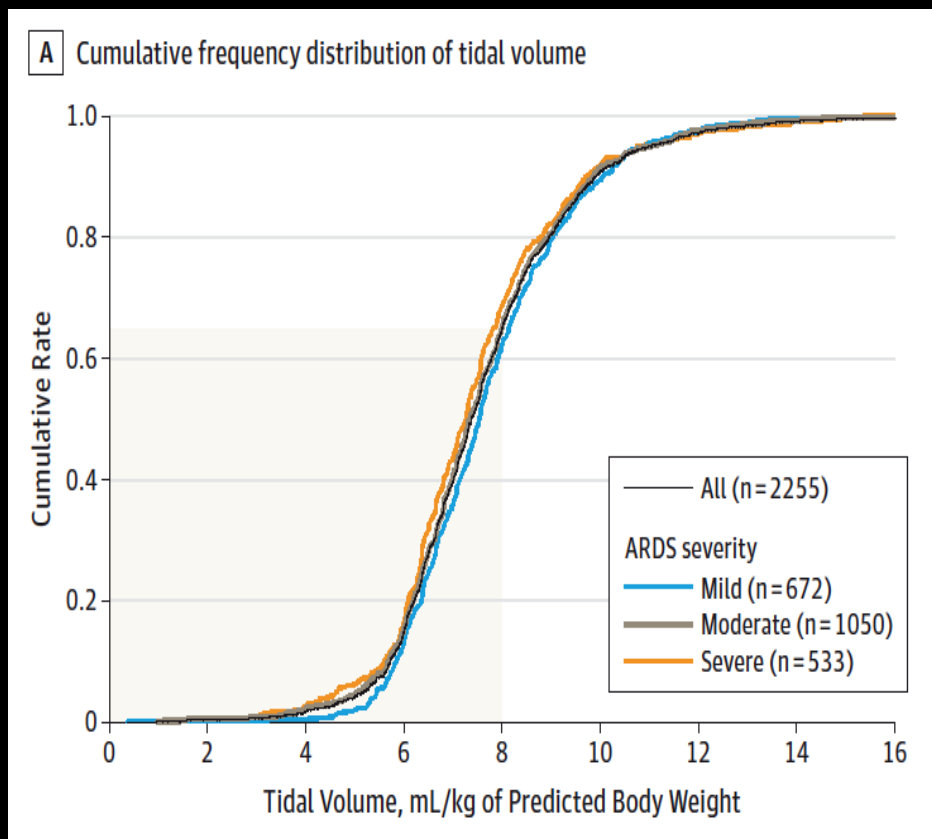
	No	Low V_T + high PEEP	High V_T + low PEEP	Odds ratio
Amato	53	13/29	17/24	0.33 [0.11 – 1.05]
Villars	95	17/50	24/45	0.41 [0.18 – 0.94]
				0.38 [0.20 – 0.75]

[METANALYSIS]

LungSafe – Practice of Ventilation in ICUs Worldwide

Bellani G JAMA. 2016 Feb 23;315(8):788-800

- international observational study
- 2,396 patients with mild, moderate or severe ARDS



Ventilation During General Anesthesia for Surgery



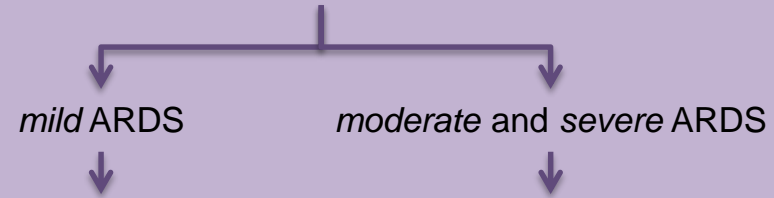
Protective ventilation includes:

Ventilation in Intensive Care Unit—patients with Uninjured Lungs



Protective ventilation includes:

Ventilation in Intensive Care Unit—patients with the Acute Respiratory Distress Syndrome (ARDS)



Protective ventilation includes:

Tidal volume size
6–8 ml/kg predicted body weight

*evidence comes from
2 RCTs [4] and
1 meta-analysis [5]*

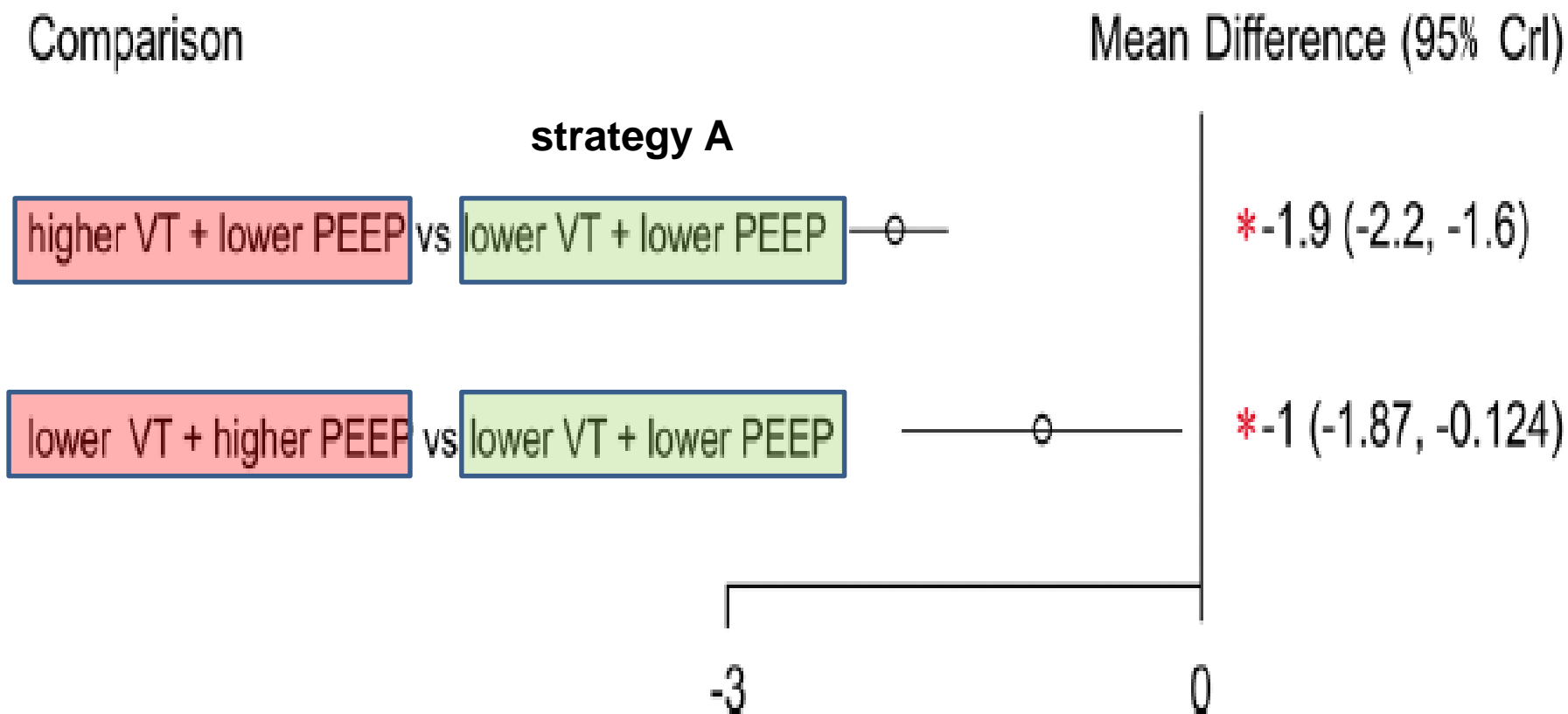
Protective ventilation includes:

Tidal volume size
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In non ARDS patients lower V_T + lower PEEP are associated with a shorter length of ICU stay

Guo L et al. Critical Care (2016) 20:226

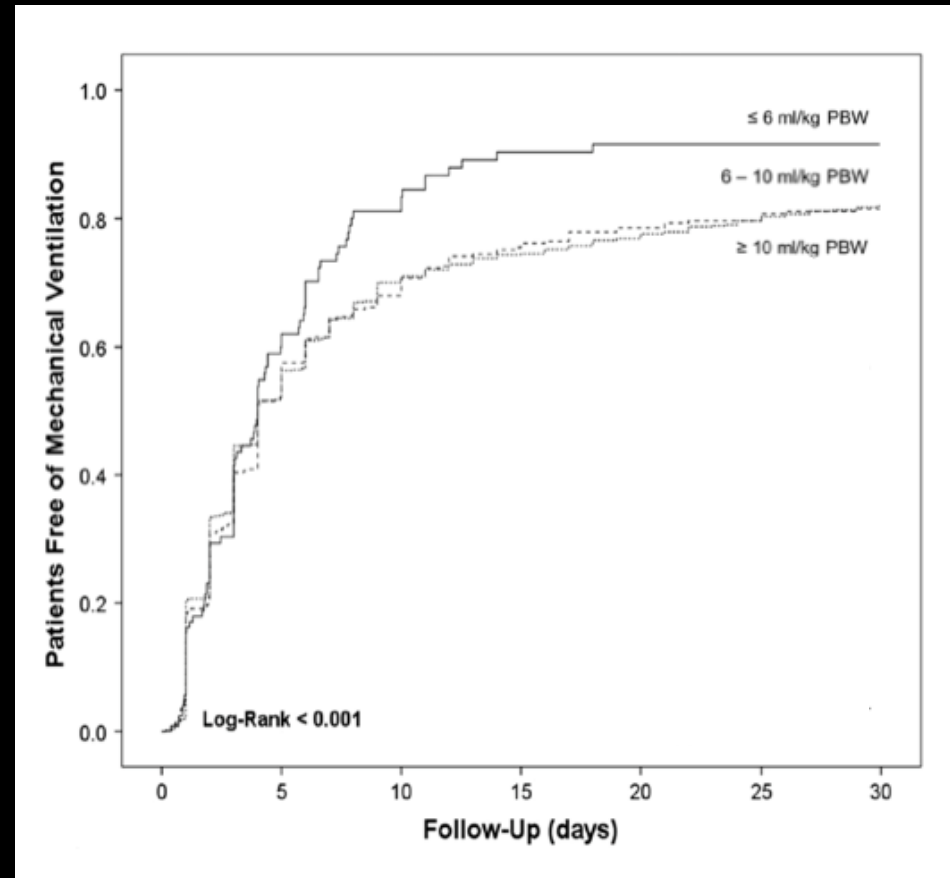


MD < 0 favors strategy A (**Low V_T /Low PEEP**)

Use of Lower Tidal Volumes Benefits Patients *without* ARDS

Serpa Neto A. *Intensive Care Med.* 2014; 40:950

- 2,184 ICU patients without ARDS from 7 studies
- outcome: duration of ventilation

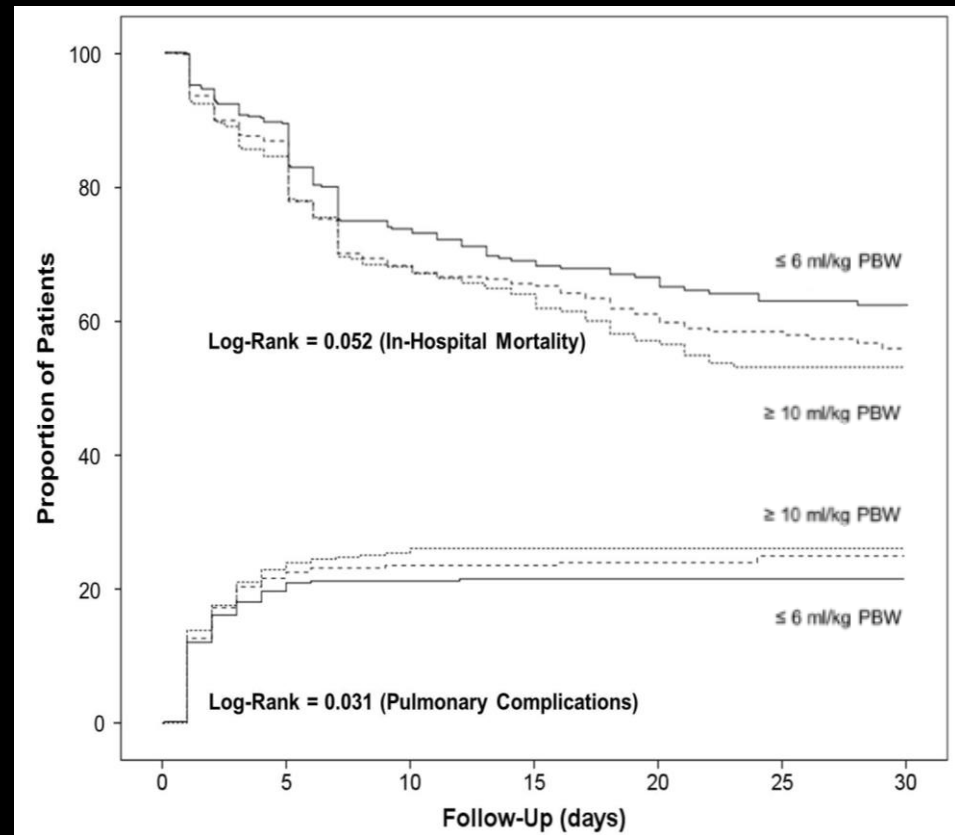


[METANALYSIS]

