Update of Management of ARDS

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Definition

- Acute onset
- Noncardiogenic pulmonary oedema
- Hypoxaemia
- The need for mechanical ventilation

2012 Berlin definition

- Timing: respiratory failure within 1 week of a known insult or new and/or worsening respiratory symptoms

- Origin: respiratory failure not fully explained by cardiac function or volume overload (need objective criterion such as echocardiography to exclude hydrostatic oedema if no risk factor is present)

- Imaging: bilateral opacities on chest radiograph or CT not fully explained by effusion, collapse or nodules

- Oxygenation: acute onset of hypoxaemia defined as PaO2/FiO2 <300 mmHg on at least PEEP 5 cmH2Oa

-- PaO2/FiO2 of 201–300 mmHg is mild ARDS

-- PaO2/FiO2 of 101–200 mmHg is moderate ARDS

-- PaO2/FiO2 ≤100 mmHg is severe ARDS

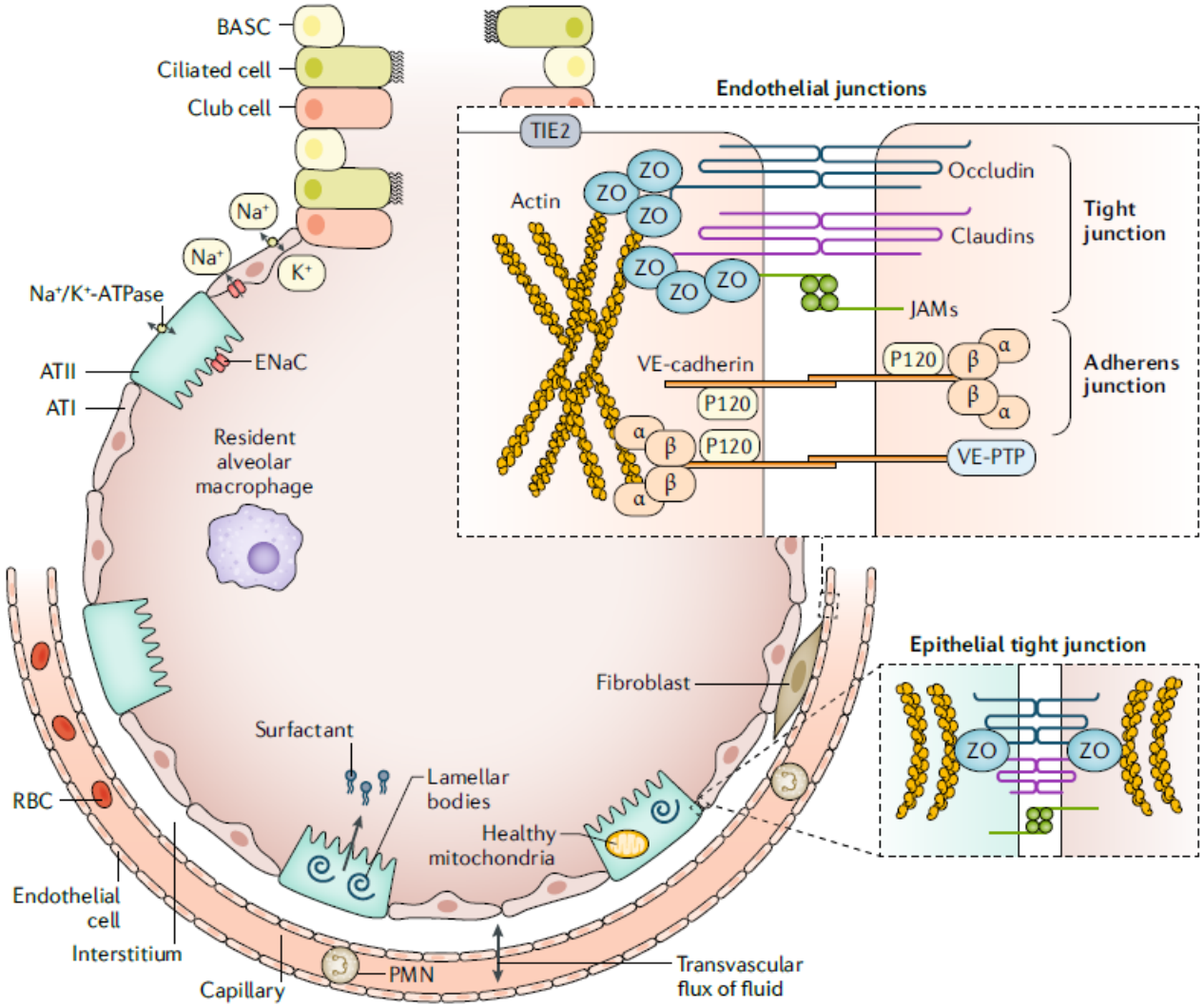
2016 Kigali modification

- Timing and origin: as in the Berlin definition

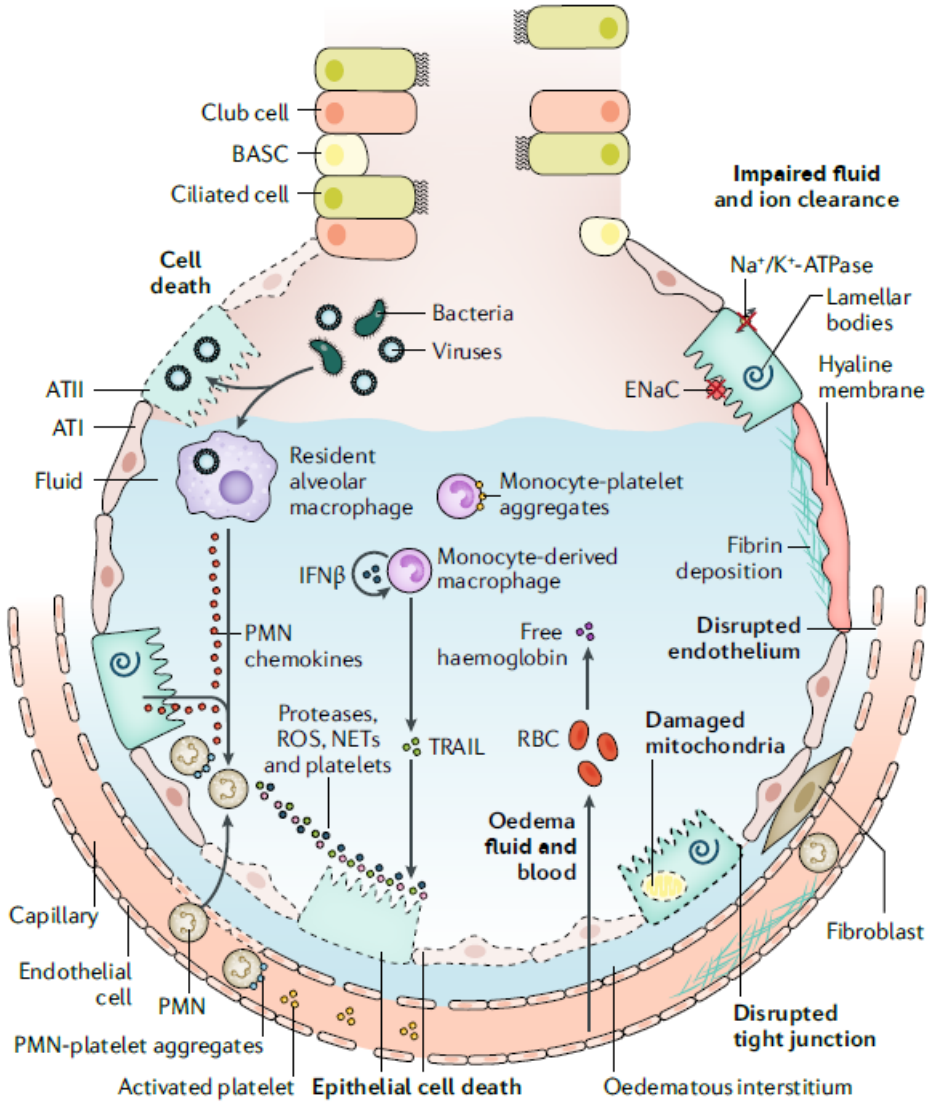
- Imaging: bilateral opacities on chest radiography or ultrasonography scan not fully explained by effusion, collapse or nodules

- Oxygenation: SpO_2/FiO_2 <315; no PEEP requirement

Normal alveolus



Injured alveolus



Nat Rev Dis Primers. 2019 Mar 14;5(1):18.

Biomarkers associated with ARDS

- **Epithelial markers (principal source)**
  - Receptor for advanced glycation end products (alveolar epithelial type 1 cells)
  - Surfactant protein D (alveolar epithelial type 2 cells)
  - Club cell 16 (airway epithelial cells)
- **Endothelial markers (principal source)**
  - von Willebrand factor (endothelium and platelets)
  - Angiopoietin 2 (endothelium and platelets)
  - Intercellular adhesion molecule 1 (endothelium, epithelium and macrophages)
  - Syndecan (endothelial glycocalyx)
  - Endocan (endothelium)

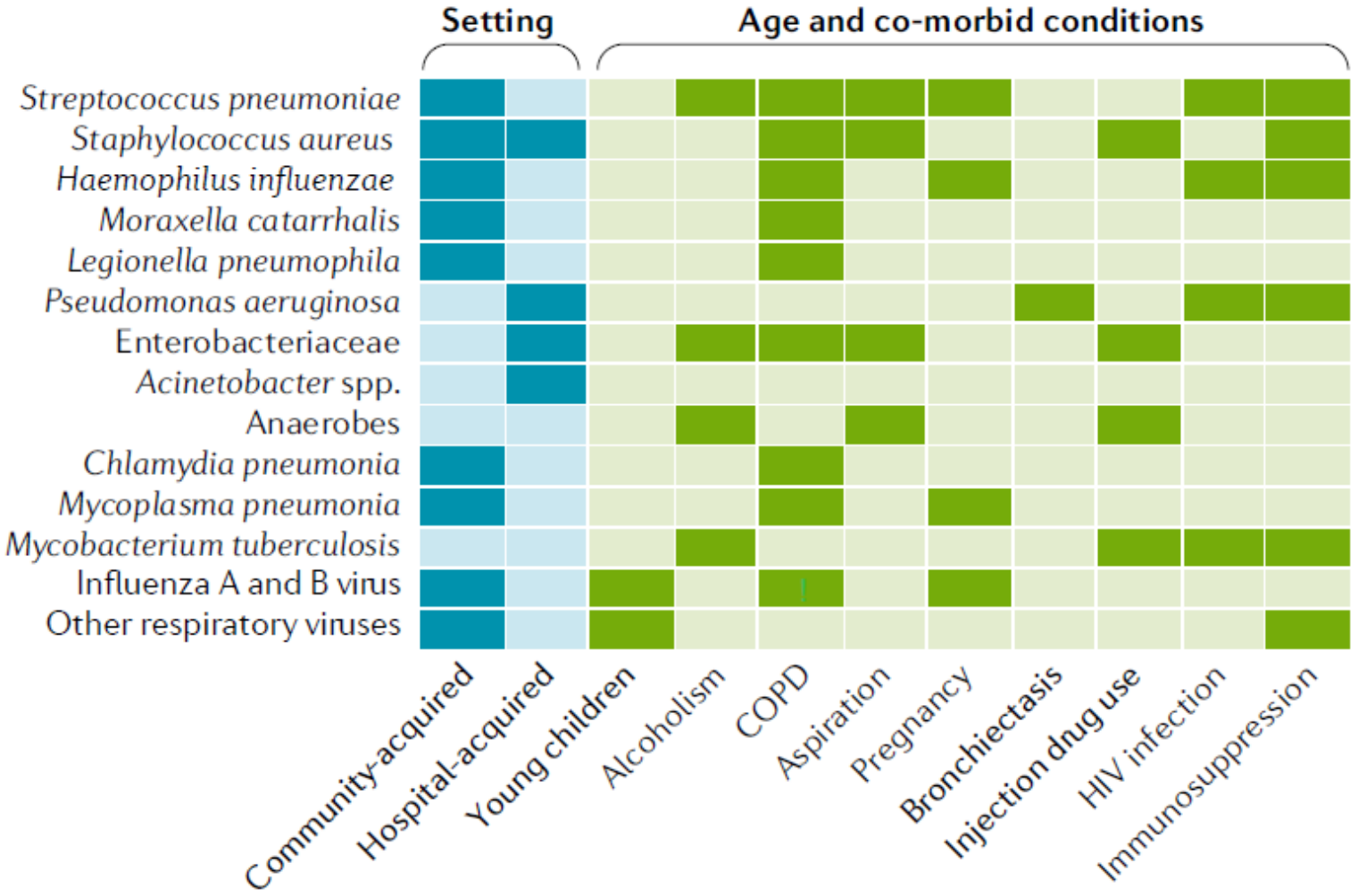
Nat Rev Dis Primers. 2019 Mar 14;5(1):18.

Biomarkers associated with ARDS

- **Inflammatory markers (principal source)**
  - IL-6 (monocytes, macrophages, neutrophils and alveolar epithelium)
  - IL-8 (monocytes, macrophages, endothelium and alveolar epithelium)
  - Soluble tumour necrosis factor receptor 1 (alveolar epithelial type 1 and type 2 cells and macrophages)
  - IL-1β, IL-1 R antagonist (monocytes, macrophages and alveolar epithelium)
  - Neutrophil extracellular traps (neutrophils)
- **Coagulation and fibrinolysis markers (principal source)**
  - Protein C (plasma)
  - Plasminogen activator inhibitor 1 (endothelium and macrophages)
- **Apoptosis markers (principal source)**
  - FAS and FasL (endothelium, alveolar epithelium and inflammatory cells)

Nat Rev Dis Primers. 2019 Mar 14;5(1):18.

