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Understanding VV ECMO Selection: Lessons learned from the BBQ

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So where to start with the literature...

- Impact factor
- NEJM- 73
- JAMA- 45
- Intensive Care Medicine- 10.2
- Organogensis- 1.0

Organogenesis it is

Bill James, baseball statistician and author, tells the story of hungry cavemen sitting about a campfire, waiting for tomatoes to ripen. One has the inspiration to throw an ox on the fire, and the first barbecue ensued and was endured. After eating, the conversation goes something like this: "There were some good parts." "Yeah, but there were some bad parts." And the smart one says, "This time, let's not eat the bones."[1]

Custer JR. Organogenesis. 2011;7:1:13-22.

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Lets see how this barbecue has evolved and what bones to avoid.

Two aspects of any therapy

- Harm from treatment
- Benefit from treatment

We must define the population least likely to accrue harm and most likely to gain benefit.

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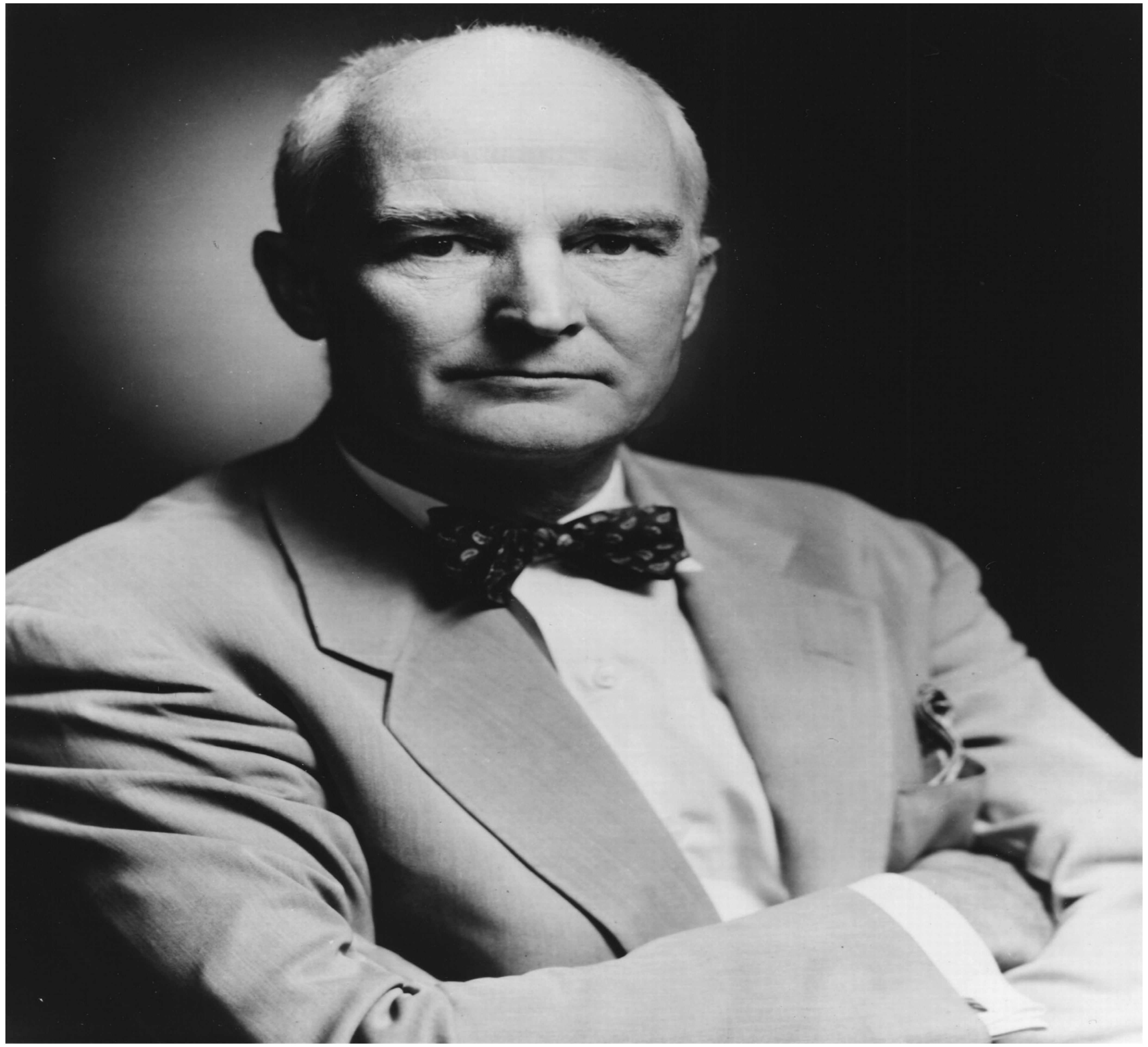
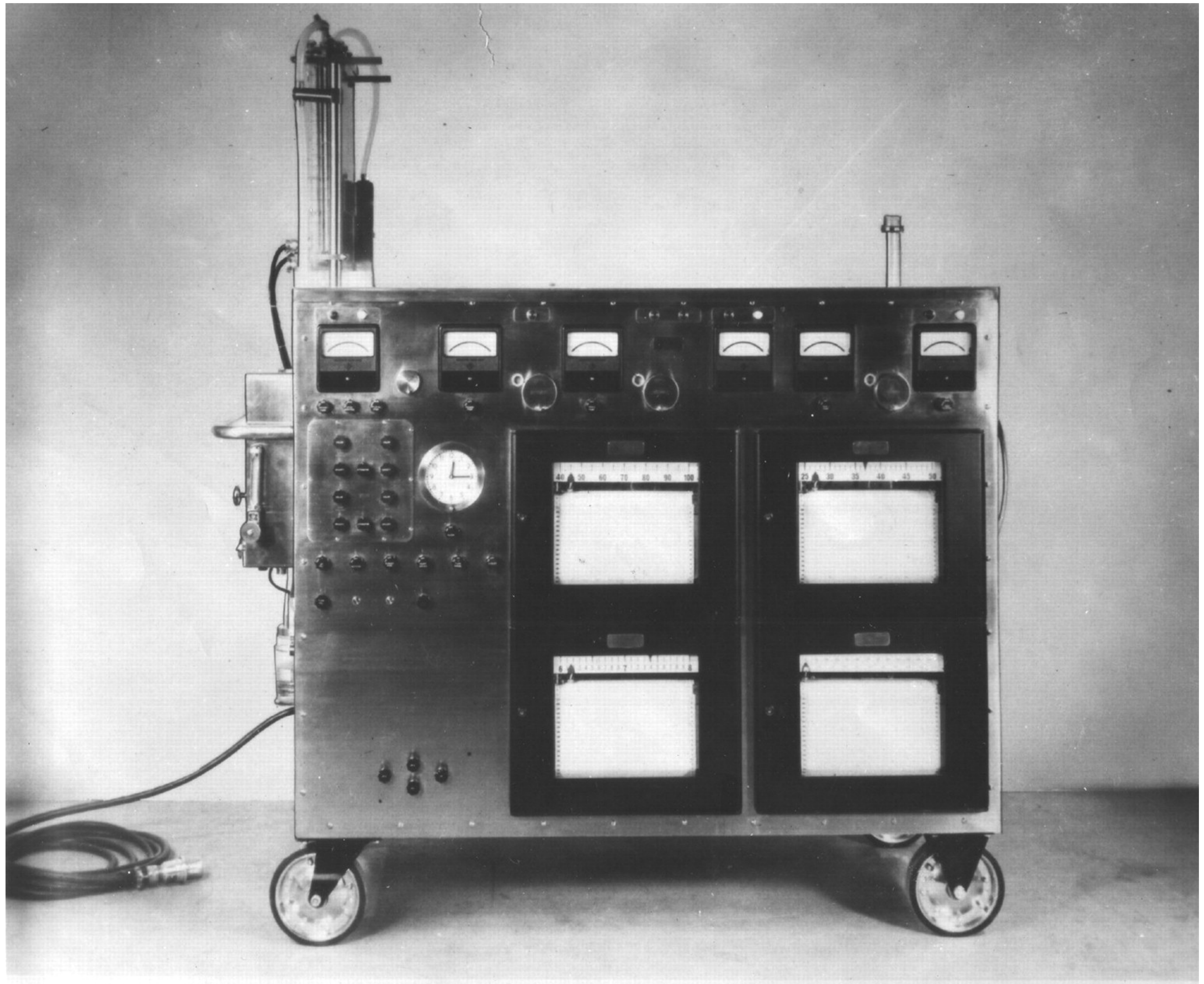
Dr. John Heysham Gibbon (1903-1973)



William S. Stoney Circulation. 2009;119:2844-2853

Gibbon-IBM Heart-Lung Machine- May 6, 1953



William S. Stoney Circulation. 2009;119:2844-2853

In his words… 1968

- “In general the difficulties encountered were foaming, hemolysis from trauma, and the production of vasoconstrictor substances in the blood from mechanical agitation… Has the heart-lung machine reached the limits of its perfection? The answer, of course, is no. Something happens to the blood during its passage through the present heart-lung machines which is detrimental to the patient…”

Gibbon JH. JAMA 1968;206:1983-1986

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Almost 50 Years of ECMO

- First successful case in 1972

PROLONGED EXTRACORPOREAL OXYGENATION FOR ACUTE POST-TRAUMATIC RESPIRATORY FAILURE (SHOCK-LUNG SYNDROME)

Use of the Bramson Membrane Lung

J. DONALD HILL, M.D., THOMAS G. O'BRIEN, M.D., JAMES J. MURRAY, M.D., LEON DONTIGNY, M.D., M. L. BRAMSON, A.C.G.I., J. J. OSBORN, M.D., AND F. GERBODE, M.D.

1979 NHLB ECMO RCT

Extracorporeal Membrane Oxygenation in Severe Acute Respiratory Failure

A Randomized Prospective Study

Warren M. Zapol, MD; Michael T. Snider, MD, PhD; J. Donald Hill, MD;
Robert J. Fallat, MD; Robert H. Bartlett, MD; L. Henry Edmunds, MD; Alan H. Morris, MD;
E. Converse Peirce II, MD; Arthur N. Thomas, MD; Herbert J. Proctor, MD; Philip A. Drinker, PhD;
Philip C. Pratt, MD; Anna Bagniewski, MA; Rupert G. Miller, Jr, PhD

Patient Outcome

Therapy*	Dead—Respiratory Improvement Never Occurred	Dead After Respiratory Improvement	Survived After Respiratory Improvement
ECMO and MV	34	4	4
MV (control)	41	3	4

*ECMO indicates extracorporeal membrane oxygenation; MV, mechanical ventilation.