Use of Lower Tidal Volumes Benefits Patients *without* ARDS

Serpa Neto A. *Crit Care Med.* 2015; 43:4155

- 2,184 ICU patients without ARDS from 7 studies
- outcome: hospital stay and ARDS development



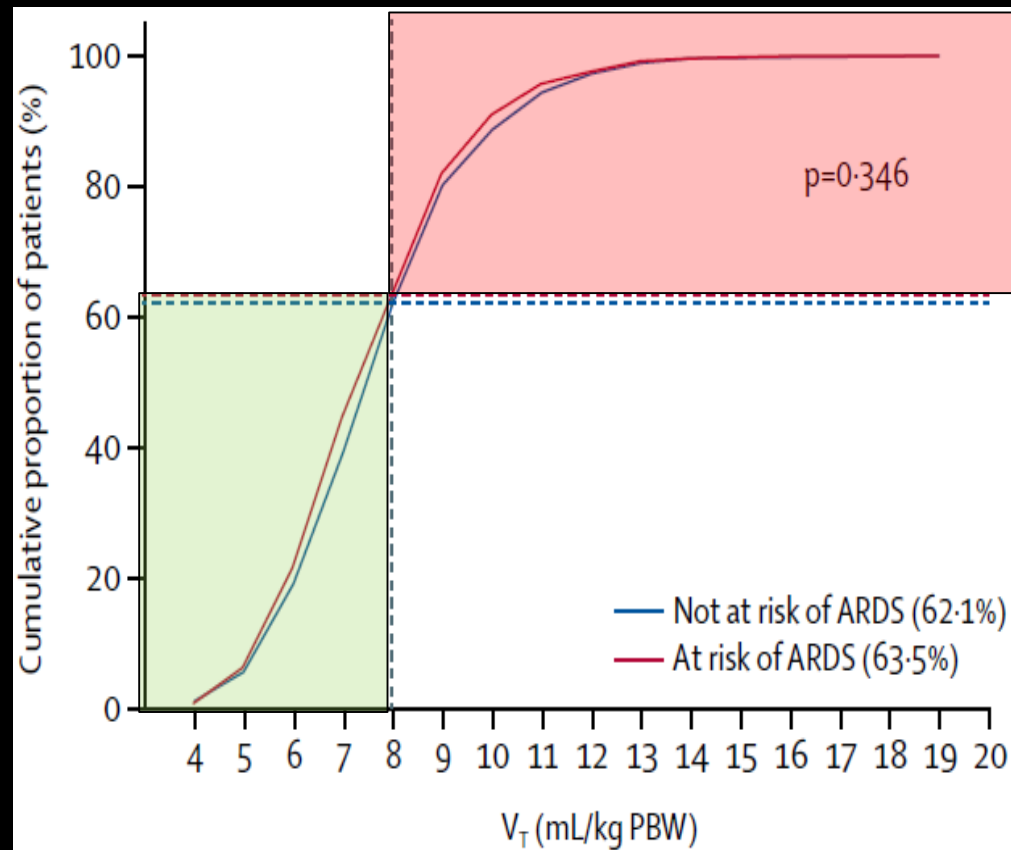
[METANALYSIS]

PRoVENT – Practice of Ventilation in ICUs Worldwide



Neto AS et al. Lancet Respir Med. 2016 Nov;4(11):882-893

- international observational study
- 1,022 patients without ARDS
- 40% of patients ($V_T > 8$ ml/Kg PBW)



4 New Trials of Low Tidal Volume Ventilation in Patients *without* ARDS

- 'PReVENT'
- 'EPALI'
- ISIC-IMIC
- a new ARDS Network trial

Ventilation During General Anesthesia for Surgery



Protective ventilation includes:

Ventilation in Intensive Care Unit—patients with Uninjured Lungs

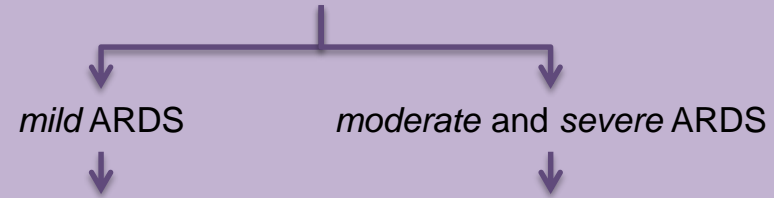


Protective ventilation includes:

Tidal volume size
6 ml/kg predicted body weight

*evidence comes from
2 RCTs [31,32], 1
meta-analysis and 2
IPD meta-analyses [17,18,33]**

Ventilation in Intensive Care Unit—patients with the Acute Respiratory Distress Syndrome (ARDS)



Protective ventilation includes:

Tidal volume size
6–8 ml/kg predicted body weight

*evidence comes from
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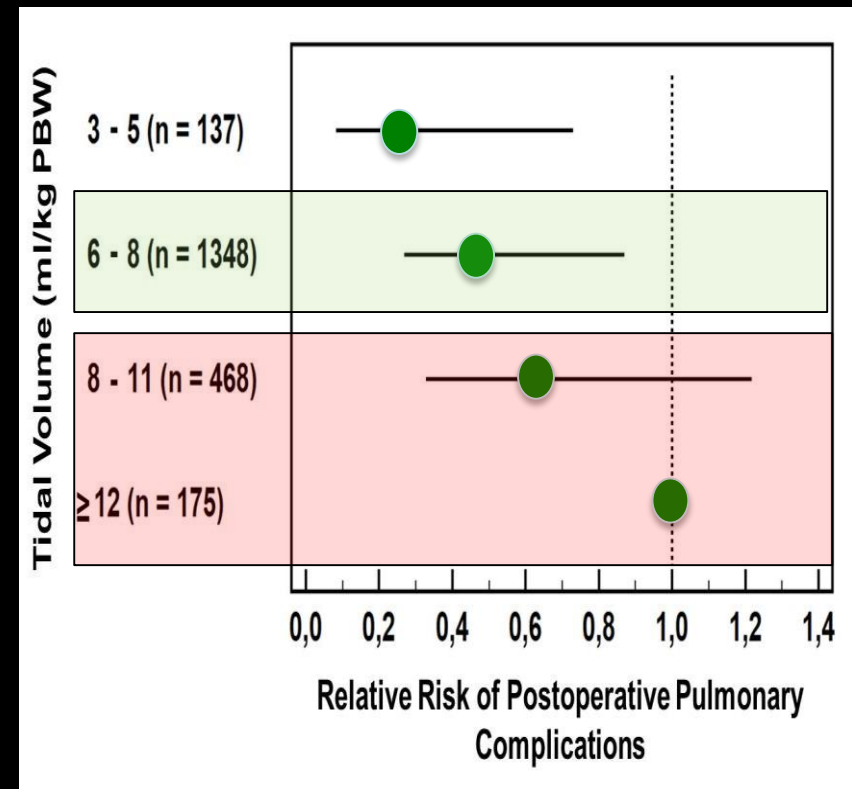
Tidal volume size
6–8 ml/kg predicted body weight

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1 meta-analysis [5]*

Intraoperative Use of Low V_T Benefits Surgery Patients without ARDS

Serpa-Neto A. et al. Anesthesiology. 2015 Jul;123(1):66-78

- 2,127 surgery patients from 15 studies of intraoperative ventilation
- outcome: PPCs

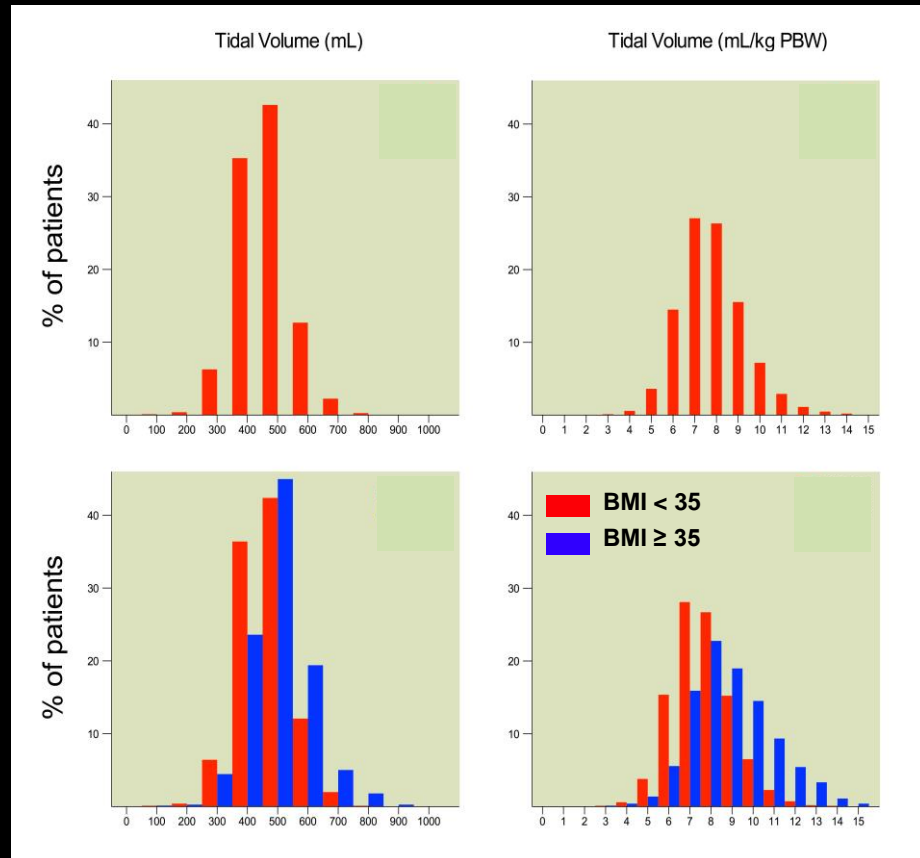


[METANALYSIS]

LAS VEGAS – Practice of Ventilation in ORs Worldwide

Hemmes S. The LAS VEGAS study [SUBMITTED]

- international observational study
- 8,241 patients
- 8.1 [7.2–9.1] mL/kg PBW



Ventilation During General Anesthesia for Surgery



Protective ventilation includes:

Tidal volume size
< 8 ml/kg predicted body weight

evidence comes from 3 RCTs [15,22,23] and 2 meta-analyses [14,18]

Ventilation in Intensive Care Unit-patients with Uninjured Lungs

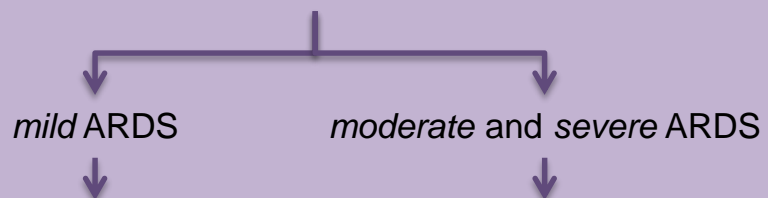


Protective ventilation includes:

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Ventilation in Intensive Care Unit-patients with the Acute Respiratory Distress Syndrome (ARDS)