Common respiratory pathogens in ARDS and associated demographic features and comorbidities



Nat Rev Dis Primers. 2019 Mar 14;5(1):18.

Prevention

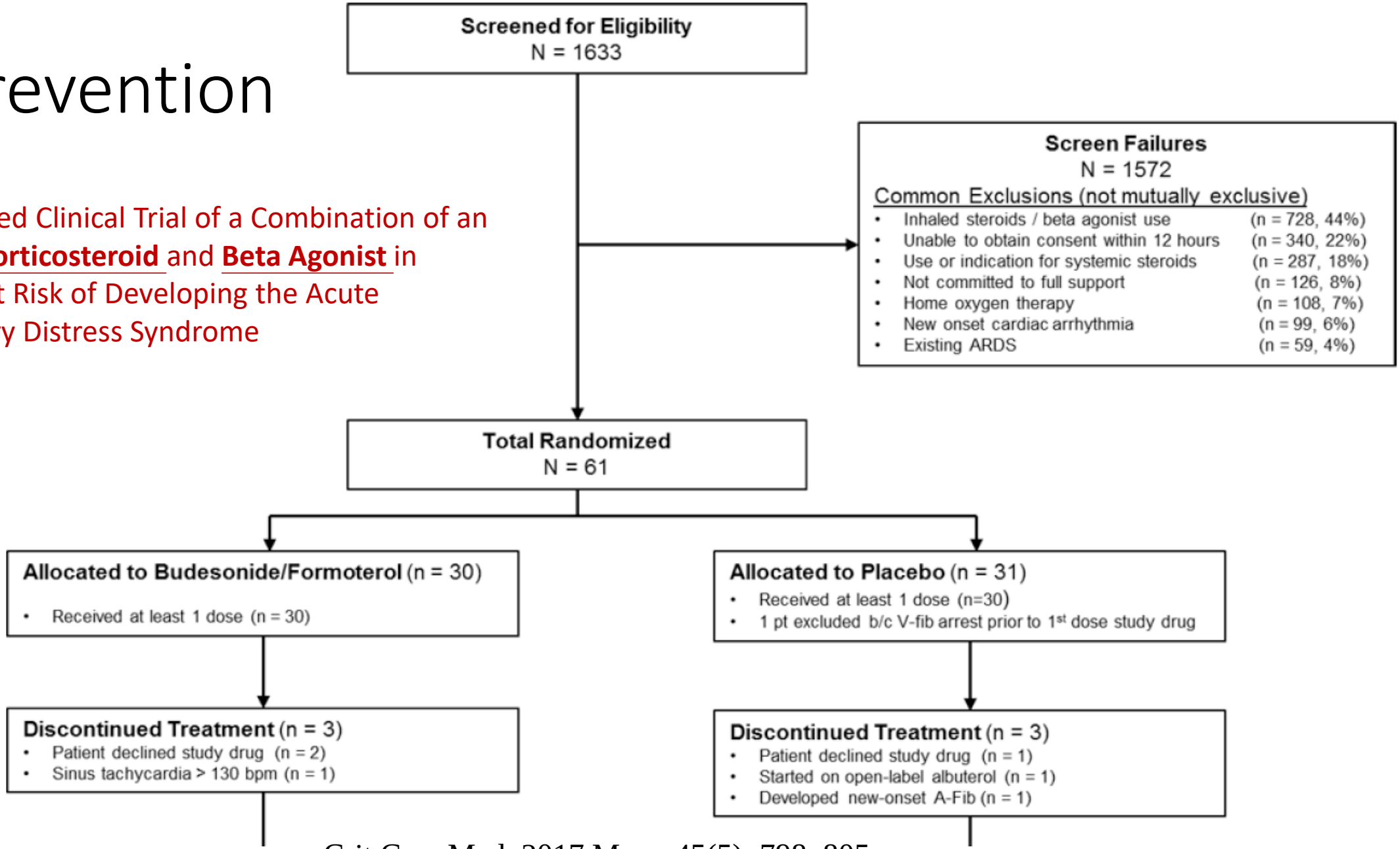
- **Steroid (negative results)**
- Ineffectiveness of high- dose methylprednisolone in preventing parenchymal lung injury and improving mortality in patients with septic shock. Am. Rev. Respir. Dis. 138, 62–68 (1988).
- Early steroid therapy for respiratory failure. *Arch. Surg.* **120**, 536–540 (1985).

Prevention

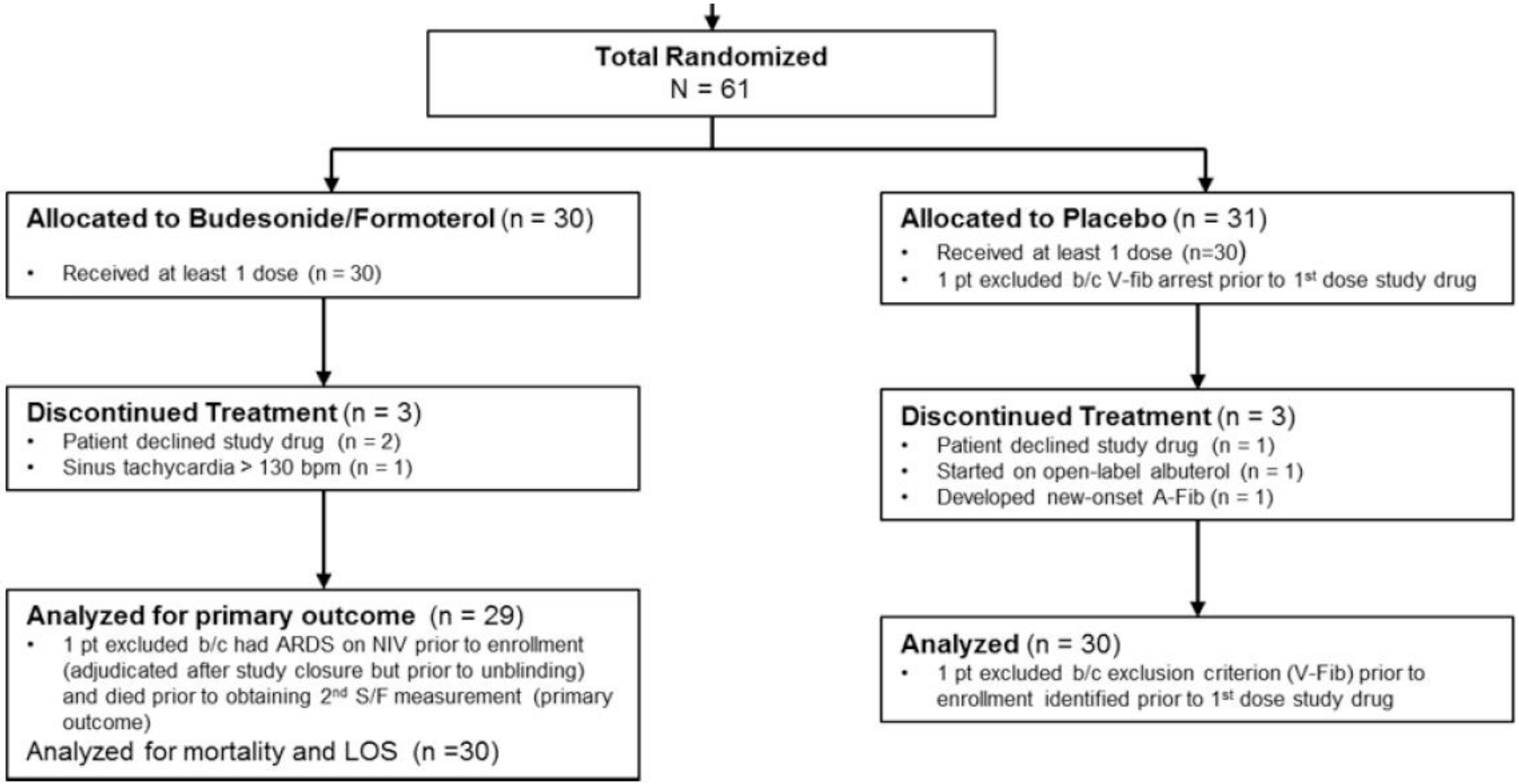
- **Aspirin**
- Effect of aspirin on development of ARDS in at- risk patients presenting to the emergency department: the LIPS- A randomized clinical trial. JAMA 315, 2406–2414 (2016).
- 7673 patients→ 7273 excluded→ 400 patients randomized
- Aspirin did not reduce the risk of ARDS at 7 days.

Prevention

Randomized Clinical Trial of a Combination of an **Inhaled Corticosteroid** and **Beta Agonist** in Patients at Risk of Developing the Acute Respiratory Distress Syndrome

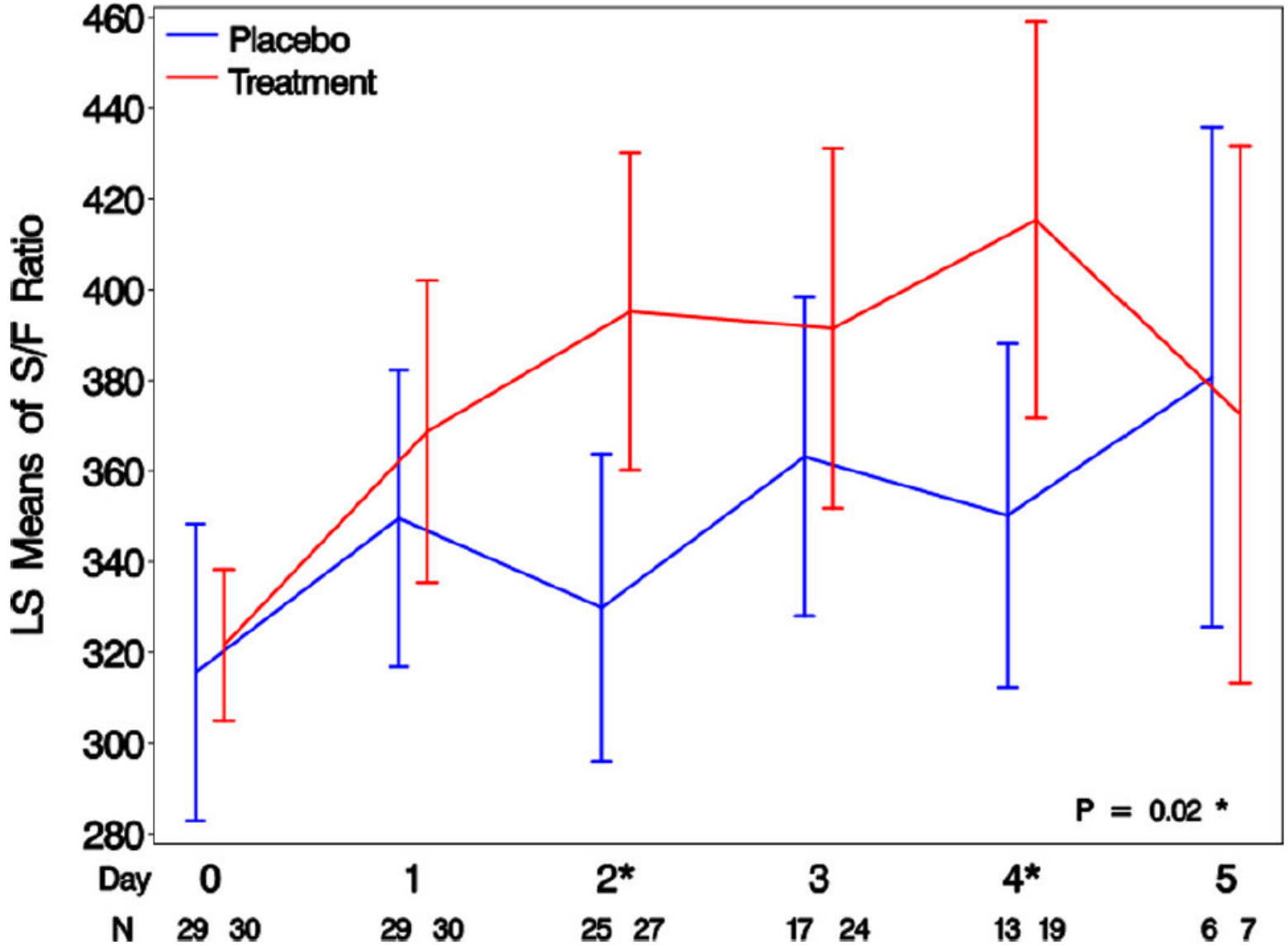


Crit Care Med. 2017 May ; 45(5): 798–805.



Crit Care Med. 2017 May ; 45(5): 798–805.

least square (LS) means of saturation divided by FiO2 (S/F) ratio



Crit Care Med. 2017 May ; 45(5): 798–805.

An Official American Thoracic Society/European Society of Intensive Care Medicine/Society of Critical Care Medicine Clinical Practice Guideline: Mechanical Ventilation in Adult Patients with Acute Respiratory Distress Syndrome

- ARDS: the recommendation is strong for mechanical ventilation using lower tidal volumes (4–8 ml/kg predicted bodyweight) and lower inspiratory pressures (plateau pressure,30 cm H2O)

  (moderate confidence in effect estimates).

- severe ARDS: the recommendation is strong for prone positioning for more than 12 h/d

  (moderate confidence in effect estimates).

