ARDS and Ventilators

Pauline Park, MD

M·TQIP

2015 Faculty Disclosure Slide

LIPS-A - NIH/NHLBI U01HL108712

EPVENT2 - NIH/NHLBI UM1HL108724

PETAL - NIH/NHLBI U01HL123031

ARDS Management: Overview 2015

➢ Low tidal volume ventilation
Prone Positioning
Early neuromuscular blockade

~~x HFOV~~
~~iNO~~

? Transpulmonary pressure guided ventilator management
ECMO

❖ Early intervention to reduce lung injury
Long Term Outcomes
Prevention in OR and ED

The Lancet · Saturday 12 August 1967

ACUTE RESPIRATORY DISTRESS IN ADULTS

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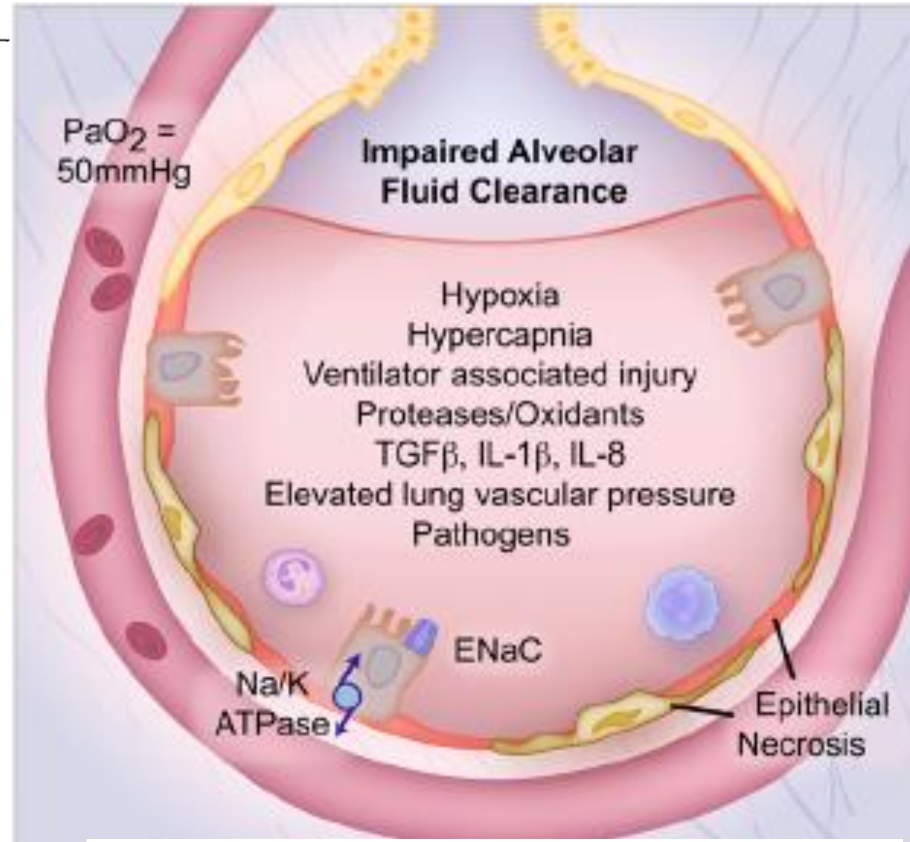
Summary The respiratory-distress syndrome in 12 patients was manifested by acute onset of tachypnœa, hypoxæmia, and loss of compliance after a variety of stimuli; the syndrome did not respond to usual and ordinary methods of respiratory therapy. The clinical and pathological features closely resembled those seen in infants with respiratory distress and to conditions in congestive atelectasis and postperfusion lung. The theoretical relationship of this syndrome to alveolar



Am J Respir Crit Care Med Vol 189, Iss 11, pp 1301–1308, Jun 1, 2014

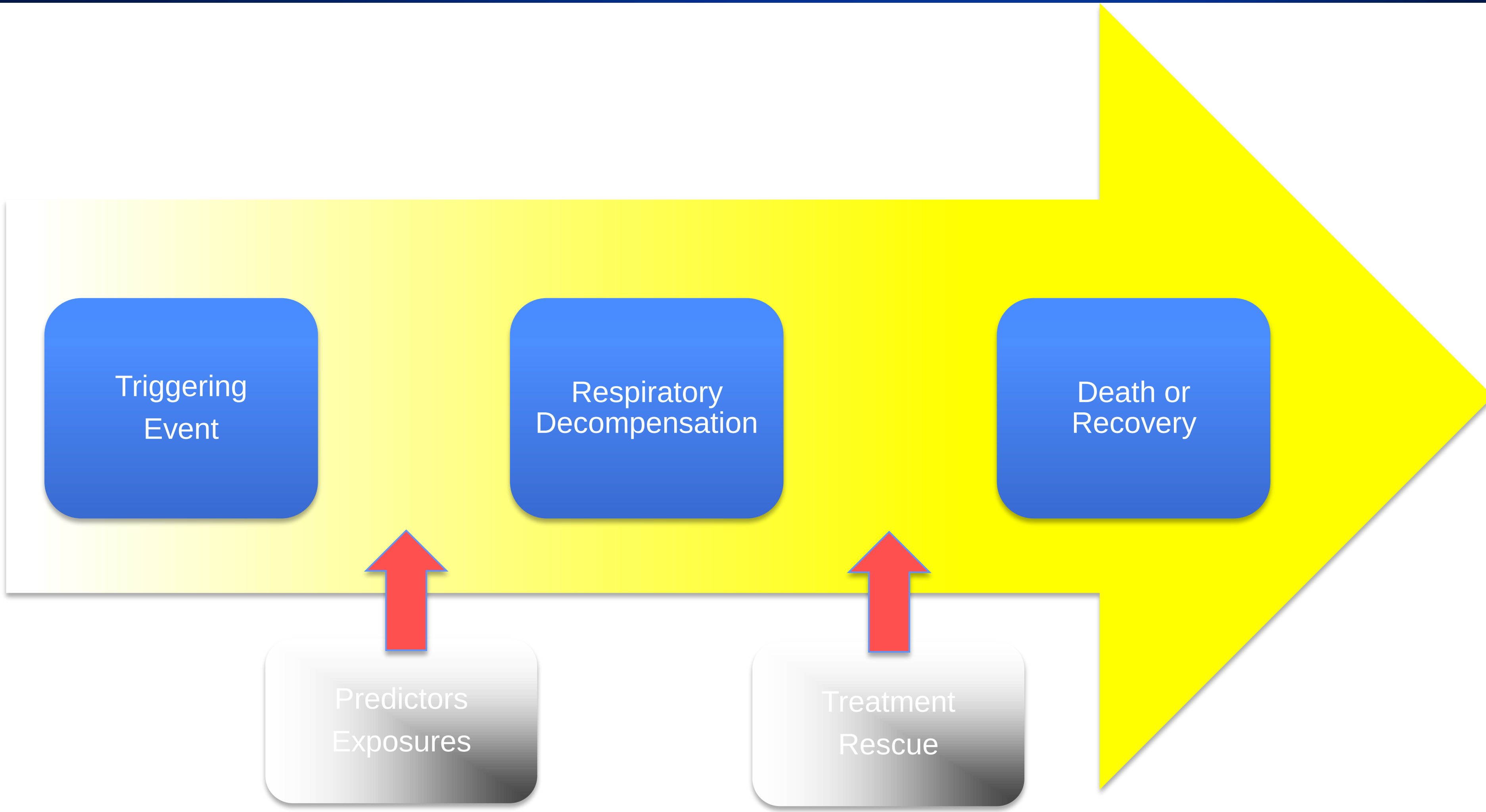
Normal Ventilation (rat lung)

(courtesy Gary Nieman, SUNY Upstate)

Injury (rat lung)

(courtesy Gary Nieman, SUNY Upstate)

Despite therapy, some patients will develop refractory hypoxemia



Acute Respiratory Distress Syndrome
The Berlin Definition

ARDS Definition Task Force, JAMA 2012 Jun 20; 307 (23): 25-26

	Mild	**Moderate**	**Severe**
Timing	Acute within one week		
Hypoxia	300 – 201	≤ 200	**≤ 100**
PEEP	≤ 5	≤ 5	≤ 10
Radiology	Bilateral	Bilateral	> 3 quadrants
Vent			Ve > 10L CRS < 40

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Hypoxia	300 – 201	$\leq$ 200	**$\leq$ 100**
PEEP	$\leq$ 5	$\leq$ 5	$\leq$ 10[illegible]
Radiology	Bilateral	Bilateral	> 3[illegible]its
Vent			[illegible]5 <[illegible]
Anticipated			
Incidence	23%	63%	14%
Mortality	10%	32%	62%

In absence of known predisposing risk factor* or not fully explained, assessment for cardiac failure required.

*Pneumonia, aspiration, inhalation, pulmonary contusion, drowning sepsis, transfusion, trauma, pancreatitis, noncardiogenic shock, drug overdose

Criteria for additional severity of disease did not enhance model and dropped from final definition

What do we actually think we know?

- Ventilation with high airway pressures is bad

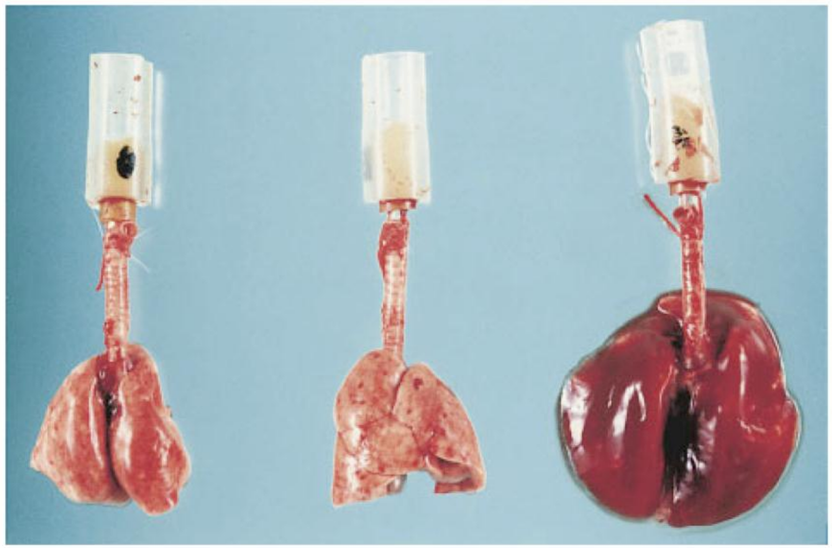
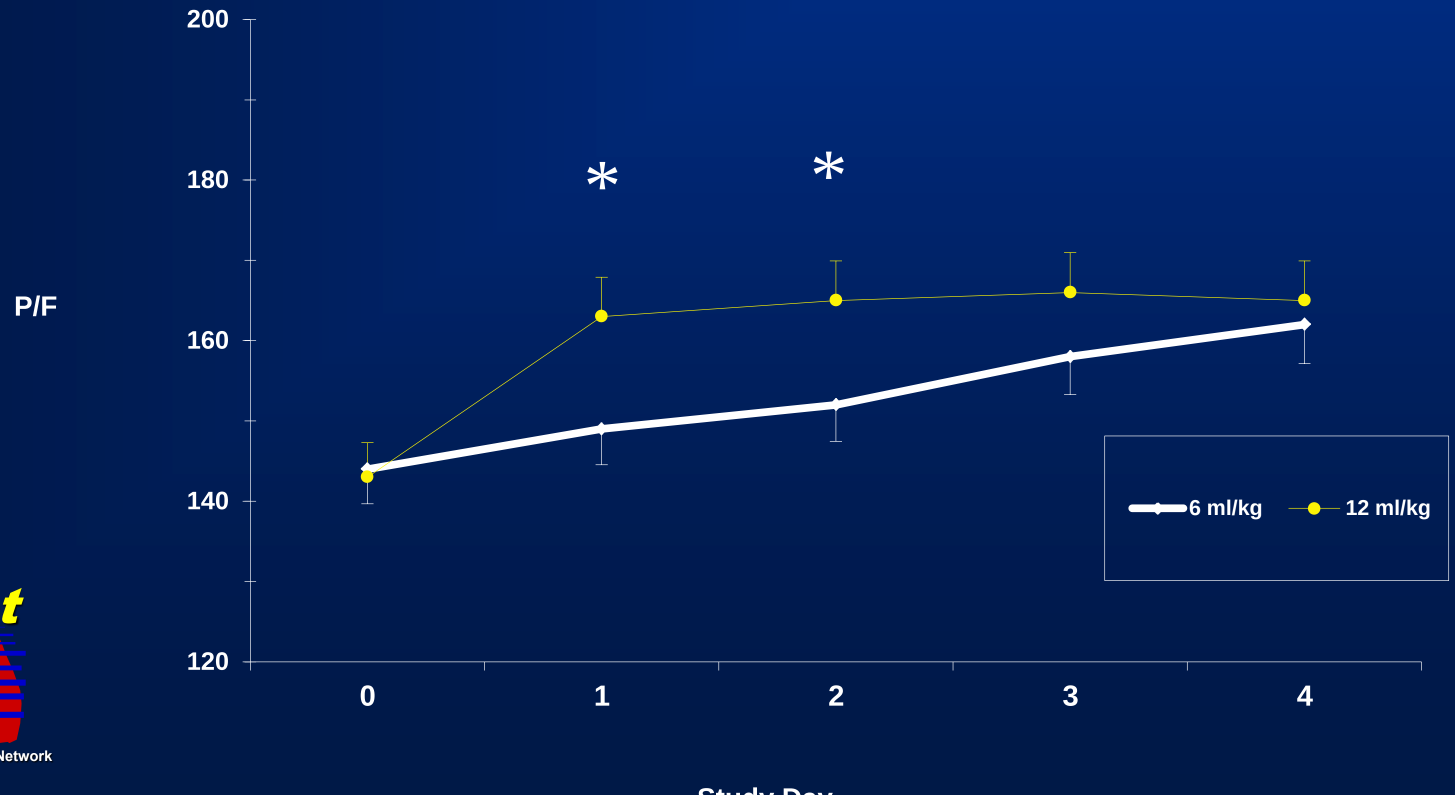


Figure 5. Macroscopic aspect of rat lungs after mechanical ventilation at 45 cm H_2O peak airway pressure. *Left*: normal lungs; *middle*: after 5 min of high airway pressure mechanical ventilation. Note the focal zones of atelectasis (in particular at the left lung apex); *right*: after 20 min, the lungs were markedly enlarged and congestive; edema fluid fills the tracheal cannula.

Am J Respir Crit Care Med Vol 157. pp 294–323, 1998

What do we actually think we know?

- Lower tidal volume ventilation with pressure limitation is good
- Correction of hypoxia is not a good surrogate for mortality