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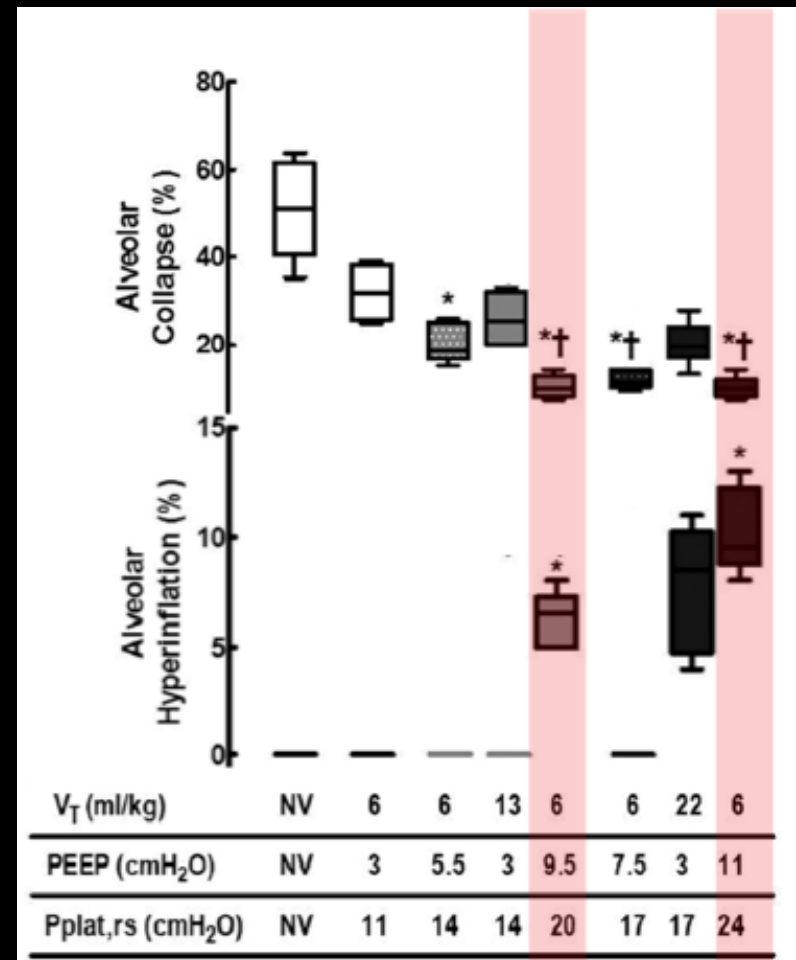
Tidal volume size
6–8 ml/kg predicted body weight

evidence comes from 2 RCTs [4] and 1 meta-analysis [5]

High PEEP Prevents Alveolar Collapse but Increases Hyperinflation

Samary C. *Anesthesiology* 2015; 123:423

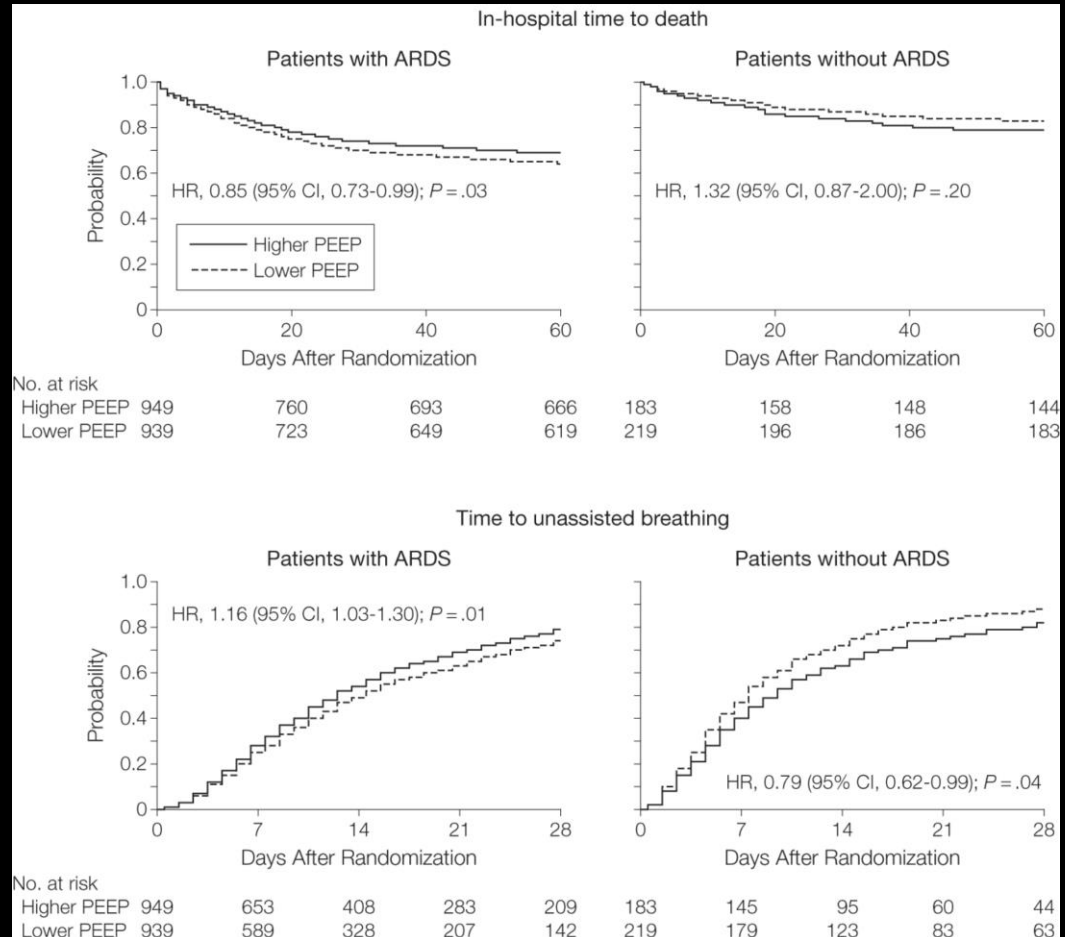
- 48 healthy rats
- intratracheal challenge with *E. coli* LPS
- 1 H of ventilation after 24 H



Use of Higher PEEP Benefits Patient with Moderate or Severe ARDS

Briel M. *JAMA* 2010; 303:865

- 2,299 ICU patients with ARDS from 3 investigations
- outcome: death



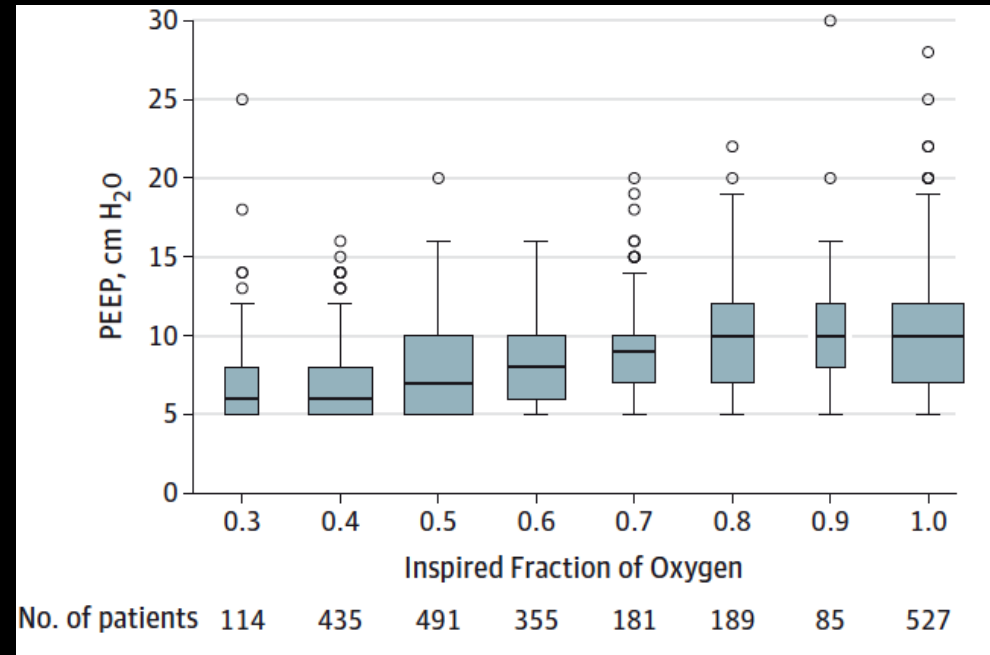
[METANALYSIS]

LungSafe – Practice of Ventilation in ICUs Worldwide

Bellani G JAMA. 2016 Feb 23;315(8):788-800

PEEP in ARDS

- international observational study
- 2,396 patients with mild, moderate or severe ARDS



Mild ARDS 7.4 cmH₂O – Moderate ARDS 8.3 cmH₂O – Severe ARDS 10.1 cmH₂O

Ventilation During General Anesthesia for Surgery



Protective ventilation includes:

Tidal volume size
< 8 ml/kg predicted body weight

*evidence comes from
3 RCTs [15,22,23] and
2 meta-analyses [14,18]*

Ventilation in Intensive Care Unit-patients with Uninjured Lungs

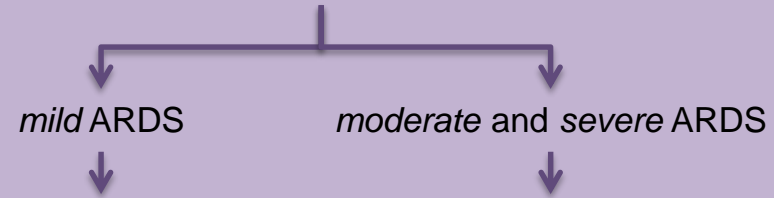


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Ventilation in Intensive Care Unit-patients with the Acute Respiratory Distress Syndrome (ARDS)



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Protective ventilation includes:

Tidal volume size
6–8 ml/kg predicted body weight

*evidence comes from
2 RCTs [4] and
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Level of PEEP
5–10 cm H₂O

*evidence comes from
3 RCTs [7,8,9] and
1 IPD meta-analysis [10]*

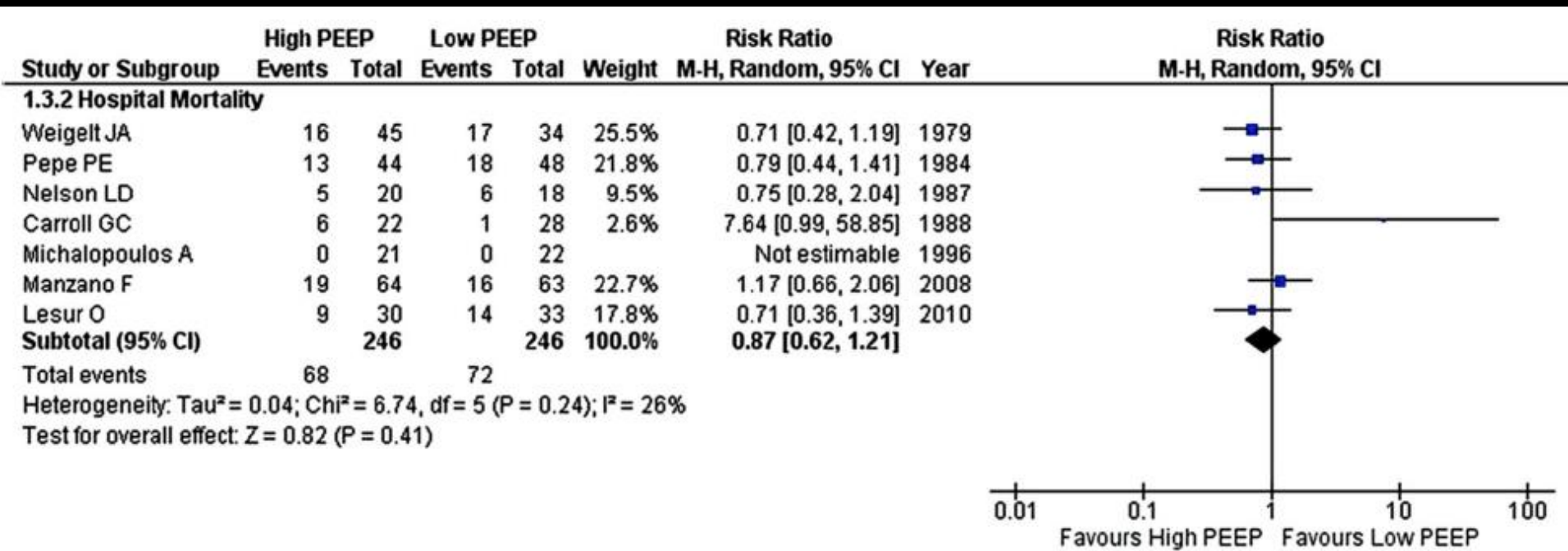
Level of PEEP
≥ 10 cm H₂O

*evidence comes from
3 RCTs [7,8,9] and
1 IPD meta-analysis [10]*

Associations between PEEP and outcome of patients without ARDS at onset of ventilation: a systematic review and meta-analysis of randomized controlled trials