Am J Respir Crit Care Med. 2017 May 1;195(9):1253-1263.

An Official American Thoracic Society/European Society of Intensive Care Medicine/Society of Critical Care Medicine Clinical Practice Guideline: Mechanical Ventilation in Adult Patients with Acute Respiratory Distress Syndrome

- moderate or severe ARDS:

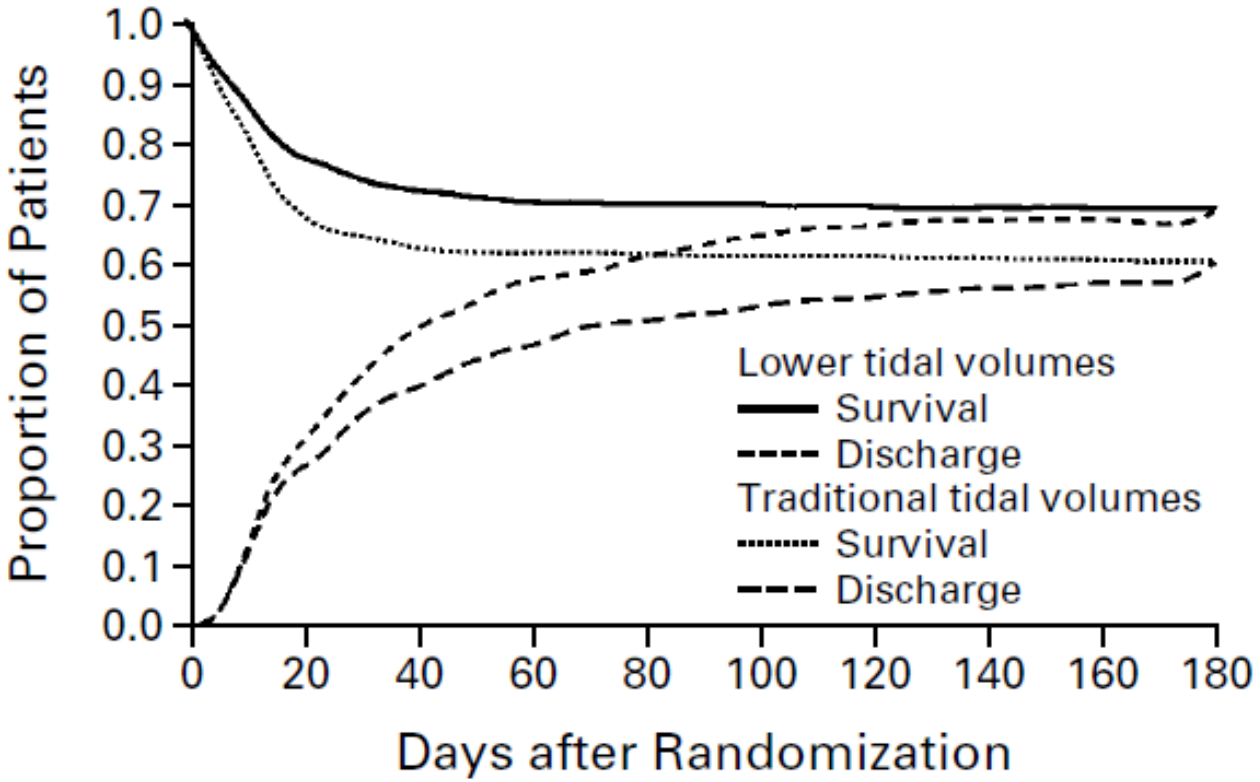
  strong against routine use of high-frequency oscillatory ventilation (high confidence in effect estimates)

  conditional for higher positive end-expiratory pressure (moderate confidence in effect estimates) and recruitment maneuvers (low confidence in effect estimates).

- Additional evidence is necessary to make a definitive recommendation for or against the use of extracorporeal membrane oxygenation in patients with severe ARDS

Am J Respir Crit Care Med. 2017 May 1;195(9):1253-1263.

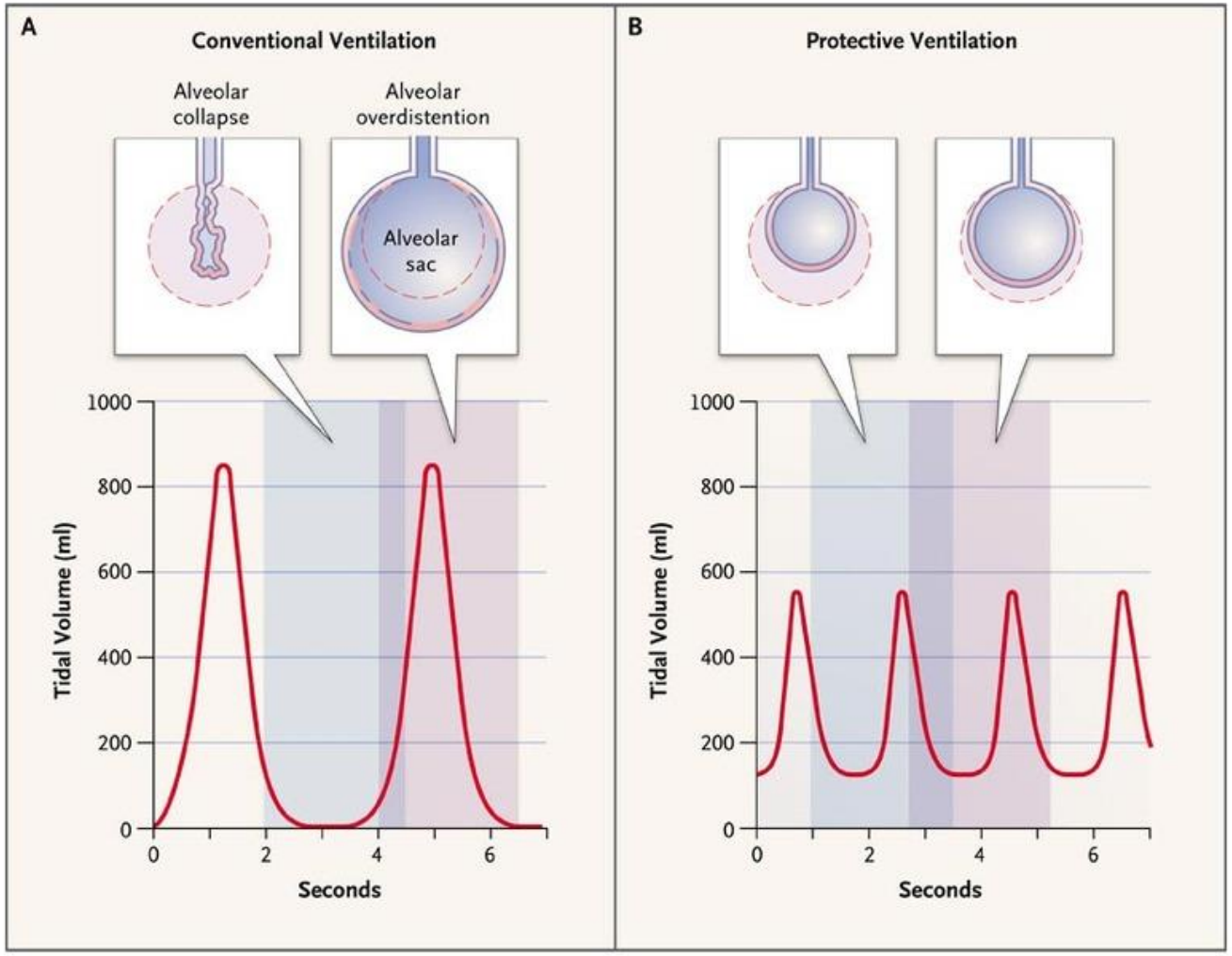
Treatment-low tidal volumes (6ml/kg)



Variable	Group Receiving Lower Tidal Volumes	Group Receiving Traditional Tidal Volumes	P Value
Death before discharge home and breathing without assistance (%)	31.0	39.8	0.007
Breathing without assistance by day 28 (%)	65.7	55.0	<0.001
No. of ventilator-free days, days 1 to 28	12±11	10±11	0.007
Barotrauma, days 1 to 28 (%)	10	11	0.43
No. of days without failure of nonpulmonary organs or systems, days 1 to 28	15±11	12±11	0.006

N Engl J Med 2000; 342:1301-1308

Treatment-low tidal volumes (6ml/kg)



https://www.nejm.org/doi/full/10.1056/nejmct074213

Low tidal volume ventilation in patients with acute respiratory distress syndrome

Initial ventilator settings	
Calculate predicted body weight (PBW)	
Male =	50 + 2.3 [height (inches) - 60] **OR**
	50 + 0.91 [height (cm) - 152.4]
Female =	45.5 + 2.3 [height (inches) - 60] **OR**
	45.5 + 0.91 [height (cm) - 152.4]
Set mode to volume assist-control	
Set initial tidal volume to 8 mL/kg PBW	
Reduce tidal volume to 7 and then to 6 mL/kg over 1 to 3 hours	
Set initial ventilator rate ≤35 breaths/min to match baseline minute ventilation	

Subsequent tidal volume adjustment
Plateau pressure goal: Pplat ≤30 cm H_2O
Check inspiratory plateau pressure with 0.5 second inspiratory pause at least every four hours and after each change in PEEP or tidal volume.
If Pplat >30 cm H_2O, decrease tidal volume in 1 mL/kg PBW steps to 5 or if necessary to 4 mL/kg PBW.
If Pplat <25 cm H_2O and tidal volume <6 mL/kg, increase tidal volume by 1 mL/kg PBW until Pplat >25 cm H_2O or tidal volume = 6 mL/kg.
If breath stacking (autoPEEP) or severe dyspnea occurs, tidal volume may be increased to 7 or 8 mL/kg PBW if Pplat remains ≤30 cm H_2O.

Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. N Engl J Med 2000; 342:1301

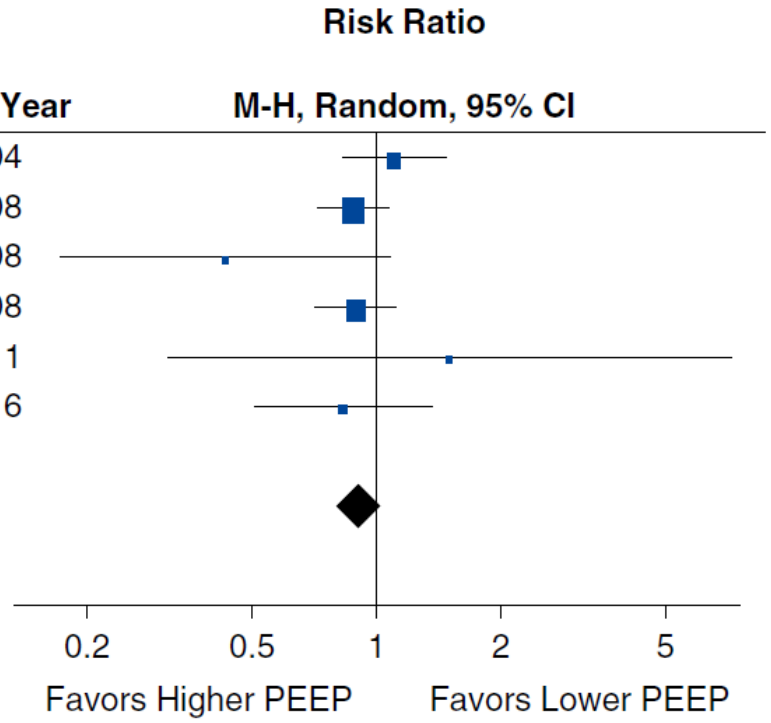
Treatment-higher PEEP

Mortality

Study or Subgroup	High Mortality Events	High Total Patients	Low Mortality Events	Low Total Patients	Weight	Risk Ratio M-H, Random, 95% CI	Year
Brower *et al.*, 2004	76	276	68	273	19.2%	1.11 [0.83, 1.46]	2004
Meade *et al.*, 2008	135	475	164	508	40.8%	0.88 [0.73, 1.06]	2008
Talmor *et al.*, 2008	5	30	12	31	1.9%	0.43 [0.17, 1.07]	2008
Mercat *et al.*, 2008	107	385	119	382	31.1%	0.89 [0.72, 1.11]	2008
Hodgson *et al.*, 2011	3	10	2	10	0.6%	1.50 [0.32, 7.14]	2011
Kacmarek *et al.*, 2016	22	99	27	101	6.4%	0.83 [0.51, 1.36]	2016
Total (95% CI)		**1275**		**1305**	**100.0%**	**0.91 [0.80, 1.03]**	
Total events	348		392				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 5.09$, df = 5 (P = 0.41); $I^2 = 2\%$

Test for overall effect: Z = 1.46 (P = 0.14)



Ann Am Thorac Soc. 2017 Oct;14(Supplement_4):S297-S303.