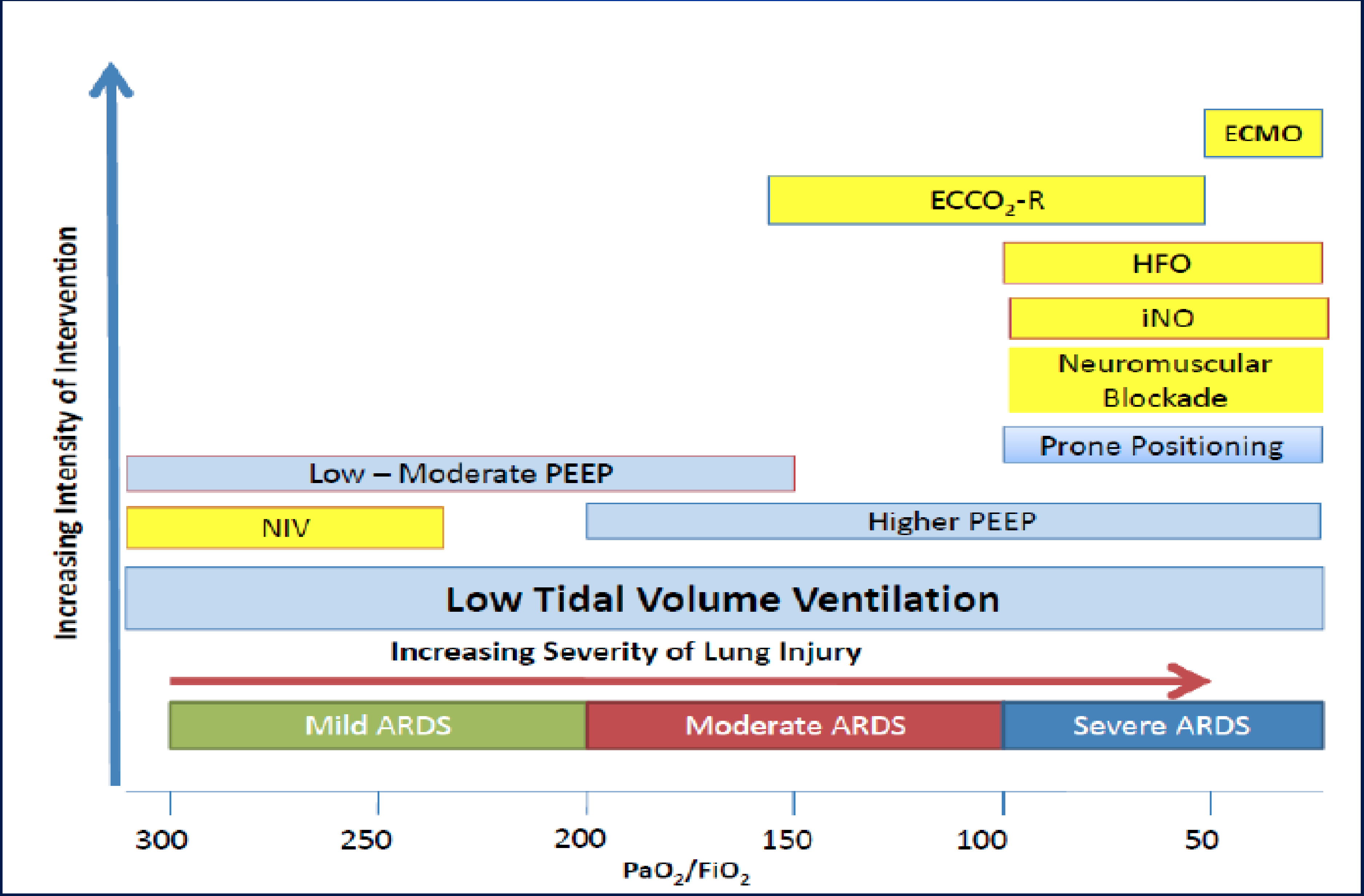


NIH NHLBI ARDS Clinical Trials Network

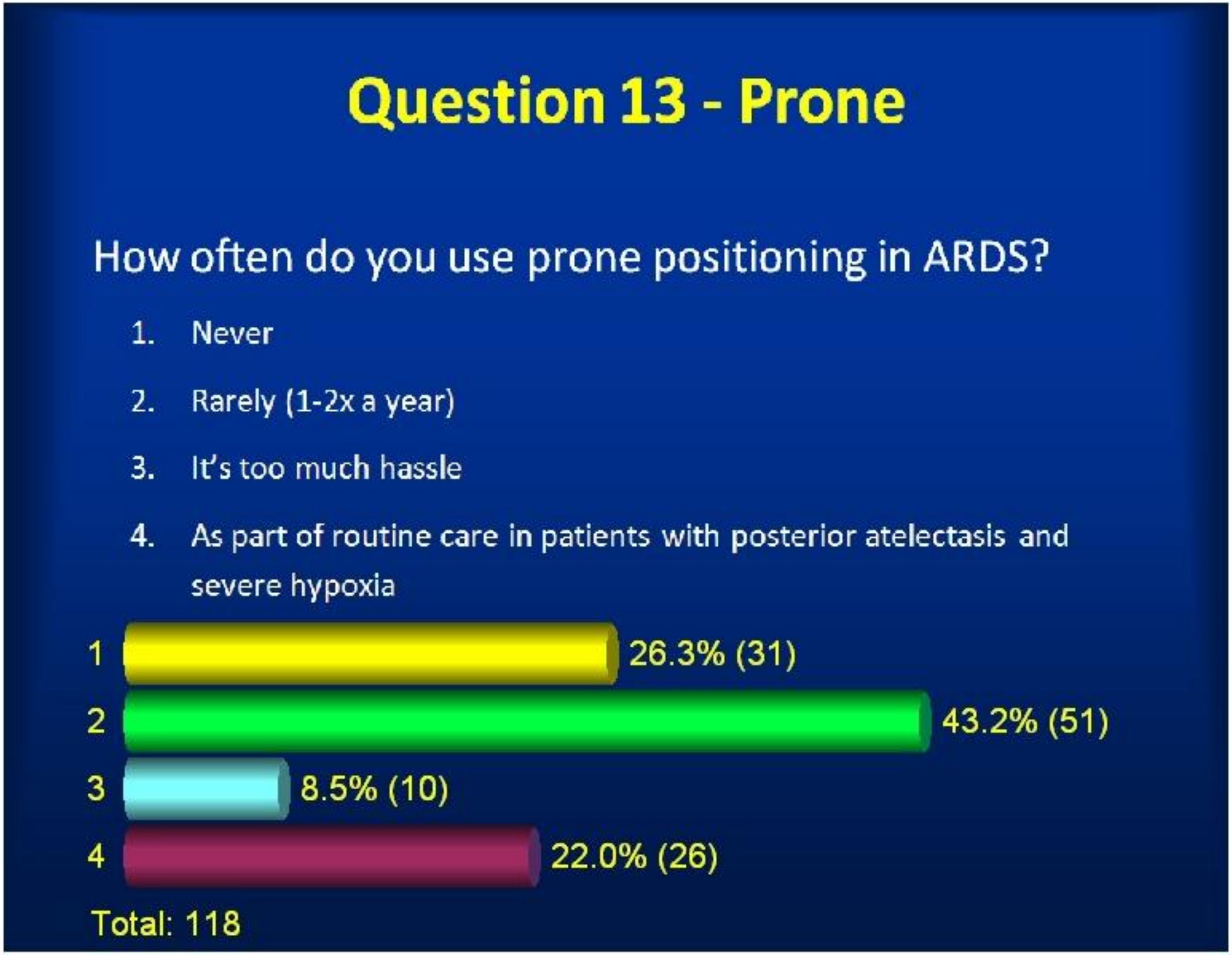
➢ Standard of Care Lung Protective Ventilation

- 6ml/kg of predicted body weight
  - Males 50 + 2.3 * (height in inches above 60")
  - Females 45.5 + 2.3 * (height in inches above 60")
- Maintain Pplat < 30 with volume titration
- Permissive hypercapnia, treat acidosis with supplemental bicarbonate

Treatment Strategies in ARDS

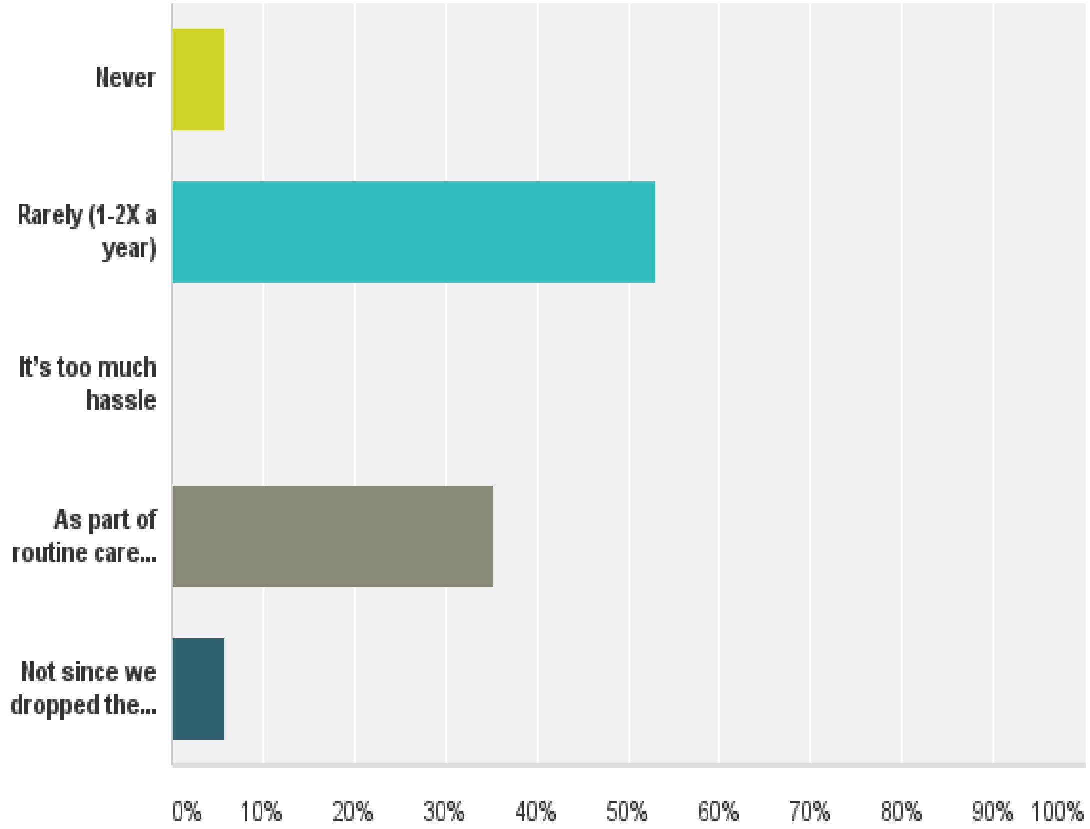


- Prone Positioning


Question 13 - Prone
How often do you use prone positioning in ARDS?
1. Never
2. Rarely (1-2x a year)
3. It's too much hassle
4. As part of routine care in patients with posterior atelectasis and severe hypoxia
1
26.3% (31)
2
43.2% (51)
3
8.5% (10)
4
22.0% (26)
Total: 118

Q9: How often do you use prone positioning in ARDS?

Answered: 17 Skipped: 1

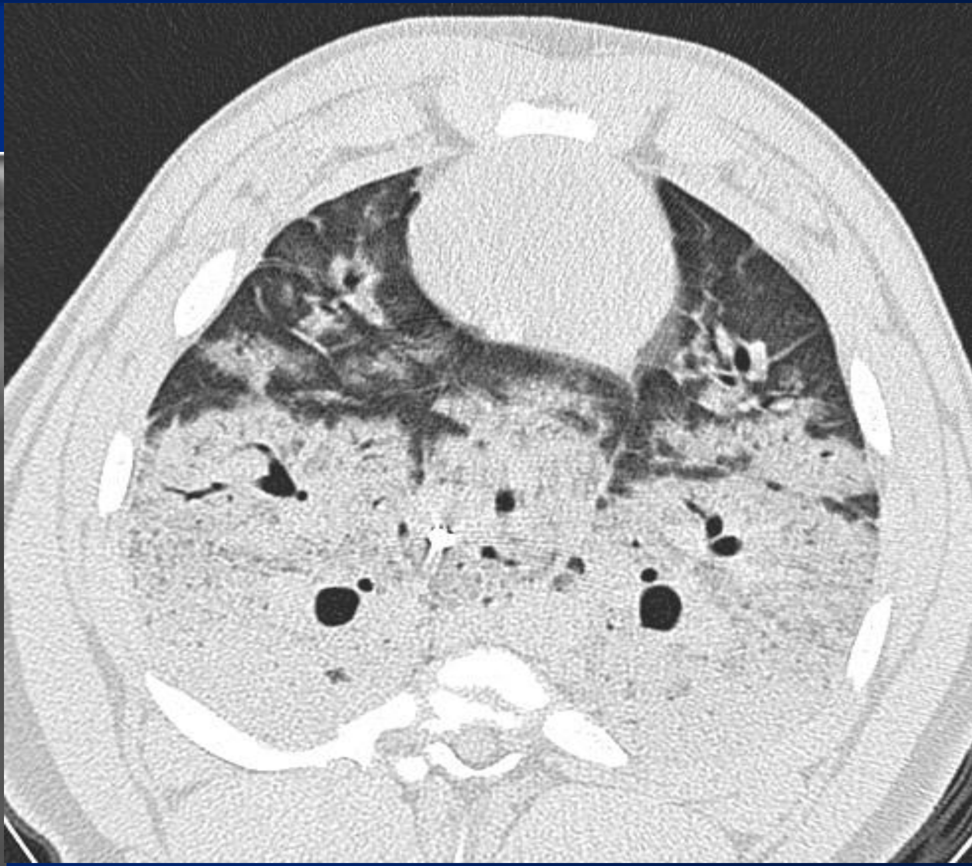


➢ Prone Positioning

- Previously, years of study, no clear impact
- Makes anatomic and physiologic sense
- Recent trial suggests mortality advantage early on in moderate to severe ARDS

ARDS

Bilateral patchy opacities



- "Baby Lung" Sitting on Top of a Consolidated Lung
- Posterior dependent lung consolidation
- Difficult to recruit

PROSEVA (Proning Patients with Severe ARDS)

The NEW ENGLAND JOURNAL of MEDICINE

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

Prone Positioning in Severe Acute Respiratory Distress Syndrome

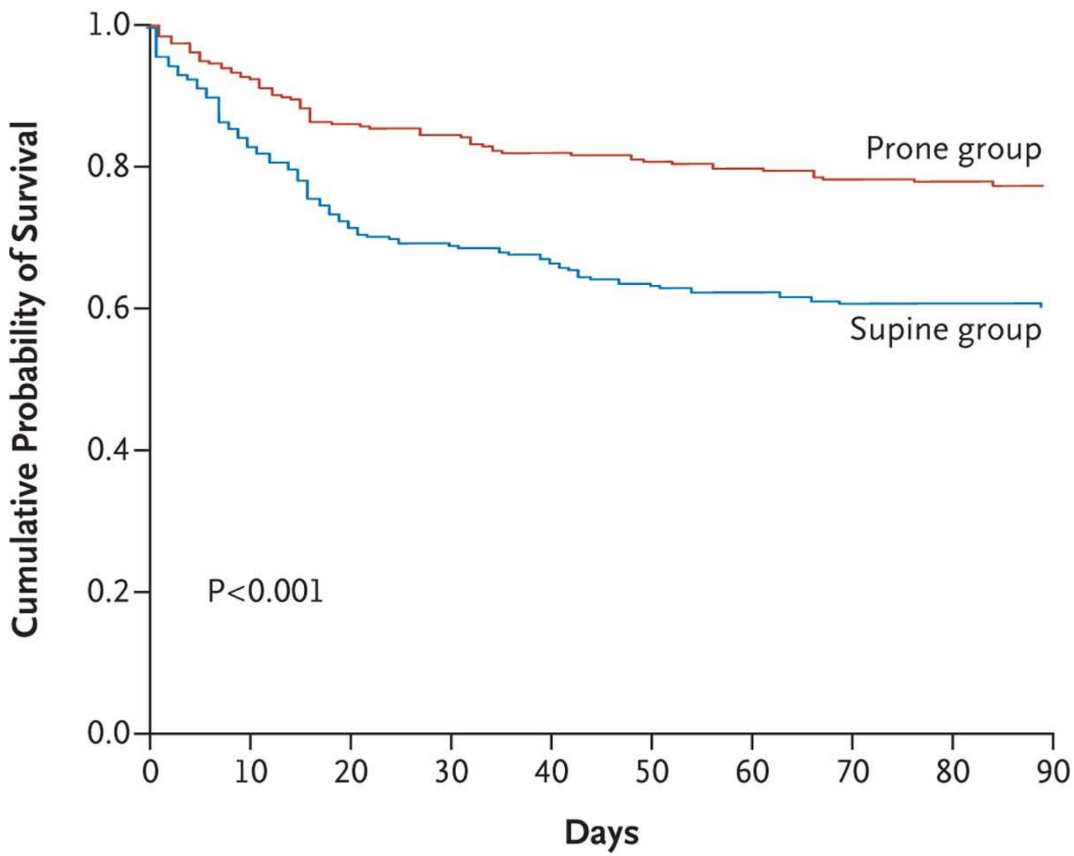
Claude Guérin, M.D., Ph.D., Jean Reignier, M.D., Ph.D., Jean-Christophe Richard, M.D., Ph.D., Pascal Beuret, M.D., Arnaud Gacouin, M.D., Thierry Boulain, M.D., Emmanuelle Mercier, M.D., Michel Badet, M.D., Alain Mercat, M.D., Ph.D., Olivier Baudin, M.D., Marc Clavel, M.D., Delphine Chatellier, M.D., 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*

Guerin C, et. al, NEJM, 368(23): 2159-68 June 6, 2013

PROSEVA - Study Overview

- Placing patients who require mechanical ventilation in the prone rather than the supine position improves oxygenation
- Enrolled Early Severe ARDS (P/F < 150 mm Hg on $FiO_2 \geq 0.6$, PEEP $\geq$ 5 cm H_2O, within 36 hours of onset)
- Prone 16 hours per day until improvement in supine position, mean 4.4 sessions per patient

PROSEVA – Probability of Survival from Randomization to Day 90



No. at Risk

Prone group	237	202	191	186	182
Supine group	229	163	150	139	136

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

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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		
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

* Plus–minus values are means ±SD. Hazard ratios are shown for mortality and successful extubation; odds ratios are shown for other outcomes. CI denotes confidence interval.

† There were no significant differences between the groups in organ dysfunction as assessed from the SOFA score (Table S4 in the Supplementary Appendix).

PROSEVA

C'est possible? Incredible effect size

- Day 28 and Day 90 Adjusted and Unadjusted Mortality OR 0.39 to 0.48 with proning

- Majority of patients in both groups received neuromuscular blockade

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

The NEW ENGLAND JOURNAL of MEDICINE

PROSEVA - Conclusions

- In this trial, the investigators found a benefit with respect to all-cause mortality with this change in body position in patients with severe ARDS

- In patients with severe ARDS, early application of prolonged prone-positioning sessions significantly decreased 28-day and 90-day mortality

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

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UM SICU Demonstrates Prone Method

- 4 people
- 2 sheets
- Easy to do
- Easy to teach
- Quick
- Easy access to patient

With flat sheet, pull patient to one side of the bed.

Tuck flat sheet around patient arm in order to protect it and move patient.

Place a second flat sheet on the bed, tuck under patient. Everything will pull through when you turn the patient.

Carefully turn the patient over and position prone by pulling the sheet. This will allow the arm and sheet to pulled across the bed.

Discard the sheet that was pulled through, position lines and tubes.

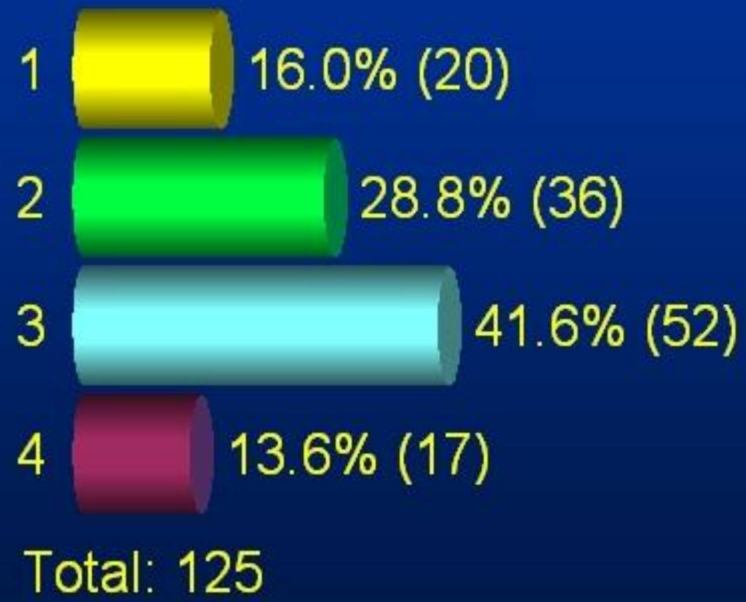
Patient now prone. Place arms in swimmers position (one positioned up toward head, one at side. Place in Reverse Trendelenberg.