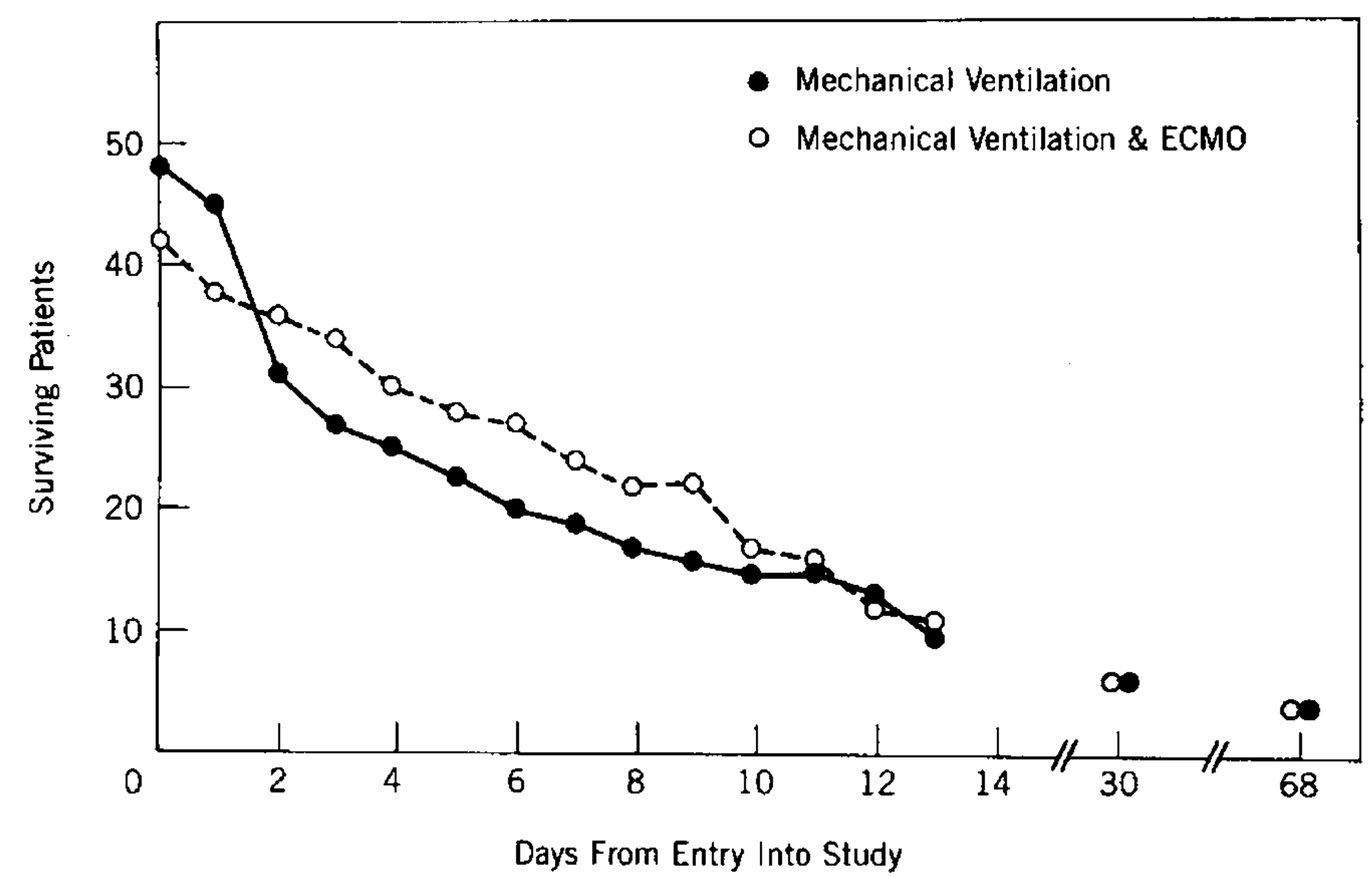

Fig 2.—Number of surviving patients treated by either mechanical ventilation alone (control group) or supplemented with partial venoarterial bypass plotted against days after entry into study. From day 2 to day 11, there were greater number of surviving patients in bypass group: ECMO, extracorporeal membrane oxygenation.

NHLB Study Assessment and Limitations

- VA Support only
- Harmful MV
- Excessive anticoagulation
- Prolonged MV prior to ECMO

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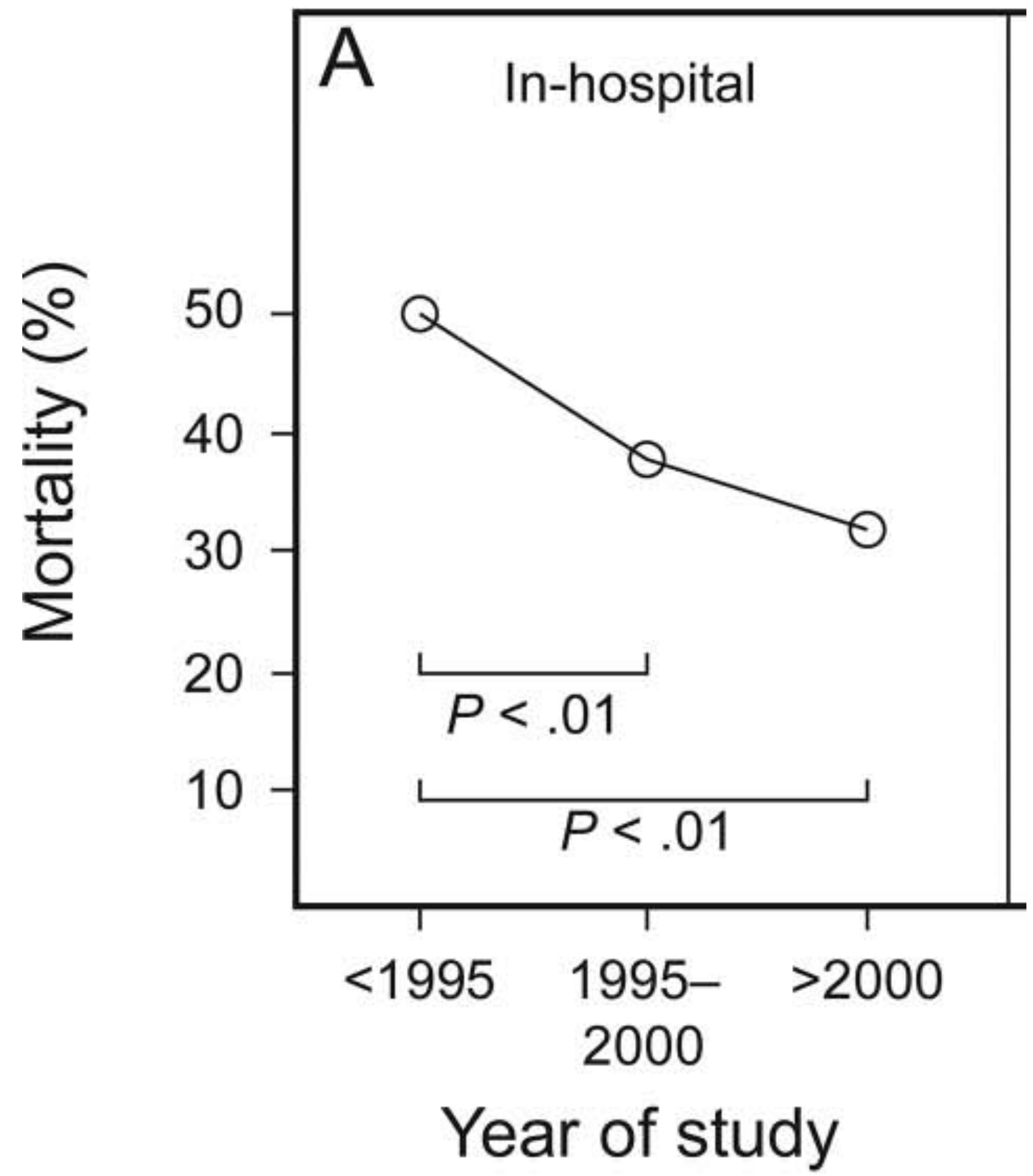
We've come a long way…

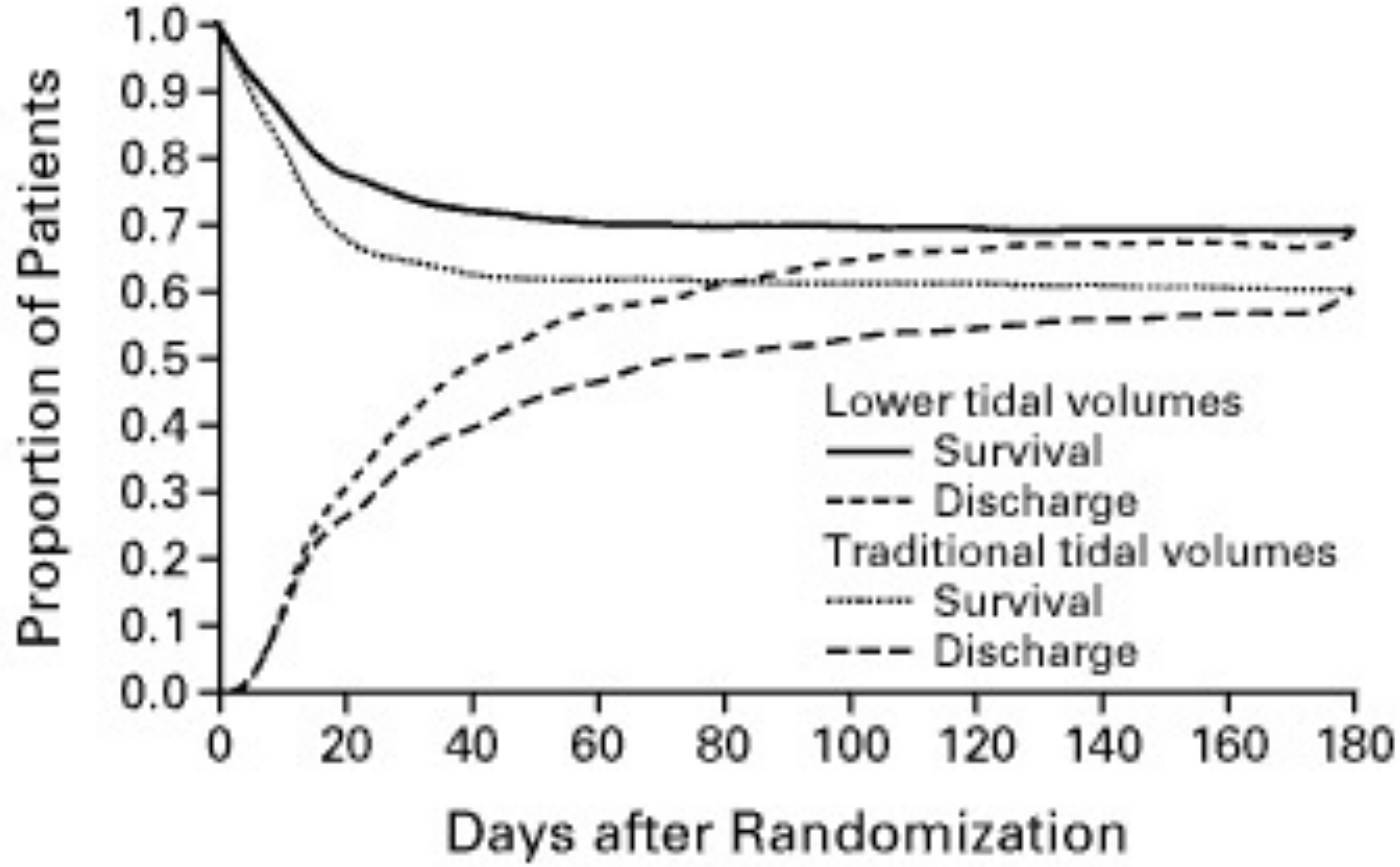
Cardiohelp System

But we are getting better at ARDS treatment



Maca J Respir Care 2017;62(1):113-122.