A higher PEEP strategy for ARDS of any severity

- **Not** significantly decrease barotrauma
- **Not** significantly decrease New organ failure
- **Not** significantly decrease ventilator-free days when compared with a lower PEEP strateg

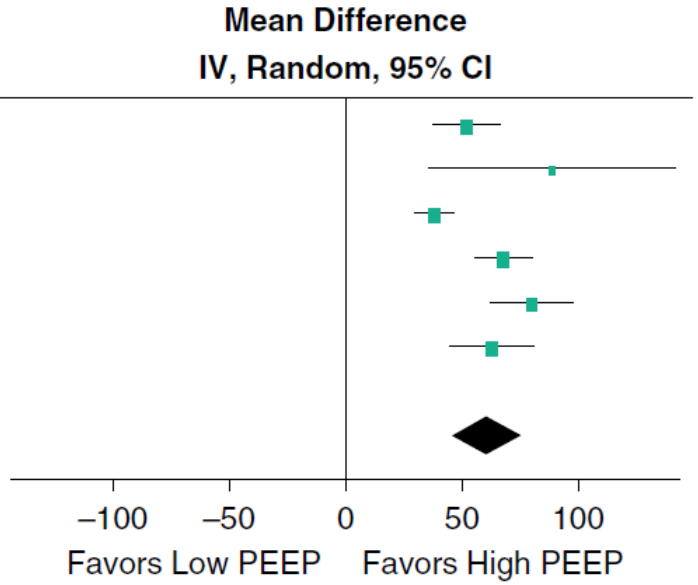
Ann Am Thorac Soc. 2017 Oct;14(Supplement_4):S297-S303.

Treatment-higher PEEP

Oxygenation

Study or Subgroup	High PEEP Mean	SD	Total	Low PEEP Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Year
Brower *et al.*, 2004	220	89	244	168	66	230	18.8%	52.00 [37.95, 66.05]	2004
Talmor *et al.*, 2008	280	126	29	191	71	29	6.1%	89.00 [36.36,141.64]	2008
Meade *et al.*, 2008	187.4	68.8	464	149.1	60.6	498	21.0%	38.30 [30.08, 46.52]	2008
Mercat *et al.*, 2008	218	97	378	150	69	371	19.6%	68.00 [55.96, 80.04]	2008
Hodgson *et al.*, 2011	220	20	10	140	20	10	17.3%	80.00 [62.47, 97.53]	2011
Kacmarek *et al.*, 2016	198.5	78.6	94	135.6	43.5	101	17.1%	62.90 [44.89, 80.91]	2016
Total (95% CI)			**1219**			**1239**	**100.0%**	**61.24 [45.92, 76.57]**	

Heterogeneity: $Tau^2 = 273.32$; $Chi^2 = 30.33$, df = 5 ($P < 0.0001$); $I^2 = 84\%$
Test for overall effect: $Z = 7.83$ ($P < 0.00001$)



Ann Am Thorac Soc. 2017 Oct;14(Supplement_4):S297-S303.

Higher PEEP

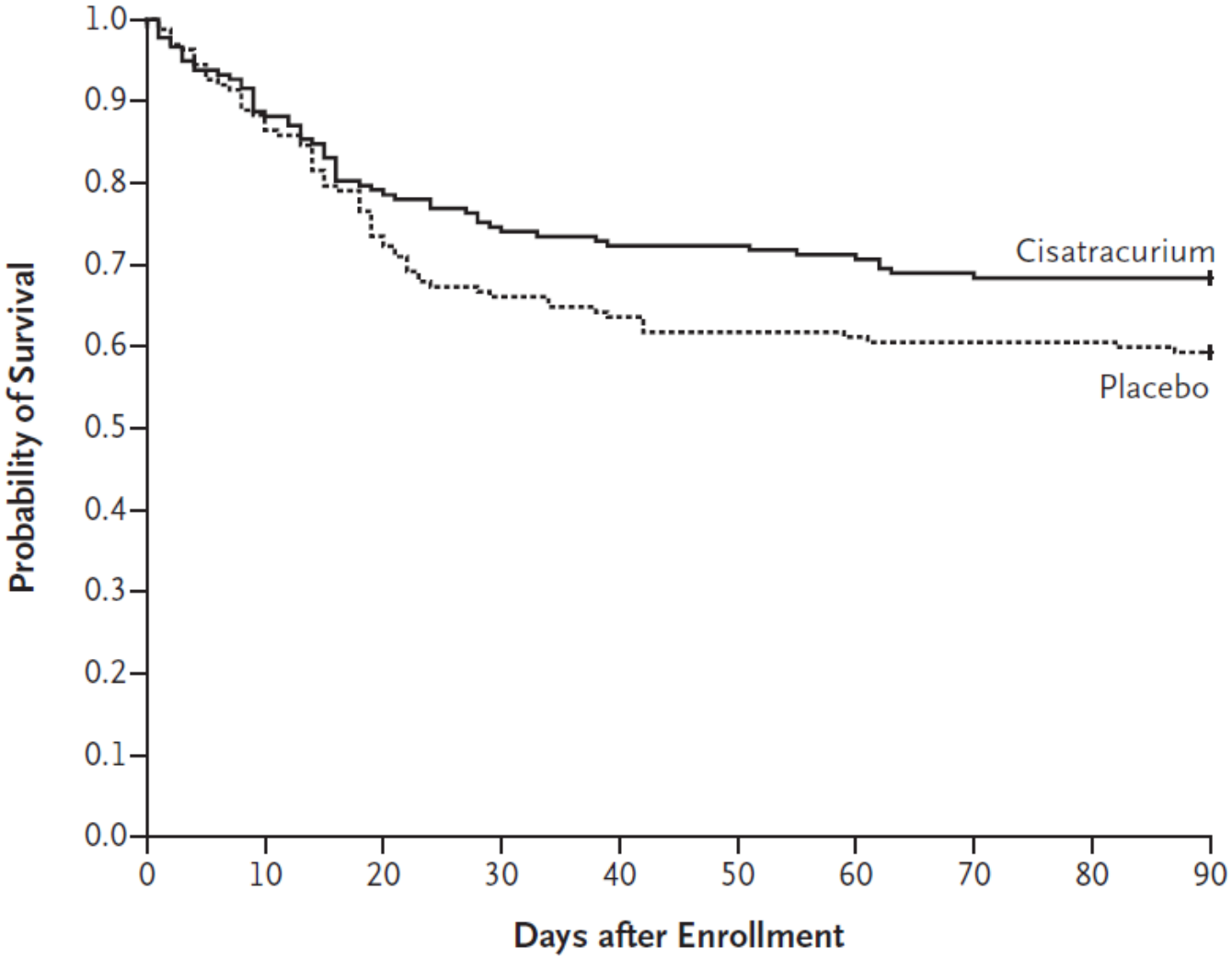
- should **not** be used among **unselected patients** with ARDS of any severity (moderate evidence).

- should be used for selected patients deemed to have greater amounts of potentially recruitable lung (e.g., moderate to severe ARDS).

- should **not** be used for patients without potential for lung recruitment with high PEEP (e.g., mild ARDS), based on moderate-level evidence.

Ann Am Thorac Soc. 2017 Oct;14(Supplement_4):S297-S303.

Treatment-neuromuscular blockade



N Engl J Med. 2010 Sep 16;363(12):1107-16.

Table 3. Secondary Outcomes, According to Study Group.*

Outcome	Cisatracurium (N=177)	Placebo (N=162)	Relative Risk with Cisatracurium (95% CI)	P Value
Death — no. (% [95% CI])				
At 28 days	42 (23.7 [18.1–30.5])	54 (33.3 [26.5–40.9])	0.71 (0.51–1.00)	0.05
In the ICU	52 (29.4 [23.2–36.5])	63 (38.9 [31.7–46.6])	0.76 (0.56–1.02)	0.06
In the hospital	57 (32.2 [25.8–39.4])	67 (41.4 [34.1–49.1])	0.78 (0.59–1.03)	0.08
No. of ventilator-free days†				
From day 1 to day 28	10.6±9.7	8.5±9.4		0.04
From day 1 to day 90	53.1±35.8	44.6±37.5		0.03
No. of days without organ failure, from day 1 to day 28				
No cardiovascular failure	18.3±9.4	16.6±10.4		0.12
No coagulation abnormalities	22.6±8.9	20.5±9.9		0.05
No hepatic failure	21.3±9.6	19.1±10.6		0.05
No renal failure	20.5±10.1	18.1±11.6		0.05
None of the four	15.8±9.9	12.2±11.1		0.01

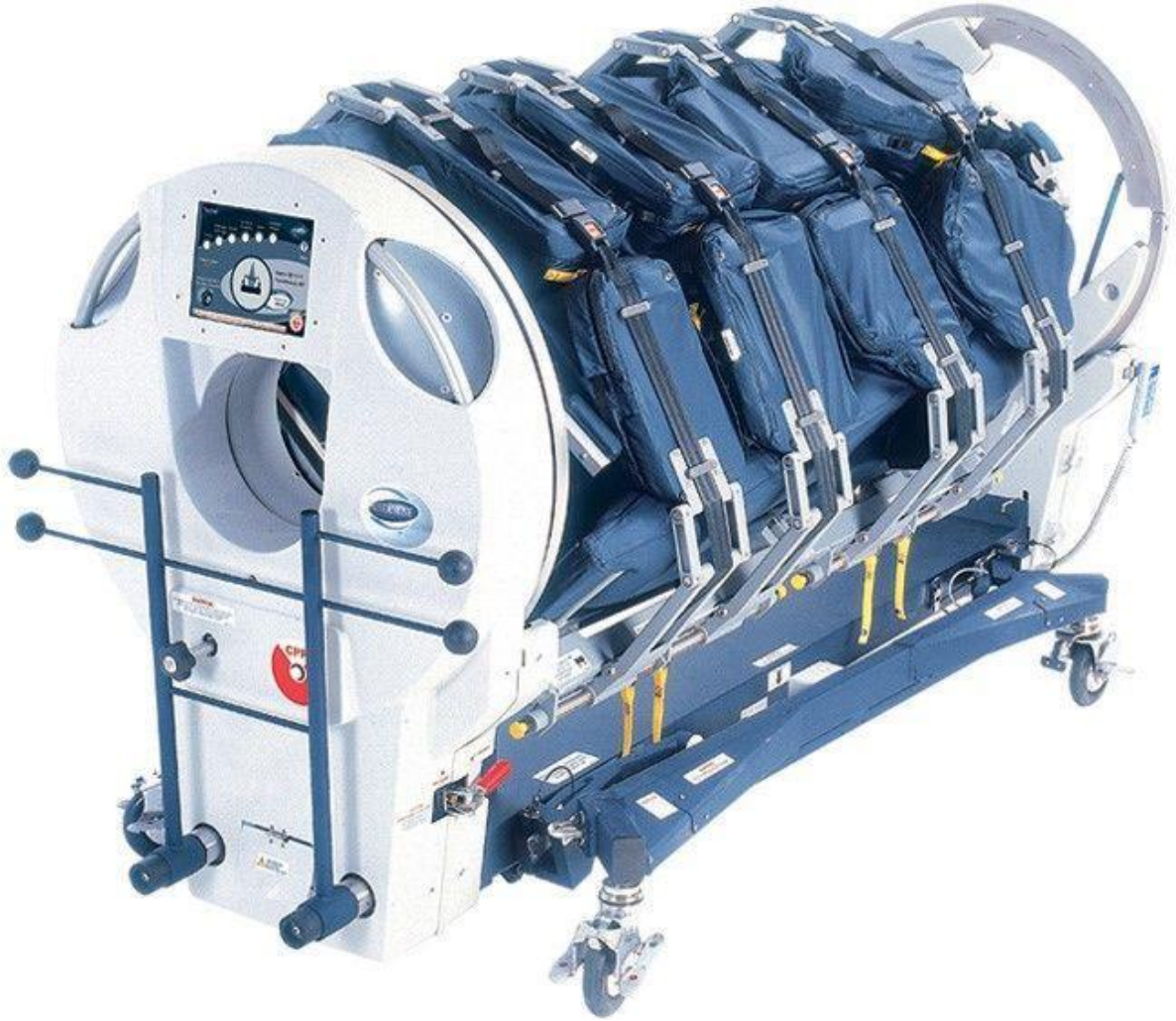
N Engl J Med. 2010 Sep 16;363(12):1107-16.

