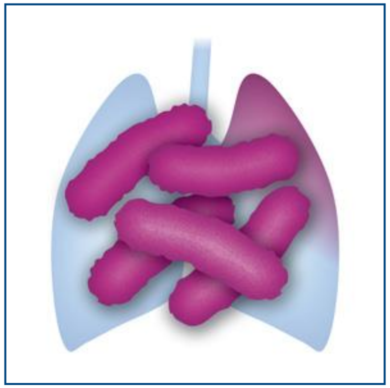
Pneumo Update Europe 2016

24-25 June, Prague

Acute Respiratory Failure & Critical Care



Paolo Pelosi, Italy

Agenda

- **New Clinical Criteria for Sepsis**
- LUNG SAFE: ARDS in the “real life”
- Low Tidal Volume in non-ARDS
- Driving pressure: the “polar star“
- High-flow oxygen nasal cannula in ARDS
- The Helmet and risk of intubation in ARDS
- Tracheostomy: Mortality and QoL

What do *YOU* call sepsis ?

RESPONSE

« Bad infection »

Infection + organ dysfunction

Hypotension
Delirium
Oliguria
DIC
…

SEPSIS – THE CONCEPTS

Sepsis
=
putrefaction

Hippocrates

Sepsis
=
infection + SIRS

1991

Sepsis
=
complex constellation of signs and symptoms

2001

Sepsis
=
Organ dysfunction associated with infection

2015

Sepsis

A“life-threatening organ dysfunction due to a dysregulated host response to infection

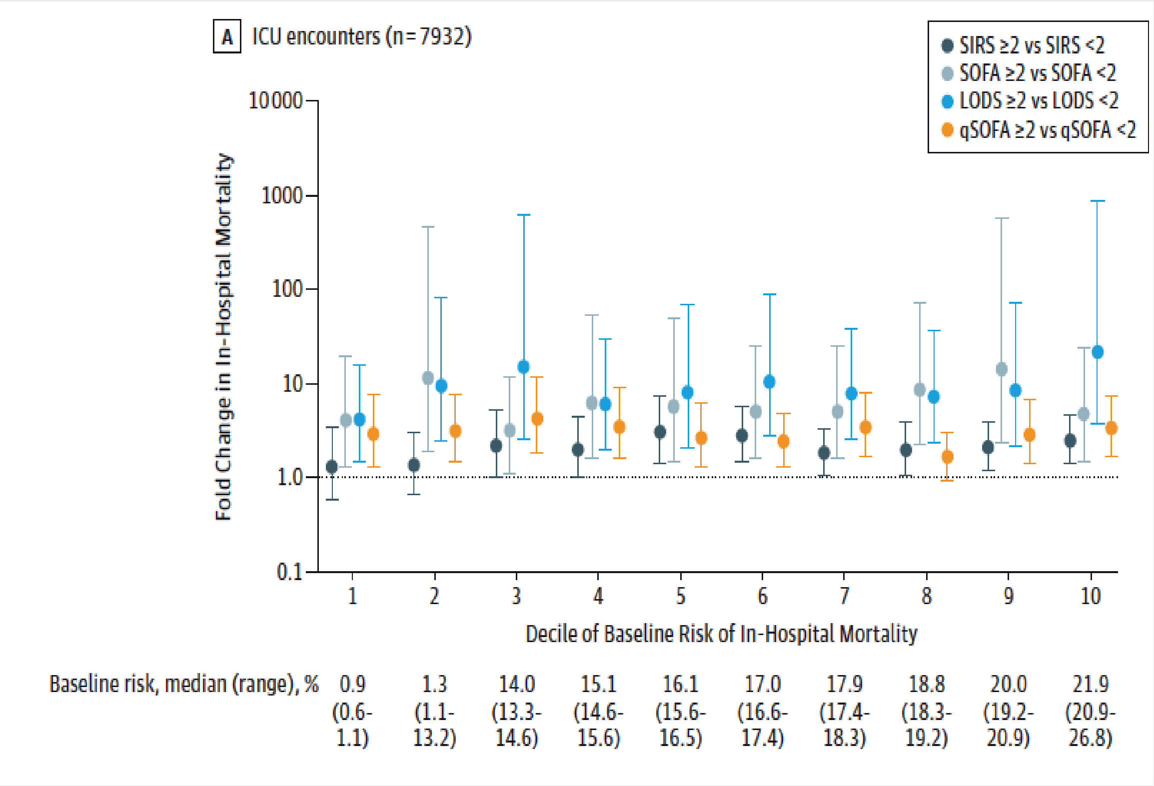
Systemic Inflammatory Response Syndrome (SIRS) Criteria (Range, 0-4 Criteria)	Sequential [Sepsis-related] Organ Failure Assessment (SOFA) (Range, 0-24 Points)	Logistic Organ Dysfunction System (LODS) (Range, 0-22 Points)[a]	Quick Sequential [Sepsis-related] Organ Failure Assessment (qSOFA) (Range, 0-3 Points)
Respiratory rate, breaths per minute	PaO_2/FIO_2 ratio	PaO_2/FIO_2 ratio	Respiratory rate, breaths per minute
White blood cell count, $10^9/L$	Glasgow Coma Scale score	Glasgow Coma Scale score	Glasgow Coma Scale score
Bands, %	Mean arterial pressure, mm Hg	Systolic blood pressure, mm Hg	Systolic blood pressure, mm Hg
Heart rate, beats per minute	Administration of vasopressors with type/dose/rate of infusion	Heart rate, beats per minute	
Temperature, °C	Serum creatinine, mg/dL, or urine output, mL/d	Serum creatinine, mg/dL	
Arterial carbon dioxide tension, mm Hg	Bilirubin, mg/dL	Bilirubin, mg/dL	
	Platelet count, $10^9/L$	Platelet count, $10^9/L$	
		White blood cell count, $10^9/L$	
		Urine output, L/d	
		Serum urea, mmol/L	
		Prothrombin time, % of standard	

Seymour CW et al. JAMA. 2016;315(8):762-774

Shankar-Ary M JAMA. 2016 Feb 23;315(8):775-87

Singer M et al. JAMA. 2016;315(8):801-810

Sepsis



- **SEPSIS in ICU settings:** SOFA score of 2 points or more with infection
- **SEPSIS in non-ICU settings:** qSOFA (consider possibility of Sepsis)

Seymour CW et al. JAMA. 2016;315(8):762-774
Shankar-Ary M JAMA. 2016 Feb 23;315(8):775-87
Singer M et al. JAMA. 2016;315(8):801-810

Special Communication | CARING FOR THE CRITICALLY ILL PATIENT

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Mervyn Singer, MD, FRCP; Clifford S. Deutschman, MD, MS; Christopher Warren Seymour, MD, MSc; Manu Shankar-Hari, MSc, MD, FFICM; Djillali Annane, MD, PhD; Michael Bauer, MD; Rinaldo Bellomo, MD; Gordon R. Bernard, MD; Jean-Daniel Chiche, MD, PhD; Craig M. Coopersmith, MD; Richard S. Hotchkiss, MD; Mitchell M. Levy, MD; John C. Marshall, MD; Greg S. Martin, MD, MSc; Steven M. Opal, MD; Gordon D. Rubenfeld, MD, MS; Tom van der Poll, MD, PhD; Jean-Louis Vincent, MD, PhD; Derek C. Angus, MD, MPH

Box 3. New Terms and Definitions

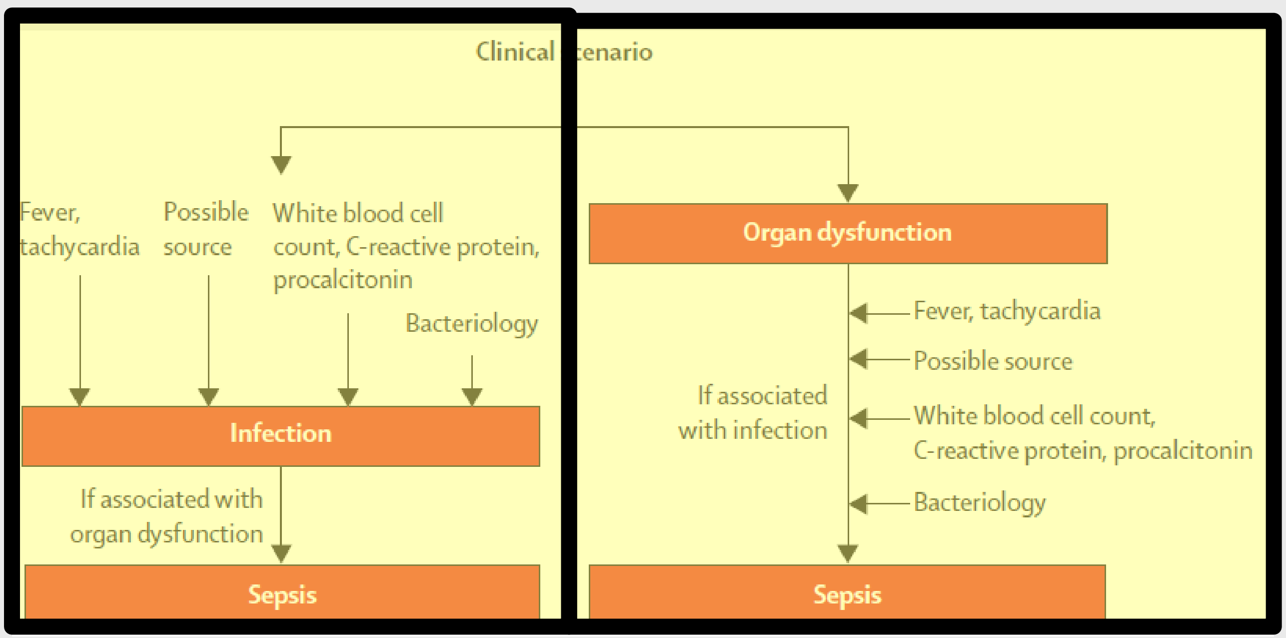
- Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.
- Organ dysfunction can be identified as an acute change in total SOFA score ≥2 points consequent to the infection.
  - The baseline SOFA score can be assumed to be zero in patients not known to have preexisting organ dysfunction.
  - A SOFA score ≥2 reflects an overall mortality risk of approximately 10% in a general hospital population with suspected infection. Even patients presenting with modest dysfunction can deteriorate further, emphasizing the seriousness of this condition and the need for prompt and appropriate intervention, if not already being instituted.
- In lay terms, sepsis is a life-threatening condition that arises when the body's response to an infection injures its own tissues and organs.

Singer M et al. JAMA. 2016;315(8):801-810

Sepsis: older and newer concepts

Jean-Louis Vincent, Jean-Paul Mira, Massimo Antonelli

Sepsis is a common complication in patients in intensive care units and a frequent reason for intensive care unit admission. Sepsis is a major cause of morbidity and mortality and, without specific antisepsis therapies, management relies on infection control and organ support. For these interventions to be most effective, they must be started early, which highlights the need for all health-care workers to be aware of sepsis so that diagnosis can be made as early as possible. In this Viewpoint, we discuss some of the earlier terms used to characterise and define sepsis, and point out some of their limitations. We then introduce some aspects of new consensus definitions, proposed by an expert panel, which highlight in particular the importance of organ dysfunction. These definitions should help provide a more standardised approach to the identification of patients with suspected sepsis in both clinical practice and clinical research.



Lancet Respir Med 2016 Mar;4(3):237-40

ALARM SIGNAL

quickSOFA (qSOFA)

to identify infected patients with poor outcomes

in prehospital, emergency room and ward settings

- additional tests to evaluate organ function
- prompt intervention
- increased surveillance / transfer to ICU?

✓ **Tachypnea** (RR ≥ 22 breaths/min)
✓ **Hypotension** (systolic BP ≤100 mmHg)
✓ **Altered Mentation**
❖ **Sat O_2 in air < 94%**

THAM = Tachypnea, Hypotension, Altered Mentation

Septic Shock

❖Septic shock can be identified using:

➢the clinical criteria of hypotension requiring vasopressor therapy to maintain mean BP 65mmHg or greater

➢having a serum lactate level greater than 2 mmol/L after adequate fluid resuscitation

Seymour CW et al. JAMA. 2016;315(8):762-774

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Singer M et al. JAMA. 2016;315(8):801-810

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- ❖ Tracheostomy: Mortality and QoL

ARDS Incidence

- ❖ **10.4% of all ICU Admissions**

- ❖ **23% of all ventilated ICU patients**

- ❖ **0.45 patients/ICU bed/4 weeks [5.5 patients / ICU bed /year]**

- ❖ **Geographic variation [cases/ICU bed/4 weeks]**
  Oceania 0.57
  Europe 0.48
  North America 0.46
  Africa 0.32
  South America 0.31
  Asia 0.27

Bellani G et al. JAMA Feb 23 2016, 315 (8): 788-800

ARDS Risk factors

ARDS Risk Factors	
Pneumonia	1794 (59%)
Non pulmonary Sepsis	484 (16%)
Aspiration	430 (14%)
Non cardiogenic shock	226 (7%)
Trauma	127 (4%)
Blood transfusion	118 (4%)
Pulmonary contusion	97 (3%)
Inhalation	72 (2%)
Drug overdose	56 (2%)
Pulmonary vasculitis	41 (1%)
Burn	9 (0.3%)
Drowning	2 (0.1%)
No risk Factor	252(8%)

Bellani G et al. JAMA Feb 23 2016, 315 (8): 788-800

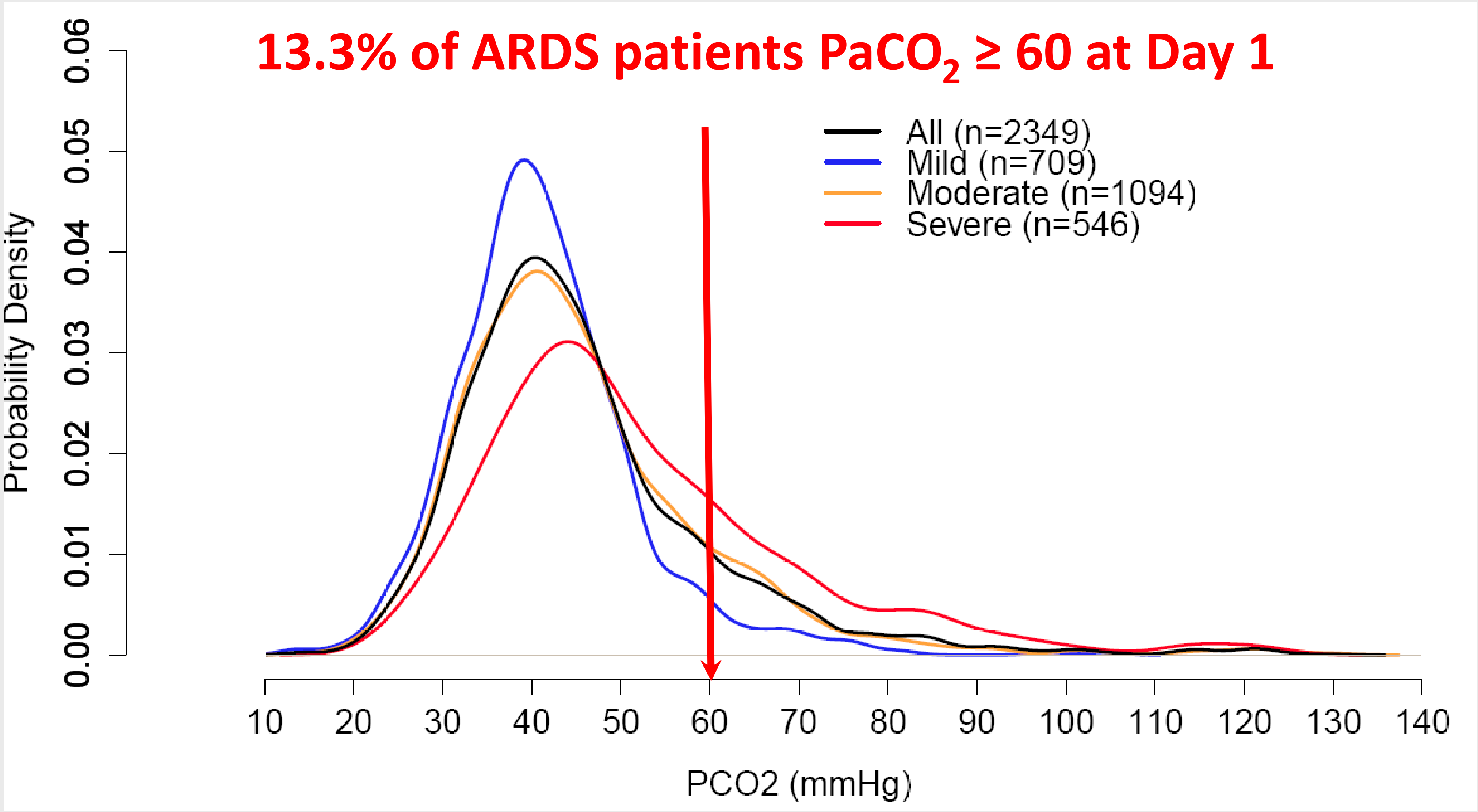
ARDS Recognition

Clinician Recognition of ARDS	All	Mild	Moderate	Severe	P value
On Day 1 (%)	**32%**	26%	34%	**42%**	<0.001
At any time (%)	**60%**	51%	65%	**78%**	<0.001

- **The absence of a risk factor for ARDS**
- **Lower numbers of nurses and physicians per ICU patient**

