ARDS Management: 2024

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- 9th Annual Advances in the Practice of
- Pulmonary and Critical Care Medicine

HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

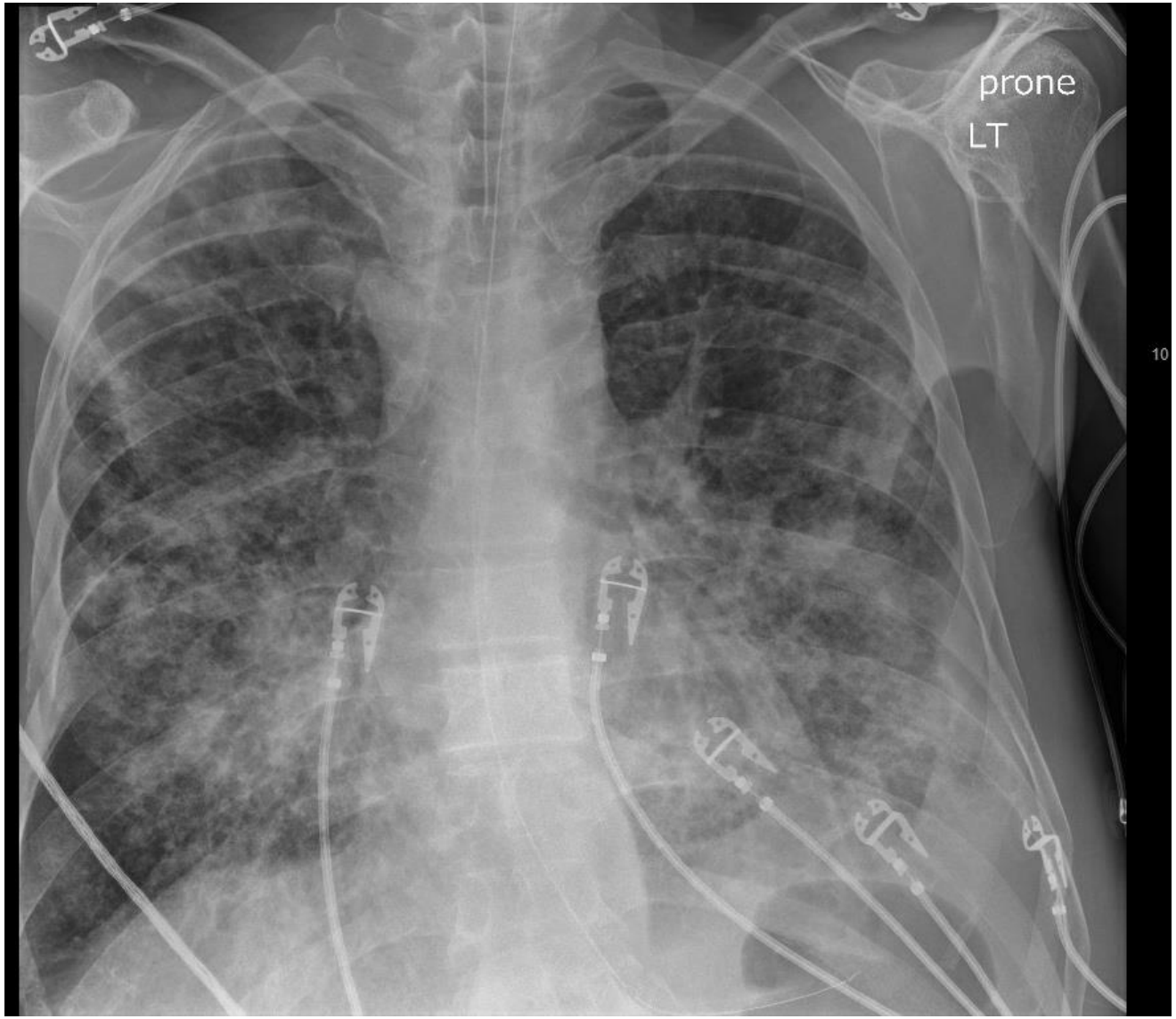
Mass General Brigham

Disclosures

- No disclosures

Aims

- ARDS
  - Definition of the syndrome
  - Incidence
  - Impact
- What is “State of the Art” 2024?
  - Setting PEEP
  - Neuromuscular blockade
  - Prone Ventilation
  - ECMO
  - Steroids
- Algorithm



Clinical Manifestations

- Hypoxemia
  - V/Q mismatch
  - Shunting
- Ventilation
  - Increased dead space
  - Reduced lung compliance

ARDS Berlin Definition		
Timing	Within 1 week of a known clinical insult or new or 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	
Oxygenation		
	Mild	200 mm Hg < PaO2/FiO2 < =300 mm Hg with PEEP or CPAP >=5 cm H2O
	Moderate	100 mm Hg < PaO2/FiO2 < =200 mm Hg with PEEP or CPAP >=5 cm H2O
	Severe	PaO2/FIO2 < =100 mm Hg with PEEP or CPAP >=5 cm H2O

Ranieri et al JAMA 2012; 307 (23) 2526-2533

Challenges with 2012 Berlin Definition

In 2024

- Improved noninvasive criteria and increased use of noninvasive criteria for evaluating oxygenation
- Increased use of HFNO (high flow nasal oxygen)
  - Patients do not meet PEEP=5 cm H20 criteria
- Increased use of Ultrasound in lung evaluation
- Challenges in resource variable setting

2023 Proposed Updates to 2012 Berlin Definition

ARDS – Not Intubated

$PaO_2/FiO_2 \leq 300$ mmHg or $SpO_2/FiO_2 \leq 315$ (if $SpO_2 \leq 97\%$) on HFNO with a flow of ≥ 30 liters per minute or NIV/CPAP with at least 5 cm H_2O expiratory pressure

ARDS – Intubated

Mild[5]:
$200 < PaO_2/FiO_2 \leq 300$ **or** $235 \leq SpO_2/FiO_2 \leq 315$ (if $SpO_2 \leq 97\%$)

Moderate:
$100 < PaO_2/FiO_2 \leq 200$ or $148 < SpO_2/FiO_2 \leq 235$ (if $SpO_2 \leq 97\%$)

Severe:
$PaO_2/FiO_2 \leq 100$ or $SpO_2/FiO_2 \leq 148$ (if $SpO_2 \leq 97\%$)

ARDS – Resource Limited

$SpO_2/FiO_2 \leq 315$ (if $SpO_2 \leq 97\%$).[6] Neither positive end-expiratory pressure or a minimum flow rate of oxygen are required for diagnosis in resource-variable settings.

Matthay et al. Am J Respir Crit Care Med 2023

ARDS

		LUNG-SAFE[2] (n=2377)
		ARDS 10.4% of all ICU Admissions 23.4% of All Patients on MV

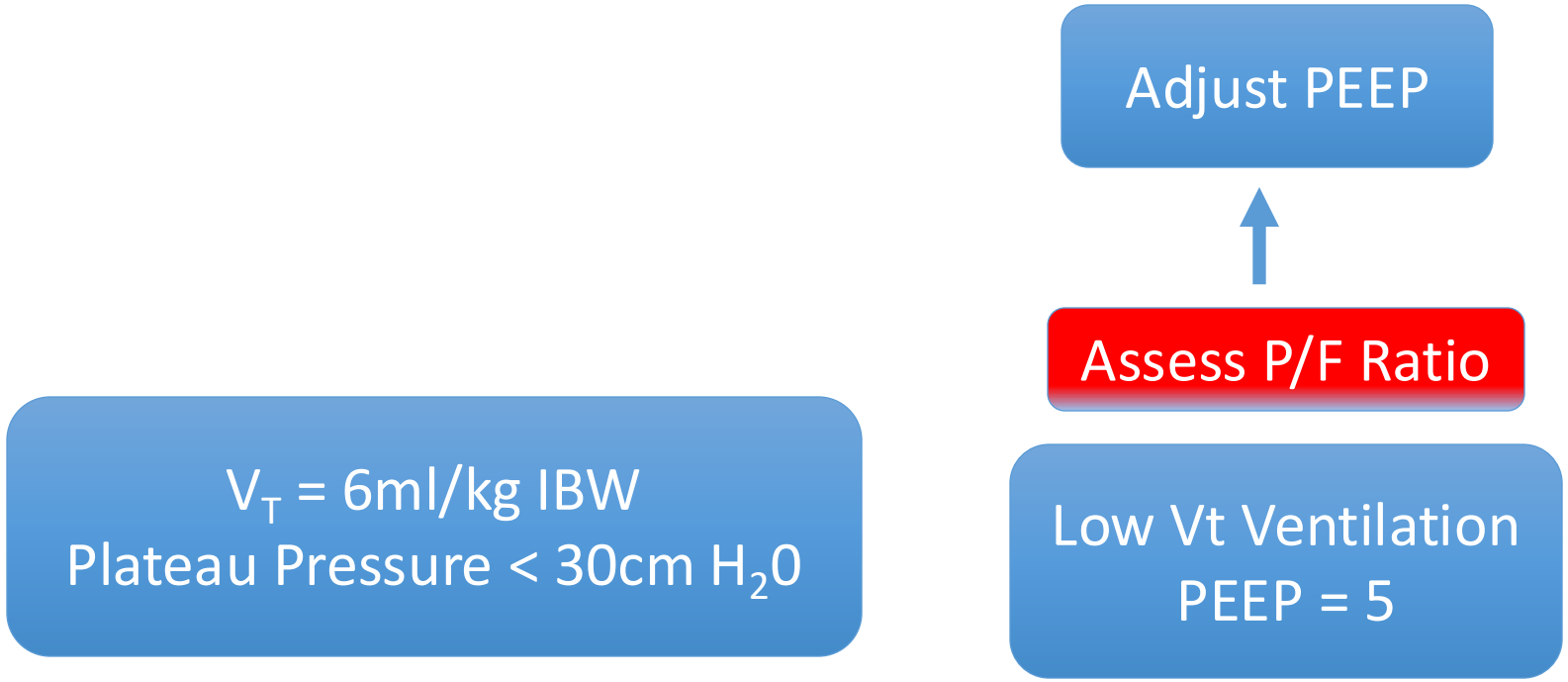
[1]Ranieri et al JAMA 2012; 307 (23) 2526-2533