➢ Neuromuscular Blockade

Question 8 - NMB

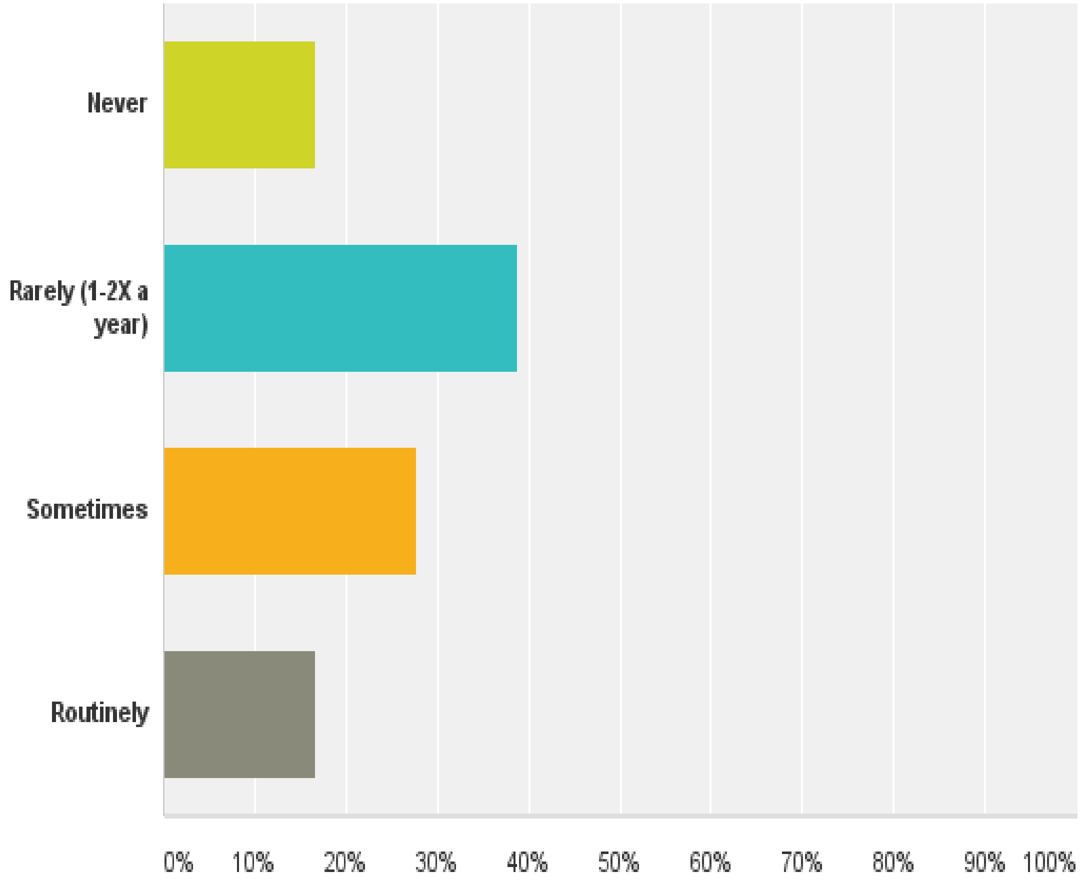
How often do you use neuromuscular blockade in initial treatment ARDS patients?

1. Never
2. Rarely (1-2x a year)
3. Sometimes
4. Routinely



Q6: How often do you use neuromuscular blockade in the initial treatment of ARDS patients?

Answered: 18 Skipped: 0



➢ Neuromuscular Blockade

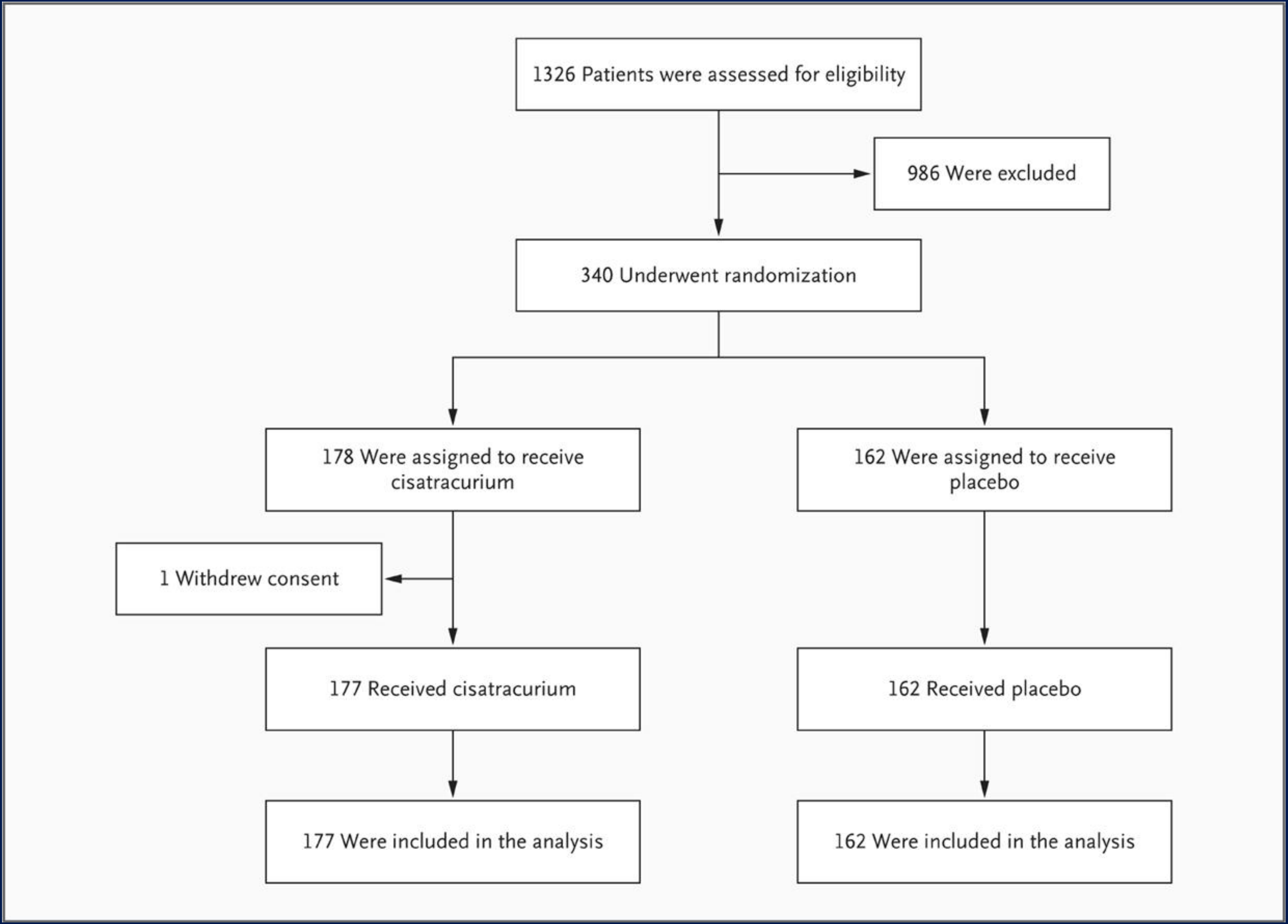
- Frequently used to facilitate controlled ventilation
- Concerns regarding long term weakness and conflict with reduction in sedation protocols
- Recent trials suggest mortality advantage early on in moderate to severe ARDS

ACURASYS – Study Overview

- The investigators induced muscle paralysis in patients with the acute respiratory distress syndrome (ARDS) by administering a neuromuscular blocking agent, cisatracurium besylate
- Continuous cisatracurium infusion for 48h in early ARDS(15mg bolus, 37.5mg per hour)
- RCT, 20 ICUs, 340 patients
- Moderate to severe ARDS (P/F <150), onset ≤ 48h
- Lung protective ventilation

Papazian L et al. N Engl J Med 2010;363:1107-1116

ACURASYS – Enrollment



Papazian L et al. N Engl J Med 2010;363:1107-1116

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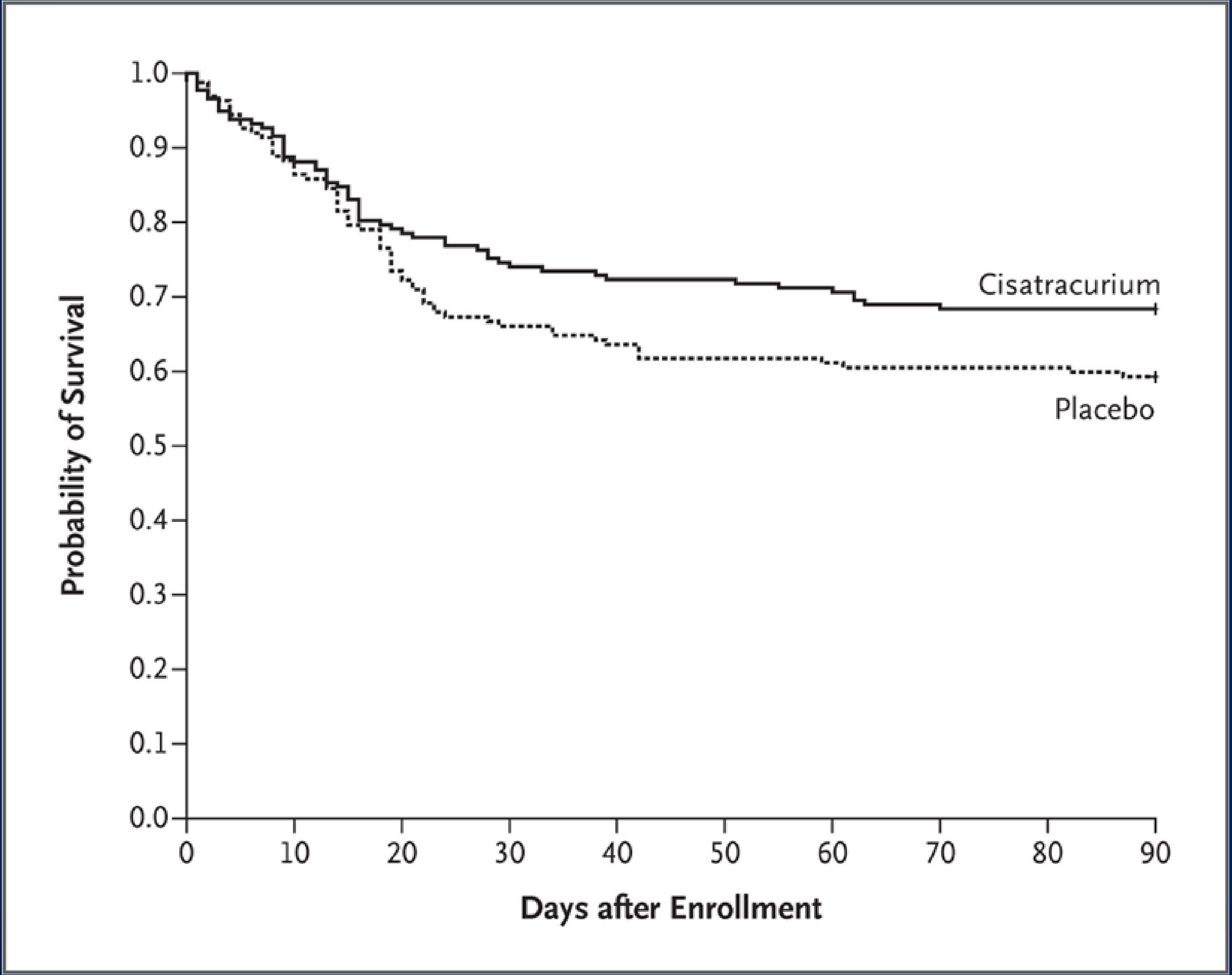
ACURASYS - Probability of Survival through Day 90



Papazian L et al. N Engl J Med 2010;363:1107-1116

The NEW ENGLAND JOURNAL of MEDICINE

ACURASYS – Results

- Reduction in mortality from 40.7% to 31.6% (hazard ratio 0.68)
- Increased oxygenation, ventilator-free days and organ-failure free days
- No observed increases in functional weakness at day 28 or ICU discharge

Papazian L et al. N Engl J Med 2010;363:1107-1116

The NEW ENGLAND JOURNAL of MEDICINE

ACURASYS – Questions

- Underpowered
- No monitoring of neuromuscular blockade
- 40% received steroids for septic shock in both arms
- But same effect size as lung protective ventilation?

Papazian L et al. N Engl J Med 2010;363:1107-1116

ACURASYS -Conclusions

- As compared with placebo, cisatracurium resulted in a lower adjusted 90-day mortality without more severe sequelae of neuromuscular blockade

- In patients with severe ARDS, early administration of a neuromuscular blocking agent improved the adjusted 90-day survival and increased the time off the ventilator without increasing muscle weakness.

x High Frequency Oscillatory Ventilation

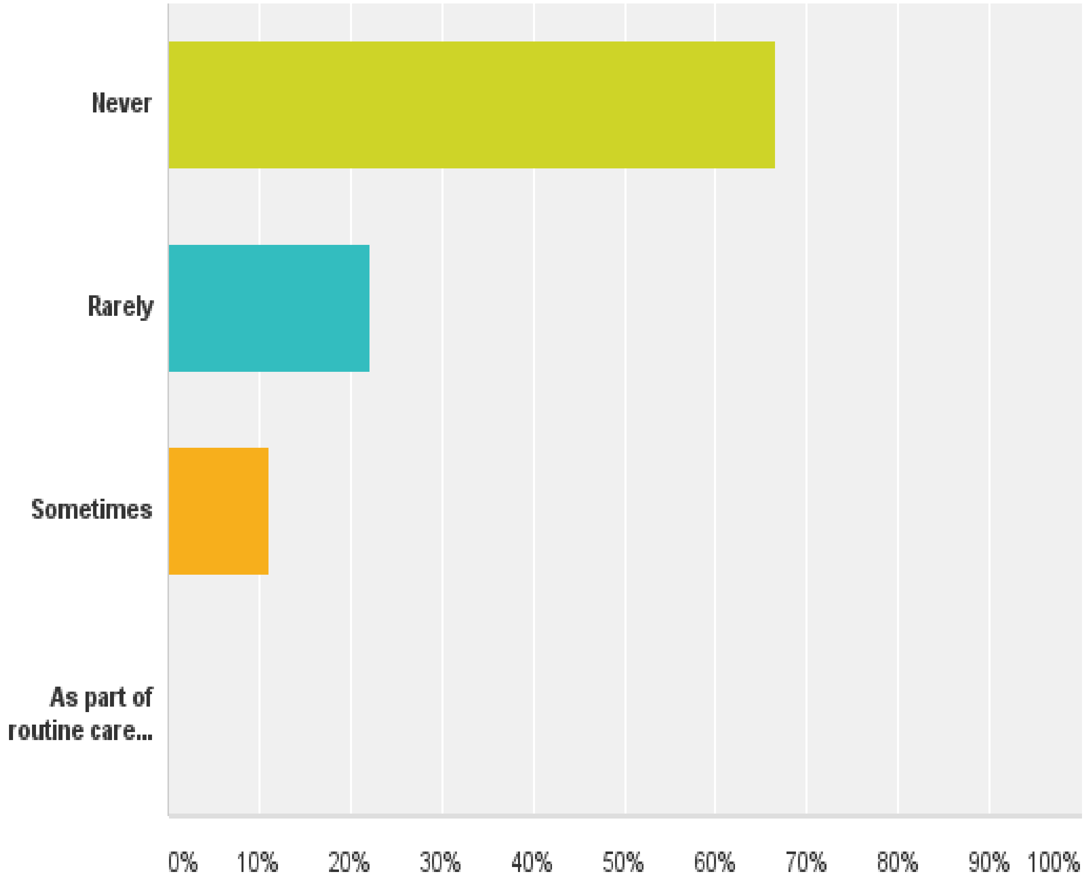
Question 2 - HFOV

How often do you use high frequency oscillatory ventilation in ARDS?

1. Never
2. Rarely (1-2x a year)
3. Sometimes
4. As part of routine care in severe ARDS

Q1: How often does your center use high frequency oscillatory ventilation (HFOV) in ARDS?

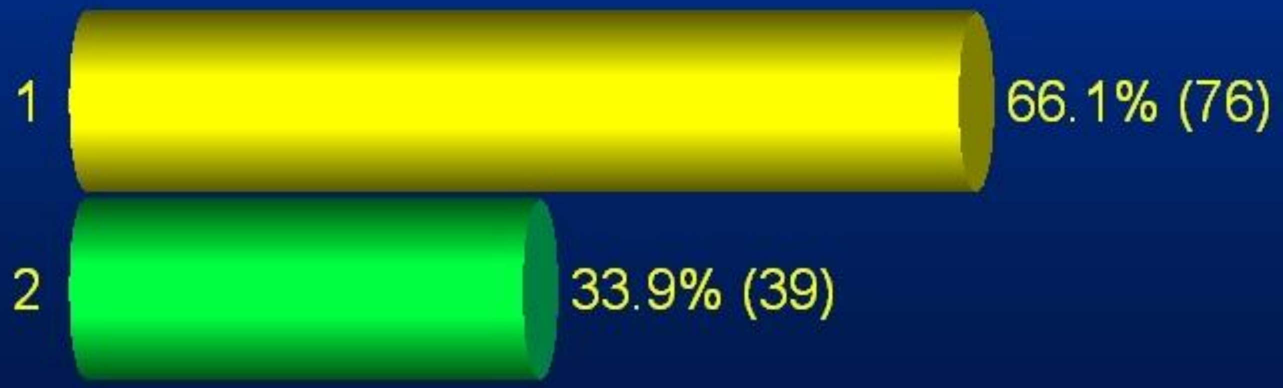
Answered: 18   Skipped: 0



Question 4 - HFOV

What do you think will be the answer?

