SDRA et SARS-CoV-2 : Place de l'ECMO

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Disclosures

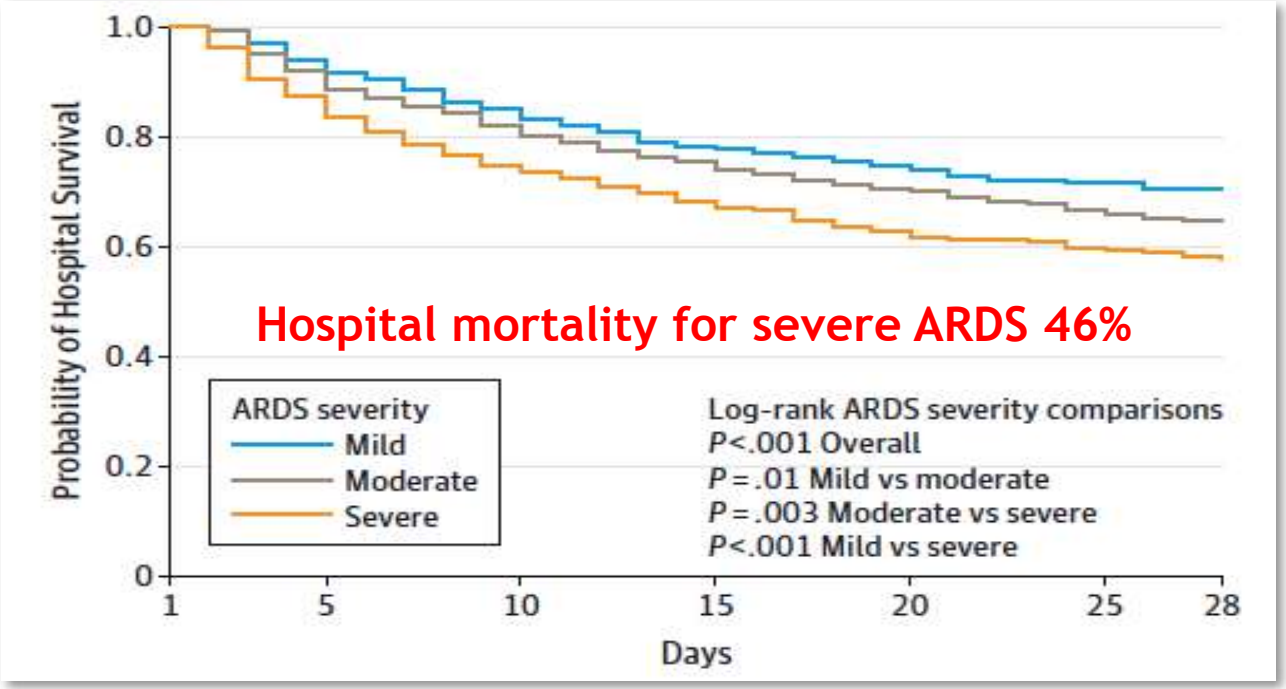
Lectures fees from:

- Getinge
- Xenios
- Dräger
- 3M

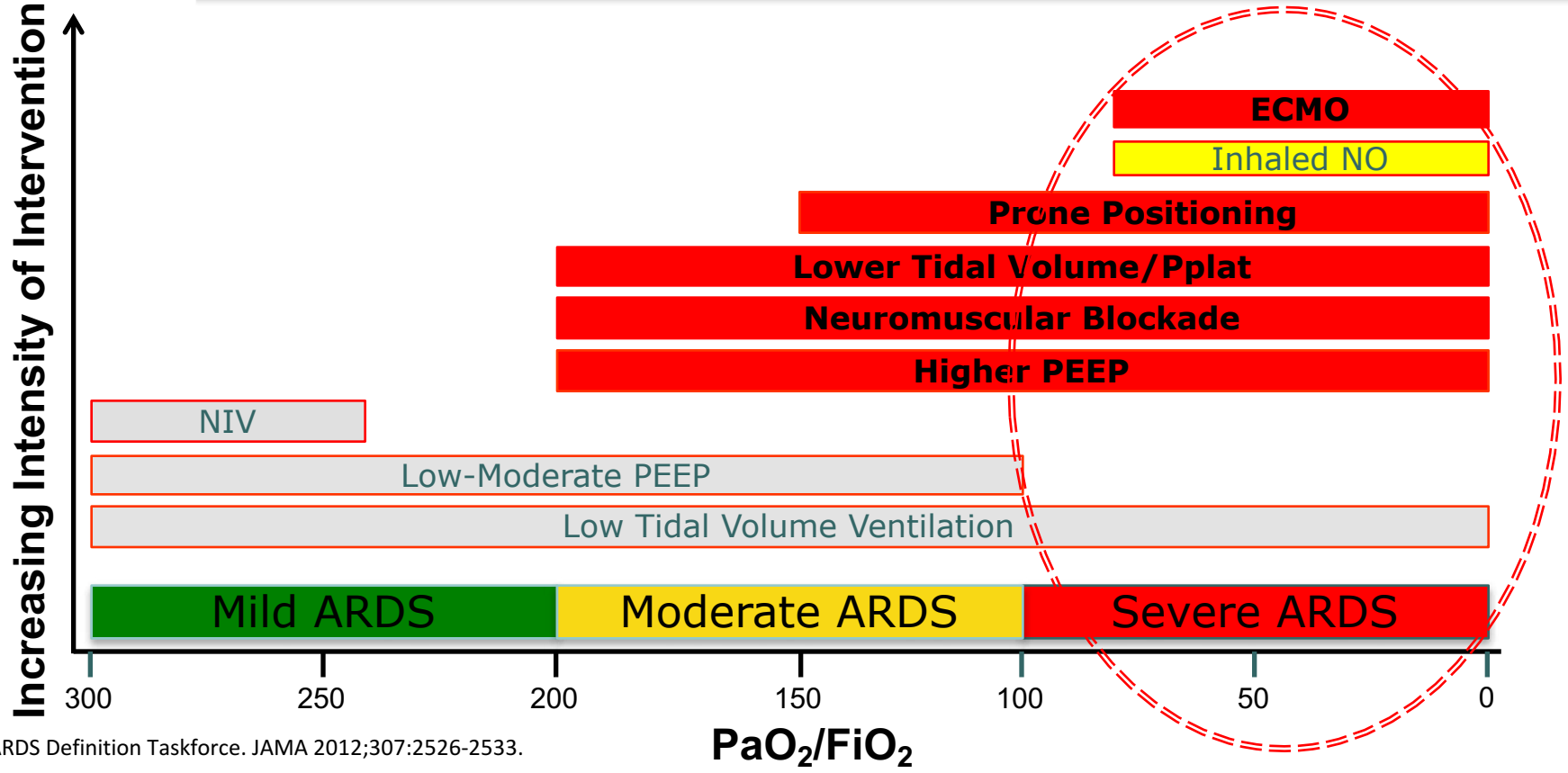
Epidemiology, Patterns of Care, and Mortality for Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries

JAMA. 2016;

Giacomo Bellani, MD, PhD; John G. Laffey, MD, MA; Tài Pham, MD; Eddy Fan, MD, PhD; Laurent Brochard, MD, HDR; Andres Esteban, MD, PhD; Luciano Gattinoni, MD, FRCP; Frank van Haren, MD, PhD; Anders Larsson, MD, PhD; Daniel F. McAuley, MD, PhD; Marco Ranieri, MD; Gordon Rubenfeld, MD, MSc; B. Taylor Thompson, MD, PhD; Hermann Wrigge, MD, PhD; Arthur S. Slutsky, MD, MASc; Antonio Pesenti, MD; for the LUNG SAFE Investigators and the ESICM Trials Group



Acute Respiratory Distress Syndrome
The Berlin Definition



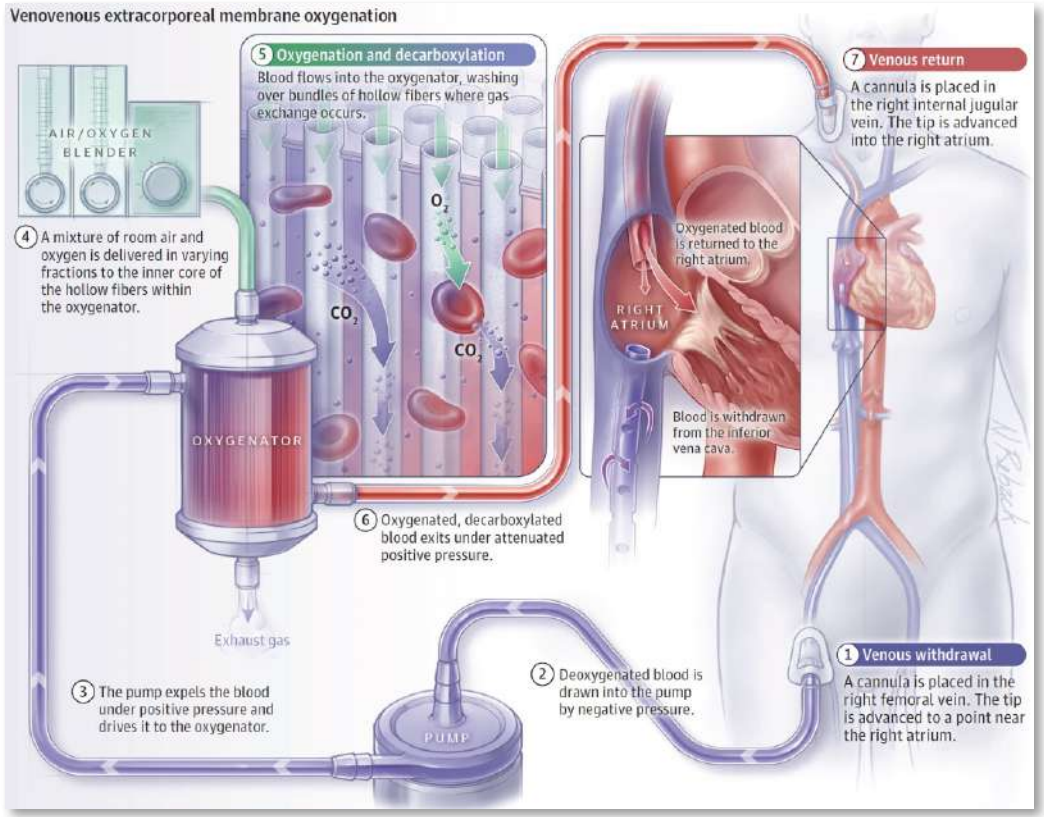
The ARDS Definition Taskforce. JAMA 2012;307:2526-2533.

