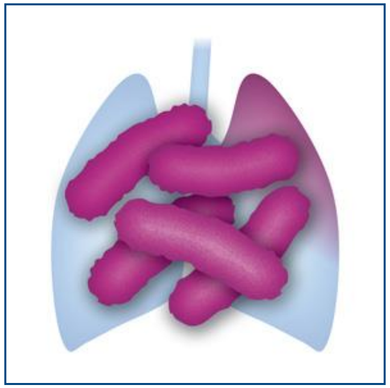
Pneumo Update Europe 2017

9-10 June, Vienna

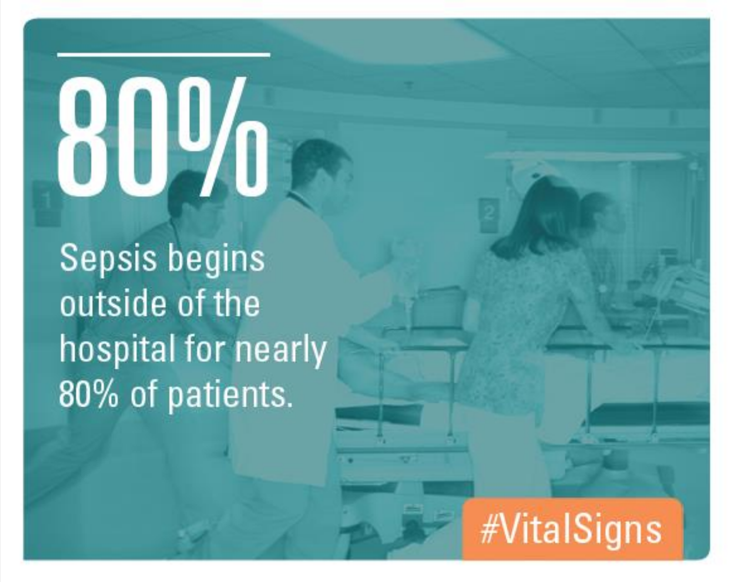
Acute Respiratory Failure & Critical Care

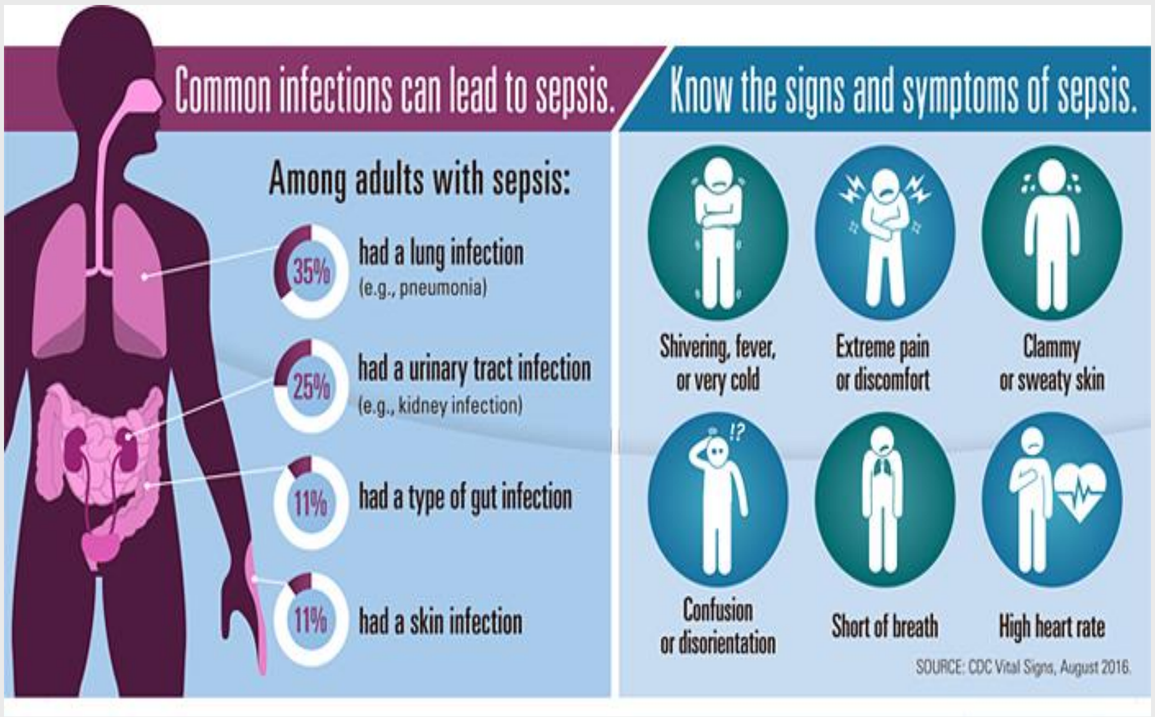


Paolo Pelosi, Italy

New Sepsis Definition

State of the Art





CDC Vital Signs
www.cdc.gov/vitalsigns/sepsis

Evolution of a concept

OLD

	≥2 of 4 SIRS		Organ dysfunction		CV collapse not responding to fluid	
infection	→	sepsis	→	severe sepsis	→	septic shock

<u>Clinical</u>

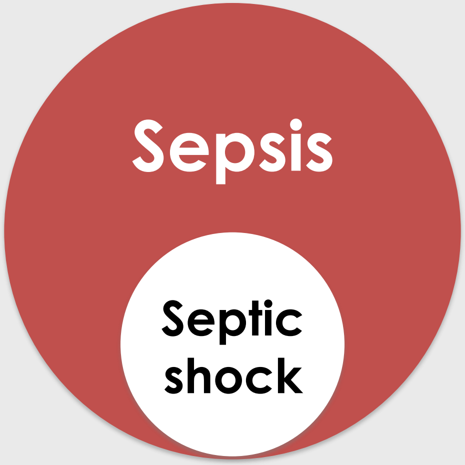
- HR > 90 beats/minute
- Temperature < 36◦ C or > 38◦ C
- Tachypnea > 20 breaths/minute, or $PaCO_2$ < 32 mmHg

<u>Laboratory</u>

- WBC < 4,000 or > 12,000/mm^3 or > 10% immature neutrophils (Bands)

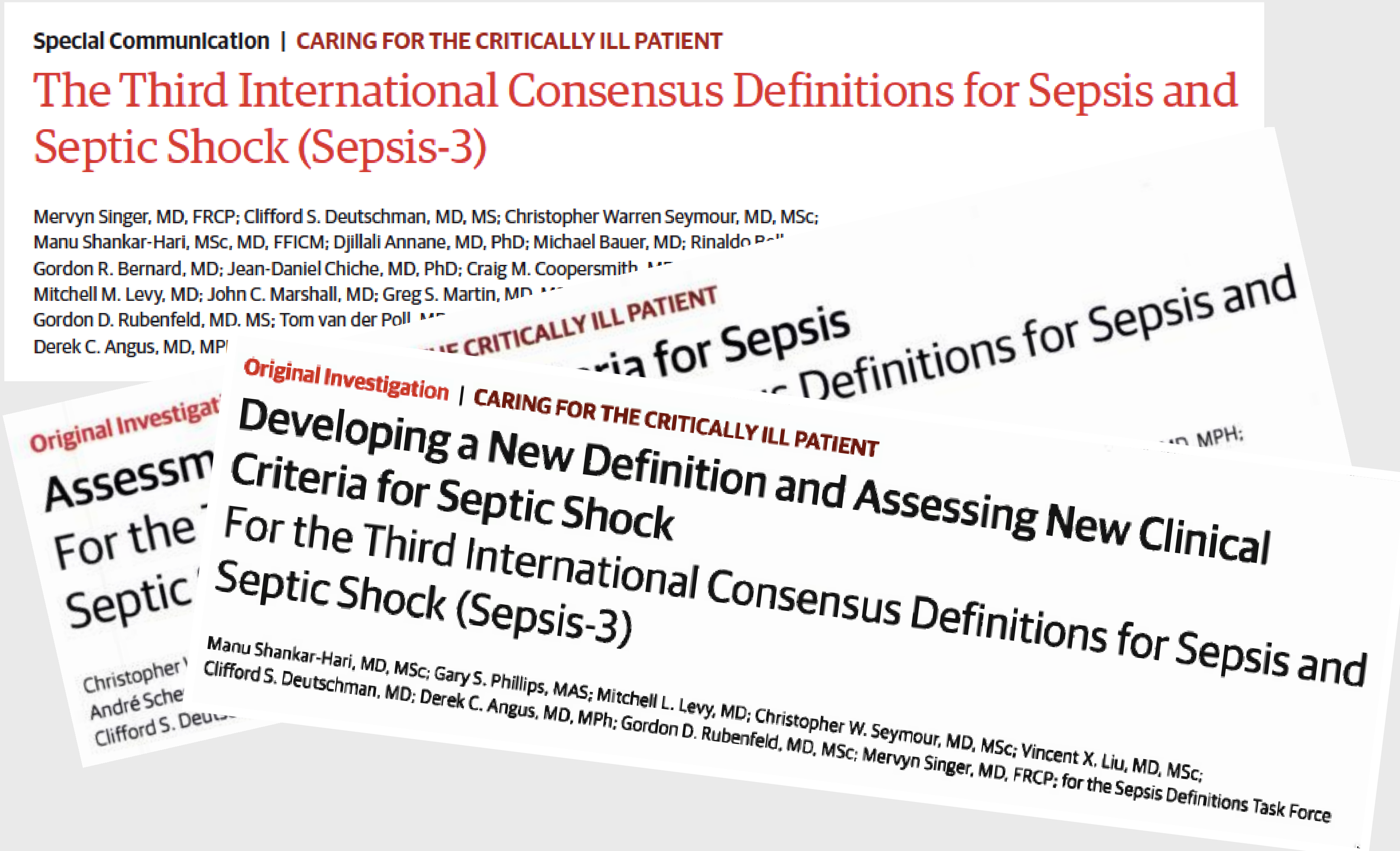
NEW

infection —“Bad”→



Organ dysfunction

New consensus on sepsis


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
Gordon R. Bernard, MD; Jean-Daniel Chiche, MD, PhD; Craig M. Coopersmith
Mitchell M. Levy, MD; John C. Marshall, MD; Greg S. Martin, MD
Gordon D. Rubenfeld, MD, MS; Tom van der Poll
Derek C. Angus, MD, MPH

Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Developing a New Definition and Assessing New Clinical Criteria for Septic Shock
For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Manu Shankar-Hari, MD, MSc; Gary S. Phillips, MAS; Mitchell L. Levy, MD; Christopher W. Seymour, MD, MSc; Vincent X. Liu, MD, MSc;
Clifford S. Deutschman, MD; Derek C. Angus, MD, MPH; Gordon D. Rubenfeld, MD, MSc; Mervyn Singer, MD, FRCP; for the Sepsis Definitions Task Force

Singer M et al. JAMA. 2016 Feb 23;315(8):801-10.

Seymour CW et al. JAMA. 2016 Feb 23;315(8):762-74.

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

Sepsis: New definition

Life-threatening organ dysfunction

caused by

Dysregulated host response to infection

New definition

Organ dysfunction characterized clinically by change in SOFA score ≥2 related to episode of new infection

variables/points	1	2	3	4
Neurological (GCS)	13-14	10-12	6-9	<6
Respiratory (P:F ratio)	<400	<300	<200 (+ resp support)	<100 (+ resp support)
Cardiovascular (systolic BP)	<70	dopamine ≤5 or dobutamine (any dose)	dopamine >5 or EPI ≤0.1 or NOREPI ≤0.1	dopamine >15 or EPI >0.1 or NOREPI >0.1
Renal (creatinine or UO)	110-170	171-299	300-440 (or <500 ml/day)	>440 (or <200 ml/day)
Haematological (platelets)	<150	<100	<50	<20
Liver (bilirubin)	20-32	33-101	102-204	>204

n.b. SOFA measured on routinely collected data - no special blood tests needed

New definition

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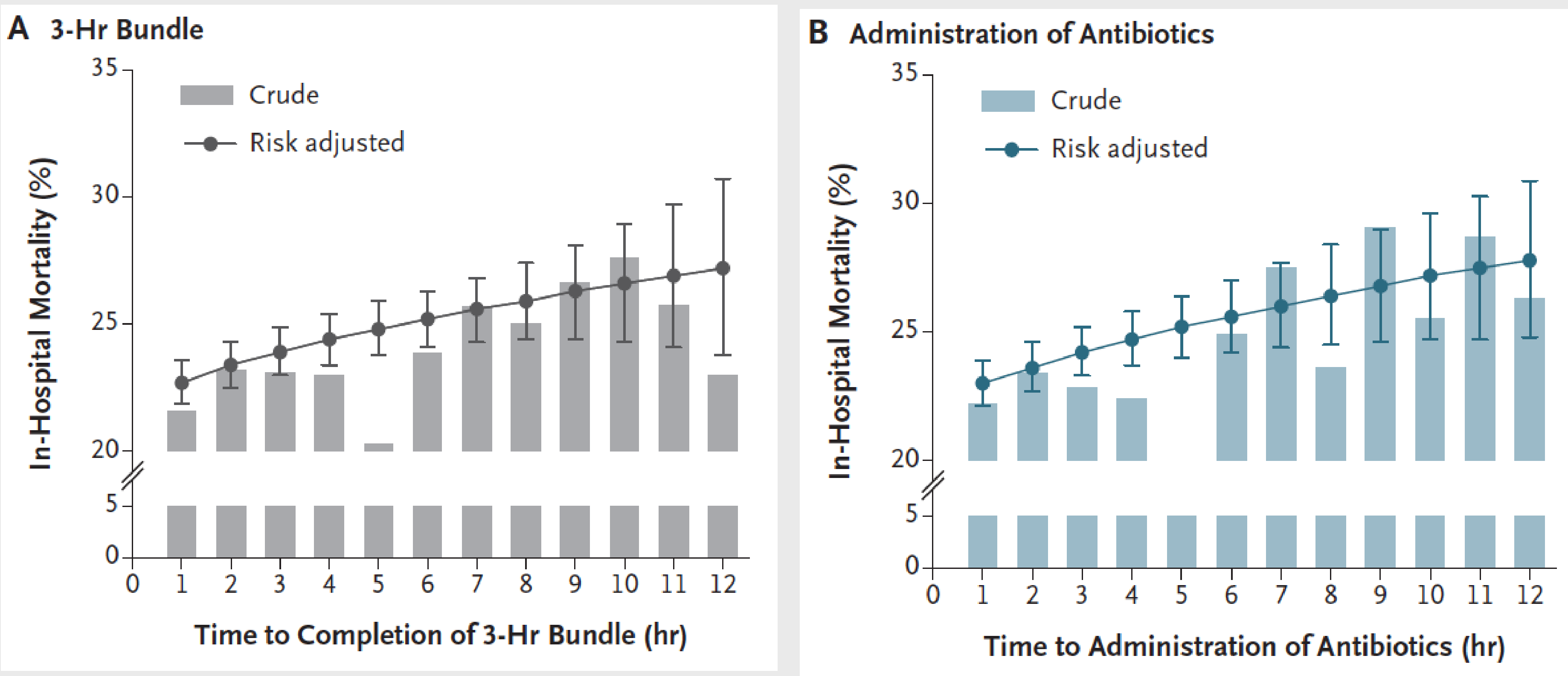
Renal (creatini[illegible]	[illegible]	[illegible]	300-440 (or <500 ml/day)	>440 (or <200 ml/day)
[illegible]	<150	<100	<50	<20
Liver (bilirubin)	20-32	33-101	102-204	>204

Infection + SOFA ≥2 = 10% risk of in-hospital mortality

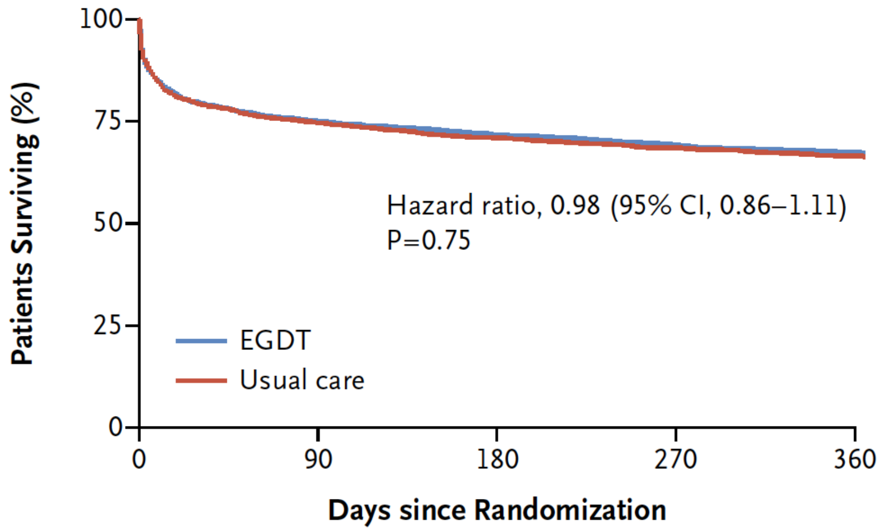
n.b. SOFA measured on routinely collected data - no special blood tests needed

Time to Treatment and Mortality during Mandated Emergency Care for Sepsis



Seymour CW., et al Online May 21, 2017 DOI: 10.1056/NEJMoa1703058

Early, Goal-Directed Therapy for Septic Shock
A Patient-Level Meta-Analysis



No. at Risk

	0	90	180	270	360
EGDT	1857	1391	1287	1209	1119
Usual care	1880	1395	1295	1206	1110

- **Most effective fluids and vasopressor regimens**
- **The role of hemodynamic monitoring**
- **Targets for resuscitation**
- **CVP and ScO_2?**

Rowan et al, N Engl J Med. 2017 Jun 8;376(23):2223-2234

Take-Home Message

New Sepsis Definition

- From Organ Dysfunction to Sepsis
- Septic Shock
- qSOFA
- Bundles (recognition and treatment within 3 hours) to improve outcome
- A new era for regulation of hospital quality

Subtopics:

- ❖New Sepsis Definition
- ❖Lung protective ventilation in non ARDS
- ❖ARDS: The LUNG SAFE
- ❖Mask vs Helmet for NIV in ARDS
- ❖High Flow Nasal Cannula in Hypoxiemic ARF
- ❖Oxygen therapy in critically ill patients

Lung protective ventilation in non ARDS

State of the Art

Is Acute Respiratory Distress Syndrome a preventable disease?