Serpa Neto et al. Ann. Intensive Care (2016) 6:109

Low PEEP = 2.0 ± 2.8 cmH₂O **High PEEP** = 9.7 ± 4.0 cmH₂O



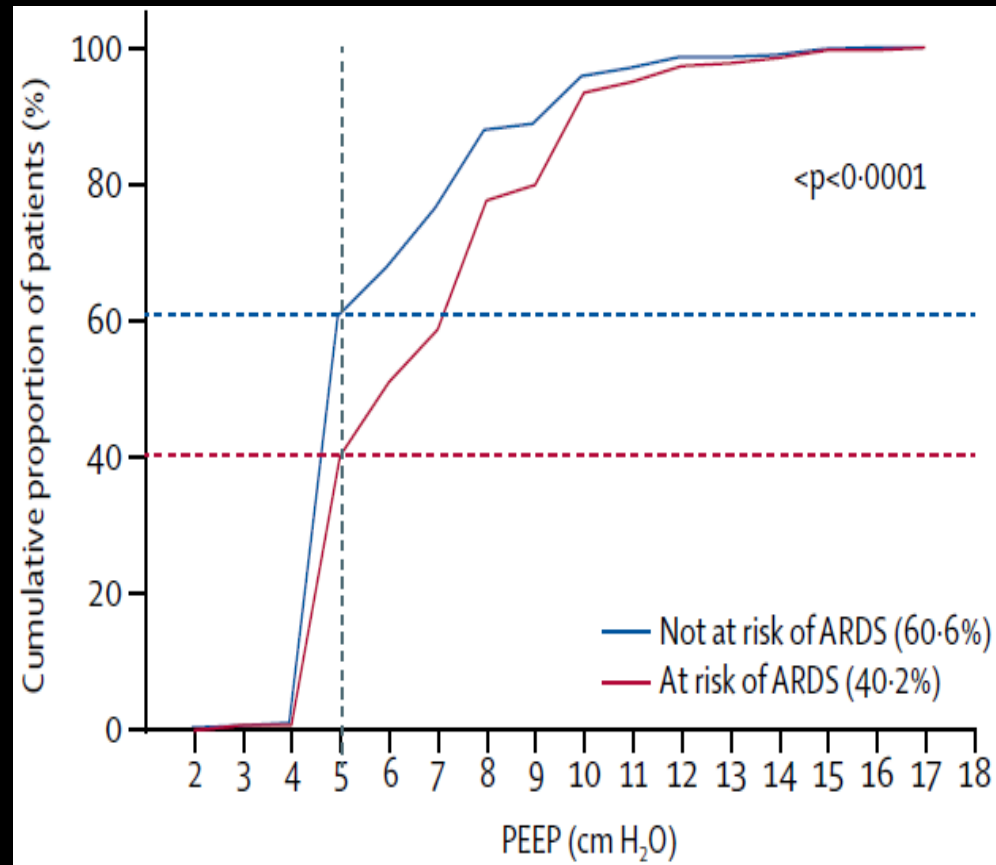
High PEEP: No effect on duration of MV – Lower rate of ARDS (high I²)

PRoVENT – Practice of Ventilation in ICUs Worldwide



Neto AS et al. Lancet Respir Med. 2016 Nov;4(11):882-893

- international observational study
- 1,022 patients without ARDS



Ventilation During General Anesthesia for Surgery



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Ventilation in Intensive Care Unit-patients with Uninjured Lungs



Protective ventilation includes:

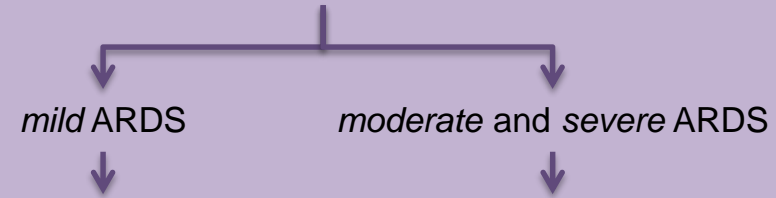
Tidal volume size
6 ml/kg predicted body weight

*evidence comes from
2 RCTs [31,32], 1
meta-analysis and 2
IPD meta-analyses [17,18,33]**

**Level of PEEP (< 6 cmH₂O)
??**

***Convincing RCT
evidence is lacking
2 meta-analysis***

Ventilation in Intensive Care Unit-patients with the Acute Respiratory Distress Syndrome (ARDS)



Protective ventilation includes:

Tidal volume size
6–8 ml/kg predicted body weight

*evidence comes from
2 RCTs [4] and
1 meta-analysis [5]*

Level of PEEP
5–10 cm H₂O

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Protective ventilation includes:

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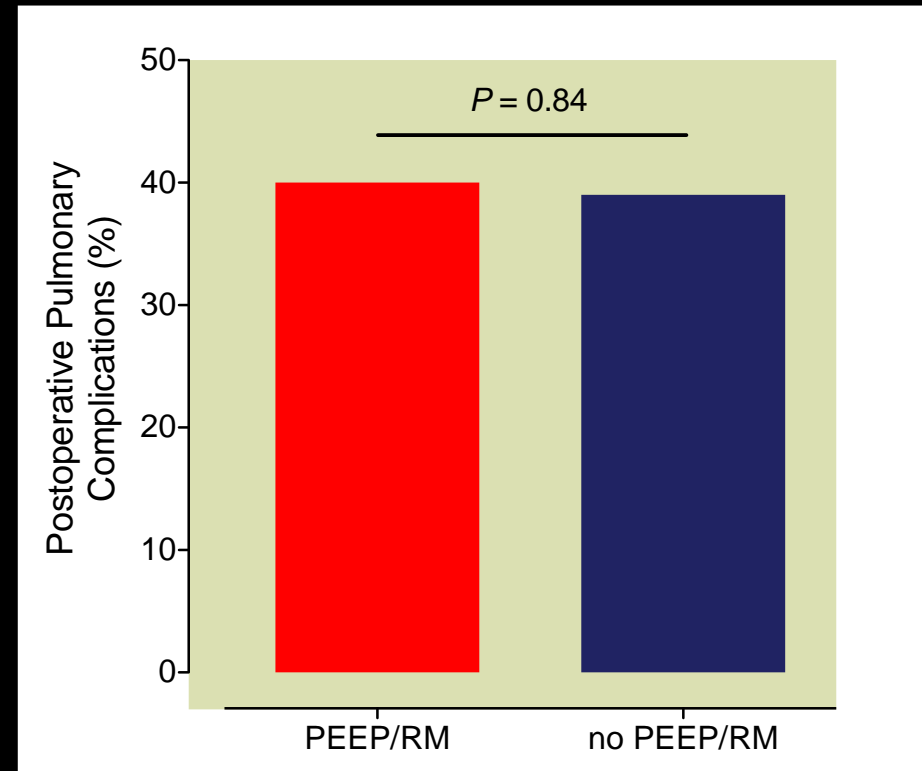
Level of PEEP
≥ 10 cm H₂O

*evidence comes from
3 RCTs [7,8,9] and
1 IPD meta-analysis [10]*

PEEP Does not Protect Surgery Patients *without* ARDS against PPCs

Hemmes S. *Lancet* 2014; 384:495

- RCT, worldwide
- 900 major abdominal surgery–patients
- 12 vs. 0–2 cm H₂O

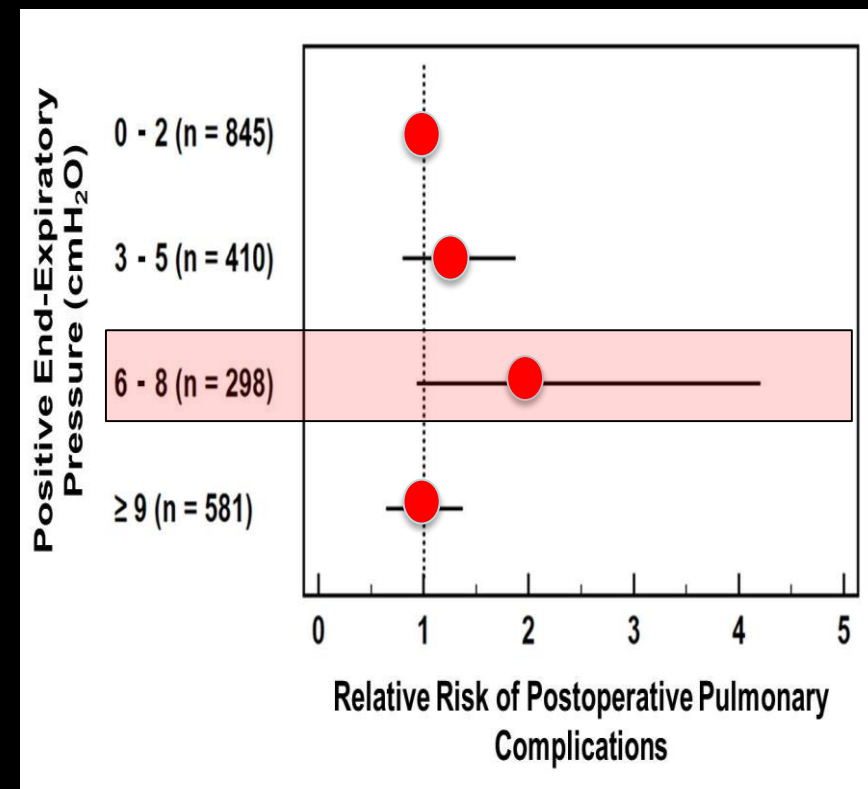


‘PROVHILO’, INTERNATIONAL MULTI-CENTER RCT

Benefit of LP–MV is Better Explained by V_T –reductions than PEEP–increases

Serpa-Neto A. et al. Anesthesiology. 2015 Jul;123(1):66-78

- 2,127 surgery pts
- from 15 studies of intraoperative ventilation
- outcome: PPC

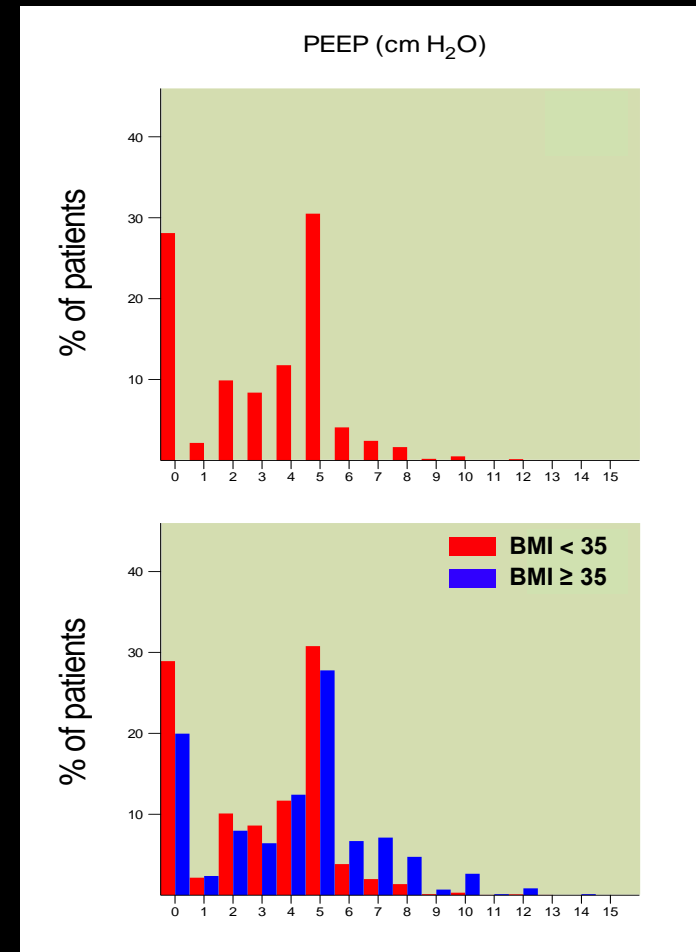


[METANALYSIS]

LAS VEGAS – Practice of Ventilation in ORs Worldwide

Hemmes S. The LAS VEGAS study [SUBMITTED]

- international study
- 8,241 patients
- PEEP 4.0 [0.0–5.0] cm H₂O; PEEP 0 and 5 cm H₂O most frequently used



Ventilation During General Anesthesia for Surgery



Protective ventilation includes:

Tidal volume size
< 8 ml/kg predicted body weight

evidence comes from 3 RCTs [15,22,23] and 2 meta-analyses [14,18]

Level of PEEP
≤ 2 cm H₂O

evidence comes from 1 RCT [25] and 1 IPD meta-analysis [14]

Ventilation in Intensive Care Unit-patients with Uninjured Lungs



Protective ventilation includes:

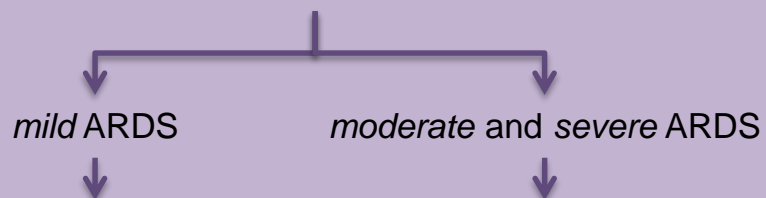
Tidal volume size
6 ml/kg predicted body weight

*evidence comes from 2 RCTs [31,32], 1 meta-analysis and 2 IPD meta-analyses [17,18,33]**

Level of PEEP (< 6 cmH₂O) ??