Or at least causing less harm

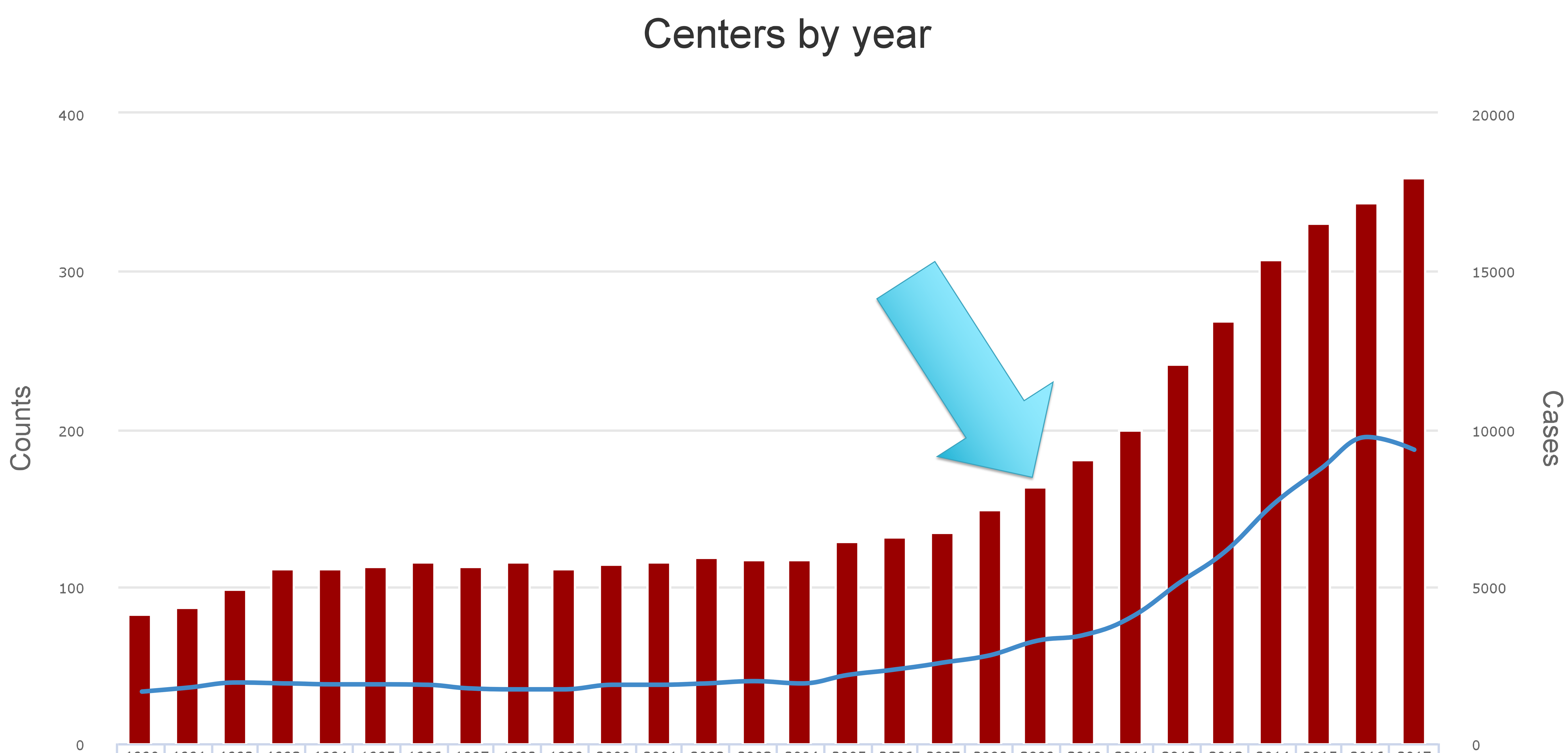


ARDS Net N Engl J Med. 2000;342(18):1301-8.

Herein lies the challenge

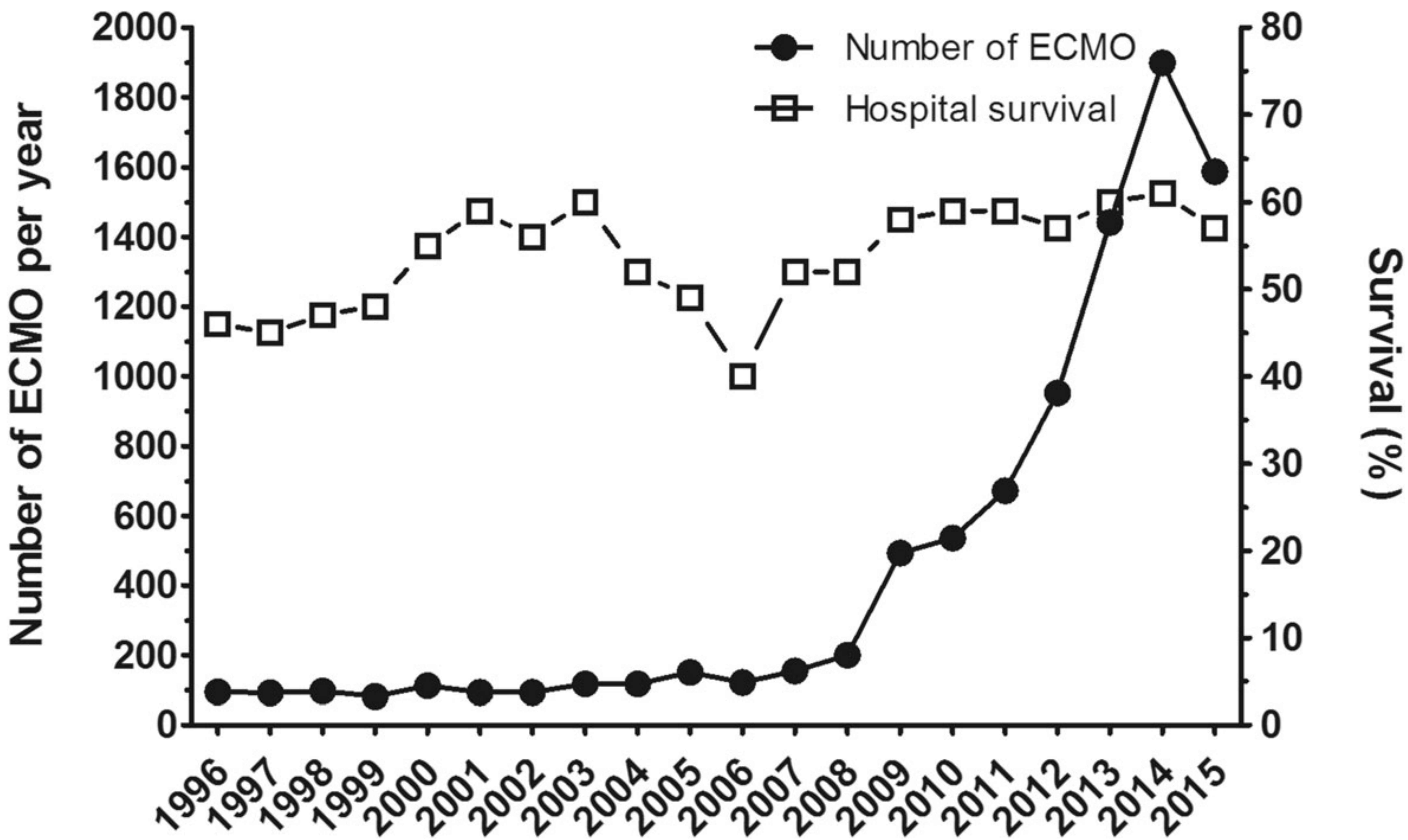
- We must select a population more likely to survive with ECMO than with standard care.
- This benefit must exceed the physiologic cost and challenge of providing ECMO support.
- Low risk ECMO, High risk ARDS or a combination of both.

And then there was H1N1



	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Counts	83	86	98	111	111	112	115	112	115	111	114	115	119	117	117	129	131	134	149	163	181	200	241	269	308	330	343	359
Cases	1644	1775	1933	1910	1879	1876	1868	1743	1720	1722	1859	1855	1908	1974	1907	2183	2346	2564	2802	3261	3443	4012	5083	6113	7583	8707	9736	9330

ELSO International Report.



Rozencwajg S. Crit Care 2016;20;392.

ECMO Survival Models

Model	N	AUROC(internal)	Year
ECMOnet	60	0.86	2009 H1N1
PRESERVE	140	0.89	2008-2012
PRESET score	108	0.85	2009-2015
Roch score	85	0.80	2009-2013
Enger et al.	284	0.75	2008-2013
RESP Score	2355	0.74	2000-2012

ECMOnet Score

- 60 Italian patients
- H1N1 in 2009
- www.ecmonet.org
  - In Italian

$$\text{ECMOnet score} = \left(\sum_{i=1}^{5} ps_i\right) - 1$$

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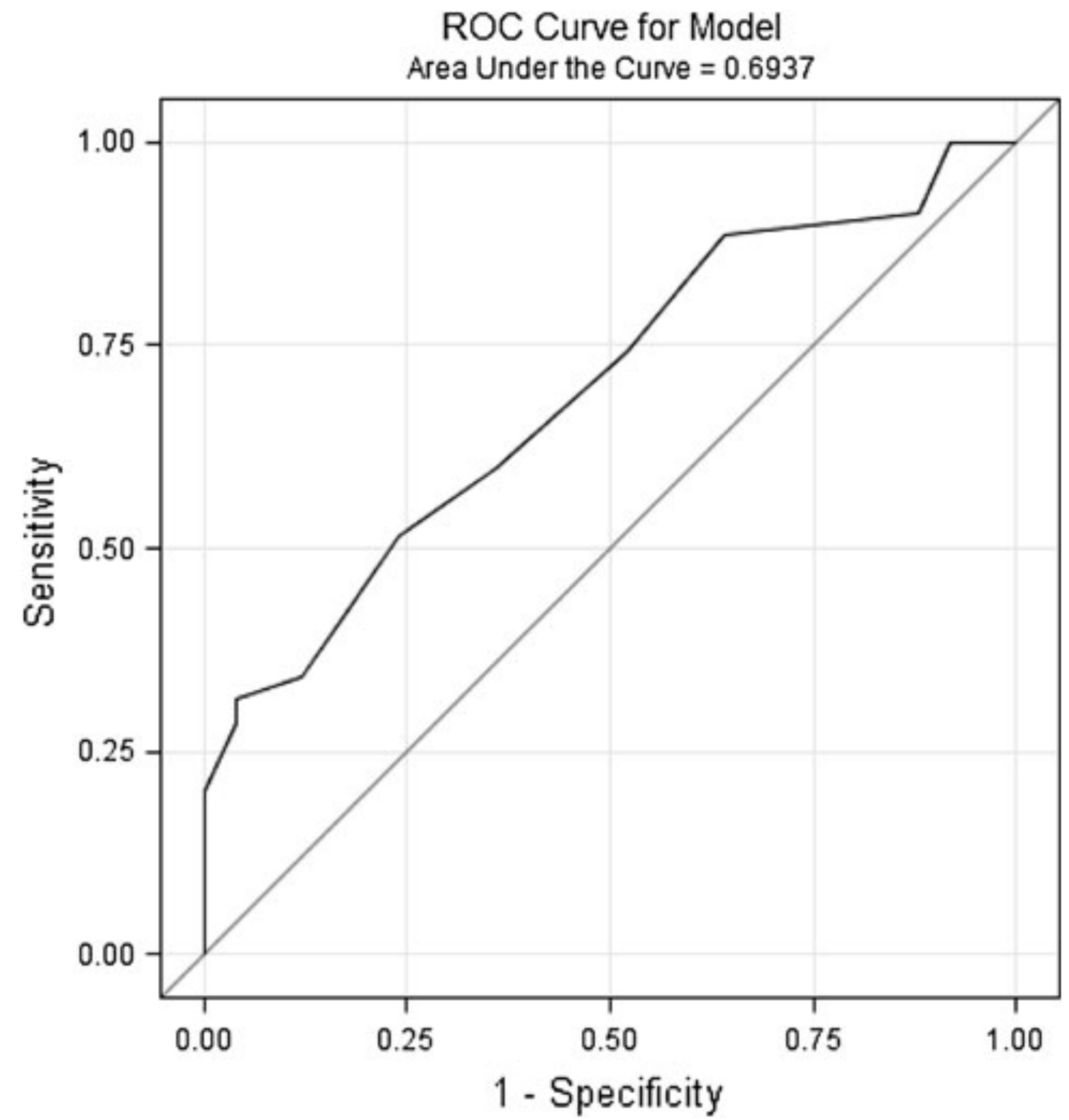
ECMOnet results