[2]Bellani et al JAMA 2016; 315 (8) 788-800

Considerations in ARDS Treatment

- HFNO
- Non-Invasive Ventilation
- Low Tidal Volume Ventilation
- PEEP Optimization
- Recruitment Maneuvers
- Neuromuscular Blockade
- Prone Ventilation
- ECMO
- Inhaled Pulmonary Vasodilators
- Corticosteroids
- Volume Management

Minimize
Ventilator Induced Lung Injury
(VILI)


Adjust PEEP
Assess P/F Ratio
V_T = 6ml/kg IBW
Plateau Pressure < 30cm H_20
Low Vt Ventilation
PEEP = 5

Methods to Optimize PEEP

- PEEP / FiO2 table
- Maximize plateau pressure
- Assess Lung Recruitment
  - Radiographic
    - Sequential CT scan
    - Use of a Table based on CT scan
  - Helium Dilution or Nitrogen Washout
  - Maximize compliance
    - P/V curve – set PEEP above lower inflection point
    - Step PEEP titration
    - Driving Pressure (End inspiratory plateau – PEEP)
- Esophageal balloon
- Electrical Impedance Tomography
- Ultrasound

Higher vs Lower Positive End-Expiratory Pressure in Patients With Acute Lung Injury and Acute Respiratory Distress Syndrome

Systematic Review and Meta-analysis

	Clinical Outcomes								
	All Patients			ARDS (PaO_2:FiO_2<200)			Non ARDS		
	Low PEEP	High PEEP	P Value	Low PEEP	High PEEP	P Value	Low PEEP	High PEEP	P Value
# Patients	1163	1136		941	951		220	184	
Death in hospital %	35.2	32.9	0.25	39.1	34.1	0.049	19.4	27.2	0.070
Death in ICU %	32.8	28.5	0.01	36.6	30.3	.001	16.8	19.6	0.71
Days unassisted breathing	11	13	0.10	7	12	0.004	19	17	0.07
Rescue Therapy	18.6	12.2	<.001	21.3	13.7	<.001	16	8	0.25

Briel M, Meade M, Mercat A, et al. Higher vs Lower Positive End-Expiratory Pressure in Patients With Acute Lung Injury and Acute Respiratory Distress SyndromeSystematic Review and Meta-analysis. *JAMA*.2010;303(9):865–873. doi:10.1001/jama.2010.218

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Titrating Positive End-Expiratory Pressure (PEEP) With an Esophageal Pressure–Guided Strategy vs an Empirical High PEEP-FIO_2 Strategy on Death and Days Free From Mechanical Ventilation Among Patients With Acute Respiratory Distress Syndrome

A Randomized Clinical Trial

Jeremy R. Beitler, MD, MPH; Todd Sarge, MD; Valerie M. Banner-Goodspeed, MPH; Michelle N. Gong, MD, MSc; Deborah Cook, MD; Victor Novack, MD, PhD; Stephen H. Loring, MD; Daniel Talmor, MD, MPH; for the EPVent-2 Study Group

- P_{ES} guided vs PEEP-FiO2 table
- 14 sites (North America)
- Moderate-Severe ARDS (PaO2:FiO2 <200mm Hg)
- P_{ES}: 102 patients
- PEEP-FiO2: 100 patients

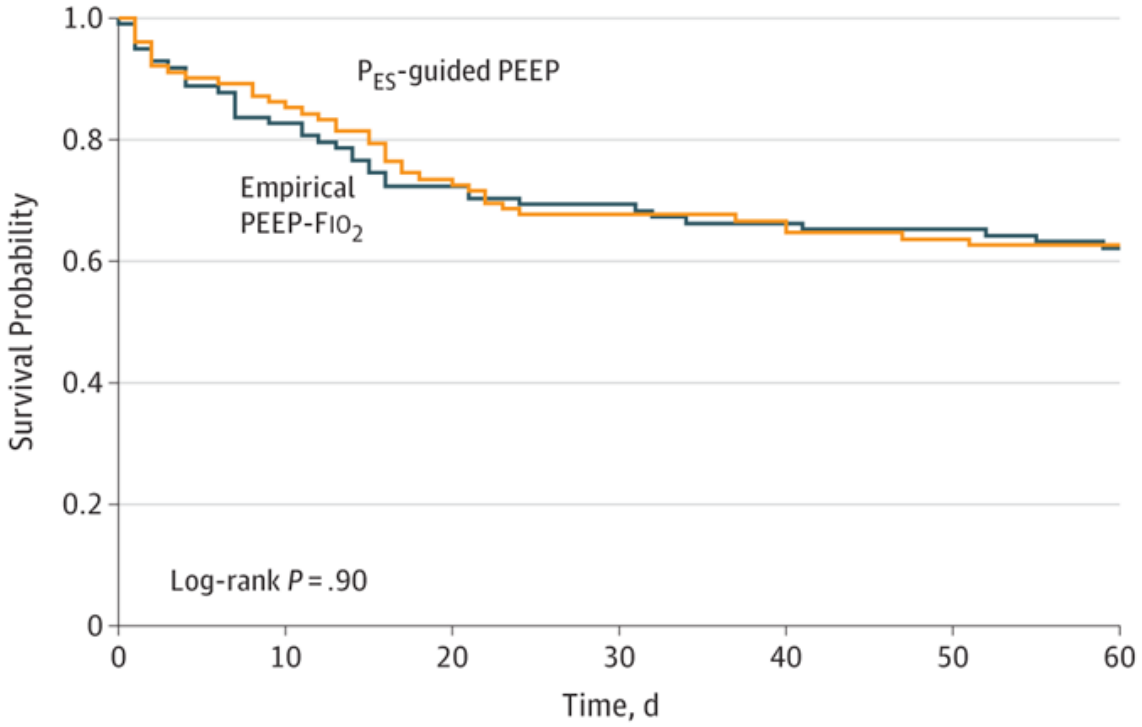
Beitler et al. JAMA 2019 Vol 321(9)

EP Vent 2 Outcomes

End Point	PES Guided	PEEP – FiO2	Absolute Diff,% (95% CI)	pValue
	(N=102)	(N=98)		
Primary				
Ranked Composite incorporating death and days free from mechanical ventilation	49.6 (41.7 to 57.5)	50.4 (42.5 to 58.3)		0.92
Secondary				
Mortality – Day 28 (%)	33 (32.4)	30 (30.6)	1.7 (-11.1 to 14.6)	0.88
Days free from MV - survivors (IQR)	22 (15 to 24)	21	0 (-1 to 2)	0.85
Mortality – Day 60 (%)	38/101 (37.6)	37/98 (37.8)	-0.1 (-13.6 to 13.3)	>0.99
ICU LOS median -thru day28 (IQR)	10 (6 to 17)	9.5 (5 to 14)	1 (-1 to 3)	0.24
Hospital LOS LOS-thru day 28 (IQR)	16 (9 to 26)	15 (8 to 24)	0 (-1 to 3)	0.58

Beitler et al. JAMA 2019 Vol 321(9)

EP Vent 2 Outcomes

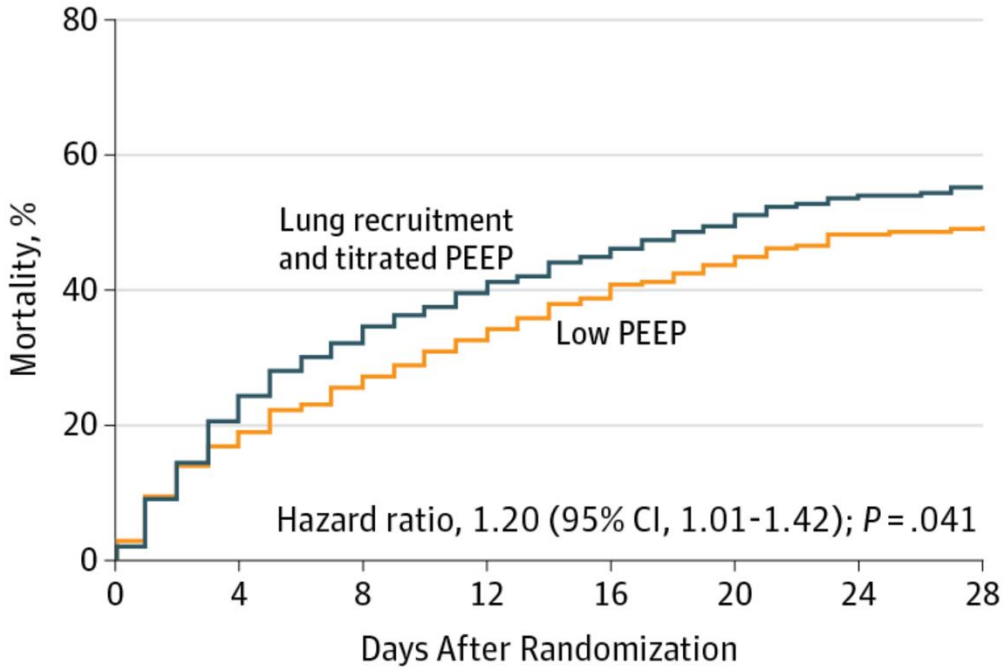


No. at risk

P_{ES}-guided PEEP	102	88	75	68	67	64	63
Empirical PEEP-FIO_2	98	81	71	68	65	64	61

Beitler et al. JAMA 2019 Vol 321(9)