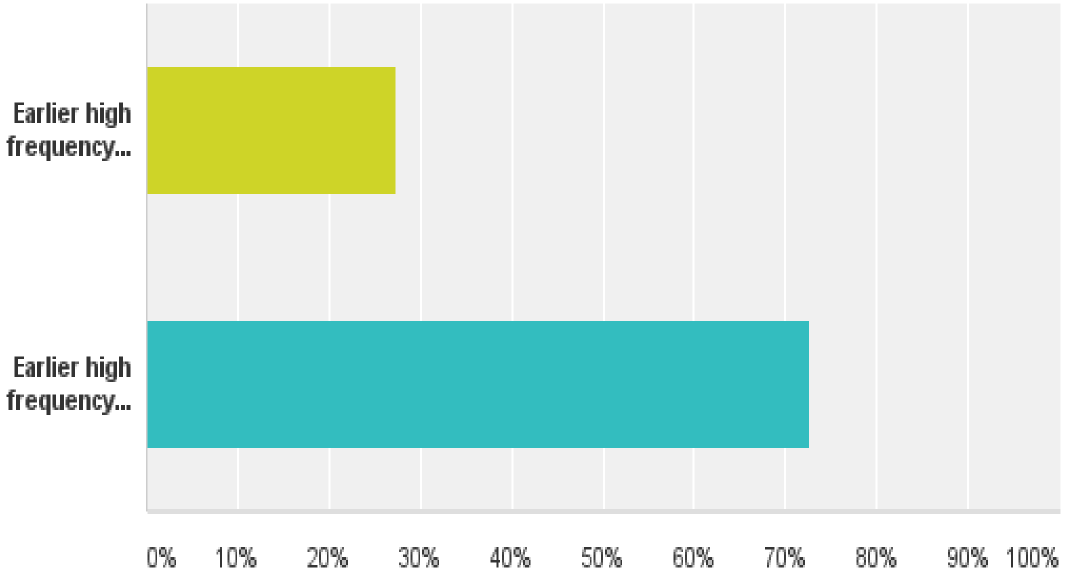
1. Earlier HFOV better
2. Earlier HFOV worse



Total: 115

Q3: What do you think will be the answer?

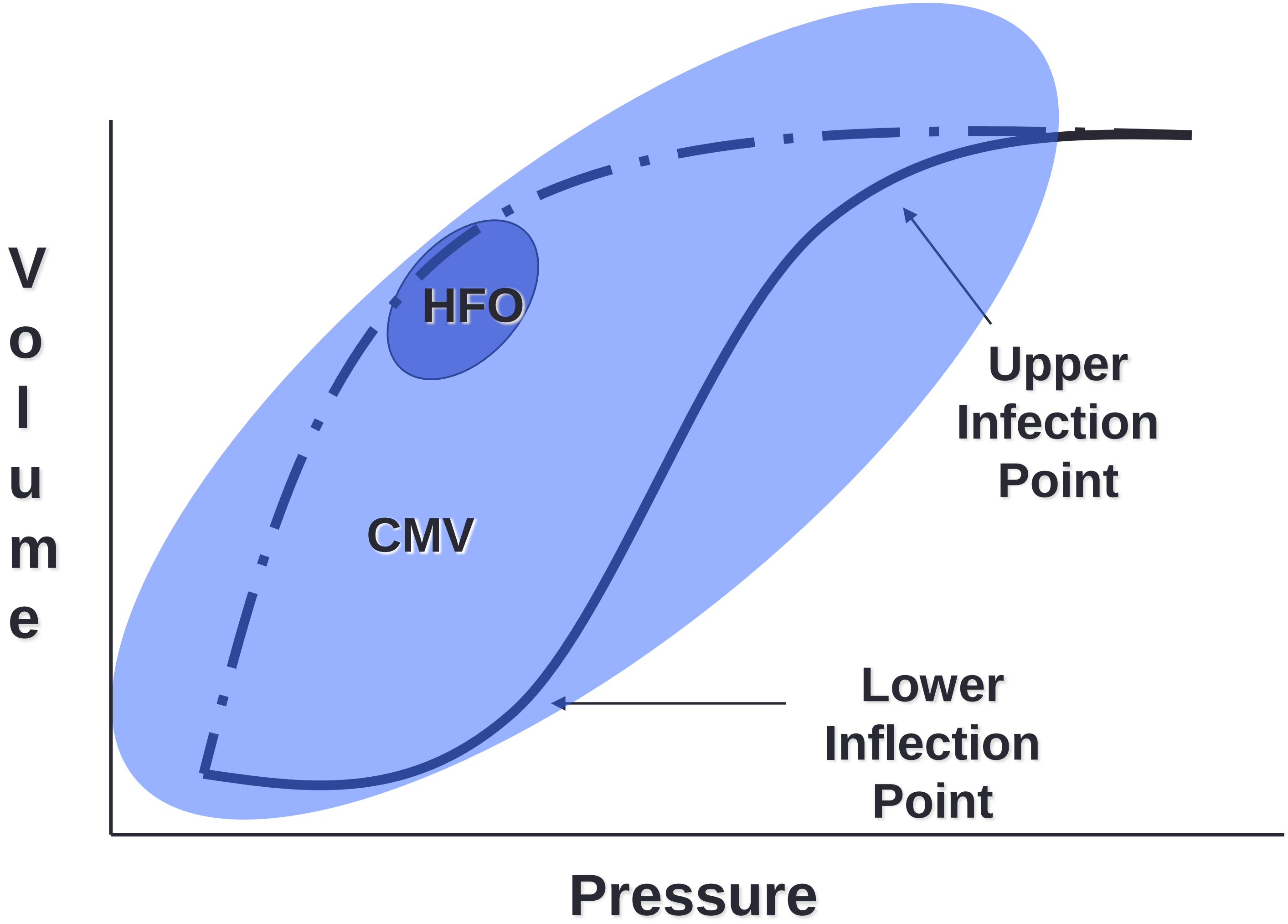
Answered: 11   Skipped: 7

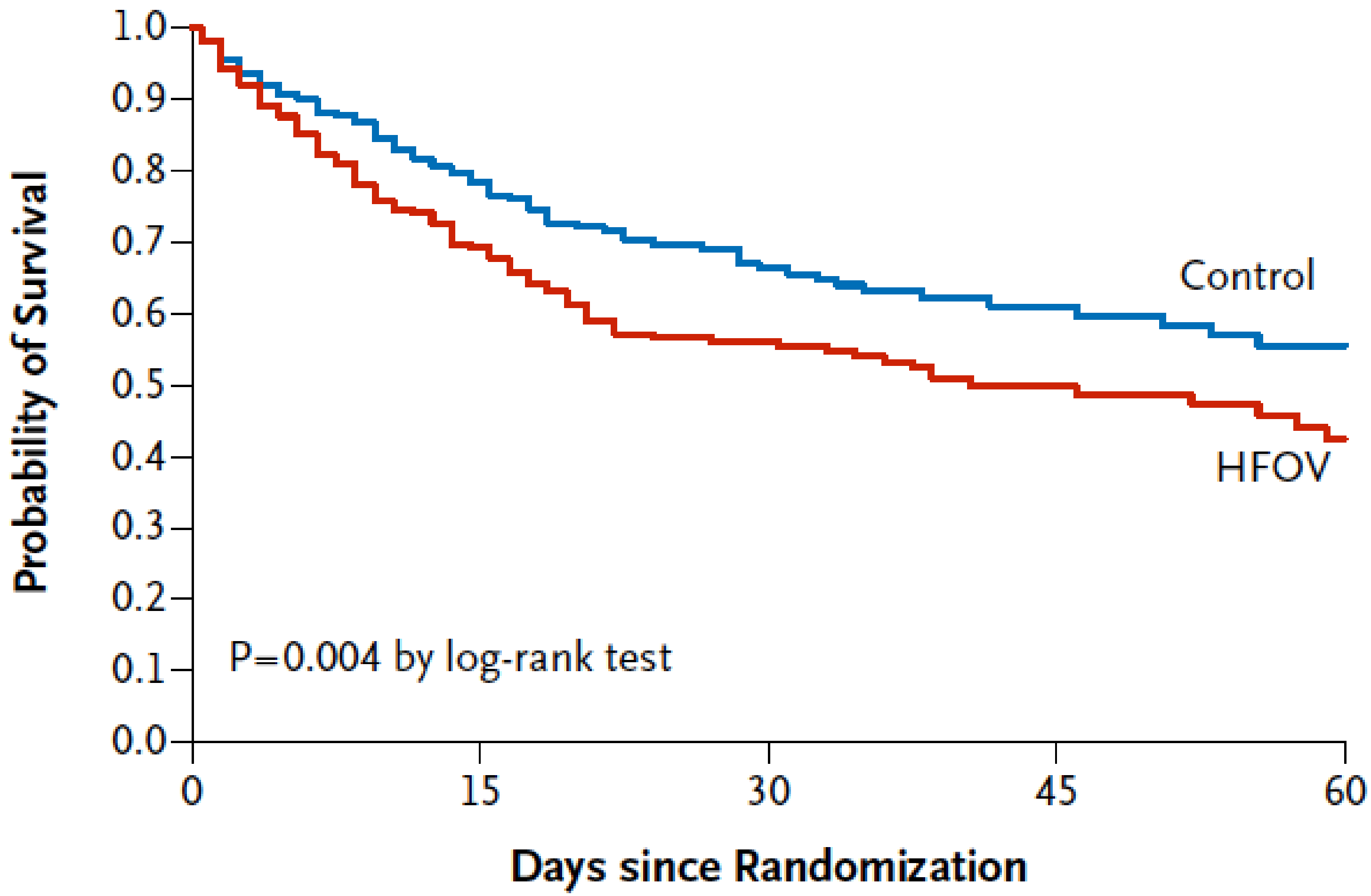


x High Frequency Oscillatory Ventilation

- 2 large randomized trials failed to show benefit, possible harm
- Usage falling off like a rock

Targeting Lung Recruitment



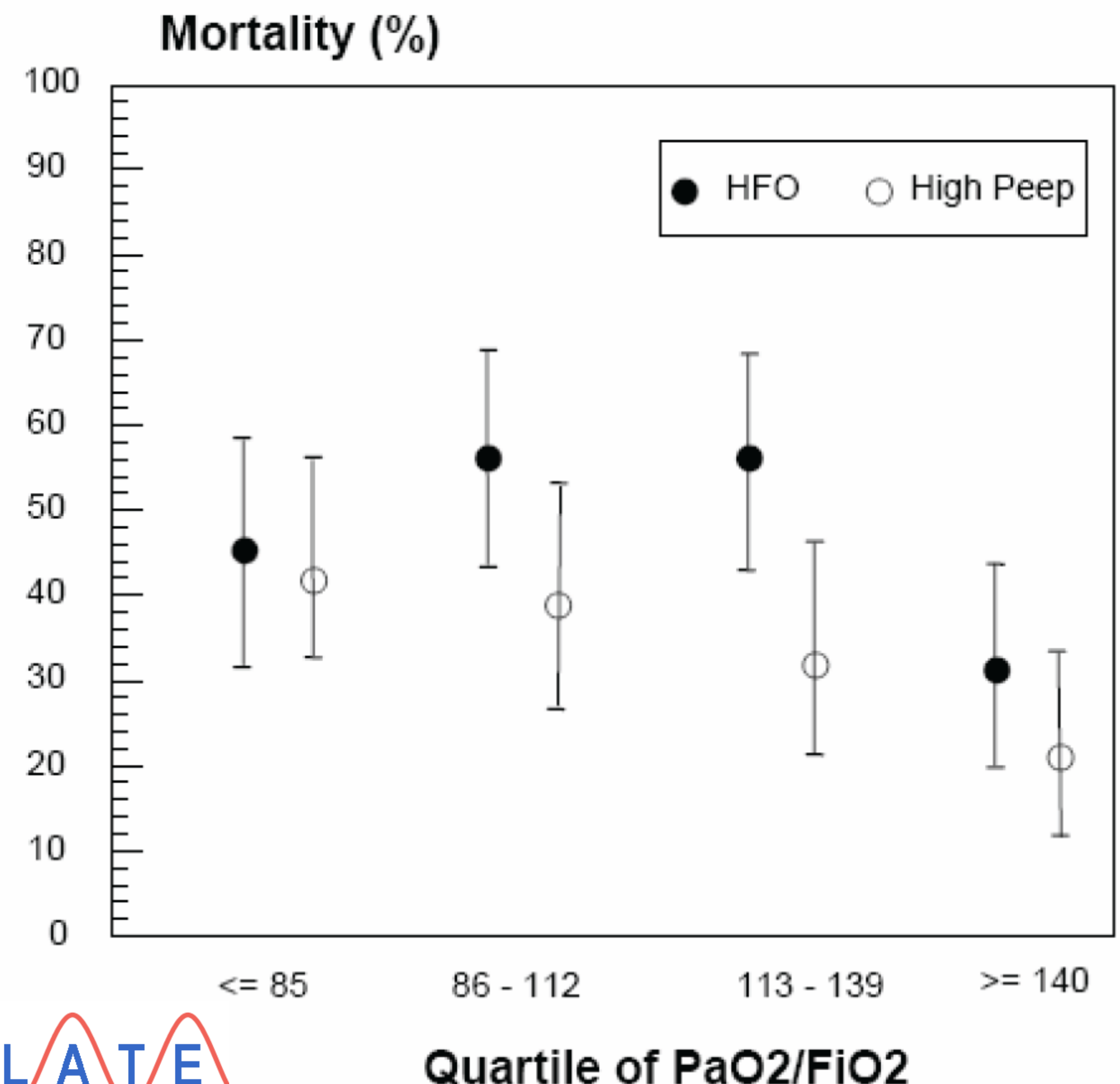


No. at Risk

HFOV	275	169	98	54	26
Control	273	181	92	54	39

OSCILLATE

Subgroup – Baseline Hypoxemia



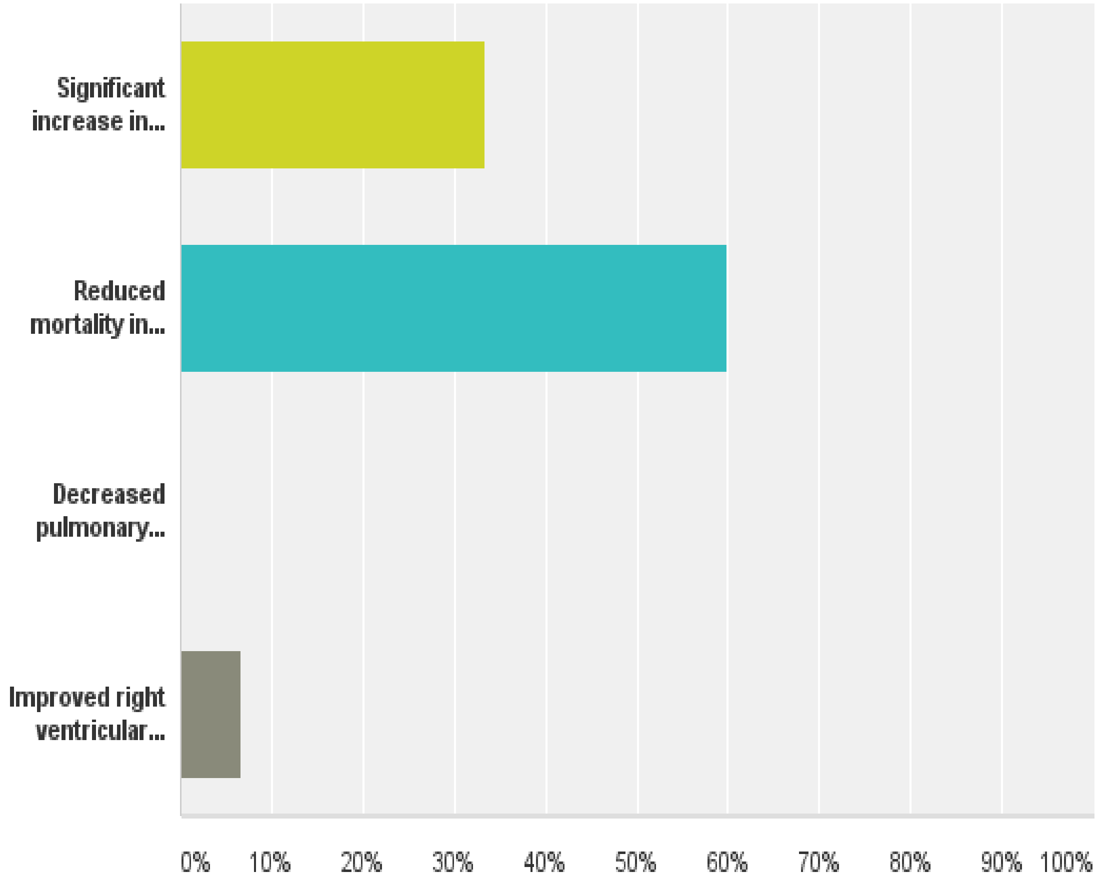
OSCILLATE

x Inhaled vasodilators

- Cannot prove a mortality benefit in ARDS
- Still used in rescue, transport

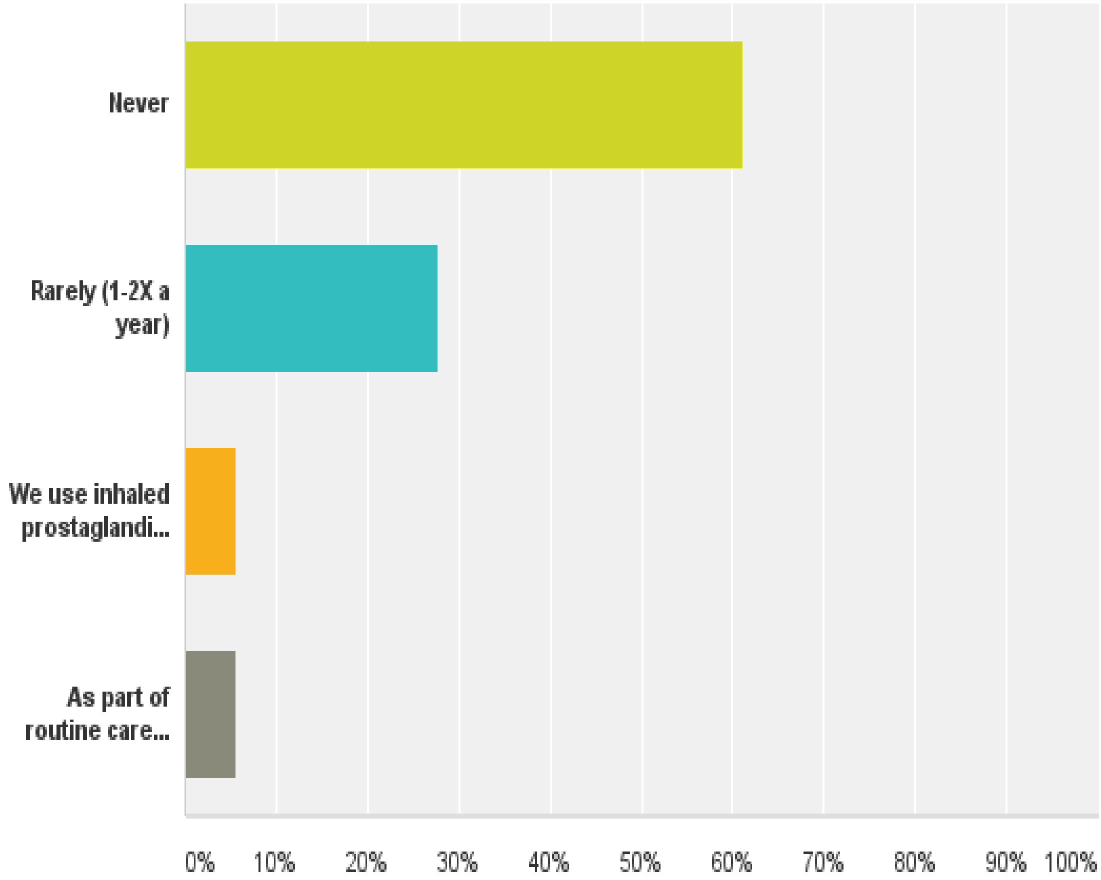
Q8: All of the following have been demonstrated as beneficial effects of inhaled nitric oxide in adult ARDS patients EXCEPT:

Answered: 15 Skipped: 3



Q7: How often do you use inhaled nitric oxide (NO) in ARDS?