Table 3. Secondary Outcomes, According to Study Group.*

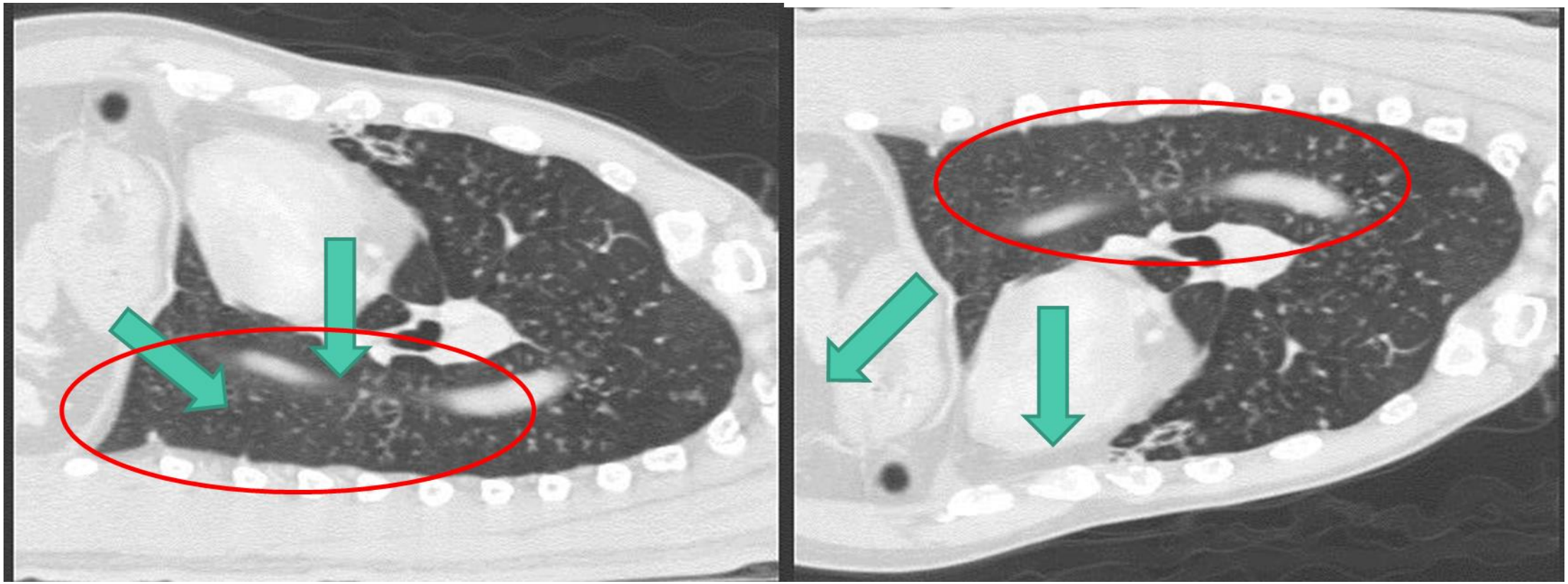
Outcome	Cisatracurium (N=177)	Placebo (N=162)	Relative Risk with Cisatracurium (95% CI)	P Value
No. of days outside the ICU				
From day 1 to day 28	6.9±8.2	5.7±7.8		0.16
From day 1 to day 90	47.7±33.5	39.5±35.6		0.03
Hospital survivors admitted to other health care facilities from day 1 to day 90 — % (95% CI)	22.3 (15.8–30.5)	18.8 (12.2–27.8)		0.52
Barotrauma — no. (% [95% CI])‡	9 (5.1 [2.7–9.4])	19 (11.7 [7.6–17.6])	0.43 (0.20–0.93)	0.03
Pneumothorax — no. (% [95% CI])	7 (4.0 [2.0–8.0])	19 (11.7 [7.6–17.6])	0.34 (0.15–0.78)	0.01
MRC score — median (IQR)§				
At day 28	55 (46–60)	55 (39–60)	1.07 (0.80–1.45)	0.49
At ICU discharge	55 (43–60)	55 (44–60)	0.92 (0.71–1.19)	0.94
Patients without ICU-acquired paresis¶				
By day 28 — no./total no. (% [95% CI])	68/96 (70.8 [61.1–79.0])	52/77 (67.5 [56.5–77.0])		0.64
By ICU discharge — no./total no. (% [95% CI])	72/112 (64.3 [55.1–72.6])	61/89 (68.5 [58.3–77.3])		0.51

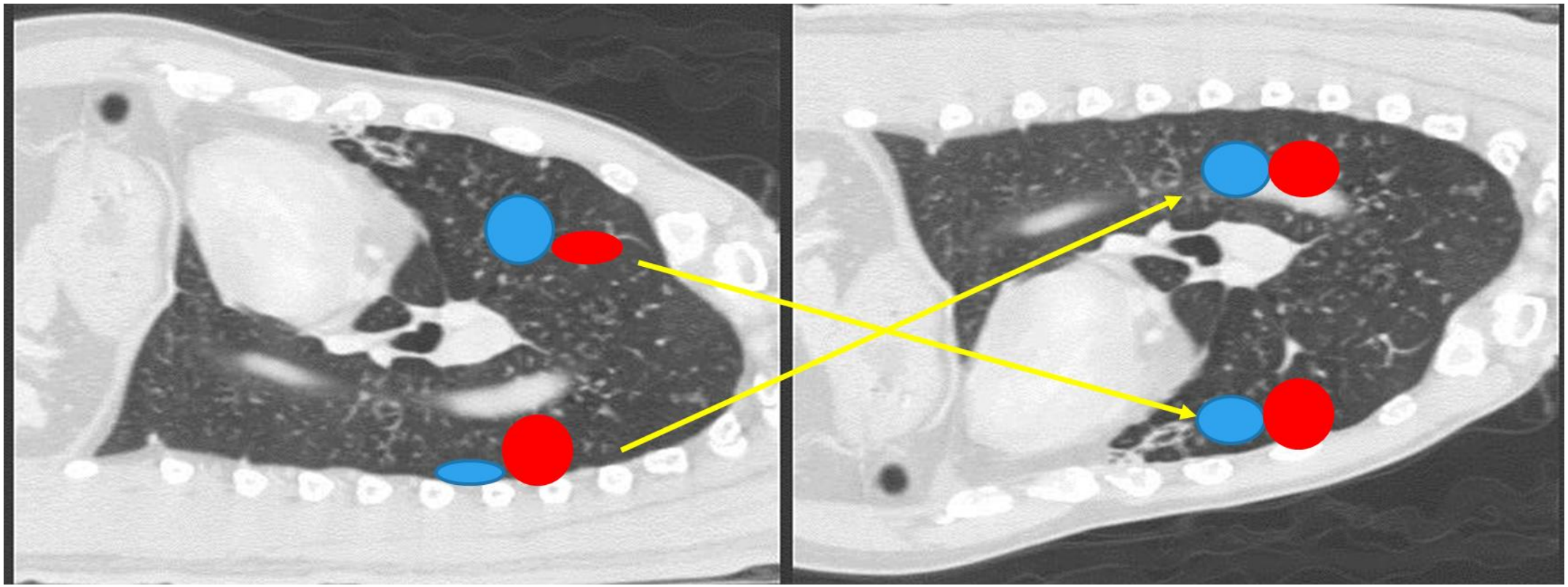
N Engl J Med. 2010 Sep 16;363(12):1107-16.

Treatment-prone position

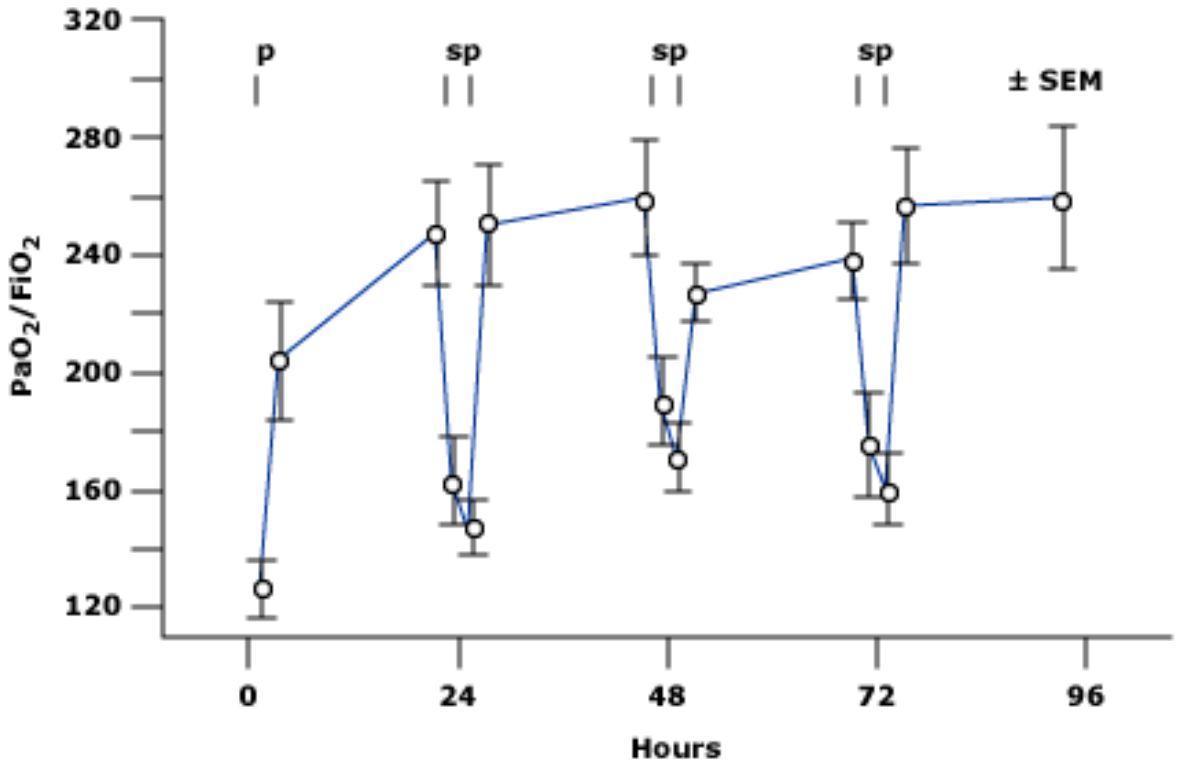


https://www.arjo.com/en-us/products/medical-beds/critical-care/rotoprone/





Course of PaO_2/FiO_2 during four consecutive 24-hour periods of prone positioning



In each period, patients were prone (p) 20 hours and supine (s) 4 hours. A benefit from prone positioning was observed during repeated transitions from supine to prone position.
Data from Fridrich, P, Krafft, P, Hochleuthner, H, et al., Anesth Analg 1996; 83:1206.

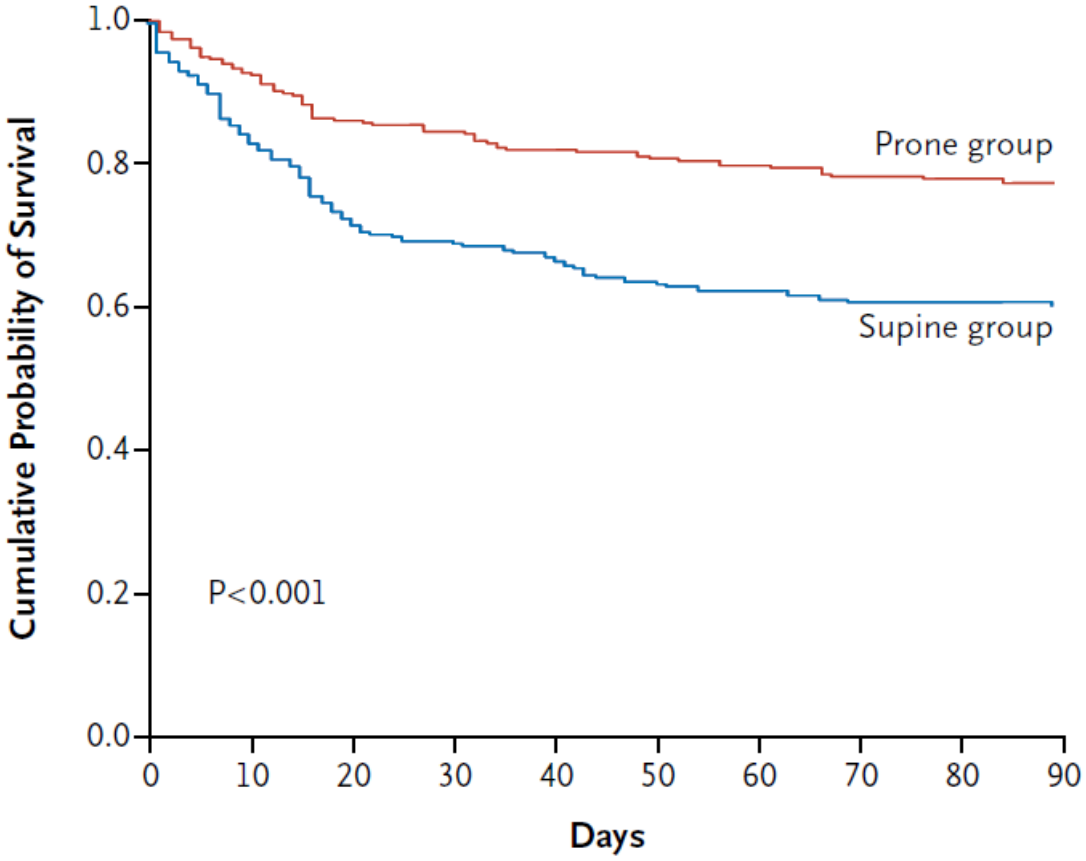
Prone positioning in severe acute respiratory distress syndrome

- endotracheal intubation and mechanical ventilation for ARDS for less than 36 hours; and severe ARDS (defined as a Pao2:Fio2 ratio of <150 mm Hg, with an Fio2 of ≥0.6, a PEEP of ≥5 cm of water, and a tidal volume of about 6 ml per kilogram of predicted body weight

- Patients assigned to the prone group had to be turned to the prone position within the first hour after randomization.
- They were placed in a completely prone position for **at least 16** consecutive hours.

N Engl J Med. 2013 Jun 6;368(23):2159-68.

Treatment-prone position



No. at Risk					
Prone group	237	202	191	186	182
Supine group	229	163	150	139	136

N Engl J Med. 2013 Jun 6;368(23):2159-68.

Table 3. Primary and Secondary Outcomes According to Study Group.*

Outcome	Supine Group (N=229)	Prone Group (N=237)	Hazard Ratio or Odds Ratio with the Prone Position (95% CI)	P Value
Mortality — no. (% [95% CI])				
At day 28				
Not adjusted	75 (32.8 [26.4–38.6])	38 (16.0 [11.3–20.7])	0.39 (0.25–0.63)	<0.001
Adjusted for SOFA score†			0.42 (0.26–0.66)	<0.001
At day 90				
Not adjusted	94 (41.0 [34.6–47.4])	56 (23.6 [18.2–29.0])	0.44 (0.29–0.67)	<0.001
Adjusted for SOFA score†			0.48 (0.32–0.72)	<0.001
Successful extubation at day 90 — no./total no. (% [95% CI])	145/223 (65.0 [58.7–71.3])	186/231 (80.5 [75.4–85.6])	0.45 (0.29–0.70)	<0.001
Time to successful extubation, assessed at day 90 — days				
Survivors	19±21	17±16		0.87
Nonsurvivors	16±11	18±14		

N Engl J Med. 2013 Jun 6;368(23):2159-68.