ART Trial – 28 Day Mortality



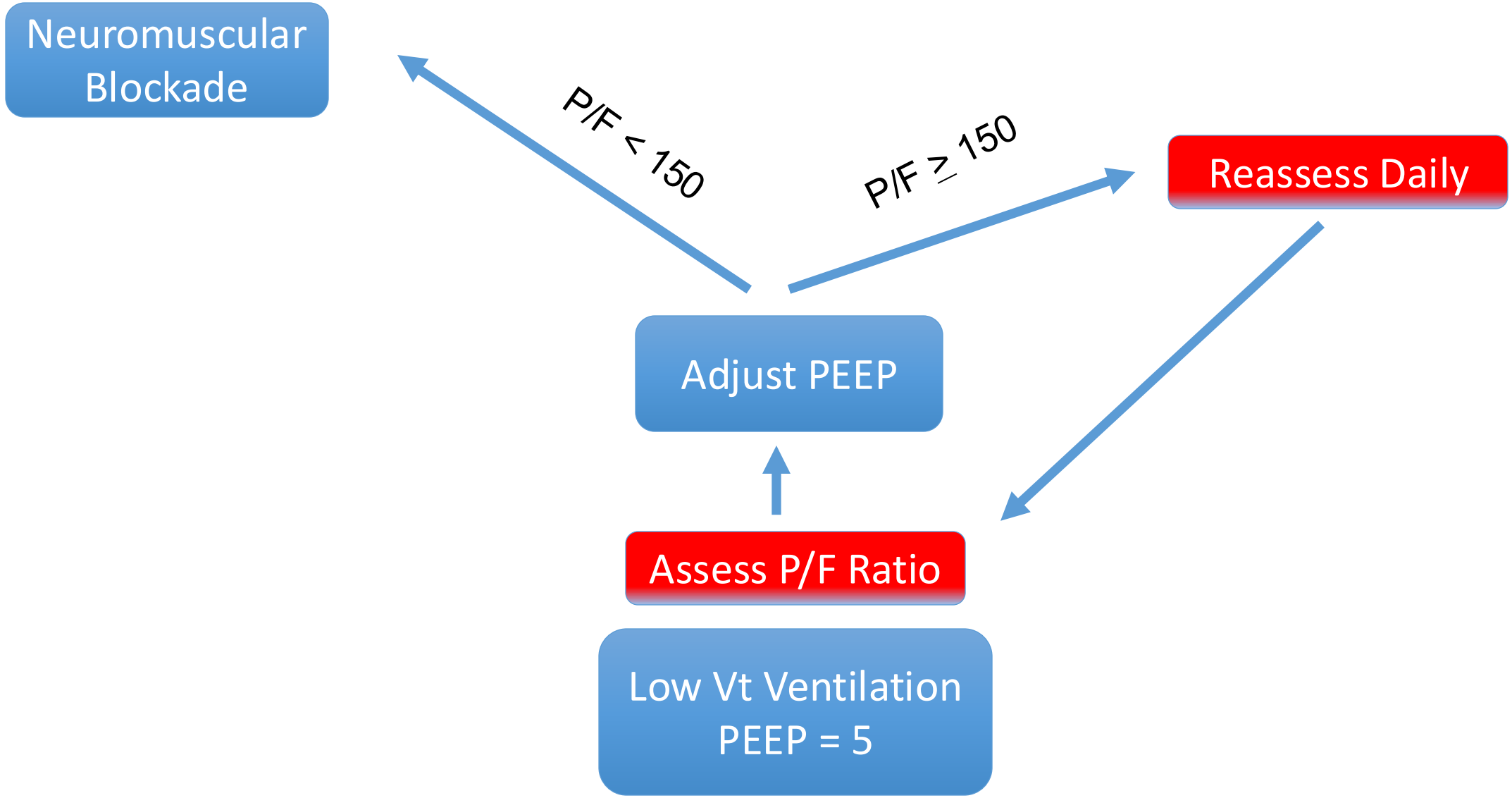
No. at risk								
Lung recruitment and titrated PEEP	501	397	340	303	276	254	233	225
Low PEEP	509	423	378	343	312	286	264	260

From: **Effect of Lung Recruitment and Titrated Positive End-Expiratory Pressure (PEEP) vs Low PEEP on Mortality in Patients With Acute Respiratory Distress Syndrome. A Randomized Clinical Trial**

JAMA. 2017;318(14):1335-1345. doi:10.1001/jama.2017.14171

PEEP 2024 ?

- Literature does not support a particular method to determine optimal PEEP
- P/F >200 – Low or High PEEP Table probably OK
- P/F < 200 – High PEEP Table
- P/F < 200 - Consider Personalizing PEEP
  - You probably don’t need to keep all alveoli open
  - Strike a balance: Avoid overdistention
  - Assess recruitability / Point of optimal compliance?
  - Data currently lacking.
- Future studies needed
  - Newer Technologies


Neuromuscular Blockade
P/F < 150
P/F ≥ 150
Reassess Daily
Adjust PEEP
Assess P/F Ratio
Low Vt Ventilation
PEEP = 5

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 16, 2010 VOL. 363 NO. 12

Neuromuscular Blockers in Early Acute Respiratory Distress Syndrome

Laurent Papazian, M.D., Ph.D., Jean-Marie Forel, M.D., Arnaud Gacouin, M.D., Christine Penot-Ragon, Pharm.D., Gilles Perrin, M.D., Anderson Loundou, Ph.D., Samir Jaber, M.D., Ph.D., Jean-Michel Arnal, M.D., Didier Perez, M.D., Jean-Marie Seghboyan, M.D., Jean-Michel Constantin, M.D., Ph.D., Pierre Courant, M.D., Jean-Yves Lefrant, M.D., Ph.D., Claude Guérin, M.D., Ph.D., Gwenaël Prat, M.D., Sophie Morange, M.D., and Antoine Roch, M.D., Ph.D., for the ACURASYS Study Investigators*

- Multicenter (20 ICU France)
- Double blind
- 340 patients
- Intervention: 48 hours of cisatricurium
  - Early (within 48 hours)
  - PaO2 : FiO2 <150
  - PEEP >5
  - Vt = 6-8ml /kg

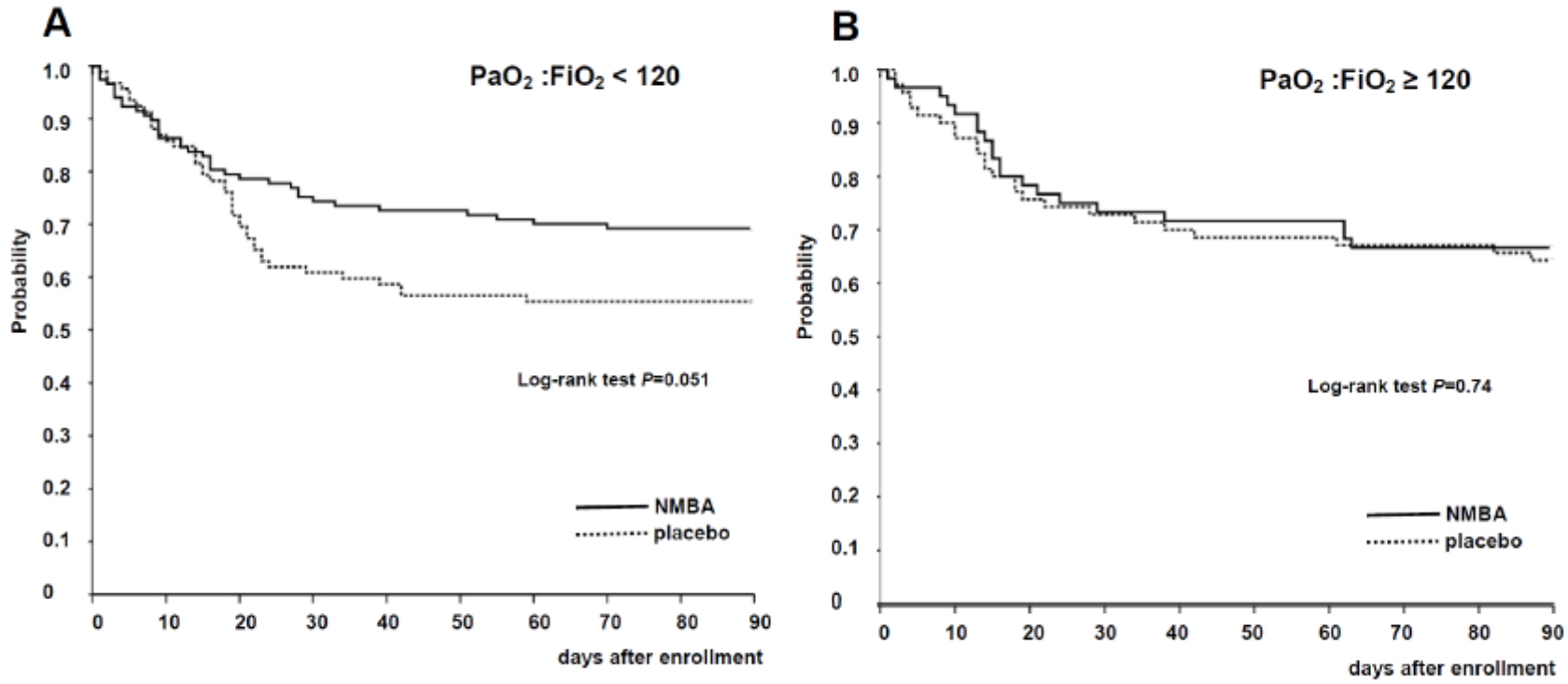
ACURASYS Primary Outcome

- Reduction of the hazard ratio of death at 90 days 0.68 (0.48-0.98; p=0.04)
  - Adjusted for PaO_2 / FiO_2
  - SAPS
  - Plateau Pressure
  - 90 Day crude mortality 31.6 vs 40.7 (p=0.08)