Table 2 The ECMOnet score

Parameter	Partial score
PreECMO hospital length of stay (days)	
≤3	0.5
4–7	1
8–11	1.5
>11	2
Bilirubin (mg/dl)	
≤0.15	0
0.16–0.65	0.5
0.66–1.15	1
1.16–1.65	1.5
1.66–2.15	2
>2.15	2.5
Creatinine (mg/dl)	
≤0.5	0
0.51–0.80	0.5
0.81–1.10	1
1.11–1.40	1.5
1.41–1.70	2
1.71–2.00	2.5
2.01–2.30	3
>2.30	3.5
Hematocrit (%)	
>40	0.5
36–40	1
31–35	1.5
≤30	2.0
Mean arterial pressure (mmHg)	
>90	0
61–90	0.5
≤60	1



Pappalardo F et al. Intensive Care Med 2013;39:275-281.

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PRESERVE Score

- 140 French patients
- Median PaO_2/FiO_2 prior to cannulation 53
- 95% VV ECMO
- $^{2}/_{3}$ of patients prone ventilation prior to ECMO
- Median time from intubation to ECMO 5 days (1-11)
- PRedicting dEath for SEvere ARDS on VV-ECMO

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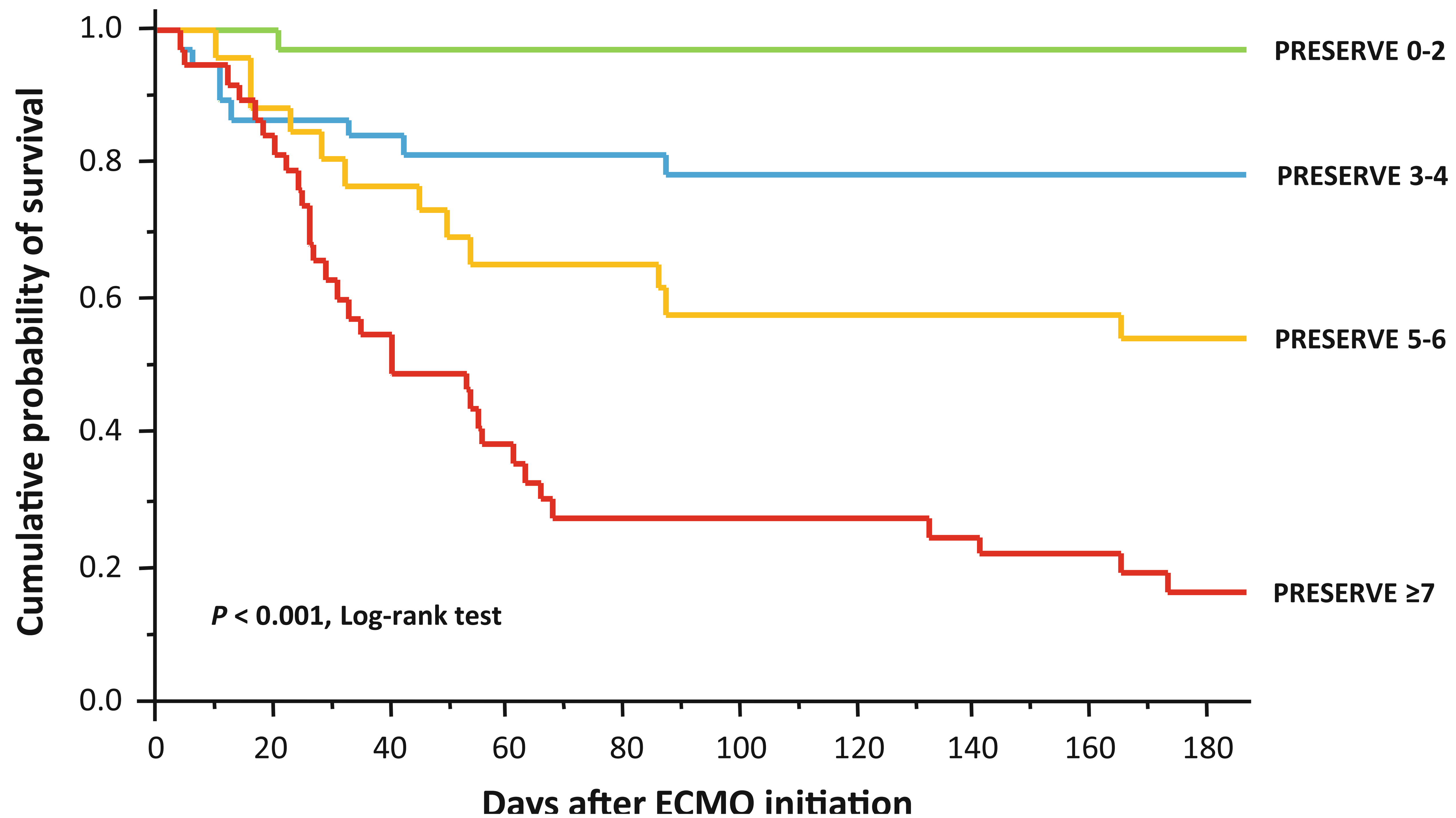
PRESERVE results

Table 4 The PRESERVE score calculated with parameters available at the time of decision to initiate ECMO

Parameter	Score
Age (years)	
<45	0
45–55	2
>55	3
Body mass index >30	−2
Immunocompromised	2
SOFA >12[a]	1
MV >6 days	1
No prone positioning before ECMO	1
PEEP < 10 cm H_2O	2
Plateau pressure >30 cm H_2O	2
Total score[c]	0–14



Schmidt M et al. Intensive Care Med 2013;39:1704-1713.

PRESET Score

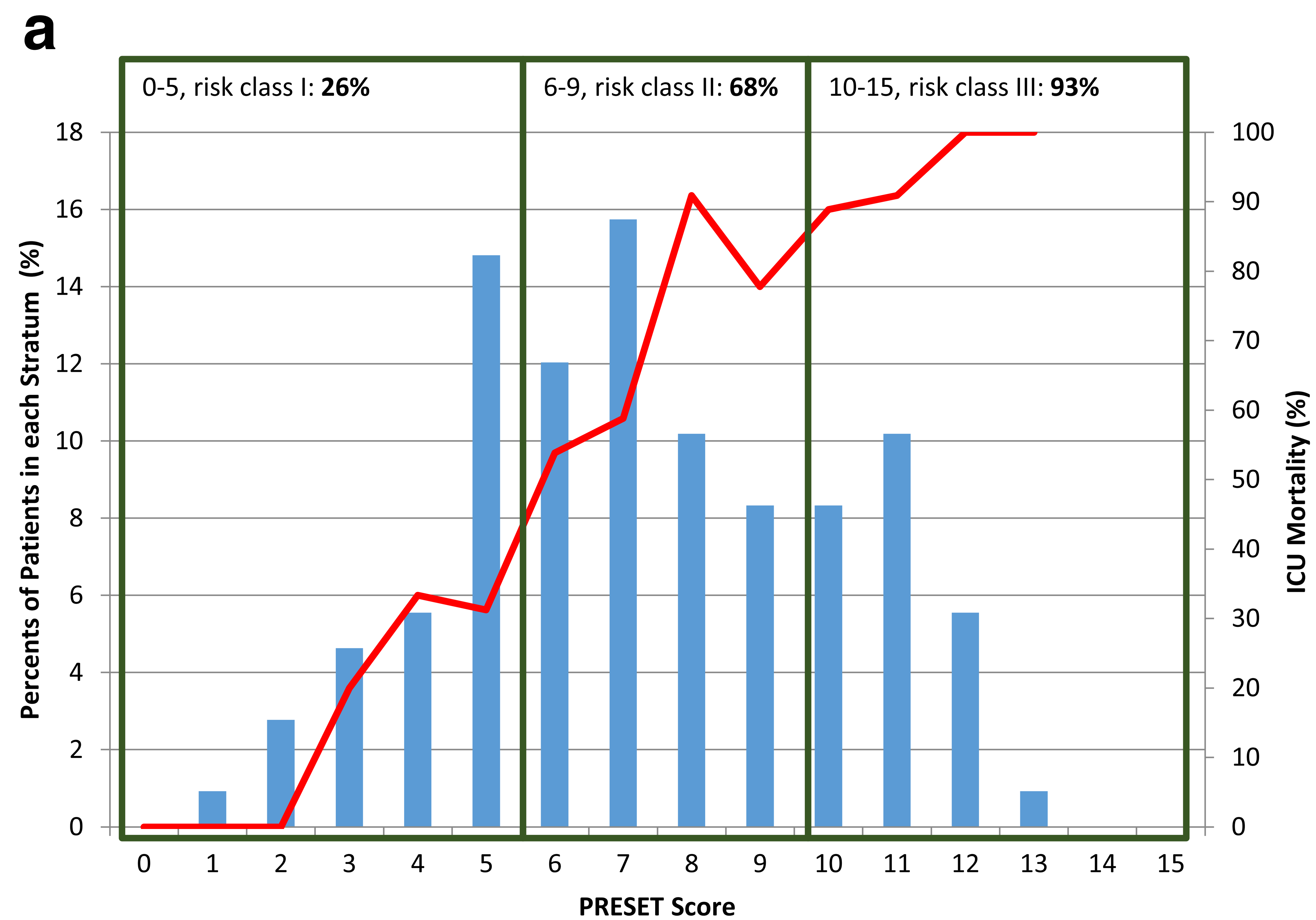
- 108 German patients
- Focused on extrapulmonary risk factors
  - MAP
  - Lactate
  - pH
  - Platelet count
  - Hospital days pre-ECMO

PRESET Score

Table 4 PRESET-Score at ECMO initiation

Variable	Points
Mean arterial pressure (mmHg)	
> 100	0
91–100	1
81–90	2
71–80	3
≤ 70	4
Lactate concentration (mmol l^{-1})	
≤ 1.50	0
1.51–3.00	1
3.01–6.00	2
6.01–10.00	3
> 10.00	4
pH_a	
> 7.300	0
7.201–7.300	1
7.101–7.200	2
≤ 7.100	3
Platelet concentration (×1000 μl^{-1})	
> 200	0
101–200	1
≤ 100	2
Hospital days pre ECMO	
≤ 2	0
3–7	1
> 7	2
Total score	0–15
ICU mortality by risk class	Mortality (%)
PRESET-Score 0–5, risk class I	26
PRESET-Score 6–9, risk class II	68
PRESET-Score 10–15, risk class III	93

ECMO extracorporeal membrane oxygenation, *ICU* intensive care unit, *PRESET-Score* PREdiction of Survival on ECMO Therapy-Score



Hilder et al. Critical Care (2017) 21:301.