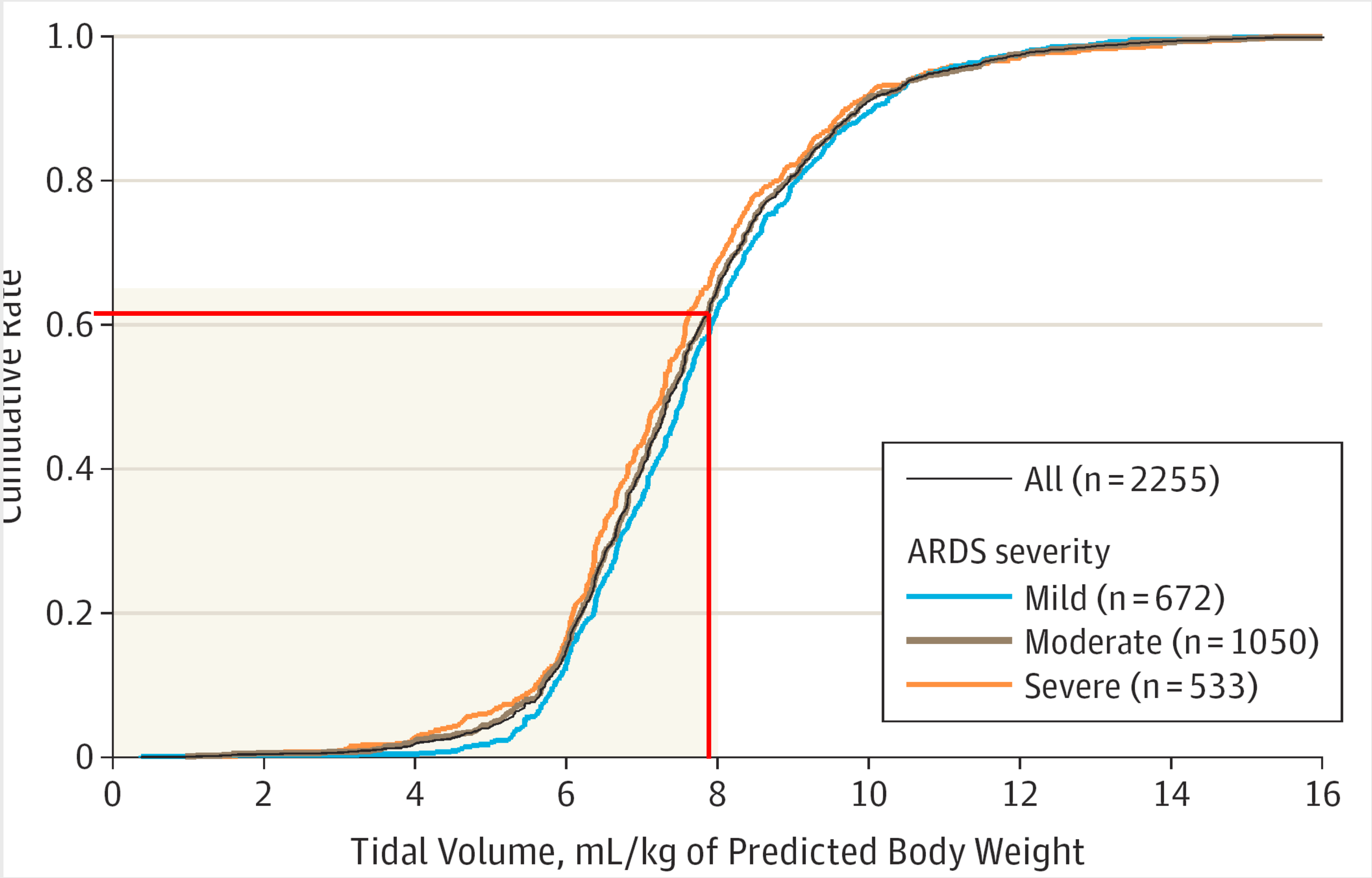
Bellani G et al. JAMA Feb 23 2016, 315 (8): 788-800

ARDS $PaCO_2$



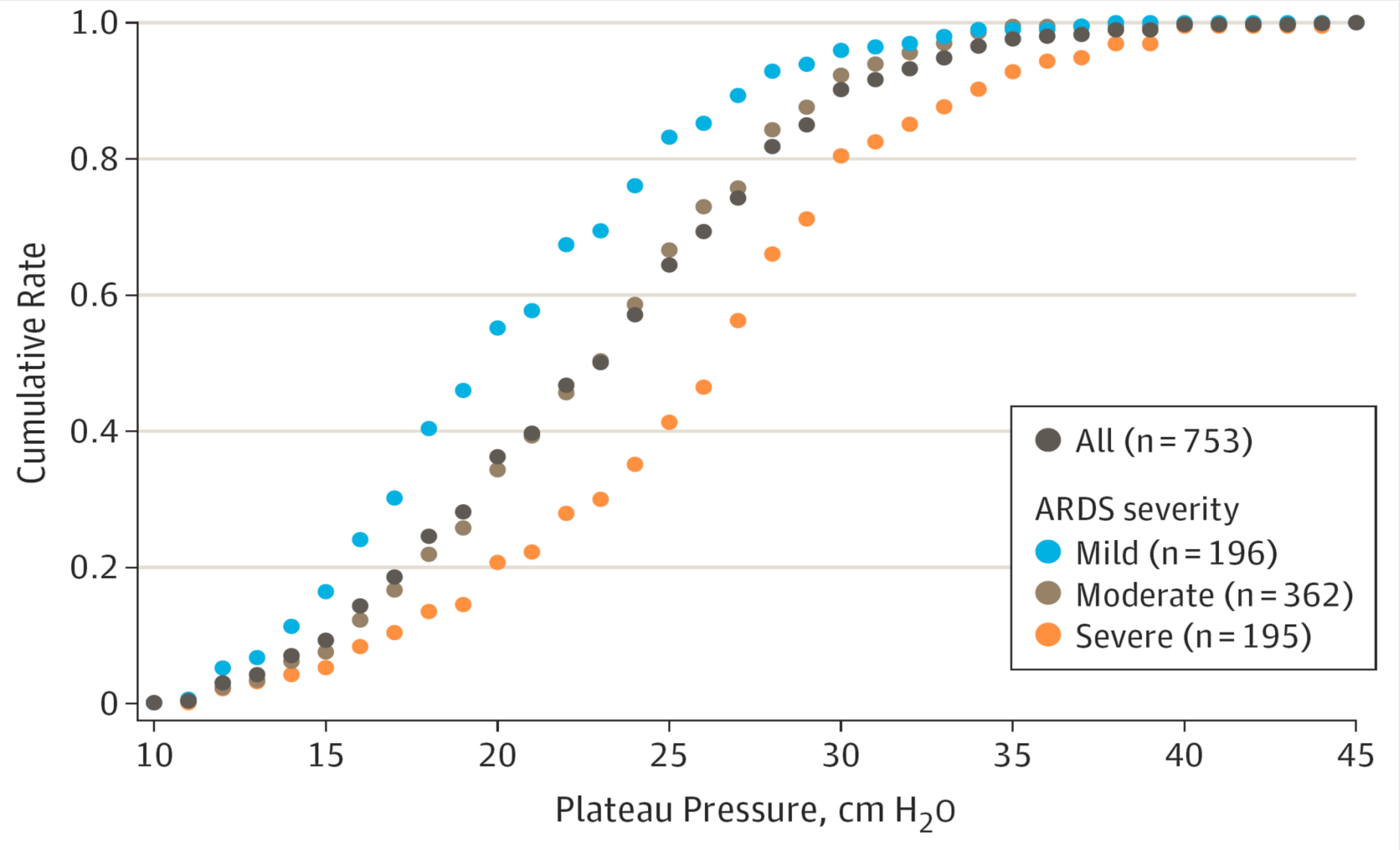
Bellani G et al. JAMA Feb 23 2016, 315 (8): 788-800

ARDS Tidal Volume



Bellani G et al. JAMA Feb 23 2016, 315 (8): 788-800

ARDS Plateau Pressure



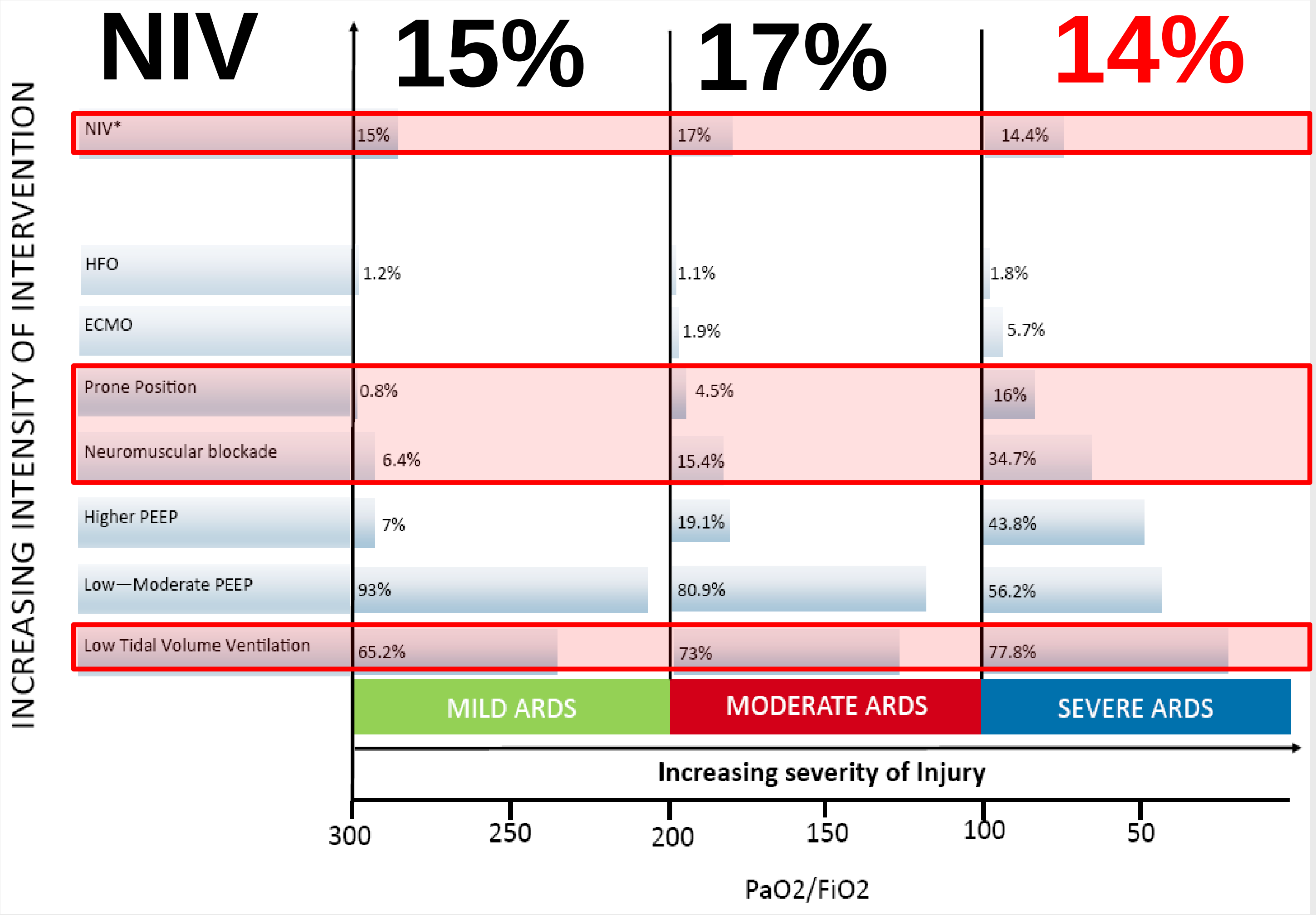
Bellani G et al. JAMA Feb 23 2016, 315 (8): 788-800

Use of adjunctive treatments

	All	Mild	Moderate	Severe	P value[2]
Neuromuscular Blockade, No. (%),	516 (21.7)	34 (6.8)	208 (18.1)	274 (37.8)	<0.001
Recruitment maneuvers, No. (%),	496 (20.9)	58 (11.7)	200 (17.4)	238 (32.7)	<0.001
Prone positioning, No. (%),	187 (7.9)	5 (1.0)	63 (5.5)	119 (16.3)	<0.001
ECMO, N (%),	76 (3.2)	1 (0.2)	27 (2.4)	48 (6.6)	<0.001
Inhaled vasodilators, No. (%),	182 (7.7)	17 (3.4)	70 (6.1)	95 (13.0)	<0.001
HFOV, No. (%),	28 (1.2)	3 (0.6)	14 (1.2)	11 (1.5)	0.347
None of the Above, No. (%),	1431 (60.2)	397 (79.7)	750 (65.2)	284 (39.0)	<0.001

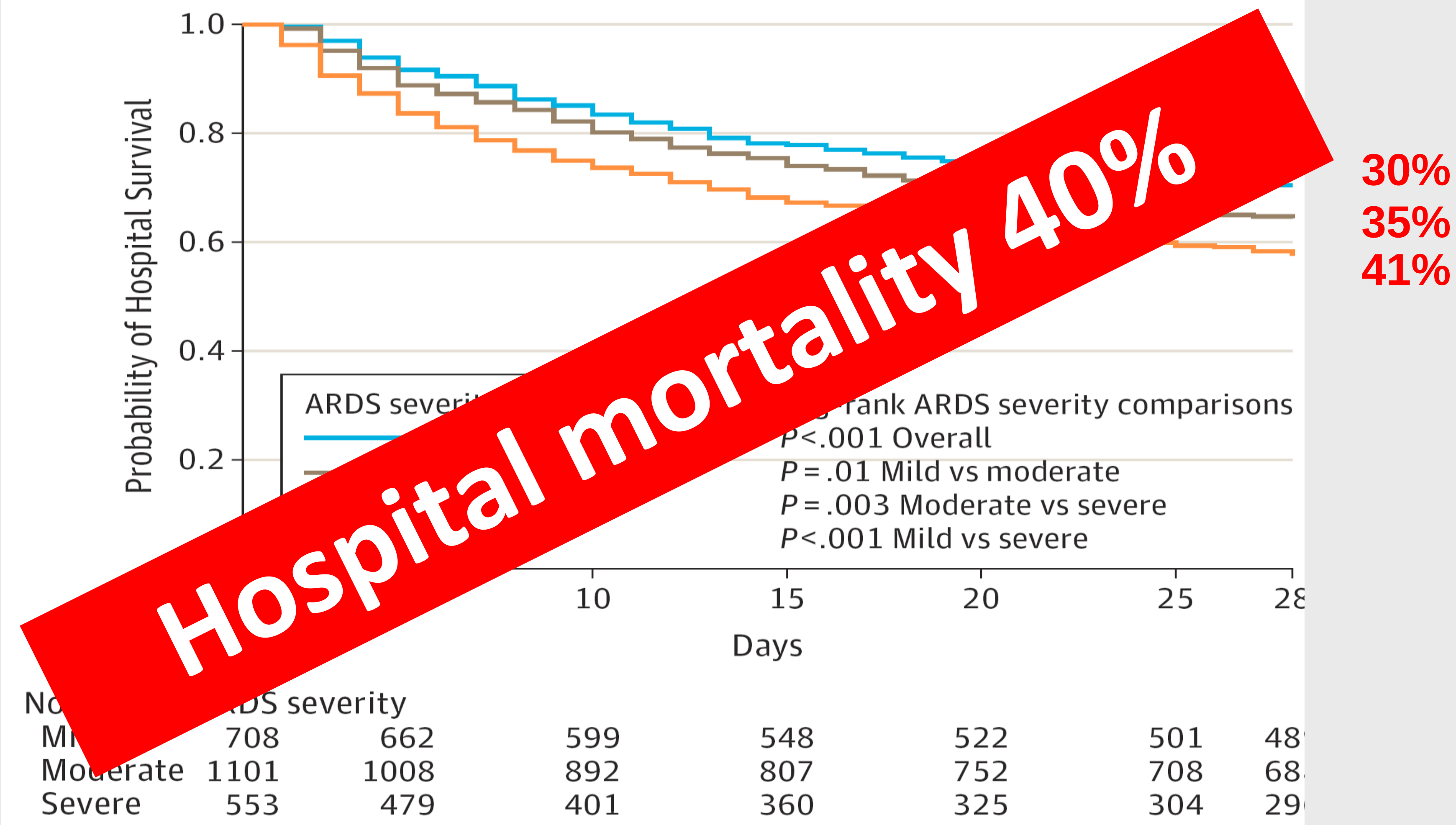
Bellani G et al. JAMA Feb 23 2016, 315 (8): 788-800