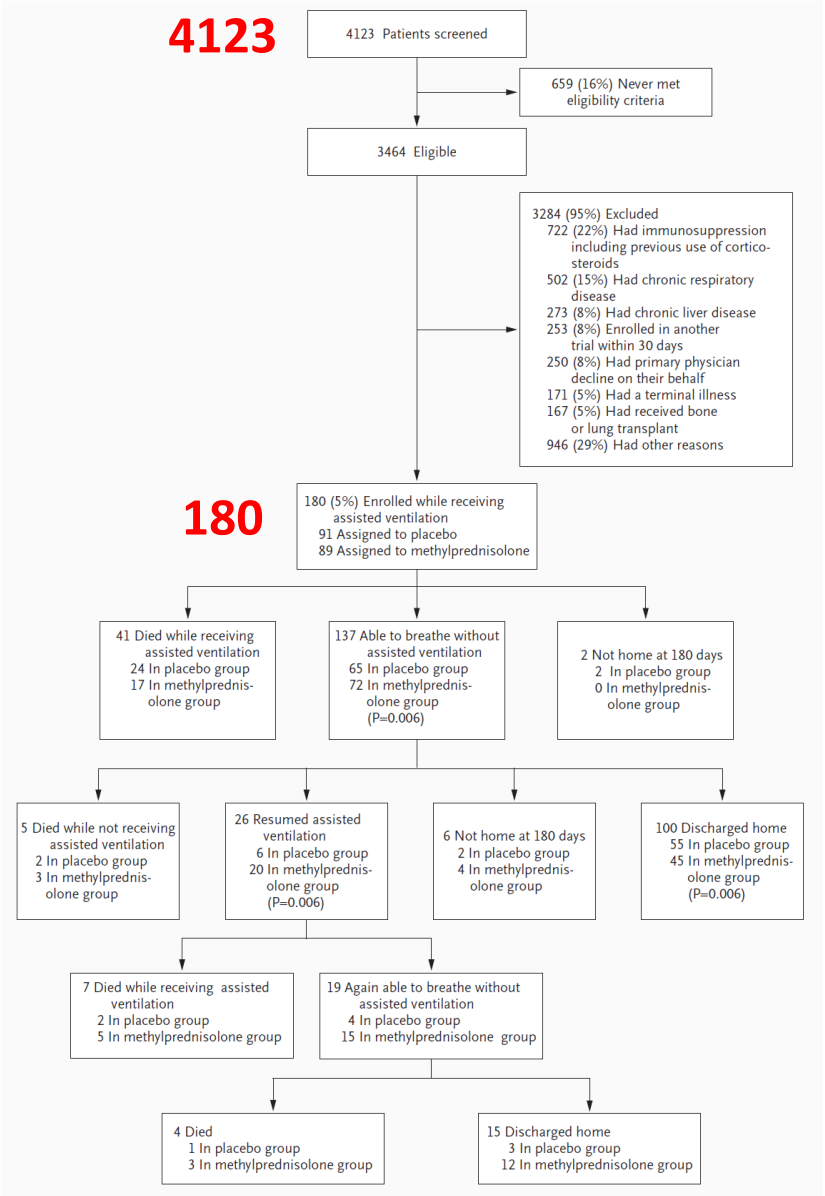
Table 3. Primary and Secondary Outcomes According to Study Group.*

Outcome	Supine Group (N = 229)	Prone Group (N = 237)	Hazard Ratio or Odds Ratio with the Prone Position (95% CI)	P Value
Length of ICU stay, assessed at day 90 — days				
Survivors	26±27	24±22		0.05
Nonsurvivors	18±15	21±20		
Ventilation-free days				
At day 28	10±10	14±9		<0.001
At day 90	43±38	57±34		<0.001
Pneumothorax — no. (% [95% CI])	13 (5.7 [3.9–7.5])	15 (6.3 [4.9–7.7])	0.89 (0.39–2.02)	0.85
Noninvasive ventilation — no./total no. (% [95% CI])				
At day 28	10/212 (4.7 [1.9–7.5])	4/228 (1.8 [0.1–3.5])	0.36 (0.07–3.50)	0.11
At day 90	3/206 (1.5 [0.2–3.2])	4/225 (1.8 [0.1–3.5])	1.22 (0.23–6.97)	1.00
Tracheotomy — no./total no. (% [95% CI])				
At day 28	12/229 (5.2 [2.3–8.1])	9/237 (3.8 [1.4–6.0])	0.71 (0.27–1.86)	0.37
At day 90	18/223 (8.1 [4.5–11.7])	15/235 (6.4 [3.3–9.5])	0.78 (0.36–1.67)	0.59

N Engl J Med. 2013 Jun 6;368(23):2159-68.

Treatment-Glucocorticoids

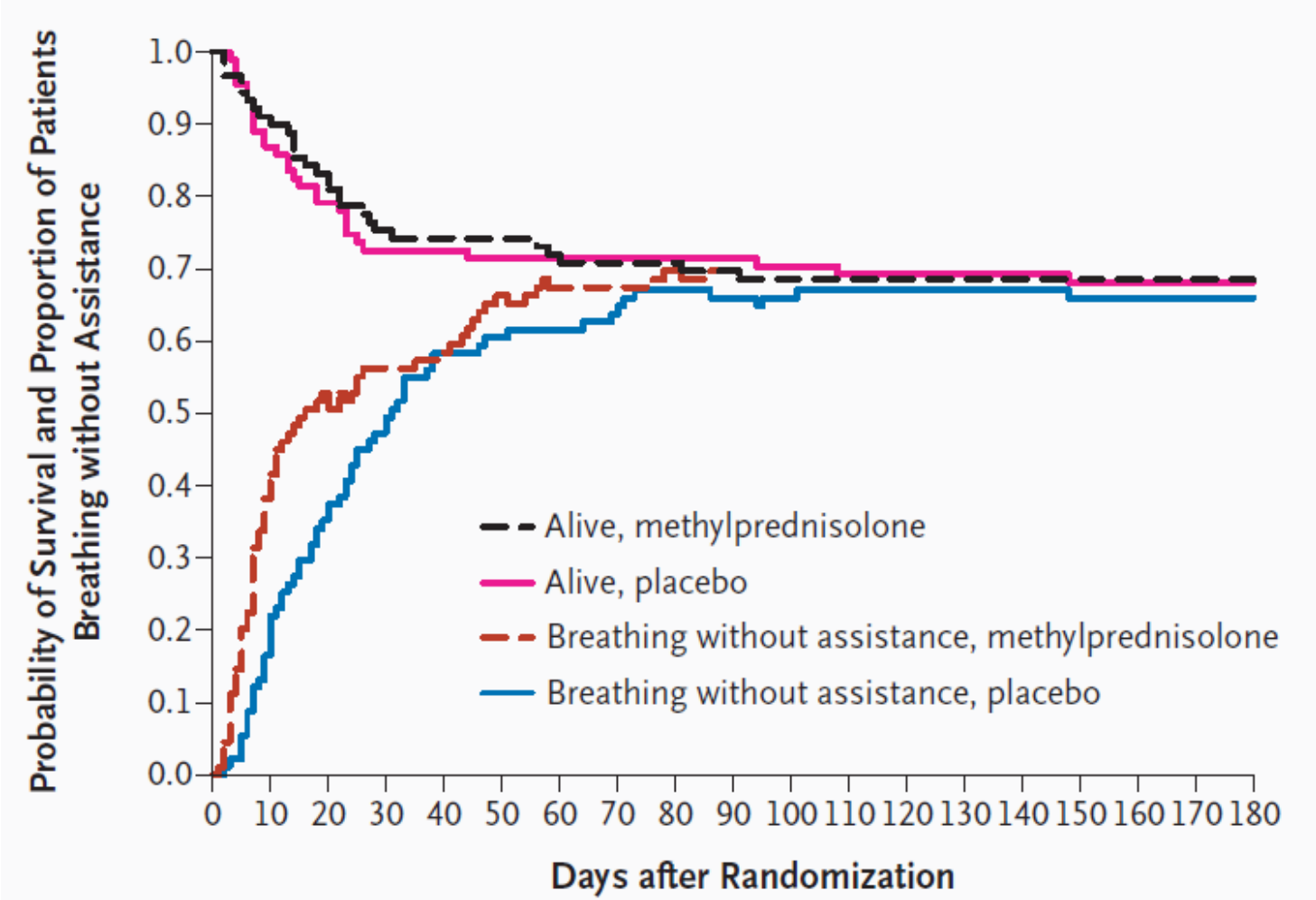
- Patients were enrolled from August 5, 1997, through November 17, 2003, at 25 hospitals of the National Heart, Lung, and Blood Institute (NHLBI) ARDS Clinical Trials Network



Methylprednisolone

- A single dose of 2 mg /kg of predicted body weight
- 0.5 mg /kg of predicted body weight every 6 hours for 14 days
- 0.5 mg /kg of predicted body weight every 12 hours for 7 days
- Then tapering of the dose.

Treatment-Glucocorticoids



N Engl J Med. 2006 Apr 20;354(16):1671-84.

Conclusion-Glucocorticoids

- Methylprednisolone did not increase infectious complications
- Methylprednisolone may have increased the risk of neuromyopathy associated with critical illness
- Should not routine use methylprednisolone in patients with persistent ARDS
- Methylprednisolone therapy may be harmful when initiated more than two weeks after the onset of ARDS

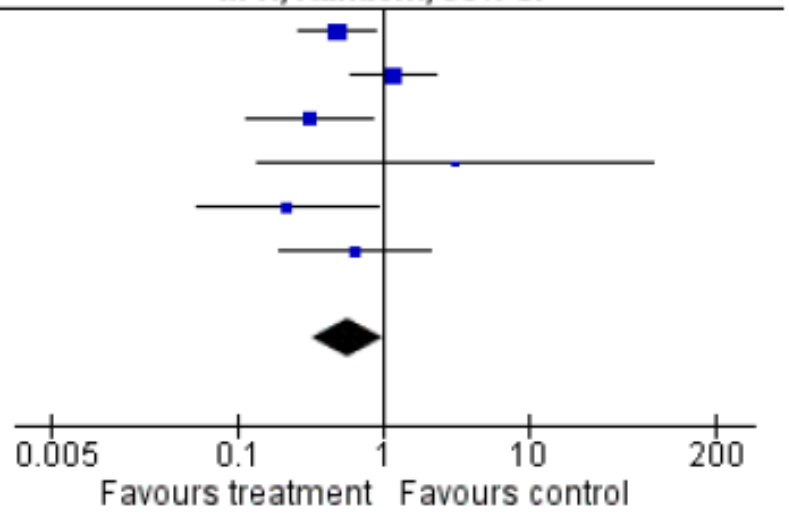
Adjunctive corticosteroids for Pneumocystis jiroveci pneumonia in patients with HIV infection

Figure 3. Forest plot of comparison: 1 Adjunctive corticosteroids versus no such treatment, outcome: 1.1 Death at 1 month; adults.

	Treatment		Control			Risk Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**
Bozzette 1990	13	123	28	128	28.1%	0.48 [0.26, 0.89]
Clement 1989	9	19	9	22	25.7%	1.16 [0.58, 2.31]
Gagnon 1990	3	12	9	11	17.6%	0.31 [0.11, 0.85]
Montaner 1990	1	18	0	19	3.0%	3.16 [0.14, 72.84]
Nielsen 1992	2	30	9	29	11.1%	0.21 [0.05, 0.91]
Walmsley 1995	4	40	6	38	14.6%	0.63 [0.19, 2.07]
Total (95% CI)		**242**		**247**	**100.0%**	**0.56 [0.32, 0.98]**
Total events	32		61			

Heterogeneity: $Tau^2 = 0.19$; $Chi^2 = 8.83$, df = 5 (P = 0.12); $I^2 = 43\%$

Test for overall effect: Z = 2.03 (P = 0.04)



Cochrane Database Syst Rev. 2015 Apr 2;(4):CD006150.

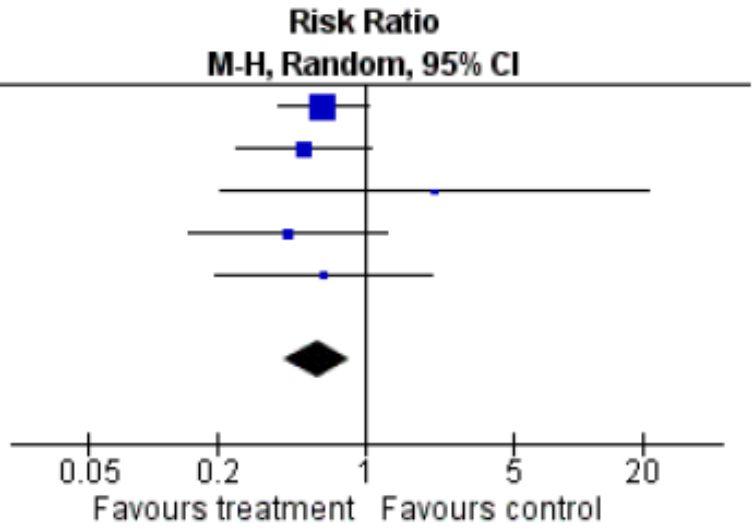
Adjunctive corticosteroids for Pneumocystis jiroveci pneumonia in patients with HIV infection

Figure 4. Forest plot of comparison: 1 Adjunctive corticosteroids versus no such treatment, outcome: 1.2 Death at 3 to 4 months; adults.