Yadav H et al. Am J respir Crit Care Med 2017 Mar 15;195(6):725-736

State of the Art

LIP: Lung Injury Prediction Score

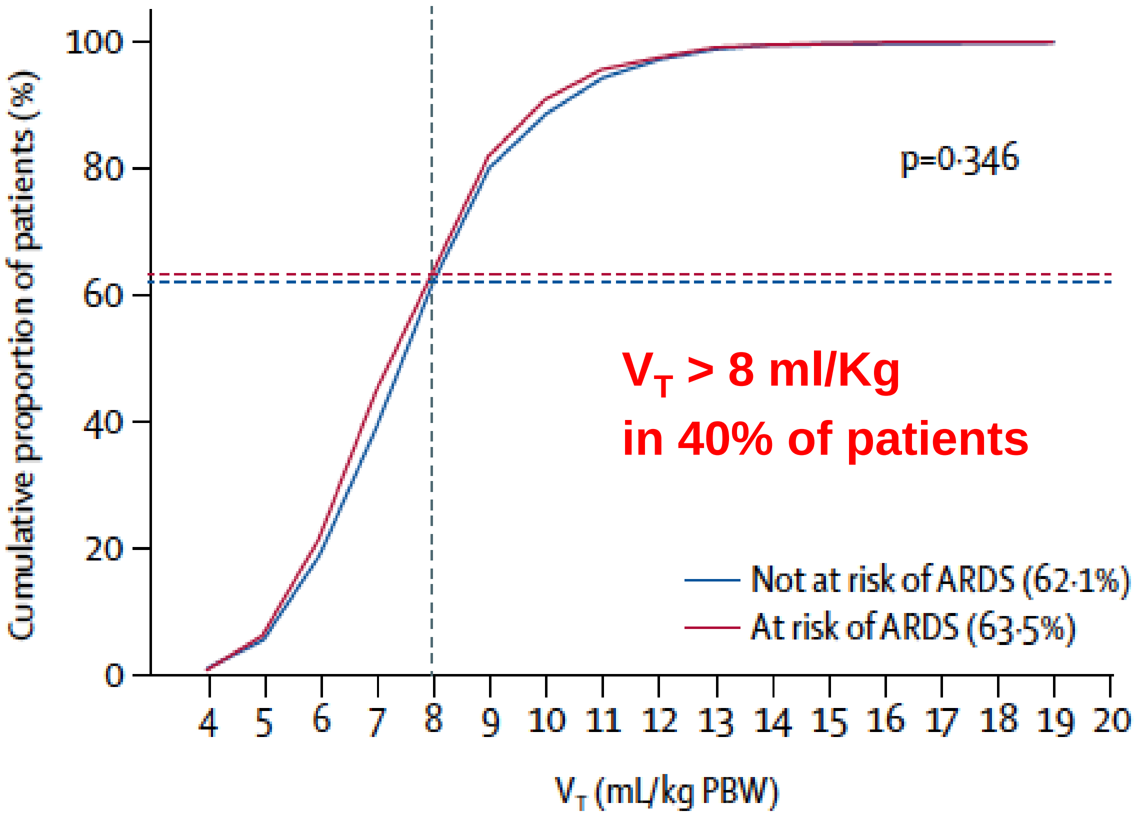
	LIPS Points	Examples
Predisposing Conditions		
Shock	2	
Aspiration	2	
Sepsis	1	(1) Patient with history of alcohol abuse
Pneumonia	1.5	with septic shock from pneumonia
High-risk surgery*		requiring $F_{IO_2} > 0.35$ in the
Orthopedic spine	1	emergency room: Sepsis + shock +
Acute abdomen	2	pneumonia + alcohol abuse +
Cardiac	2.5	$F_{IO_2} > 0.35$
Aortic vascular	3.5	1 + 2 + 1.5 + 1 + 2 = 7.5
High-risk trauma		(2) Motor vehicle accident with
Traumatic brain injury	2	traumatic brain injury, lung contusion,
Smoke inhalation	2	and shock requiring $F_{IO_2} > 0.35$
Near drowning	2	Traumatic brain injury + lung
Lung contusion	1.5	contusion + shock+ $F_{IO_2} > 0.35$
Multiple fractures	1.5	2 + 1.5 + 2 + 2 = 7.5
Risk modifiers		
Alcohol abuse	1	
Obesity (BMI > 30)	1	(3) Patient with history of diabetes
Hypoalbuminemia	1	mellitus and urosepsis with shock
Chemotherapy	1	Sepsis + shock + diabetes
$F_{IO_2} > 0.35$ (> 4 L/min)	2	1 + 2 − 1 = 2
Tachypnea (RR > 30)	1.5	
$Sp_{O_2} < 95\%$	1	
Acidosis (pH < 7.35)	1.5	
Di		

De ... ry rate;
Sp_{O_2}
* A
† Only if sepsis.

Higher than 4

Gajic O et al Am J Respir Crit Care Med 183:462–470, 2011

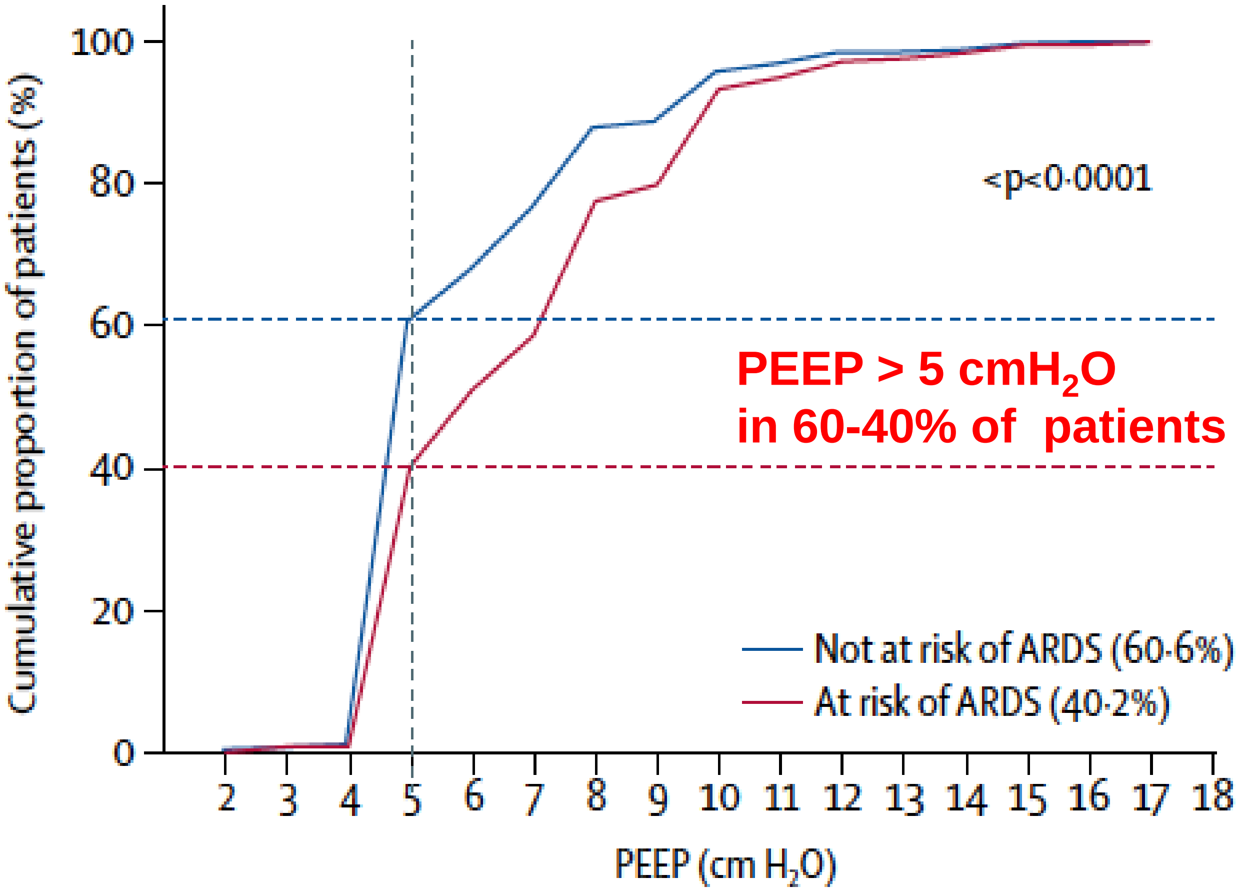
Tidal volume



1,022 patients without ARDS

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

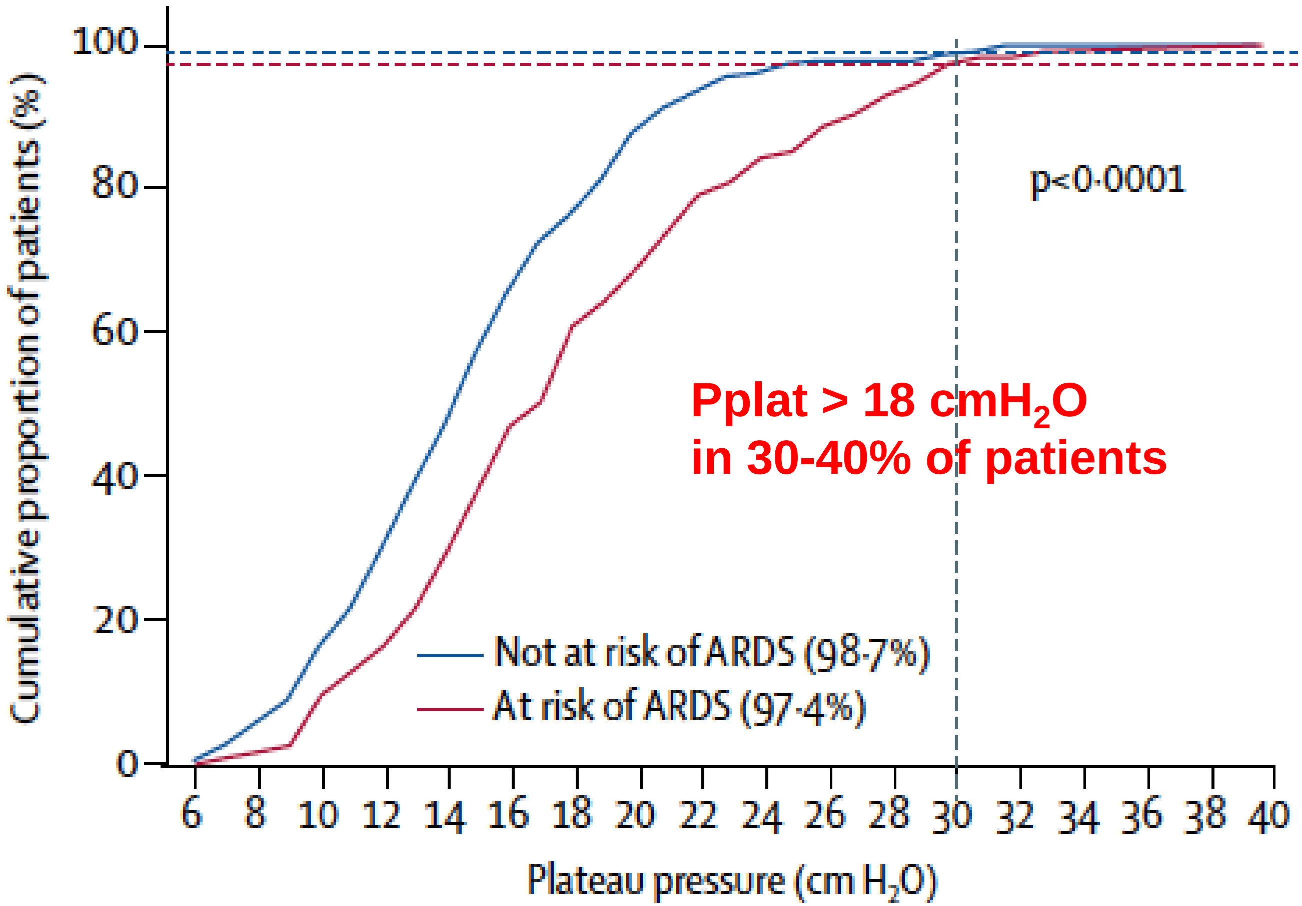
Posiivr End-Expiratory Pressure



1,022 patients without ARDS

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

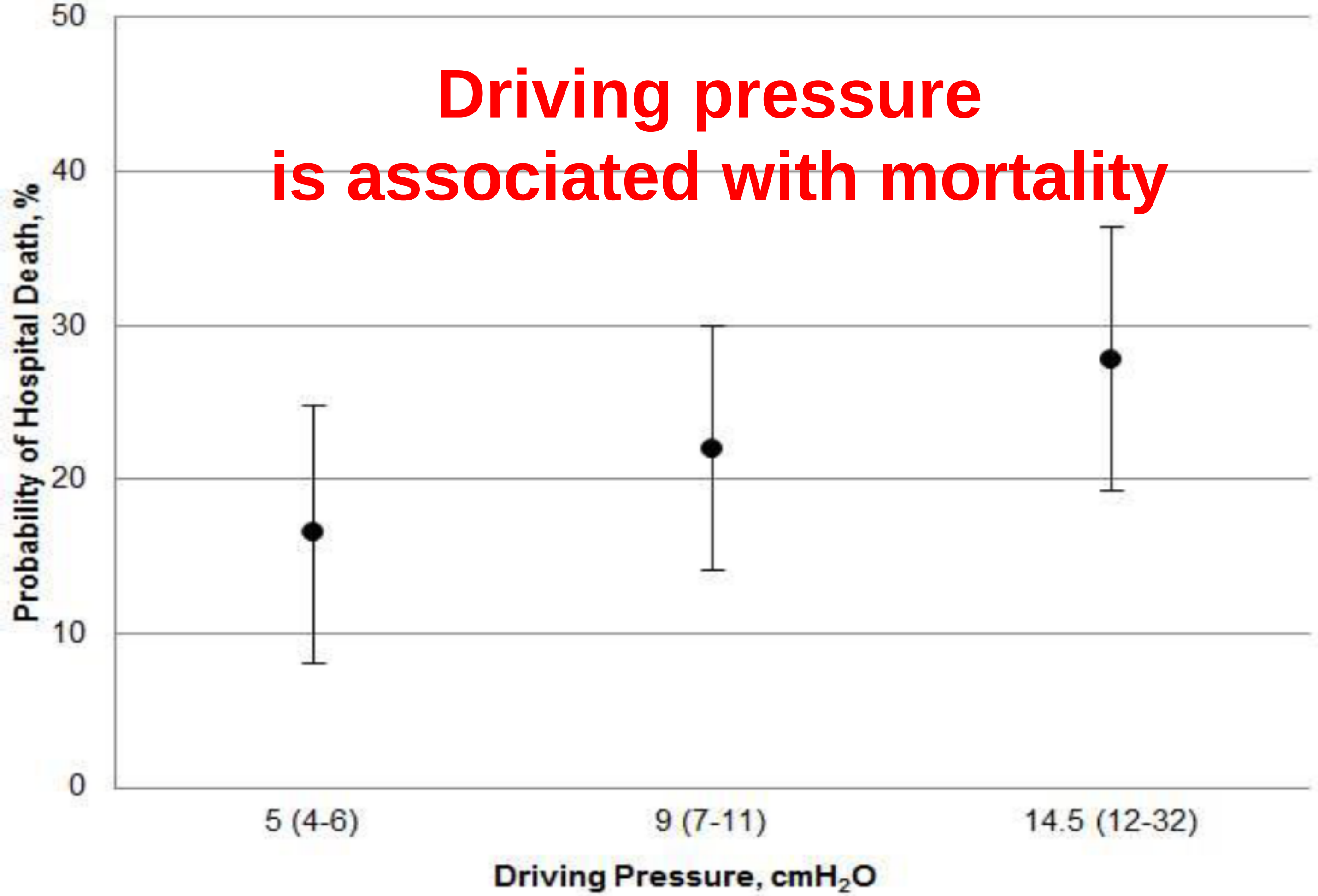
Plateau pressure



1,022 patients without ARDS

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

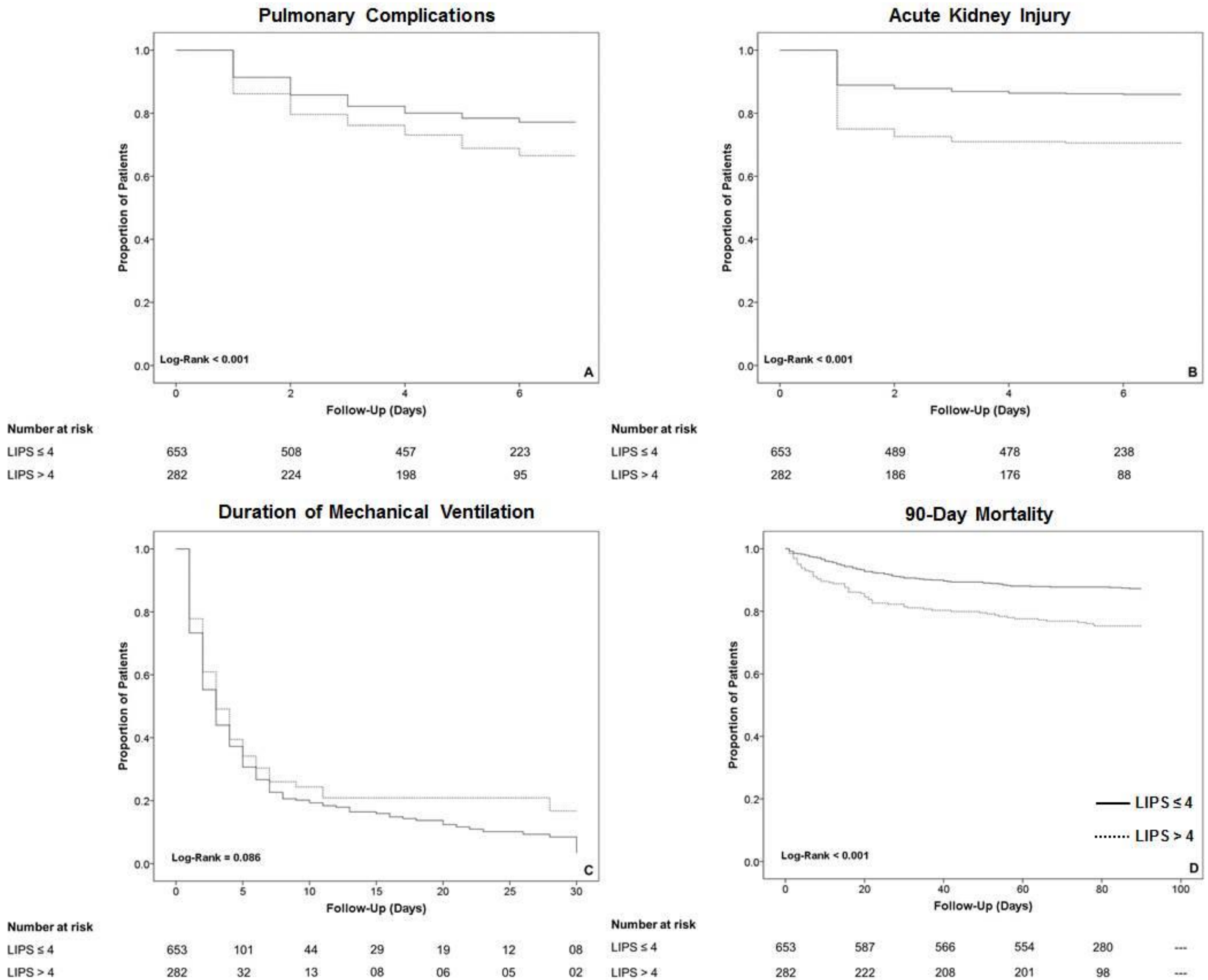
Driving pressure



1,022 patients without ARDS

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

Lung Injury Score and Outcome



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

Factors associated with pulmonary complications

Reasons for ICU admission

- Emergency surgery 11.0
- Clinical condition 6.2

Ventilatory parameters

- V_T ml/Kg PBW 1.2
- RR b/min 1.1

- Transfusions in 1w 2.4

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

Take-Home Message

Lung protective ventilation in non ARDS

- Around a third of patients receiving mechanical ventilation in the ICU were at risk of ARDS.