Convincing RCT evidence is lacking 2 meta-analysis

Ventilation in Intensive Care Unit-patients with the Acute Respiratory Distress Syndrome (ARDS)



Protective ventilation includes:

Tidal volume size
6–8 ml/kg predicted body weight

evidence comes from 2 RCTs [4] and 1 meta-analysis [5]

Level of PEEP
5–10 cm H₂O

evidence comes from 3 RCTs [7,8,9] and 1 IPD meta-analysis [10]

Protective ventilation includes:

Tidal volume size
6–8 ml/kg predicted body weight

evidence comes from 2 RCTs [4] and 1 meta-analysis [5]

Level of PEEP
≥ 10 cm H₂O

evidence comes from 3 RCTs [7,8,9] and 1 IPD meta-analysis [10]

Driving Pressure - Power: the “Polar stars”

Samary CS et al. Anesthesiology. 2015 Aug;123(2):423-33.

Cressoni M. et al. Anesthesiology. 2016 May;124(5):1100-8

$$\Delta P = P_{\text{plat,rs}} - PEEP = V_T / C_{\text{st}} = V_T / EELV$$

$$\text{Stress } \sigma = \Delta F / \Delta S \text{ (PL)}$$

$$\text{Energy} = \Delta P^2 \times (2 \times E_{\text{st}})$$

$$\text{Strain } \varepsilon = \Delta L / L_0 \text{ (} V_T / EELV \text{)}$$

$$\text{Power} = \text{Energy} / \text{Time}$$

$$\Delta P = V_T / C_{\text{st,rs}} = V_T / EELV$$

$$\text{Intensity} = \text{Power} / \text{Area}$$

ΔP

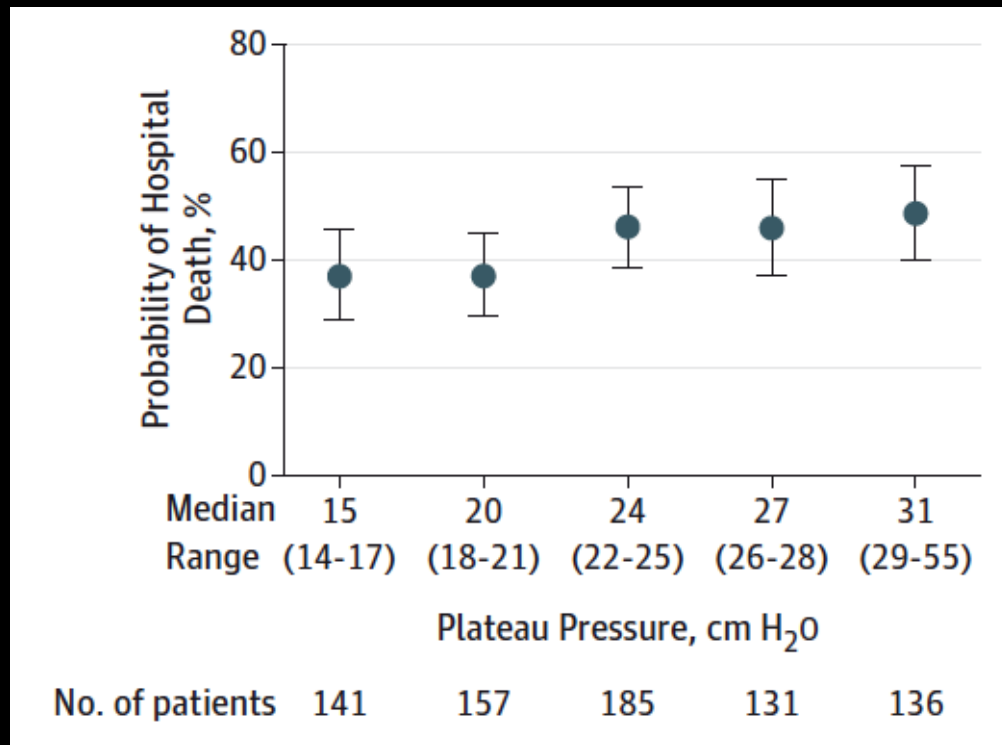
Power

LungSafe – Practice of Ventilation in ICUs Worldwide

Bellani G JAMA. 2016 Feb 23;315(8):788-800

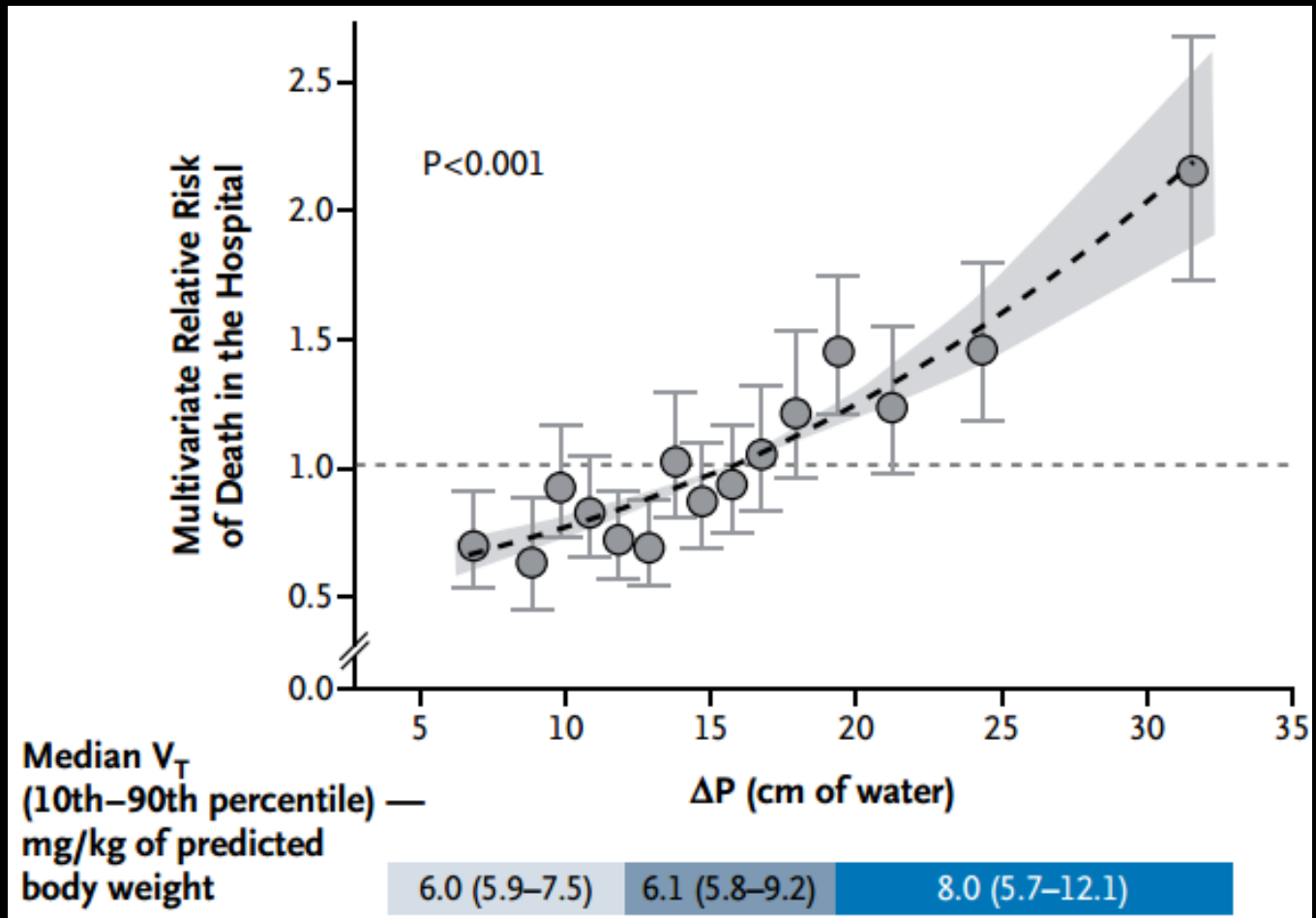
Pplat and Mortality in ARDS

- international observational study
- 2,396 patients with mild, moderate or severe ARDS



Driving pressure and survival in the ARDS

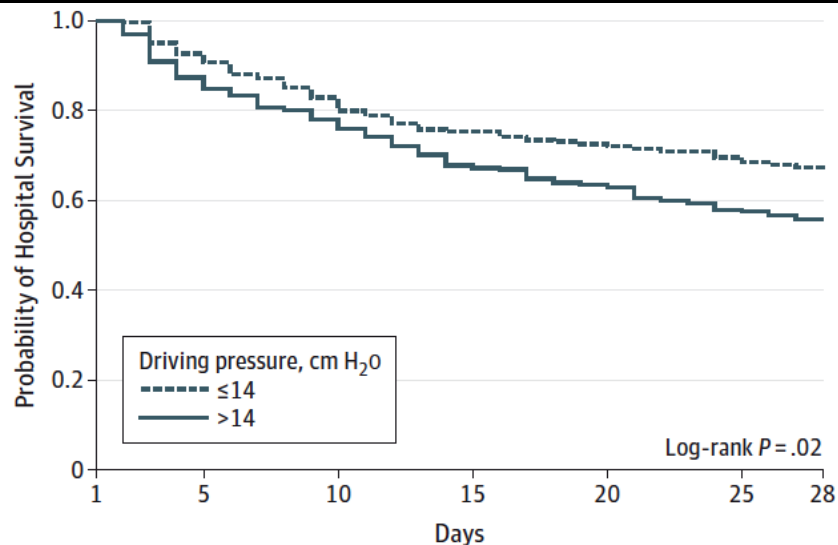
Amato MBP, et al. N Engl J Med 2015;372:747-55



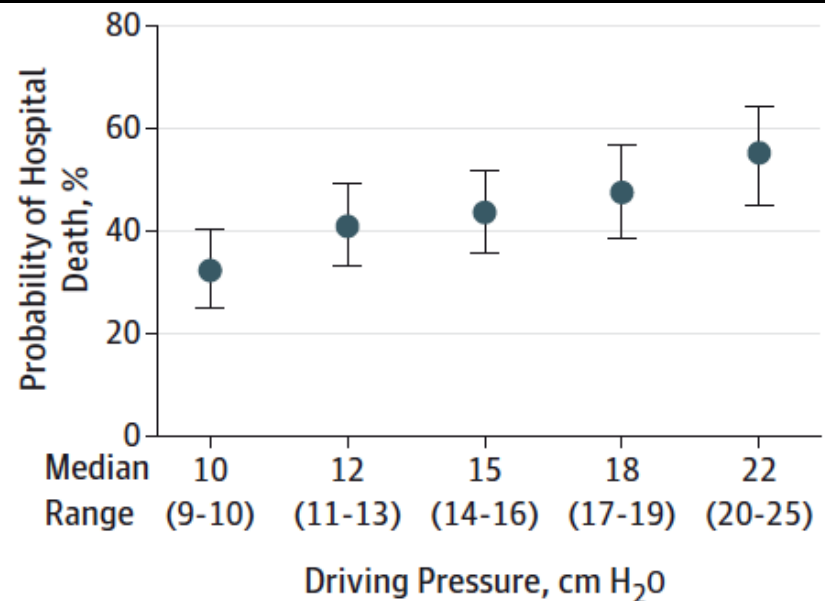
LungSafe – Practice of Ventilation in ICUs Worldwide

Bellani G JAMA. 2016 Feb 23;315(8):788-800

- 2,396 pts with mild, moderate or severe ARDS



No. at risk		Driving pressure, cm H ₂ O							
		≤14	>14	≤14	>14	≤14	>14	≤14	>14
1	370	342	306	277	266	254	245		
5	342	298	262	225	211	192	185		
10									
15									
20									
25									
28									



No. of patients	155	149	154	120	125
Median	10	12	15	18	22
Range	(9-10)	(11-13)	(14-16)	(17-19)	(20-25)

IPD Metaanalysis of studies in ARDS–patients Receiving ELS

Serpa-Neto A et al Intensive Care Med. 2016 Sep 1. [Epub ahead of print]

- 653 patients from 12 studies
- RR for hospital death
- median settings in the first 3 days