Extracorporeal Life Support for Adults With Respiratory Failure and Related Indications

A Review

Daniel Brodie, MD; Arthur S. Slutsky, MD; Alain Combes, MD, PhD

JAMA. 2019;322(6):557-568. doi:10.1001/jama.2019.9302



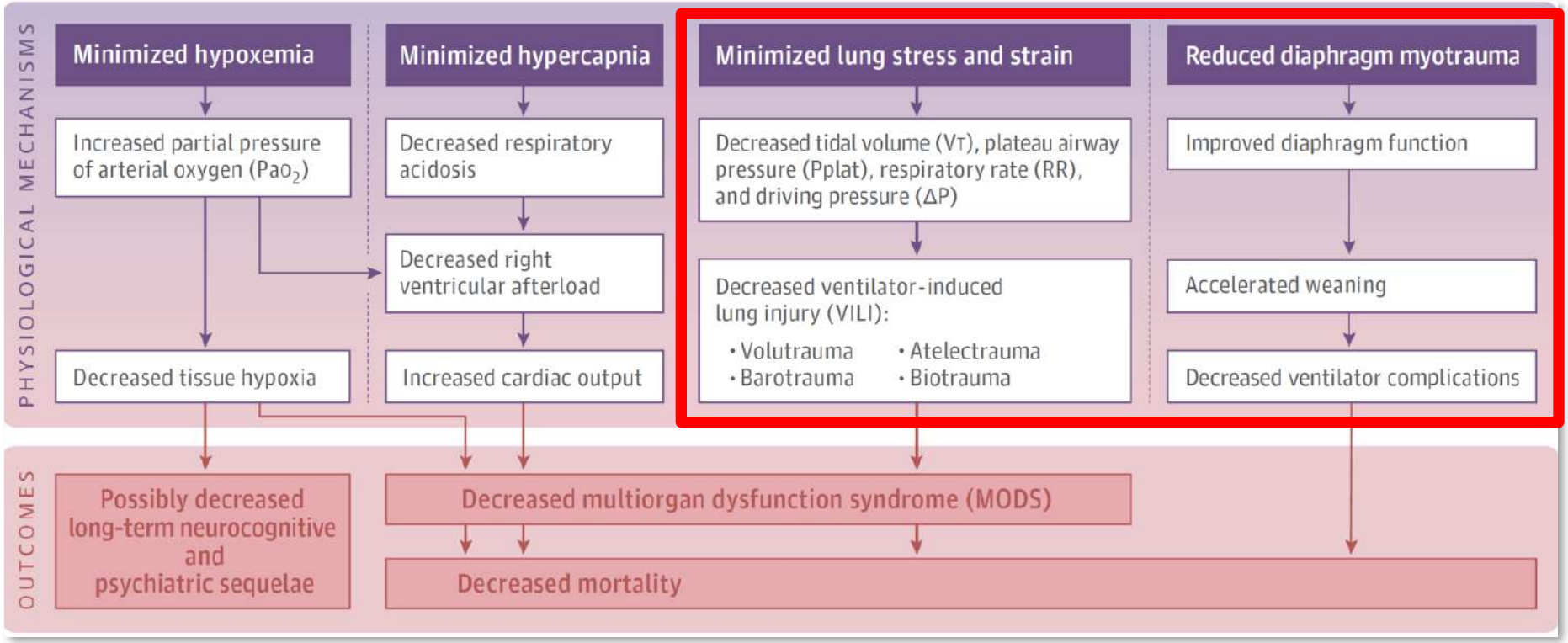
To replace pulmonary function

To allow the lungs to rest…

To allow healing of the lungs…

Potential Physiologic Mechanisms of Benefit of ECLS for Respiratory Failure

JAMA. 2019;322(6):557-568. doi:10.1001/jama.2019.9302



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 24, 2018 VOL. 378 NO. 21

Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome

A. Combes, D. Hajage, G. Capellier, A. Demoule, S. Lavoué, C. Guervilly, D. Da Silva, L. Zafrani, P. Tirot, B. Veber, E. Maury, B. Levy, Y. Cohen, C. Richard, P. Kalfon, L. Bouadma, H. Mehdaoui, G. Beduneau, G. Lebreton, L. Brochard, N.D. Ferguson, E. Fan, A.S. Slutsky, D. Brodie, and A. Mercat, for the EOLIA Trial Group, REVA, and ECMONet*

EOLIA objectives

- EOLIA trial designed to determine the effect of
  - Early initiation of ECMO
  - In patients with the most severe forms of ARDS

Inclusion Criteria

- American–European Consensus Conference definition for ARDS criteria
- Intubated and on MV for <7 days
- MV optimization before inclusion
  - F_IO_2 ≥80%
  - V_T = 6 ml/kg PBW
  - Trial of PEEP ≥10 cm H_2O

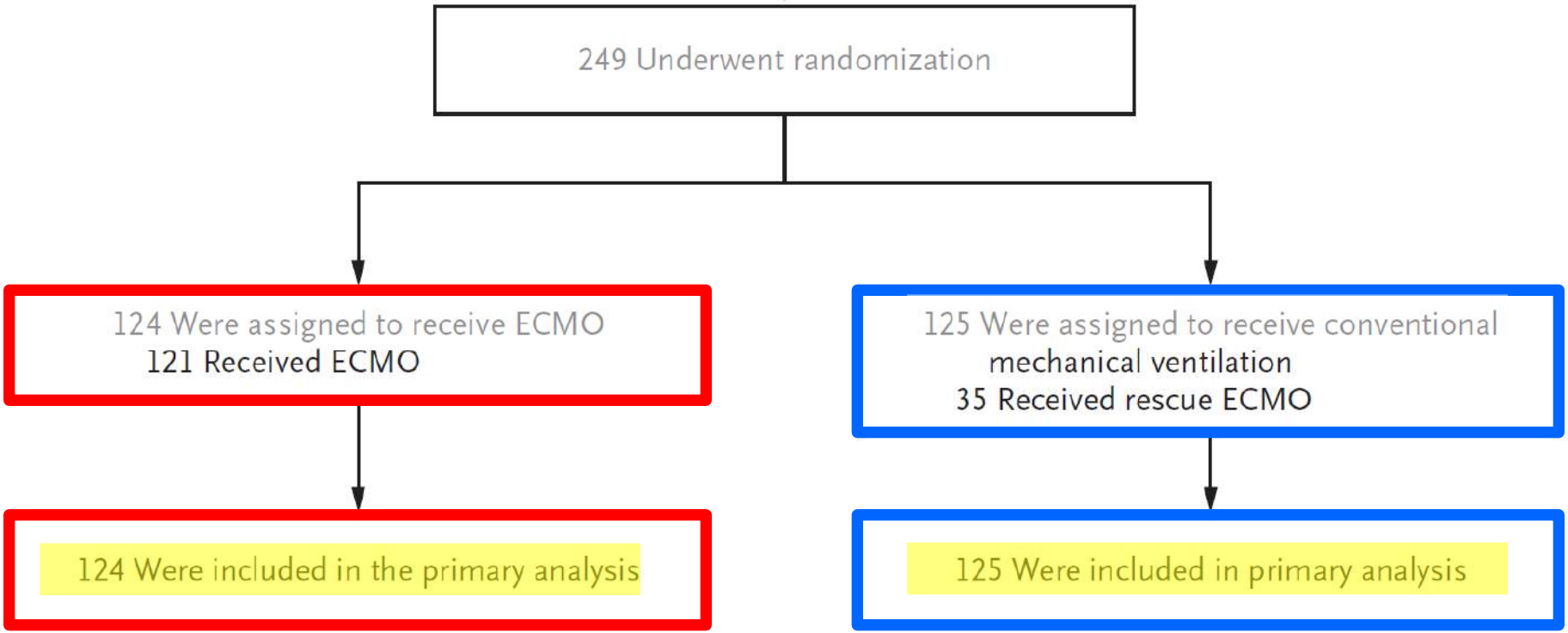
Inclusion Criteria

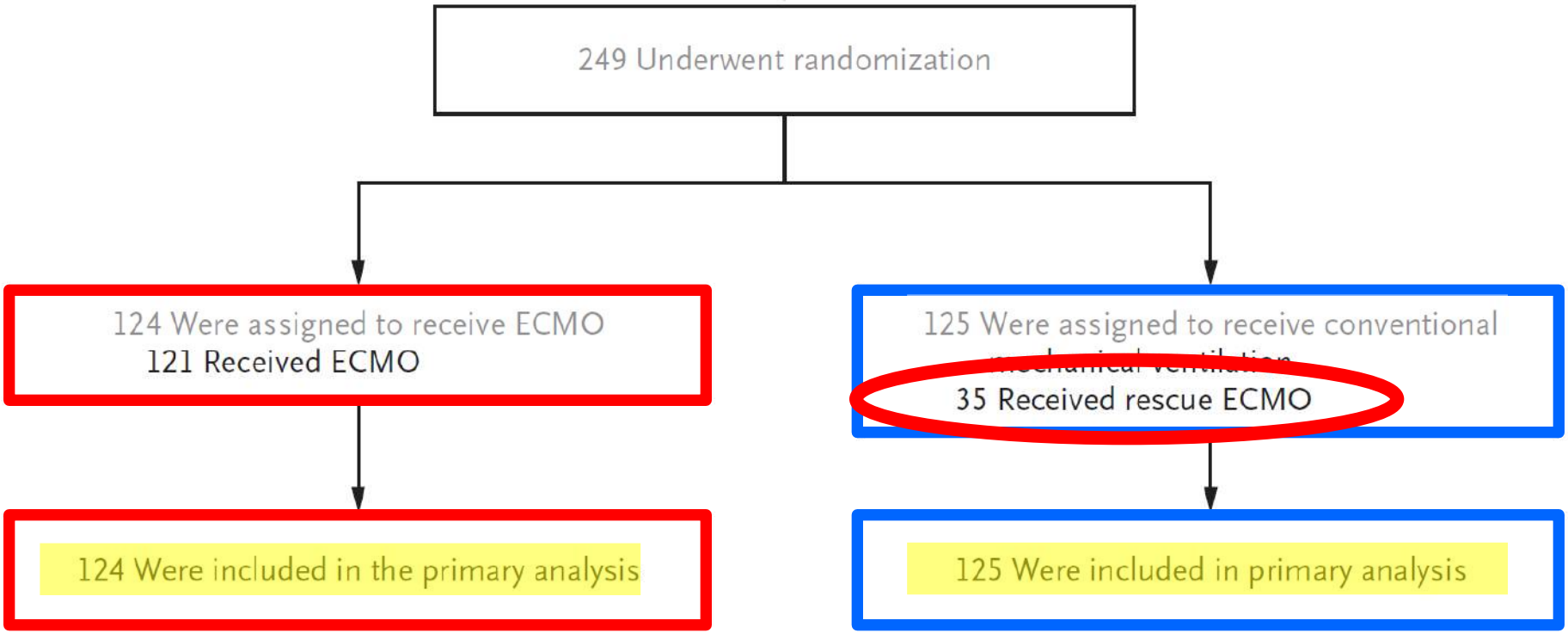
- One of the 3 following disease severity criteria