ARDS: Adjunctive treatments



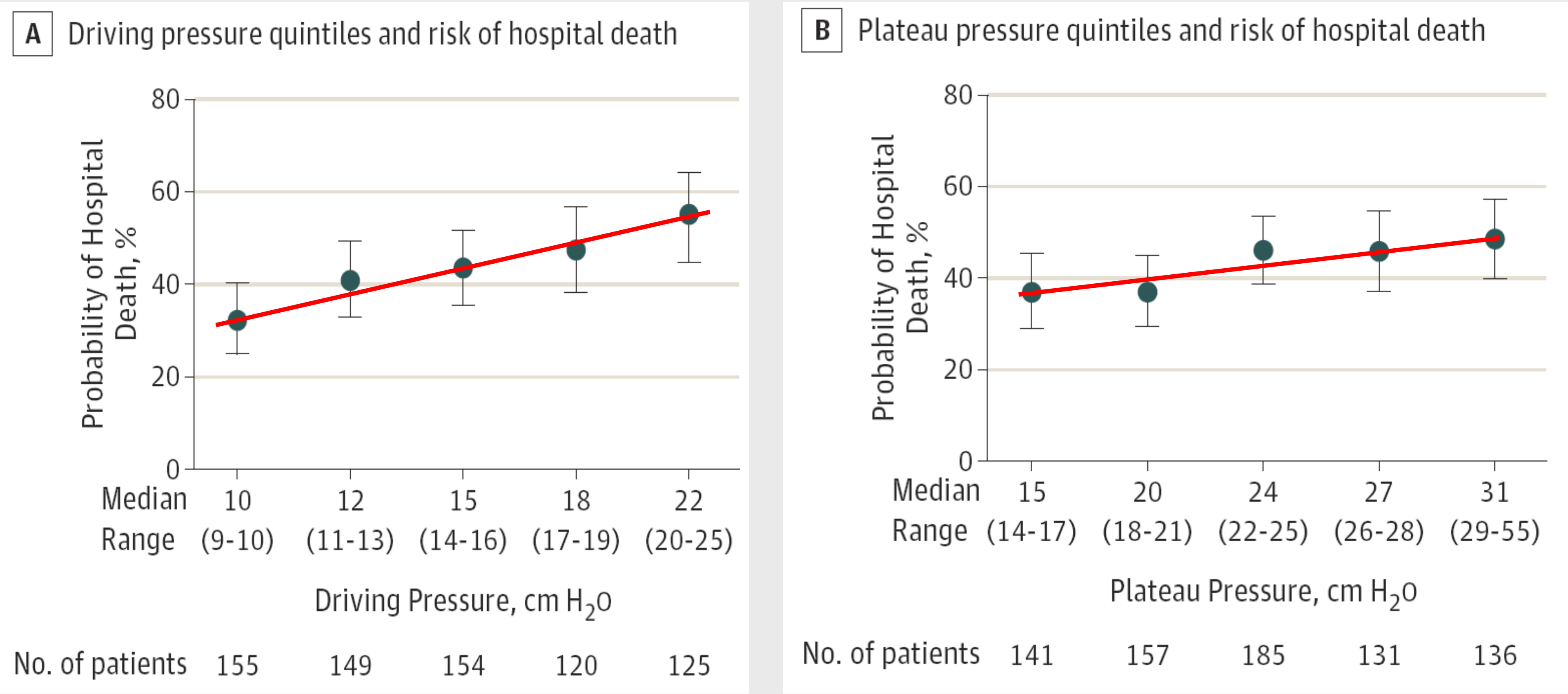
Bellani G et al. JAMA Feb 23 2016, 315 (8): 788-800

ARDS and Survival



Bellani G et al. JAMA Feb 23 2016, 315 (8): 788-800

△ *vs* Plateau P and Survival



Bellani G et al. JAMA Feb 23 2016, 315 (8): 788-800

LUNG SAFE

- ARDS has relatively high Incidence
  - Varied from 10.0 - 10.7% of ICU admissions across the different continents
- Clinician recognition of ARDS was low
  - 40% of all cases not being diagnosed.
  - Clinician recognition rates still <80% in severe ARDS
- More than 1/3 of all pts with ARDS received a VT >8 mL/kg PBW
- PEEP 10 cmH_2O or less even in severe ARDS
- Plateau and driving pressure rarely measured
- Adjunctive measures were used relatively infrequently
  - 22% received NMB
  - 21% received recruitment maneuvers
  - 8% received Prone positioning
  - 3% received ECMO

Bellani G et al. JAMA Feb 23 2016, 315 (8): 788-800

LUNG SAFE

- ❖ **ARDS continues to have a hospital mortality of 40%**

  Despite advances in supportive care.

  increase in mortality with each increase in ARDS severity category. Overall, 40% of patients with ARDS died in the Hospital

- ❖ **A higher driving pressure is associated with increased risk of death**

  caution as Pplat was available in a minority of patients.

  <80% in severe ARDS

Bellani G et al. JAMA Feb 23 2016, 315 (8): 788-800

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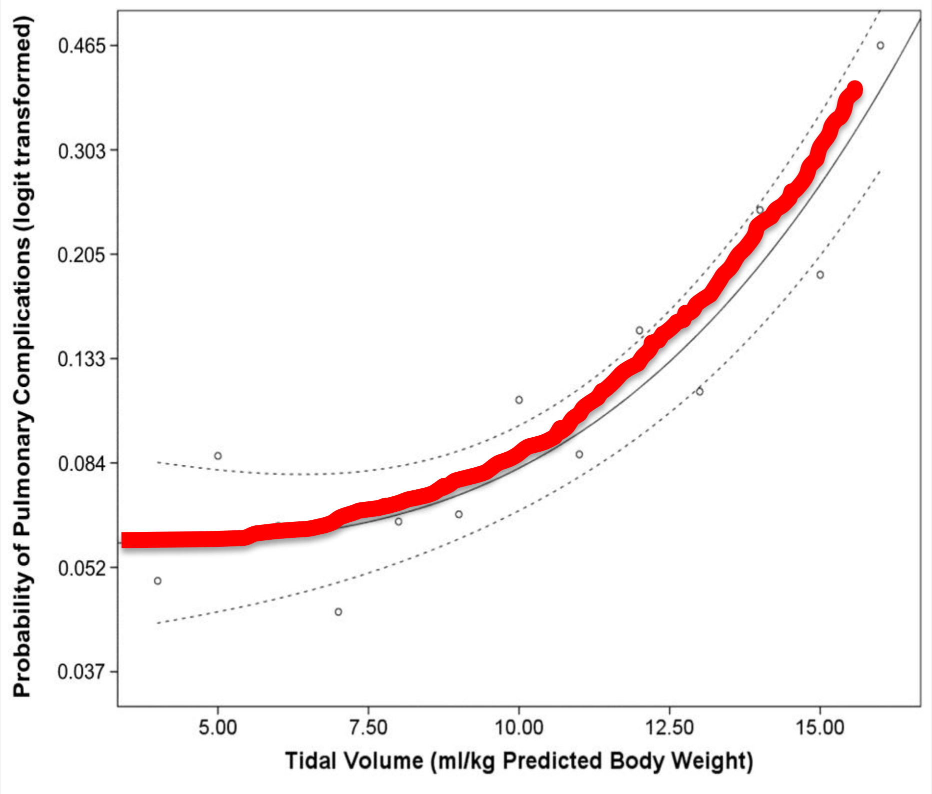
- ❖ Tracheostomy: Mortality and QoL

Lung protective ventilation with low V_T and the occurrence of pulmonary complications in non ARDS patients: a systematic review and meta-analysis



Serpa Neto A. et al. Crit Care Med. 2015 Oct;43(10):2155-63

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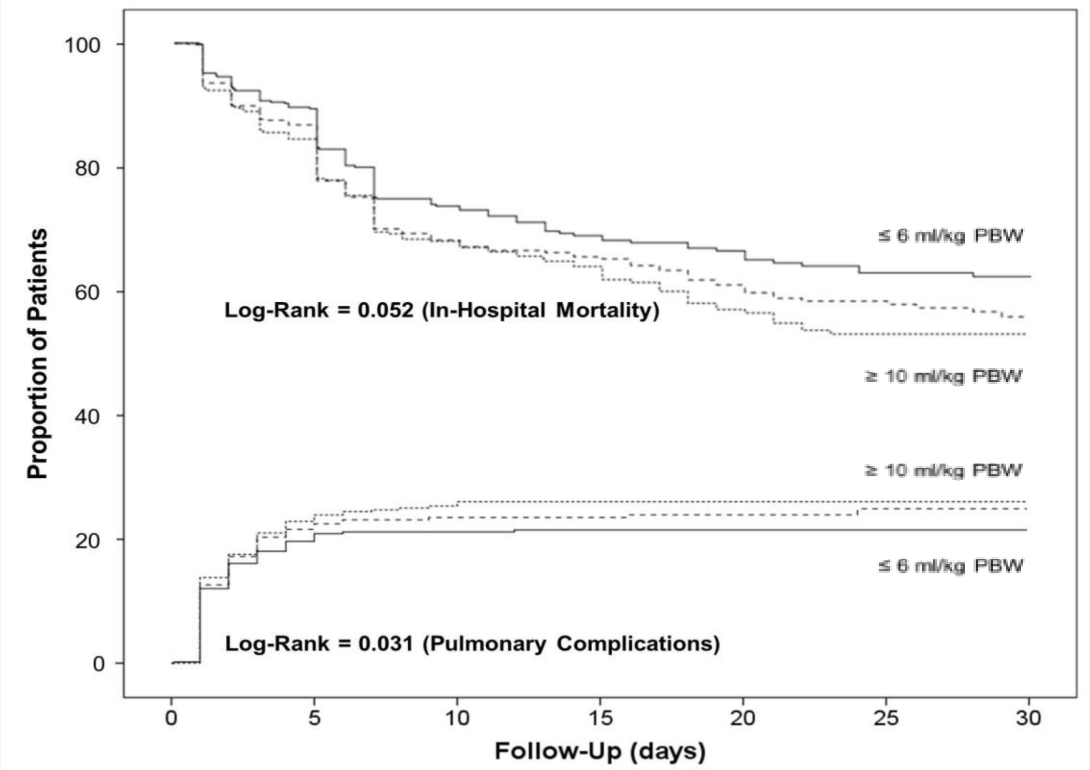

Serpa Neto A. et al. Crit Care Med. 2015 Oct;43(10):2155-63

To prevent or cure acute respiratory distr
syndrome: that is the question!

Paolo Pelosi[a] and Patricia R.M. Ro

Protective mechanical ventilation
in ALL patients
JUST DO IT!

Pelosi P Rocco PR Curr Opin Crit Care 2014 Feb;20(1):1-2.

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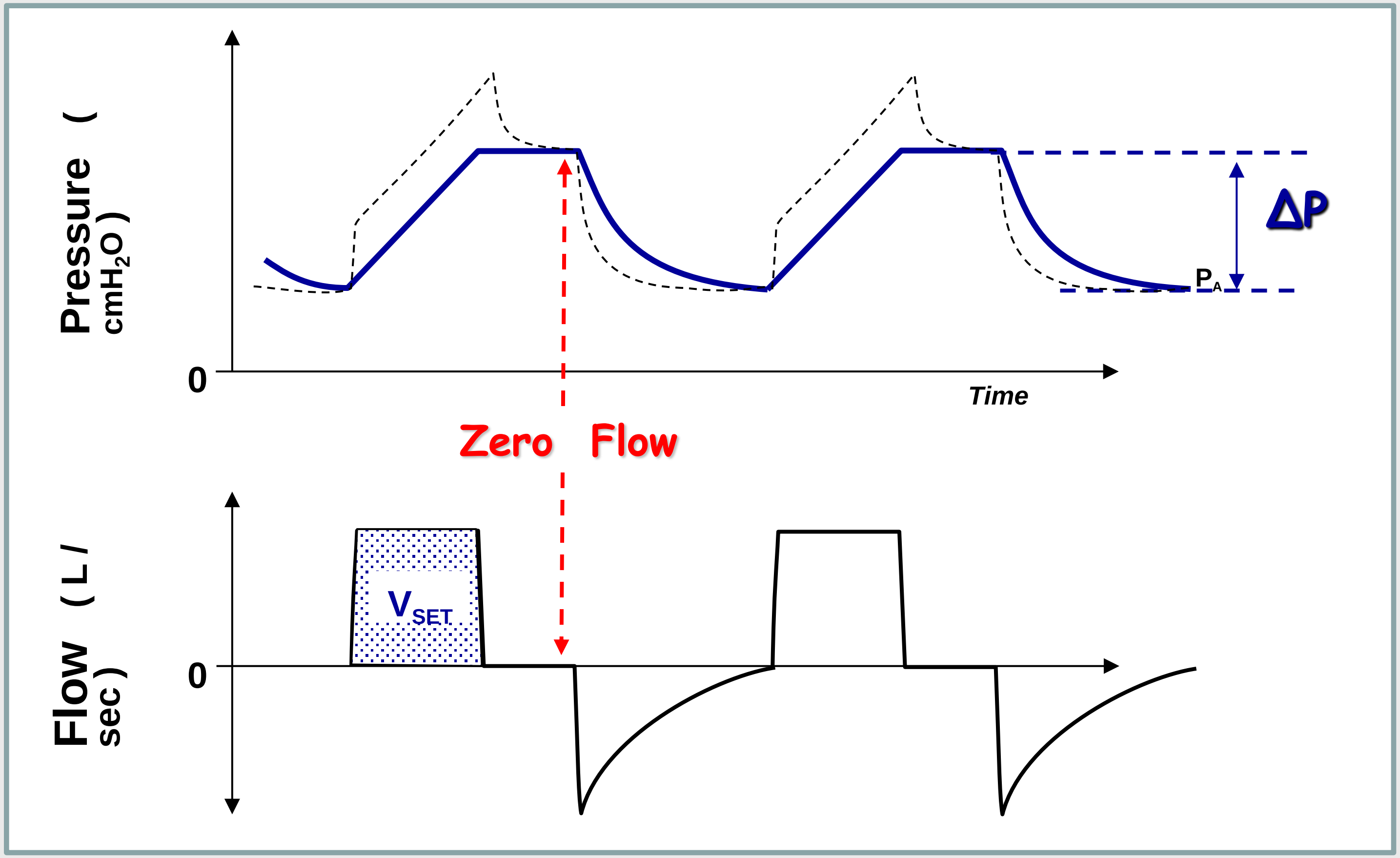
Δpressure is the "polar star"

ΔP = Pplat,rs – PEEP = V_T/Cst = V_T/EELV



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

Cressoni M et al. Anesthesiology. 2016 Feb 12. [Epub ahead of print]

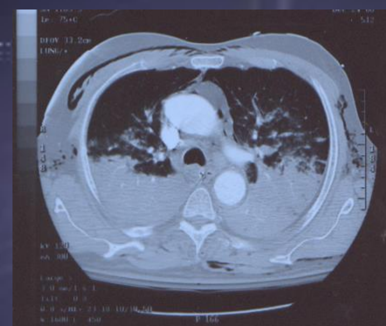
Δpressure is the "polar star"

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

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

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

ΔP



Strain $\varepsilon = \Delta L/L0$ (V_T/EELV)