- Pulmonary complications occur frequently in patients at risk of ARDS and their clinical outcome is worse compared with those not at risk of ARDS.

- There is potential for improvement in the management of patients without ARDS.

- Further refinements are needed for prediction of ARDS.

Subtopics:

- New Sepsis Definition
- Lung protective ventilation in non ARDS
- ARDS: The LUNG SAFE
- Mask vs Helmet for NIV in ARDS
- High Flow Nasal Cannula in Hypoxiemic ARF
- Oxygen therapy in critically ill patients

ARDS: The LUNG SAFE

State of the Art

	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 $\geq$ 5 cmH_2O	**$100 < PaO_2/FiO_2 \leq 200$** with PEEP $\geq$ 5 cmH_2O	**$PaO_2/FiO2 \leq 100$** with PEEP $\geq$ 5 cmH_2O

ARDS definition Task Force **JAMA 2012 Jun 20;307(23):2526-33.**

Risk factors for ARDS

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%)

10.4% of all ICU Admissions

23% of all MV ICU patients

0.45 patients/ICU bed/4 weeks
[5.5 patients / ICU bed /year]

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

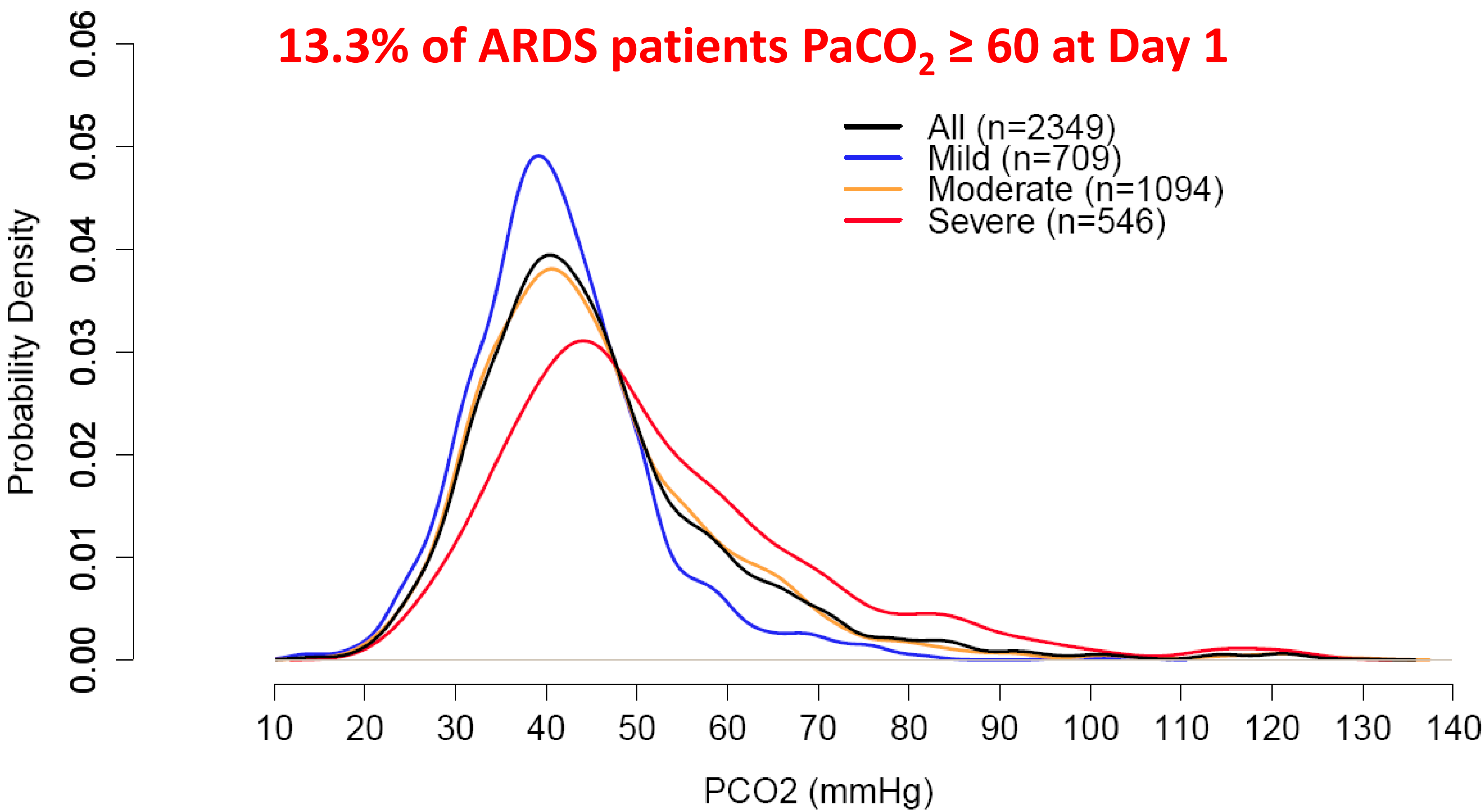
Recognition of ARDS

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

- Factors associated with under-recognition of ARDS:
  - The absence of a risk factor for ARDS
  - Lower numbers of nurses and physicians per ICU patient

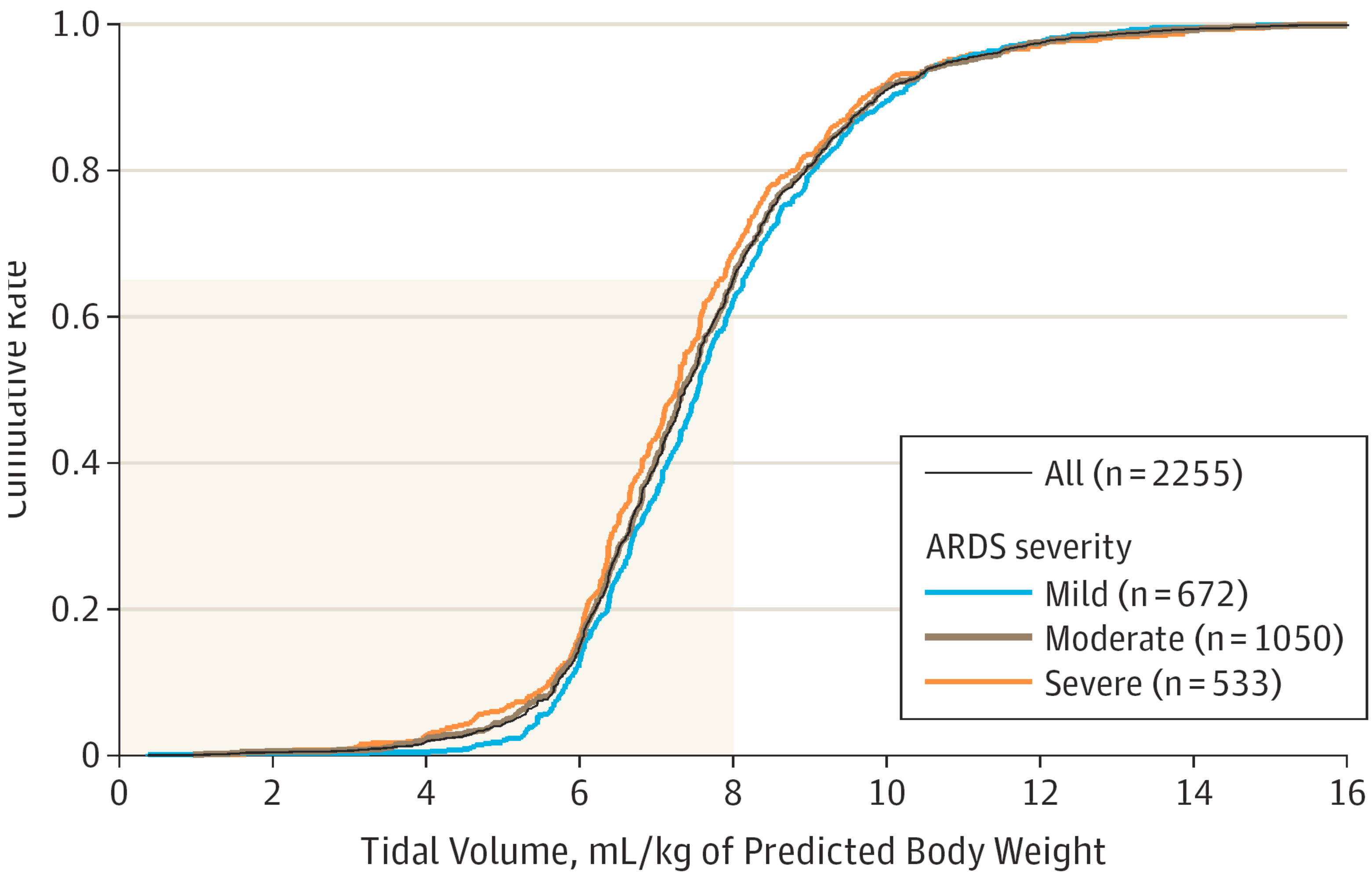
Bellani G et al. JAMA Feb 23 2016, 315 (8): 788-800

Arterial PCO_2



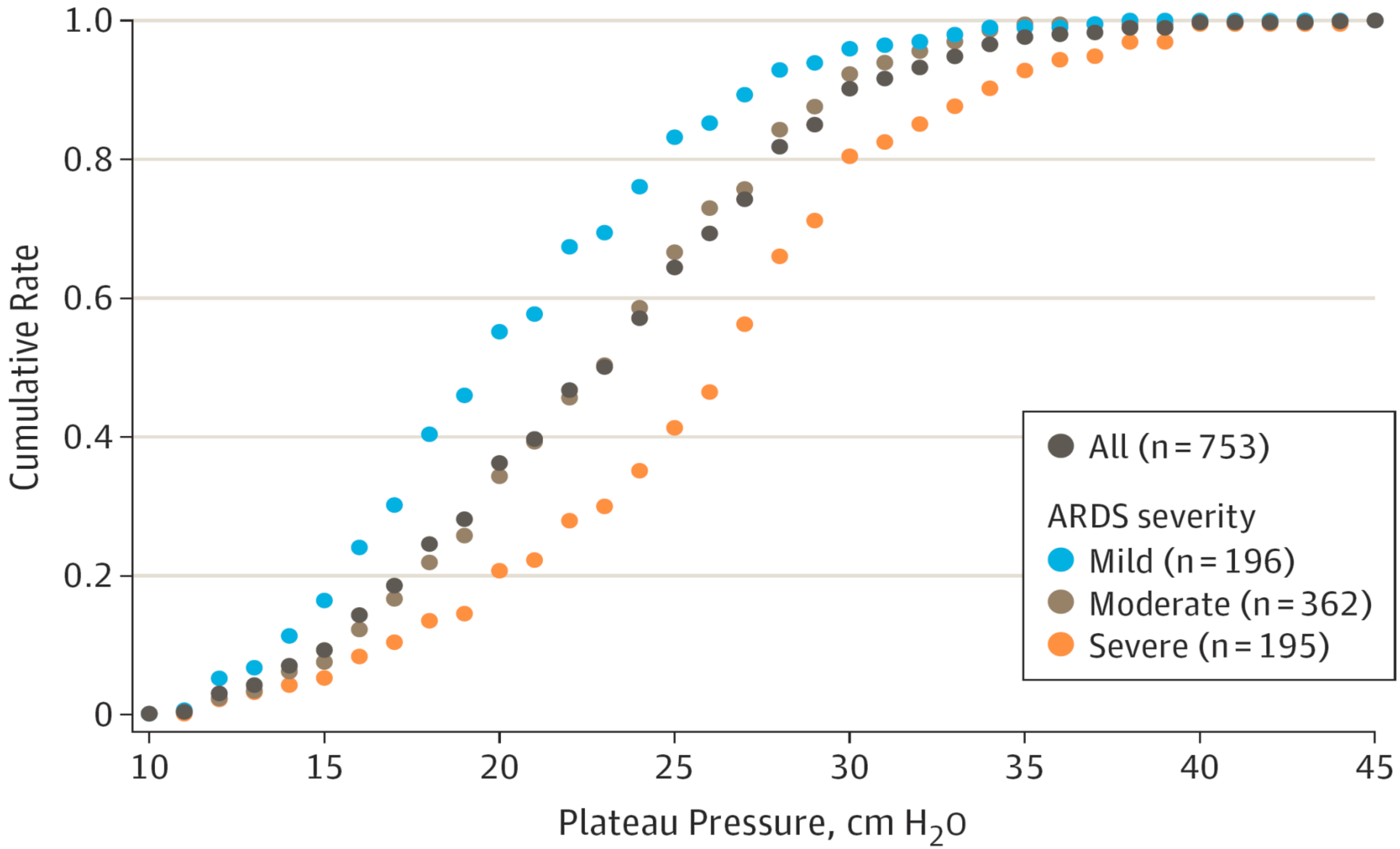
Bellani G et al. JAMA Feb 23 2016, 315 (8): 788-800

Tidal volume



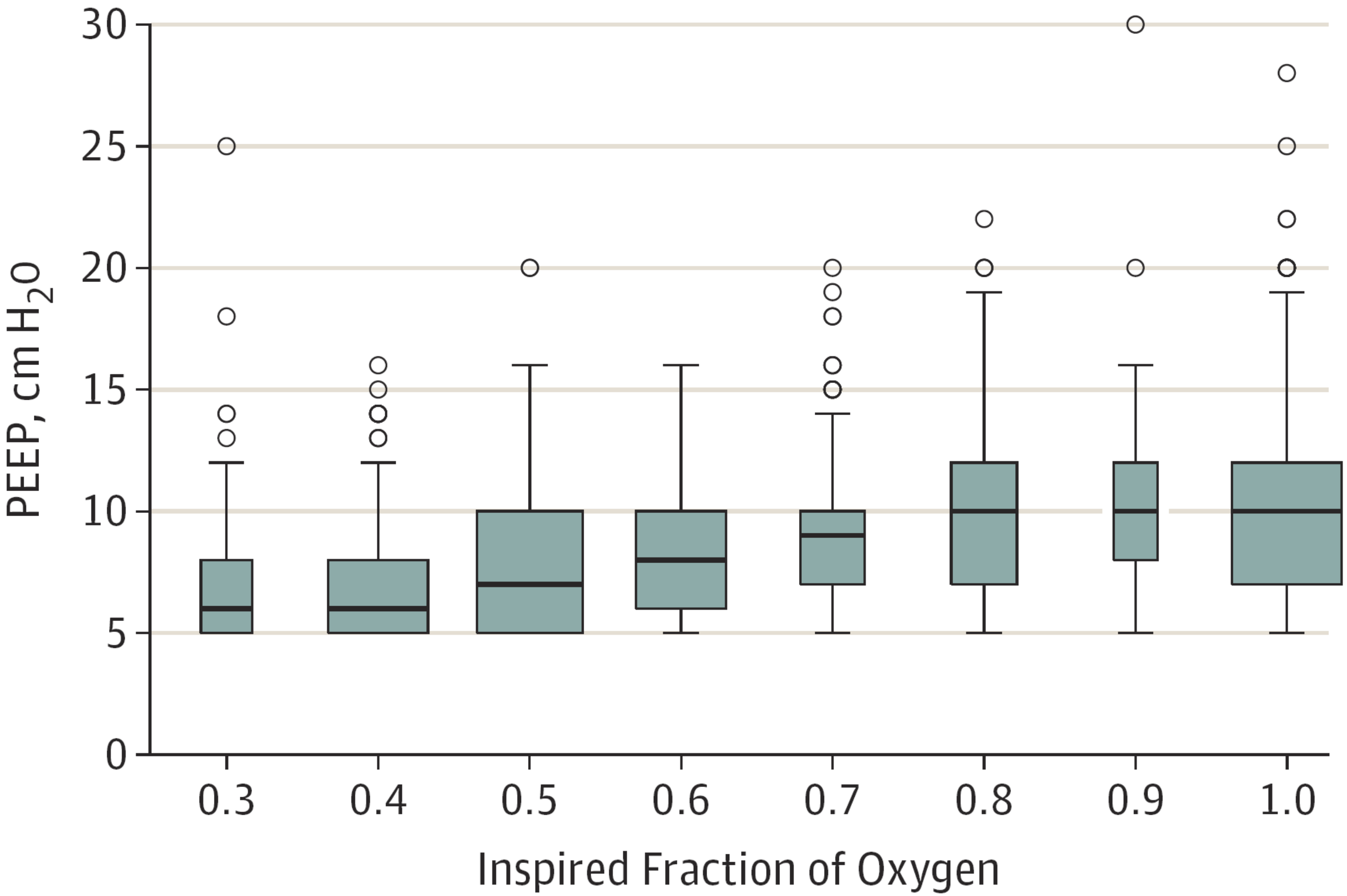
Bellani G et al. JAMA Feb 23 2016, 315 (8): 788-800