Answered: 18 Skipped: 0

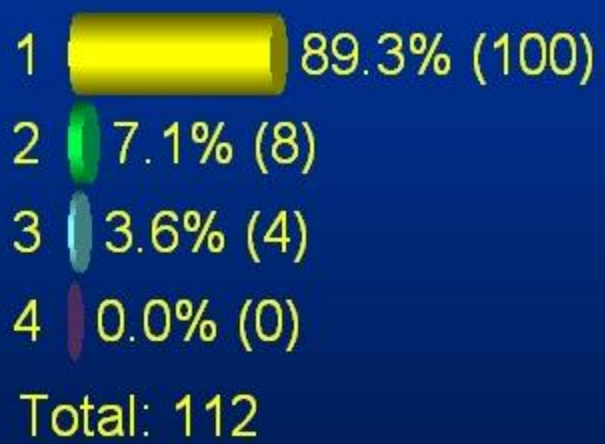


? Transpulmonary Pressure-guided ventilator management (Pes)

Question 5 - Ptp

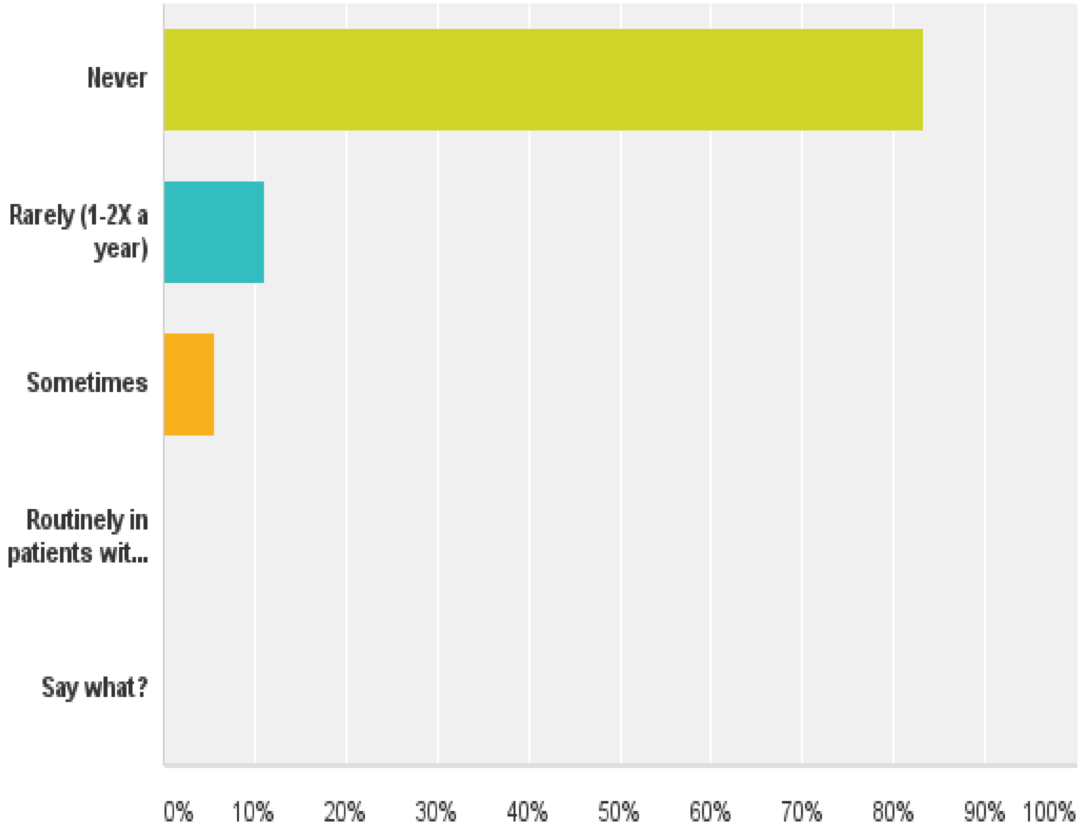
How often do you use esophageal pressure monitoring and transpulmonary pressure guided ventilator titration in ARDS?

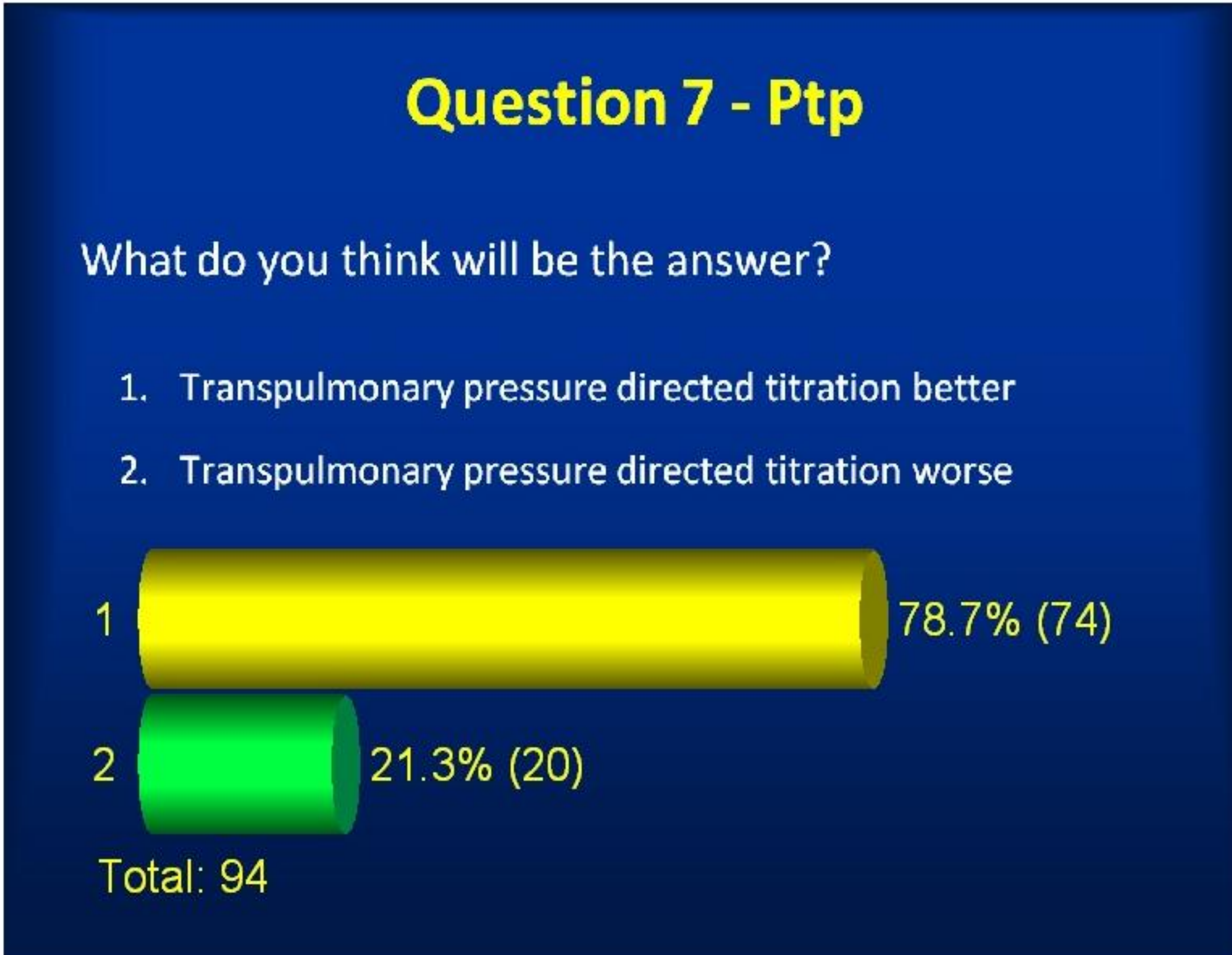
1. Never
2. Rarely (1-2x a year)
3. Sometimes
4. Routinely in patients with high BMI



Q4: How often do you use esophageal pressure monitoring and transpulmonary pressure guided ventilator titration in ARDS?

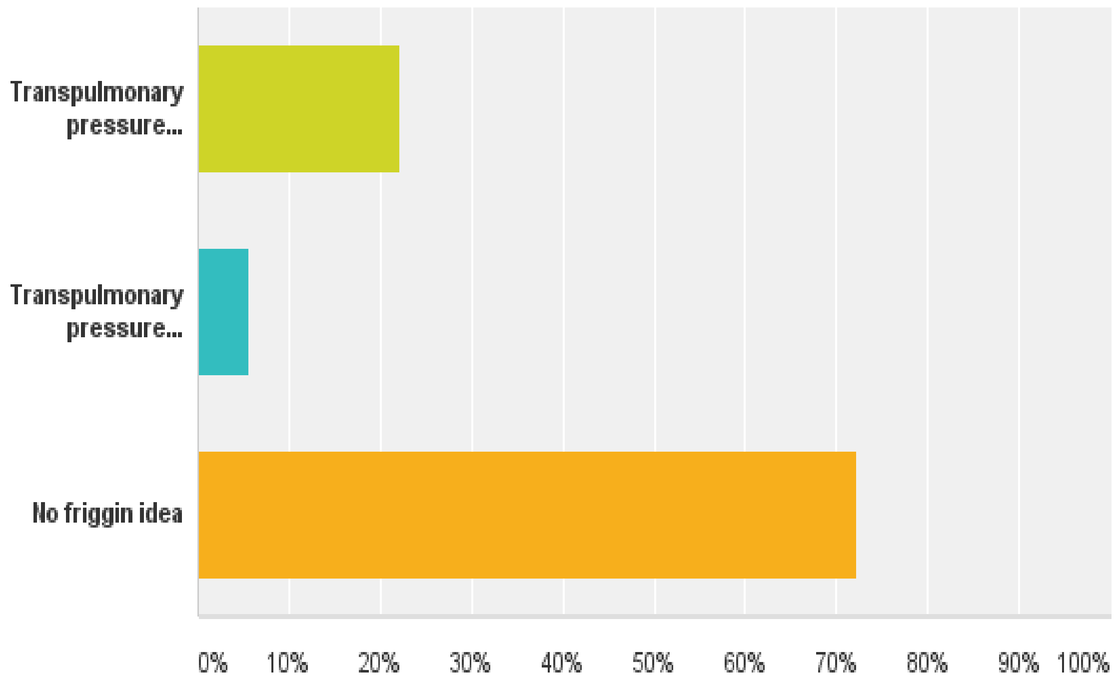
Answered: 18 Skipped: 0



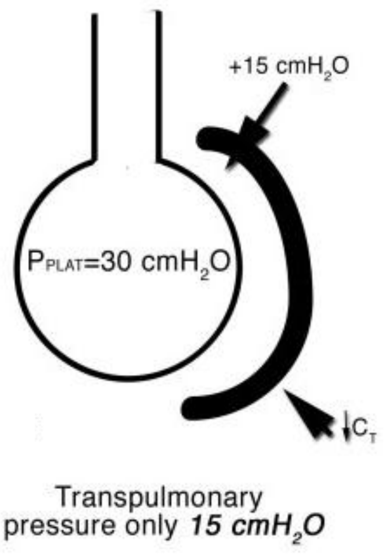

Question 7 - Ptp
What do you think will be the answer?
1. Transpulmonary pressure directed titration better
2. Transpulmonary pressure directed titration worse
1
78.7% (74)
2
21.3% (20)
Total: 94

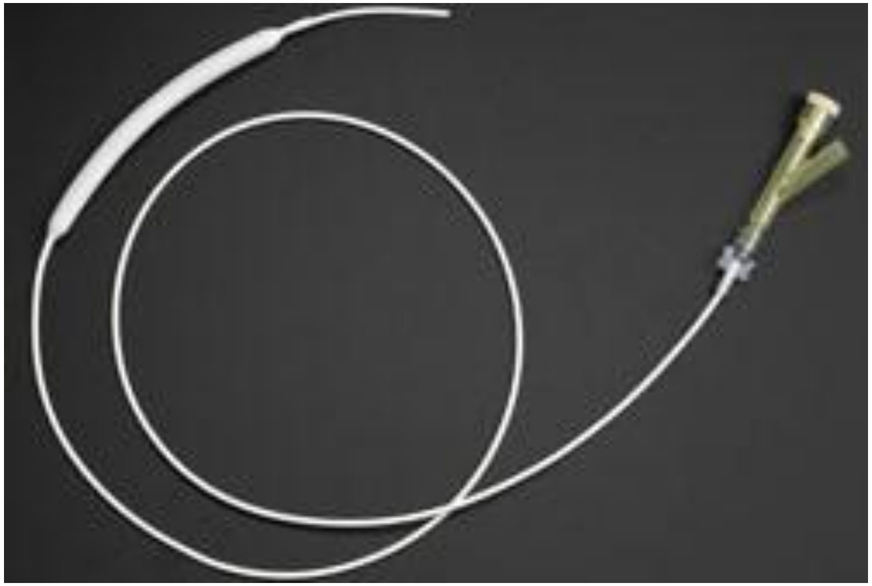
Q5: What do you think will be the answer?

Answered: 18   Skipped: 0



Ptp - Esophageal balloon catheter





Ptp ≈ airway pressure – esophageal pressure

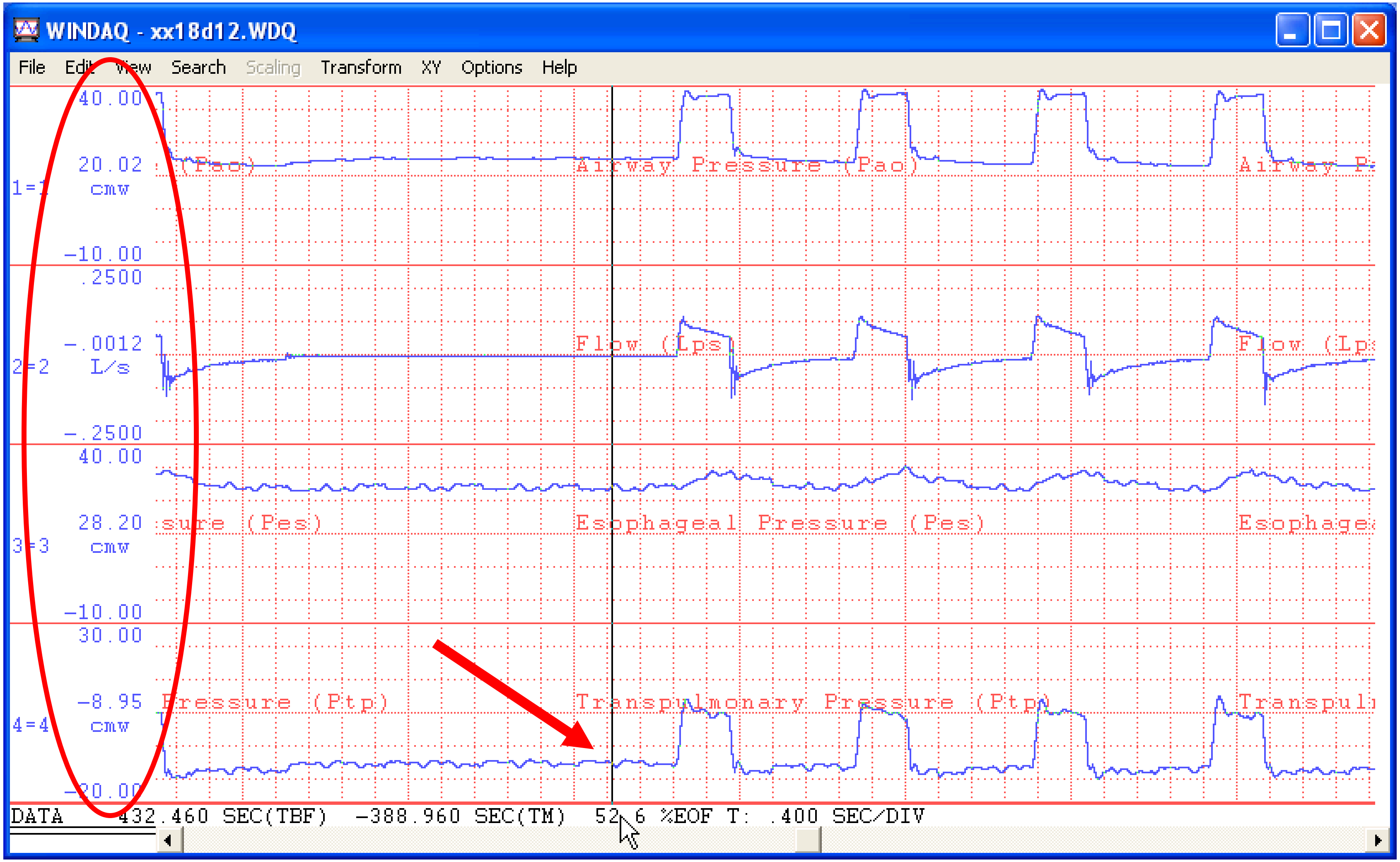
Mechanical Ventilation Guided by Esophageal Pressure in Acute Lung Injury

Daniel Talmor, M.D., M.P.H., Todd Sarge, M.D., Atul Malhotra, M.D., Carl R. O'Donnell, Sc.D., M.P.H., Ray Ritz, R.R.T., Alan Lisbon, M.D., Victor Novack, M.D., Ph.D., and Stephen H. Loring, M.D.