Power = Energy / Time

Power

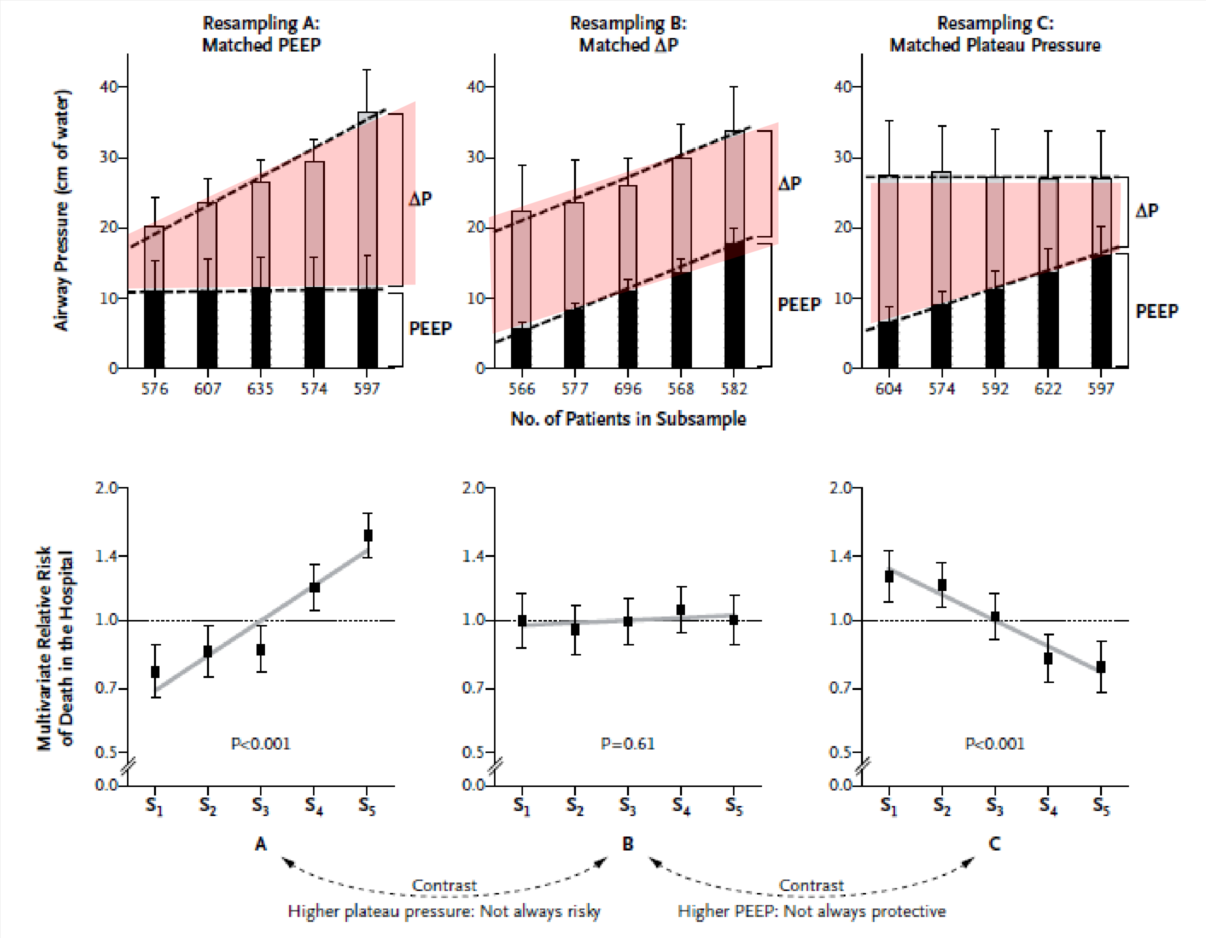
$\Delta P = V_T/C_{st,rs} = V_T/EELV$

Intensity = Power/Area

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

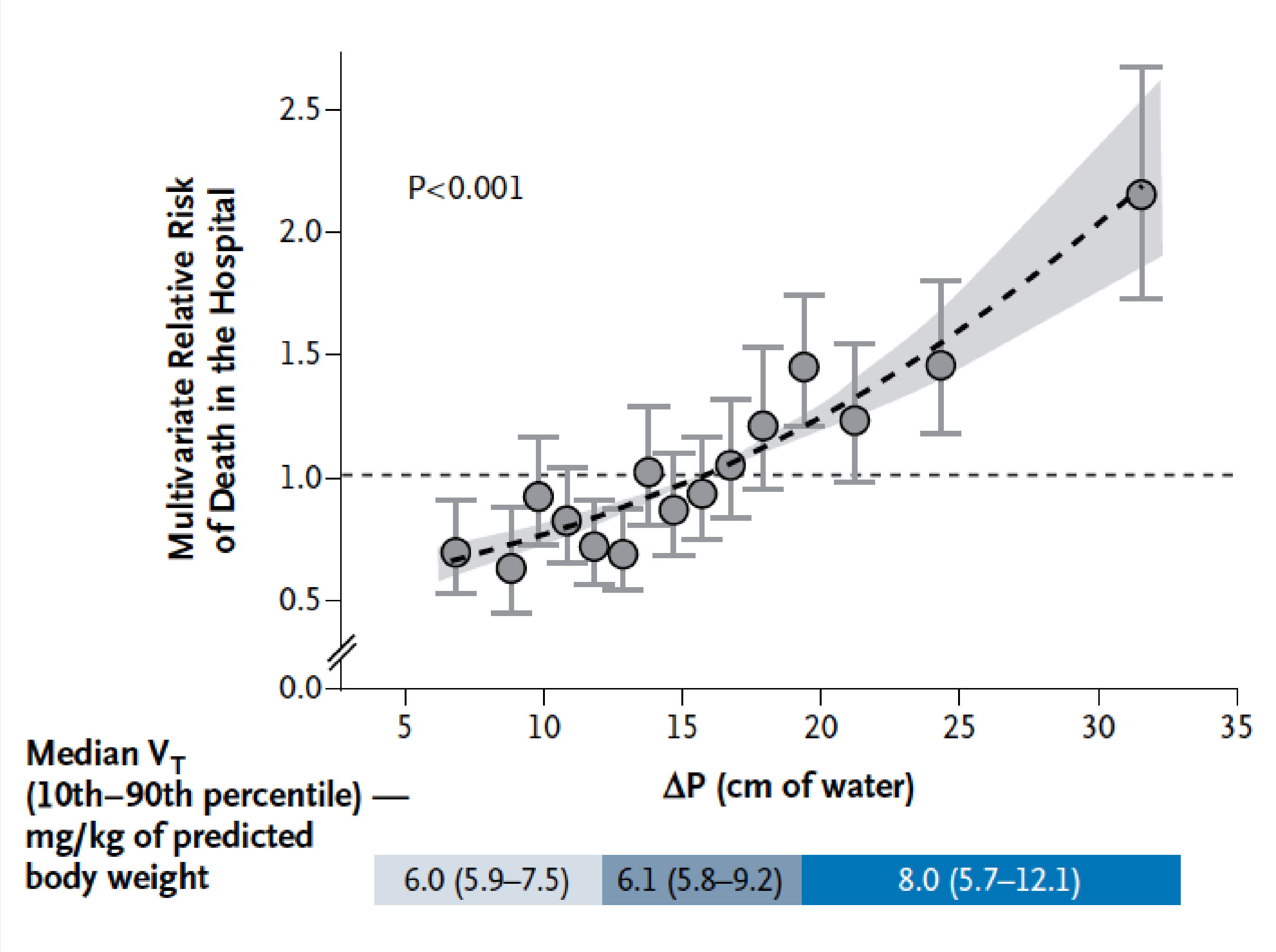
Cressoni M et al. Anesthesiology. 2016 Feb 12. [Epub ahead of print]

Driving pressure and survival in the ARDS



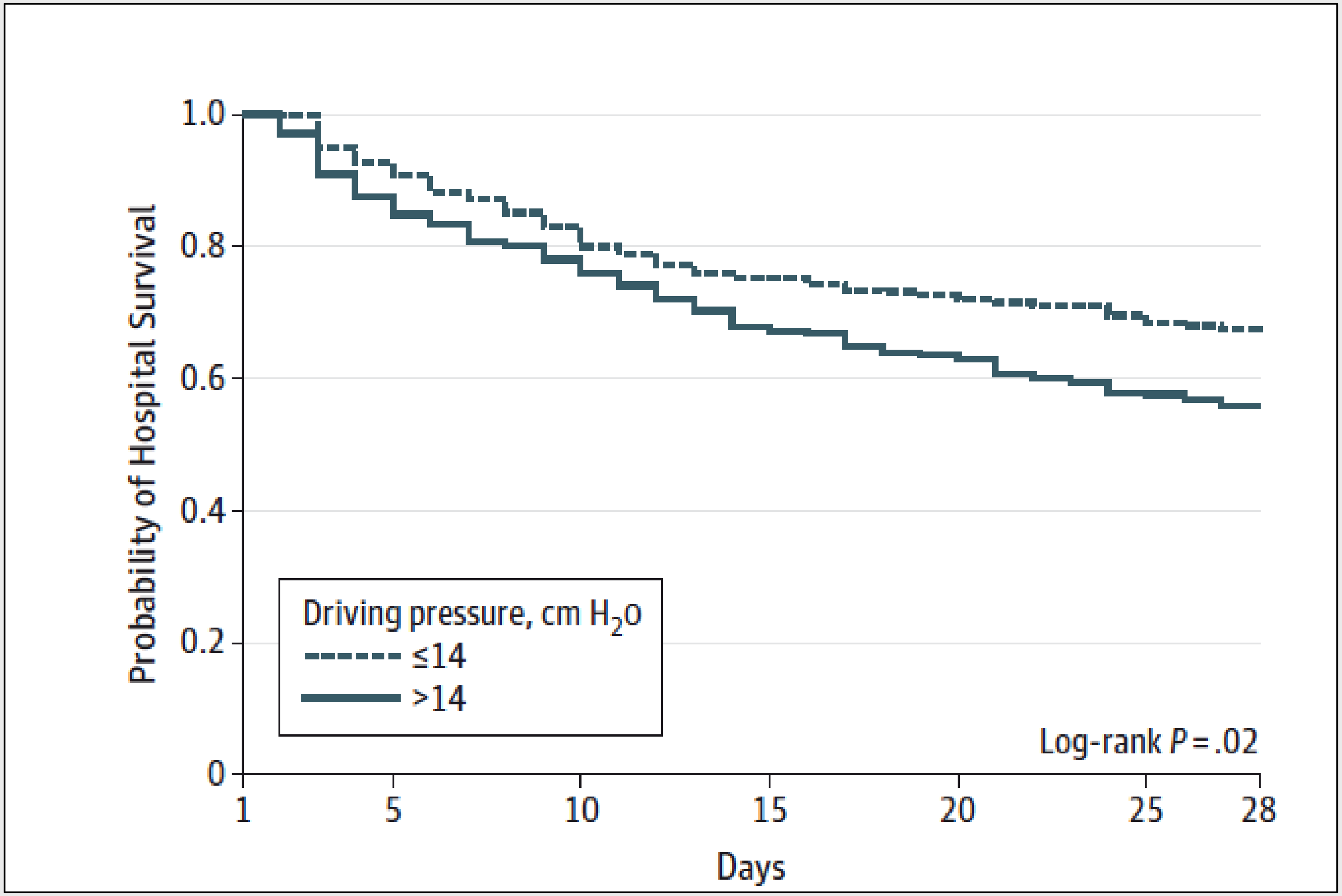
Amato MBP, et al. N Engl J Med 2015;372:747-55

Driving pressure and survival in the ARDS



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

Driving pressure and survival in the ARDS



Bellani G et al. Lung Safe *JAMA* 2016; 315:788–13

Associations between ∆pressure and Associations between outcome in pateints with severe ARDS: a pooled individual patient data analysis

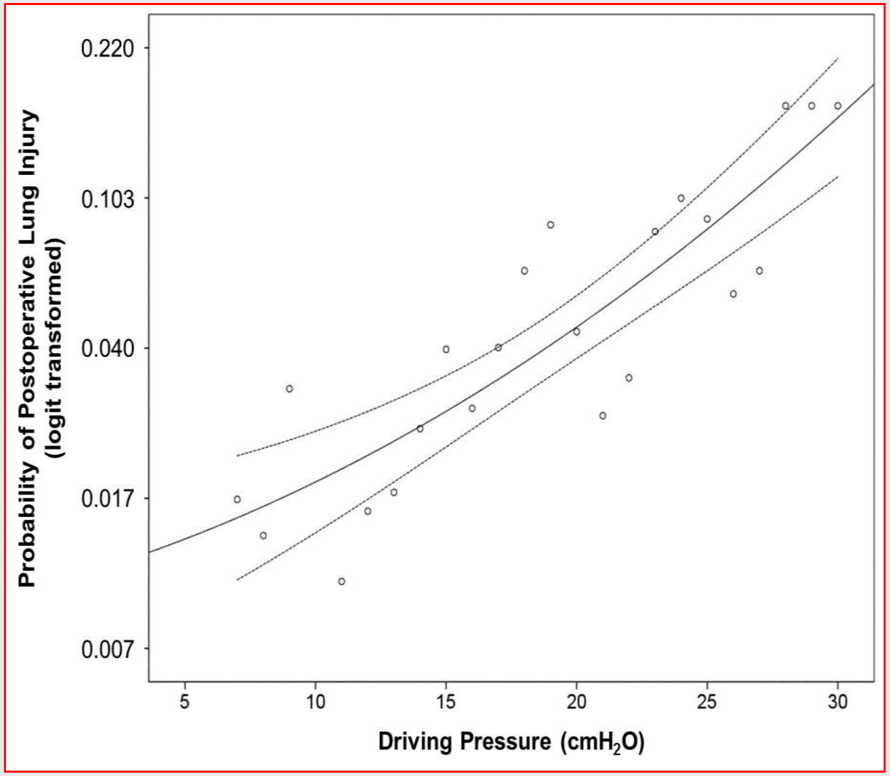
	OR (95%CI), *p*	HR (95%CI), *p*
Age, years	1.04 (1.01 – 1.08), 0.011	1.03 (1.01 – 1.05), 0.008
BMI, kg/m^2	0.94 (0.88 – 1.00), 0.052	0.93 (0.88 – 0.97), 0.002
Time between MV-ECMO		
≤ 24 hours	1.00 (Reference)	1.00 (Reference)
24 – 72 hours	1.49 (0.44 – 4.98), 0.518	1.36 (0.57 – 3.26), 0.488
> 72 hours	2.47 (0.94 – 6.48), 0.066	1.04 (0.53 – 2.04), 0.915
Ventilatory Parameters[a]		
FiO_2, %	1.05 (1.01 – 1.08), 0.007	1.03 (1.01 – 1.06), 0.008
Driving pressure, cmH_2O	1.14 (1.02 – 1.27), 0.018	1.13 (1.07 – 1.21), < 0.001
Laboratory Parameters[a]		
Lactate	1.02 (1.00 – 1.03), 0.007	1.02 (1.01 – 1.02), < 0.001

Serpa-Neto A et al. **(Submitted)**

Fan E et al. Intensive Care Med 2016 [Epub Ahead of Print]

Association between ∆pressure and development of PPCs in patients undergoing MV for general anaesthesia: a meta-analysis of individual patient data.

- ❖ **2.679 patients from 15 RCTs**
- ❖ **Driving P as an independent variable**
- ❖ **mediation analysis**



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

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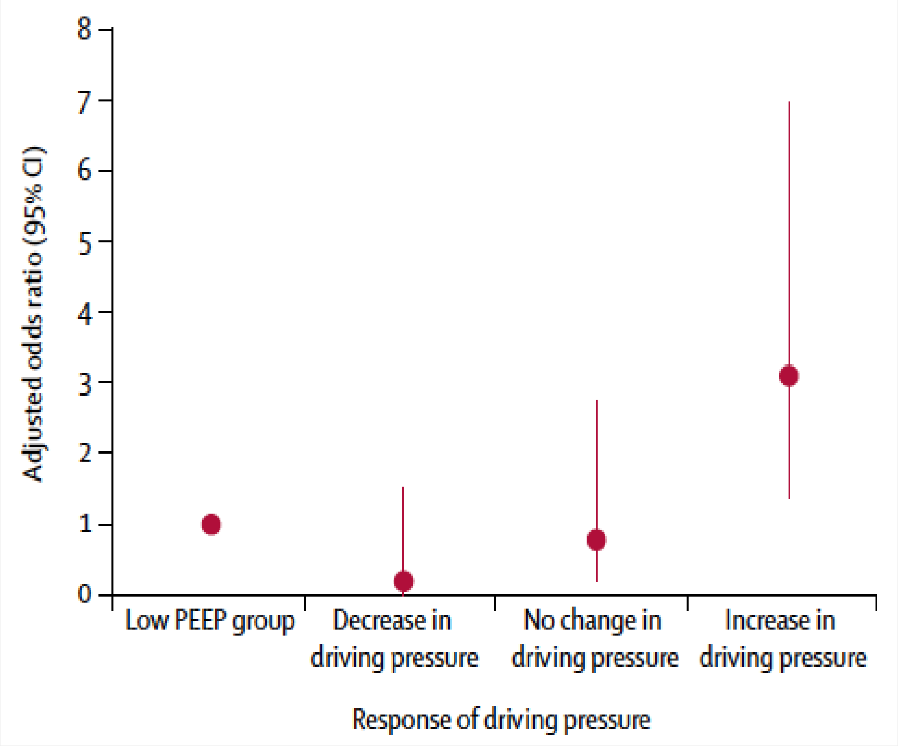

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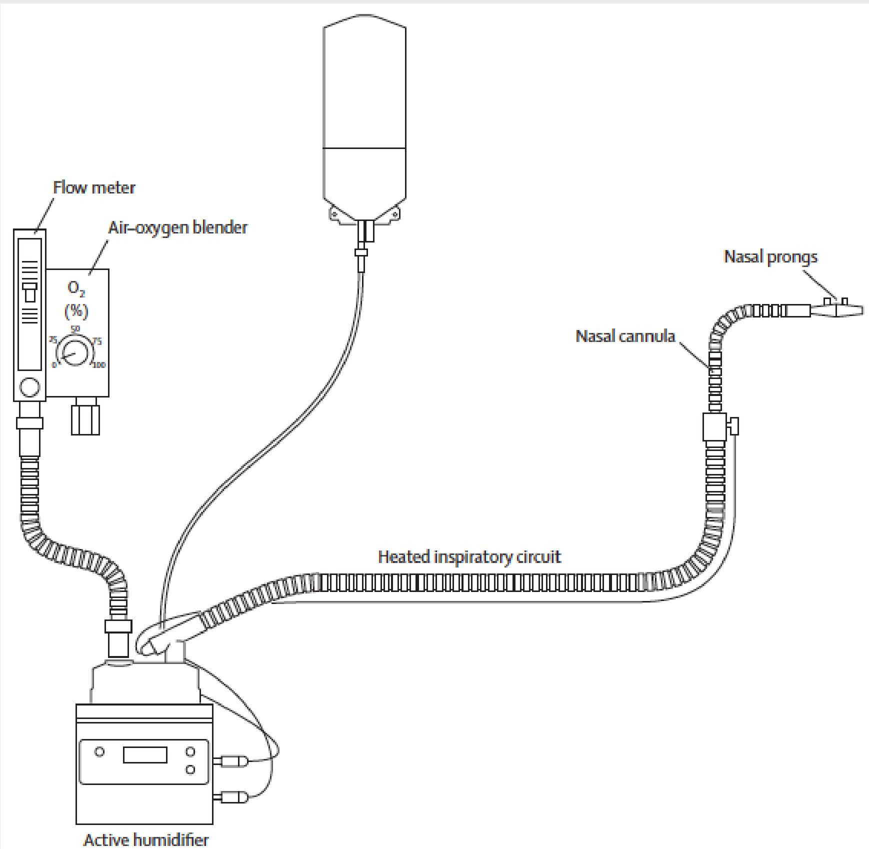
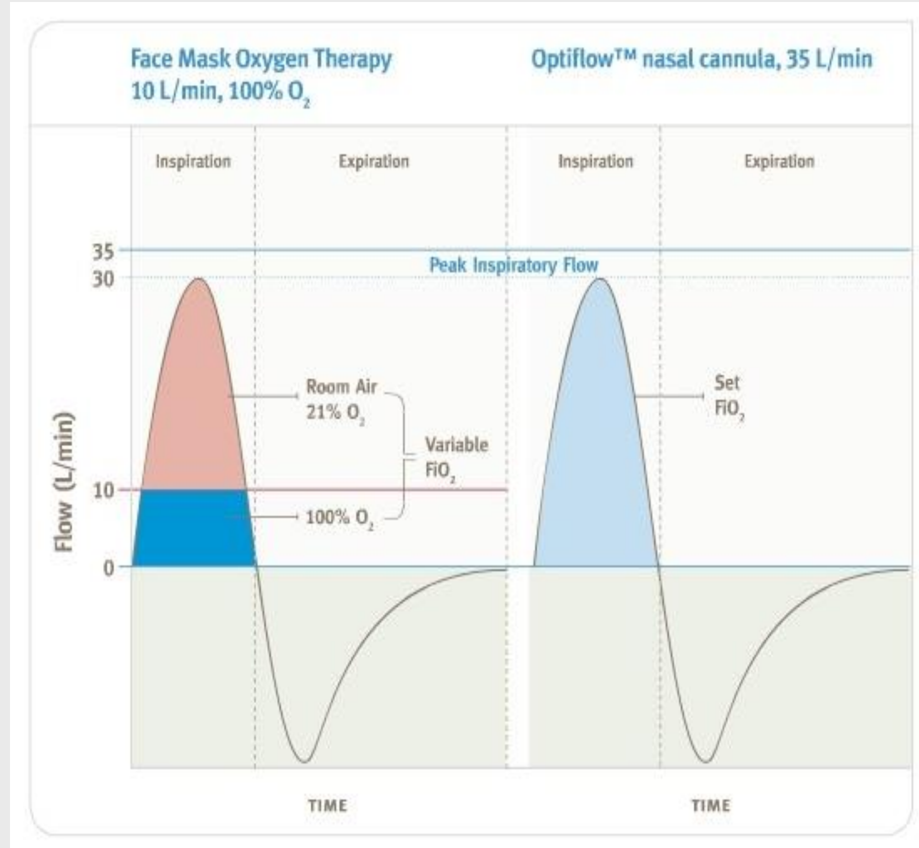
High-flow nasal cannula oxygen