Plateau pressure



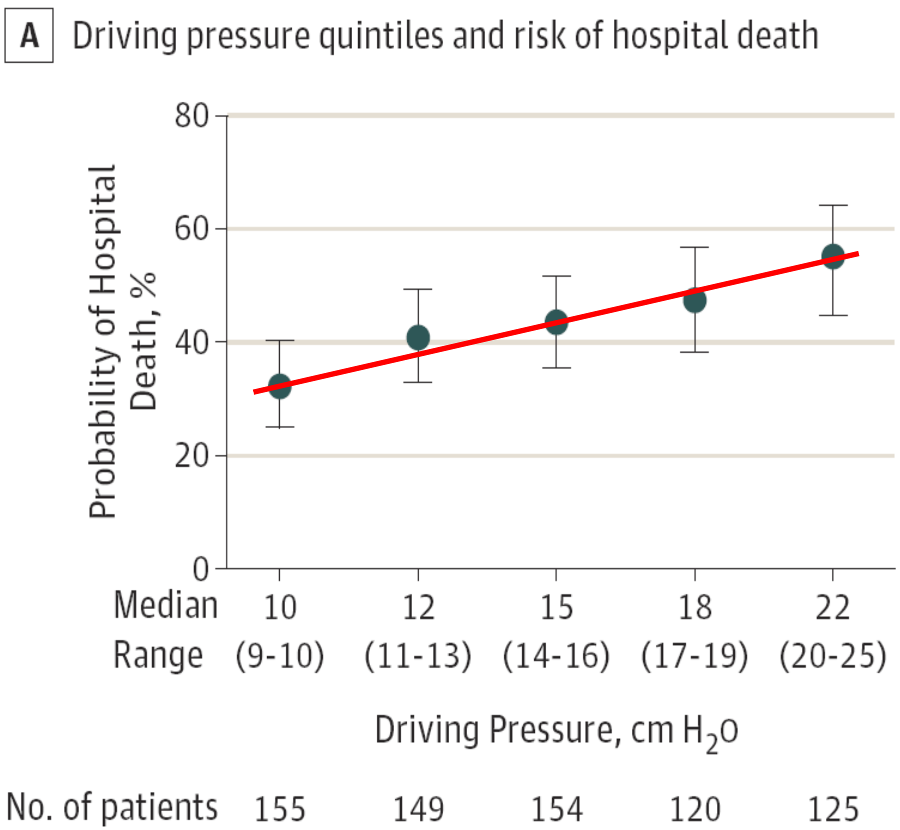
Bellani G et al. JAMA Feb 23 2016, 315 (8): 788-800

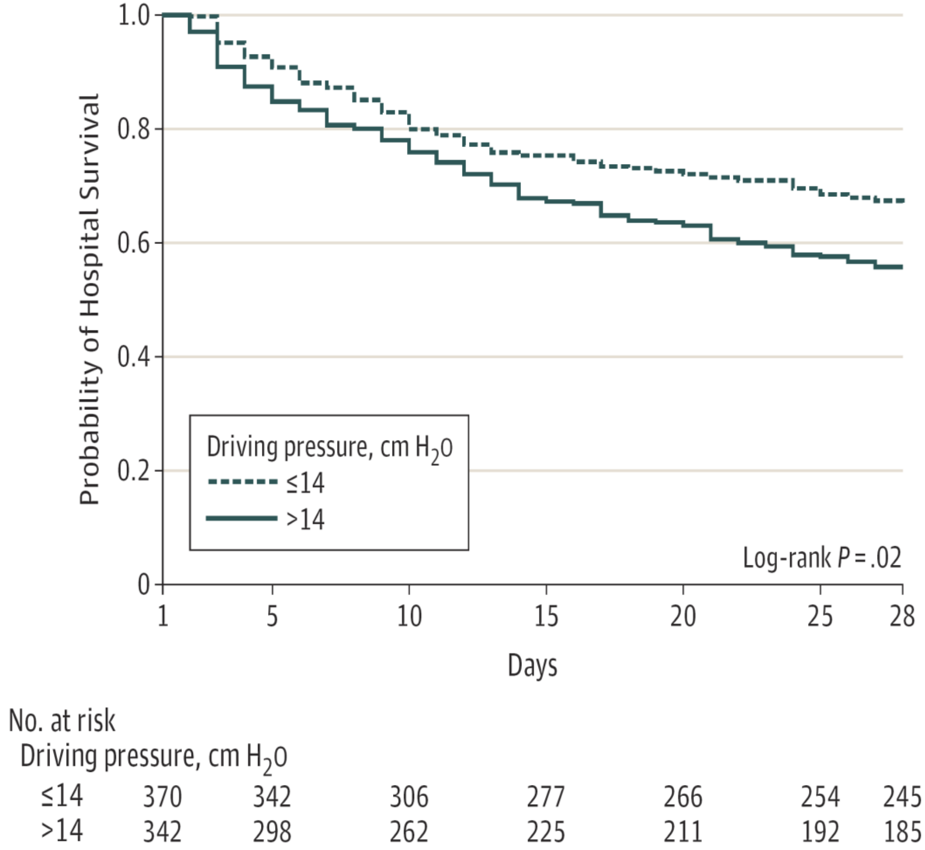
Positive End-Expiratory Pressure



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

ΔPressure *vs* Plateau Pressure





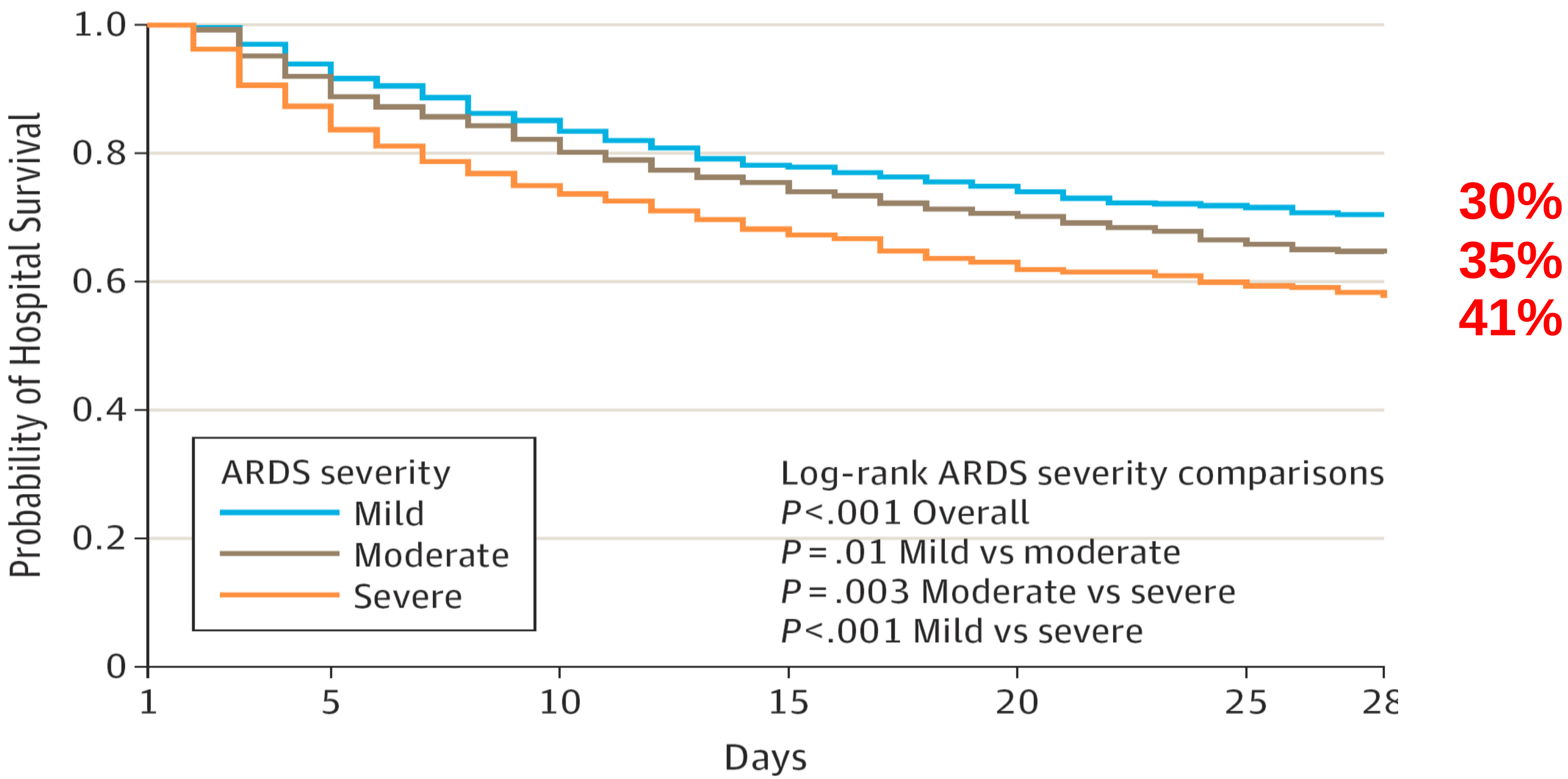
Bellani G et al. JAMA Feb 23 2016, 315 (8): 788-800

Use of Adjunctive Measures

	All	Mild	Moderate	Severe	P value
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

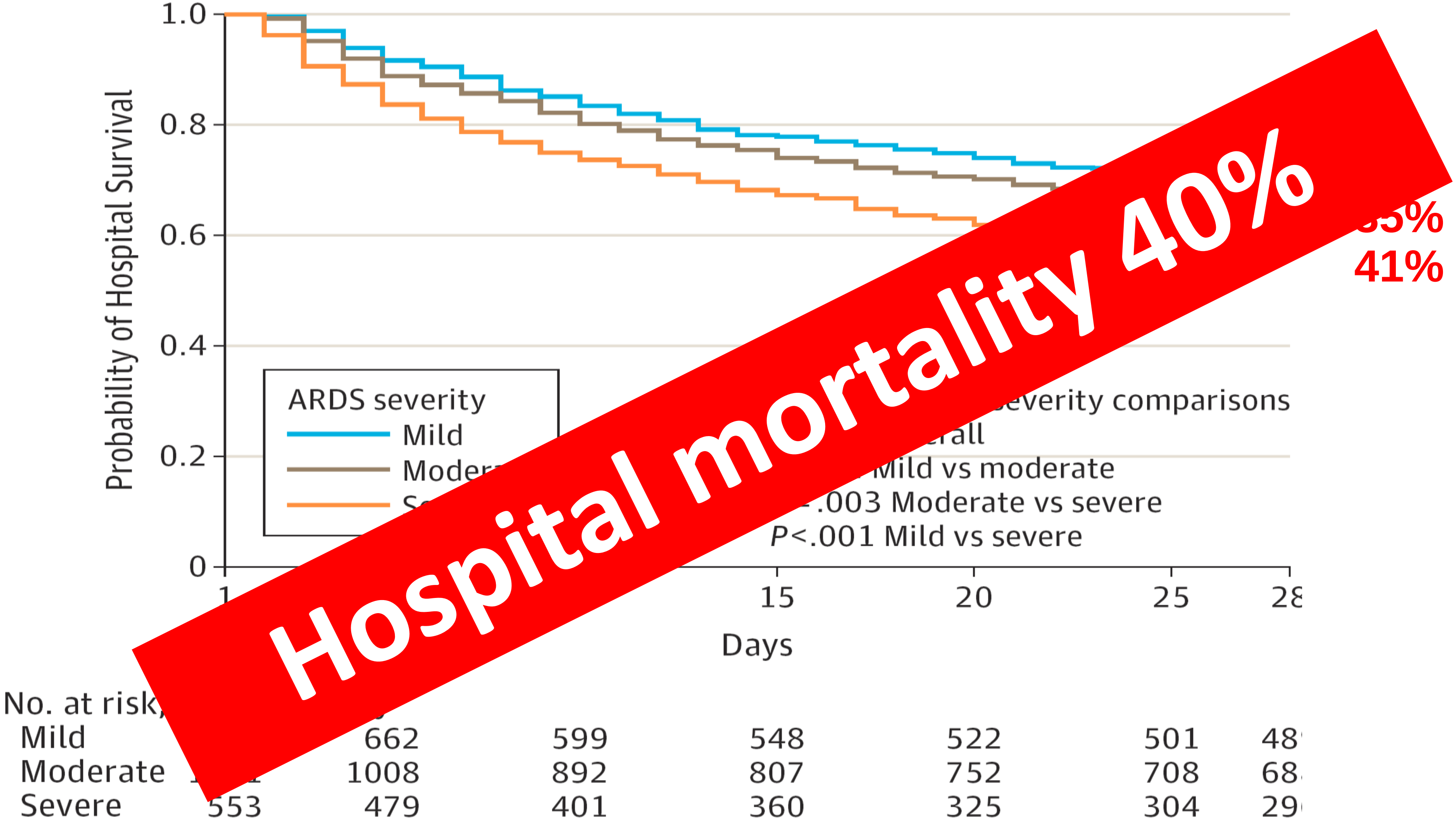
ARDS Survival to Day 28



No. at risk, ARDS severity							
Mild	708	662	599	548	522	501	[illegible]
Moderate	1101	1008	892	807	752	708	[illegible]
Severe	553	479	401	360	325	304	[illegible]

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

ARDS Survival to Day 28



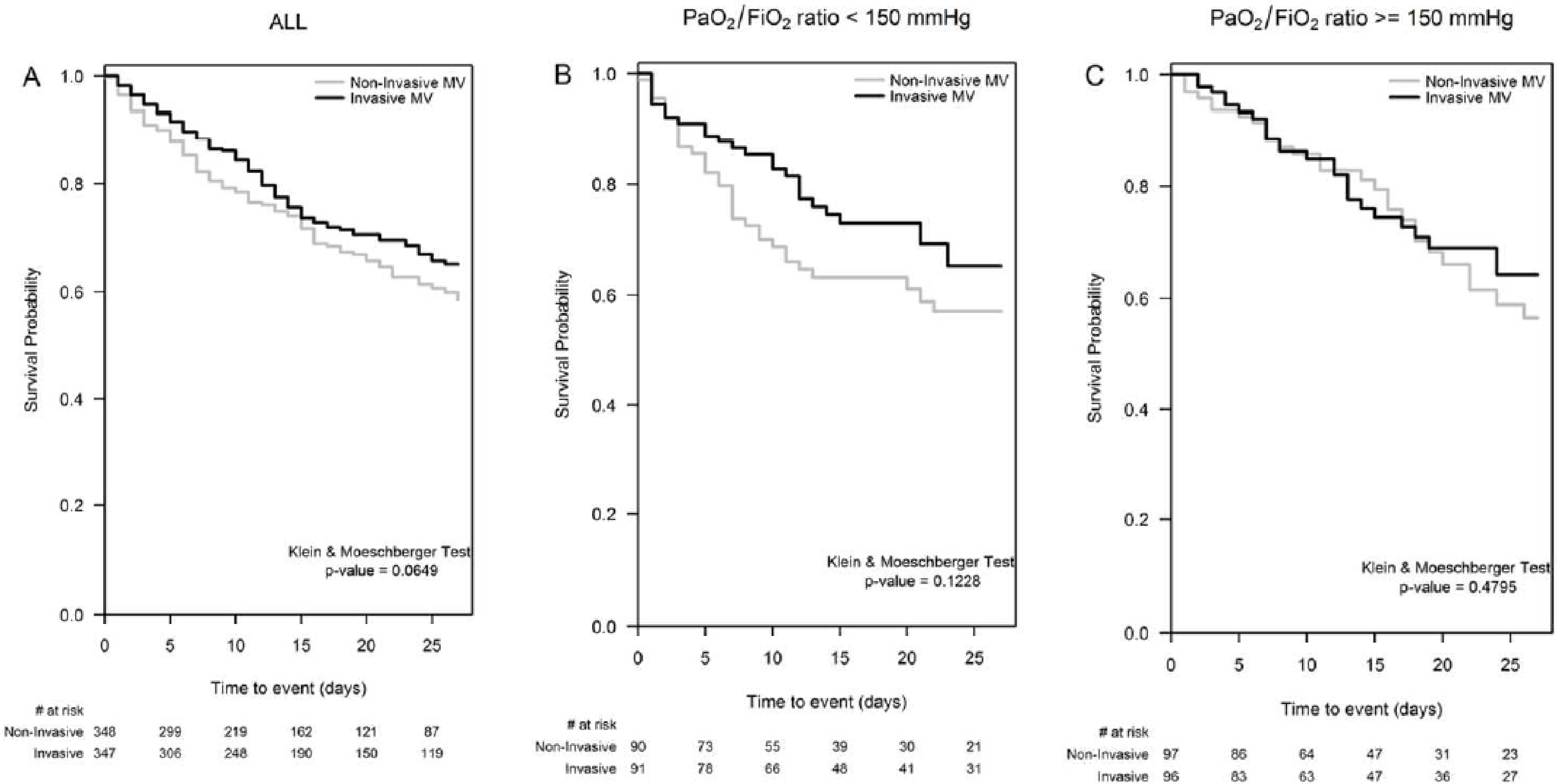
Bellani G et al. JAMA Feb 23 2016, 315 (8): 788-800