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Bozzette 1990	20	123	33	128	52.3%	0.63 [0.38, 1.04]
Gagnon 1990	5	12	9	11	24.6%	0.51 [0.25, 1.05]
Montaner 1990	2	18	1	19	2.4%	2.11 [0.21, 21.32]
Nielsen 1992	4	30	9	29	11.5%	0.43 [0.15, 1.24]
Walmsley 1995	4	40	6	38	9.2%	0.63 [0.19, 2.07]
Total (95% CI)		**223**		**225**	**100.0%**	**0.59 [0.41, 0.85]**
Total events	35		58			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.77$, df = 4 (P = 0.78); $I^2 = 0\%$

Test for overall effect: Z = 2.88 (P = 0.004)



Cochrane Database Syst Rev. 2015 Apr 2;(4):CD006150.

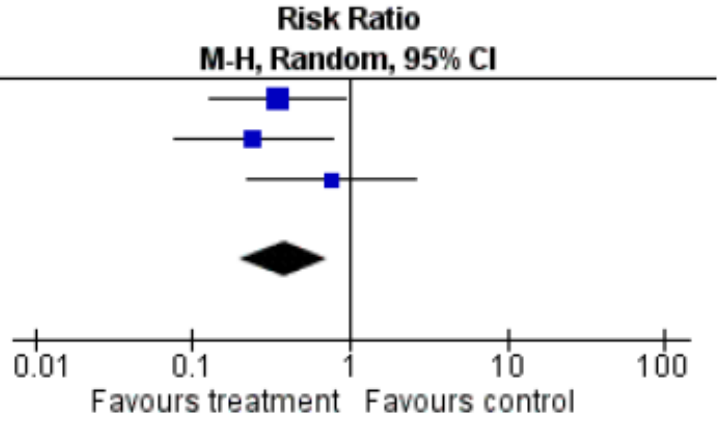
Adjunctive corticosteroids for Pneumocystis jiroveci pneumonia in patients with HIV infection

Figure 6. Forest plot of comparison: 1 Adjunctive corticosteroids versus no such treatment, outcome: 1.4 Need for mechanical ventilation at 1 month; adults.

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Bozzette 1990	5	123	15	128	42.6%	0.35 [0.13, 0.93]
Nielsen 1992	3	30	12	29	30.6%	0.24 [0.08, 0.77]
Walmsley 1995	4	40	5	38	26.8%	0.76 [0.22, 2.62]
Total (95% CI)		**193**		**195**	**100.0%**	**0.38 [0.20, 0.73]**
Total events	12		32			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.83$, df = 2 (P = 0.40); $I^2 = 0\%$

Test for overall effect: Z = 2.94 (P = 0.003)



Cochrane Database Syst Rev. 2015 Apr 2;(4):CD006150.

Treatment- Extracorporeal carbon dioxide removal ($ECCO_2R$)

- similar in concept to ECMO
- lower flow rate and does not significantly oxygenate the patient.
- a primary treatment for hypercarbic respiratory failure
- an adjunct to reduce potentially injurious levels of mechanical ventilator support in hypoxemic respiratory failure.

https://link.springer.com/chapter/10.1007/978-3-319-33341-0_10

Treatment-ECMO

Table 1. Characteristics of the Patients at Randomization.*

Characteristic	ECMO Group (N = 124)	Control Group (N = 125)
Age — yr	51.9±14.2	54.4±12.7
Male sex — no. (%)	87 (70)	90 (72)
Immunocompromised condition — no. (%)	27 (22)	27 (22)
SOFA score†	10.8±3.9	10.6±3.5
Median time since intubation (interquartile range) — hr	34 (15–89)	34 (17–100)
Cause of ARDS — no. (%)		
Pneumonia		
Bacterial	54 (44)	58 (46)
Viral	26 (21)	20 (16)
Other	44 (35)	47 (38)
Pao_2:Fio_2 — mm Hg	73±30	72±24
PEEP — cm of water	11.7±3.9	11.8±3.7
Tidal volume — ml/kg of predicted body weight	6.0±1.3	6.1±0.9

N Engl J Med. 2018 May 24;378(21):1965-1975.

Treatment-ECMO

Table 1. Characteristics of the Patients at Randomization.*

Characteristic	ECMO Group (N=124)	Control Group (N=125)
Respiratory rate — breaths/min	30.4±4.7	31.2±4.5
Plateau pressure — cm of water	29.8±5.5	29.5±4.8
Driving pressure — cm of water	17.8±7.0	17.7±5.8
Respiratory-system compliance — ml/cm of water	25.0±11.5	25.4±10.8
Arterial blood pH	7.24±0.13	7.24±0.12
Pao_2 — mm Hg‡	69±25	68±22
$Paco_2$ — mm Hg	57±15	57±16
Prone positioning — no. (%)§	70 (56)	78 (62)
Inhaled nitric oxide or prostacyclin — no. (%)§	64 (52)	68 (54)
Recruitment maneuvers — no. (%)§	22 (18)	34 (27)
Neuromuscular blockade — no. (%)§	114 (92)	120 (96)

N Engl J Med. 2018 May 24;378(21):1965-1975.

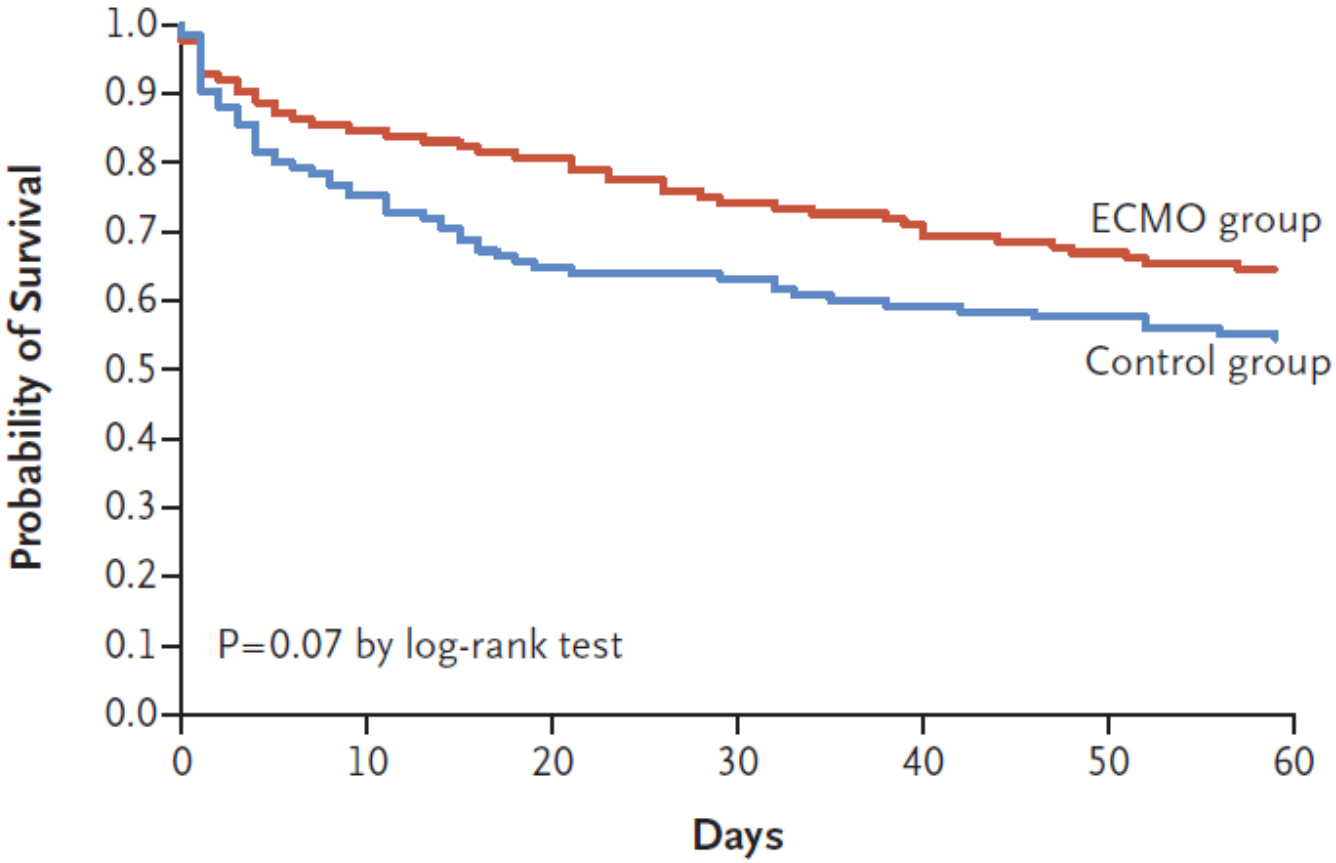
Treatment-ECMO

Table 2. End Points.*

End Point	ECMO Group (N=124)	Control Group (N=125)	Relative Risk or Difference (95% CI)†	P Value
Primary end point: mortality at 60 days — no. (%)	44 (35)	57 (46)	0.76 (0.55 to 1.04)	0.09
Key secondary end point: treatment failure at 60 days — no. (%)‡	44 (35)	72 (58)	0.62 (0.47 to 0.82)	<0.001
Other end points				
Mortality at 90 days — no. (%)	46 (37)	59 (47)	−10 (−22 to 2)	
Median length of stay (interquartile range) — days				
In the ICU	23 (13–34)	18 (8–33)	5 (−1 to 10)	
In the hospital	36 (19–48)	18 (5–43)	18 (6 to 25)	
Median days free from mechanical ventilation (interquartile range)§	23 (0–40)	3 (0–36)	20 (−5 to 32)	
Median days free from vasopressor use (interquartile range)§	49 (0–56)	40 (0–53)	9 (0 to 51)	
Median days free from renal-replacement therapy (interquartile range)§	50 (0–60)	32 (0–57)	18 (0 to 51)	
Prone position — no. (%)¶	82 (66)	113 (90)	−24 (−34 to −14)	
Recruitment maneuvers — no. (%)¶	27 (22)	54 (43)	−21 (−32 to −10)	
Inhaled nitric oxide or prostacyclin — no. (%)¶	75 (60)	104 (83)	−23 (−33 to −12)	
Glucocorticoids — no. (%)¶	80 (65)	82 (66)	−1 (−13 to 11)	

N Engl J Med. 2018 May 24;378(21):1965-1975.

Treatment-ECMO



No. at Risk							
ECMO	124	105	100	92	88	83	80
Control	125	94	81	79	74	72	69

N Engl J Med. 2018 May 24;378(21):1965-1975.

Treatment-$ECCO_2R$

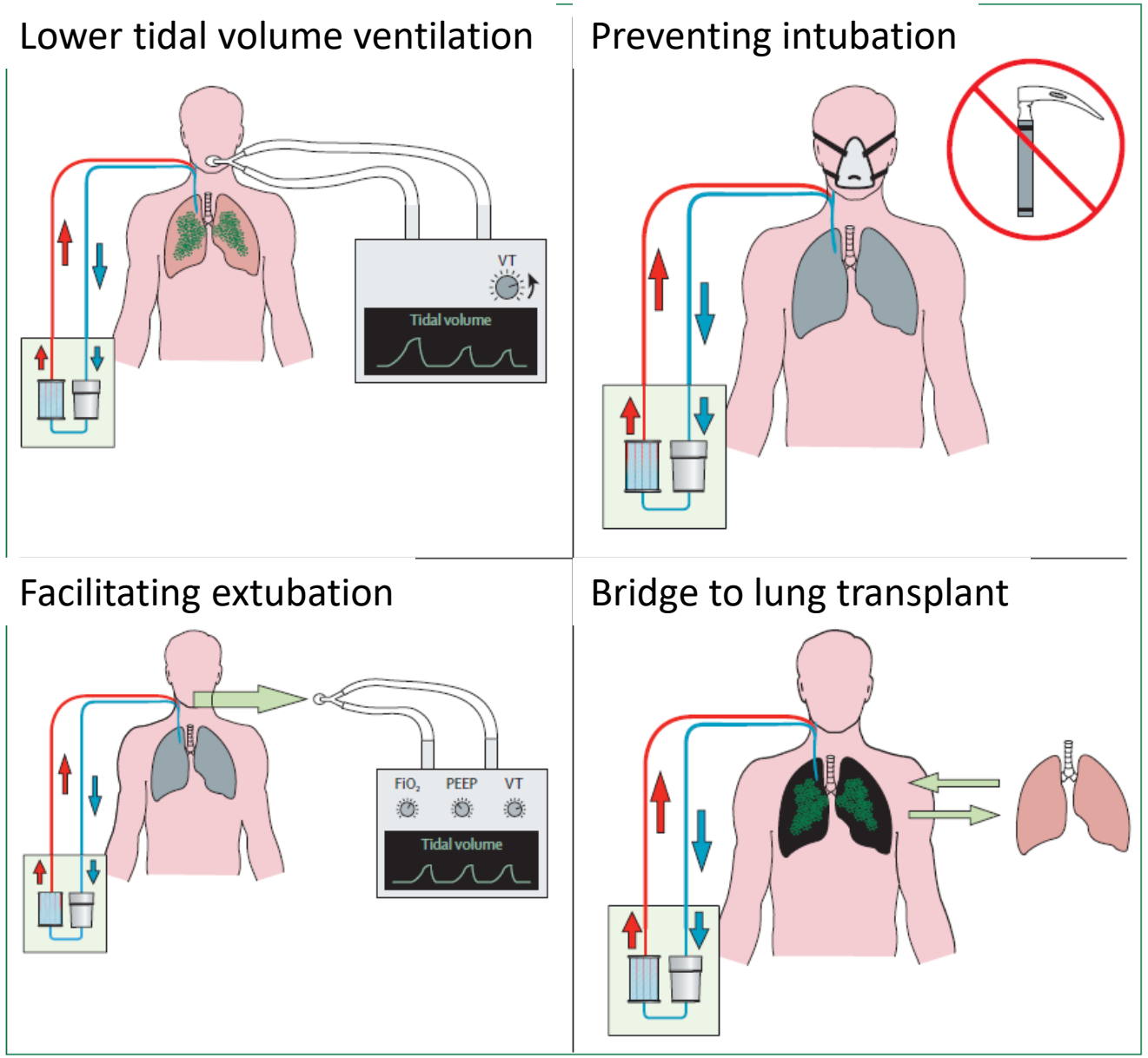
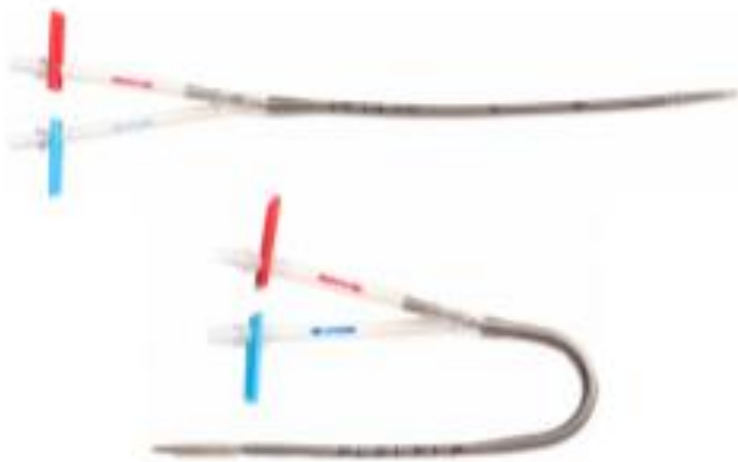