Levy SD et al. Lancet 2016; 387: 1867–78

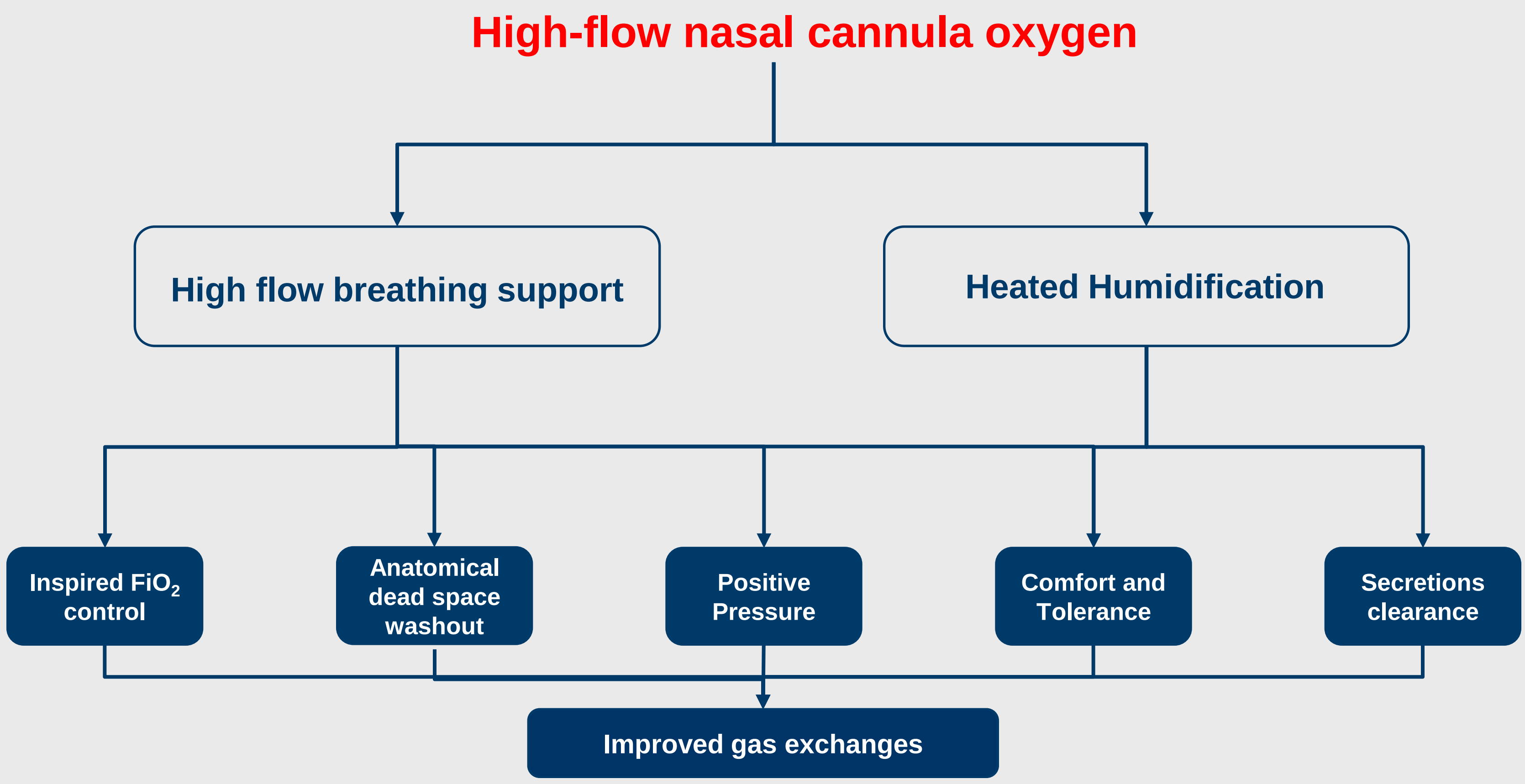
Roca et al. Critical Care (2016) 20:109

Papazian L et al. Intensive Care Med 2016 (Epub Ahead of Print)

High-flow nasal cannula oxygen

> How does it work ?

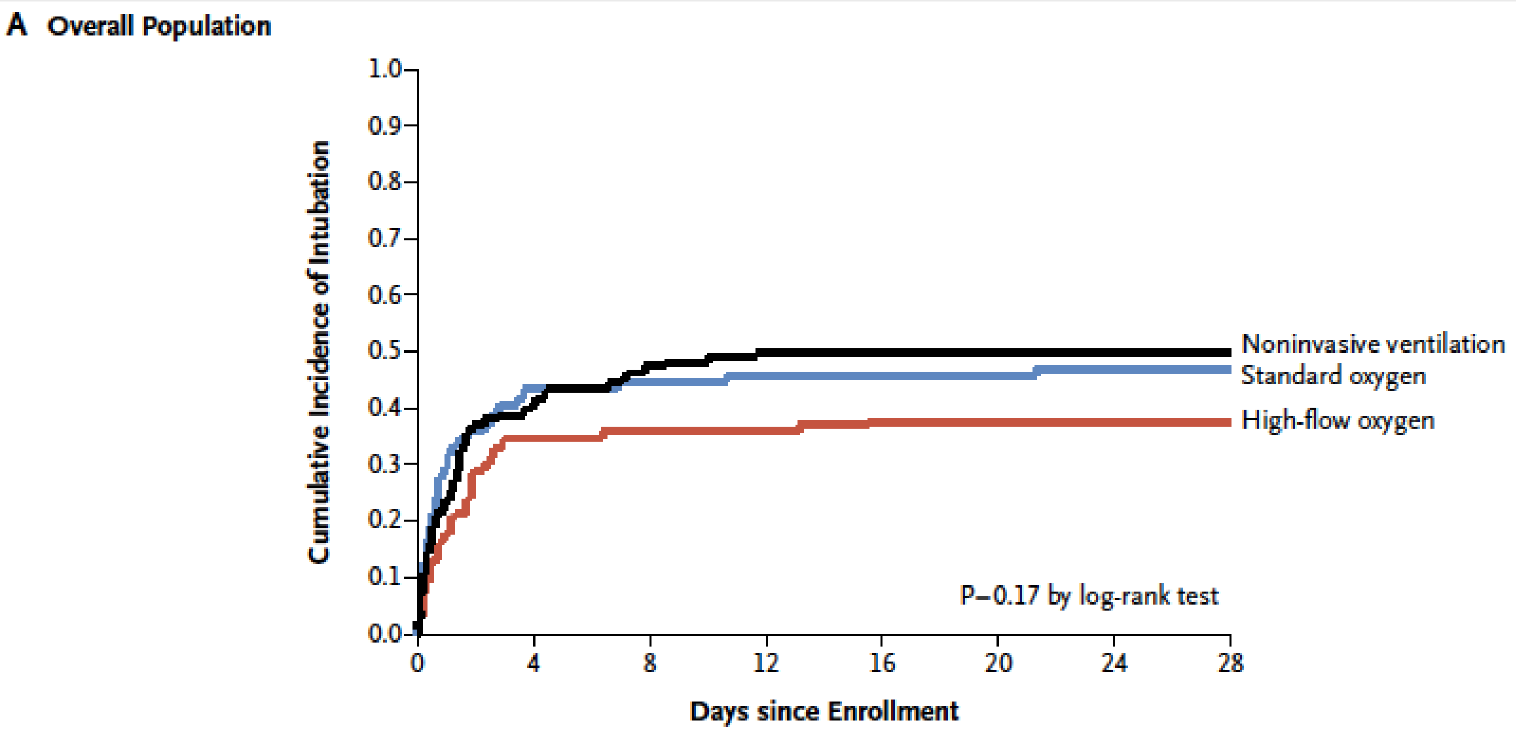
- Two basics, five benefits :



Papazian L et al. Intensive Care Med 2016 (Epub Ahead of Print)

High-Flow Oxygen through Nasal Cannula in Acute Hypoxemic Respiratory Failure

- ❖ high-flow oxygen therapy, standard oxygen therapy delivered through a face mask, or noninvasive positive-pressure ventilation



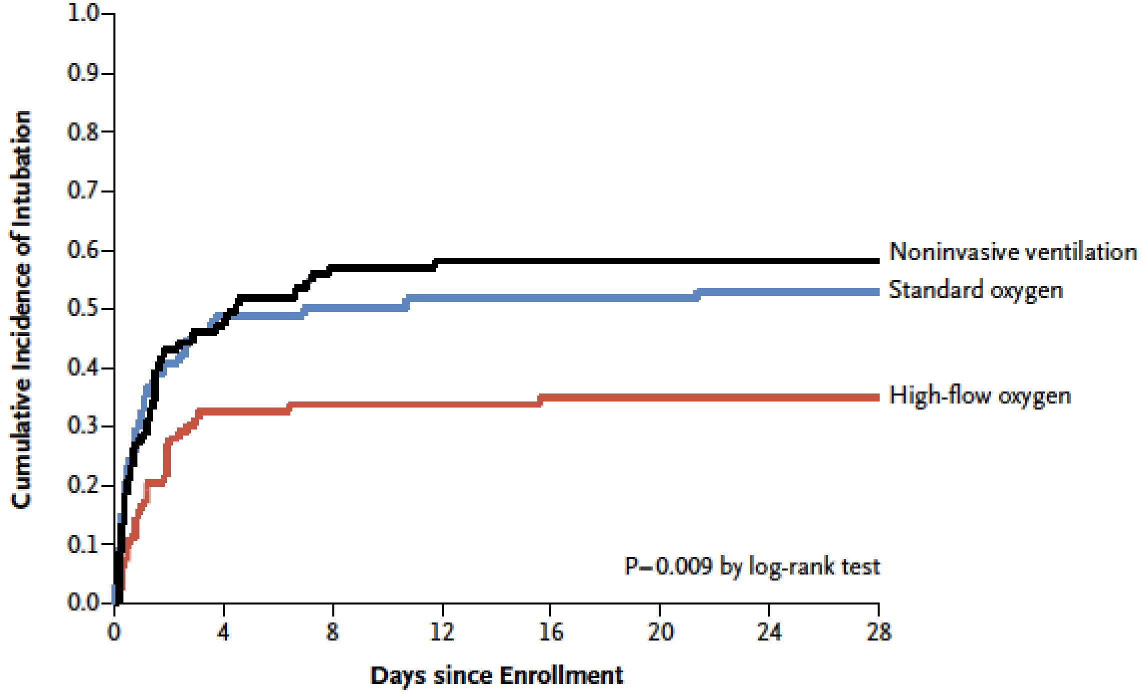
No. at Risk								
High-flow oxygen	106	68	67	67	65	65	65	65
Standard oxygen	94	52	50	49	49	49	48	48
Noninvasive ventilation	110	64	57	53	53	53	53	52

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

High-Flow Oxygen through Nasal Cannula in Acute Hypoxemic Respiratory Failure

❖ high-flow oxygen therapy, standard oxygen therapy delivered through a face mask, or noninvasive positive-pressure ventilation

B Patients with a Pa_{O_2}:F_{IO_2} ≤200 mm Hg



No. at Risk

High-flow oxygen	83	55	54	54	53	53	53	53
Standard oxygen	74	37	35	34	34	34	33	33
Noninvasive ventilation	81	41	34	32	32	32	32	32

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

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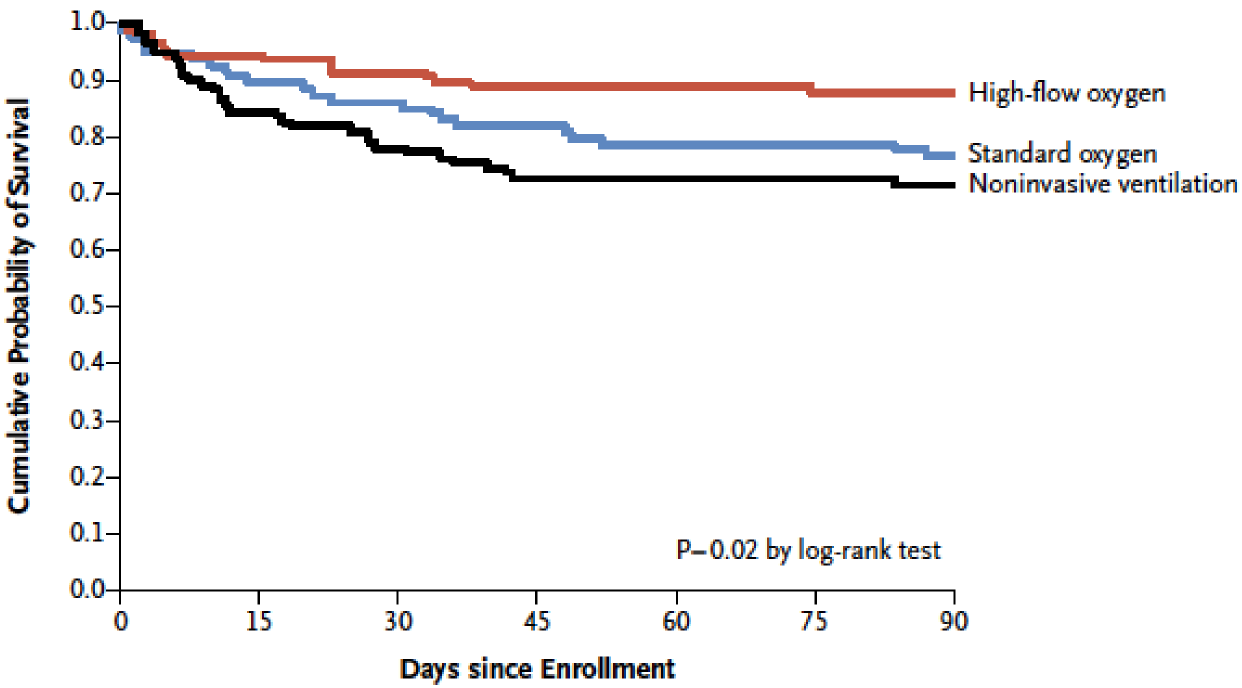


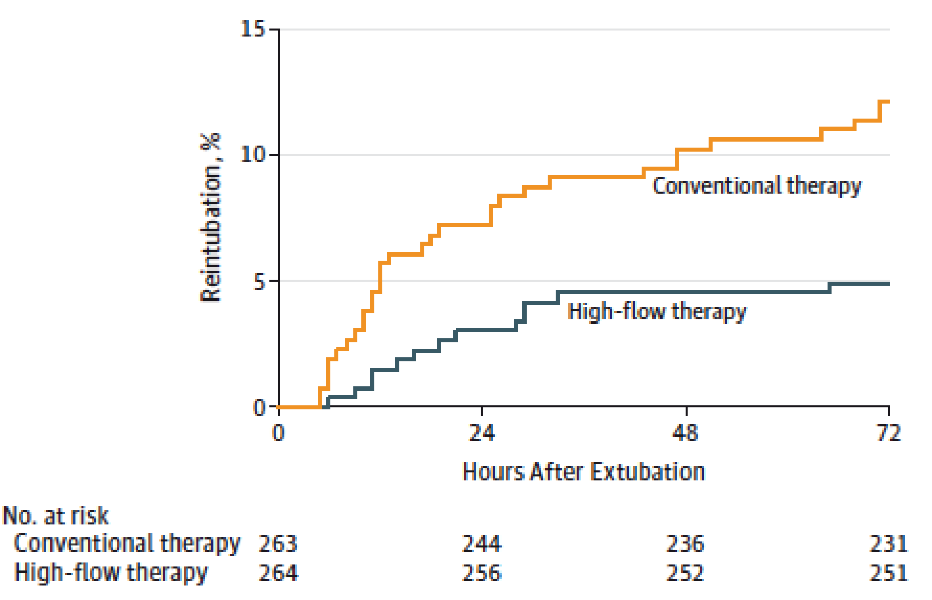
No. at Risk

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

Effect of Postextubation High-Flow Nasal Cannula vs Conventional Oxygen Therapy on Reintubation in Low-Risk Patients: A Randomized Clinical Trial

- **Low risk for reintubation** was defined as younger than 65 years; Acute Physiology and Chronic Health Evaluation II score less than 12 on day of extubation; body mass index less than 30; adequate secretions management; simple weaning; 0 or 1 comorbidity; and absence of heart failure, moderate-to-severe COPD, airway patency problems, and prolonged MV
- **high-flow or conventional oxygen therapy** for 24 hours after extubation.