Roch Score

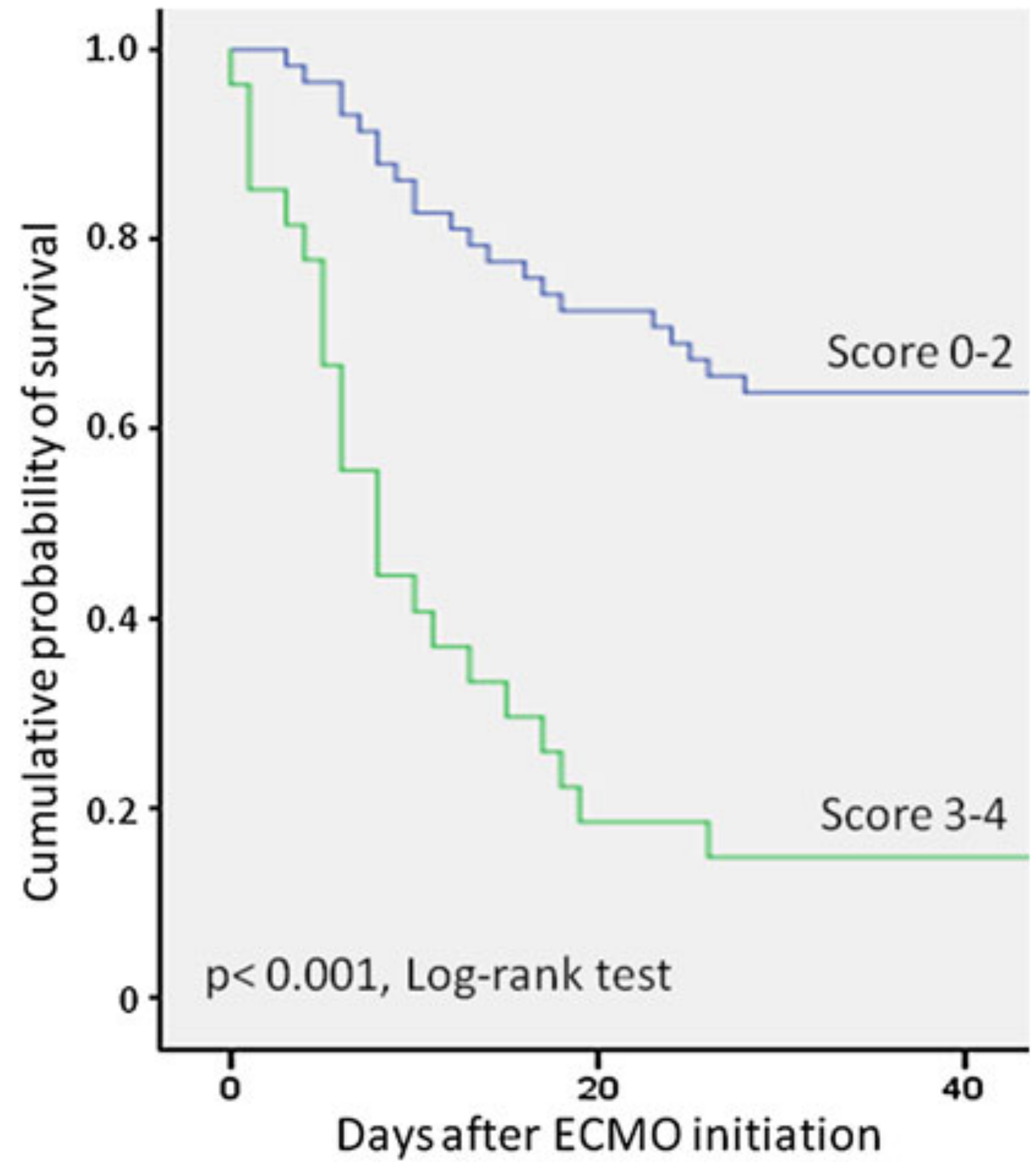
- 85 French patients
- Cannulation at OSH then transfer to ECMO center

Roch Score

Table 3 Hospital mortality score calculated with parameters available just before ECMO initiation

Parameter	Partial score ps_i
SOFA	
<9	0
9–11	1
≥12	2
Age	
<45 years	0
≥45 years	1
Influenza pneumonia	
Yes	0
No	1
Total score	0–4

A higher score was associated with higher hospital mortality
SOFA sequential organ failure assessment



Roch A. Intensive Care Med (2014) 40:74–83

Enger et al.

- 284 German patients
- Later coined UKR Pre-ECMO Score
- Evaluation Pre-EMCO and Day 1 post cannulation

Enger Model- UKR Pre-ECMO Score

Model 1 (pre-ECMO)

Age (per five years)

Immunocompromised state

Minute ventilation (L/minute)

Pre-ECMO hemoglobin (g/dL)

Pre-ECMO lactate (mmol/L)

Intercept

Model 2 (Day 1)

Age (per five years)

Immunocompromised state

Minute ventilation (L/minute)

Pre-ECMO hemoglobin (g/dL)

Day 1 FiO_2 (per 10%)

Day 1 fibrinogen (mg/dL)

Day 1 norepinephrine (µg/minute/10 kg)

Day 1 C-reactive protein (mg/L)

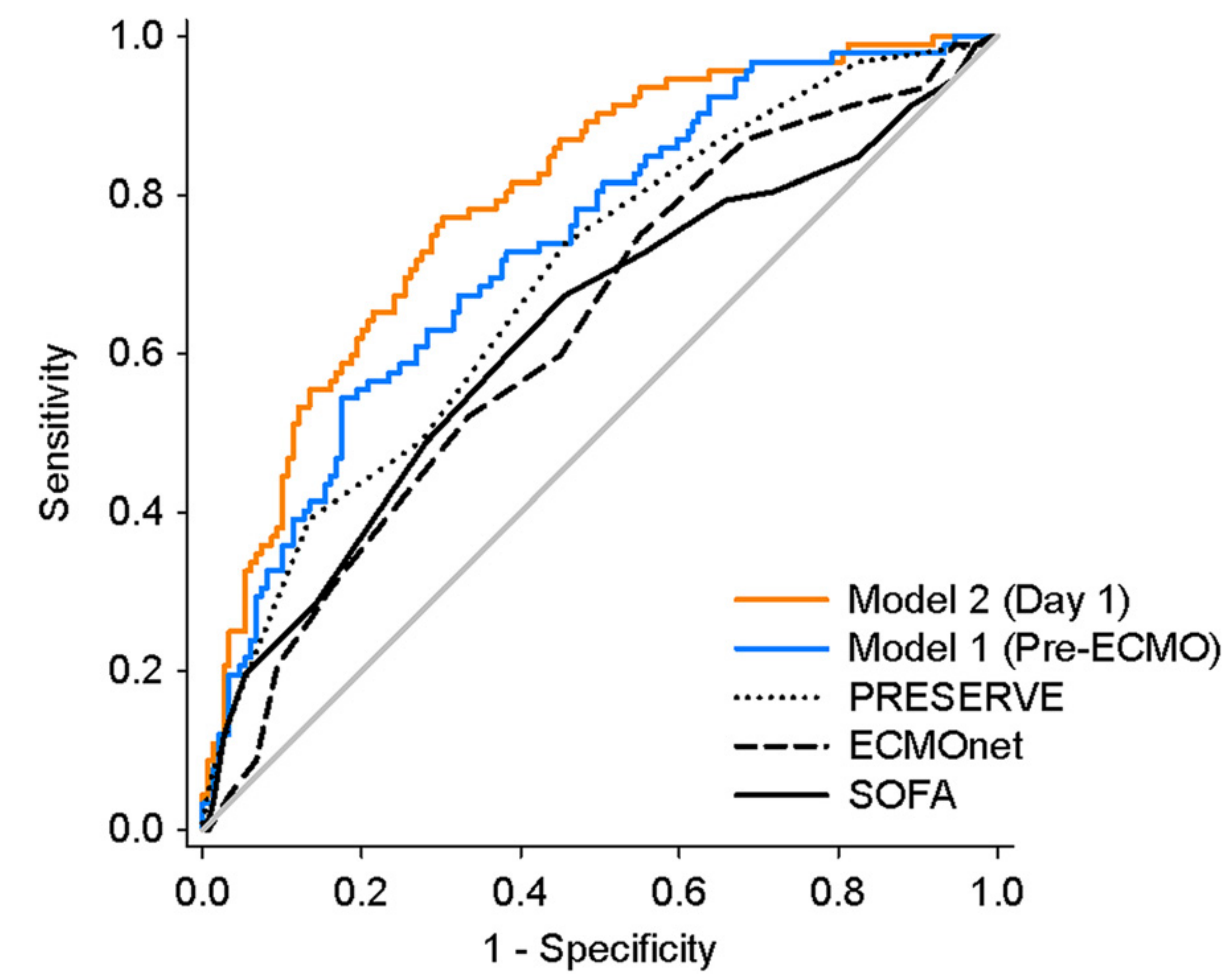


Figure 1 Comparison of the receiver-operating curves for all risk prediction tools (n = 241). Neither the ECMOnet nor the PRESERVE score had significantly better discrimination compared to the SOFA score ($P = 0.67$ and 0.25, respectively). Model 1 improved discrimination compared to the SOFA and the ECMOnet score ($P = 0.03$ and 0.009, respectively). Addition of parameters available one day after ECMO initiation further enhanced discrimination compared to both Model 1 and the PRESERVE score ($P = 0.03$ and $P = 0.003$, respectively). Further statistical comparison is given in Table 2. ECMO, extracorporeal membrane oxygenation; SOFA, Sequential Organ Failure Assessment.

Enger et al. Critical Care 2014, 18:R67

RESP Score

- 2355 patients from international ELSO database
- Negative scores indicate mortality

Citation.

RESP Score

Parameter	Score
Age, yr	
18 to 49	0
50 to 59	−2
⩾60	−3
Immunocompromised status*	−2
Mechanical ventilation prior to initiation of ECMO	
<48 h	3
48 h to 7 d	1
>7 d	0
Acute respiratory diagnosis group (select only one)	
Viral pneumonia	3
Bacterial pneumonia	3
Asthma	11
Trauma and burn	3
Aspiration pneumonitis	5
Other acute respiratory diagnoses	1
Nonrespiratory and chronic respiratory diagnoses	0
Central nervous system dysfunction†	−7
Acute associated (nonpulmonary) infection‡	−3
Neuromuscular blockade agents before ECMO	1
Nitric oxide use before ECMO	−1
Bicarbonate infusion before ECMO	−2
Cardiac arrest before ECMO	−2
Pa_{CO_2}, mm Hg	
<75	0
⩾75	−1
Peak inspiratory pressure, cm H_2O	
<42	0
⩾42	−1
Total score	−22 to 15

Hospital Survival by Risk Class		
Total RESP Score	Risk Class	Survival
⩾6	I	92%
3 to 5	II	76%
−1 to 2	III	57%
−5 to −2	IV	33%
⩽−6	V	18%

Schmidt et al Am J Respir Crit Care Med189(11);1374–1382.