	NMB	Control		
	(n=177)	(n=162)	RR	P value
Death (@ 90 days)	31.6	40.7		0.08

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

ACURASYS –Mortality and P/F ratio



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

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 23, 2019 VOL. 380 NO. 21

Early Neuromuscular Blockade in the Acute Respiratory Distress Syndrome

The National Heart, Lung, and Blood Institute PETAL Clinical Trials Network*

- ROSE Trial – Reevaluation of Systemic Early Neuromuscular Blockade
- Neuromuscular blockade (NMB) with Cisatracurium and deep sedation to usual care with lighter sedation.
- Moderate to Severe ARDS PaO_2: FiO_2 <150mmHg
- 1006 patients
- 48 US Hospitals

The National Heart, Lung, and Blood Institute PETAL Clinical Trials Network. N Engl J Med 2019;380:1997-2008

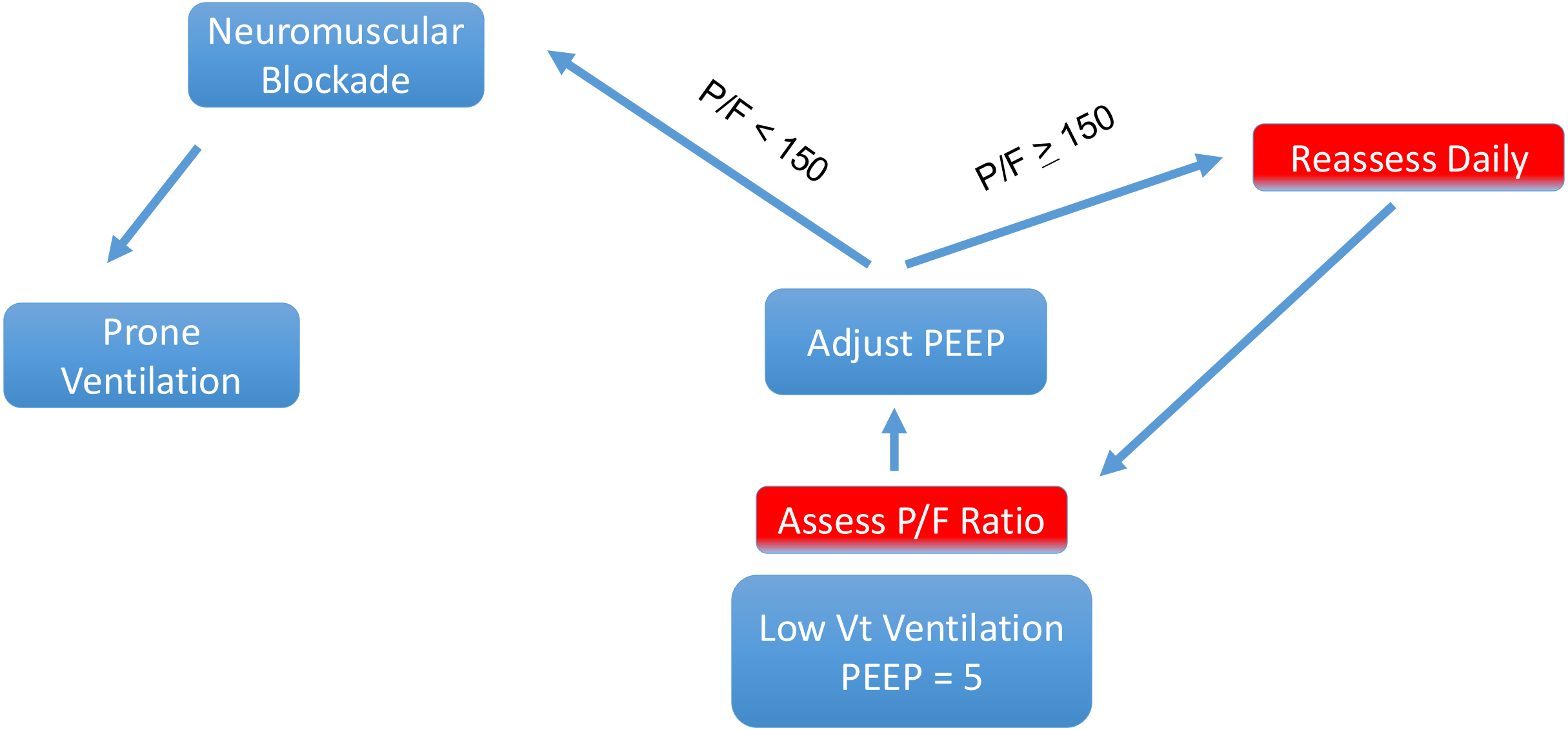
ROSE Trial Outcomes

End Point	NMB	Control	Between Group Difference (95% CI)	pValue
	(N=501)	(N=505)		
Primary				
In Hospital Death - Day 90 (%)	213 (42.5)	216 (42.8)	-0.3 (-6.4 to 5.9)	0.93
Secondary				
In Hospital Death – Day 28 (%)	184 (36.7)	187 (37.0)	-0.3 (-6.3 to 5.7)	
Days free from MV – Day 28	9.6 ± 10.4	9.9 ± 10.9	-0.3 (-1.7 to 1.0)	
Days Not in ICU – Day 28	9.0 ± 9.4	9.4 ± 9.8	-0.4 (-1.6 to 0.8)	
Days Not in Hospital – Day 28	5.7 ± 7.8	5.9 ± 8.1	-0.2 (-1.1 to 0.8)	

The National Heart, Lung, and Blood Institute PETAL Clinical Trials Network. N Engl J Med 2019;380:1997-2008

Neuromuscular Blockade 2024 ?

- Not to be used for all patients with Moderate – Severe ARDS
- May have role in patients in selected patients
  - Ongoing ventilator dyssynchrony despite optimization of ventilator settings and sedation
- Mechanism of action: Reduce dyssynchrony – reduce VILI


Neuromuscular Blockade
P/F < 150
P/F ≥ 150
Reassess Daily
Prone Ventilation
Adjust PEEP
Assess P/F Ratio
Low Vt Ventilation
PEEP = 5

Prone Ventilation

- Initial report 1976
  - Piehl and Brown Crit Care Med 1976;4;12-14
  - Increase PaO2 = 47 torr
- Multiple reports of improved oxygenation
- Mechanism of improved oxygenation
  - Recruitment of dorsal regions of lung
  - Improved ventilation – perfusion matching
  - Reduction of alveolar shunt
- Utilized as rescue therapy

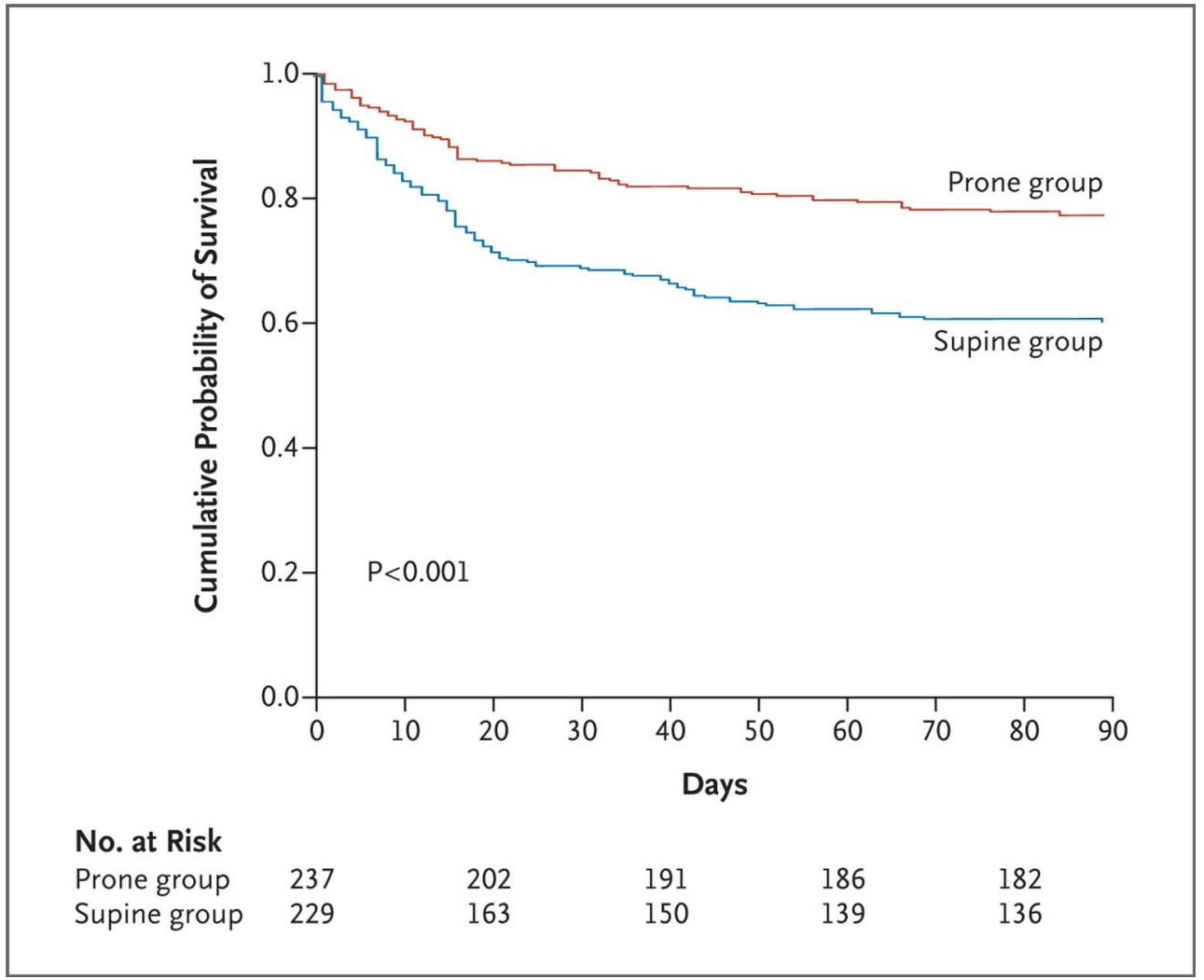
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 6, 2013 VOL. 368 NO. 23