Figure: Potential indications for extracorporeal carbon dioxide removal

Hemolung Cartridge

- Membrane oxygenator with integrated centrifugal pump



Hemolung Catheter

- 15.5 Fr dual lumen venous Catheter with insertion accessories, percutaneous, single-stick venous access, femoral (26cm) and jugular (17cm) available

https://www.alung.com/training-support-global/cr4/

Hemolung Controller

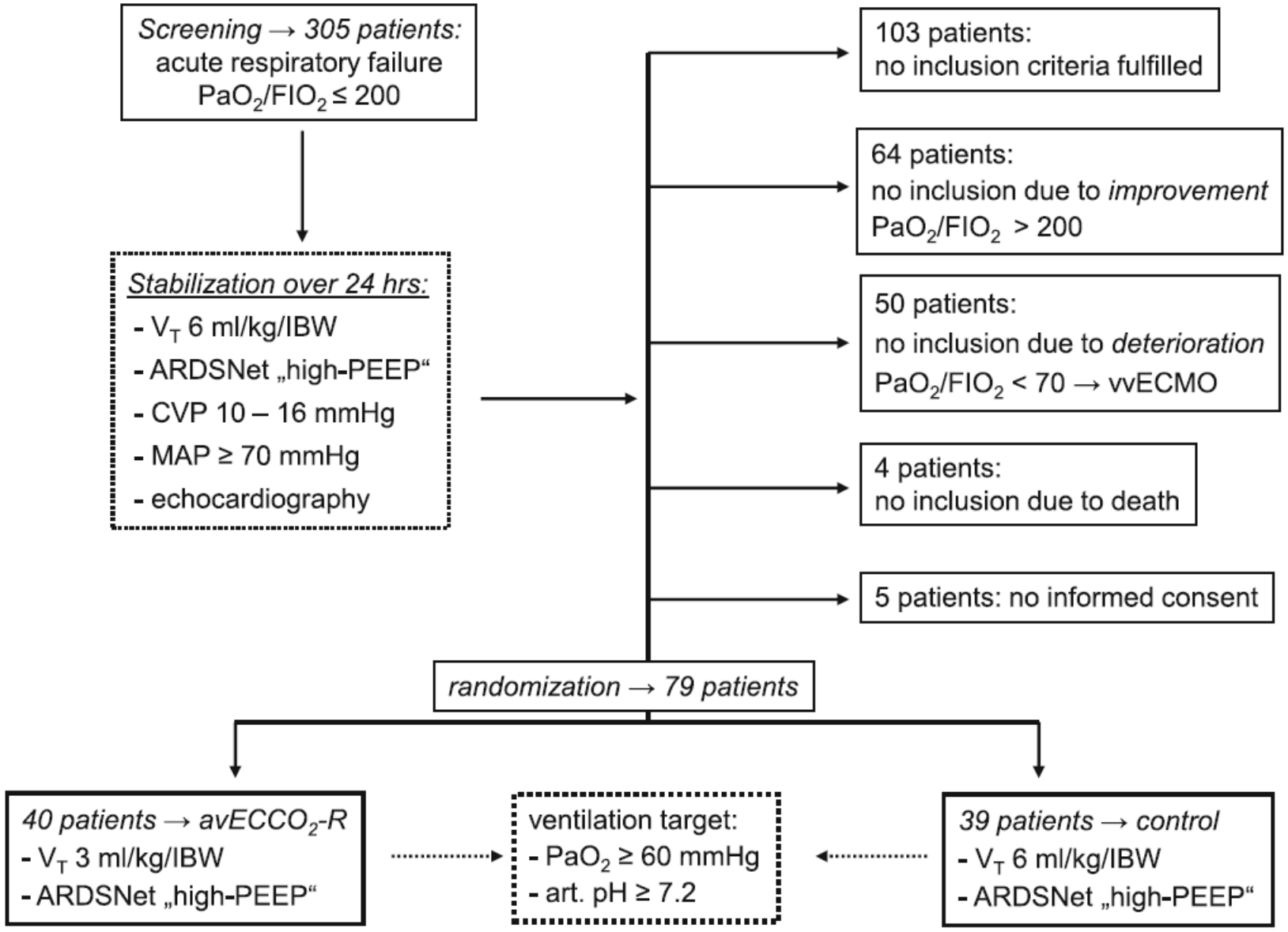
- Controls the Cartridge pump speed and gas flow while providing real-time monitoring of CO_2 removal and blood flow, bubble detection and other operating alarms
- Infusion pump: continuous saline infusion to prevent bearing damage

https://www.alung.com/training-support-global/cr4/

Treatment-ECCO$_2$R- ultra- protective strategy

- removes CO2 from the venous blood using a moderate (0.5-1 l per min) extracorporeal blood flow.
- permits the use of very low tidal volume (3–4 ml per kg PBW) without causing severe respiratory acidosis
- the benefit on outcomes in patients with ARDS **remains unknown**

Treatment-ECCO$_2$R



Intensive Care Med. 2013 May;39(5):847-56.

Treatment-$ECCO_2R$

Table 1 Baseline characteristics of the patients

	avECCO$_2$-R ($n = 40$)	Control ($n = 39$)
Age (years)	49.8 ± 12	48.7 ± 17
Gender (male/female)	38/2	30/9
Lung Injury Score (Murray)	2.8 ± 0.7	2.7 ± 0.8
Body mass index (kg/m^2)	28.6 ± 5	28.8 ± 5
Source of ARDS		
Pulmonary/non-pulmonary ARDS	31/9	37/2
Non-pulmonary		
SIRS/Sepsis	5	1
Massive transfusion	1	0
Trauma	3	1
Pulmonary		
Pneumonia	24 (58 % bacterial)	21 (62 % bacterial)
Aspiration	1	6
Lung contusion	6	9
Inhalation	1	0
Comorbidities		
Diabetes mellitus	2	3
COPD	5	3
Arterial hypertension	10	7
Coronary artery disease	1	1
Chronic renal impairment	2	0
Other	19	15
Atrial fibrillation	3	2
Alcohol use disorder	2	3
Obesity	2	3

Intensive Care Med. 2013 May;39(5):847-56.

Treatment-ECCO$_2$R

Table 3 Outcome parameters of the study

	All patients			Subgroup: PaO_2/FIO_2 <150		
	avECCO$_2$-R	Control	*p*	avECCO$_2$-R	Control	*p*
Ventilator-free-days-28	10.0 ± 8	9.3 ± 9	0.779	11.3 ± 7.5	5.0 ± 6.3	0.033
Ventilator-free-days-60	33.2 ± 20	29.2 ± 21	0.469	40.9 ± 12.8	28.2 ± 16.4	0.033
Non-pulmonary organ failure free days-60	21.0 ± 14	23.9 ± 15	0.447	24.1 ± 7.5	29.0 ± 17.7	0.428
Lung injury score on day 10	2.2 ± 0.6	2.1 ± 0.5	0.854	2.3 ± 0.8	2.2 ± 0.5	0.601
Length of stay in hospital (days)	46.7 ± 33	35.1 ± 17	0.113	42.0 ± 16.6	40.3 ± 15.7	0.815
Length of stay in ICU (days)	31.3 ± 23	22.9 ± 11	0.144	25.9 ± 13.1	31.0 ± 12.7	0.258
In-hospital mortality	7/40 (17.5 %)	6/39 (15.4 %)	1.000	1/21 (4.8 %)	1/10 (10 %)	0.563

Intensive Care Med. 2013 May;39(5):847-56.

Treatment-$ECCO_2R$

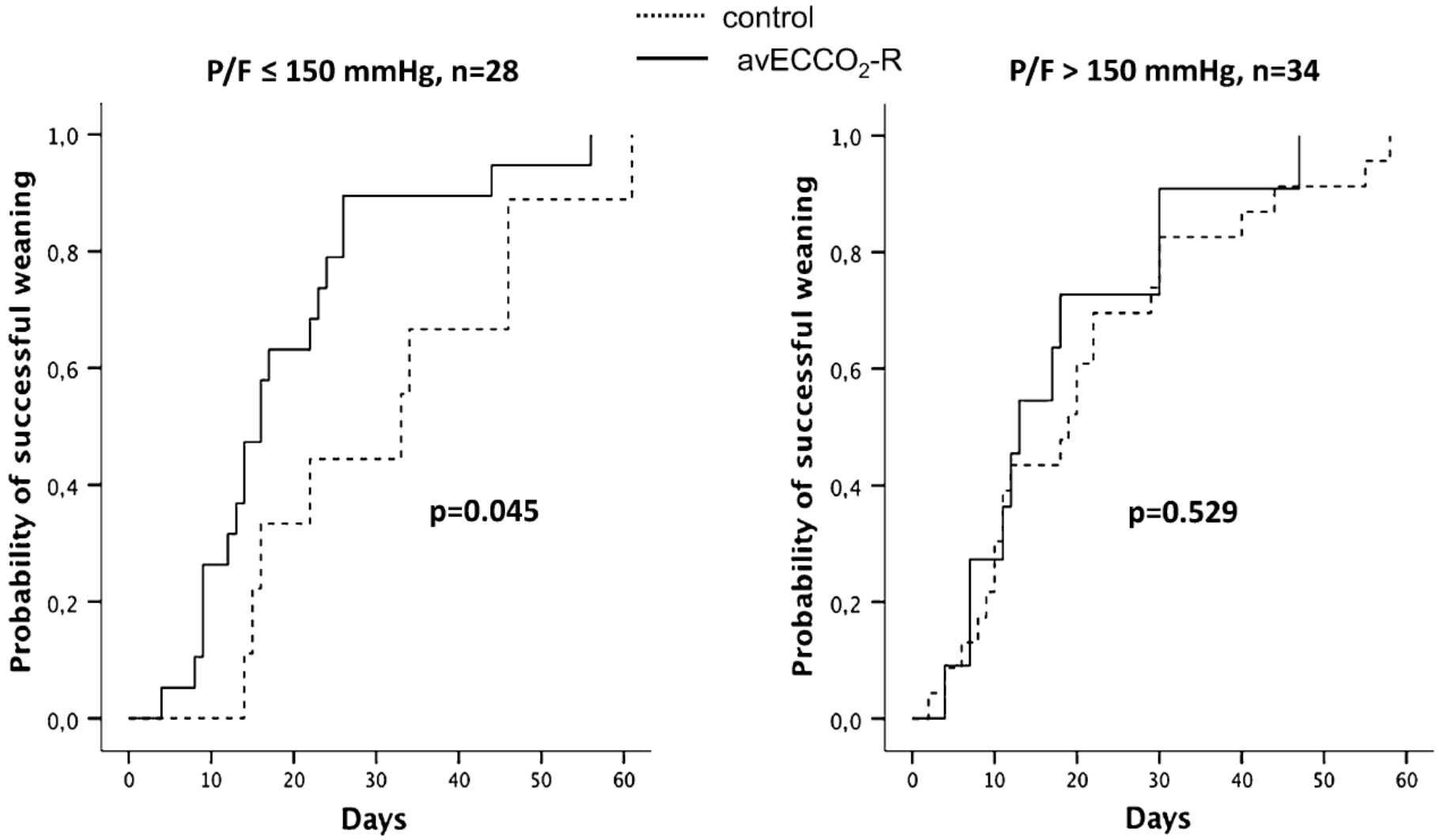


Fig. 2 Post-hoc analysis: probability of successful weaning in patients presenting with PaO_2/FIO_2 ≤150 versus >150 (only surviving patients)

Intensive Care Med. 2013 May;39(5):847-56.

Thanks for your attention