Potentially modifiable factors contributing to outcome from ARDS:

- Higher PEEP
- Lower peak inspiratory, plateau and driving pressures
- Lower respiratory rate
- Higher number of ICU beds

Laffey JG et al. **Intensive Care Med. 2016 Dec;42(12):1865-1876**

Non Invasive Ventilation in ARDS



NIV is used in about 15% pts with ARDS, irrespective of the severity of hypoxemia

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

Take-Home Message

ARDS: The Lung Safe

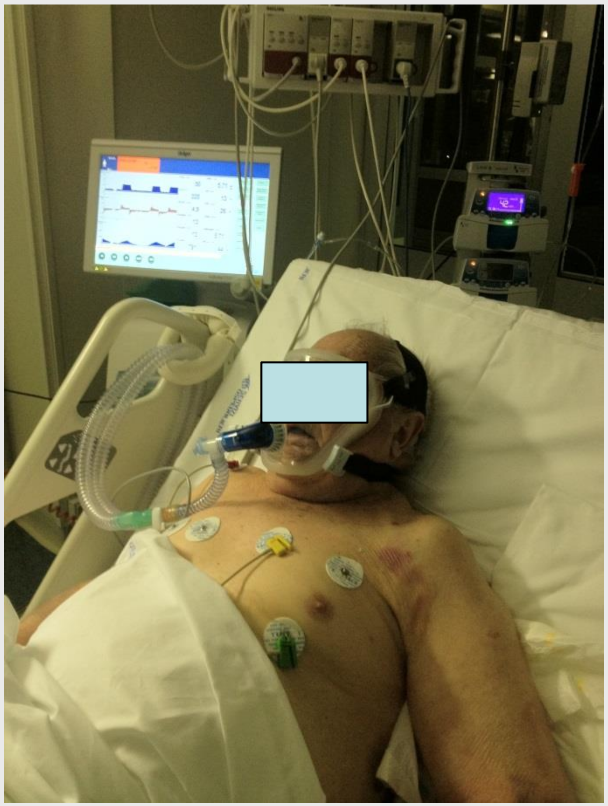
- ARDS is underrecognized and associated with high mortality
- Some potential modifiable factors are associated with imporved survival
- NIV is used irrespective of ARDS severity and associated with higher mortality in moderate to severe ARDS

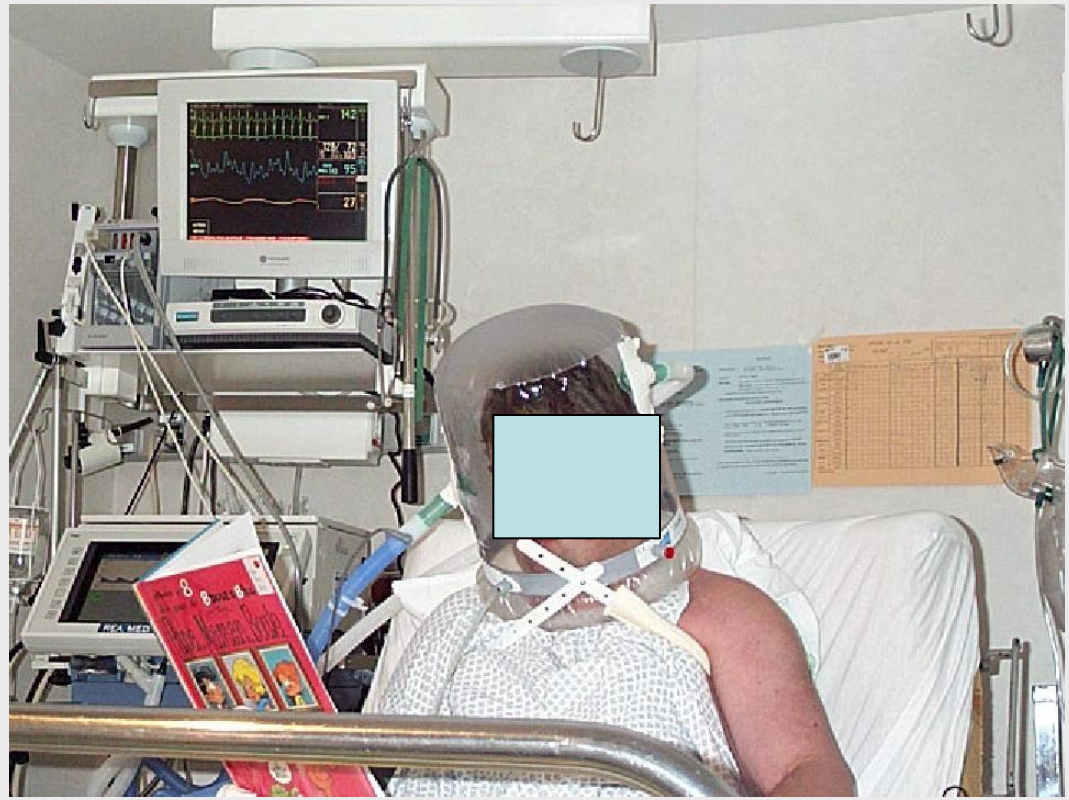
Subtopics:

- ❖New Sepsis Definition
- ❖Lung protective ventilation in non ARDS
- ❖ARDS: The LUNG SAFE
- ❖Mask vs Helmet for NIV in ARDS
- ❖High Flow Nasal Cannula in Hypoxiemic ARF
- ❖Oxygen therapy in critically ill patients

Mask vs Helmet for NIV in ARDS

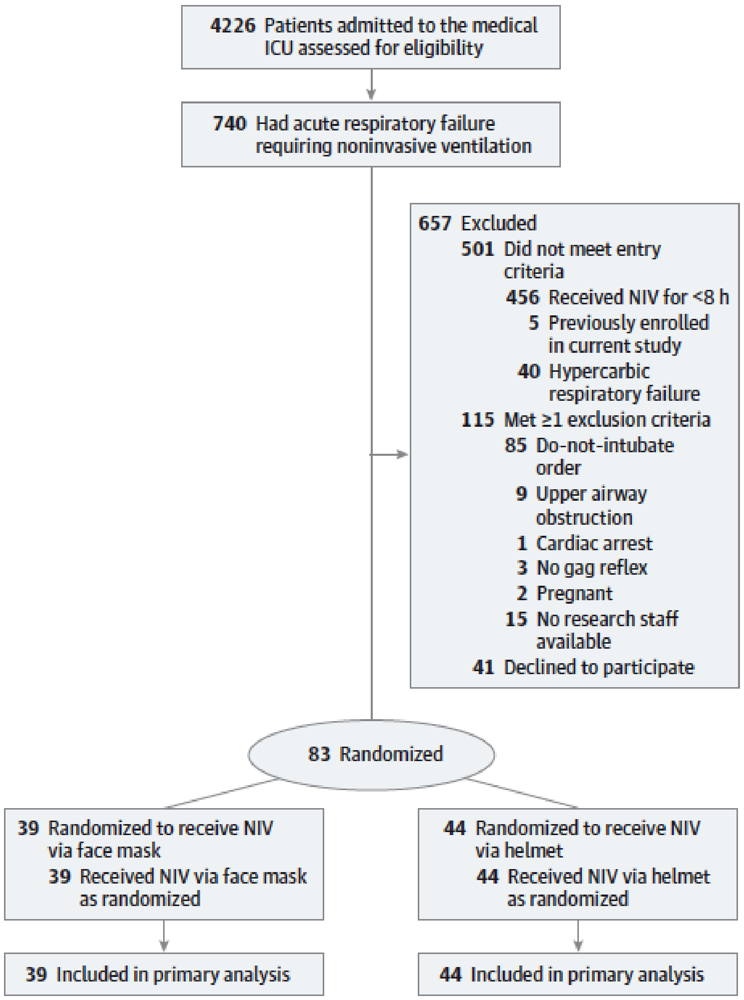
State of the Art





Bello G et al. **Clin Chest Med. 2016 Dec;37(4):711-721**

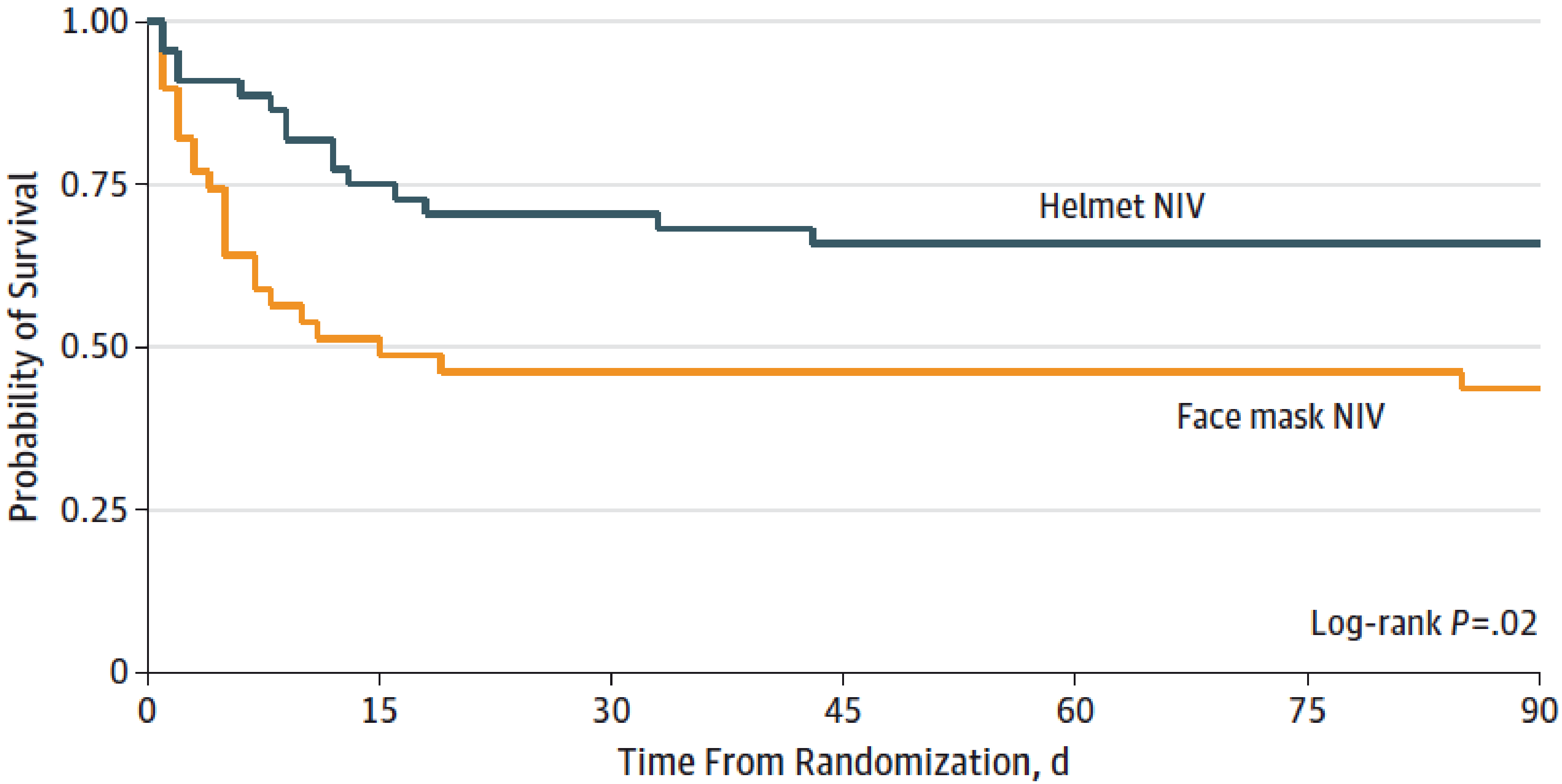
Patient characteristics



Characteristic	No. (%) of Patients Receiving Noninvasive Ventilation, Face Mask (n = 39)	Helmet (n = 44)
Reason for Acute Respiratory Failure		
Pneumonia	14 (36)	23 (52)
Aspiration	5 (13)	3 (7)
Extrapulmonary ARDS	6 (15)	3 (7)
Pneumonia due to immunosuppression[b]	14 (36)	15 (34)
Respiratory and Hemodynamic Parameter, Median (IQR)		
Duration of NIV before randomization, median, h	13 (8-19.7)	10.3 (8.3-13.4)
Inspiratory positive airway pressure, cm H_2O	10 (10-15)	12 (10-14.5)
Expiratory positive airway pressure, cm H_2O	5 (5-8)	5 (5-8)
SpO_2, %	95 (91-99)	97 (95-99)
FIO_2, %	60 (50-80)	60 (40-90)
PaO_2:FIO_2	144 (90-223)	118 (93-170)
Shock, No. (%)	12 (31)	9 (20)

Patel BK et al. JAMA. 2016 Jun 14;315(22):2435-41.

Survival at 90 d



No. at risk

	0	15	30	45	60	75	90
Face mask	39	20	18	18	18	18	17
Helmet	44	33	31	29	29	29	29

Patel BK et al. **JAMA. 2016 Jun 14;315(22):2435-41.**

Primary and secondary outcomes

	Face Mask (n = 39)	Helmet (n = 44)	Absolute Difference (95% CI)	*P* Value
Primary outcome, No. (%)				
Endotracheal intubation	24 (61.5)	8 (18.2)	−43.3 (−62.4 to −24.3)	<.001
Reason for intubation				
Respiratory failure	20 (83.3)	3 (37.5)	−45.3 (−82.5 to −9.1)	.01
Circulatory failure	3 (12.5)	0 (0)	−12.5 (−25.7 to 0.7)	.55
Neurologic failure	1 (4.2)	5 (62.5)	58.3 (24.8 to 92.8)	.001
Secondary outcomes, median (IQR), d				
Ventilator-free days	12.5 (0.49-28)	28 (13.7-28)	8.4 (13.4 to 3.4)	<.001
ICU length of stay	7.8 (3.9-13.8)	4.7 (2.5-8.7)	−2.76 (−6.07 to 0.54)	.04
Hospital length of stay	15.2 (7.8-19.7)	10.1 (6.5-15.9)	−2.92 (−8.47 to 2.63)	.16
Mortality, No. (%)				
Hospital	19 (48.7)	12 (27.3)	−21.4 (−41.9 to −1.0)	.04
90 d[a]	22 (56.4)	15 (34.1)	−22.3 (−43.3 to −1.4)	.02

Patel BK et al. **JAMA. 2016 Jun 14;315(22):2435-41.**

Take-Home Message

Mask vs Helmet for NIV in ARDS

- Among patients with ARDS, treatment with helmet NIV resulted in a significant reduction of intubation rates.
- There was also a statistically significant reduction in 90-day mortality with helmet NIV.

Subtopics:

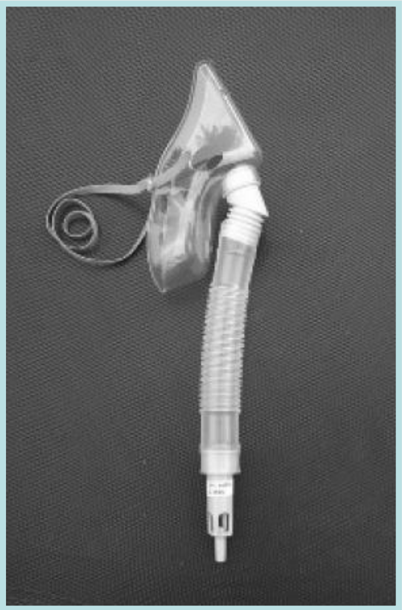
- New Sepsis Definition
- Lung protective ventilation in non ARDS
- ARDS: The LUNG SAFE
- Mask vs Helmet for NIV in ARDS
- High Flow Nasal Cannula in Hypoxiemic ARF
- Oxygen therapy in critically ill patients

High Flow Nasal Cannula in Hypoxiemic ARF

State of the Art

Simple face mask

High-concentration reservoir mask



Venturi mask

Nasal cannulae

Delivered FiO_2 is dependent on insp. flow & breathing pattern

O'Driscoll BR et al. Thorax 2008;63 (suppl VI):1-68

State of the Art

- **High flows of inspired gas up to 60 L/min**
- **Full humidification (37° C, 100 RH, 44 mg H_2O/L)**