Prone Positioning in Severe Acute Respiratory Distress Syndrome

Claude Guérin, M.D., Ph.D., Jean Reignier, M.D., Ph.D., Jean-Christophe Richard, M.D., Ph.D., Pascal Beuret, M.D., Arnaud Gacouin, M.D., Thierry Boulain, M.D., Emmanuelle Mercier, M.D., Michel Badet, M.D., Alain Mercat, M.D., Ph.D., Olivier Baudin, M.D., Marc Clavel, M.D., Delphine Chatellier, M.D., Samir Jaber, M.D., Ph.D., Sylvène Rosselli, M.D., Jordi Mancebo, M.D., Ph.D., Michel Sirodot, M.D., Gilles Hilbert, M.D., Ph.D., Christian Bengler, M.D., Jack Richecoeur, M.D., Marc Gainnier, M.D., Ph.D., Frédérique Bayle, M.D., Gael Bourdin, M.D., Véronique Leray, M.D., Raphaele Girard, M.D., Loredana Baboi, Ph.D., and Louis Ayzac, M.D., for the PROSEVA Study Group*

- Multicenter, Randomized
- Prone vs control (low VT and PEEP:FiO2 table)
- 466 patients
- Early application (within 36 hrs of initiation of MV); PaO2 / FiO2 <150
- Prone dose = 16 hours
- Outcome: Proportion of deaths from any cause within 28 days after enrollment



Guérin C et al. N Engl J Med 2013;368:2159-2168

Guerin et al. N Engl J Med 368;23

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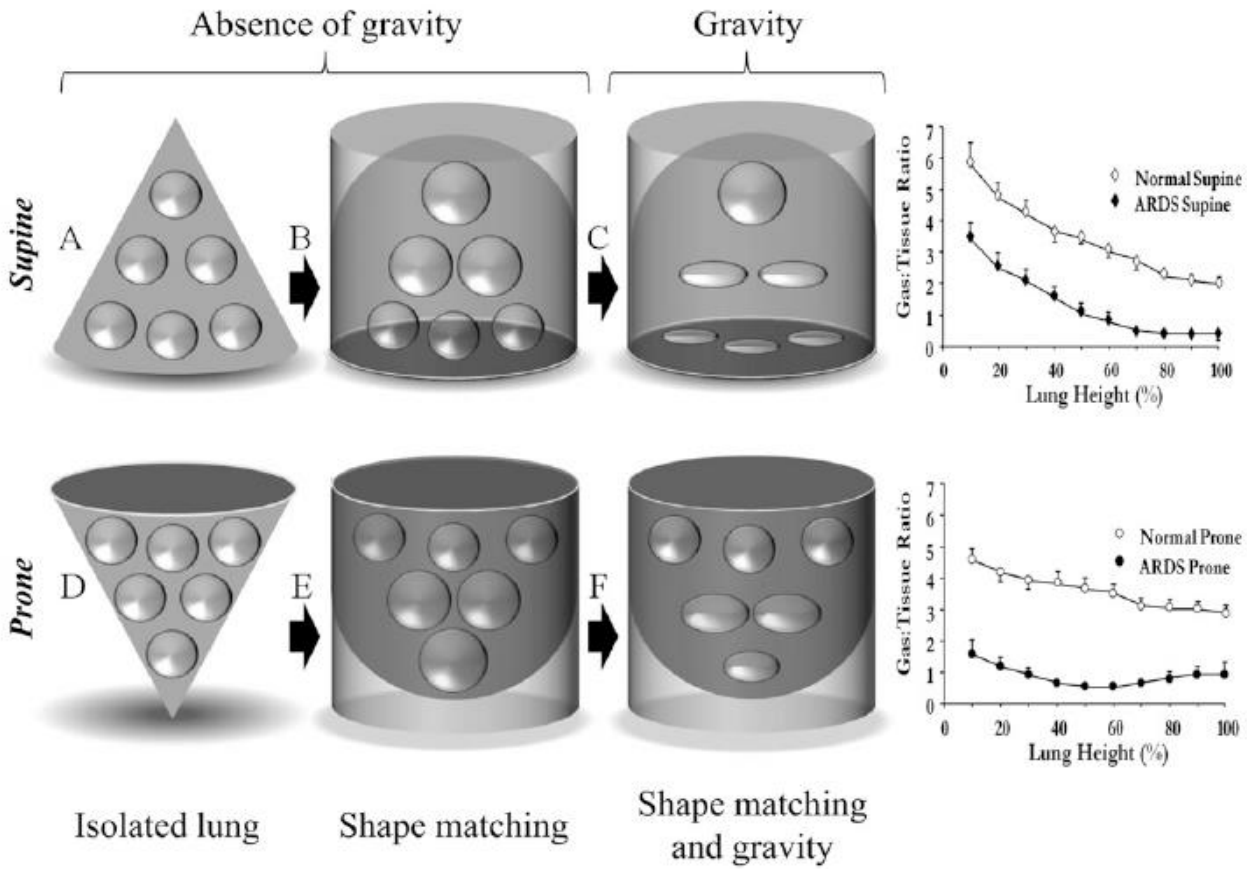
BWH BRIGHAM AND WOMEN'S HOSPITAL

HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

Mass General Brigham

Prone Ventilation Studies

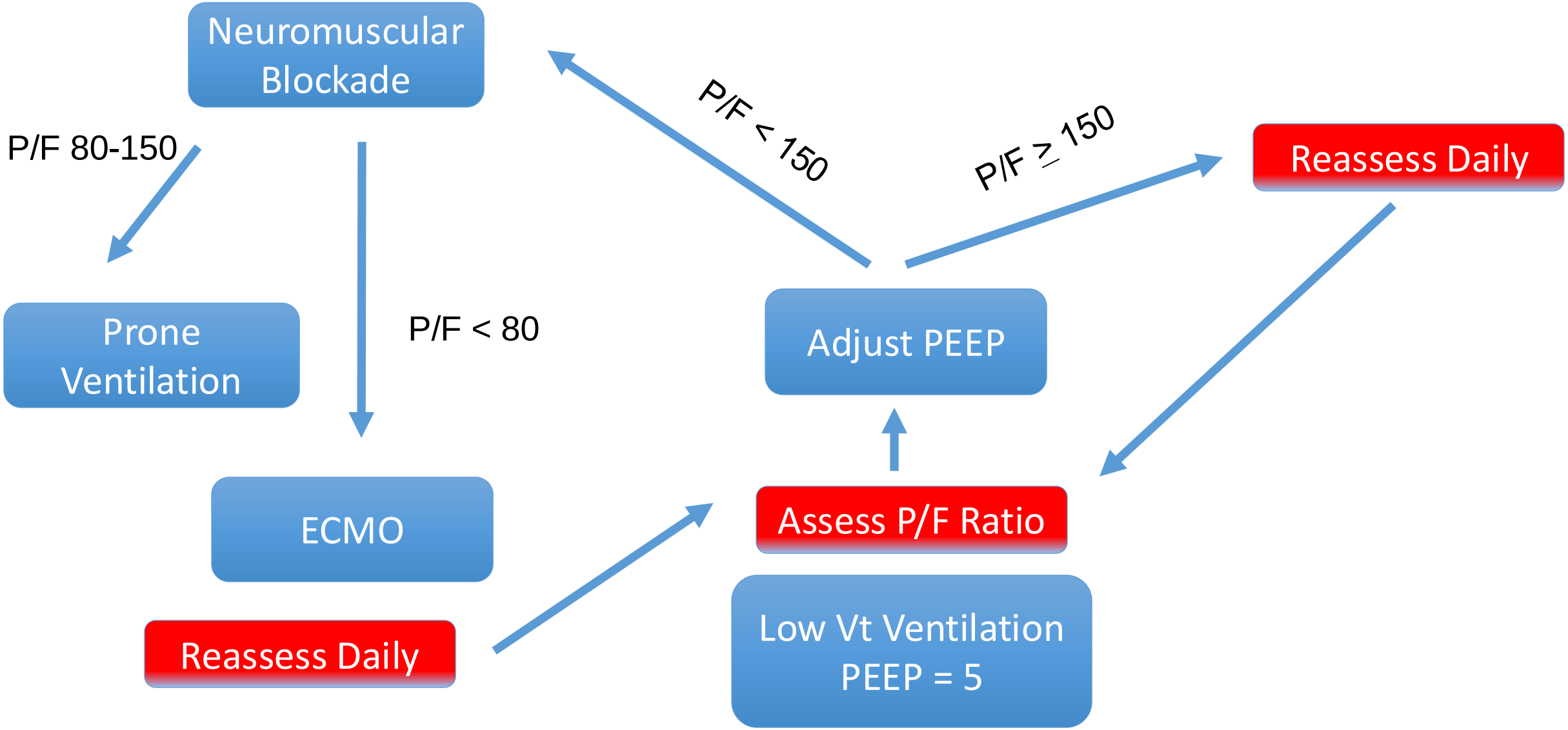
	2001	2004	2006	2009	2014
	Prone-Supine			Prone-Supine II	PROSEVA
	Gattinoni	Guerin	Mancebo	Taccone	Guerin
Patients	304	791	142	342	474
Proning Dose	>=6	>=8	20	>=20	>=16
PaO2:FiO2	<=300	<=300	<=200	100-200; <100	<150
Time Enrolled	Not early	Not early	<48 hrs	<72 hrs	<36 hrs
Mortality	ICU	28 day	ICU	28 day	28 day
Prone	50.7%	32.4%	43%	31%	16%
Control	48%	31.5%	58%	32.8%	32.8%
RR	1.05	1.02	0.74	0.97	0.48
		p=0.77	p=0.12	p=0.72	p<0.0001



Gattinoni et al. Prone Positioning in ARDS Am J Respir Crit Care Med 188 (11) 1286-1293