  - PaO_2:FIO_2 <50 mmHg for >3 hours
    - *Despite potential use of inhaled NO, recruitment maneuvers*
    - *Prone position, HFO ventilation, almitrine infusion*
  - PaO_2:FIO_2 <80 mmHg for >6 hours
    - *Despite similar criteria as above*
  - pH <7.25 with $PaCO_2$ $\geq$60 mmHg for >6 hours
    - *Resulting from MV settings to keep Pplat ≤32 cm H_2O*
    - *Despite respiratory rate increased to 35/minute*

Rescue ECMO for Controls

- Refractory hypoxemia
  - SaO_2 <80% for >6 hours
- Despite mandatory trial of
  - Prone positioning AND
  - Recruitment maneuver AND
  - iNO or inhaled prostacyclin
- AND If the treating physician felt that
  - Patient had no irreversible multi-organ failure AND
  - ECMO might change the outcome


249 Underwent randomization
124 Were assigned to receive ECMO
121 Received ECMO
125 Were assigned to receive conventional mechanical ventilation
35 Received rescue ECMO
124 Were included in the primary analysis
125 Were included in primary analysis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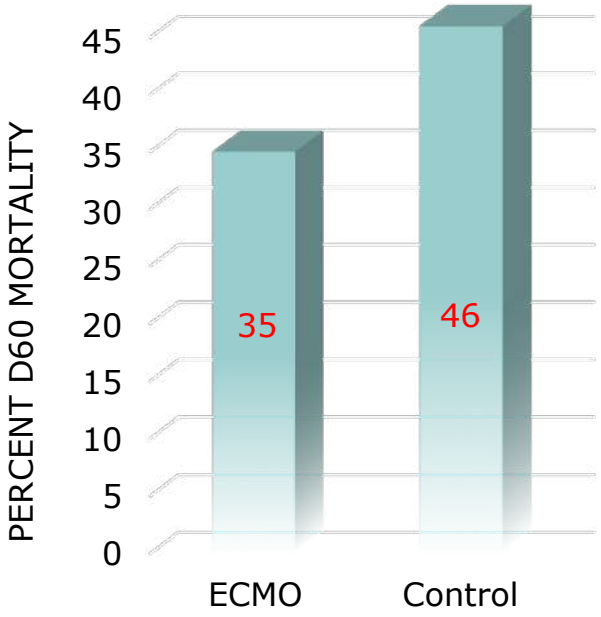
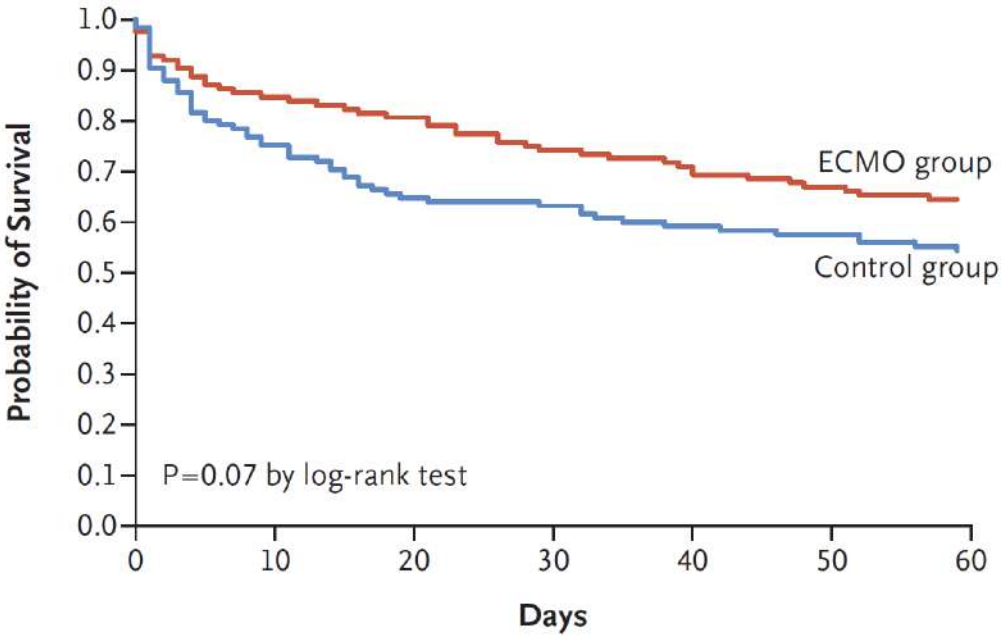
Primary Endpoint

Relative Risk, 0.76, 95% CI, 0.55-1.04; P=0.087

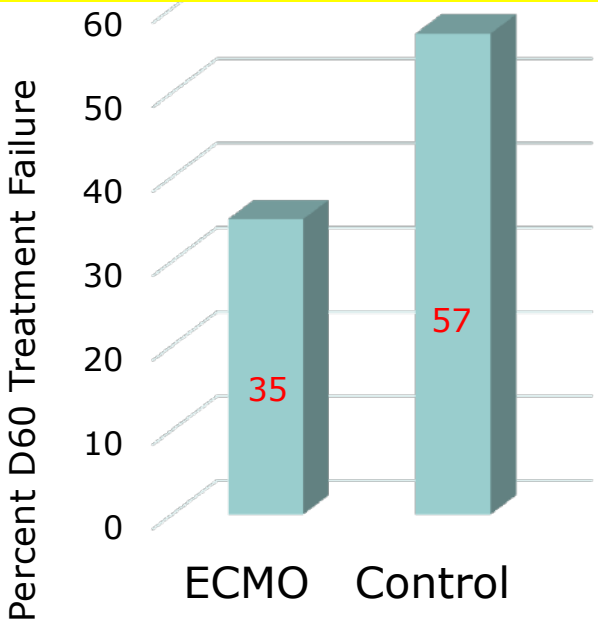


Hazard Ratio, 0.70; 95% CI, 0.47-1.04, P=0.074 by log-rank test

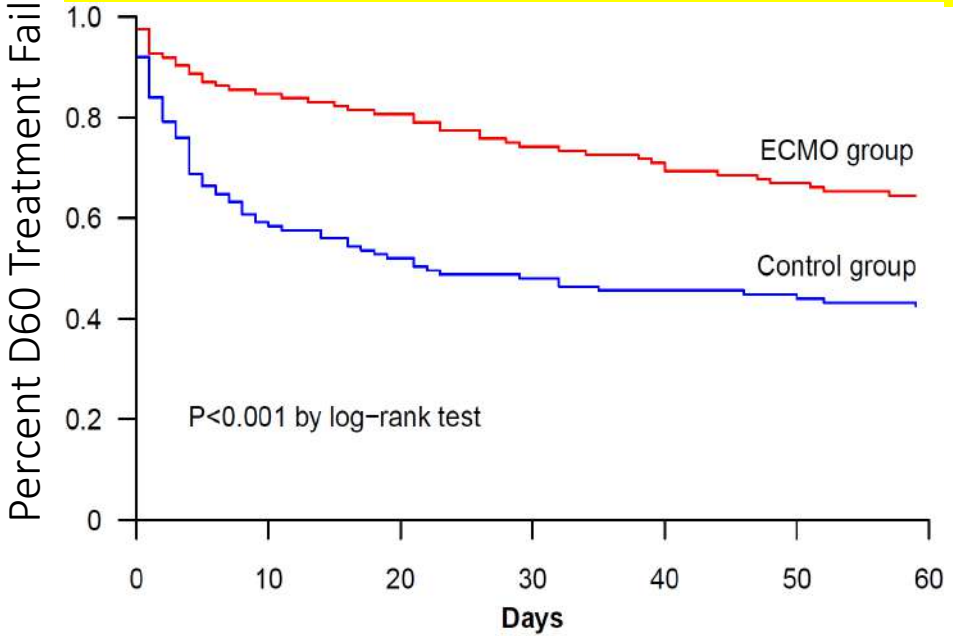


Key Secondary Endpoint

Relative Risk, 0.62; 95% CI, 0.47-0.82; P<0.001



Hazard ratio, 0.48; 95% CI, 0.34-0.70, P <0.001 by log-rank test



Death in ECMO group patients; Death or Crossover to ECMO in control patients

Endpoint at D60

	ECMO Group (N = 124)	Control Group (N = 125)	Median Difference (95% CI)
Days alive and free of vasopressor use	49 [0–56]	40 [0–53]	9 (0 to 51)
Days alive and free of cardiac failure (SOFA)	48 [0–56]	41 [0–53]	7 (0 to 51)
Days alive and free of dialysis	50 [0–60]	32 [0–57]	18 (0 to 51)
Days alive and free of renal failure (SOFA)	46 [0–60]	21 [0–56]	25 (6 to 53)
Days alive and free of prone position	59 [0–59]	46 [0–57]	13 (5 to 59)
Days alive and free of NO/prostacyclin	59 [0–60]	39 [0–58]	20 (4 to 59)

Why early ECMO?