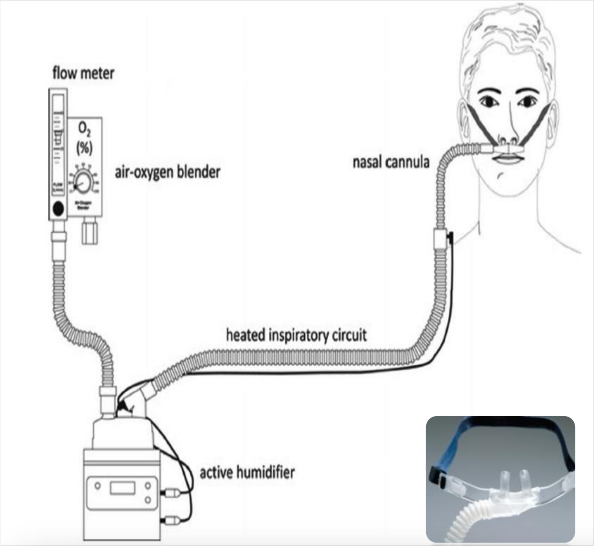
1) Accurate FiO_2 delivery

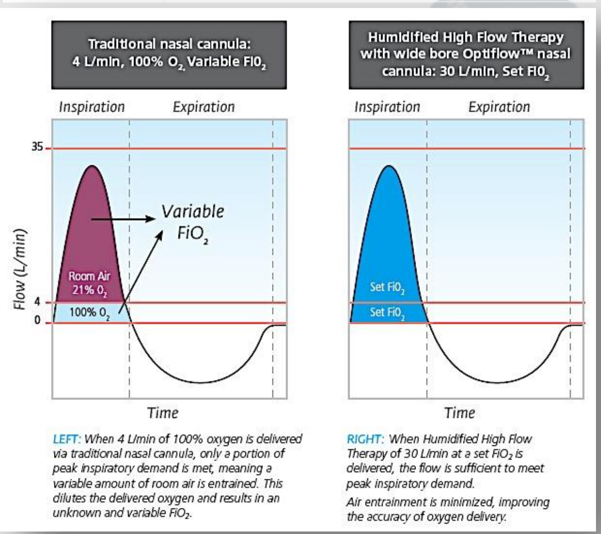
2) Washout of nasopharyngeal VDT

3) Provision of a small PEEP/CPAP

4) Increased lung volume

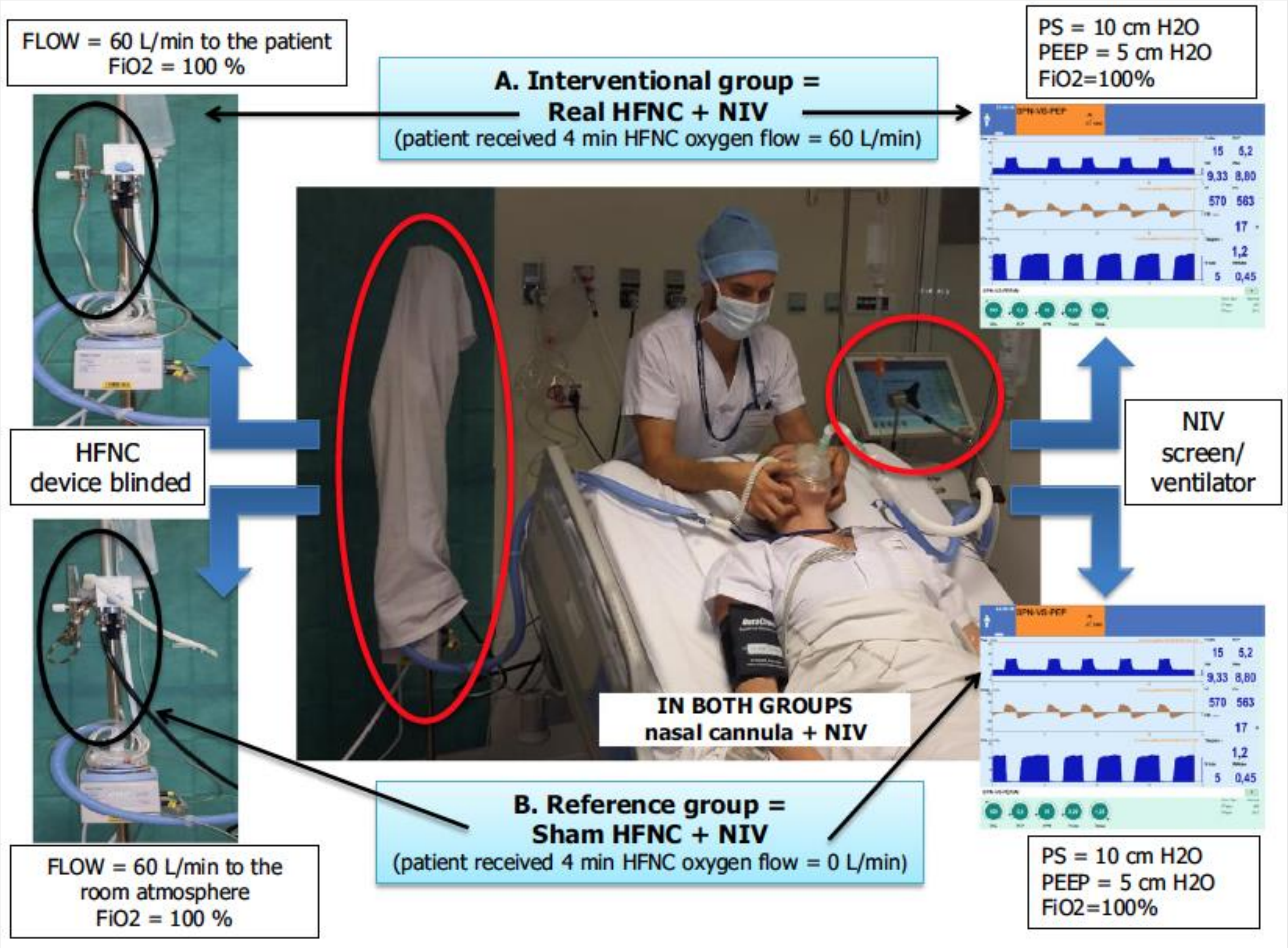
5) Improved comfort and compliance





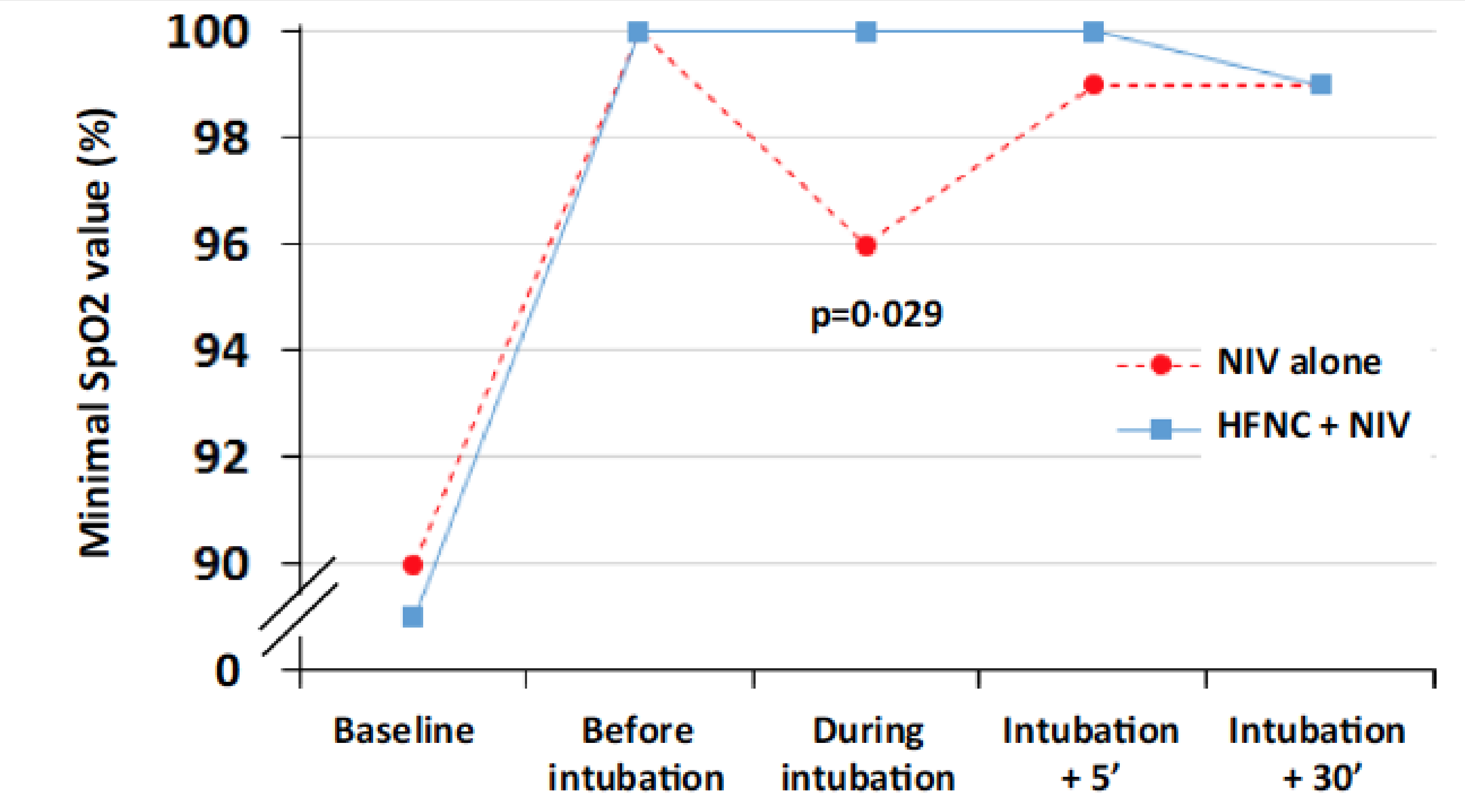
Papazian L et al. Intensive Care Med. 2016 Sep;42(9):1336-49

Apnoeic oxygenation via high-flow nasal cannula oxygen with NIV preoxygenation for intubation in hypoxaemic patients



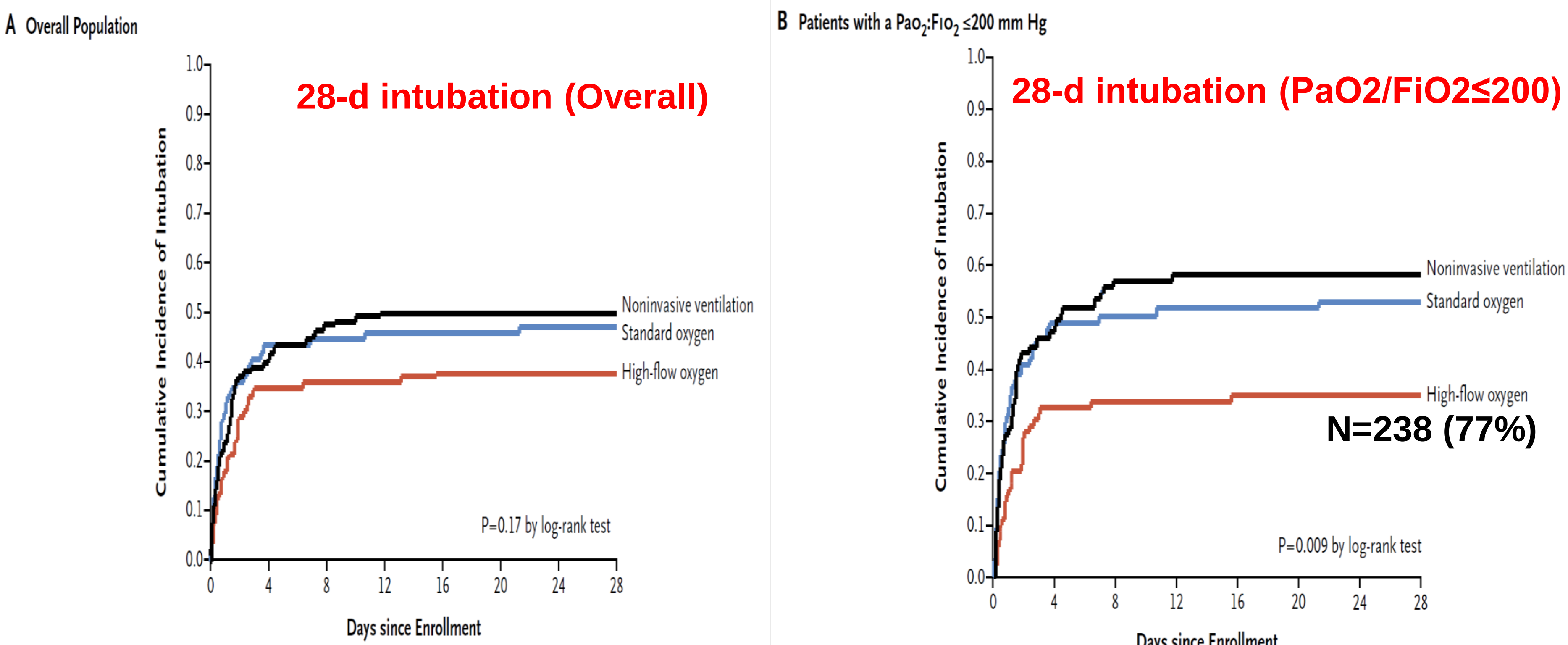
Jaber S et al. Intensive Care Med (2016) 42:1877–1887

Apnoeic oxygenation via high-flow nasal cannula oxygen with NIV preoxygenation for intubation in hypoxaemic patients



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

HFNC vs O_2 vs NIV in hypoxemic ARF



A — No. at Risk

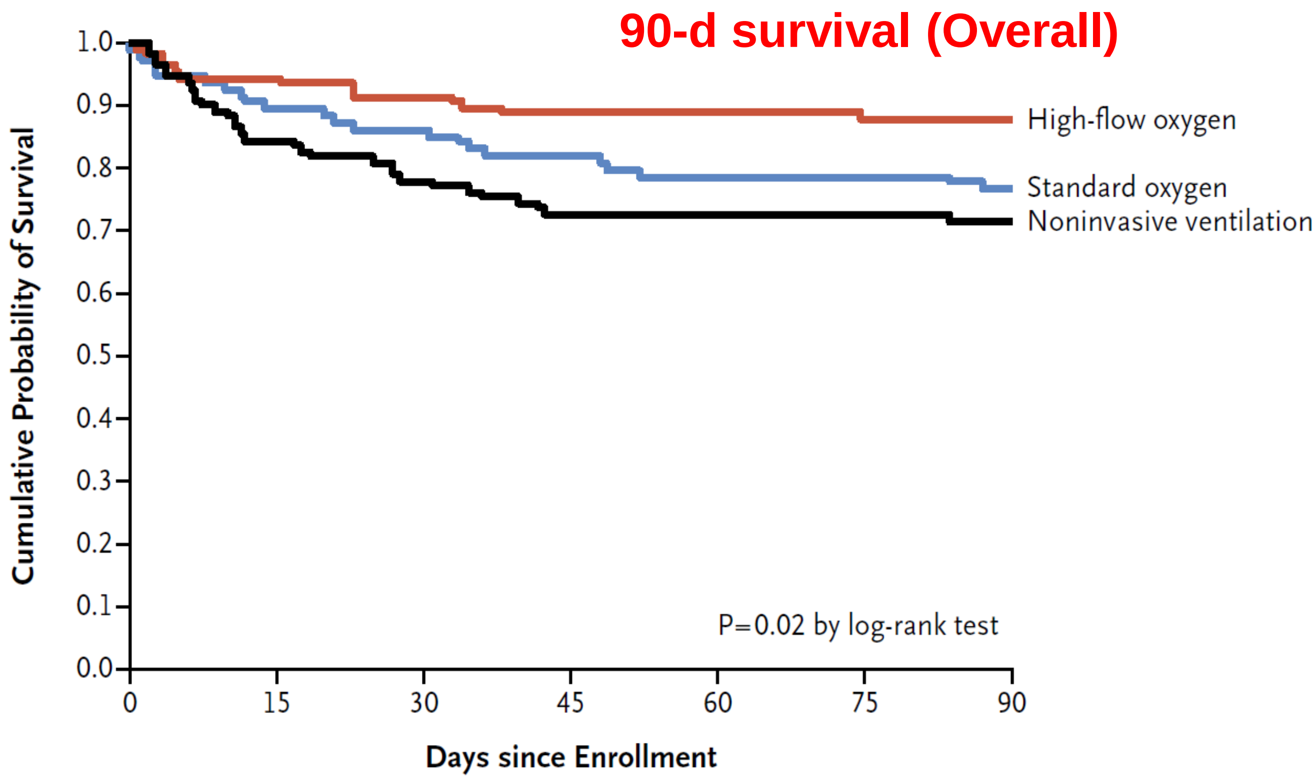
High-flow oxygen	106	68	67	67	65	65	65	65
Standard oxygen	94	52	50	49	49	49	48	48
Noninvasive ventilation	110	64	57	53	53	53	53	52

B — 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 J-P et al. NEJM 2015;372:2185-96

HFNC vs O_2 vs NIV in hypoxemic ARF

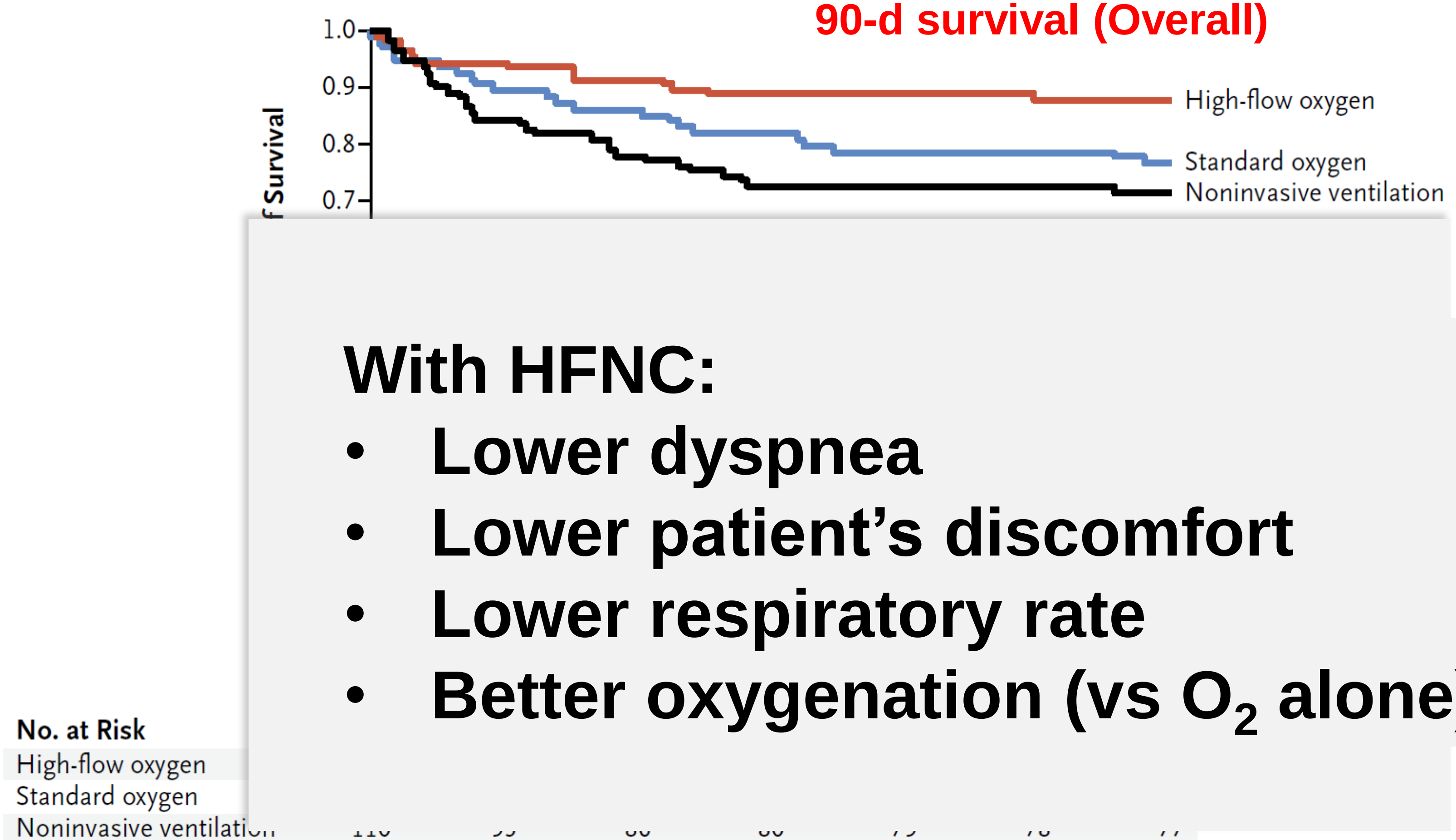


No. at Risk							
High-flow oxygen	106	100	97	94	94	93	93
Standard oxygen	94	84	81	77	74	73	72
Noninvasive ventilation	110	93	86	80	79	78	77