Prone Ventilation

- Indicated if PaO2:FiO2 ratio <150
  - Contraindications
    - Elevated intracranial pressure
    - Spinal instability
- Be prepared: Multidisciplinary team
- Perform early
- Proning duration of 16 hours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P/F < 150
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Reassess Daily
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Assess P/F Ratio
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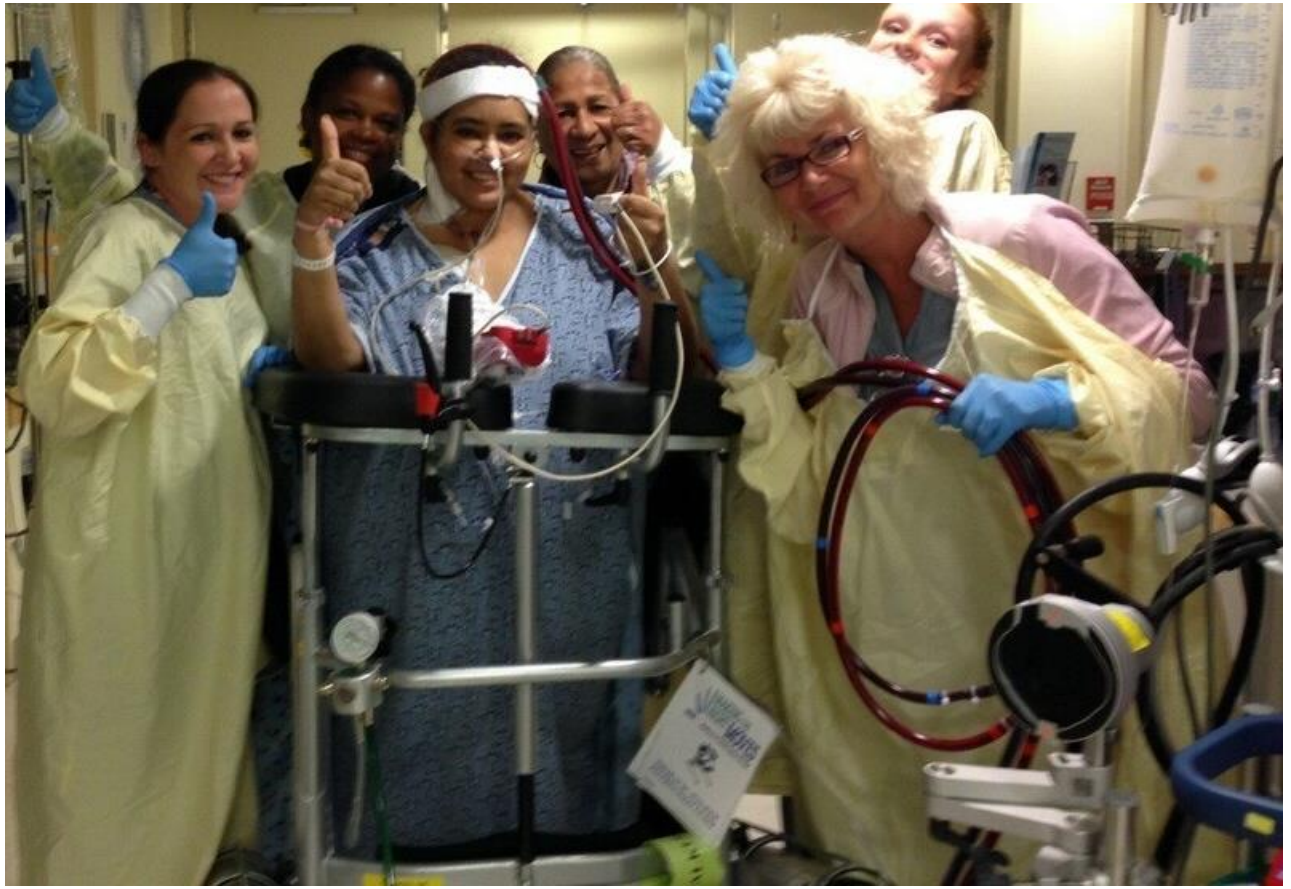
Low Vt Ventilation
PEEP = 5

VV ECMO for ARDS



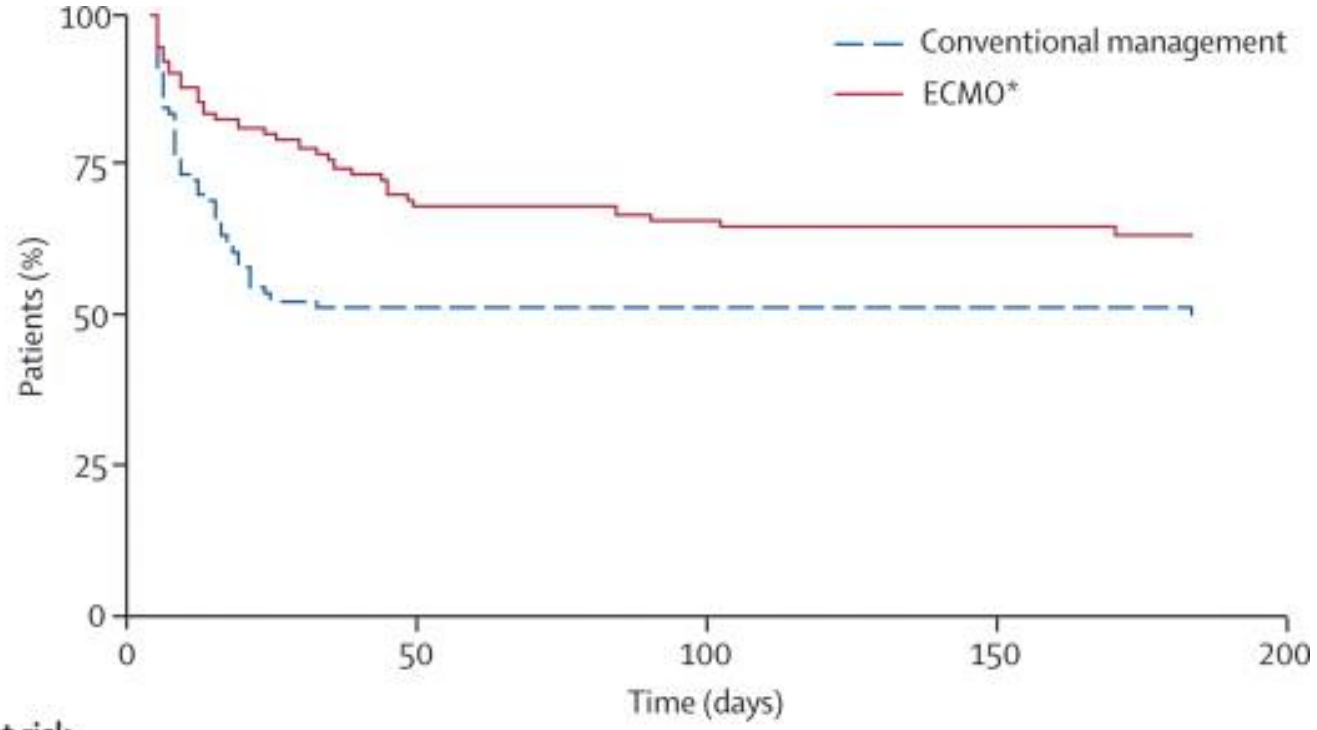
Extra-Corporeal Membrane Oxygenation (ECMO)

- 1979 – ECMO & MV vs. MV
  - 90 Patients, 9 centers, Randomized Prospective
  - Mortality ECMO = 90.5% vs MV= 91.7%
  - Zapol et al. JAMA 242: 2193-2196, 1979
- 1994 – PIRV & ECMO vs MV
  - 40 patients, 1 center, Randomized Prospective
  - 30 Day Mortality ECMO=42% vs 33% (p=0.8)
  - Morris et al. Am J Resp Crit Care Med 1994; 149:295-305

Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial

Giles J Peek, Miranda Mugford, Ravindranath Tiruvoipati, Andrew Wilson, Elizabeth Allen, Mariamma M Thalanany, Clare L Hibbert, Ann Truesdale, Felicity Clemens, Nicola Cooper, Richard K Firmin, Diana Elbourne, for the CESAR trial collaboration

- Multicenter
- 180 Patients
- Murray Score 3.0 or higher (P/F, CXR quadrants, PEEP, compliance)
- Conventional Management vs ECMO
- Primary Outcome – Death or Severe Disability at 6 months
- Peek et al. Lancet Volume 374, Issue 9698, 2009, 1351–1363



Kaplan-Meier survival estimates. Randomized to ECMO, but did not necessarily receive this treatment.