RESP Score

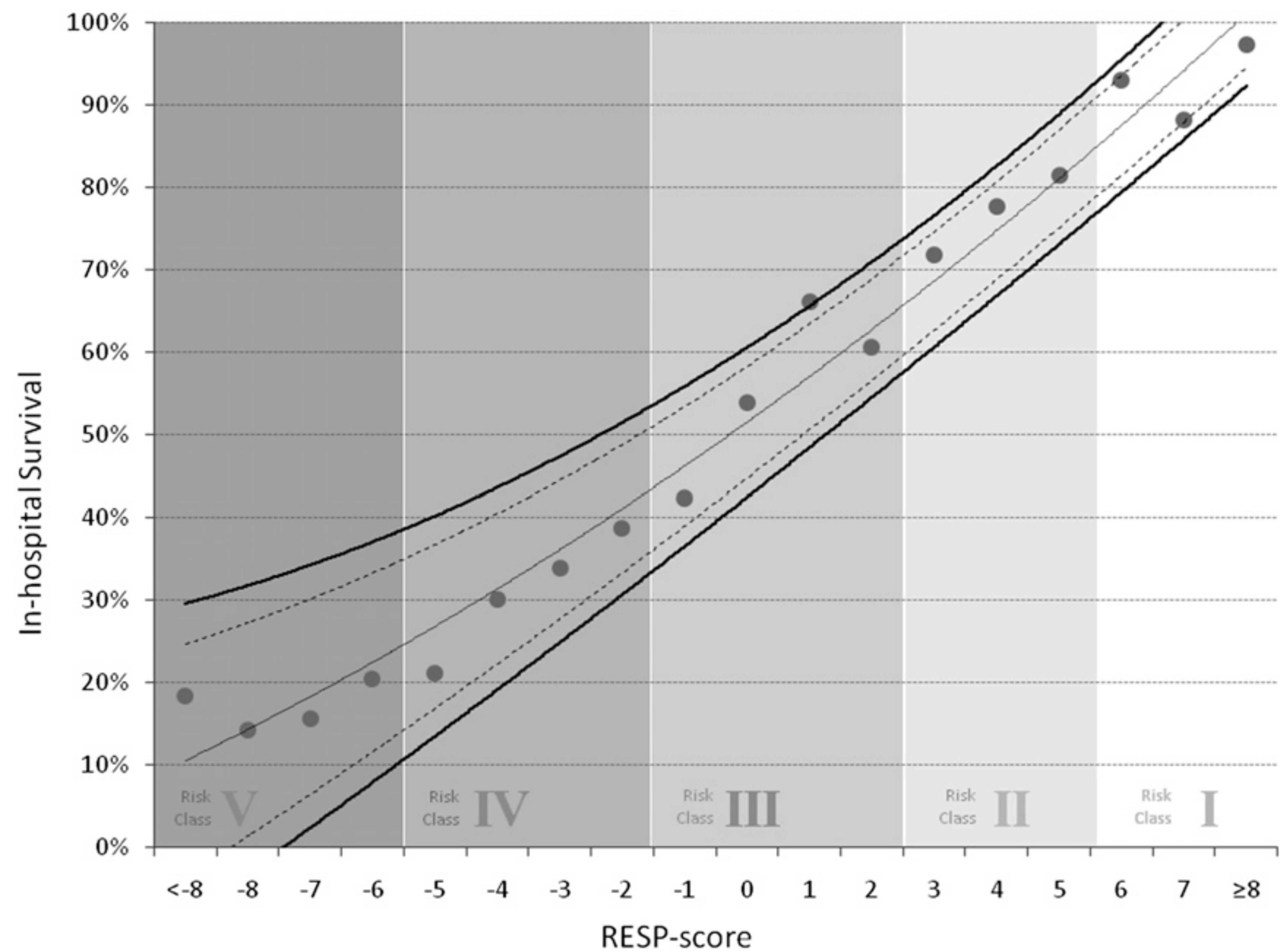


Figure 2. Individual observed survival regarding the Respiratory Extracorporeal Membrane Oxygenation Survival Prediction (RESP) score within 95% confidence interval. Each *dot* represents the observed survival percentage in the study population (n = 2,355) used to derive the RESP score. *Curved dotted gray lines* and *curved black lines* represent 95 and 99% confidence intervals, respectively, for predicted survival at each score level.

Schmidt et al Am J Respir Crit Care Med189(11);1374–1382.

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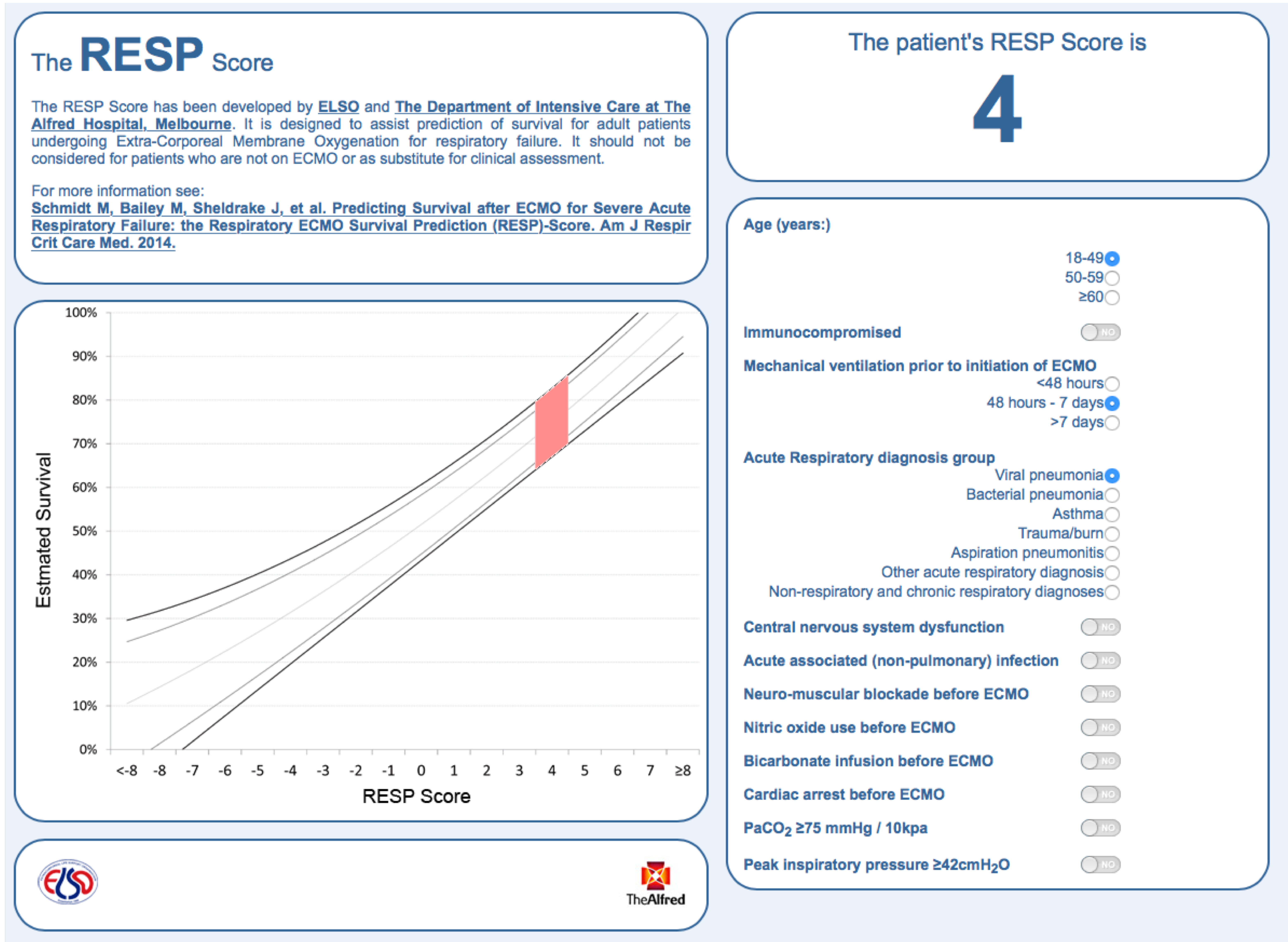
respscore.com



Effect of BMI

Variable	BMI <40 kg/m^2 (n = 43)	BMI ≥40 kg/m^2 (n = 12)	*p* Value	BMI ≥50 kg/m^2 (n = 6)	*p* Value[a]
Intensive care unit LOS (d)	15.5 (IQR: 6–37.5)	28 (IQR: 13.5–46.5)	0.35	33 (IQR: 25–45)	0.13
Hospital LOS (d)	28 (IQR: 7–55)	35 (IQR: 13.5–50)	0.77	42 (IQR: 31–45)	0.22
Weaned from ECMO	27 (63%)	9 (75%)	0.51	6 (100%)	0.16
Bridge to recovery	26 (60%)	9 (75%)	0.50	6 (100%)	0.08
Bridge to transplantation	1 (2%)	0 (0%)	1	0 (0%)	1
Complications					
Major bleeding/thrombosis	13 (30%)	5 (42%)	0.50	3 (50%)	0.38
HITT	2 (5%)	3 (25%)	0.06	1 (17%)	0.33
CVA	3 (7%)	1 (8%)	1	0 (0%)	1
Hospital or 30-d mortality	18 (42%)	4 (33%)	0.74	0 (0%)	0.07

[a] Compared with BMI < 40 kg/m^2.