Frat J-P et al. NEJM 2015;372:2185-96

HFNC vs O_2 vs NIV in hypoxemic ARF

90-d survival (Overall)



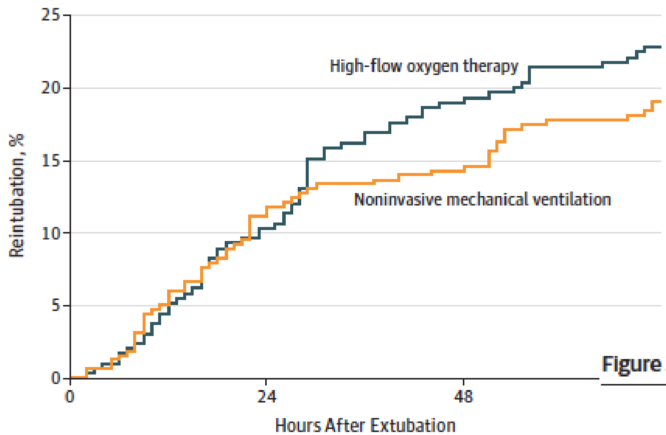
With HFNC:

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

Frat J-P et al. NEJM 2015;372:2185-96

HFNC vs NIV after extubation in hypoxiemic ARF

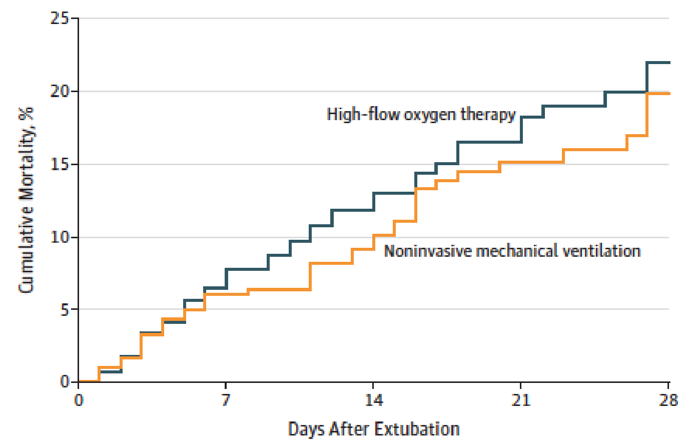
Figure 2. Kaplan-Meier Analysis of Time From Extubation to Reintubation



No. at risk

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

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

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

Use of HFNC in Stable COPD: Rationale and Physiology

- Improvement of lung mucociliary clearance
- Anatomical dead space and PaCO2 washout
- HFNC may provide a mild distending pressure
- Attenuation of inspiratory resistance
  - By providing adequate flow
  - By supplying adequately warmed and humidified gas

Compared to SB or Standard O2
- increase tidal volume
-decrease respiratory rate
-decrease minute ventilation

- Increase of expiratory resistance
- Matching patient's inspiratory flow (stable FiO2)
- Better comfort and quality of life

Pisani L et al **COPD: Journal of Chronic Obstructive Pulmonary Disease (Epub Ahead of Print 2017)**

Take-Home Message

HFNC in hypoxiemic ARF

- better than conventional, low-flow devices in terms of gas exchange, respiratory rate, inspiratory effort and comfort
- safer than face mask, with less interface displacement and less oxygen desaturations
- equivalent to NIV after extubation (prevention – treatment)
- equivalent to standard O_2 to prevent PPCs
- escalation of treatment (intubation) should not be delayed in patients not improving under NFNC

HFNC in COPD

- Potential benefits but large studies required

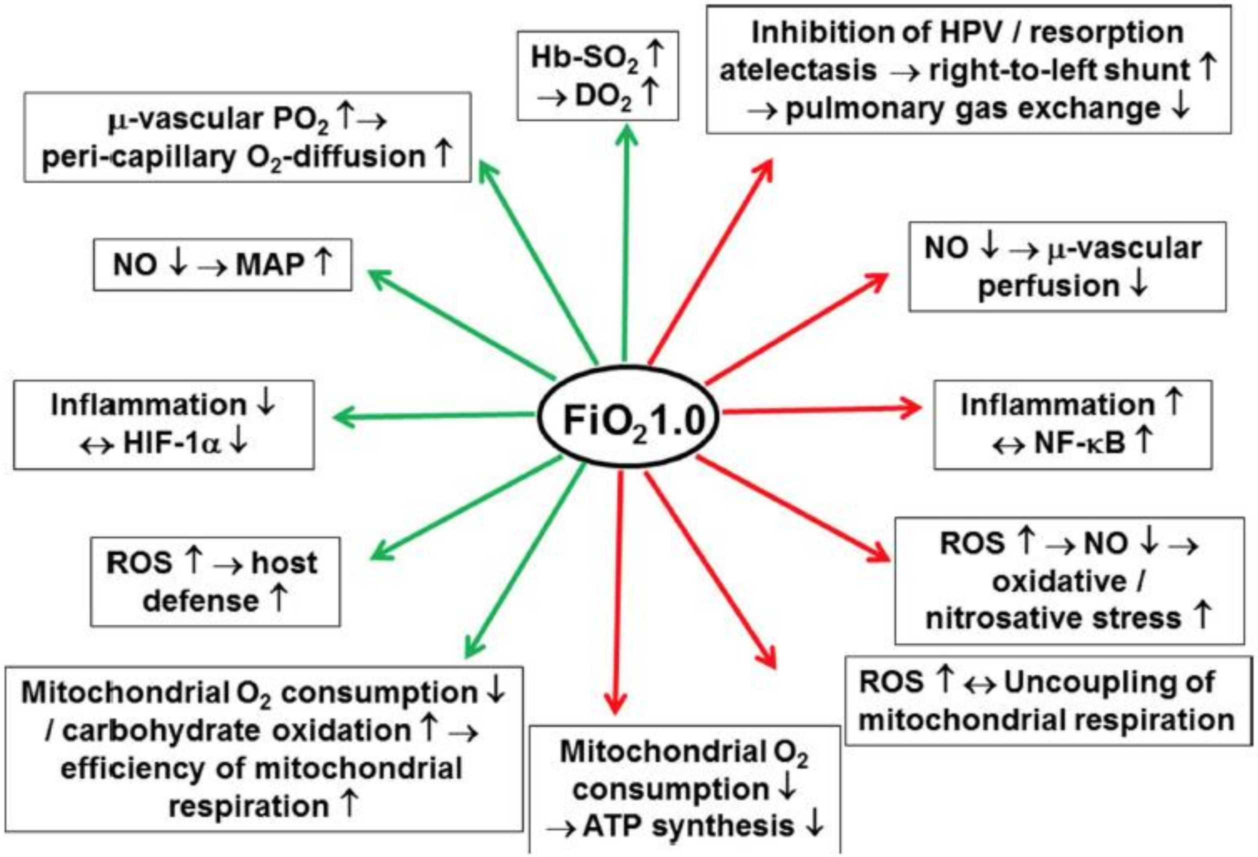
Subtopics:

- ❖New Sepsis Definition
- ❖Lung protective ventilation in non ARDS
- ❖ARDS: The LUNG SAFE
- ❖Mask vs Helmet for NIV in ARDS
- ❖High Flow Nasal Cannula in Hypoxiemic ARF
- ❖Oxygen therapy in critically ill patients

Oxygen therapy
in critically ill patients

State of the Art

Beneficial and negative effects of hyperoxia

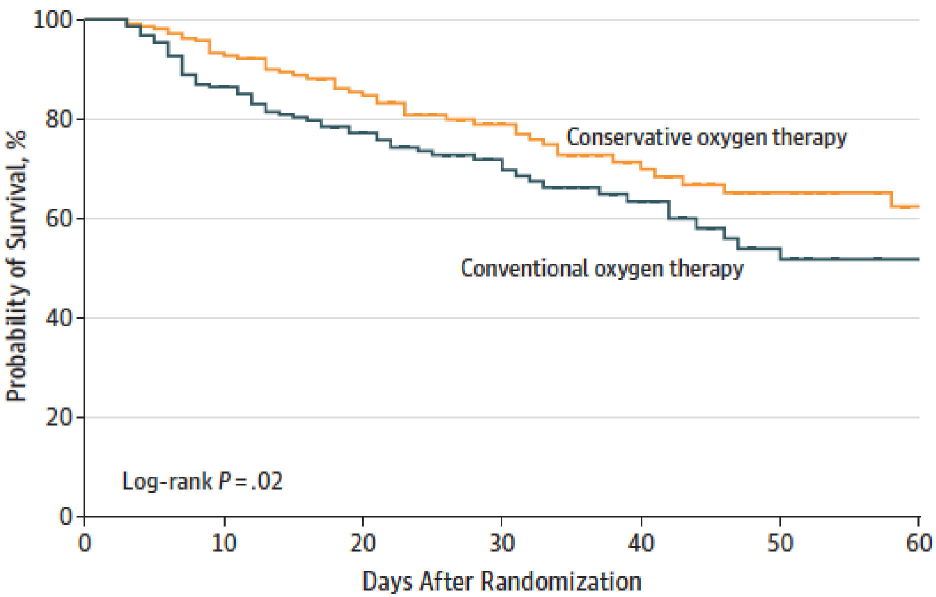


Hafner et al. Ann. Intensive Care (2015) 5:42

Conservative vs Conventional Oxygen Therapy on Mortality Among Patients in ICU

Conservative Group: PaO_2 between 70 and 100 mmHg or arterial oxyhemoglobin saturation (SpO_2) between 94% and 98%(conservative group)
***Conventional Group*:** according to standard ICU practice, to allow PaO_2 values up to 150 mmHg or SpO_2 values between 97%and 100%

	Oxygen Therapy, No. (%)			
	Conservative (n = 216)	Conventional (n = 218)	Absolute Risk Difference (95% CI)	*P* Value
Primary outcome				
ICU mortality	25 (11.6)	44 (20.2)	0.086 (0.017 to 0.150)	.01



No. at risk	0	10	20	30	40	50	60
Conservative oxygen therapy	216	201	188	181	173	170	169
Conventional oxygen therapy	218	189	172	163	158	152	152

Girardis M et al. JAMA. 2016 Oct 18;316(15):1583-1589

Conservative vs Conventional Oxygen Therapy on Mortality Among Patients in ICU

Secondary outcomes				
Hospital mortality	52 (24.2)	74 (33.9)	0.099 (0.013 to 0.182)	.03
New organ failure during ICU stay	41 (19.0)	56 (25.7)	0.067 (−0.012 to 0.145)	.09
Respiratory failure	14 (6.5)	14 (6.4)	−0.126 (−0.189 to −0.064)	.98
Shock	8 (3.7)	23 (10.6)	0.068 (0.020 to 0.120)	.006
Liver failure	4 (1.9)	14 (6.4)	0.046 (0.008 to 0.088)	.02
Renal failure	26 (12.0)	21 (9.6)	−0.024 (−0.084 to 0.035)	.42
New infections during ICU stay	39 (18.1)	50 (22.9)	0.049 (−0.027 to 0.124)	.21
Respiratory	30 (13.9)	37 (17.0)	0.031 (−0.038 to 0.099)	.37
Bacteremia	11 (5.1)	22 (10.1)	0.050 (0.000 to 0.090)	.049
Surgical site[a]	10 (7.2)	12 (9.1)	0.019 (−0.048 to 0.088)	.68
Surgical revision[a]	18 (12.9)	16 (12.1)	−0.008 (−0.088 to 0.073)	.84
Mechanical ventilation-free hours, median (IQR)	72 (35 to 110)	48 (24 to 96)	24 (0 to 46)	.02
ICU length of stay, median (IQR), d	6 (4 to 10)	6 (4 to 11)	0 (0 to 2)	.33
Hospital length of stay, median (IQR), d	21 (13 to 38)	21 (12 to 34)	0 (−5 to 1)	.21

Girardis M et al. JAMA. 2016 Oct 18;316(15):1583-1589

Take-Home Message

Oxygen Therapy in critically ill patients

- Among critically ill patients with an ICU length of stay of 72 hours or longer, a conservative protocol for oxygen therapy compared with conventional therapy resulted in a lower ICU mortality.

Liberation from Mechanical Ventilation: An Official American College of Chest Physicians/American Thoracic Society Clinical Practice Guideline

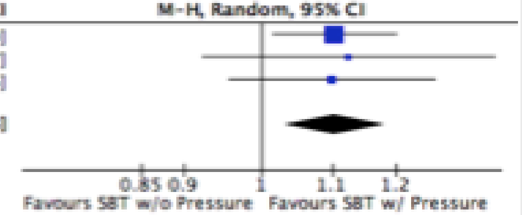
Quellette DR et al. CHEST (2016), doi: 10.1016/j.chest.2016.10.036

SBT with and without pressure

SBT, 1 — Successful SBT

Study or Subgroup	SBT with Pressure Events	SBT with Pressure Total	SBT without Pressure Events	SBT without Pressure Total	Weight	Risk Ratio M-H, Random, 95% CI
Esteban 1997	205	238	192	246	65.1%	1.10 [1.02, 1.20]
Haberthur 2002	54	60	24	30	11.6%	1.13 [0.92, 1.37]
Matic 2004	120	150	80	110	23.3%	1.10 [0.96, 1.26]
Total (95% CI)		**448**		**386**	**100.0%**	**1.11 [1.03, 1.18]**
Total events	379		296			

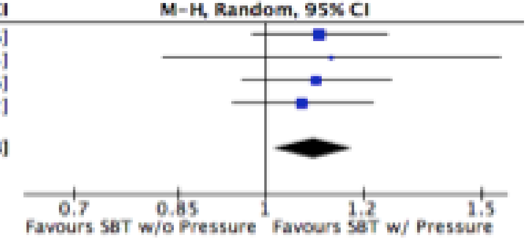
Heterogeneity: Tau² = 0.00; Chi² = 0.04, df = 2 (P = 0.98); I² = 0%
Test for overall effect: Z = 2.91 (P = 0.004)



SBT, 1 — Extubation Success

Study or Subgroup	SBT with Pressure Events	SBT with Pressure Total	SBT without Pressure Events	SBT without Pressure Total	Weight	Risk Ratio M-H, Random, 95% CI
Esteban 1997	167	238	156	246	34.5%	1.11 [0.98, 1.26]
Haberthur 2002	43	60	19	30	5.5%	1.13 [0.83, 1.55]
Matic 2004	120	150	80	110	28.1%	1.10 [0.96, 1.26]
Zhang 2014	78	93	90	115	31.8%	1.07 [0.94, 1.22]
Total (95% CI)		**541**		**501**	**100.0%**	**1.09 [1.02, 1.18]**
Total events	408		345			

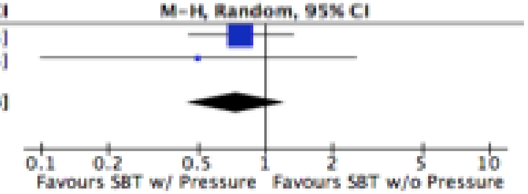
Heterogeneity: Tau² = 0.00; Chi² = 0.18, df = 3 (P = 0.98); I² = 0%
Test for overall effect: Z = 2.40 (P = 0.02)



SBT, 1 — Short-Term Mortality

Study or Subgroup	SBT with Pressure Events	SBT with Pressure Total	SBT without Pressure Events	SBT without Pressure Total	Weight	Risk Ratio M-H, Random, 95% CI
Esteban 1997	21	238	28	246	90.1%	0.78 [0.45, 1.33]
Matic 2004	2	30	4	30	9.9%	0.50 [0.10, 2.53]
Total (95% CI)		**268**		**276**	**100.0%**	**0.74 [0.45, 1.24]**
Total events	23		32			

Heterogeneity: Tau² = 0.00; Chi² = 0.25, df = 1 (P = 0.61); I² = 0%
Test for overall effect: Z = 1.15 (P = 0.25)



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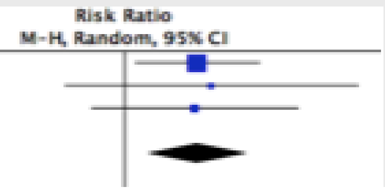
Quellette DR et al. CHEST (2016), doi: 10.1016/j.chest.2016.10.036

SBT with and without pressure

		Study or Subgroup	SBT with Pressure Events	SBT with Pressure Total	SBT without Pressure Events	SBT without Pressure Total	Weight	Risk Ratio M-H, Random, 95% CI
SBT, 1	Successful SBT	Esteban 1997	205	238	192	246	65.1%	1.10 [1.02, 1.20]
		Haberthur 2002	54	60	24	30	11.6%	1.13 [0.92, 1.37]
		Matic 2004	120	150	80	110	23.3%	1.10 [0.96, 1.26]
		Total (95% CI)		448		386	100.0%	1.11 [1.03, 1.18]
		Total events	379		296			

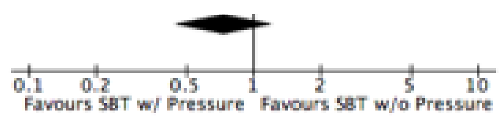


1. **For acutely hospitalized patients ventilated more than 24 hours, we suggest that the initial SBT be conducted with inspiratory pressure augmentation (5-8 cm H_2O) rather than without (T-piece or CPAP).** (Conditional recommendation, Moderate quality evidence)

   Remarks: This recommendation relates to how to conduct the initial SBT, but does not inform how to ventilate prolonged weaning patients between SBTs.