Giles J Peek, Miranda Mugford, Ravindranath Tiruvoipati, Andrew Wilson, Elizabeth Allen, Mariamma M Thalanany, Clare L Hibbert, Ann Truesdale, Felicity Clemens, Nicola Cooper, Richard K Firmin, Diana Elbourne

Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial

Volume 374, Issue 9698, 2009, 1351–1363

http://dx.doi.org/10.1016/S0140-6736(09)61069-2

CESAR Criticisms

- Lack of specified ventilator management protocol in control arm
- 30% of patients did not receive protective lung ventilation
- All ECMO at one center
- 75% of the intervention group received ECMO
- Early cessation of trial

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*

- Conventional support vs ECMO
  - Crossover allowed
- Very severe ARDS
- 240 Patients
- Primary Outcome: Mortality at 60 days

Combes et al. NEJM 2018 Vol 378(21)

EOLIA Trial

- Entry Criteria
  - Mechanical Ventilation < 7 days
  - "Very Severe ARDS"
    - PaO_2 / FiO_2 ratio <50mg Hg x 3 hours
    - PaO_2 / FiO_2 ratio <80mg Hg x 6 hours
    - pH <7.25 with $PaCO_2$ >=60 mmHg x 6hrs
- Cross Over for refractory hypoxemia
  - 35 patients in control arm (mean 6.5 days)
  - 57% mortality
- Endpoints
  - Mortality
  - Key Endpoint – Death and crossover to ECMO

Combes et al. NEJM 2018 Vol 378(21)

EOLIA Outcomes

End Point	ECMO Group	Control Group	Relative Risk	pValue
	(N=124)	(N=125)		
Primary				
Mortality at 60 days %	44 (35)	57 (46)	0.76 (0.55 to 1.04)	0.09
Key Secondary EndPoint				
Treatment Failure at 60 days	44 (35)	72 (58)	0.62 (0.47 to 0.82)	<0.001

Of note for several secondary endpoints, ECMO was significantly better than the control group

- days alive and free of the need for vasopressor therapy
- days alive and free of the need for renal replacement therapy
- days alive and free of the need for prone positioning

Combes et al. NEJM 2018 Vol 378(21)

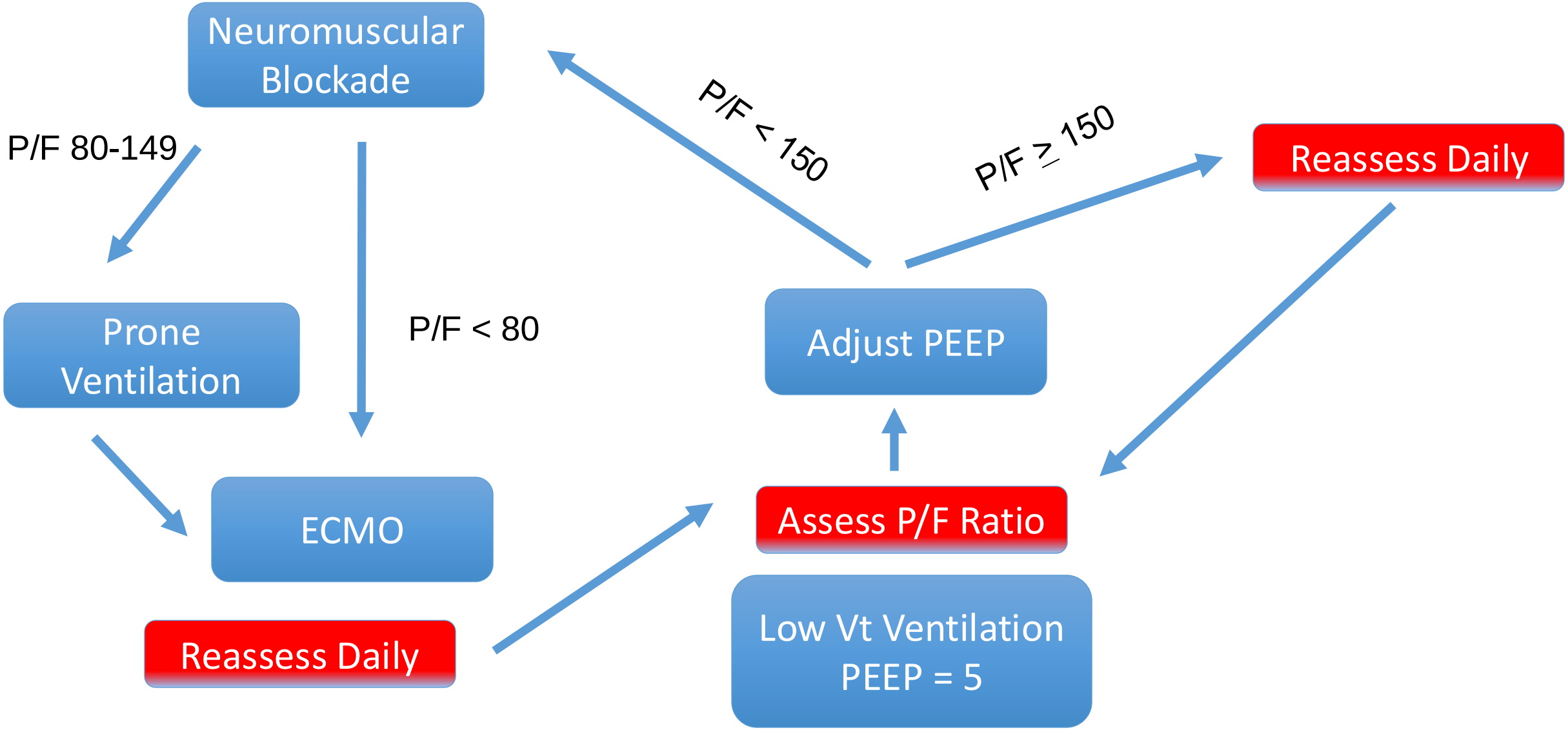
EOLIA

- Stopped early for futility (after 249 pts)
- Trial powered for 20% reduction mortality (?unrealistic)

- Method of improved mortality?
  - “Lung rest”, very low VT.

ECMO

- Use in patients with very severe hypoxemic respiratory failure
- Always use basic strategies first
  - PEEP optimization, NMB, prone ventilation.
- Patient should have potentially reversible etiology of ARDS
  - Bridge to recovery
  - Bridge to transplant
- Equity concerns
- Higher institutional volume associated with better outcomes.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Low Vt Ventilation
PEEP = 5

Steroids in ARDS

- Benefits
  - Reduce pro-inflammatory mediators
  - Reduce oxygen radicals made by neutrophils
  - Contribute to resolution of inflammation
- Risks
  - Hyperglycemia
  - GI bleed
  - Neuromuscular weakness
  - Infectious complications

Steroids in ARDS

- Indicated
  - PJP [1]
  - Covid-19 [2]
  - Severe Community Acquired PNA [3]
- All ARDS?
  - ATS Clinical Practice Guidelines
    - “Conditional recommendation; moderate certainty of evidence” [4]

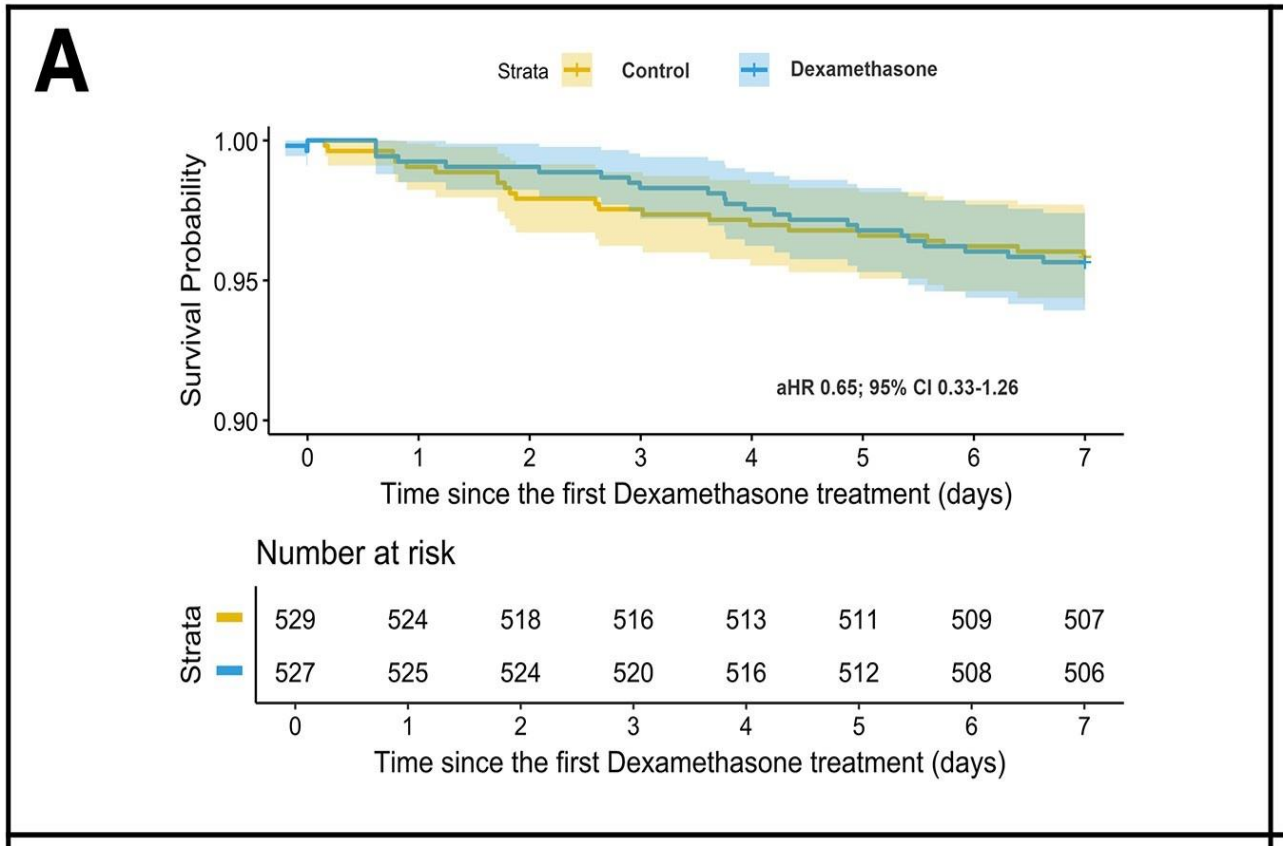
[1] Ewald H,et al . Adjunctive corticosteroids for Pneumocystis jiroveci pneumonia in patients with HIV infection. Cochrane Database Syst Rev 2015;2015:CD006150.

[2] WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group; Sterne, J.A.C et al. Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19: A Meta-analysis. JAMA 2020, 324, 1330–1341

[3] Dequin PF, et al. CRICS-TriGGERSep Network. Hydrocortisone in severe community acquired pneumonia. N Engl J Med 2023;388:1931–1941.