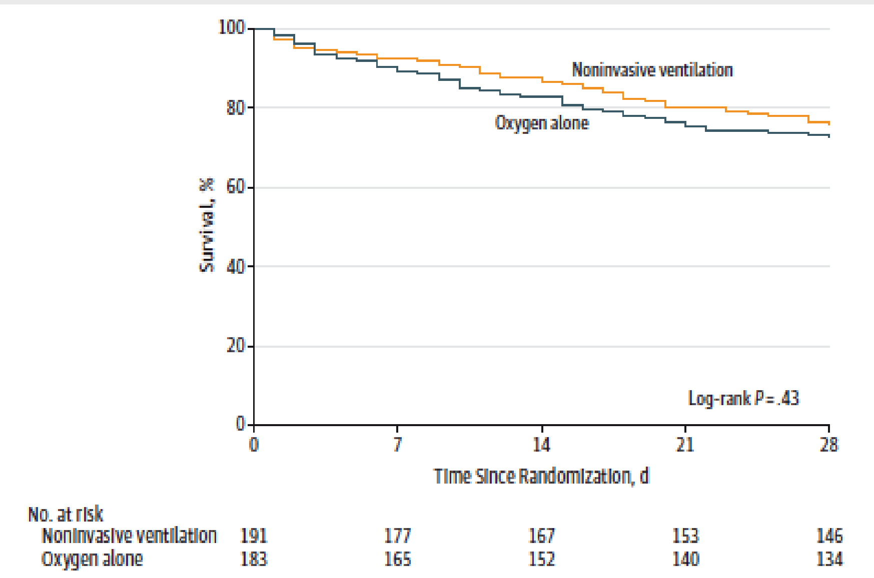


	Oxygen Therapy	
	High-Flow (n = 264)	Conventional (n = 263)
Exploratory Outcomes, No. (%)		
Respiratory-causes reintubation[a]	4 (1.5)	23 (8.7)
Immediate postextubation stridor	2 (0.9)	9 (4.1)
Laryngeal edema requiring reintubation [a]	0	7 (3.1)

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

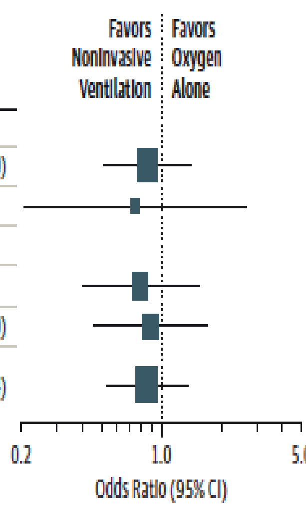
Effect of Noninvasive Ventilation vs Oxygen Therapy on Mortality Among Immunocompromised Patients With Acute Respiratory Failure
A Randomized Clinical Trial

❖ **early noninvasive ventilation or oxygen therapy alone**



✓ **2/5 of patients with high-flow oxygen nasal cannulas**

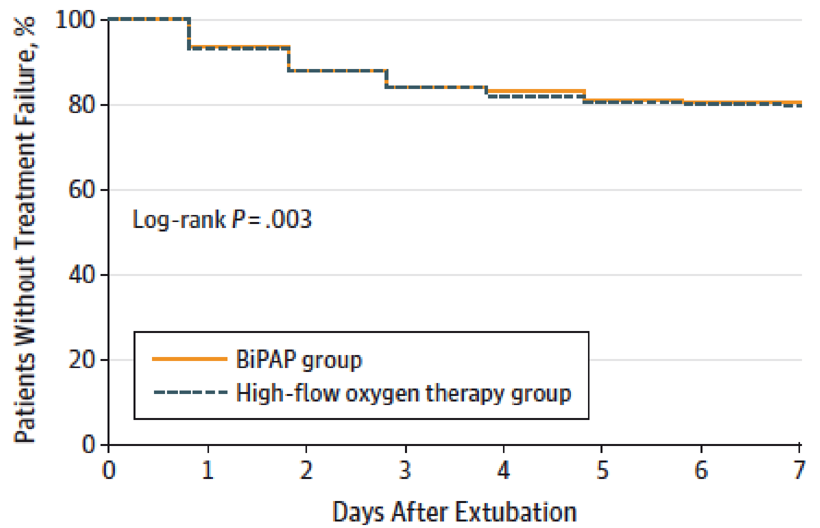
Source	No. of Deaths/Total No. Oxygen Alone	Noninvasive Ventilation	Odds Ratio (95% CI)
Underlying Conditions			
Solid tumors or hematologic malignancies	43/150	41/161	0.85 (0.51-1.40)
Immunosuppressive treatment or organ transplant	7/33	5/30	0.74 (0.2-2.63)
Oxygen flow at randomization[b]			
>9 L/min	26/77	24/84	0.78 (0.4-1.53)
≤9 L/min	24/106	22/107	0.88 (0.46-1.70)
All patients	50/183	46/191	0.84 (0.53-1.34)



Lemiale V et al. JAMA. 2015 Oct 27;314(16):1711-9.

High-Flow Nasal Oxygen vs Noninvasive Positive Airway Pressure in Hypoxemic Patients After Cardiothoracic Surgery A Randomized Clinical Trial

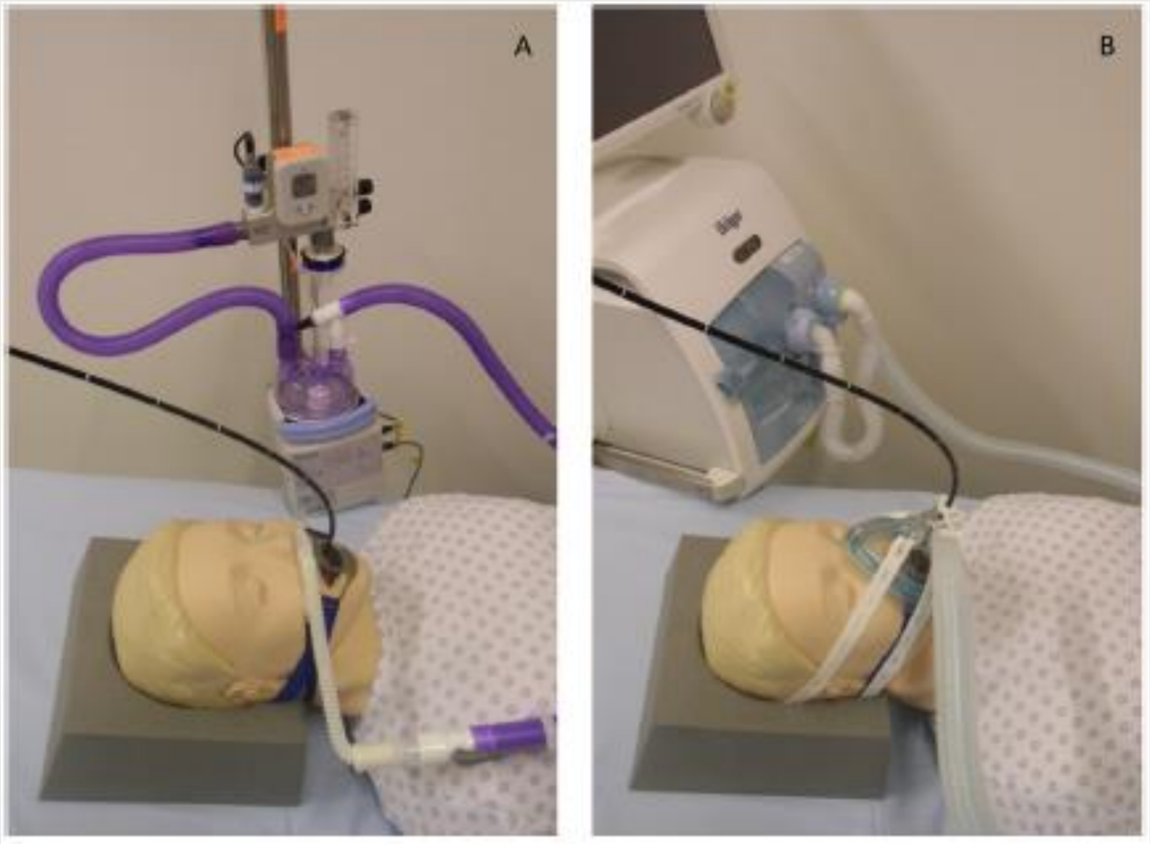
- **high-flow nasal oxygen therapy**: delivered continuously through a nasal cannula (flow, 50 L/min; fraction of inspired oxygen [F_{IO2}], 50%) (n = 414)
- **BiPAP**: delivered with a full-face mask for at least 4 hours per day (pressure support level, 8 cmH_2O; positive end-expiratory pressure, 4 cmH_2O; F_{IO2}, 50%)



No. at risk								
BiPAP	416	385	363	348	339	333	331	329
High-flow oxygen therapy	414	385	361	346	342	334	333	331

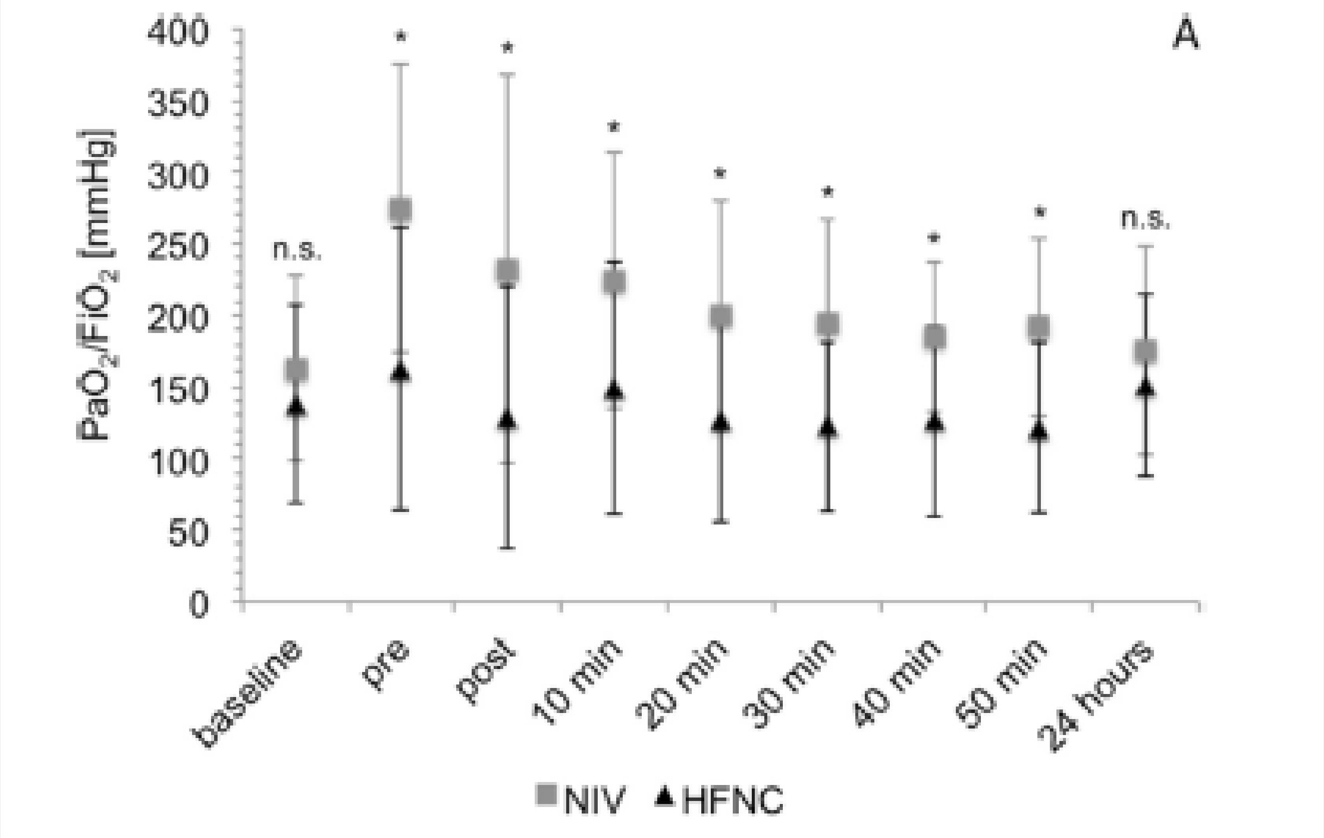
Stephan F et al. JAMA. 2015 Jun 16;313(23):2331-9

High-flow nasal cannula oxygen versus non-invasive ventilation in patients with acute hypoxaemic respiratory failure undergoing flexible bronchoscopy - a prospective RCT



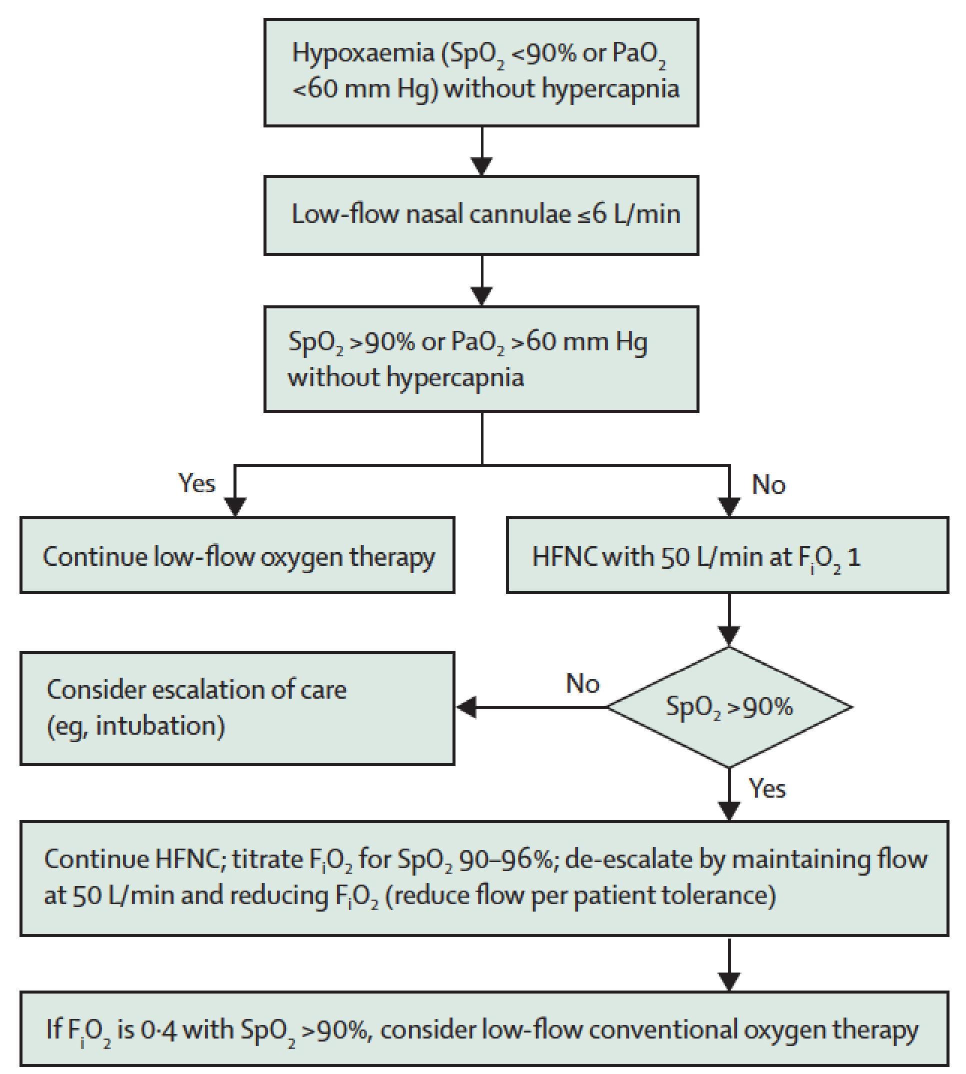
Simon et al. Critical Care (2014) 18:712.

High-flow nasal cannula oxygen versus non-invasive ventilation in patients with acute hypoxaemic respiratory failure undergoing flexible bronchoscopy - a prospective RCT



Simon et al. Critical Care (2014) 18:712.