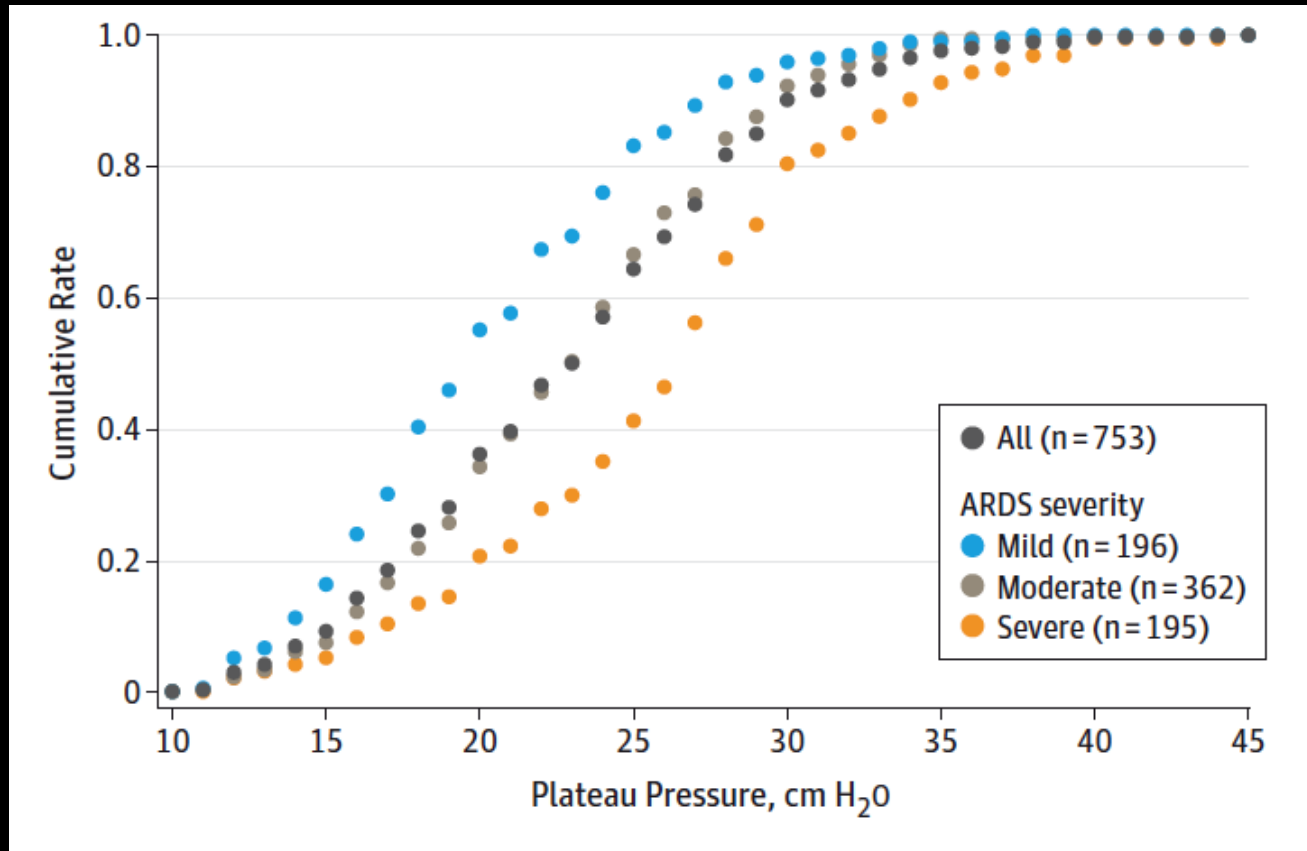
	ALL N = 653	ECMO N = 545	ECCO ₂ R N = 108
RR [95%–CI] (<i>p</i> -value) for hospital death			
V _T , ml/kg PBW	0.97 [0.87–1.08] (<i>p</i> = 0.602)	0.94 [0.83–1.06] (<i>p</i> = 0.294)	1.03 [0.80–1.32] (<i>p</i> = 0.817)
PEEP, cm H ₂ O	0.97 [0.92–1.02] (<i>p</i> = 0.249)	0.97 [0.91–1.03] (<i>p</i> = 0.323)	0.92 [0.83–1.02] (<i>p</i> = 0.125)
Pplat, cm H ₂ O	1.03 [0.97–1.09] (<i>p</i> = 0.298)	1.03 [0.97–1.10] (<i>p</i> = 0.308)	0.94 [0.81–1.10] (<i>p</i> = 0.454)
ΔP, cm H ₂ O	1.07 [1.02–1.12] (<i>p</i> = 0.004)	1.06 [1.01–1.12] (<i>p</i> = 0.029)	1.19 [1.04–1.35] (<i>p</i> = 0.009)
adjusted for risk of death, age and severity of ARDS			

[METANALYSIS]

LungSafe – Practice of Ventilation in ICUs Worldwide

Bellani G JAMA. 2016 Feb 23;315(8):788-800

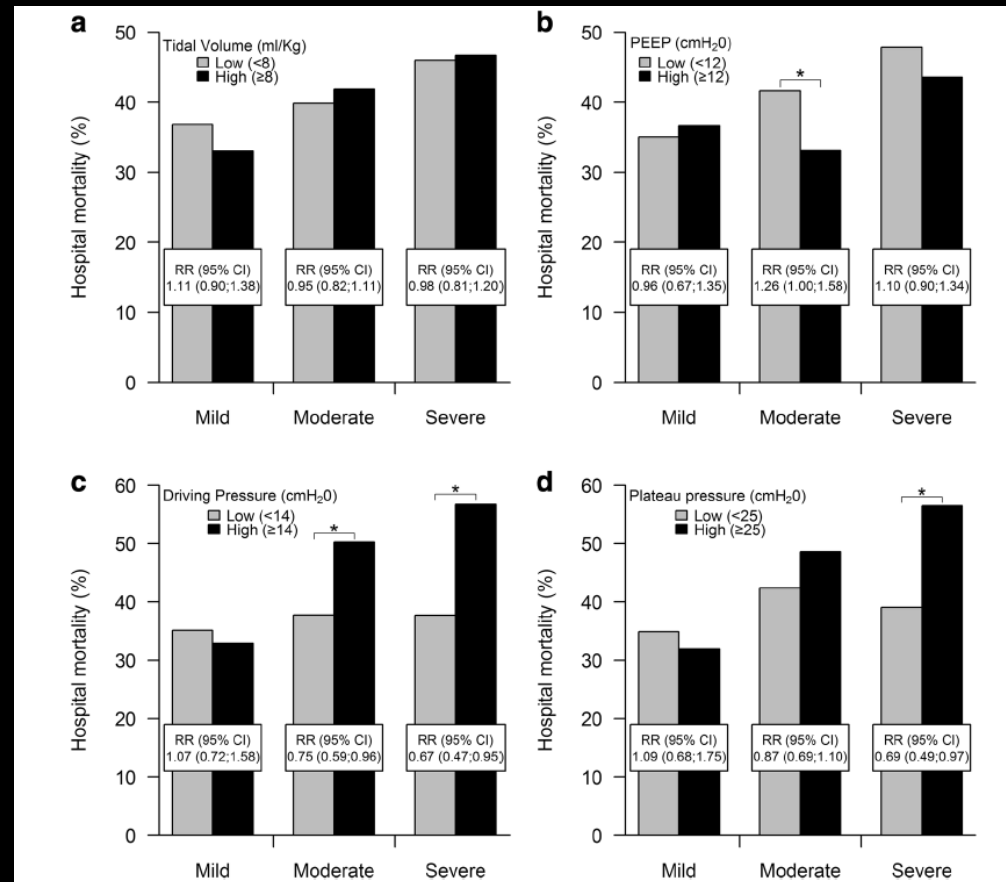
- 2,396 pts with mild, moderate or severe ARDS



LungSafe – Potentially modifiable factors contributing to outcome from ARDS

Laffey GC et al. Intensive Care Med 2016 (Epub Ahead of Print)

- 2,396 pts with mild, moderate or severe ARDS
- Higher PEEP, lower plateau and driving P, & lower respiratory rate are associated with better survival



Ventilation During General Anesthesia for Surgery



Protective ventilation includes:

Tidal volume size
< 8 ml/kg predicted body weight

evidence comes from 3 RCTs [15,22,23] and 2 meta-analyses [14,18]

Level of PEEP
≤ 2 cm H₂O

evidence comes from 1 RCT [25] and 1 IPD meta-analysis [14]

Ventilation in Intensive Care Unit-patients with Uninjured Lungs



Protective ventilation includes:

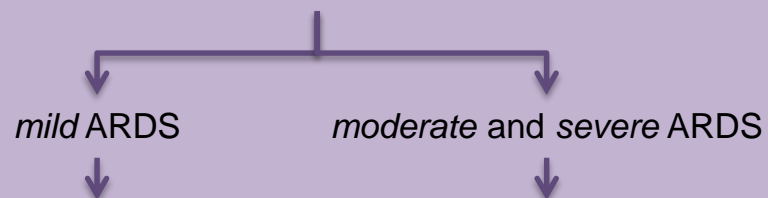
Tidal volume size
6 ml/kg predicted body weight

*evidence comes from 2 RCTs [31,32], 1 meta-analysis and 2 IPD meta-analyses [17,18,33]**

Level of PEEP (< 6 cmH₂O) ??

Convincing RCT evidence is lacking 2 meta-analysis

Ventilation in Intensive Care Unit-patients with the Acute Respiratory Distress Syndrome (ARDS)



Protective ventilation includes:

Tidal volume size
6–8 ml/kg predicted body weight

evidence comes from 2 RCTs [4] and 1 meta-analysis [5]

Level of PEEP
5–10 cm H₂O

evidence comes from 3 RCTs [7,8,9] and 1 IPD meta-analysis [10]

Driving pressure (< 15 cmH₂O)
Pplat (< 25-27 cmH₂O)

suggestion comes from several studies and 1 IPD meta-analysis [10]

Protective ventilation includes:

Tidal volume size
6–8 ml/kg predicted body weight

evidence comes from 2 RCTs [4] and 1 meta-analysis [5]

Level of PEEP
≥ 10 cm H₂O

evidence comes from 3 RCTs [7,8,9] and 1 IPD meta-analysis [10]

Driving pressure (< 15 cmH₂O)
Pplat (< 25-27 cmH₂O)

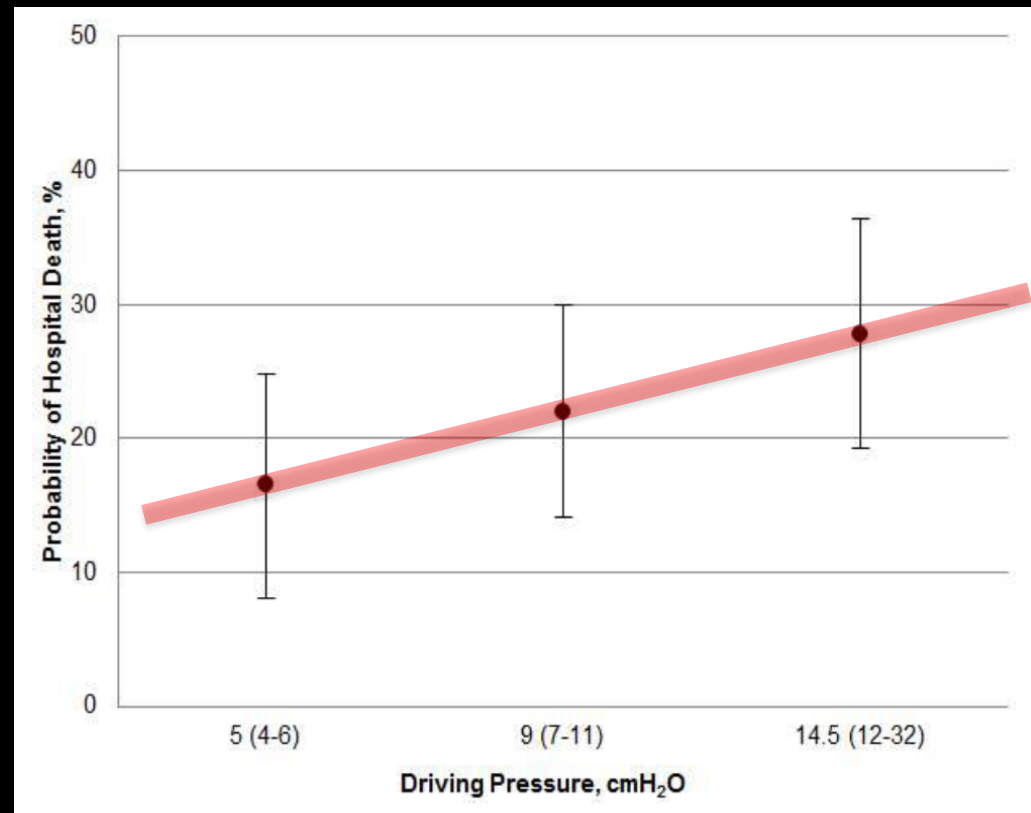
suggestion comes from several studies and 1 IPD meta-analysis [10]