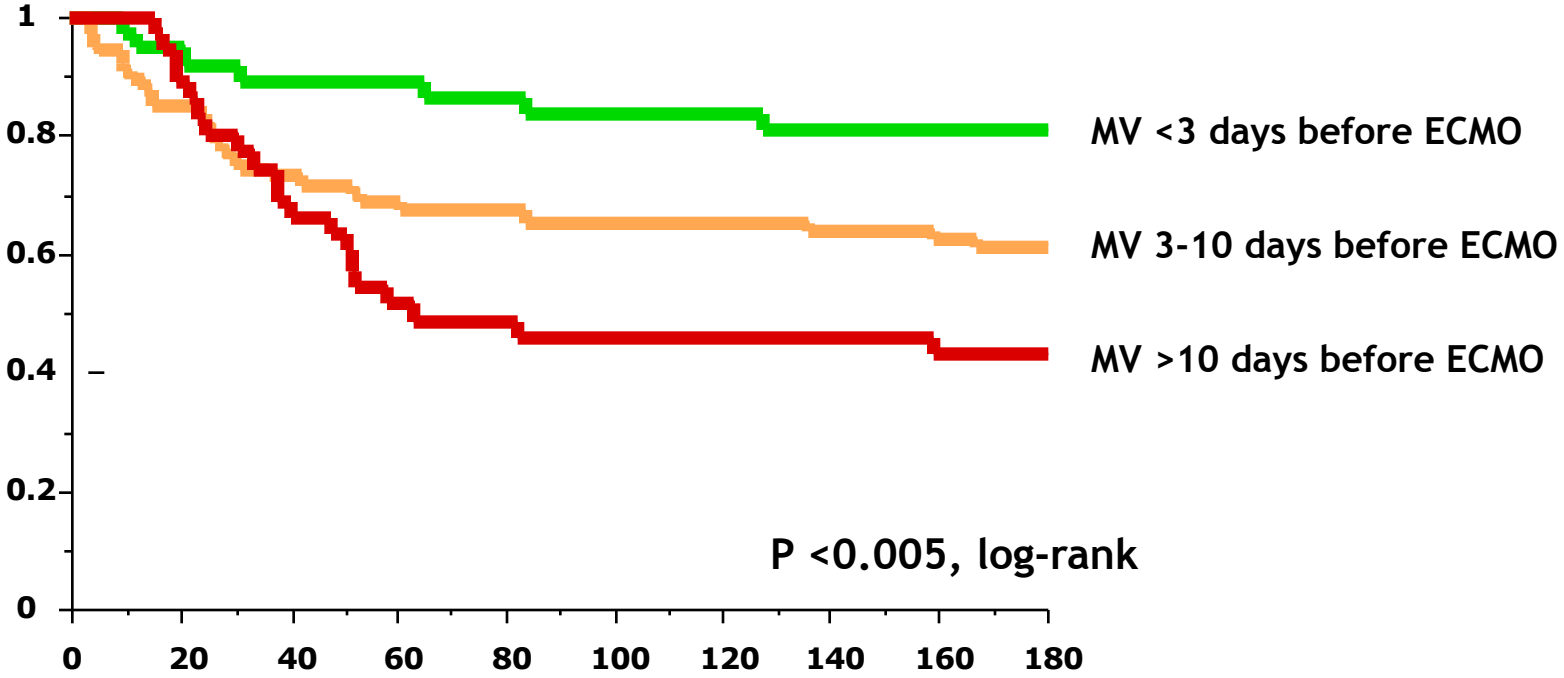
To rapidly decrease the intensity of MV

Matthieu Schmidt
Elie Zogheib
Hadrien Rozé
Xavier Repesse
Guillaume Lebreton
Charles-Edouard Luyt
Jean-Louis Trouillet
Nicolas Bréchot
Ania Nieszkowska
Hervé Dupont
Alexandre Ouattara
Pascal Leprince
Jean Chastre
Alain Combes

The PRESERVE mortality risk score and analysis of long-term outcomes after extracorporeal membrane oxygenation for severe acute respiratory distress syndrome

Intensive Care Med 2013

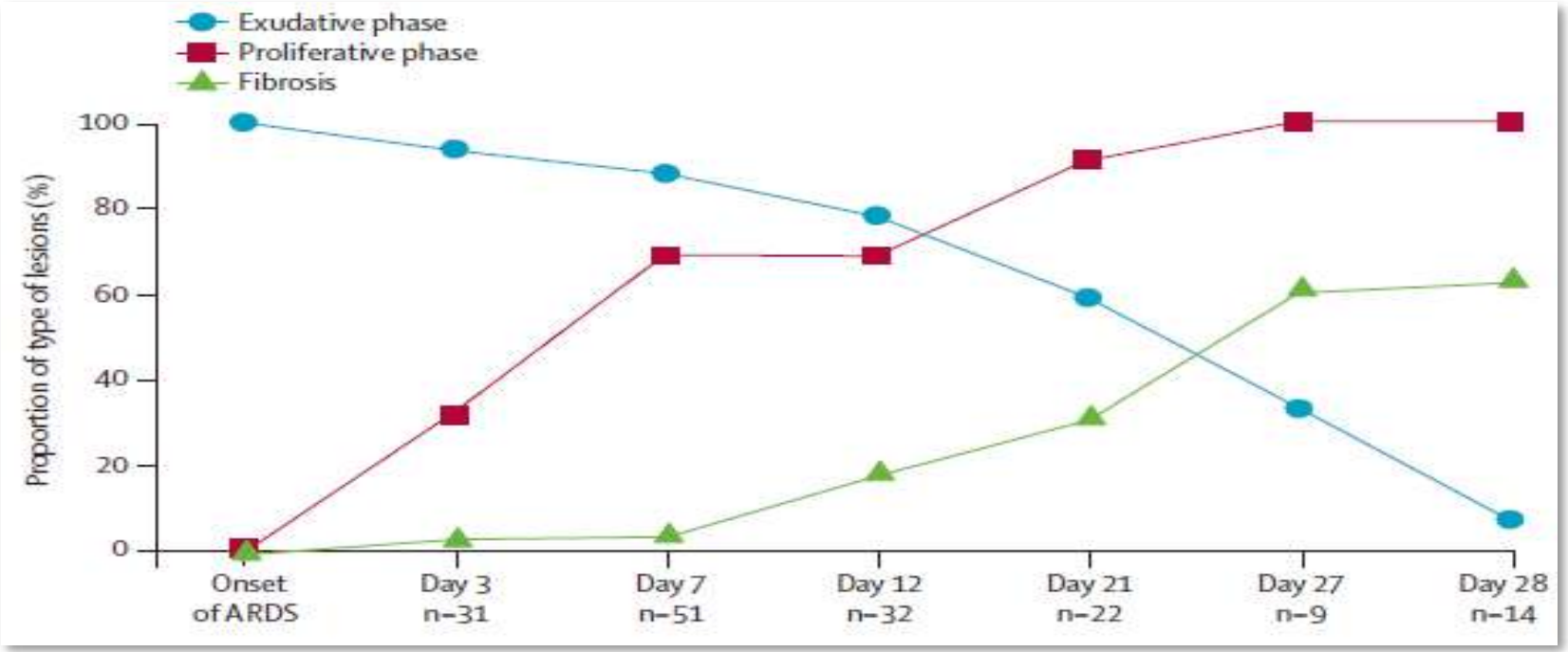
N=140



Chronology of histological lesions in acute respiratory distress syndrome with diffuse alveolar damage: a prospective cohort study of clinical autopsies

Arnaud W Thille, Andrés Esteban, Pilar Fernández-Segoviano, José-María Rodriguez, José-Antonio Aramburu, Patricio Vargas-Errázuriz, Ana Martín-Pellicer, José A Lorente, Fernando Frutos-Vivar

The Lancet Respiratory Medicine - July 2013



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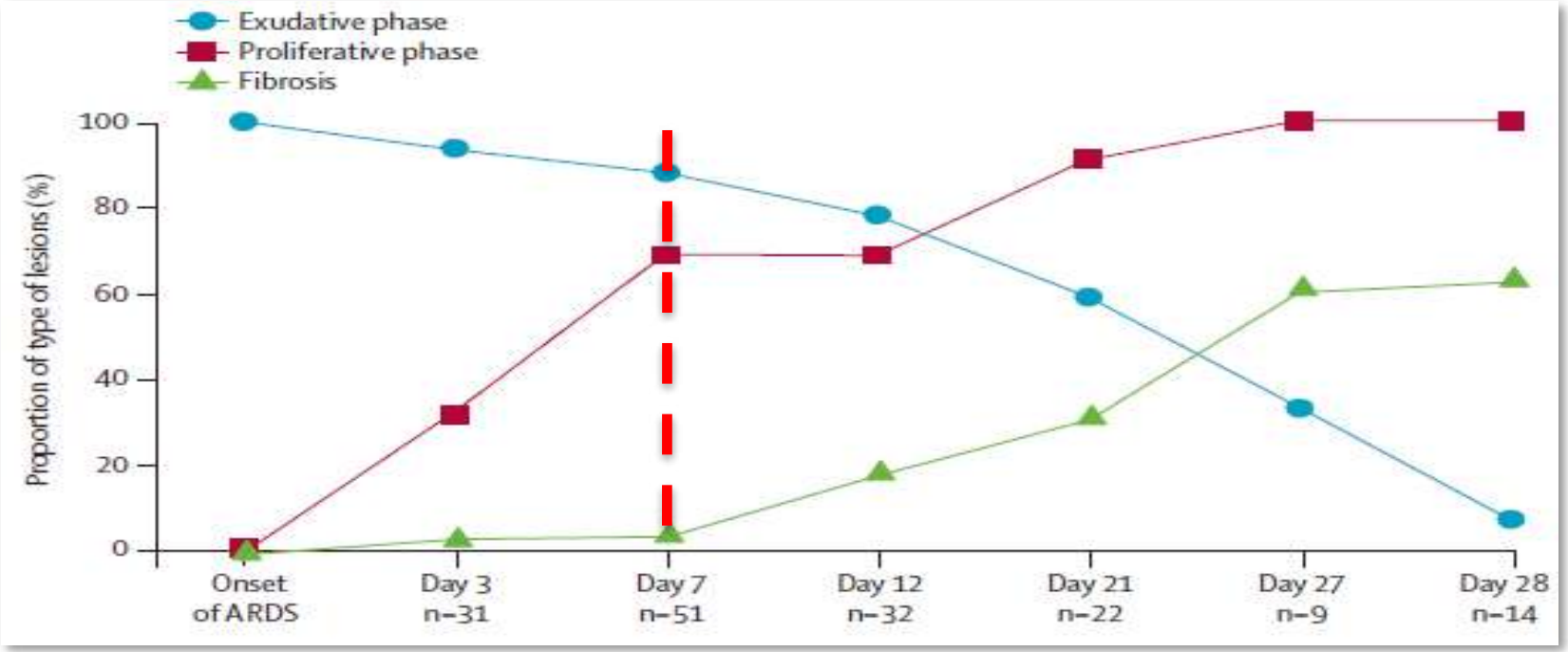