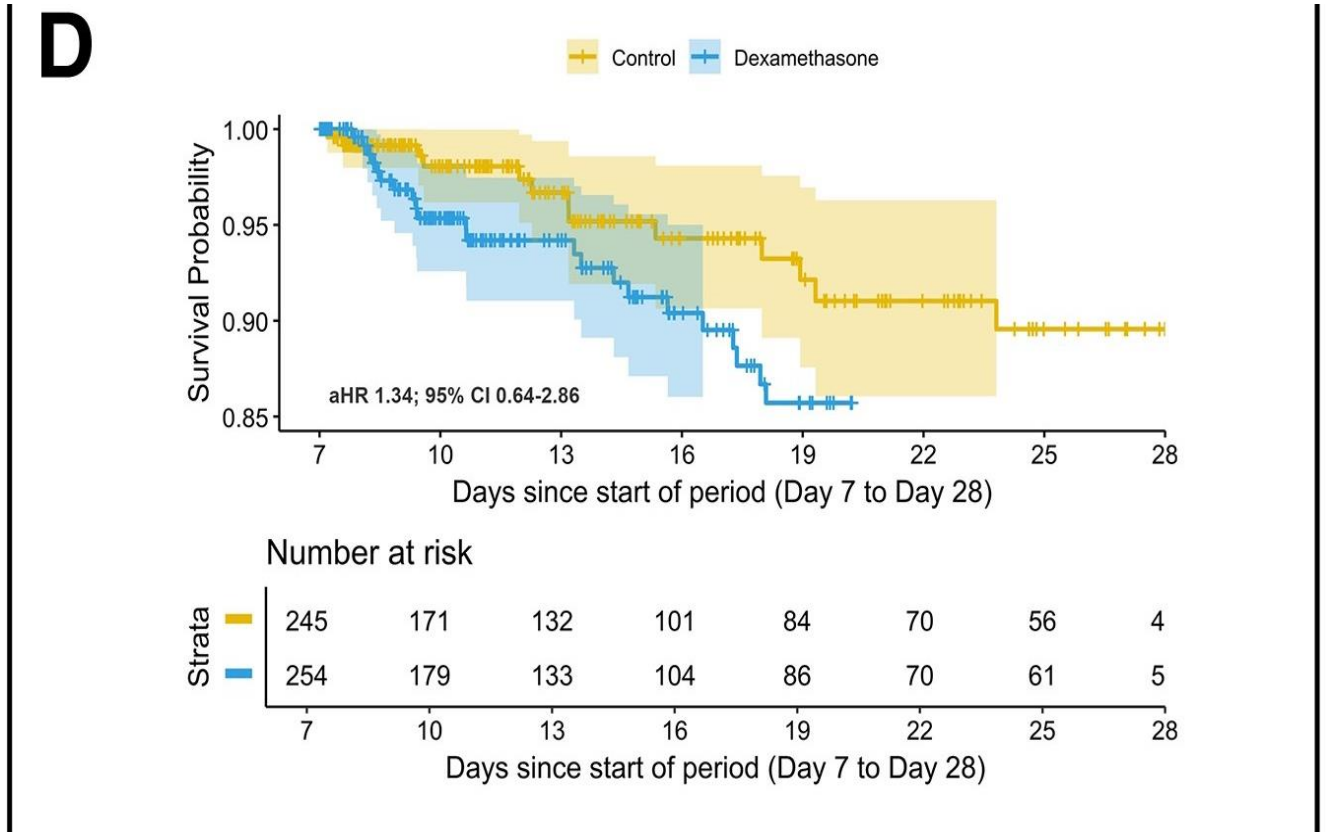
[4] Qadir N, et al. An update on management of adult patients with acute respiratory distress syndrome: an official American Thoracic Society Clinical practice guideline. Am J Respir Crit Care Med. 2024;209(1):24–36.

Time to death in the 0- to 6-day period in the entire study cohort



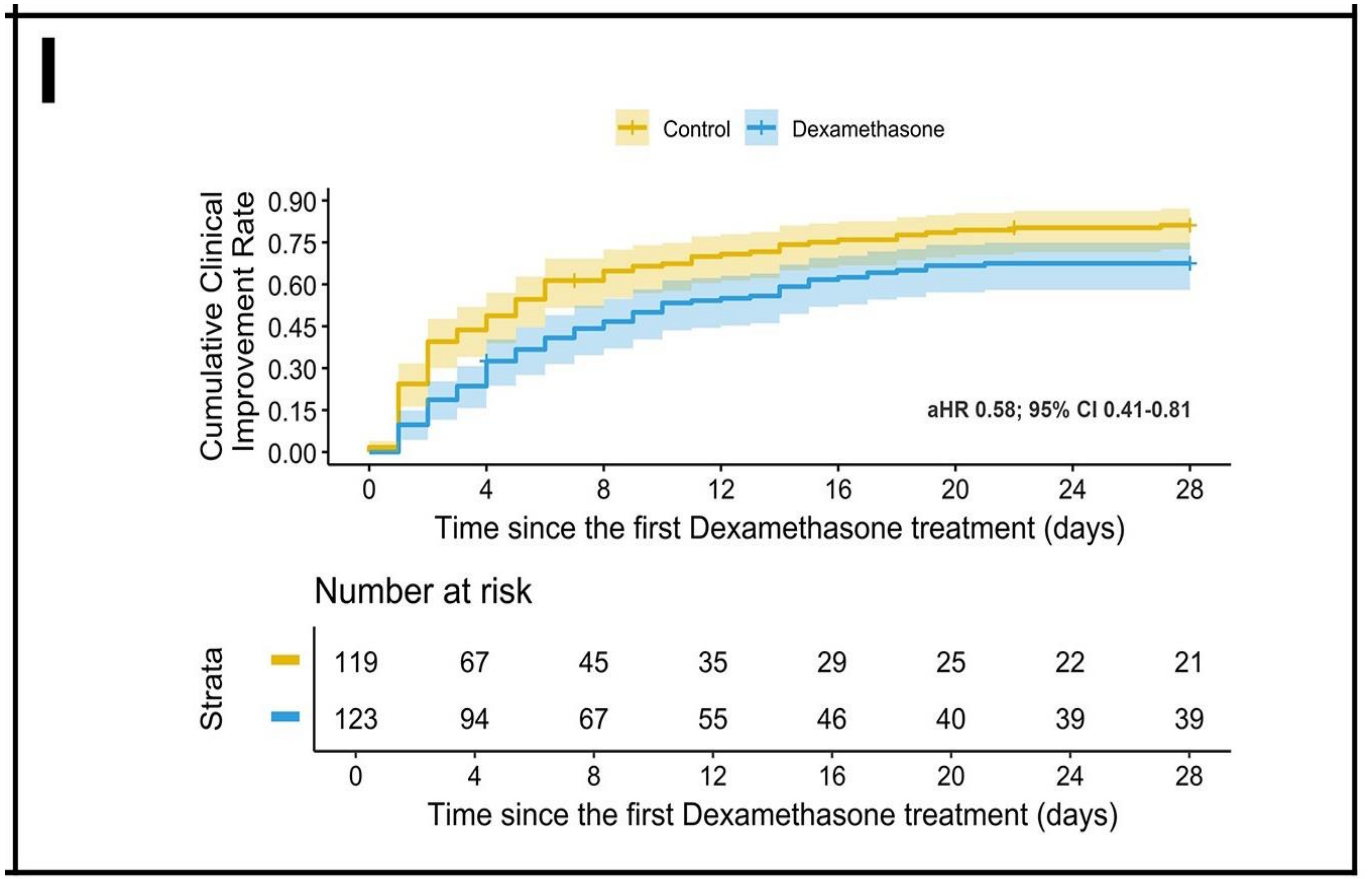
J Clin Endocrinol Metab, dgae734, https://doi.org/10.1210/clinem/dgae734

Time to death in the 7- to 28 day period in the entire study cohort



J Clin Endocrinol Metab, dgae734, https://doi.org/10.1210/clinem/dgae734

Cumulative Time to Clinical Improvement 0 to 28 Day Period in Severe Covid-19 Subgroup



J Clin Endocrinol Metab, dgae734, https://doi.org/10.1210/clinem/dgae734

Steroids in ARDS: Future Directions

- More data needed
  - Type of corticosteroid
  - Timing
  - Dose

- Upcoming Trials
  - GuARDS Trial (UK Center for Inflammation Research)
    - Glucocorticoids in adults with Acute Respiratory Distress Syndrome (GuARDS Trial)
    - RCT to recruit up to 1708 adult patients with ARDS, in approximately 65 ICUs throughout the UK
  - CORT-E2 (Canadian Critical Care Trials Group)
    - Corticosteroids Early and Extended Domains of the PRACTICAL platform RCT
    - Open label randomized trial to evaluate if:
      - Early corticosteroids will improve survival (Early Cohort) in patients with non-COVID AHRF; and
      - Extending corticosteroids (Extended Cohort) will improve survival in those with AHRF still requiring invasive or non-invasive respiratory despite already receiving 10 days of corticosteroids

Where to go next (2024)?

- Identifying ARDS subphenotypes
  - Radiographic appearance
  - Hyper vs hypo inflammatory subtype
- Directing treatment at subphenotypes
  - Ventilatory management strategies
  - Volume resuscitation
  - Immunomodulatory anti-inflammatory therapy
- Research questions (as posed by ESICM ARDS Guidelines)
  - Stability of subphenotypes
  - Are subphenotypes reproducible across populations
  - Accuracy and reproducibility of rapid subphenotype classification

Notes for Practice

- P/F ratio key for prognosis / rx.
- Optimize PEEP
  - For Moderate-Severe ARDS High PEEP:FiO2 table
- If PaO2/FiO2 < =150 consider neuromuscular blockade
  - If ongoing dyssynchrony
- If PaO2/FiO2 < =150 initiate prone ventilation
  - Early
  - Proning dose 16 hrs
- If very severe ARDS or failing above consider ECMO
- Consider corticosteroids in select populations