PRoVENT – Practice of Ventilation in ICUs Worldwide



Neto AS et al. Lancet Respir Med. 2016 Nov;4(11):882-893

- international observational study
- 1,022 patients without ARDS

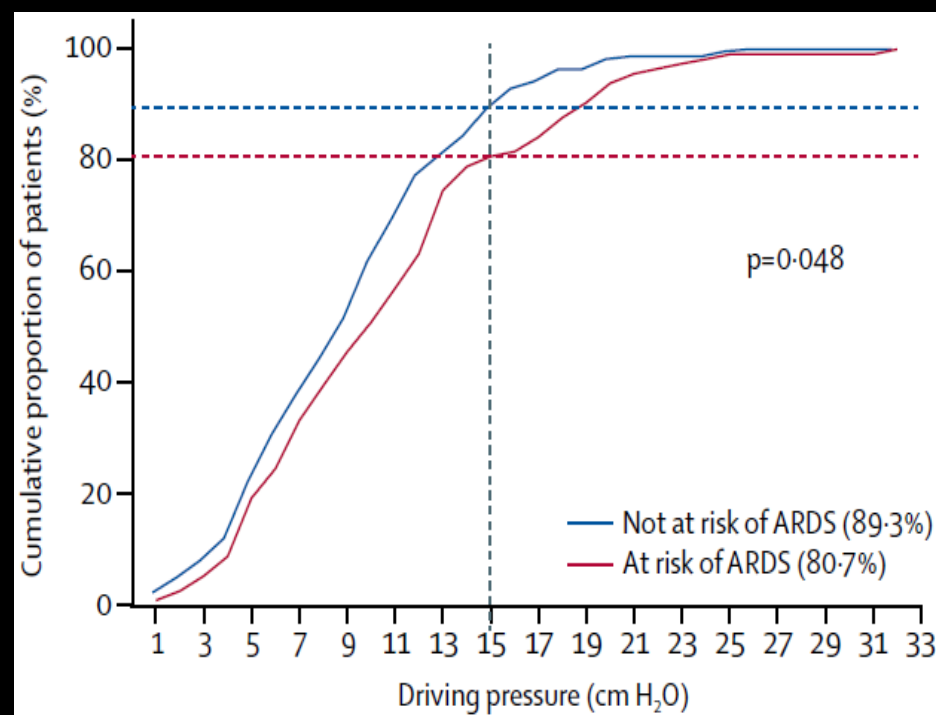
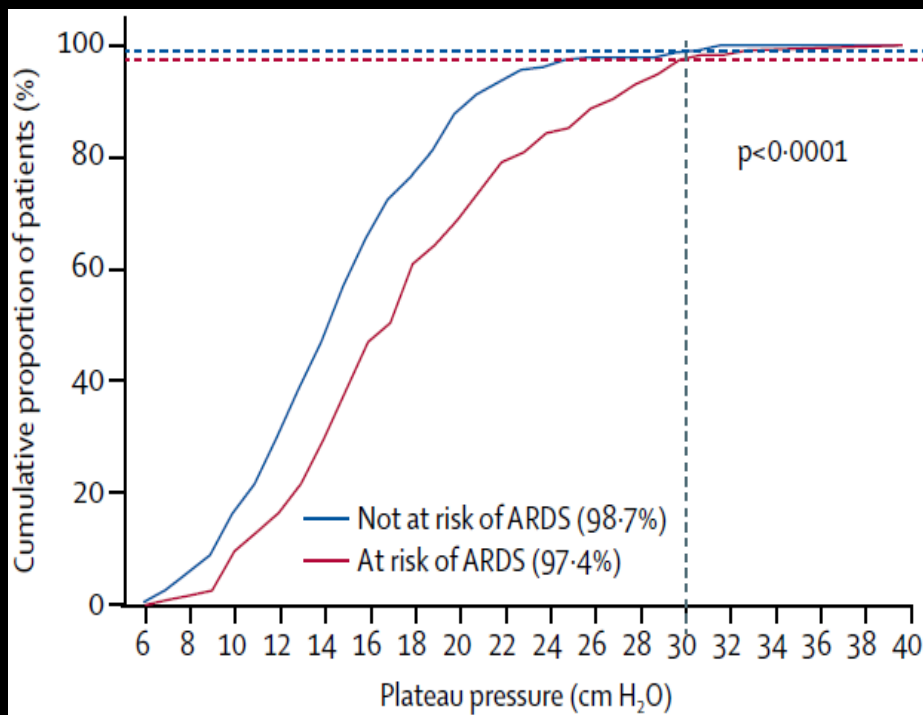


PRoVENT – Practice of Ventilation in ICUs Worldwide



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- 1,022 patients without ARDS



Ventilation During General Anesthesia for Surgery



Protective ventilation includes:

Tidal volume size
< 8 ml/kg predicted body weight

evidence comes from 3 RCTs [15,22,23] and 2 meta-analyses [14,18]

Level of PEEP
≤ 2 cm H₂O

evidence comes from 1 RCT [25] and 1 IPD meta-analysis [14]

Ventilation in Intensive Care Unit-patients with Uninjured Lungs



Protective ventilation includes:

Tidal volume size
6 ml/kg predicted body weight

*evidence comes from 2 RCTs [31,32], 1 meta-analysis and 2 IPD meta-analyses [17,18,33]**

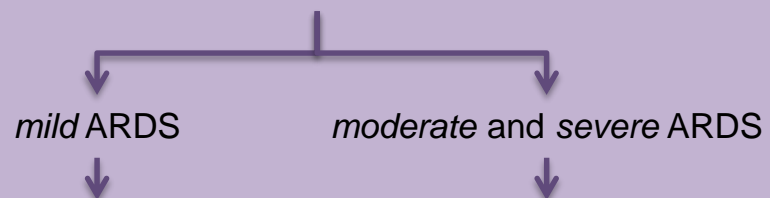
**Level of PEEP (< 6 cmH₂O)
??**

***Convincing RCT evidence is lacking
1 meta-analysis***

**Driving pressure (< 13 cmH₂O)
Plateau pressure (< 20 cmH₂O)
??**

studies are lacking

Ventilation in Intensive Care Unit-patients with the Acute Respiratory Distress Syndrome (ARDS)



Protective ventilation includes:

Tidal volume size
6–8 ml/kg predicted body weight

evidence comes from 2 RCTs [4] and 1 meta-analysis [5]

Level of PEEP
5–10 cm H₂O

evidence comes from 3 RCTs [7,8,9] and 1 IPD meta-analysis [10]

Driving pressure (< 15 cmH₂O)
Pplat (< 25-27 cmH₂O)

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Protective ventilation includes:

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Level of PEEP
≥ 10 cm H₂O

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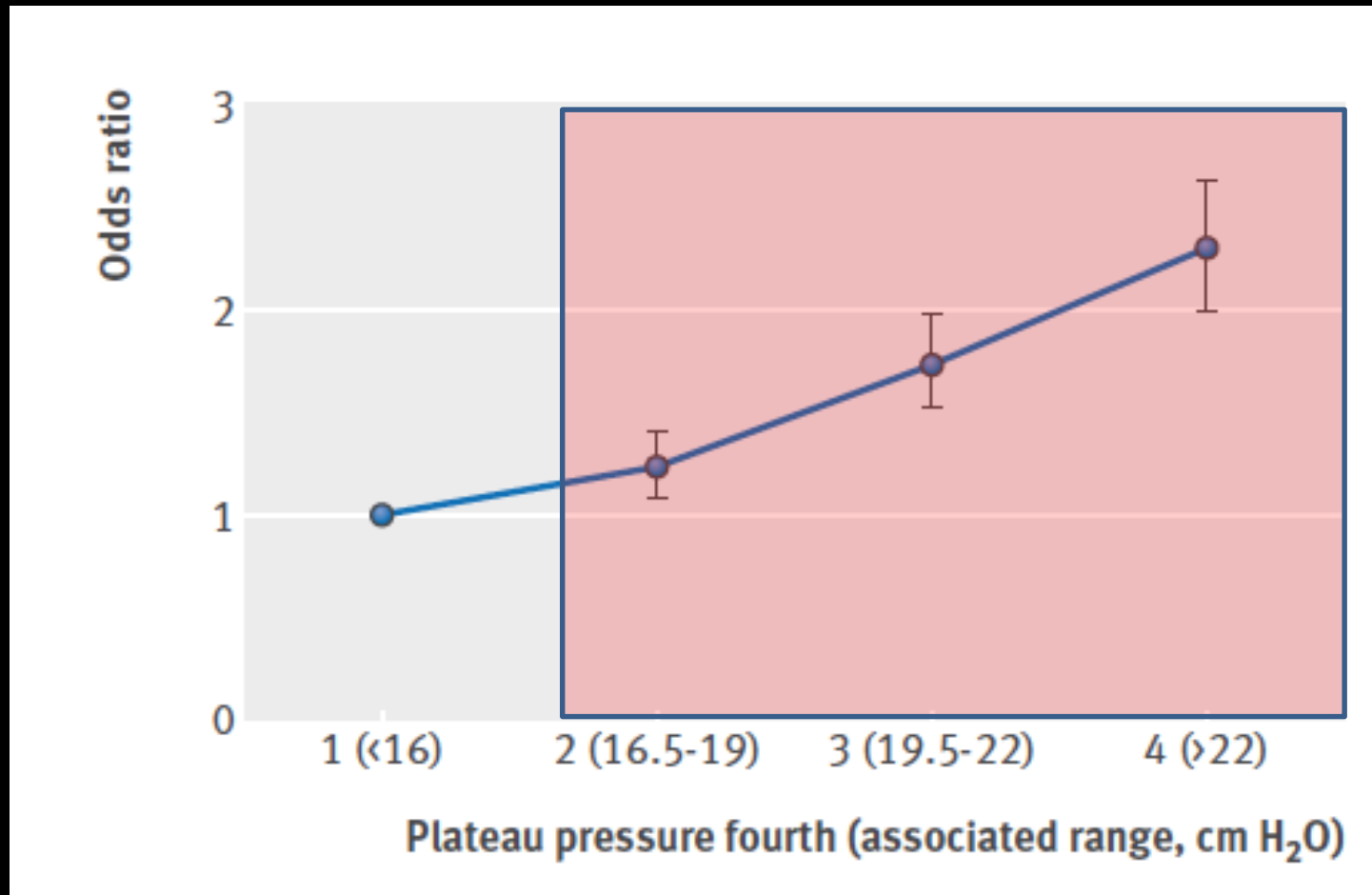
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Intraoperative protective mechanical ventilation and risk of postoperative respiratory complications: hospital based registry study