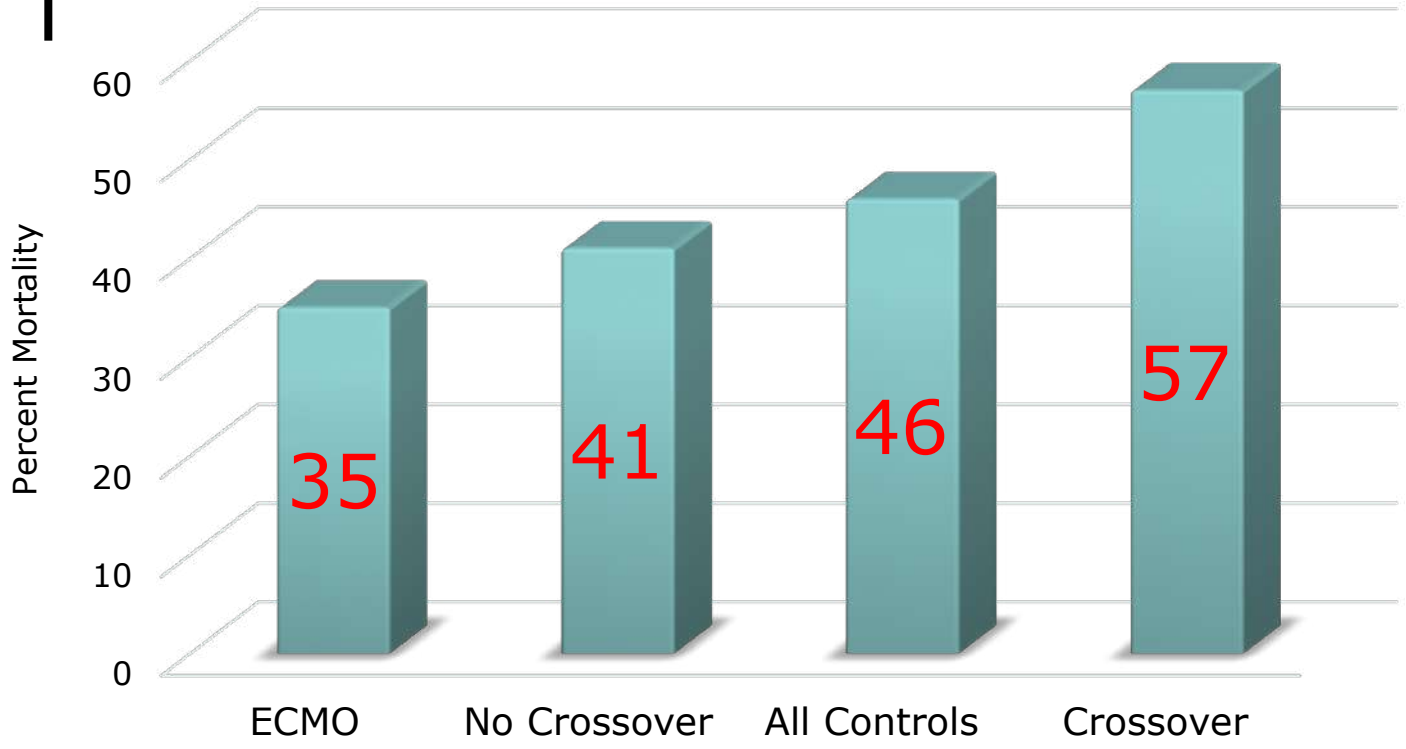
Crossover to ECMO in Controls

- 28% (35/125) of controls received rescue ECMO
  - Refractory hypoxemia, 6.5±9.7 days post randomization
- These patients had more severe ARDS at baseline
  - Higher Plateau pressure:
    - 31.7±5.5 vs 28.5±4.1 cm H_2O
  - Higher Driving pressure:
    - 20.2±6.1 vs 16.6±5.3 cm H_2O
  - Lower Respiratory system compliance:
    - 21.3±9.2 vs 27.1±11.0 ml/cm H_2O
  - More quadrants with infiltrate on chest Xray:
    - 3.7±0.6 vs 3.3±0.9

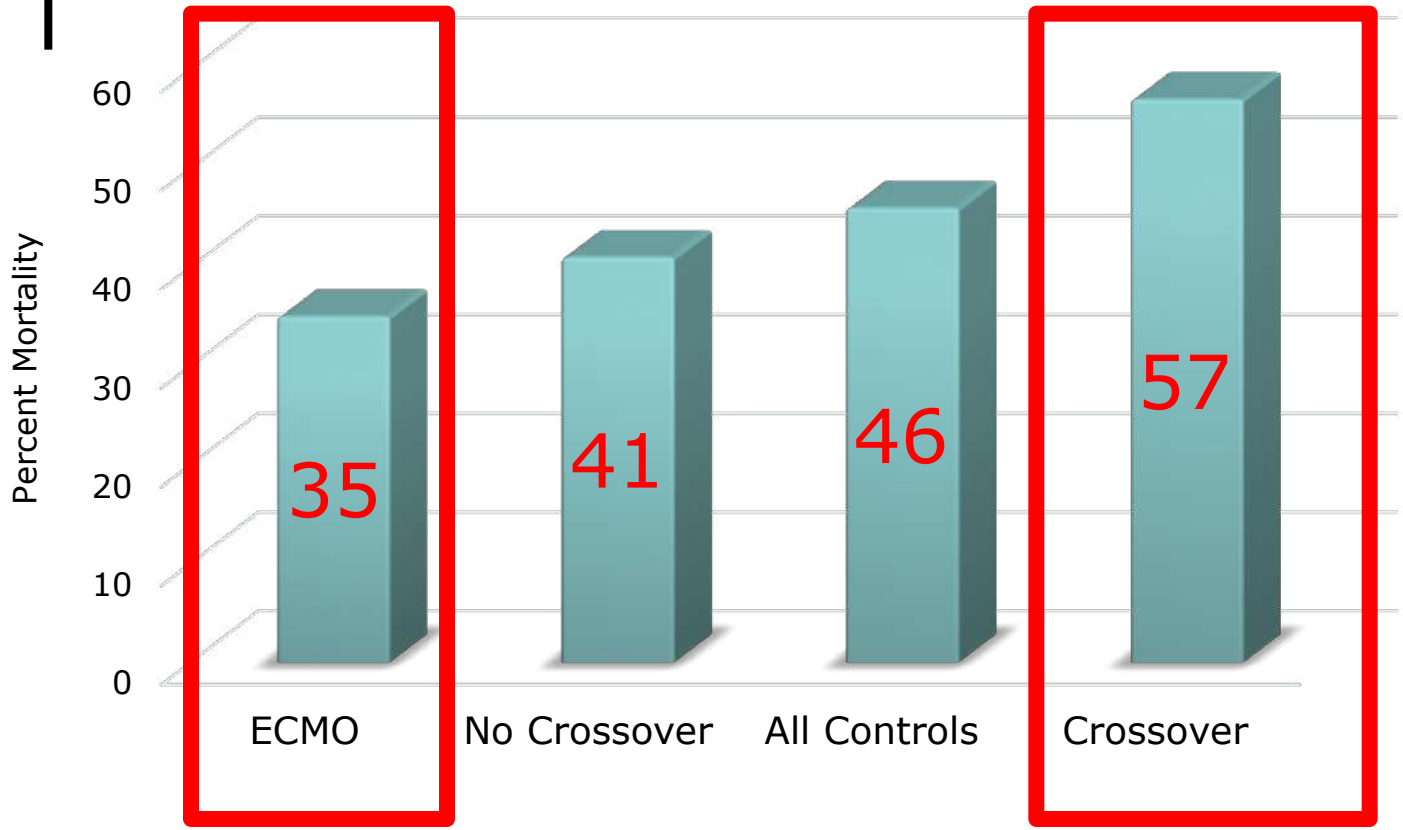
Crossover to ECMO in Controls

- Before crossover, of the 35 controls who had ECMO
  - 9 had cardiac arrest
  - 7 had severe right heart failure
  - 11 developed renal failure requiring dialysis
- Venoarterial ECMO applied to 7 patients
  - 6 under cardiopulmonary resuscitation

Control Crossover Outcomes



Control Crossover Outcomes



Early ultra-protective ventilation

Matthieu Schmidt
Elie Zogheib
Hadrien Rozé
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Charles-Edouard Luyt
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The PRESERVE mortality risk score and analysis of long-term outcomes after extracorporeal membrane oxygenation for severe acute respiratory distress syndrome