Kon et al. Ann Thorac Surg 2015;100:1855–60

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Understanding the balance

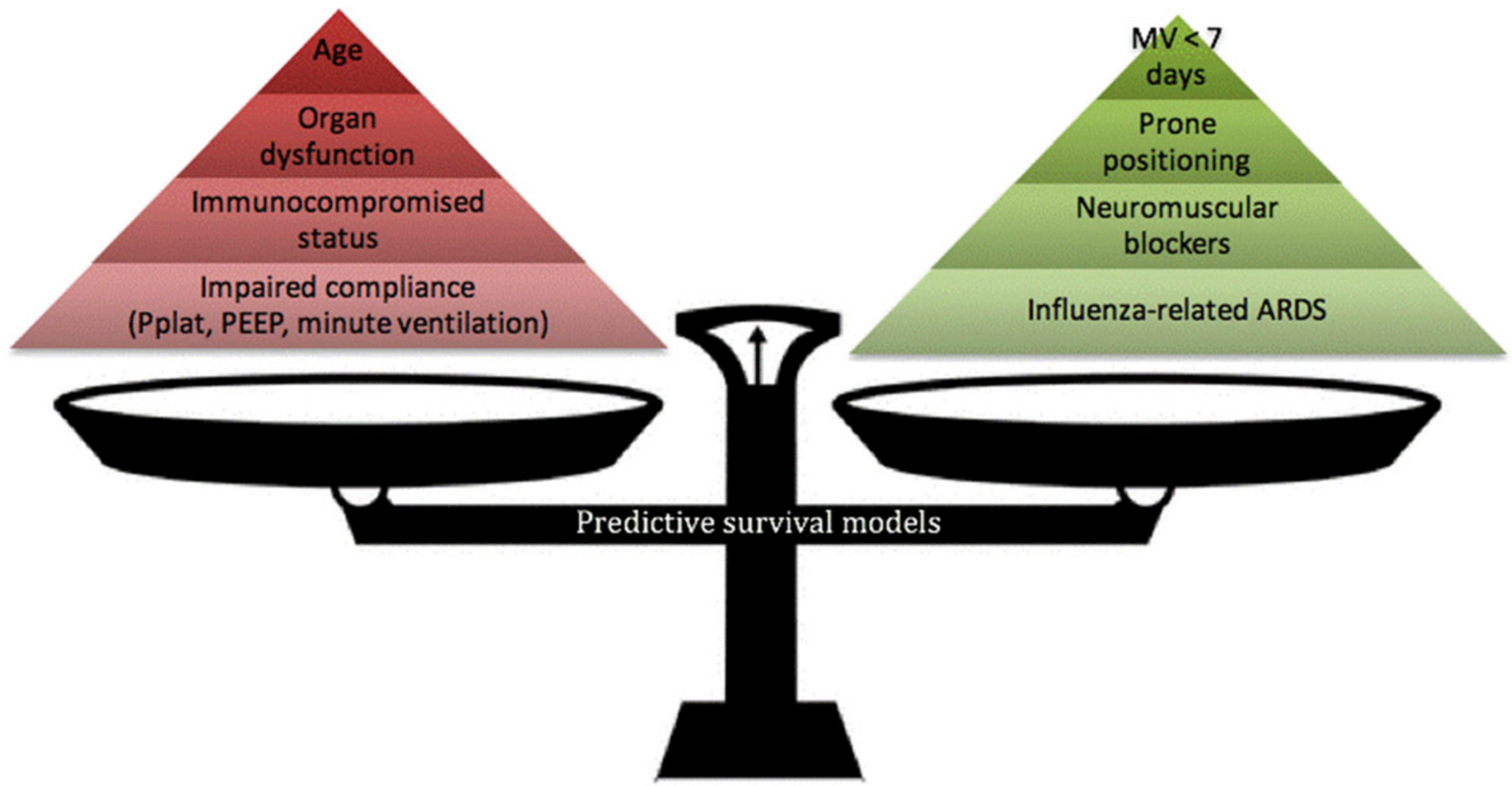


Fig. 2 Pre-ECMO factors associated with mortality on VV-ECMO according to published predictive survival models. *Red pyramid*, risk factors; *green pyramid*, protective factors: the higher the factor, the heavier impact on mortality according to published predictive survival models. *ARDS* acute respiratory distress syndrome, *MV* mechanical ventilation, *Pplat,* plateau pressure *PEEP* positive end-expiratory pressure

Rozencwajg S. Crit Care 2016;20;392.

What predicts ARDS mortality?

- Stratification and Outcome of ARDS (STANDARDS) Network
- Simplified score
  - Age
  - PaO_2/FiO_2
  - APPS (Airway plateau pressure score)
- AUC 0.80 for score >7
- Outperforms APACHE II score (AUC 0.66)

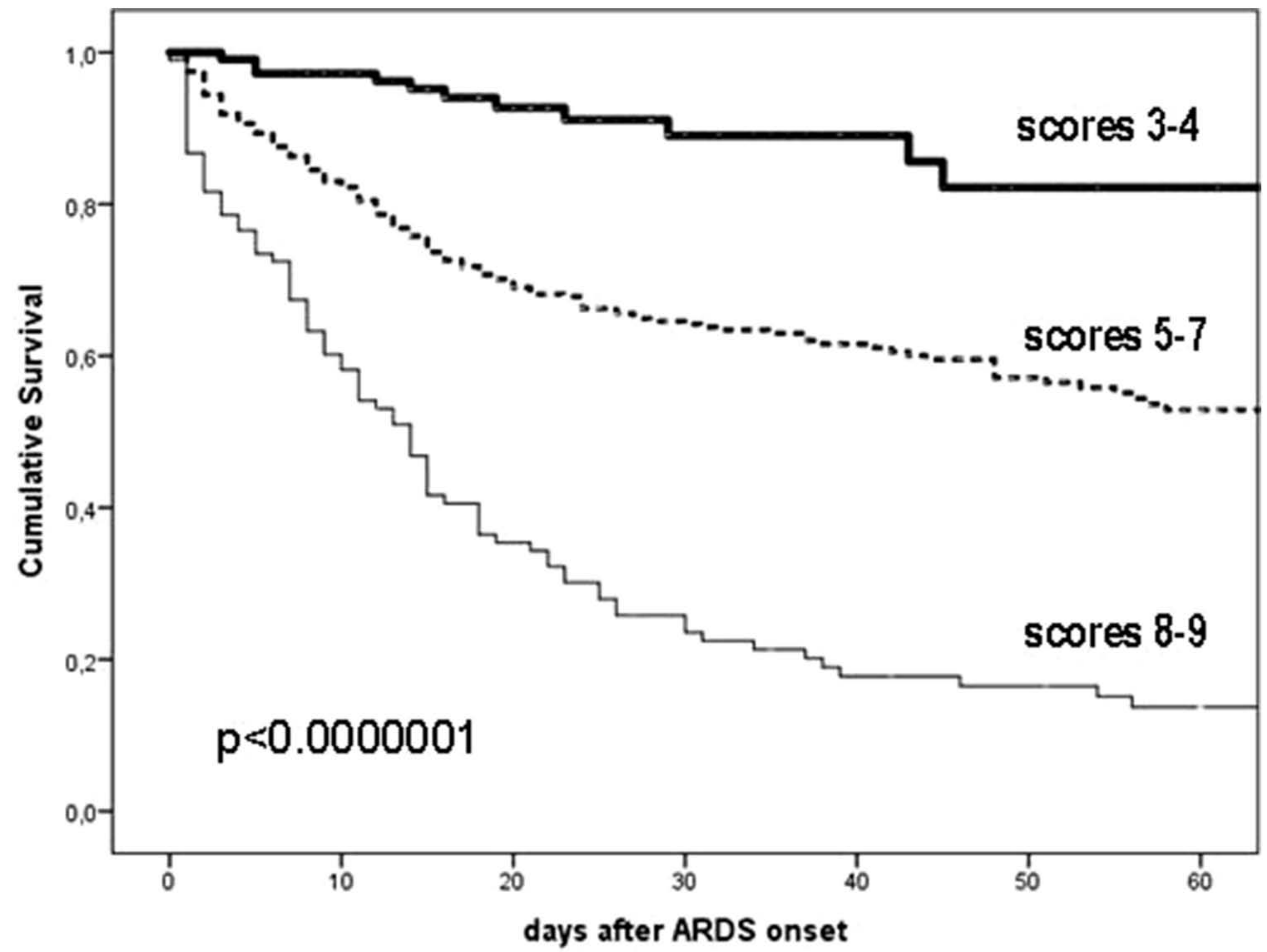
Vilar J. Crit Care Med. 2016;44:1361-9.

STANDARDS Network Score

TABLE 3. A 9-Point Acute Respiratory Distress Syndrome Outcome Score (Age, Pao_2/Fio_2, and Plateau Pressure Score)

Variables	Range of Values	Score
Age, yr	< 47	1
	47–66	2
	> 66	3
Pao_2/Fio_2, mm Hg	> 158	1
	105–158	2
	< 105	3
Plateau pressure, cm H_2O	< 27	1
	27–30	2
	> 30	3
Total score		3–9

Total score is equal to the sum of the points for each category of high-risk tertiles, based on the values at 24 hr after acute respiratory distress syndrome diagnosis.



Vilar J. Crit Care Med. 2016;44:1361-9.

Murray Score

- Quadrants of consolidation (0-4)
- PaO_2/F_iO_2 ratio (0-4)
- PEEP (0-4)
- Pulmonary compliance (0-4)
  - V_T/(PIP-PEEP)
- ELSO transfer recommendation
  - 2.5 consider ECMO referral
  - 3.0 ECMO referral

Murray J. Am Rev Respir Dis. 1988;138(3):720-3.

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Hail CESAR? 2009

“La morte di Cesare” Vincenzo Camuccini (1804)

CESAR Key points

- Inclusion
  - Severe but potentially reversible respiratory failure:
    - Murray score >2.5
    - Uncompensated hypercapnea with pH<7.20
  - 18-65 y/o
  - Duration of high pressure and/or high FiO_2 ventilation <7 days

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CESAR Key points

- Referral to ECMO Center v. Conventional Management
- Unfortunately other differences in care
  - Increased steroid use (84% v. 64%)
  - Increased use of MARS (17% v 0%)
  - Less HFOV (7% v. 14%)
  - Low volume Low pressure ventilation (93% v. 70%)

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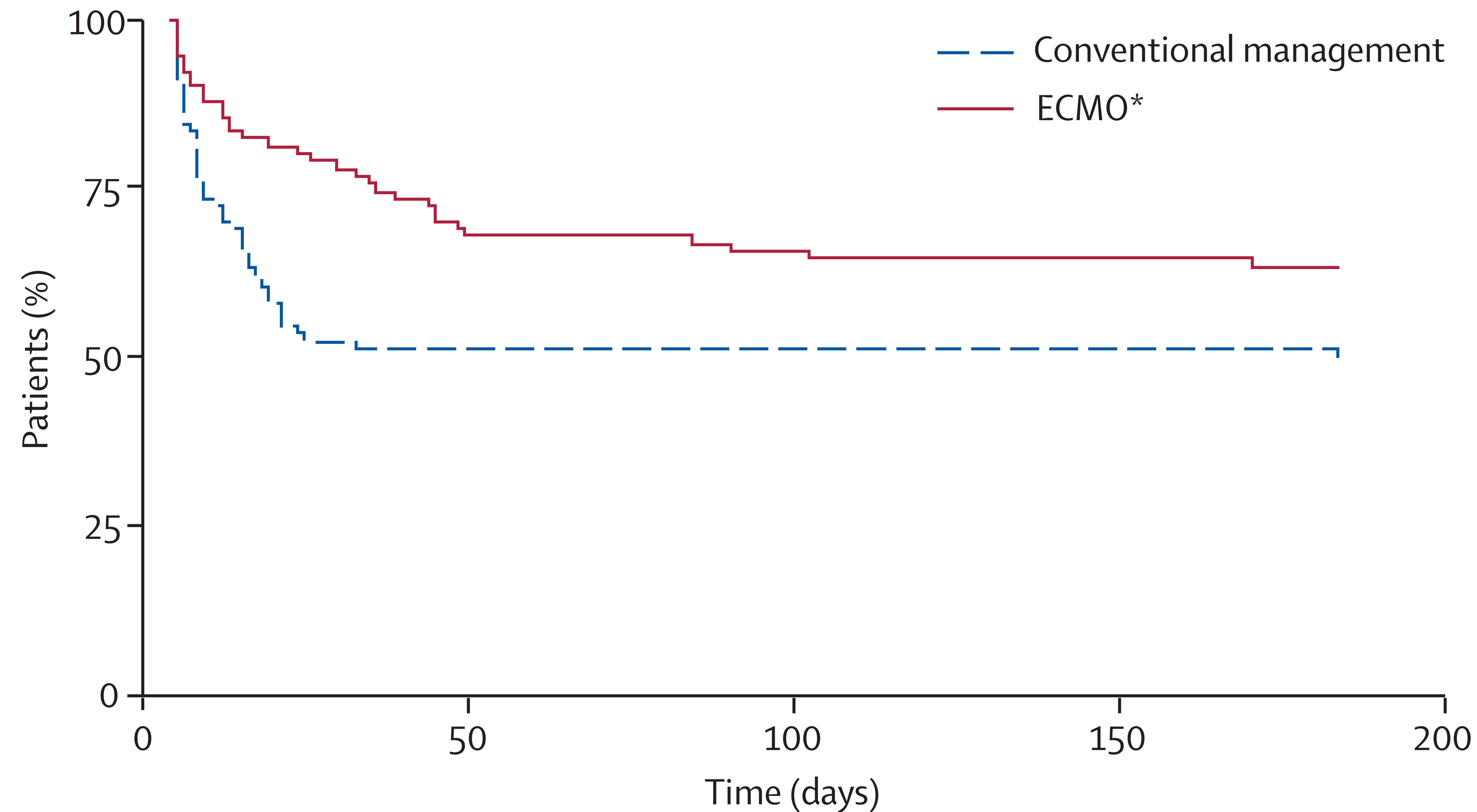
CESAR Result



Patients at risk

Conventional management	90	45	44	44	0
ECMO*	90	61	59	58	0

Figure 2: **Kaplan-Meier survival estimates**
ECMO=extracorporeal membrane oxygenation. *Patients were randomly allocated to consideration for treatment by ECMO, but did not necessarily receive this treatment.