Ladha K et al. BMJ 2015;351:h3646

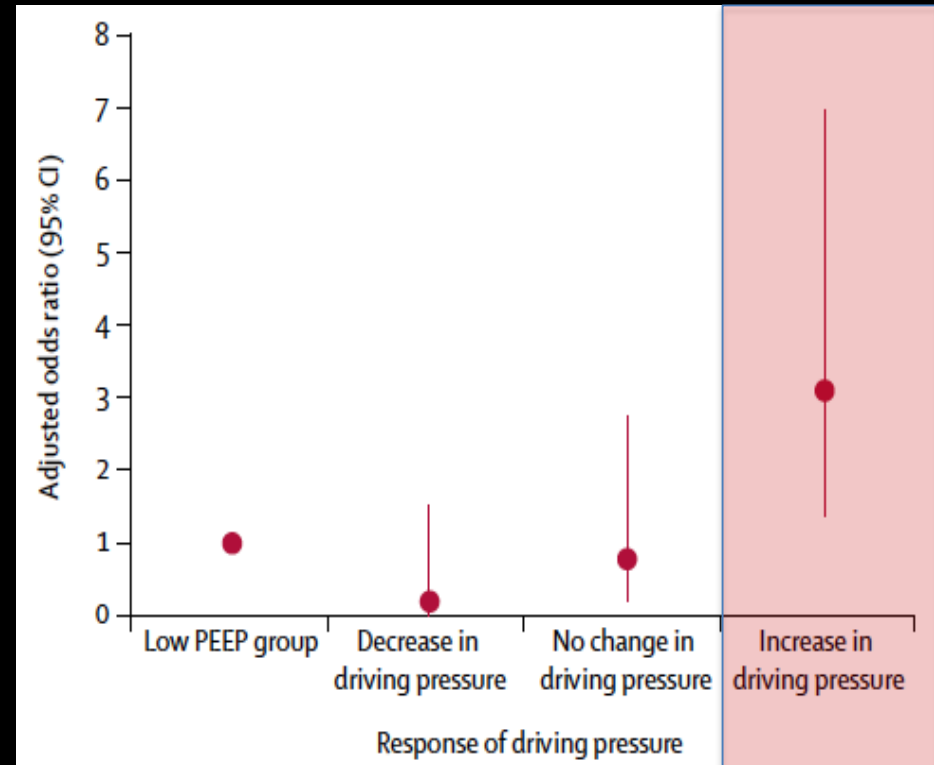
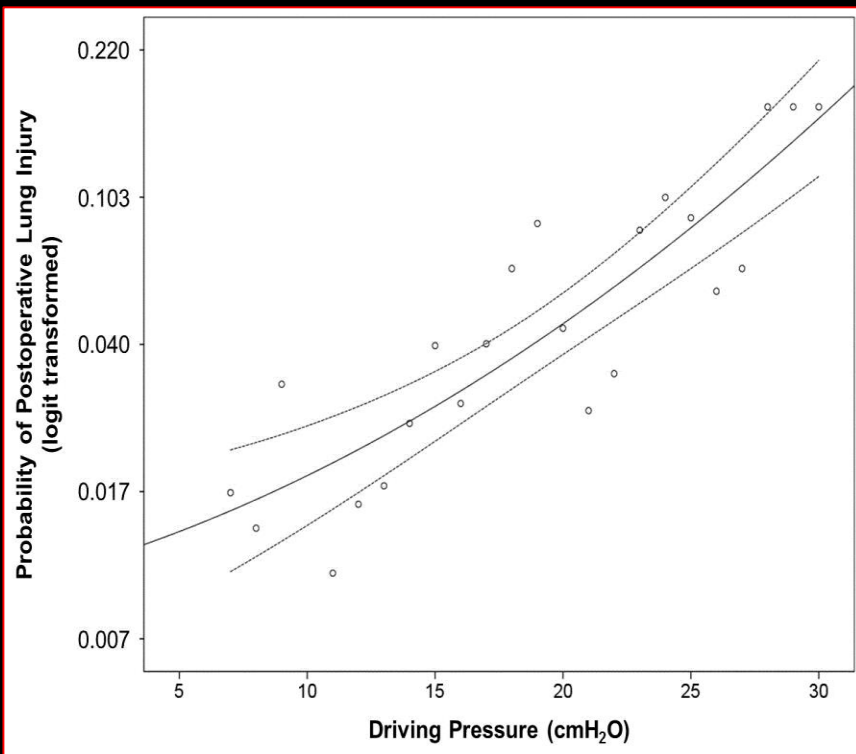
Postoperative Pulmonary Complications



Driving Pressure (ΔP_{rs}) & PPCs

Serpa-Neto A et al. Lancet Respir Med. 2016 Mar 3. pii: S2213-2600

HIGHER DRIVING PRESSURES (>13 cmH₂O)
INCREASE THE RISK OF PPCs
2.679 patients from 15 RCTs



Ventilation During General Anesthesia for Surgery



Protective ventilation includes:

Tidal volume size
< 8 ml/kg predicted body weight

evidence comes from 3 RCTs [15,22,23] and 2 meta-analyses [14,18]

Level of PEEP
≤ 2 cm H₂O

evidence comes from 1 RCT [25] and 1 IPD meta-analysis [14]

Driving pressure (<13 cmH₂O)
Plateau pressure (< 17 cmH₂O)

suggestion comes from several studies and 1 IPD meta-analysis [10]

Ventilation in Intensive Care Unit-patients with Uninjured Lungs



Protective ventilation includes:

Tidal volume size
6 ml/kg predicted body weight

*evidence comes from 2 RCTs [31,32], 1 meta-analysis and 2 IPD meta-analyses [17,18,33]**

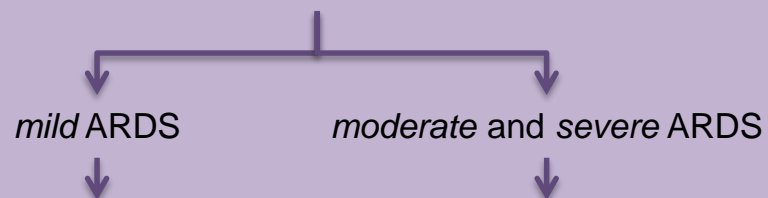
**Level of PEEP (< 6 cmH₂O)
??**

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Ventilation in Intensive Care Unit-patients with the Acute Respiratory Distress Syndrome (ARDS)



Protective ventilation includes:

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suggestion comes from several studies and 1 IPD meta-analysis [10]

JUST DO IT !

*Protective Mechanical Ventilation
In ALL patients*



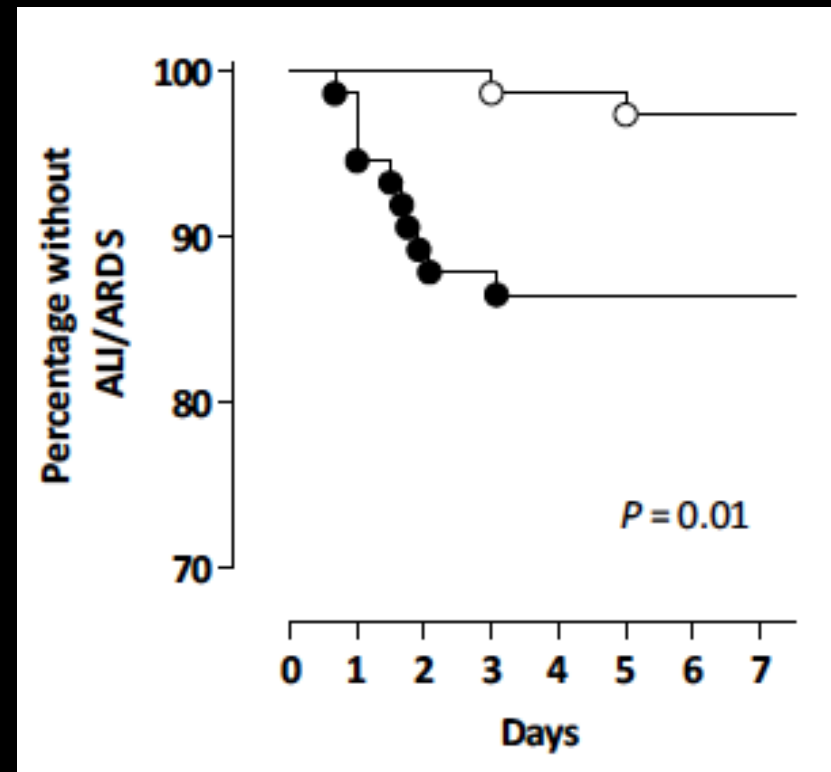
LOWER IS BETTER

...except higher PEEP in severe ARDS (?)

Use of Lower Tidal Volumes Benefits Patients *without* ARDS

Determann R. *Crit Care* 2010; 14:R1

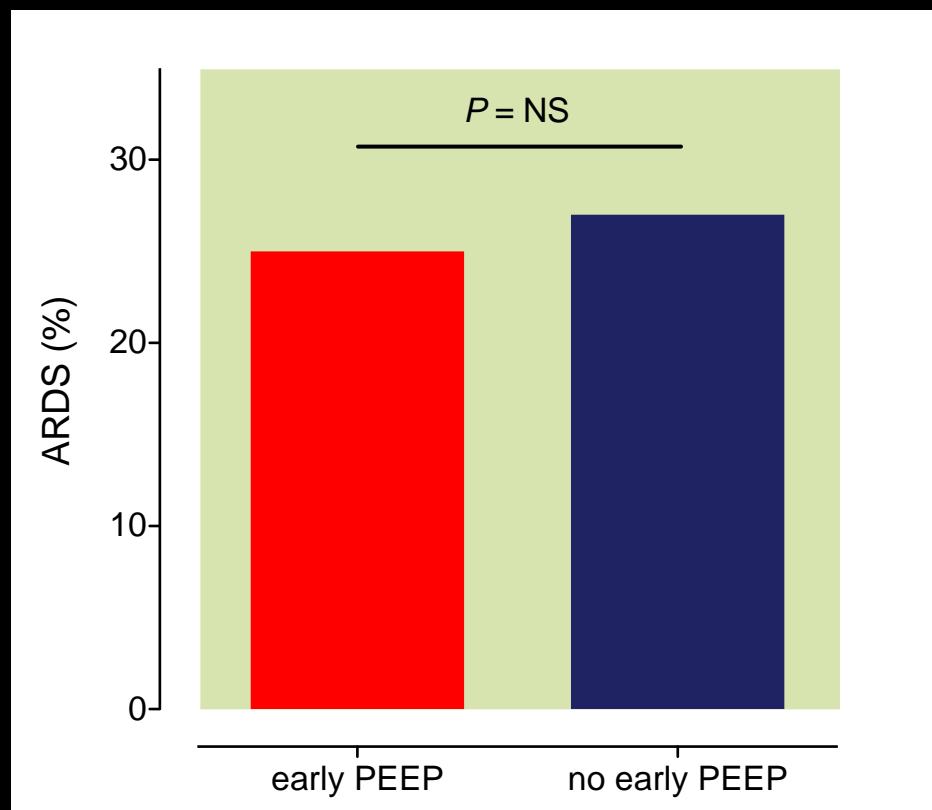
- RCT, the Netherlands
- 150 patients at risk for ARDS
- 6 vs. 10 ml/kg
- stopped early



Use of Higher PEEP Does not Benefit Patients *without* ARDS

Pepe P. *New England J Med.* 1984; 311:281

- RCT, USA
- 92 ICU patients without ARDS
- 8 vs. 0 cm H₂O PEEP

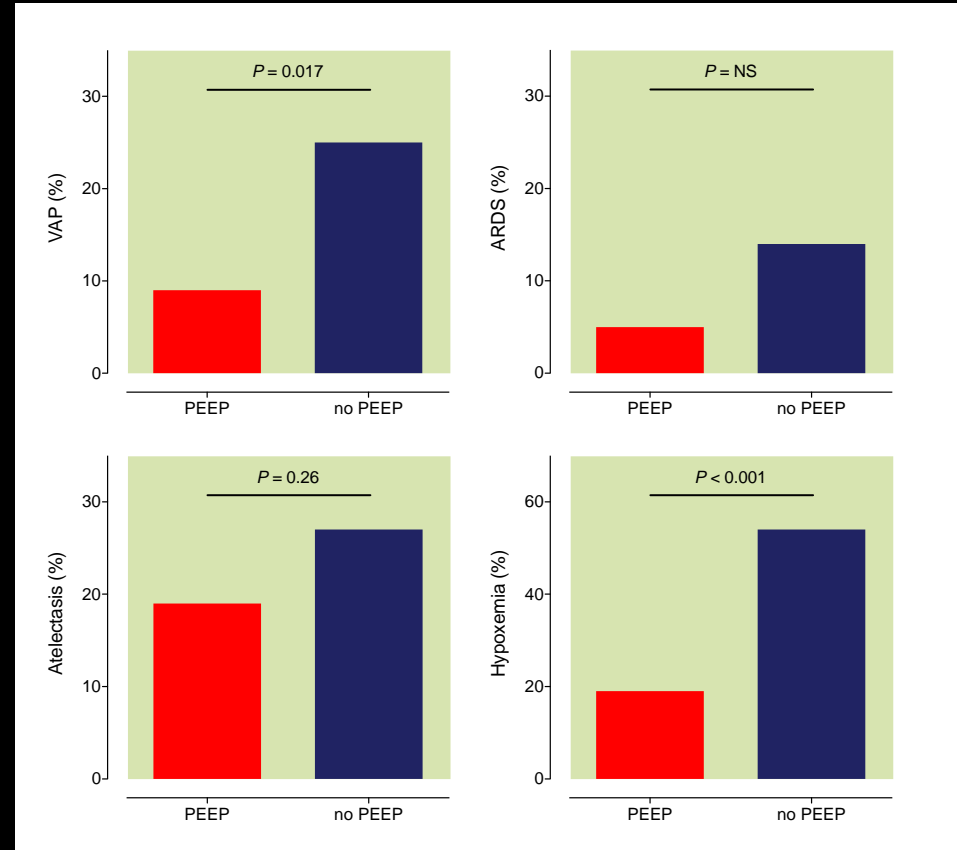


[RANDOMIZED CONTROLLED TRIAL]

Use of Higher PEEP May Benefit Patient *without* ARDS

Manzano F. *Crit Care Med* 2008; 36:2225

- RCT, Spain
- 131 ICU patients without ARDS
- 5–8 vs. 0 PEEP
- no mortality or LOS differences



[RANDOMIZED CONTROLLED TRIAL]