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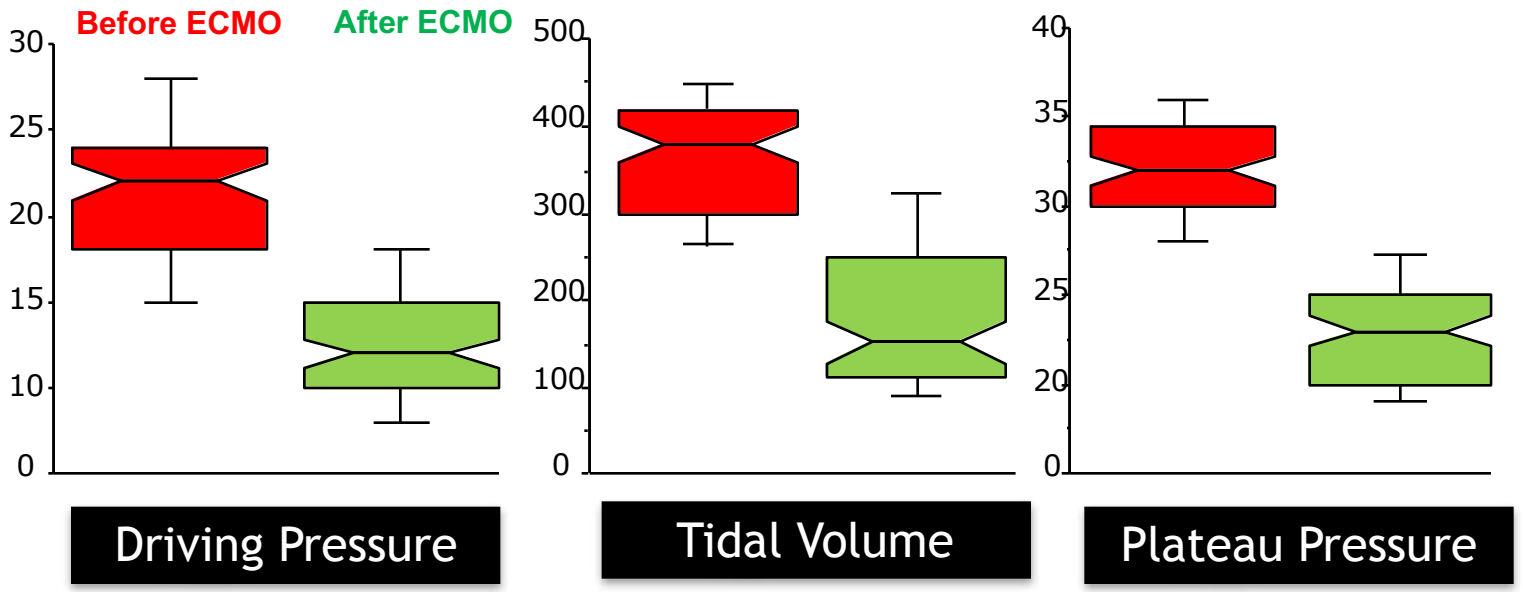
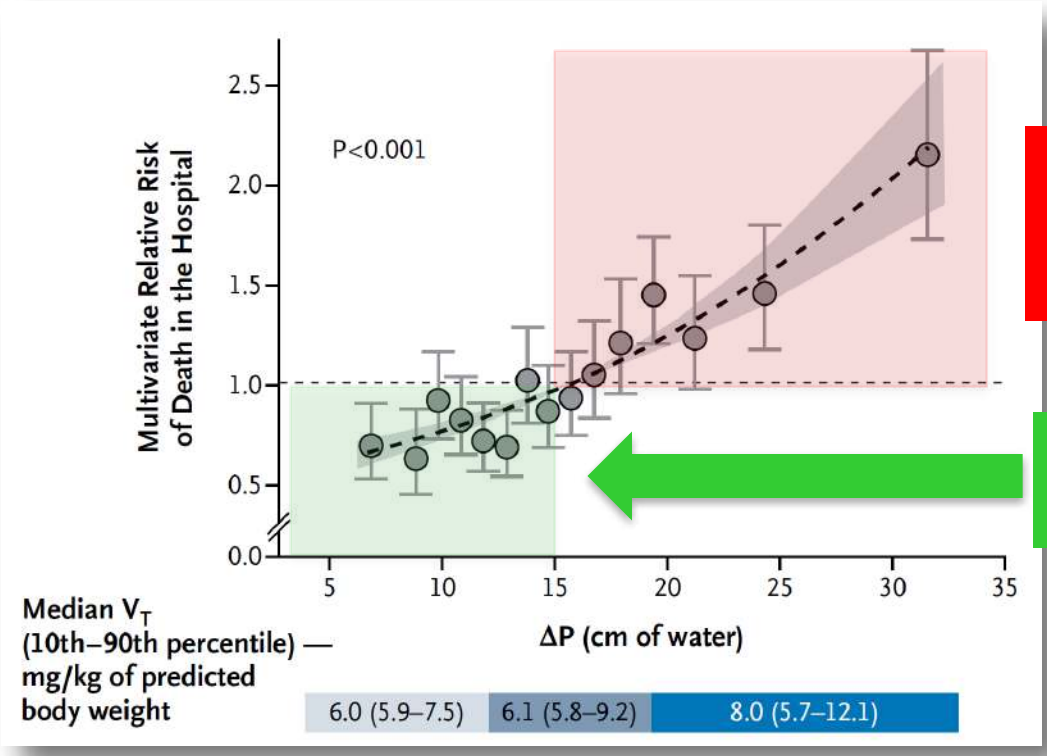


Driving Pressure and Survival in the Acute Respiratory Distress Syndrome

Marcelo B.P. Amato, M.D., Maureen O. Meade, M.D., Arthur S. Slutsky, M.D., Laurent Brochard, M.D., Eduardo L.V. Costa, M.D., David A. Schoenfeld, Ph.D., Thomas E. Stewart, M.D., Matthias Briel, M.D., Daniel Talmor, M.D., M.P.H., Alain Mercat, M.D., Jean-Christophe M. Richard, M.D., Carlos R.R. Carvalho, M.D., and Roy G. Brower, M.D.

N Engl J Med 2015;372:747-55.



Not advocated on ECMO

Target on ECMO

Mechanical Ventilation Management during Extracorporeal Membrane Oxygenation for Acute Respiratory Distress Syndrome

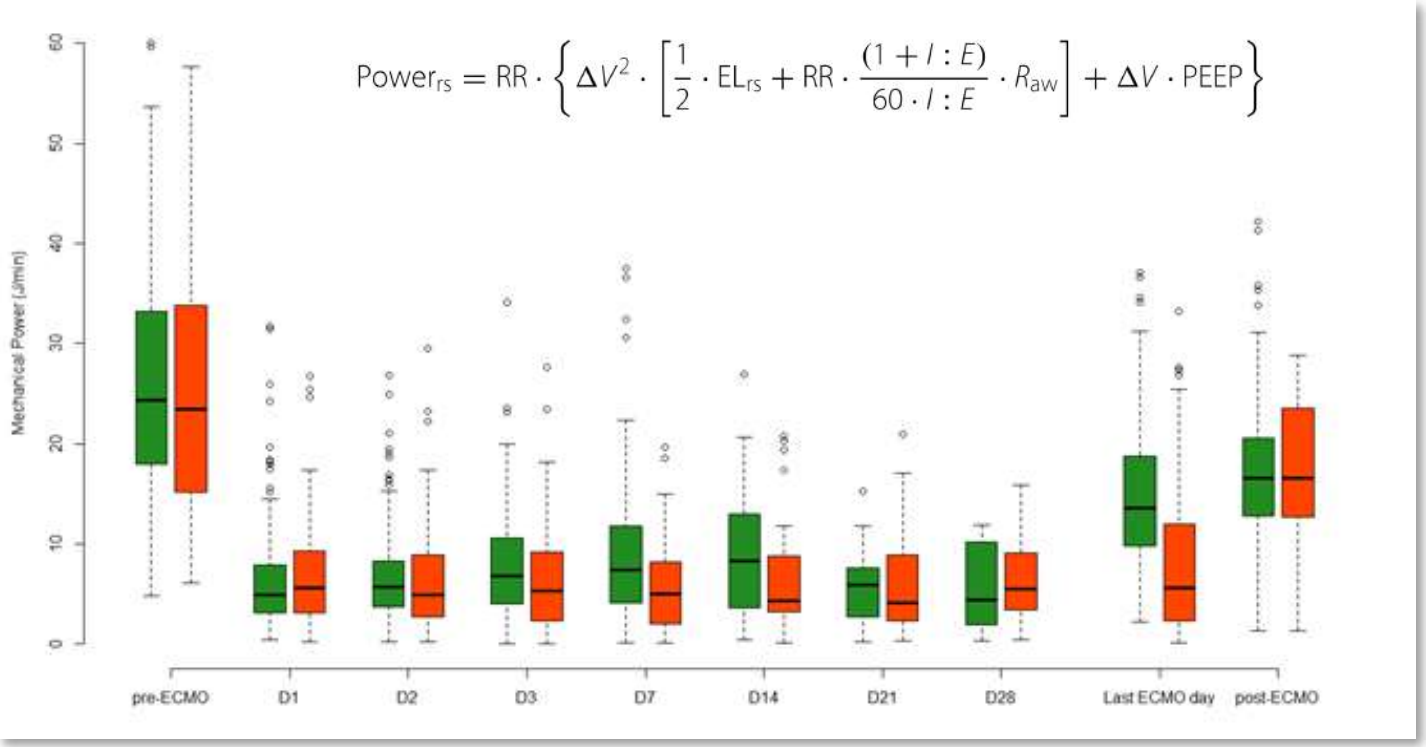
An International Multicenter Prospective Cohort

Matthieu Schmidt[1,2], Tài Pham[3,4], Antonio Arcadipane[5], Cara Agerstrand[6], Shinichiro Ohshimo[7], Vincent Pellegrino[8], Alain Vuylsteke[9], Christophe Guervilly[10], Shay McGuinness[11], Sophie Pierard[12], Jeff Breeding[13], Claire Stewart[14], Simon Sin Wai Ching[15], Janice M. Camuso[16], R. Scott Stephens[17], Bobby King[18], Daniel Herr[19], Marcus J. Schultz[20], Mathilde Neuville[21,22], Elie Zogheib[23,24], Jean-Paul Mira[25,26,27], Hadrien Rozé[28], Marc Pierrot[29], Anthony Tobin[30], Carol Hodgson[8,31], Sylvie Chevret[32,33], Daniel Brodie[6]* and Alain Combes[1,2]*, for the International ECMO Network (ECMONet) and the LIFEGARDS Study Group

AJRCCM 2019

N=350

$$\text{Power}_{rs} = RR \cdot \left\{ \Delta V^2 \cdot \left[\frac{1}{2} \cdot EL_{rs} + RR \cdot \frac{(1 + I:E)}{60 \cdot I:E} \cdot R_{aw} \right] + \Delta V \cdot PEEP \right\}$$



ECMO for COVID-19 related severe ARDS

Initial mistrust regarding ECMO…

- New disease with unknown outcome

- Health system were rapidly overwhelmed
- Scarce resource in times of high demand

- Expected long ICU stay when ICU beds are already lacking…fear of bed-blockers?

- Initial alarm about the outcomes

- Poor outcome reported in very small case series from China…experience of the center ?