- Used esophageal balloon catheter to estimate transpulmonary pressure to guide PEEP settings
- 61 patients randomized
- Altered PEEP settings: down or to 5 cm H_2O in 40%
  up 6 – 10 cmH_2O in 40%
- Increased P/F ratio
  Mortality signal at 180 days
- Phase II trial funded and enrollment has begun

NEJM 2008; 359: 2095-104

HOLDS – END EXPIRATORY



Position cursor near end of the hold

Question 5

A 56 year old man is admitted to the ICU with ARDS and sepsis 4 days after emergency colectomy and splenectomy following an MVC. His height is 65 inches; his weight is 285 pounds. On lung protective ventilator settings, FiO2 0.80, PEEP 15 cmH_2O his:

Peak inspiratory pressure (PIP) is 35 cm H_2O
Plateau pressure (P_{plat}) is 30 cm H_2O
End expiratory airway pressure (Paw) is 20 cm H_2O
Esophageal balloon pressure (Pes) is 17 cm H_2O.

Transpulmonary pressure (Ptp_{exp}) is estimated by the formula:

A. Pes-PEEP

B. PEEP-Pes

C. Pplat-Paw

D. Paw-Pes

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Transpulmonary pressure (Ptp_{exp}) is estimated by the formula:

A. Pes-PEEP

B. PEEP-Pes

C. Pplat-Paw

D. Paw-Pes

Beth Israel Deaconess Medical Center | A teaching hospital of Harvard Medical School

EPVENT II-PROTOCOL

A PHASE II PROSPECTIVE RANDOMIZED CONTROLLED TRIAL OF VENTILATION DIRECTED BY ESOPHAGEAL PRESSURE MEASUREMENTS.

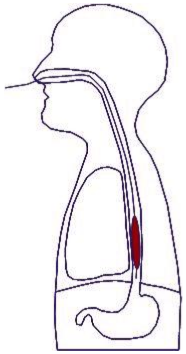
WILL ENROLL 200 PATIENTS WITH MODERATE TO SEVERE ARDS BY THE BERLIN CONFERENCE DEFINITION IN SEVEN ACADEMIC MEDICAL CENTERS IN NORTH AMERICA

BETH ISRAEL DEACONESS MEDICAL CENTER

BOSTON, MA

DANIEL TALMOR MD MPH, BIDMC

VENTILATION PROTOCOLS- EPVENT GROUP



Measure Ptpexp during an end-expiratory hold.

Increase (or decrease) PEEP to achieve Ptpexp = 0

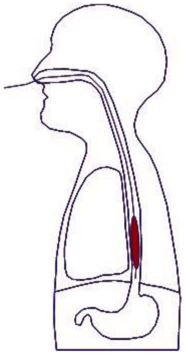
- Incrementally changes according to the formula: [new PEEP] = [initial PEEP] – Ptpexp

Repeat this procedure until Ptpexp = 0.

- If this formula dictates an increase in PEEP of more than 10 cmH2O, increase PEEP in increments of 10 cmH2O or less

When Ptpexp = 0, reassess oxygenation

VENTILATION PROTOCOLS- CONTROL AND EPVENT GROUPS



The control group PEEP and tidal volume will be managed without reference to the esophageal pressure measurements.

FIO2 and PEEP must be kept within one column of this table, moving right or left one column at a time as required.

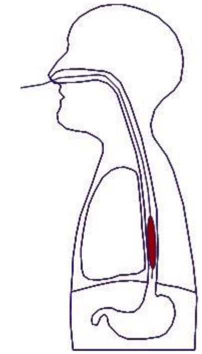
Table 4- Oxygenation Management Table – Control Group

Step	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
F_IO_2	0.3	0.3	0.3	0.4	0.4	0.4	0.4	0.4	0.5	0.5	0.6	0.7	0.8	0.8	0.9	1.0	1.0
PEEP	5	8	10	10	12	14	16	18	18	20	20	20	20	22	22	22	24

Table 1- Oxygenation Management Table - EPVent group

Step	1	2	3	4	5	6	7	8	9	10	11	12	13
F_IO_2	0.3	0.4	0.5	0.5	0.6	0.6	0.7	0.7	0.8	0.8	0.9	0.9	1.0
Ptp_{exp}	0	0	0	2	2	3	3	4	4	5	5	6	6

VENTILATION PROTOCOLS- CONTROL AND EPVENT GROUPS



91 patients enrolled in US/Canada as of December, 2014

Table 4- Oxygenation Management Table – Control Group

Step	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
F_IO_2	0.3	0.3	0.3	0.4	0.4	0.4	0.4	0.4	0.5	0.5	0.6	0.7	0.8	0.8	0.9	1.0	1.0
PEEP	5	8	10	10	12	14	16	18	18	20	20	20	20	22	22	22	24

Table 1- Oxygenation Management Table - EPVent group

Step	1	2	3	4	5	6	7	8	9	10	11	12	13
F_IO_2	0.3	0.4	0.5	0.5	0.6	0.6	0.7	0.7	0.8	0.8	0.9	0.9	1.0
Ptp_{exp}	0	0	0	2	2	3	3	4	4	5	5	6	6

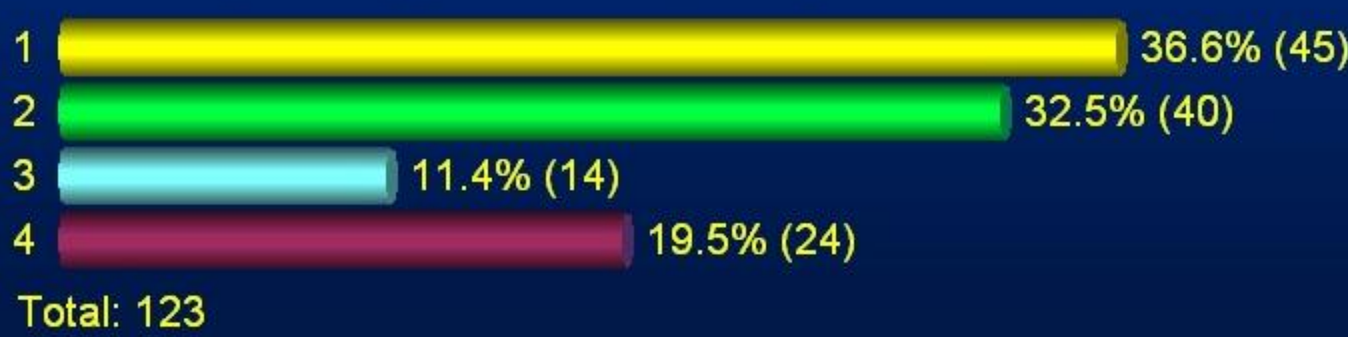
Harvard Medical School

? Extracorporeal Membrance Oxygenation (ECMO)

Question 15 - ECMO

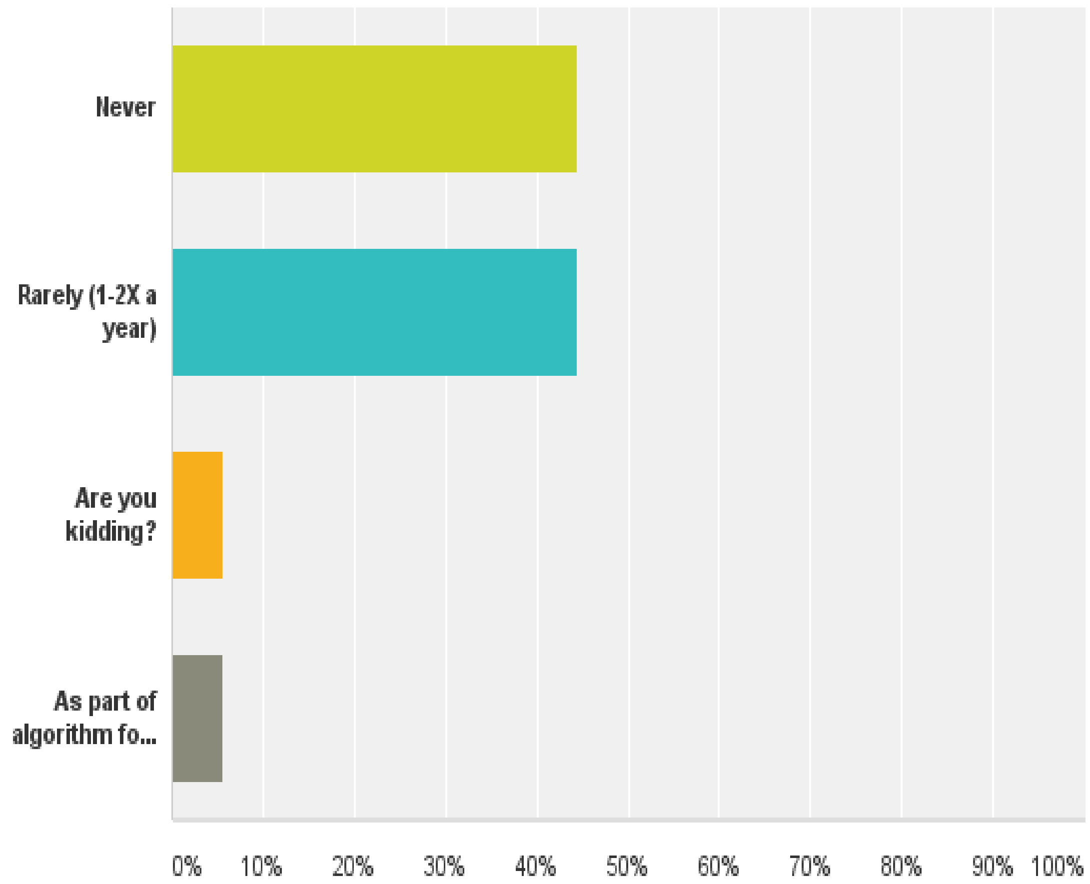
How often do you use or refer for ECMO in ARDS?

1. Never
2. Rarely (1-2x a year)
3. Are you kidding?
4. As part of algorithm for care in patients with severe ARDS



Q11: How often do you use or refer for extracorporeal membrane oxygenation (ECMO) in ARDS?

Answered: 18 Skipped: 0



Question 16 - ECMO

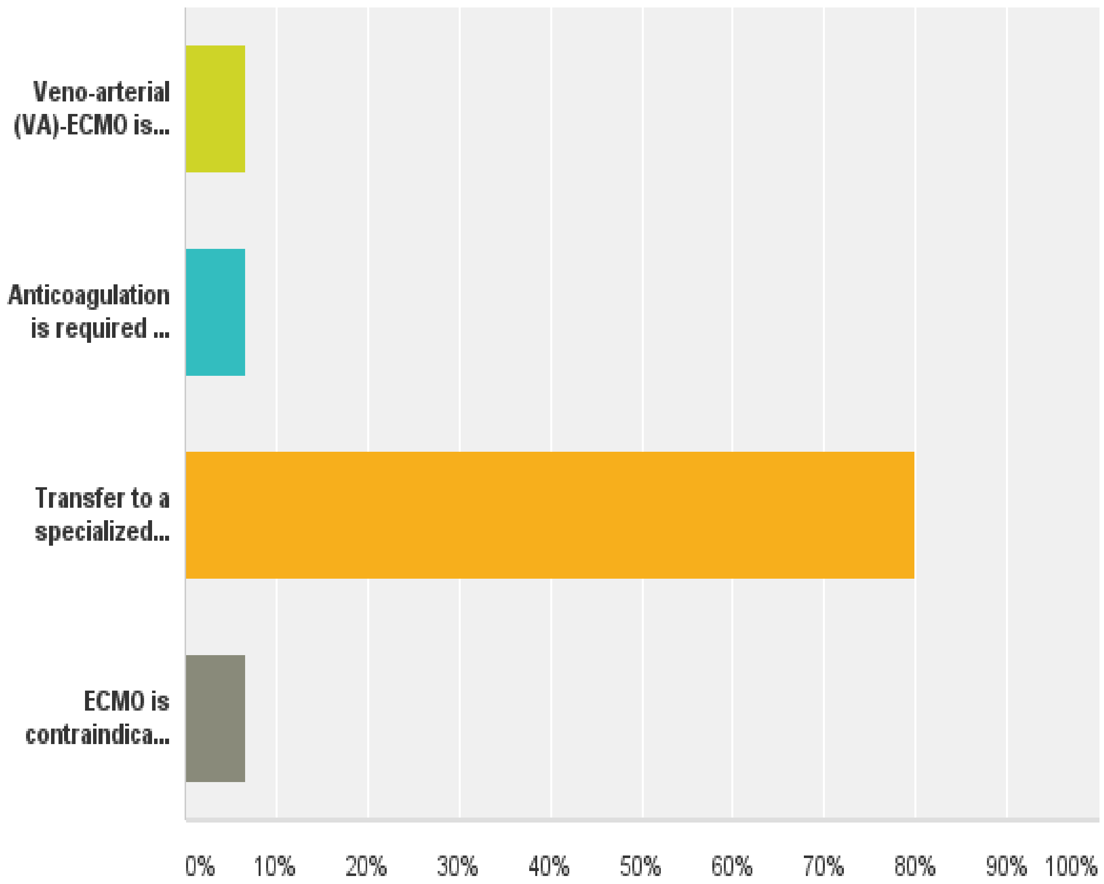
Which of the following is true regarding ECMO in adult patients with ARDS?

1. VA-ECMO is associated with decreased mortality compared to VV-ECMO
2. Anticoagulation is required but is not associated with increased complications
3. **Transfer to a specialized center with ECMO capabilities is associated with decreased mortality**
4. ECMO is contraindicated after ≥ 5 days of mechanical ventilation

Answer: 3 Total: 92

Q12: Which of the following is true regarding ECMO in adult patients with ARDS?