SBT, 1	Term Mortality	Total (95% CI)		268		276	100.0%	0.74 [0.45, 1.24]
		Total events	23		32			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.25$, df = 1 (P = 0.61); $I^2 = 0\%$
Test for overall effect: Z = 1.15 (P = 0.25)



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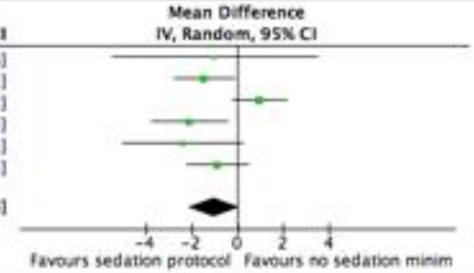
Protocolized sedation vs no sedation minimization

Sedation, 2 — Duration of Ventilation

Study or Subgroup	Protocolized Sedation Mean	SD	Total	No Sedation Minimization Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Anifantaki 2009	7.7	13.5	49	8.7	8.35	48	5.3%	-1.00 [-5.46, 3.46]
Brook 1999	3.71	5.57	162	5.17	6.4	159	21.3%	-1.46 [-2.77, -0.15]
Bucknall 2008	4.83	6.1	153	3.89	4.3	159	22.5%	0.94 [-0.24, 2.12]
Girard 2008	7.1	7	167	9.2	8.4	168	18.2%	-2.10 [-3.76, -0.44]
Kress 2000	4.9	4.52	68	7.3	9.41	60	11.6%	-2.40 [-5.01, 0.21]
Mansouri 2013	0.79	1.8	96	1.67	6.7	105	21.1%	-0.88 [-2.21, 0.45]
Total (95% CI)			**695**			**699**	**100.0%**	**-1.00 [-2.14, 0.14]**

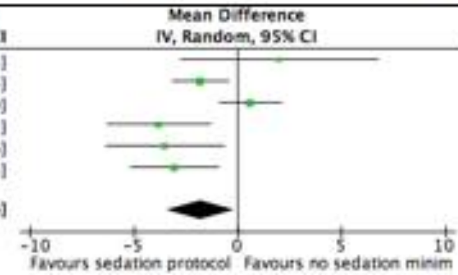
Heterogeneity: Tau² = 1.14; Chi² = 13.20, df = 5 (P = 0.02); I² = 62%
Test for overall effect: Z = 1.72 (P = 0.09)



Sedation, 2 — ICU LOS

Study or Subgroup	Protocolized Sedation Mean	SD	Total	No Sedation Minimization Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Anifantaki 2009	14	13.5	49	12	10.17	48	8.1%	2.00 [-2.75, 6.75]
Brook 1999	5.7	5.9	162	7.5	6.5	159	21.9%	-1.80 [-3.16, -0.44]
Bucknall 2008	6.6	7.2	153	6	6.2	159	21.2%	0.60 [-0.89, 2.09]
Girard 2008	9.1	9.4	167	12.9	13.48	168	16.2%	-3.80 [-6.29, -1.31]
Kress 2000	6.4	6	68	9.9	9.7	60	14.5%	-3.50 [-6.34, -0.66]
Mansouri 2013	4.04	4.15	96	7.08	10.12	105	18.1%	-3.04 [-5.15, -0.93]
Total (95% CI)			**695**			**699**	**100.0%**	**-1.78 [-3.41, -0.14]**

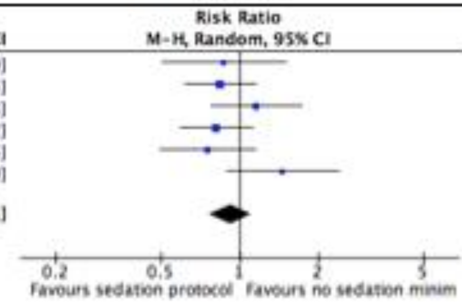
Heterogeneity: Tau² = 2.71; Chi² = 17.11, df = 5 (P = 0.004); I² = 71%
Test for overall effect: Z = 2.13 (P = 0.03)



Sedation, 2 — Short-Term Mortality

Study or Subgroup	Protocolized Sedation Events	Total	No Sedation Minimization Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Anifantaki 2009	16	49	18	48	9.9%	0.87 [0.51, 1.50]
Brook 1999	49	162	57	159	23.7%	0.84 [0.62, 1.15]
Bucknall 2008	39	153	35	159	16.5%	1.16 [0.78, 1.73]
Girard 2008	47	167	58	168	23.0%	0.82 [0.59, 1.12]
Kress 2000	24	68	28	60	15.2%	0.76 [0.50, 1.15]
Mansouri 2013	28	96	21	105	11.7%	1.46 [0.89, 2.39]
Total (95% CI)		**695**		**699**	**100.0%**	**0.93 [0.77, 1.11]**
Total events	203		217			

Heterogeneity: Tau² = 0.01; Chi² = 6.38, df = 5 (P = 0.27); I² = 22%
Test for overall effect: Z = 0.81 (P = 0.42)



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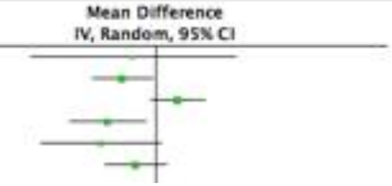
Protocolized sedation vs no sedation minimization

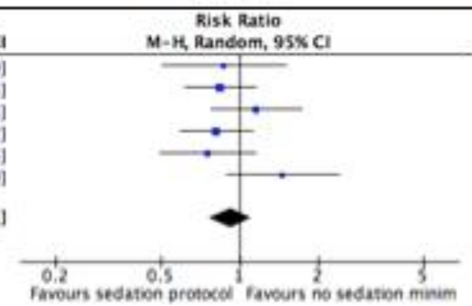
		Study or Subgroup	Protocolized Sedation Mean	SD	Total	No Sedation Minimization Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Sedation, 2	Duration of Ventilation	Anifantaki 2009	7.7	13.5	49	8.7	8.35	48	5.3%	-1.00 [-5.46, 3.46]
		Brook 1999	3.71	5.57	162	5.17	6.4	159	21.3%	-1.46 [-2.77, -0.15]
		Bucknall 2008	4.83	6.1	153	3.89	4.3	159	22.5%	0.94 [-0.24, 2.12]
		Girard 2008	7.1	7	167	9.2	8.4	168	18.2%	-2.10 [-3.76, -0.44]
		Kress 2000	4.9	4.52	68	7.3	9.41	60	11.6%	-2.40 [-5.01, 0.21]
		Mansouri 2013	0.79	1.8	96	1.67	6.7	105	21.1%	-0.88 [-2.21, 0.45]



2. For acutely hospitalized patients ventilated for more than 24 hours, we suggest protocols attempting to minimize sedation. (Conditional recommendation, Low quality of evidence)

Remarks: There is insufficient evidence to recommend any protocol over another.

		Study or Subgroup	Protocolized Sedation Events	Total	No Sedation Minimization Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Sedation, 2	Short-Term Mortality	Anifantaki 2009	16	49	18	48	9.9%	0.87 [0.51, 1.50]
		Brook 1999	49	162	57	159	23.7%	0.84 [0.62, 1.15]
		Bucknall 2008	39	153	35	159	16.5%	1.16 [0.78, 1.73]
		Girard 2008	47	167	58	168	23.0%	0.82 [0.59, 1.12]
		Kress 2000	24	68	28	60	15.2%	0.76 [0.50, 1.15]
		Mansouri 2013	28	96	21	105	11.7%	1.46 [0.89, 2.39]
		Total (95% CI)		**695**		**699**	**100.0%**	**0.93 [0.77, 1.11]**
		Total events	203		217			
		Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 6.38$, df = 5 (P = 0.27); $I^2 = 22\%$						
		Test for overall effect: Z = 0.81 (P = 0.42)						



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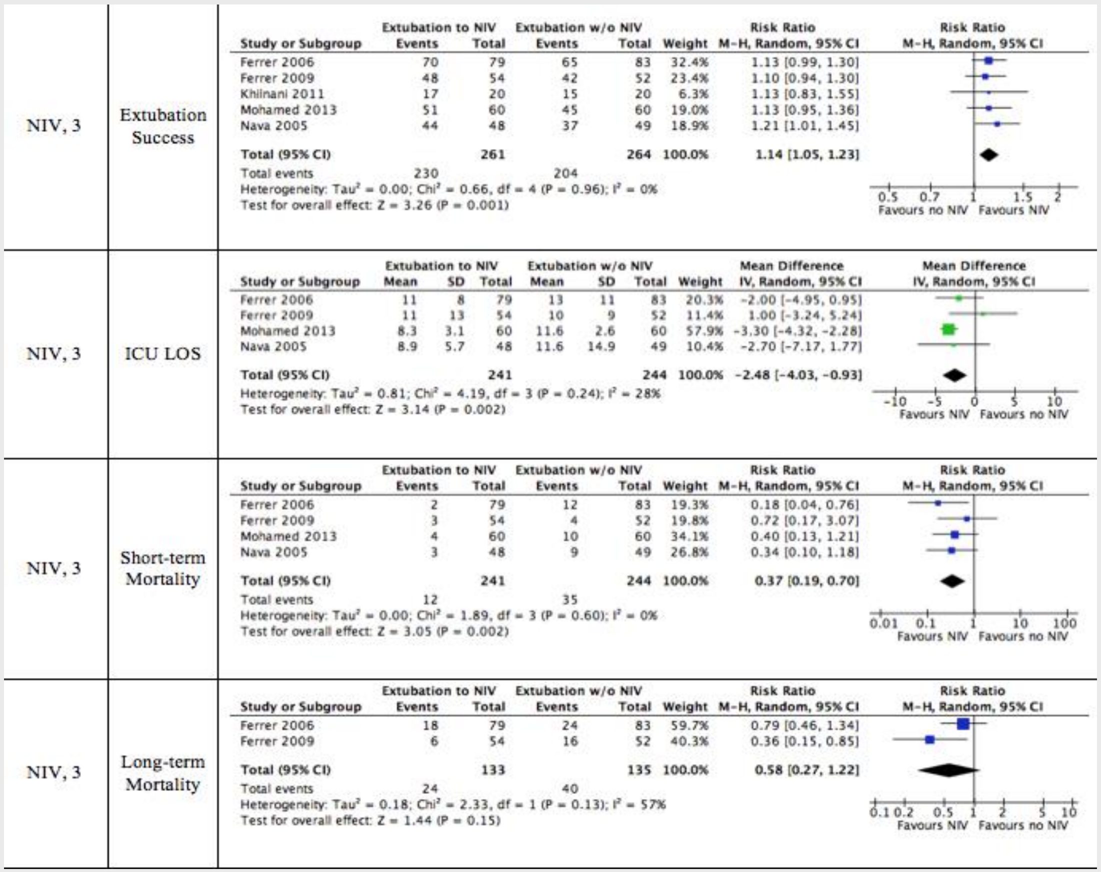
Quellette DR et al. CHEST (2016), doi: 10.1016/j.chest.2016.10.036

Extubation with and without NIV



NIV, 3 — Extubation Success

Study or Subgroup	Extubation to NIV Events	Extubation to NIV Total	Extubation w/o NIV Events	Extubation w/o NIV Total	Weight	Risk Ratio M-H, Random, 95% CI
Ferrer 2006	70	79	65	83	32.4%	1.13 [0.99, 1.30]
Ferrer 2009	48	54	42	52	23.4%	1.10 [0.94, 1.30]
Khilnani 2011	17	20	15	20	6.3%	1.13 [0.83, 1.55]
Mohamed 2013	51	60	45	60	19.0%	1.13 [0.95, 1.36]
Nava 2005	44	48	37	49	18.9%	1.21 [1.01, 1.45]
Total (95% CI)		**261**		**264**	**100.0%**	**1.14 [1.05, 1.23]**
Total events	230		204			

Heterogeneity: Tau² = 0.00; Chi² = 0.66, df = 4 (P = 0.96); I² = 0%
Test for overall effect: Z = 3.26 (P = 0.001)

NIV, 3 — ICU LOS

Study or Subgroup	Extubation to NIV Mean	SD	Total	Extubation w/o NIV Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Ferrer 2006	11	8	79	13	11	83	20.3%	-2.00 [-4.95, 0.95]
Ferrer 2009	11	13	54	10	9	52	11.4%	1.00 [-3.24, 5.24]
Mohamed 2013	8.3	3.1	60	11.6	2.6	60	57.9%	-3.30 [-4.32, -2.28]
Nava 2005	8.9	5.7	48	11.6	14.9	49	10.4%	-2.70 [-7.17, 1.77]
Total (95% CI)			**241**			**244**	**100.0%**	**-2.48 [-4.03, -0.93]**

Heterogeneity: Tau² = 0.81; Chi² = 4.19, df = 3 (P = 0.24); I² = 28%
Test for overall effect: Z = 3.14 (P = 0.002)

NIV, 3 — Short-term Mortality

Study or Subgroup	Extubation to NIV Events	Extubation to NIV Total	Extubation w/o NIV Events	Extubation w/o NIV Total	Weight	Risk Ratio M-H, Random, 95% CI
Ferrer 2006	2	79	12	83	19.3%	0.18 [0.04, 0.76]
Ferrer 2009	3	54	4	52	19.8%	0.72 [0.17, 3.07]
Mohamed 2013	4	60	10	60	34.1%	0.40 [0.13, 1.21]
Nava 2005	3	48	9	49	26.8%	0.34 [0.10, 1.18]
Total (95% CI)		**241**		**244**	**100.0%**	**0.37 [0.19, 0.70]**
Total events	12		35			

Heterogeneity: Tau² = 0.00; Chi² = 1.89, df = 3 (P = 0.60); I² = 0%
Test for overall effect: Z = 3.05 (P = 0.002)

NIV, 3 — Long-term Mortality

Study or Subgroup	Extubation to NIV Events	Extubation to NIV Total	Extubation w/o NIV Events	Extubation w/o NIV Total	Weight	Risk Ratio M-H, Random, 95% CI
Ferrer 2006	18	79	24	83	59.7%	0.79 [0.46, 1.34]
Ferrer 2009	6	54	16	52	40.3%	0.36 [0.15, 0.85]
Total (95% CI)		**133**		**135**	**100.0%**	**0.58 [0.27, 1.22]**
Total events	24		40			

Heterogeneity: Tau² = 0.18; Chi² = 2.33, df = 1 (P = 0.13); I² = 57%
Test for overall effect: Z = 1.44 (P = 0.15)

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Quellette DR et al. CHEST (2016), doi: 10.1016/j.chest.2016.10.036

Extubation with and without NIV

3. **For patients at high risk for extubation failure who have been receiving mechanical ventilation for more than 24 hours, and who have passed an SBT, we recommend extubation to preventative NIV** (Strong recommendation, moderate quality of evidence).

   Remarks: Patients at high risk for failure of extubation may include those patients with hypercapnia, COPD, CHF, or other serious co-morbidities. Physicians may choose to avoid extubation to NIV in selected patients for patient-specific factors including but not limited to the inability to receive ventilation through a mask or similar interface. Physicians who choose to use NIV should apply such treatment immediately after extubation to realize the outcome benefits.

List of Abbreviations

- ΔP: Driving Pressure
- LIS: Lung Injury Score
- PEEP: Positive End-Expiratory Pressure

List of References

1. CDC Vital Signs www.cdc.gov/vitalsigns/sepsis
2. Singer M et al. JAMA. 2016 Feb 23;315(8):801-10.
3. Seymour CW et al. JAMA. 2016 Feb 23;315(8):762-74
4. Shankar-Hari M etal. JAMA. 2016 Feb 23;315(8):775-87
5. Vincent et al., Lancet Respir Med 2016. Online Feb. 22
6. Seymour CW et al published on line May 21 – 2017
7. Yadav H et al. Am J Respir Crit Care Med 2017;195(6):725-736
8. Gajic O et al Am J Respir Crit Care Med 183:462–470, 2011
9. Serpa-Neto A et al. Lancet Respir Med. 2016;4(11):882-893
10. ARDS Task Force JAMA 2012 Jun 20;307(23):2526-33
11. Bellani G et al. JAMA Feb 23 2016, 315 (8): 788-800
12. Laffey JG et al. Intensive Care Med. 2016;42(12):1865-1876

List of References

13. Bellani G et al. Am J Respir Crit Care Med 2017;195(1):67-77
14. Bello G et al. Clin Chest Med. 2016 Dec;37(4):711-721
15. Patel BK et al. JAMA. 2016 Jun 14;315(22):2435-41
16. O'Driscoll BR et al. Thorax 2008;63 (suppl VI):1-68
17. Papazian L et al. Intensive Care Med. 2016;42(9):1336-49
18. Jaber S et al. Intensive Care Med (2016) 42:1877–1887
19. Frat J-P et al. NEJM 2015;372:2185-96
20. Hernandez G et al. JAMA. 2016;316(15):1565-1574
21. Pisani L et al COPD: Journal of Chronic Obstructive Pulmonary Disease (Epub Ahead of Print 2017)
22. Hafner et al. Ann. Intensive Care (2015) 5:42;

List of References

23. Girardis M et al. JAMA. 2016 Oct 18;316(15):1583-1589

24. Umbrello M et al. Respir Care. 2016 Apr;61(4):542-55

25. Zambon M et al. Intensive Care Med. 2017 Jan;43(1):29-38

26. Chiumello D et al. Respir Care. 2016 May;61(5):689-99

27. Herridge MS et al. Am J Respir Crit Care Med. 2016 Oct 1;194(7):831-844

23. Quellette DR et al. CHEST (2016), doi: 10.1016/j.chest.2016.10.036