Letter to the Editor

Poor survival with extracorporeal membrane oxygenation in acute respiratory distress syndrome (ARDS) due to coronavirus disease 2019 (COVID-19): Pooled analysis of early reports

Journal of Crit Care 2020

Authors	ECMO: n=	ECMO -Survivors: n (%)
Ruan Q et al. *2020*	7	0 (0%)
Wu et al. *2020*	1	0 (%)
Yang X et al. *2020*	6	1 (16.6%)
Zhou F et al. *2020*	3	0 (0%)

Letter to the Editor

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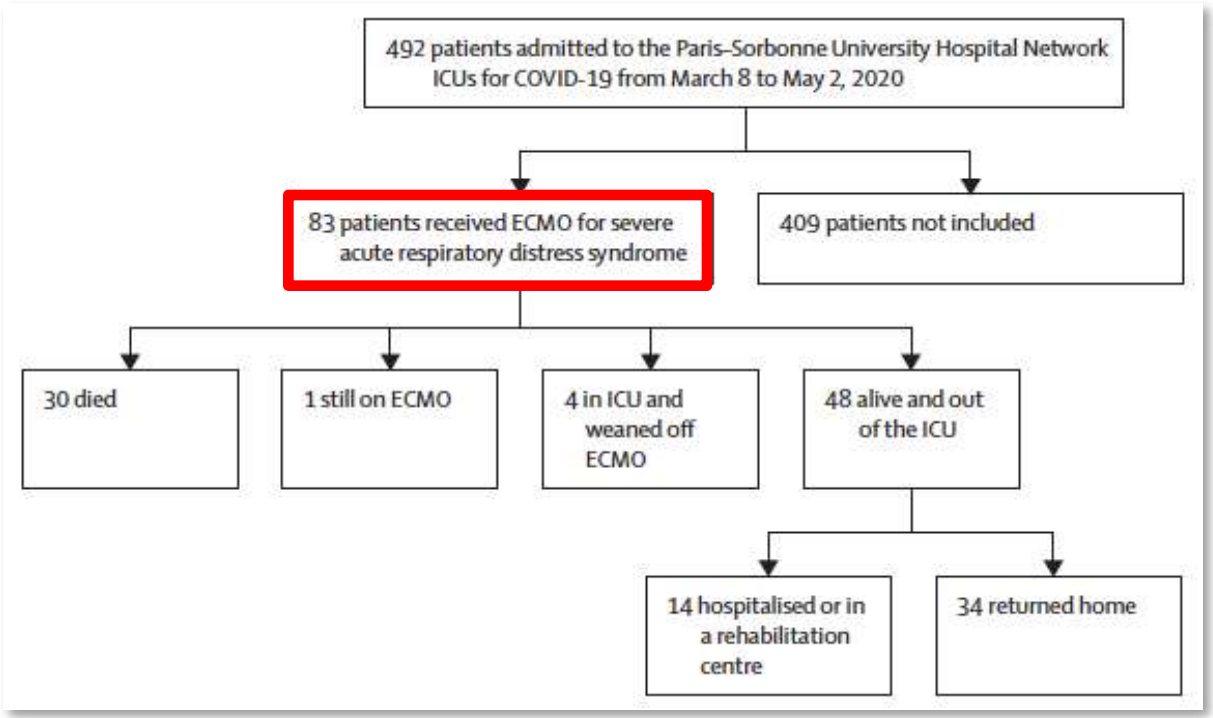
Zhou F et al. *2020*	3	0 (0%)

94% mortality

Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome associated with COVID-19: a retrospective cohort study

*Matthieu Schmidt, David Hajage, Guillaume Lebreton, Antoine Monsel, Guillaume Voiriot, David Levy, Elodie Baron, Alexandra Beurton, Juliette Chommeloux, Paris Meng, Safaa Nemlaghi, Pierre Bay, Pascal Leprince, Alexandre Demoule, Bertrand Guidet, Jean Michel Constantin, Muriel Fartoukh, Martin Dres, Alain Combes, for the Groupe de Recherche Clinique en REanimation et Soins intensifs du Patient en Insuffisance Respiratoire aiguE (GRC-RESPIRE) Sorbonne Université, and the Paris-Sorbonne ECMO-COVID investigators**

Lancet Respir Med 2020



Strict application of the EOLIA criteria

- ✓Age <70
- ✓Intubated for less than 7 days
- ✓Prone positioning was highely recommended

2. Meeting 1 of the 3 following criteria of severity:
   a. PaO_2/FiO_2 ratio <50 mm Hg with FiO_2 ≥80% for >3 hours, despite optimization of mechanical ventilation (Vt set at 6 ml/kg and trial of PEEP≥10 cm H2O) and despite possible recourse to usual adjunctive therapies (NO, recruitment maneuvers, prone position, HFO ventilation, almitrine infusion) OR
   b. PaO_2/FiO_2 ratio <80 mm Hg with FiO_2 ≥80% for >6 hours, despite optimization of mechanical ventilation (Vt set at 6 ml/kg and trial of PEEP≥10 cm H2O) and despite possible recourse to usual adjunctive therapies (NO, recruitment maneuvers, prone position, HFO ventilation, almitrine infusion) OR
   c. pH <7.25 (with $PaCO_2$ ≥60 mm Hg) for >6 hours (RR increased to 35 /min) resulting from MV settings adjusted to keep Pplat ≤32 cm H2O (first, Vt reduction by steps of 1 mL/kg to 4 mL/kg then PEEP reduction to a minimum of 8 cm H2O

Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome associated with COVID-19: a retrospective cohort study

*Matthieu Schmidt, David Hajage, Guillaume Lebreton, Antoine Monsel, Guillaume Voiriot, David Levy, Elodie Baron, Alexandra Beurton, Juliette Chommeloux, Paris Meng, Safaa Nemlaghi, Pierre Bay, Pascal Leprince, Alexandre Demoule, Bertrand Guidet, Jean Michel Constantin, Muriel Fartoukh, Martin Dres, Alain Combes, for the Groupe de Recherche Clinique en REanimation et Soins intensifs du Patient en Insuffisance Respiratoire aiguE (GRC-RESPIRE) Sorbonne Université, and the Paris-Sorbonne ECMO-COVID investigators**

Lancet Respir Med 2020

	All patients (N=83)
Age, years	49 (41–56)
Sex	
Male	61 (73%)
Female	22 (27%)
Body-mass index, kg/cm²	30·4 (27·9–34·1)
Simplified Acute Physiology Score II	45 (29–56)
RESP score	4 (2–5)
Total SOFA score‡	12 (9–13)
Comorbidities	
Hypertension	32 (39%)
Diabetes	26 (31%)
Ischaemic cardiomyopathy	4 (5%)
Chronic respiratory disease, COPD, or asthma	9 (11%)
Active smoker	2 (2%)
Immunocompromised§	3 (4%)
Time from first symptoms to ICU admission, days	7 (5–10)
Time from first symptoms to intubation, days	8 (6–11)
Time from intubation to ECMO, days	4 (3–6)
Retrieval on ECMO by mobile ECMO retrieval team from another hospital	61 (73%)

Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome associated with COVID-19: a retrospective cohort study

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Lancet Respir Med 2020

Ventilation parameters

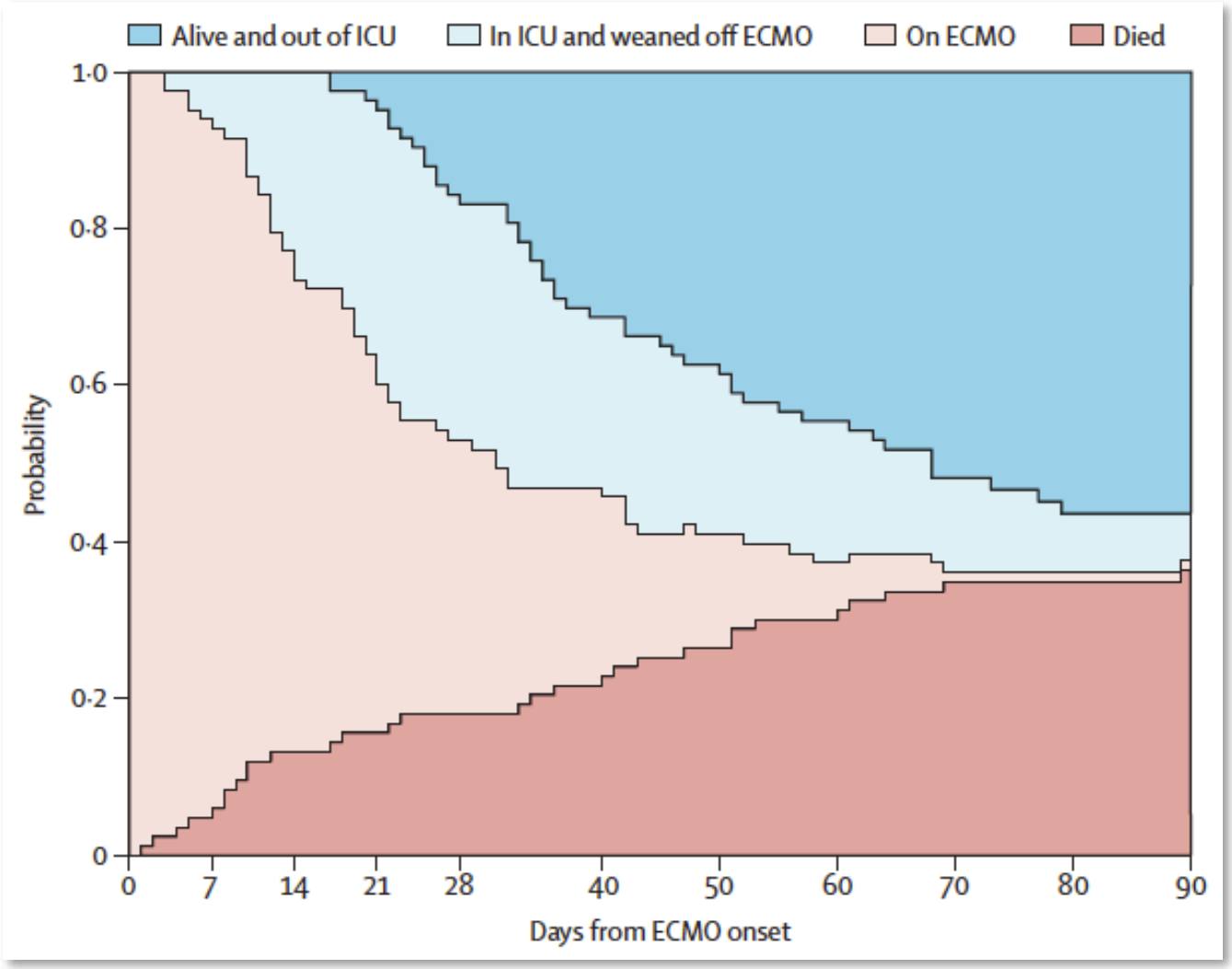
FiO_2	100 (100–100)
Positive end-expiratory pressure, cm H_2O‡	14 (12–14)
Tidal volume, mL/kg predicted bodyweight‡	6·0 (5·7–6·4)
Respiratory rate, breaths per min‡	29 (28–30)
Plateau pressure, cm H_2O‡	32 (29–33)
Driving pressure, cm H_2O¶	18 (16–21)
Static compliance, mL/cm H_2O‡	22·1 (18·1–26·5)
Mechanical power, J/min‖	24·7 (22·0–27·3)
Ventilatory ratio‡	2·7 (2·3–3·2)