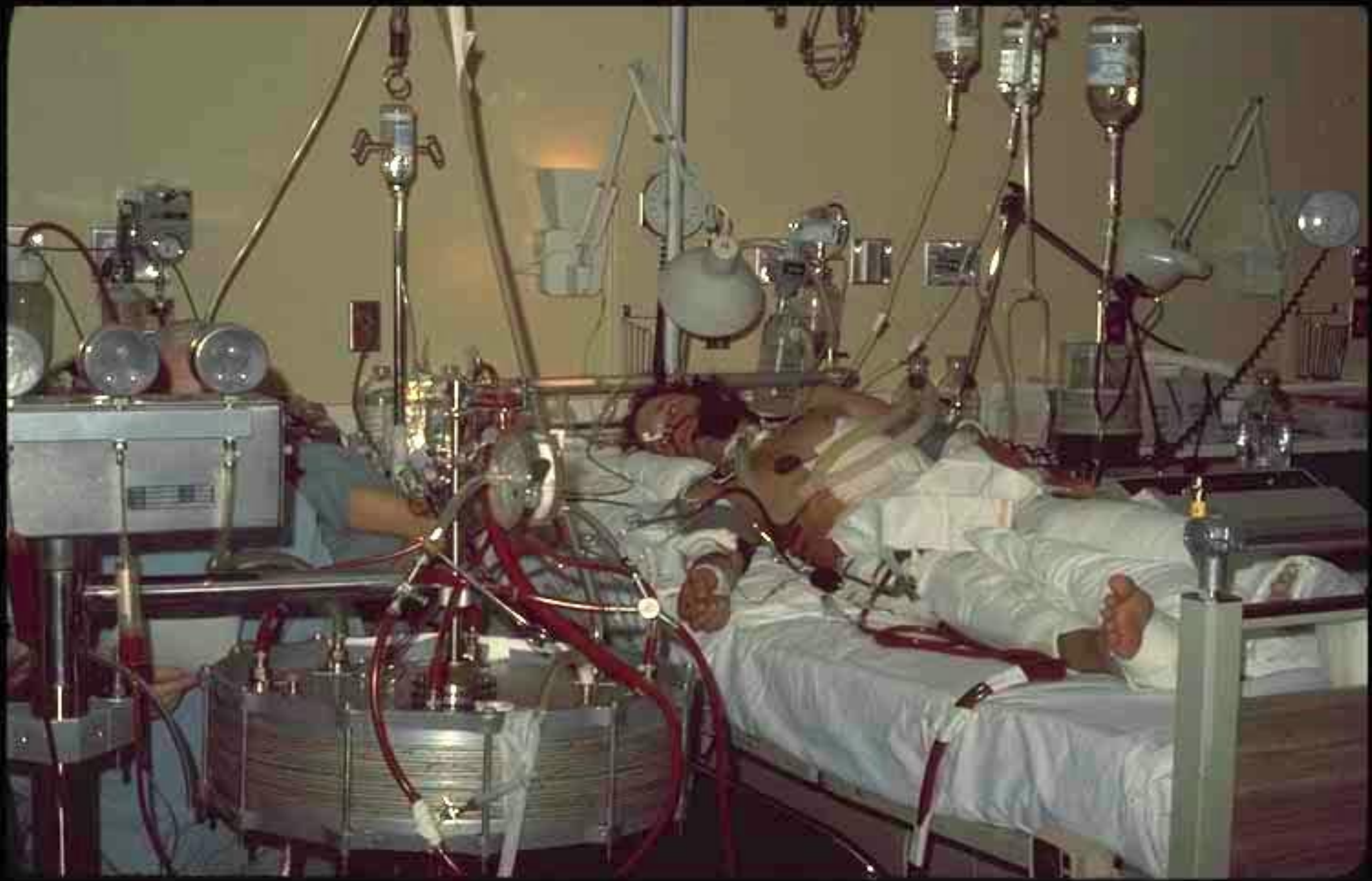
Answered: 15 Skipped: 3



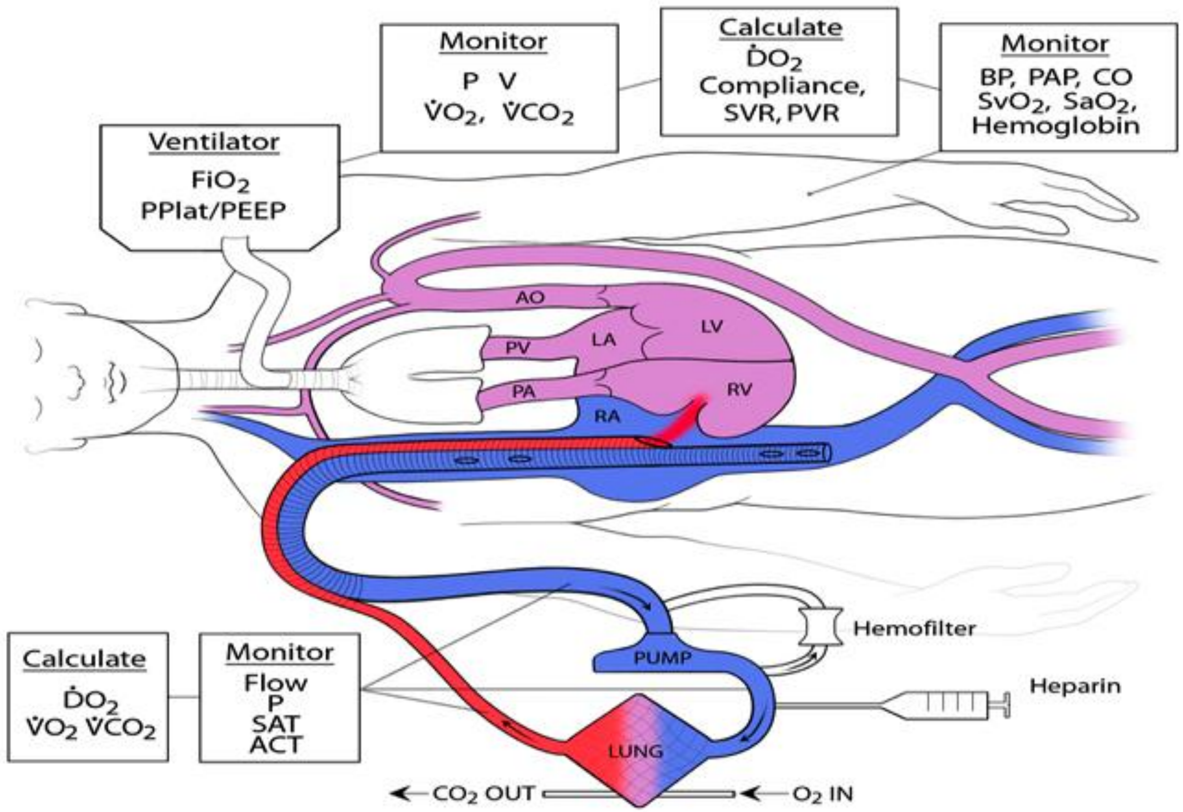
? Extracorporeal Membrance Oxygenation (ECMO)

- Resurgent interest with more compact systems, favorable results in influenza H1N1
- Continuous life support, resource and labor-intensive, conclusive trials contraversial
- Some evidence for regionalization

Bartlett

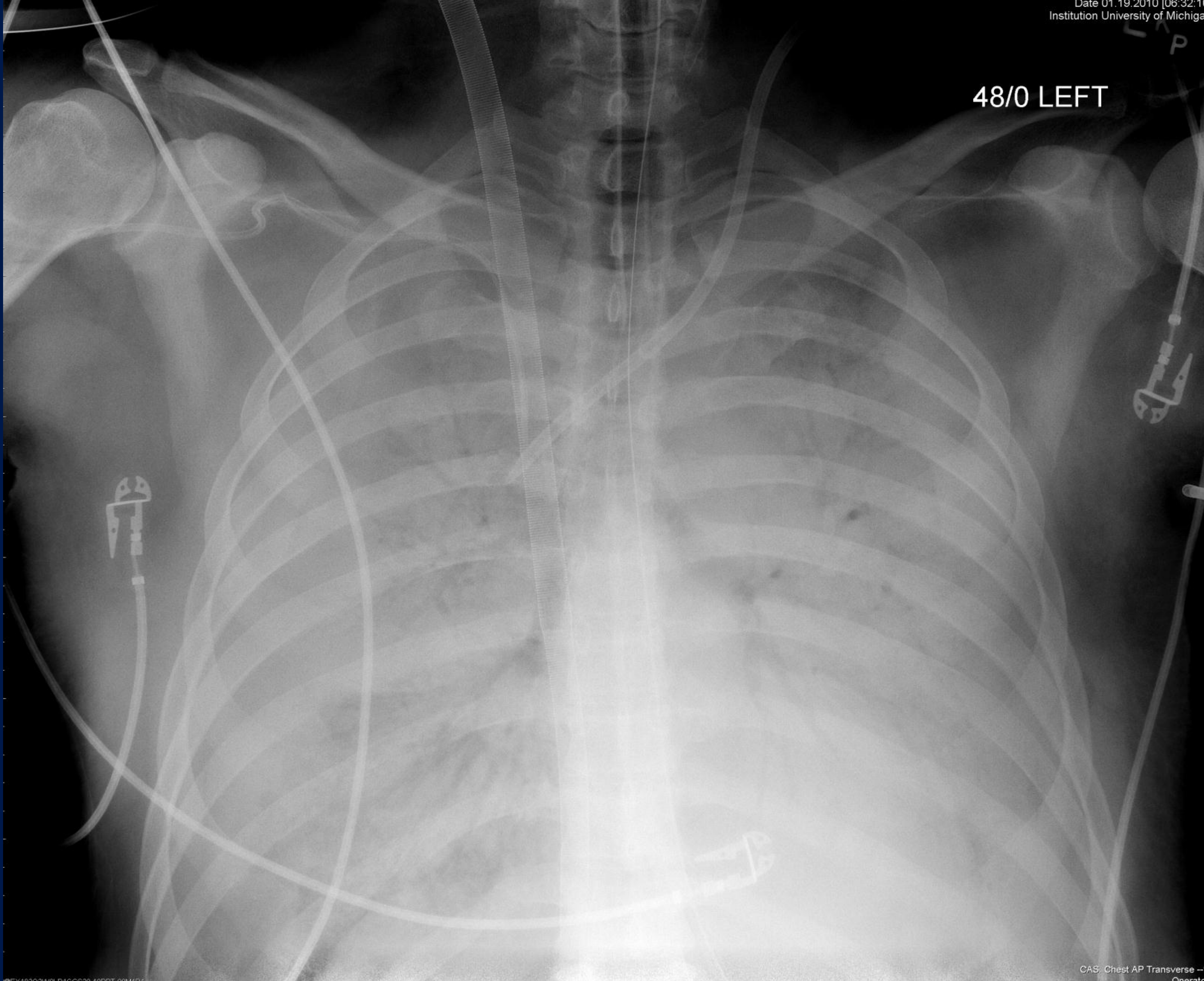


First successful ECLS Patient; ARDS/ trauma
Santa Barbara, Ca, 1971.
J Donald Hill MD and Maury Bramson BME



RHB

Veno-venous ECLS with a double lumen cannula


Date 01.19.2010 [06:32:10]
Institution University of Michigan
48/0 LEFT
CAS: Chest AP Transverse --%
Operator:

Afghanistan to Regensburg ECMO transport

PHOTOS BY SETH ROBBINS/Stars and Stripes

Dr. Matthias Amann, left, and Dr. Alois Philipp make preparations to transport a 22-year-old soldier to the university hospital in Regensburg, Germany. Philipp helped develop the ECMO machine that was used on the wounded soldier during an evacuation.

Lifesaving INNOVATION

Portable heart-lung machine used in combat evacuation

BY SETH ROBBINS
Stars and Stripes

LANDSTUHL, Germany — A U.S. team for the first time in a combat evacuation has used an innovative and portable heart-lung machine, saving a 22-year-old soldier wounded in Afghanistan.

the most serious lung injuries and evacuate them to Germany.

Within hours, Wanek and her team were bound for Kandahar.

When they got there Wednesday, they operated on him for five hours and tried several different ventilators, but all of them failed.

"I just could not improve his oxygenation

The ECMO machine

STARS AND STRIPES

October, 2010

Severe Thoracic Trauma

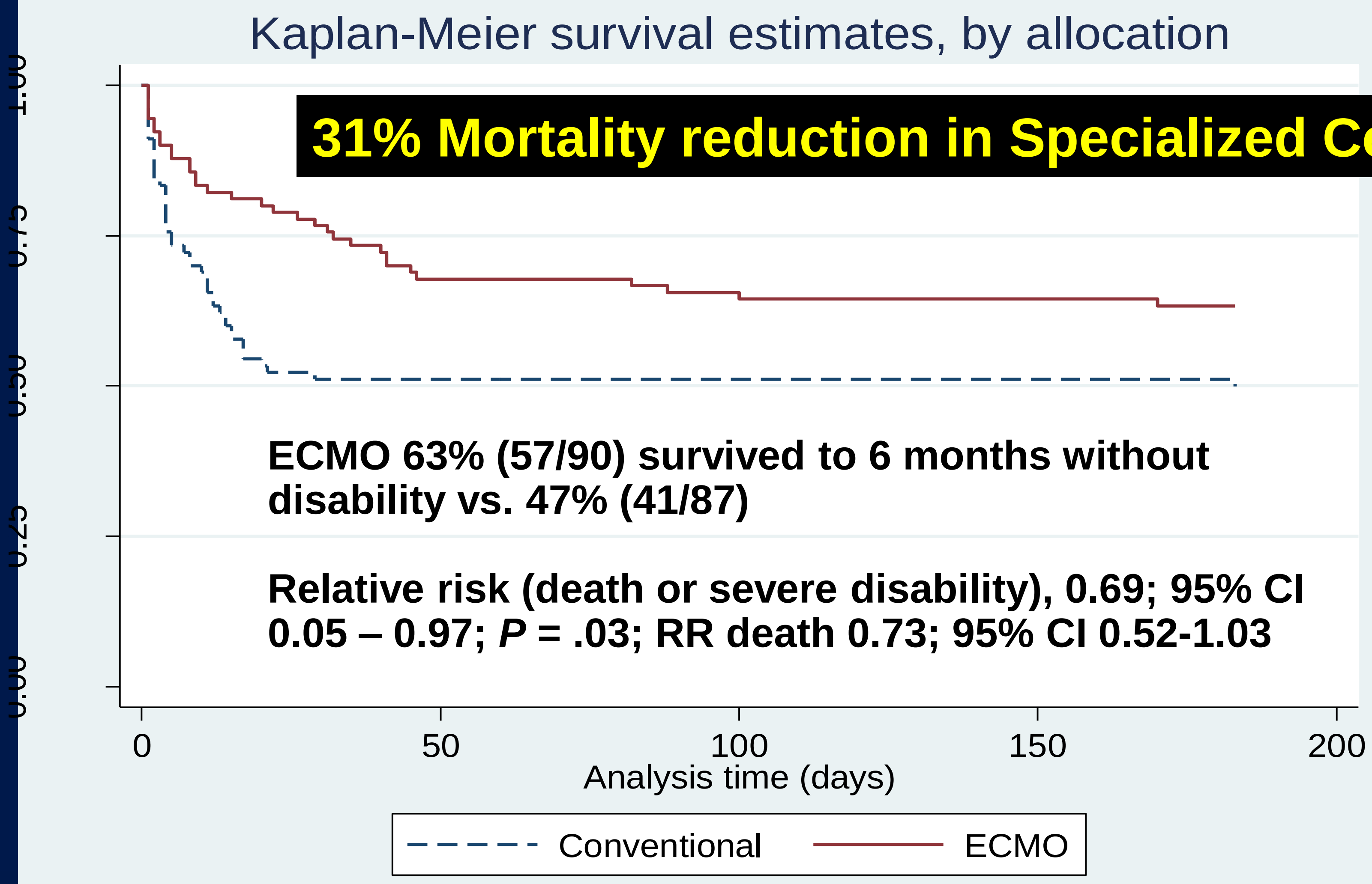
- Transmediastinal Gunshot Wound
- Combat Casualty
- Damage Control Thoracic Surgery
- Hilar Clamp for initial control

- Right pneumonectomy
- Severe ARDS
- ECMO Support initiated at a Level III Hospital in Afghanistan
- Continued by ALRT in-flight to Landstuhl Germany

Complete recovery, empyema complication

Conventional Ventilation or
ECMO for
Severe
Adult
Respiratory Failure

CESAR



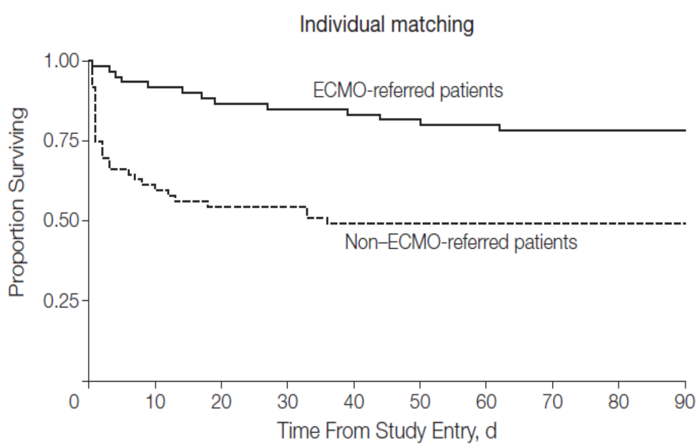
Giles Peek
CESAR 2007

Table 2. Deaths Analyzed by Matching Methods

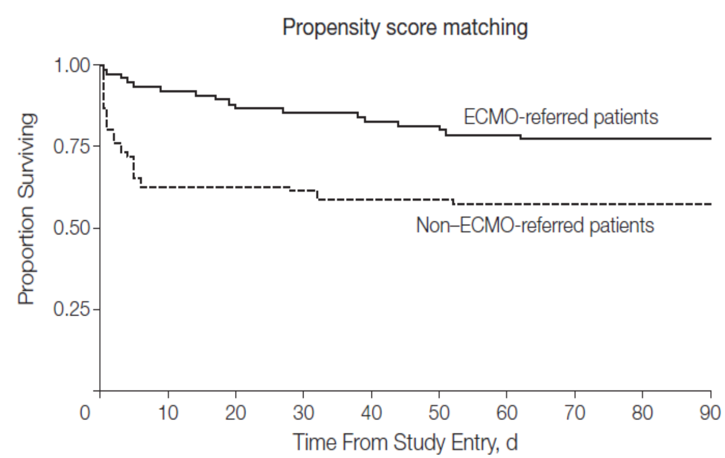
	No. of Deaths/ Total No. of Patients (%)			
	ECMO-Referred	Non–ECMO-Referred	RR (95% CI)	*P* Value
Matching method				
Propensity score	18/75 (24.0)	35/75 (46.7)	0.51 (0.31-0.84)	.008
GenMatch	18/75 (24.0)	38/75 (50.7)	0.47 (0.31-0.72)	.001
Individual	14/59 (23.7)	31/59 (52.5)	0.45 (0.26-0.79)	.006

Abbreviations: ECMO, extracorporeal membrane oxygenation; RR, relative risk.

80 referred for ECMO; 69 received (86.3%); hospital mortality 27.5%



No. at risk	0	10	20	30	40	50	60	70	80	90
ECMO-referred patients	59	54	51	50	49	48	47	46	46	46
Non–ECMO-referred patients	59	36	32	32	29	29	29	29	29	29



No. at risk	0	10	20	30	40	50	60	70	80	90
ECMO-referred patients	75	69	66	64	62	61	59	58	58	58
Non–ECMO-referred patients	75	47	47	46	44	44	43	43	43	43

Noah MA, et al. JAMA 2011;306(15):1659-1668.