High-flow nasal cannula oxygen



Levy SD et al. Lancet 2016; 387: 1867–78

Agenda

- ❖ New Clinical Criteria for Sepsis
- ❖ LUNG SAFE: ARDS in the “real life”
- ❖ Low Tidal Volume in non-ARDS
- ❖ Driving pressure: the “polar star“
- ❖ High-flow oxygen nasal cannula in ARDS
- ❖ **The Helmet and risk of intubation in ARDS**
- ❖ Tracheostomy: Mortality and QoL

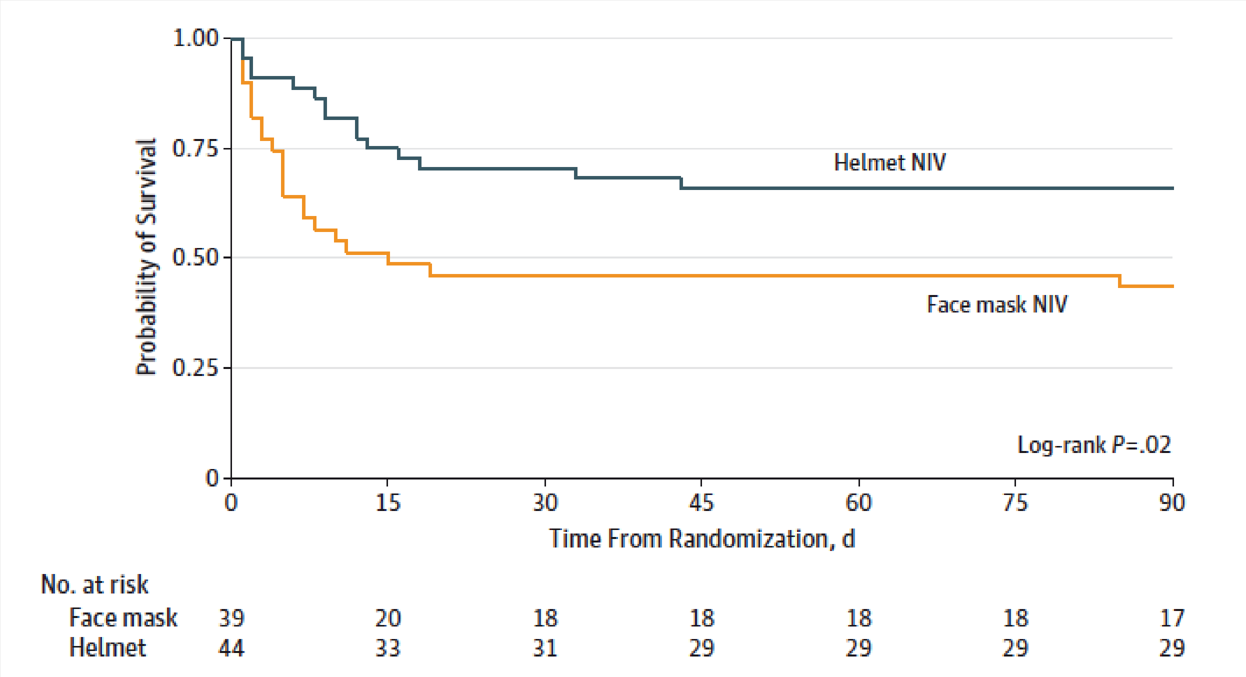
The Helmet

- ❖ **Equally effective as mask to improve gas exchange and to reduce intubation rate**
- ❖ **Better tolerated than mask for continuous and prolonged use (days !)**
- ❖ **Reduces complications related to mask**

Antonelli, Conti, Pelosi et al. Crit Care Med 2002; 30: 602-606
Antonelli, Pennisi, Pelosi et al. Anaesthesiology 2004; 100: 16-24

Effect of Noninvasive Ventilation Delivered by Helmet vs Face Mask on the Rate of Endotracheal Intubation in Pts With ARDS: A Randomized Clinical Trial

- ❖ patients with ARDS requiring NIV delivered by face mask for at least 8 hours
- ❖ face mask NIV or switch to a helmet for NIV support



Patel BK et al. JAMA. 2016 May 15. doi: 10.1001

Agenda

- ❖ New Clinical Criteria for Sepsis
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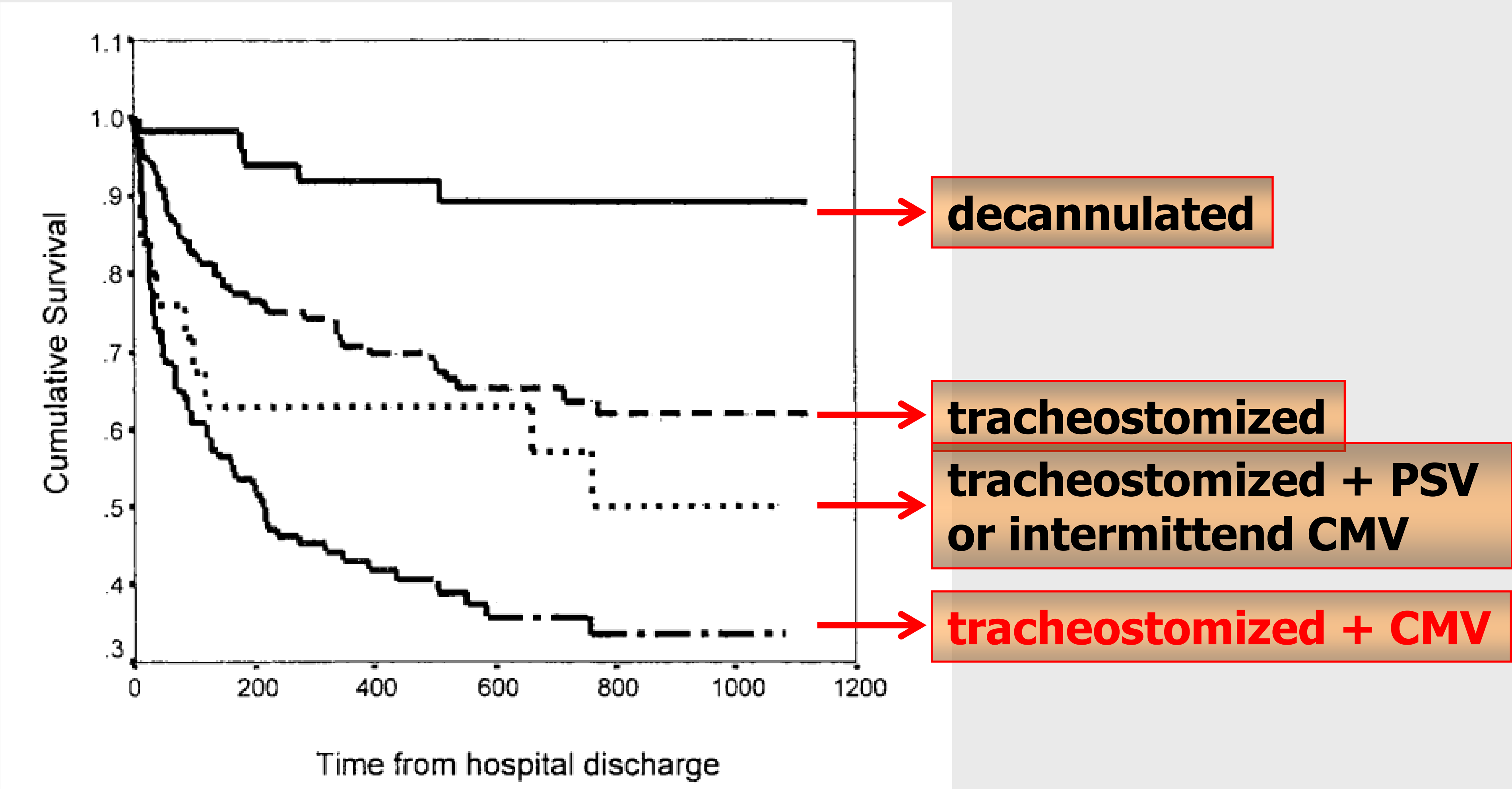
- ❖ The Helmet and risk of intubation in ARDS
- ❖ **Tracheostomy: Mortality and QoL**

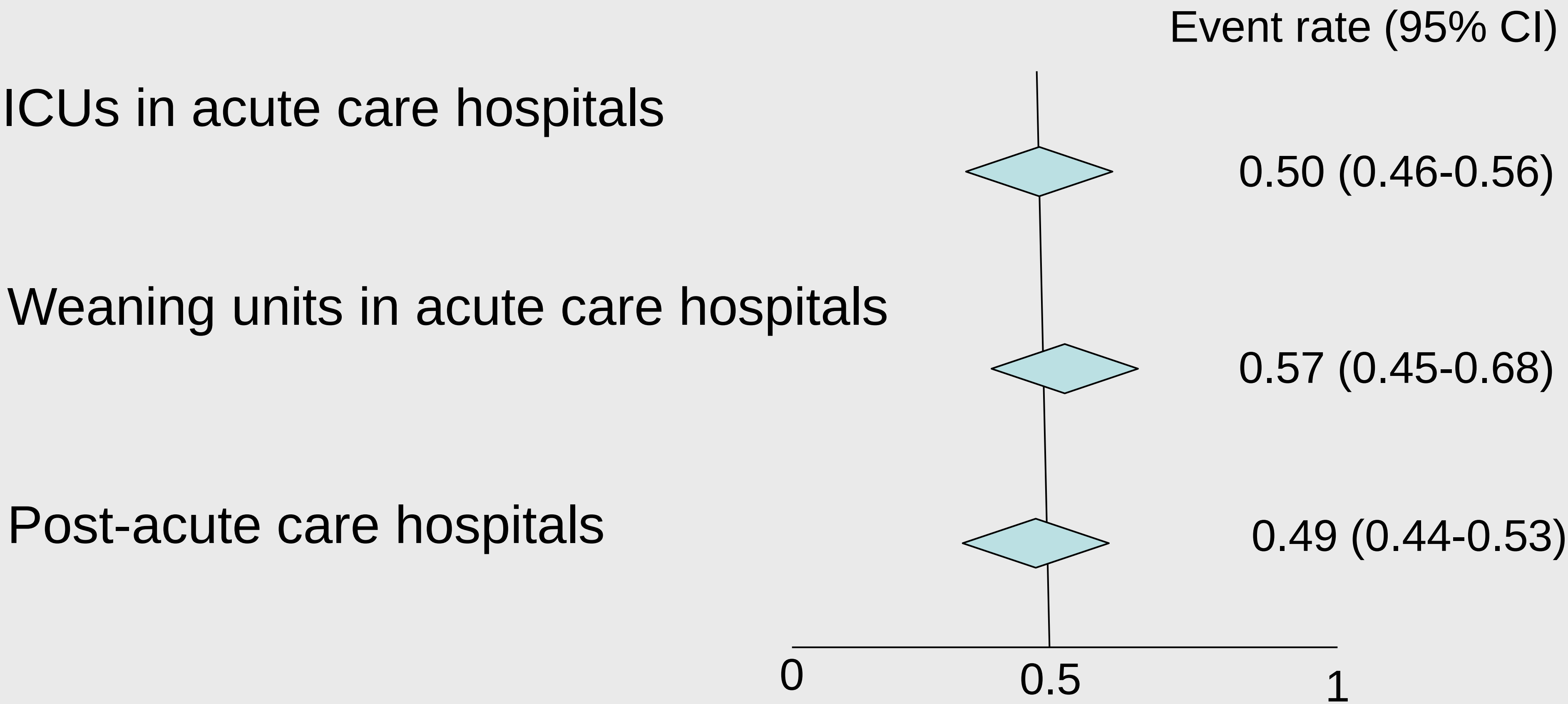
Hospital and Long-term Outcome After Tracheostomy for Respiratory Failure



Engoren M et al. Chest 2004; 125:220–227

Long-term survival of critically ill patients treated with prolonged mechanical ventilation: a systematic review and meta-analysis

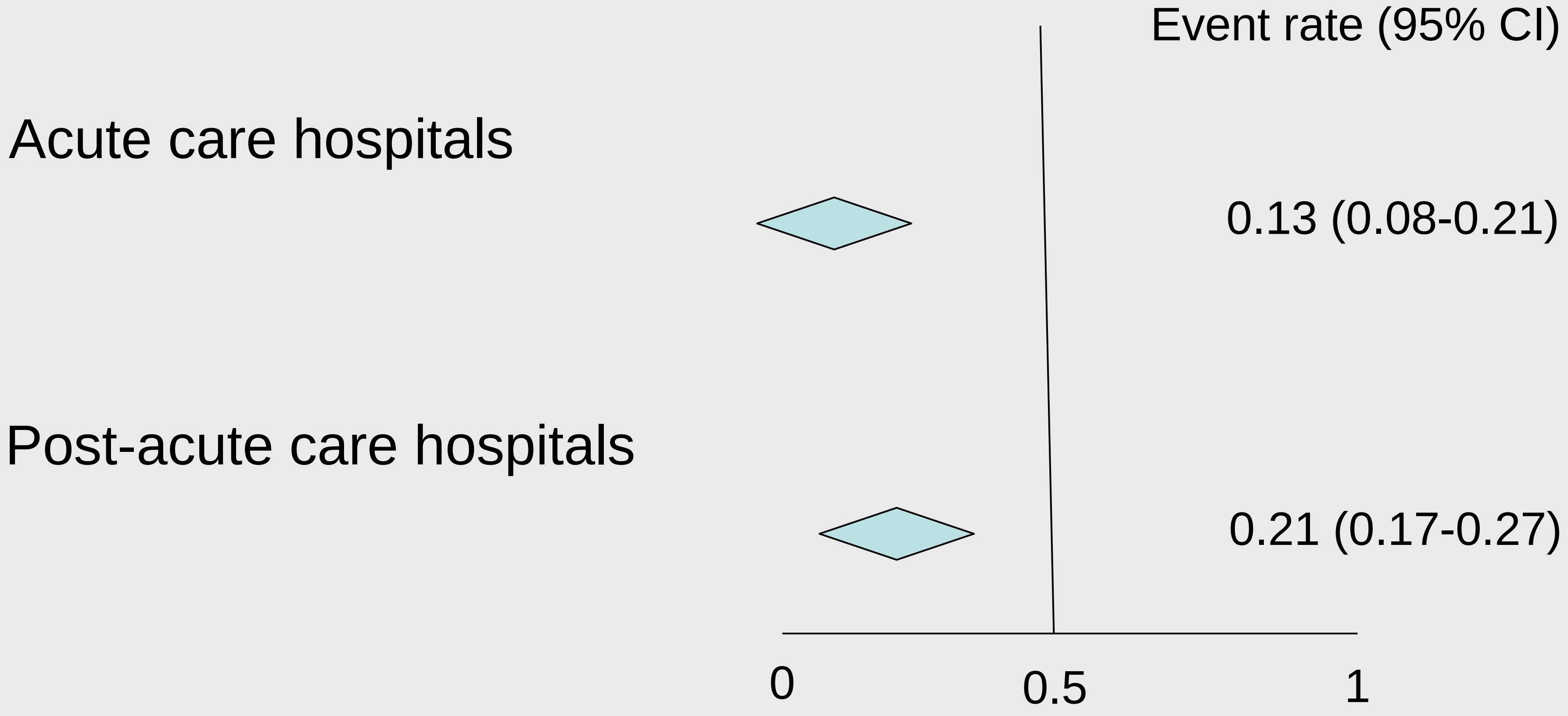
Pts successfully liberated from the ventilator in the hospital



Damuth E et al. Lancet Respir Med 2015;3: 544–53

Long-term survival of critically ill patients treated with prolonged mechanical ventilation: a systematic review and meta-analysis

Proportion of patients discharged to home from the hospital



Damuth E et al. Lancet Respir Med 2015;3: 544–53

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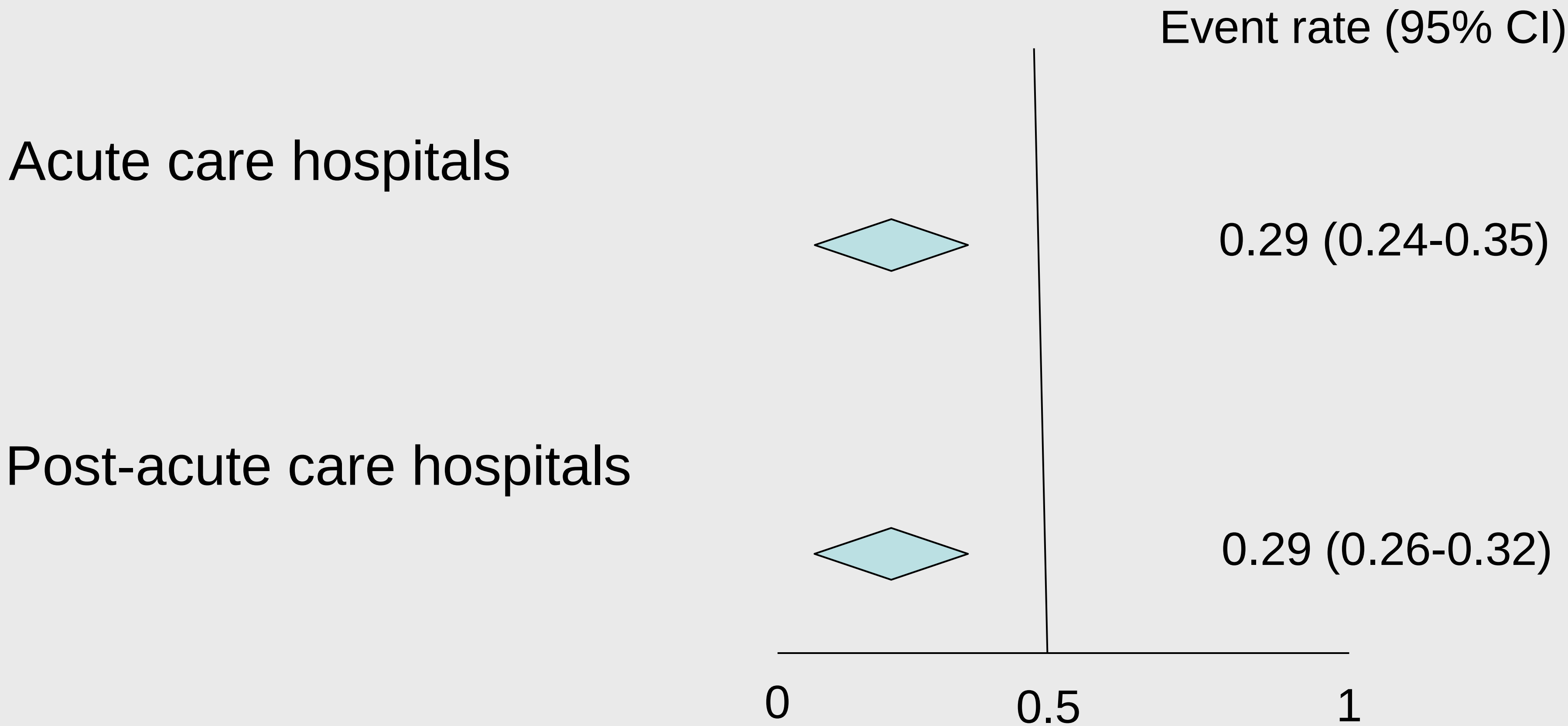
Mortality at Hospital discharge