Last blood-gas values pre-ECMO

pH	7·32 (7·24–7·38)
PaO_2/FiO_2	60 (54–68)
$PaCO_2$, mm Hg	57 (50–68)
Plasma bicarbonate, mmol/L	27 (24–32)
SaO_2‡	90% (83–92)
Arterial lactate, mmol/L	1·6 (1·3–2·0)

Rescue therapy pre-ECMO

Any	82 (99%)
Neuromuscular blockade	80 (96%)
Prone-positioning	78 (94%)
Inhaled nitric oxide or prostacyclin	28 (34%)
Steroids	6 (7%)
Almitrine	1 (1%)
Renal replacement therapy	4 (5%)


Alive and out of ICU
In ICU and weaned off ECMO
On ECMO
Died
1·0
0·8
0·6
0·4
0·2
0
Probability
0
7
14
21
28
40
50
60
70
80
90
Days from ECMO onset

	State occupation probability (95% CI)*	Mean days in each state (95% CI)†
Day 28		
On ECMO	35% (26–46)	18·5 (16·7–20·4)
In ICU and weaned off ECMO	30% (21–41)	5·5 (4·0–7·0)
Alive and out of ICU	17% (10–27)	0·8 (0·4–1·4)
Died	18% (11–28)	3·2 (1·8–4·8)
Day 60		
On ECMO	6% (3–14)	24·6 (21·0–28·6)
In ICU and weaned off ECMO	18% (11–28)	14·4 (11·2–17·8)
Alive and out of ICU	45% (35–56)	11·4 (8·0–14·3)
Died	31% (22–42)	11·0 (7·0–15·4)
Day 90		
On ECMO	1% (0–8)	25·4 (21·4–29·8)
In ICU and weaned off ECMO	6% (2–15)	16·2 (12·4–20·5)
Alive and out of ICU	56% (46–67)	27·6 (21·0–32·9)
Died	36% (27–48)	21·4 (14·7–28·5)

Extracorporeal membrane oxygenation support in COVID-19: an international cohort study of the Extracorporeal Life Support Organization registry

Ryan P Barbaro*, Graeme MacLaren*, Philip S Boonstra, Theodore J Iwashyna, Arthur S Slutsky, Eddy Fan, Robert H Bartlett, Joseph E Tonna, Robert Hyslop, Jeffrey J Fanning, Peter T Rycus, Steve J Hyer, Marc M Anders, Cara L Agerstrand, Katarzyna Hryniewicz, Rodrigo Diaz, Roberto Lorusso†, Alain Combes†, Daniel Brodie†, for the Extracorporeal Life Support Organization‡

www.thelancet.com **Published online September 25, 2020**

	Full cohort (n=1035)		ARDS cohort* (n=779)	
	N	Median (IQR) or n (%)	N	Median (IQR) or n (%)
Non-invasive ventilation				
Non-invasive ventilation before intubation	1032	606 (59%)	776	434 (56%)
BiPAP	1032	185 (18%)	776	119 (15%)
CPAP	1032	140 (14%)	776	80 (10%)
HFNC	1032	357 (35%)	776	285 (37%)
Pre-ECMO intubation (days)	914	4·0 (1·8–6·4)	688	4·3 (2·0–6·5)
Conventional ventilation†	951	942 (99%)	729	721 (99%)
PEEP (cm H_2O)	868	14 (12–16)	661	15 (12–18)
PIP (cm H_2O)	699	33 (30–38)	532	34 (30–38)
FiO_2	888	1·0 (0·90–1·0)	672	1·0 (0·90–1·0)
PaO_2:FiO_2 (mm Hg)	868	72 (59–94)	657	72 (60–93)
$PaCO_2$ (mm Hg)	896	60 (50–74)	678	60 (50–74)
Pre-ECMO support				
Prone positioning	1019	612 (60%)	766	464 (61%)
Neuromuscular blockade	1015	729 (72%)	762	567 (74%)
Inhaled pulmonary vasodilators	1019	293 (29%)	766	242 (32%)
Any vasoactive support	1015	606 (60%)	758	447 (59%)
Norepinephrine	1015	561 (55%)	762	416 (55%)

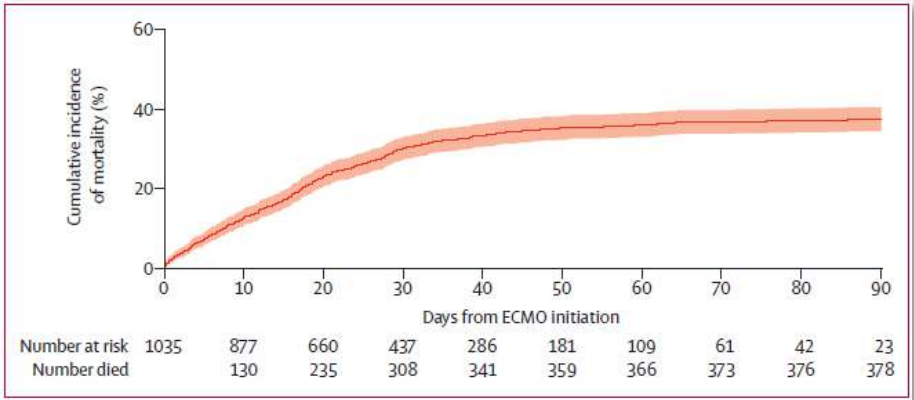


Figure 2: **Cumulative incidence of mortality from time of ECMO initiation**

Extracorporeal membrane oxygenation support in COVID-19: an international cohort study of the Extracorporeal Life Support Organization registry

Ryan P Barbaro*, Graeme MacLaren*, Philip S Boonstra, Theodore J Iwashyna, Arthur S Slutsky, Eddy Fan, Robert H Bartlett, Joseph E Tonna, Robert Hyslop, Jeffrey J Fanning, Peter T Rycus, Steve J Hyer, Marc M Anders, Cara L Agerstrand, Katarzyna Hryniewicz, Rodrigo Diaz, Roberto Lorusso†, Alain Combes†, Daniel Brodie†, for the Extracorporeal Life Support Organization‡

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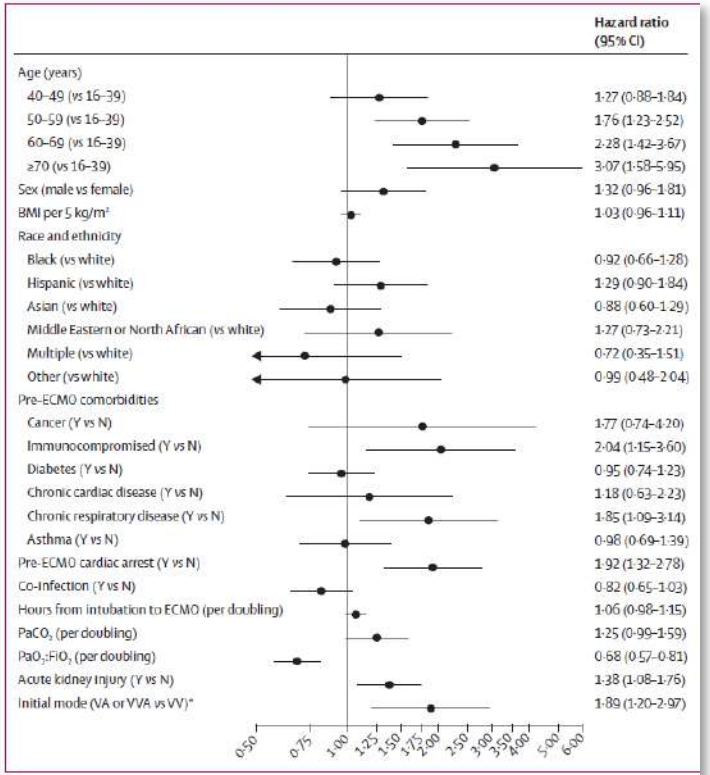

Figure 3: Cox model for factors associated with in-hospital mortality in patients with COVID-19 supported with ECMO

Comparison with the results from EOLIA…

Characteristic	COVID-19 ECMO patients (N=83)	EOLIA ECMO-group patients (N=124)
Age, years	48·0±11·0	51·9±14·2
Immunocompromised	3 (4)	27 (22)
ICU admission to ECMO, days	4 (3–6)	2 (1–4)
PaO2/FiO2	62±18	73±30
Pre-ECMO prone-positioning	78 (94)	70 (56)
On-ECMO prone-positioning	67 (81)	12 (10)
Haemorrhage requiring transfusion	35 (42)	57 (46)
Pulmonary embolism	16 (19)	0
Haemorrhagic stroke	4 (5)	3 (2)
Antibiotic-treated VAP	72 (87)	48 (39)
ECMO support	20 (10-40)	11 (7-18)
ICU lenght of stay	36 (23-60)	23 (13 -34)
60-day mortality	31%	35%

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Proning ECMO patients to reduce VILI and enhance ECMO weaning ?

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Which anticoagulation?

- UFH to a target aPTT of 50 to 55 seconds or anti-Xa activity between 0.2 and 0.3 IU/mL
- Target **aPTT of 60 to 75 seconds** or **anti-Xa activity between 0.3 and 0.5 IU/mL** for **COVID-19 patients**

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Conclusion

- VV-ECMO indication should not differ between COVID-19 patients and other patients with severe ARDS
- Strict application of EOLIA criteria
- Be prepared of (very) long ICU and hospital stays: role of the experience and preparedness of the health-care system..
- Must be performed in experienced center:
  - ✓ appropriate organisation of personnel, equipment, facilities, and systems
  - ✓ clinical expertise

Conclusion

- **Survival of these patients is similar** to that reported in studies on ECMO support for severe ARDS published in the past few years.

- **ECMO should be considered at an early stage** for patients developing profound respiratory failure, despite optimised conventional care, including prone-positioning.