Peek et al. Lancet 2009;374:1351-63.

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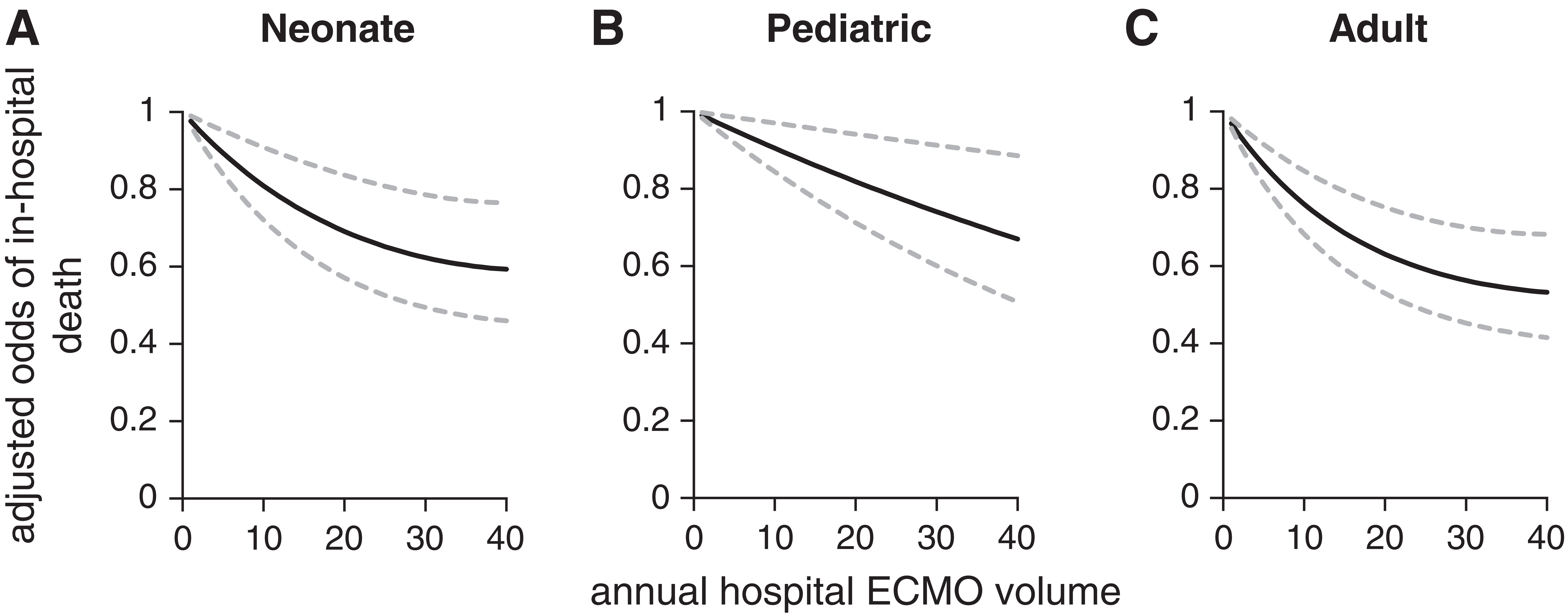
Effect of Center Volume



Barbora RP. J Am J Respir Crit Care Med 2015;191(8):894-901.

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Diseases that do well

- Pneumonia
  - Influenza/viral
- Aspiration
- Pulmonary contusion
- Primary graft dysfunction following lung transplant
- Steroid responsive lung disease

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And those that don't

- Profound septic shock
- Acute/subacute pulmonary fibrosis
- Irreversible lung injury (i.e. Bleomycin lung injury)
- Cryptogenic Organizing Pneumonia
- Debility/Immobility/Frailty
- MSOF

Time for new data

EOLIA: ECMO to rescue Lung Injury in severe ARDS

- RCT ECMO v. Conventional Care
- Conventional care
  - VT 6mL/kg
  - Plateau pressure 28-30cm H_2O
  - Allows iNO and prone ventilation

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EOLIA:ECMO to rescue Lung Injury in severe ARDS

- Inclusion
  - ARDS
  - MV <6days
  - One of the three criteria following optimization
    - PaO_2/FiO_2 < 50mmHg with FiO_2>80% for >3h
    - PaO_2/FiO_2 < 80mmHg with FiO_2>80% for >6h
    - pH <7.25 and $PaCO_2$ >60mmHg for >6h with plat <32

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EOLIA:ECMO to rescue Lung Injury in severe ARDS

- Exclusion
  - MV >7days
  - BMI >45
  - Chronic respiratory insufficiency
  - HIT
  - Oncologic disease not expected to survive 5yrs
  - Moribund (SAPS II >90)

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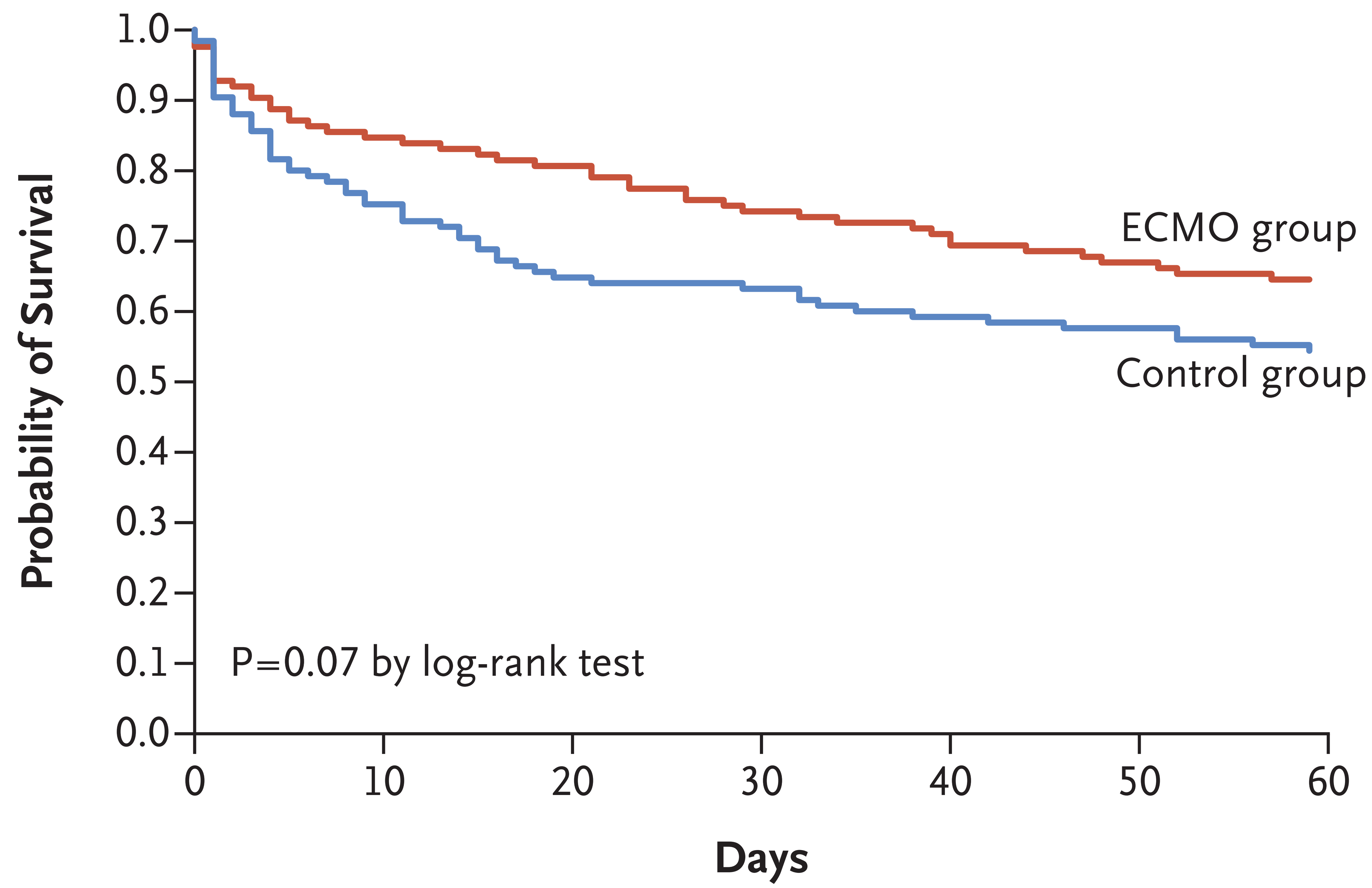
EOLIA Results



No. at Risk

ECMO	124	105	100	92	88	83	80
Control	125	94	81	79	74	72	69

Figure 2. **Kaplan–Meier Survival Estimates in the Intention-to-Treat Population during the First 60 Days of the Trial.**

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EOLIA: ECMO to rescue Lung Injury in severe ARDS

- Controversy with early termination
  - Unable to meet significance with predetermined enrolment
- 28% Control arm cross over

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UPMC Respiratory Failure ECMO Selection and Exclusion

Pre-ECMO optimization

- ARDSnet settings
- Recruitment trial
- Optimal peep trial
- Paralysis
- Diuretic trial if tolerated
- Transfusion to Hgb 12
- Fever control to T<38.5
- Prone positioning trial

UPMC VV ECMO Selection Criteria

- Reversible disease process
- Failed pre-ECMO optimization
- Failure to maintain PaO_2 > 55mmHg or Sat >88% on 100% FiO_2
- Unable to maintain pH >7.2 due to hypercarbia with elevated plateau pressures

UPMC VV ECMO Exclusion Criteria

- Absolute
  - Baseline advanced lung disease not actively on transplant list. This includes any home O_2 requirement (except OSA)
  - Age > 65
  - Known anoxic brain injury
  - Active GI bleeding
  - Pan-resistant pneumonia
  - Cirrhosis MELD >20
  - Malignancy without surgical cure
  - Advanced HIV/AIDS (well controlled HIV is not an exclusion)
  - Moribund patients

UPMC VV ECMO Exclusion Criteria

- Relative
  - >10 days of mechanical ventilation
  - > 7 days of high pressure or high FiO_2
  - Mild stroke or ICH may be considered

UPMC VV ECMO results

- Overall survival to discharge 2013 to 2017
  - 181 cases 62%
- 2015-2017 subset data
  - Bridge to lung transplant 55%
  - Respiratory failure trauma 56%
  - Respiratory failure 59%
  - Post lung transplant 83%

VV ECMO tips

- Optimize aggressively
- Prone early
- Adhere to ARDSnet
- Remember that neither ECMO nor mechanical ventilation are curative but rather support devices
- Call ECMO team early when you need help and advice.
- MEDCALL 412-647-7000

Thanks