Damuth E et al. Lancet Respir Med 2015;3: 544–53

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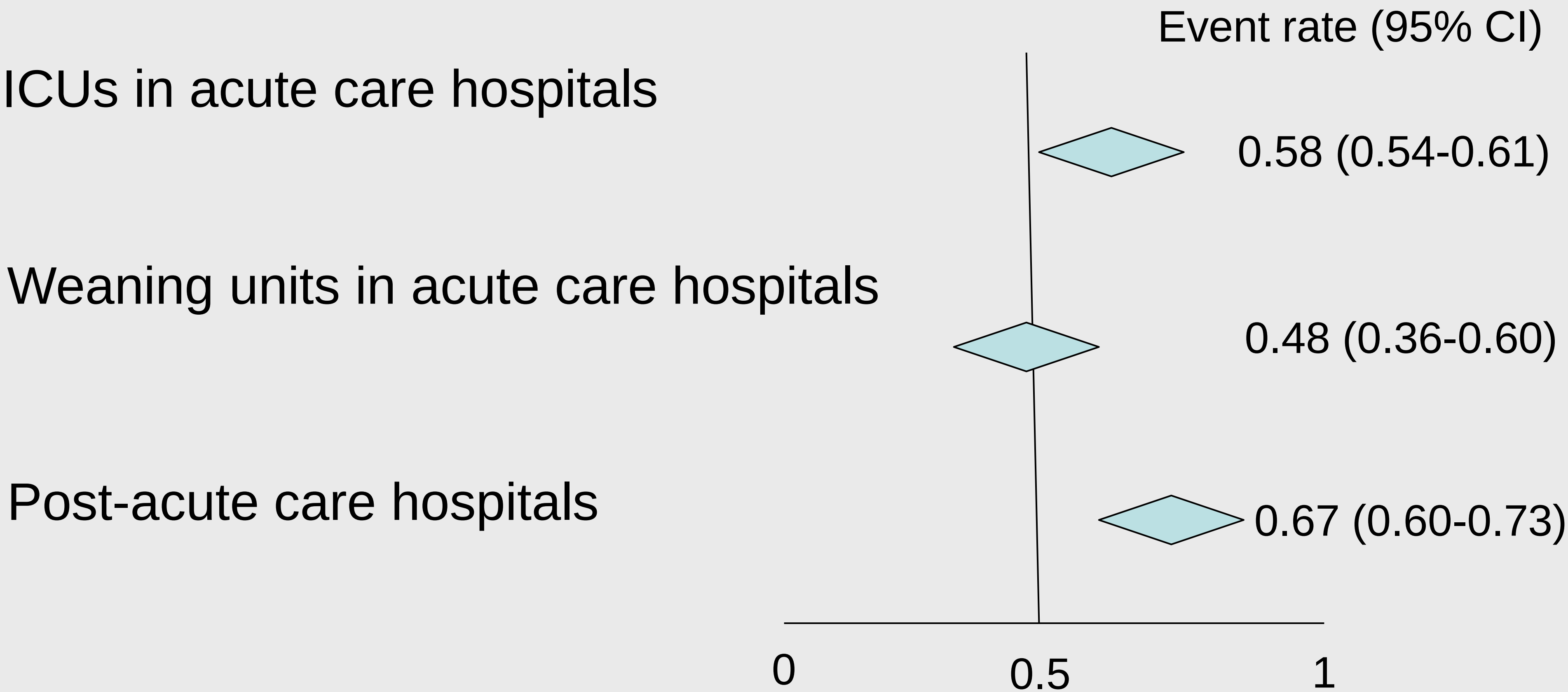
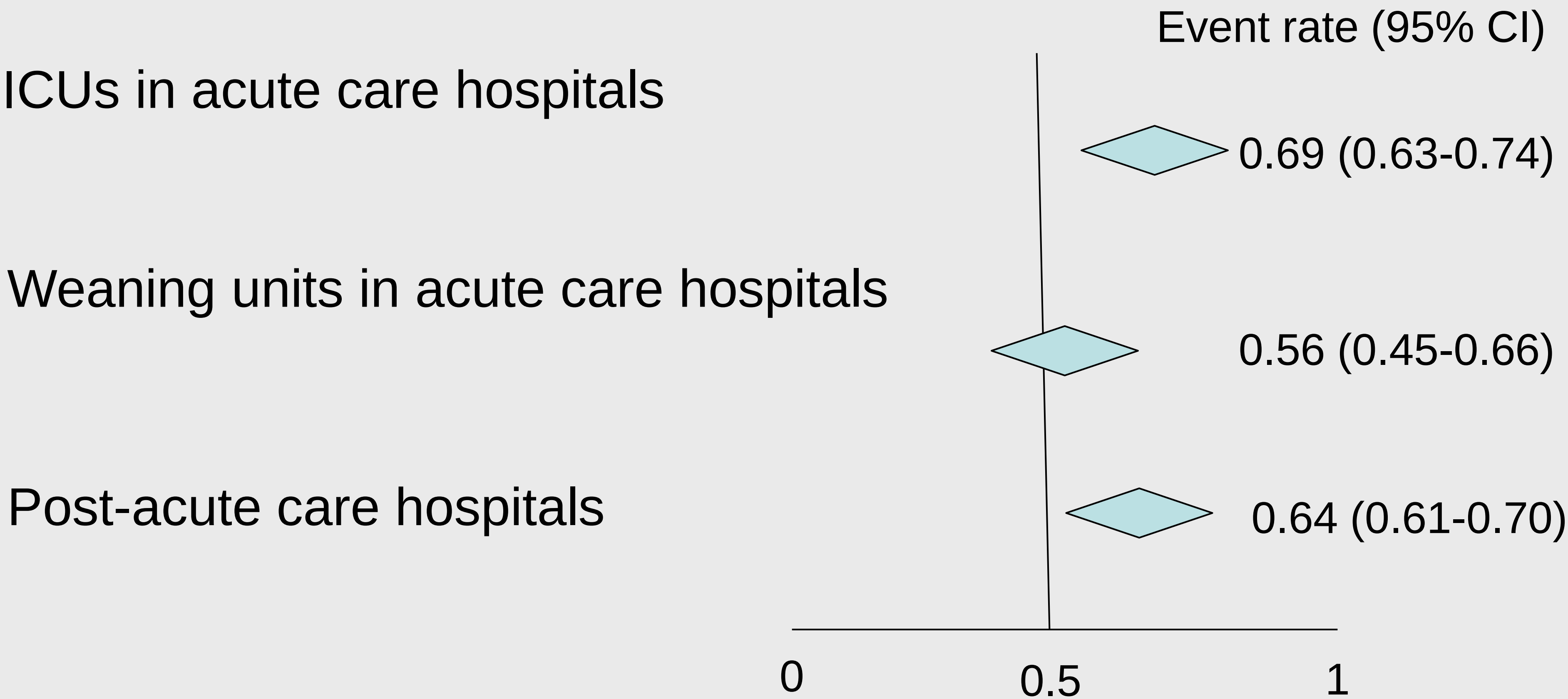
Mortality at 1 year



Damuth E et al. Lancet Respir Med 2015;3: 544–53

Long-term survival of critically ill patients treated with prolonged mechanical ventilation: a systematic review and meta-analysis

Mortality at timepoints beyond 1 year



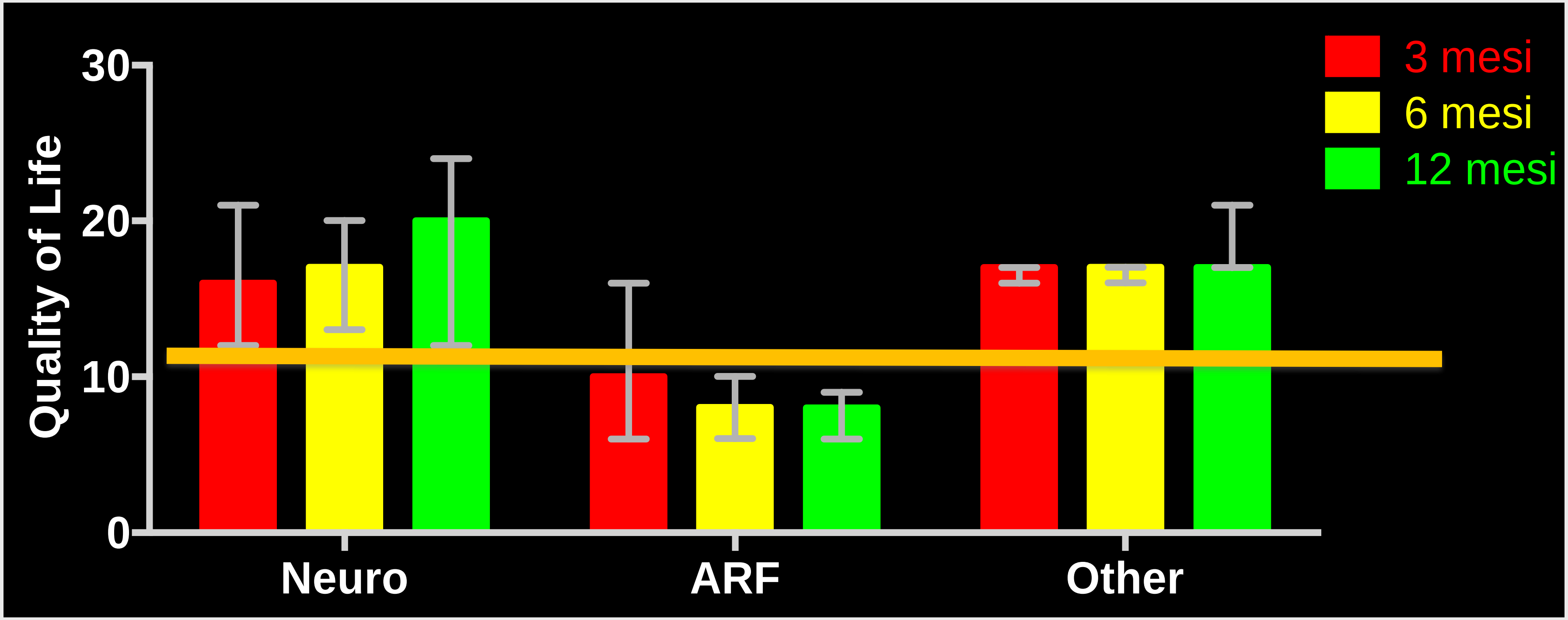
Damuth E et al. Lancet Respir Med 2015;3: 544–53

Mortality and QoL after percutaneous tracheostomy in ICU: An observational study

Mortality 1 yr **88%**

Mortality 1 yr **78%**

Mortality 1 yr **92%**



QoL = 11: mild disability

QoL = 12-15: moderate disability

QoL >15: severe disability

Vargas M et al. **(Submitted)**

The RECOVER Program: Disability Risk Groups & One Year Outcome after ≥ 7 Days of Mechanical Ventilation

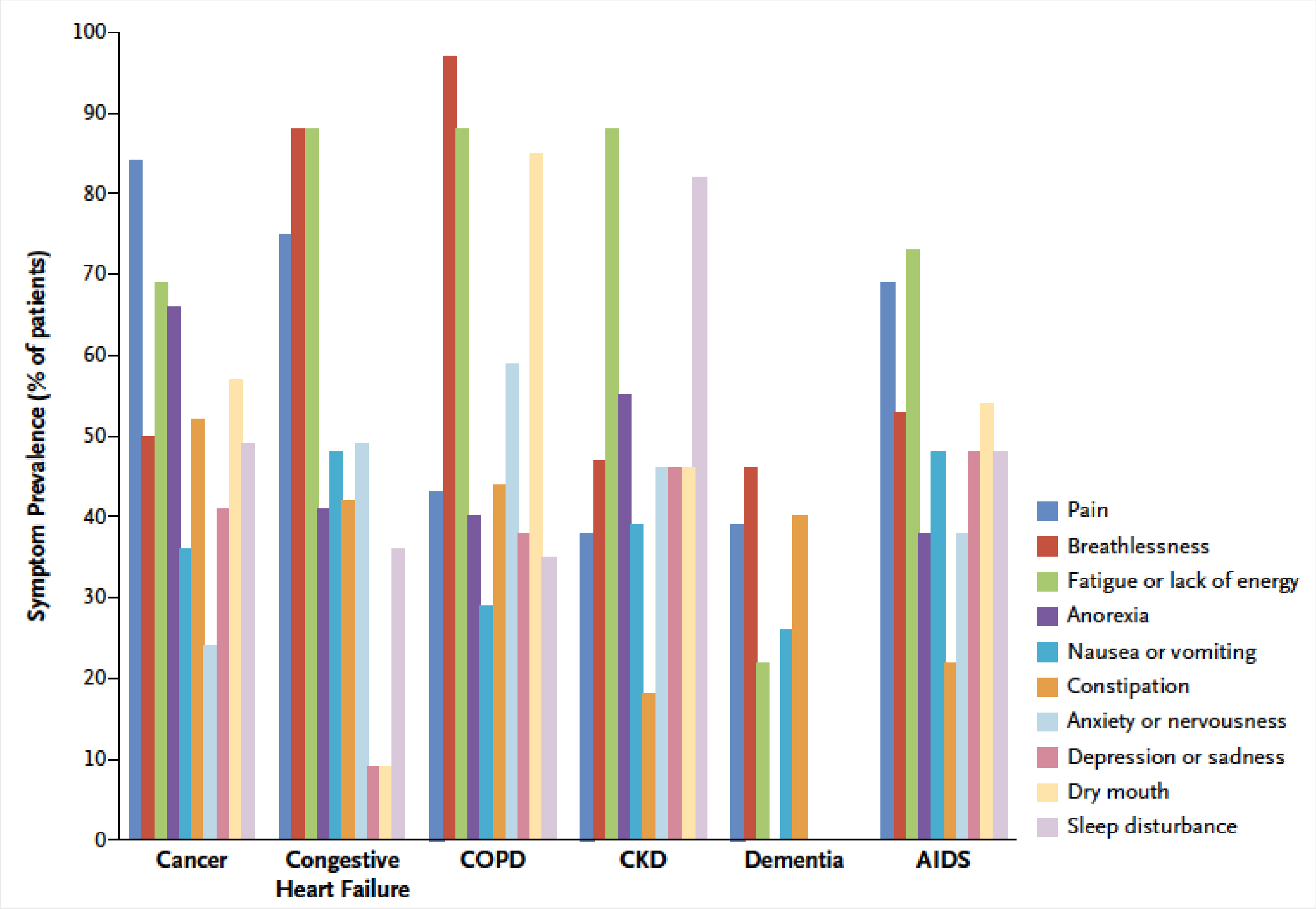
Risk factors for mortality over 1 year after ICU discharge

	HR	95% CI	Pr(>|z|)
FIM at day 7 after ICU discharge (per 30 points)	0.76	0.58, 1.00	0.0536
Age by decade	1.27	1.07, 1.51	0.0056
Female	0.99	0.62, 1.58	0.9661
ICU LOS by week	1.07	1.02, 1.13	0.0093
Charlson score per point	1.35	1.21, 1.51	<0.0001

Herridge MA et al. Am J Respir Crit Care Med 2016 (Epub Ahead of Print).

Palliative Care for the Seriously Ill

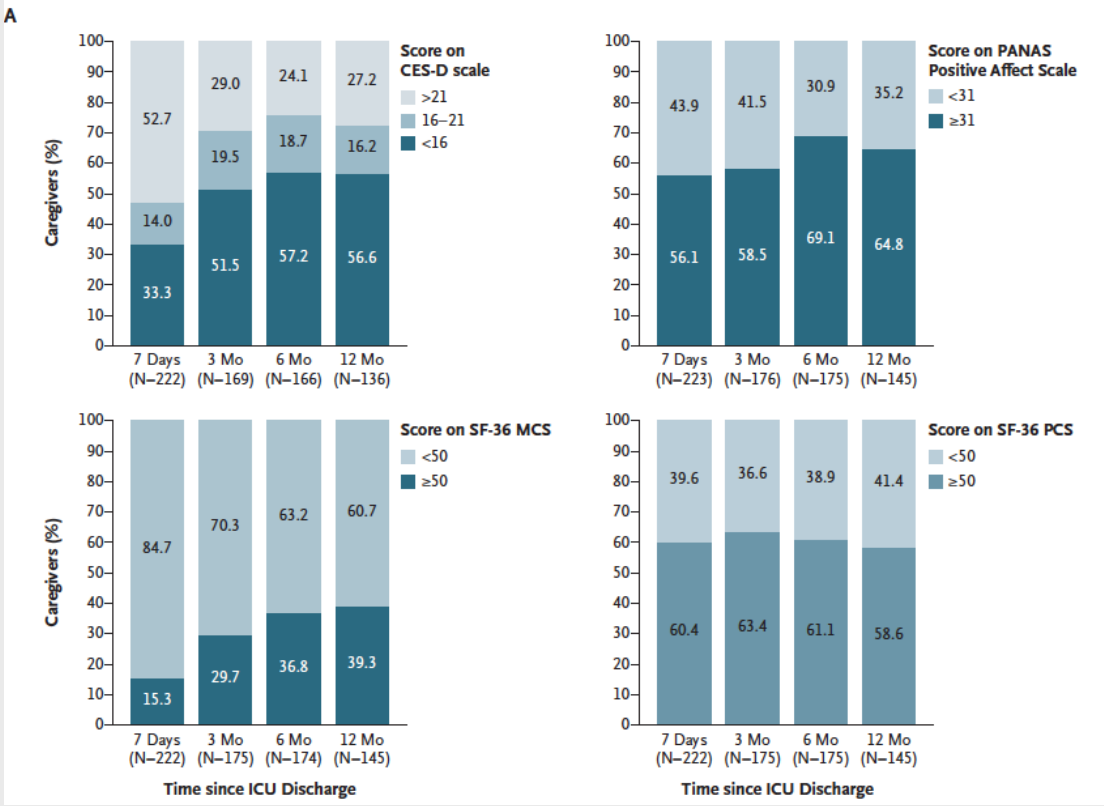
Symptom Prevalence in Advanced Illness



Kelley AS et al. N Engl J Med 2015;373:747-55

One-Year Outcomes in Caregivers of Critically Ill Patients

Caregiver Outcomes during 1° Year after Patient Discharge from an ICU



- ❖ Center for Epidemiologic Studies Depression (CES-D)
- ❖ Positive Affect Scale of the Positive and Negative Affective Schedule (PANAS)
- ❖ Mental Component Summary (MCS)
- ❖ Physical Component Summary (PCS)

Cameron JI et al. N Engl J Med 2016;374:1831-41

Conclusions

- New Sepsis and Septic shock definition (NO SIRS):
  - qSOFA for sepsis outside ICU
  - SOFA for sepsis and septic shock in ICU
- In ARDS, protective MV is rarely applied
- Protective ventilation in non-ARDS
- Driving pressure the “polar star“
- High-flow oxygen NC better than NPPV in ARDS
- Helmet reduces the risk of intubation in ARDS
- Tracheostomy is associated with high mortality and poor QoL

List of References

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