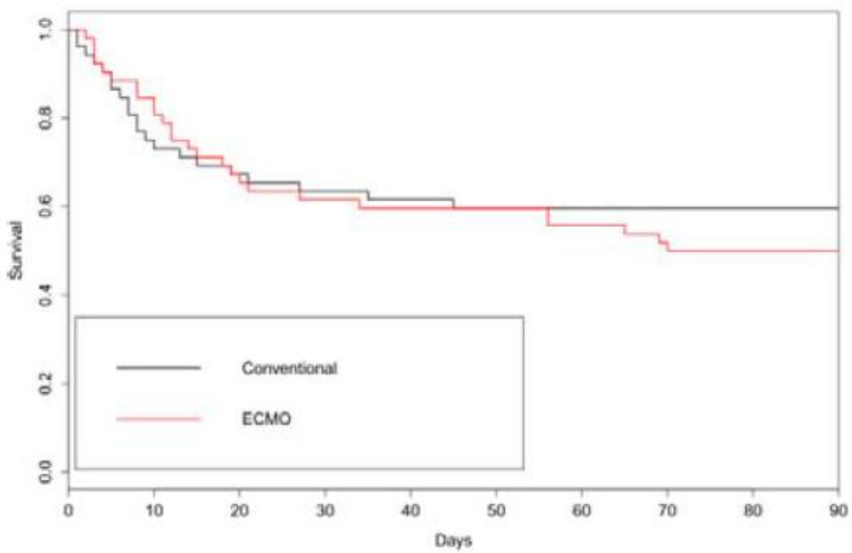
Extracorporeal Membrane Oxygenation for Pandemic Influenza A(H1N1)–induced Acute Respiratory Distress Syndrome

A Cohort Study and Propensity-matched Analysis

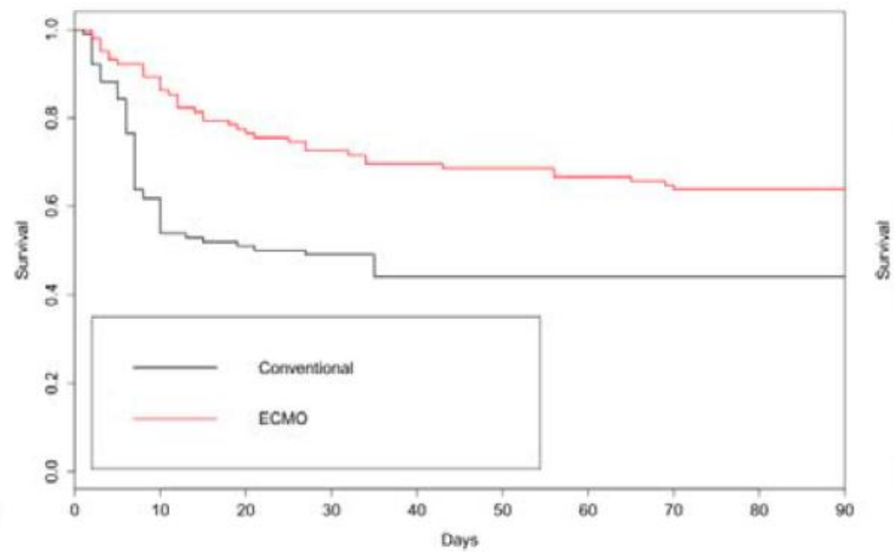
Tài Pham[1,2], Alain Combes[3,4], Hadrien Rozé[5], Sylvie Chevret[2,6], Alain Mercat[7,8], Antoine Roch[9,10], Bruno Mourvillier[11,12], Claire Ara-Somohano[13,14], Olivier Bastien[15,16], Elie Zogheib[17], Marc Clavel[18,19], Adrien Constan[1], Jean-Christophe Marie Richard[20,21,22], Christian Brun-Buisson[1,23,24], and Laurent Brochard[20,21,24]; for the REVA Research Network*

Matched 52/123 pts receiving ECMO; mortality varies with replacement

REVA main analysis
(matched sample without replacement)



REVA matched sample with replacement



Pham T, et al. AJRCCM 187 (3): 276-85 2013

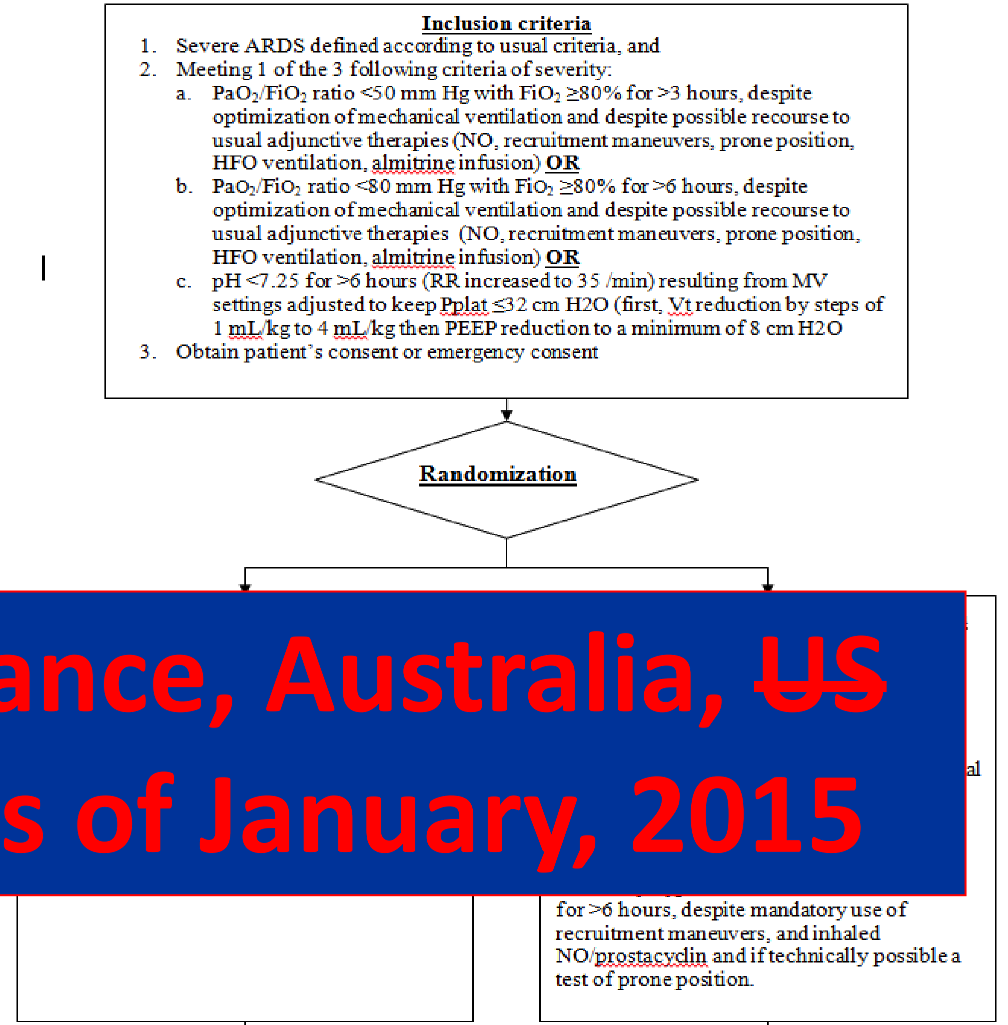
EOLIA ECMO Trial

- **E**CMO to rescue **L**ung **I**njury in severe **A**RDS
- Multicenter ECMO trial

Enrolling in France, Australia, ~~US~~

157 patients as of January, 2015

- Control cohort with modern ARDS ventilator management, and rescue strategies allowed



Judgement criteria

Primary endpoint: all-cause mortality at D60

Secondary outcomes:

– Mortality at D30 and D90, in the ICU and in-hospital

– Number of days, between inclusion and D60, alive without mechanical ventilation, without hemodynamic support and without organ failure

– Number of patients developing pneumothorax between D1 and D60

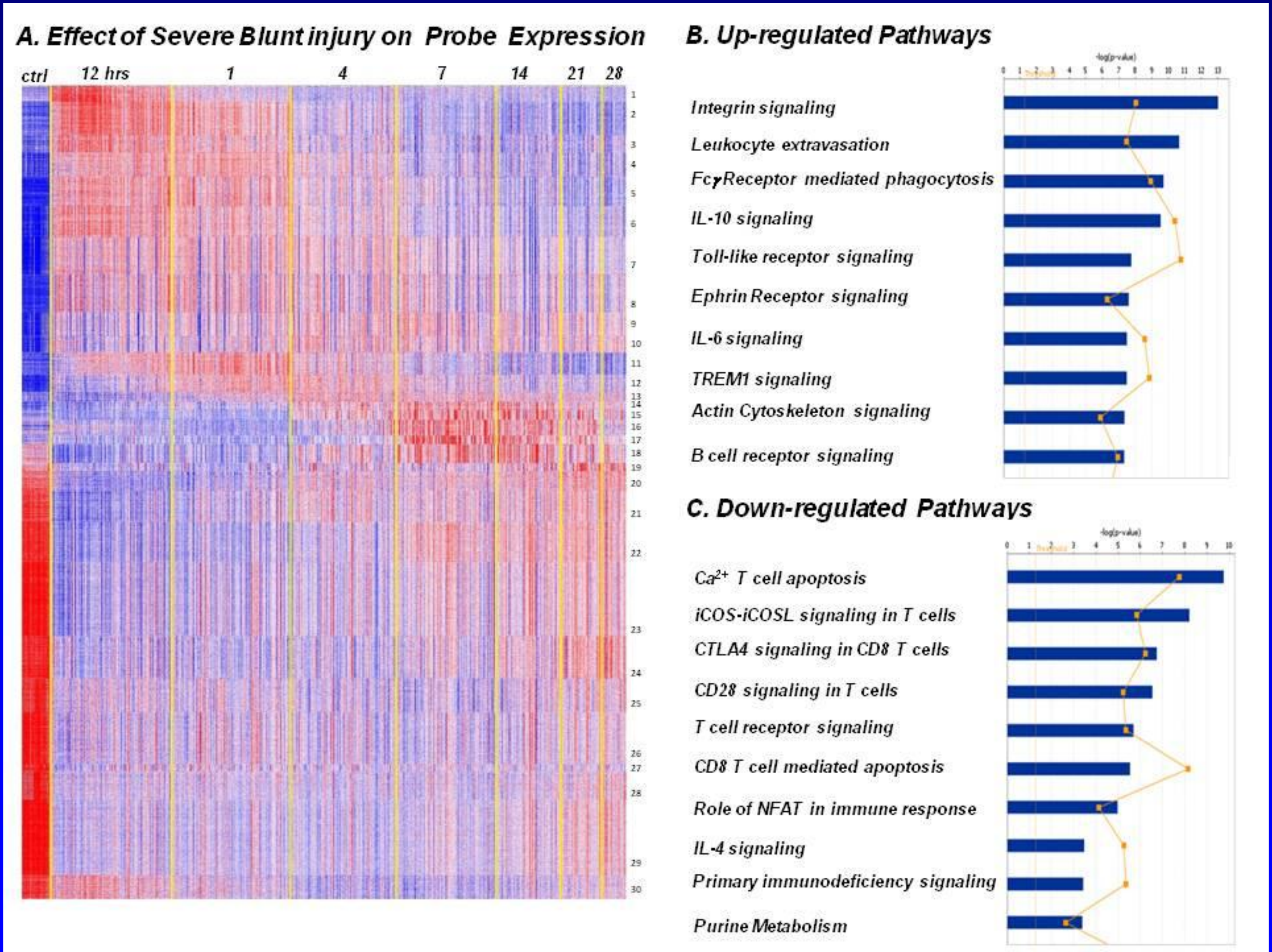
– Number of infectious, neurological and hemorrhagic complications

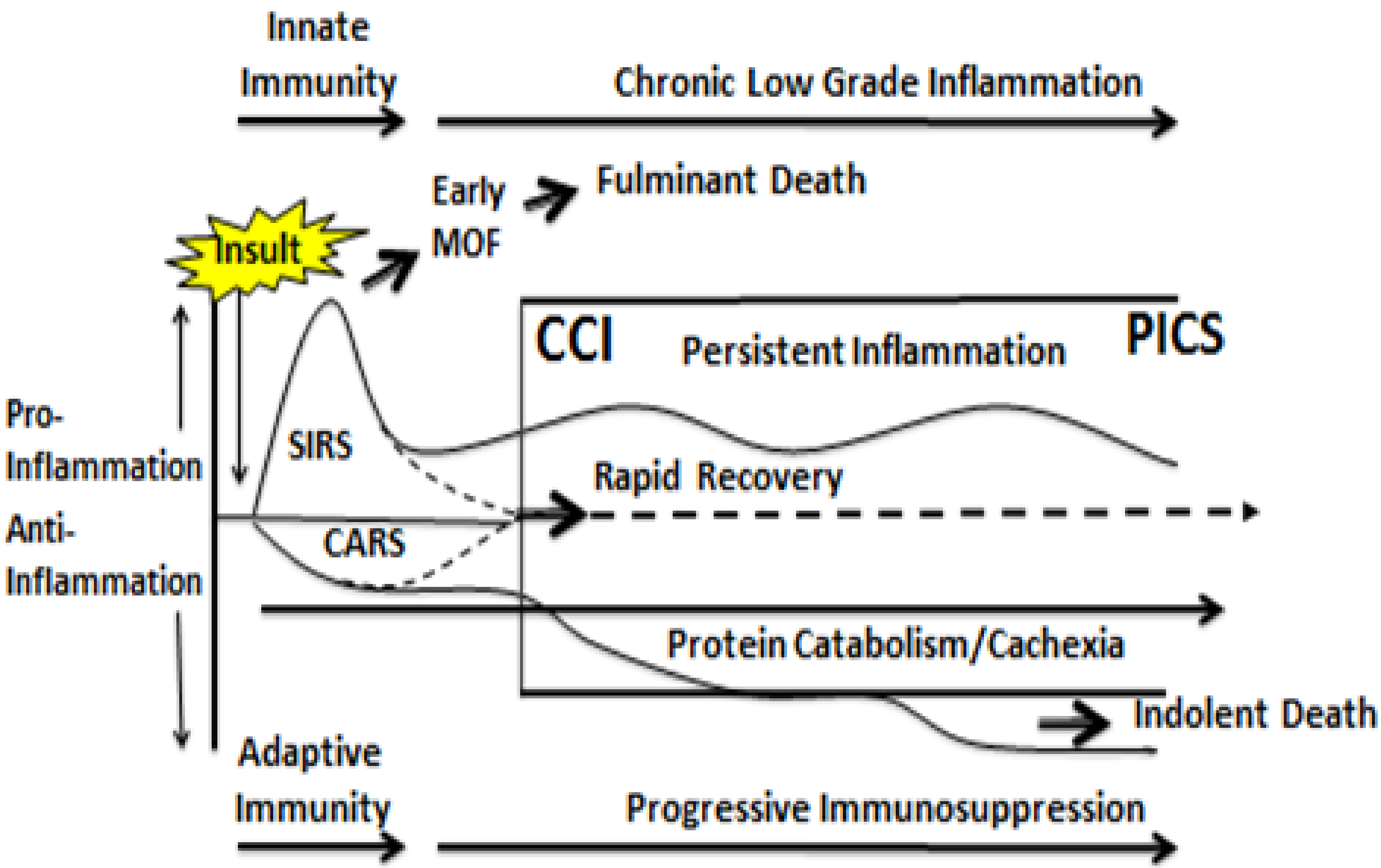
– Duration of mechanical ventilation, and ICU and hospital stays

❖ Long Term Outcomes

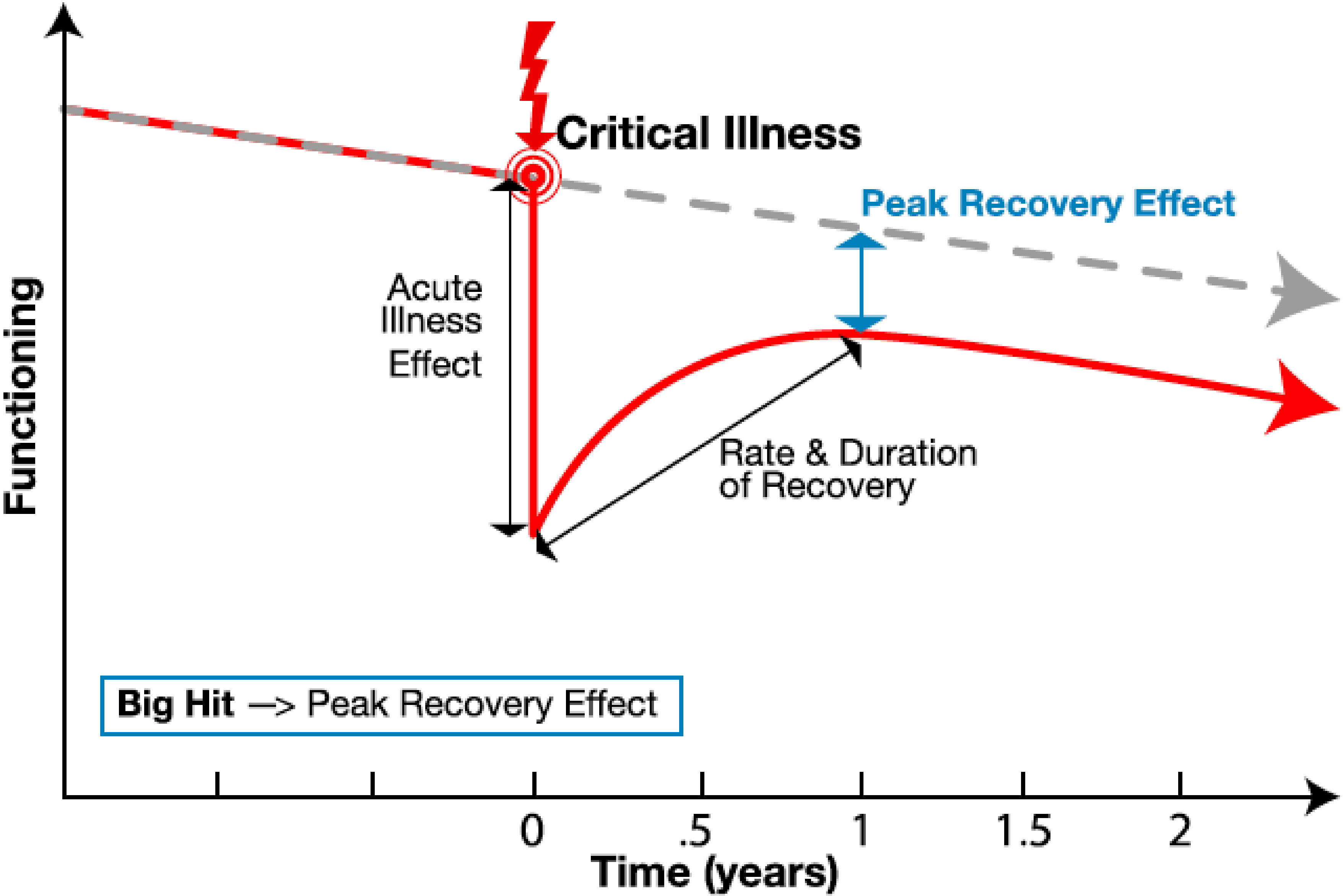
- Increased awareness of critical care myopathy, persistent inflammation, immunosuppression and catabolism syndrome
- Just discharging the patient from the ICU is not sufficient any more

A "Genomic Storm" induced by severe blunt trauma



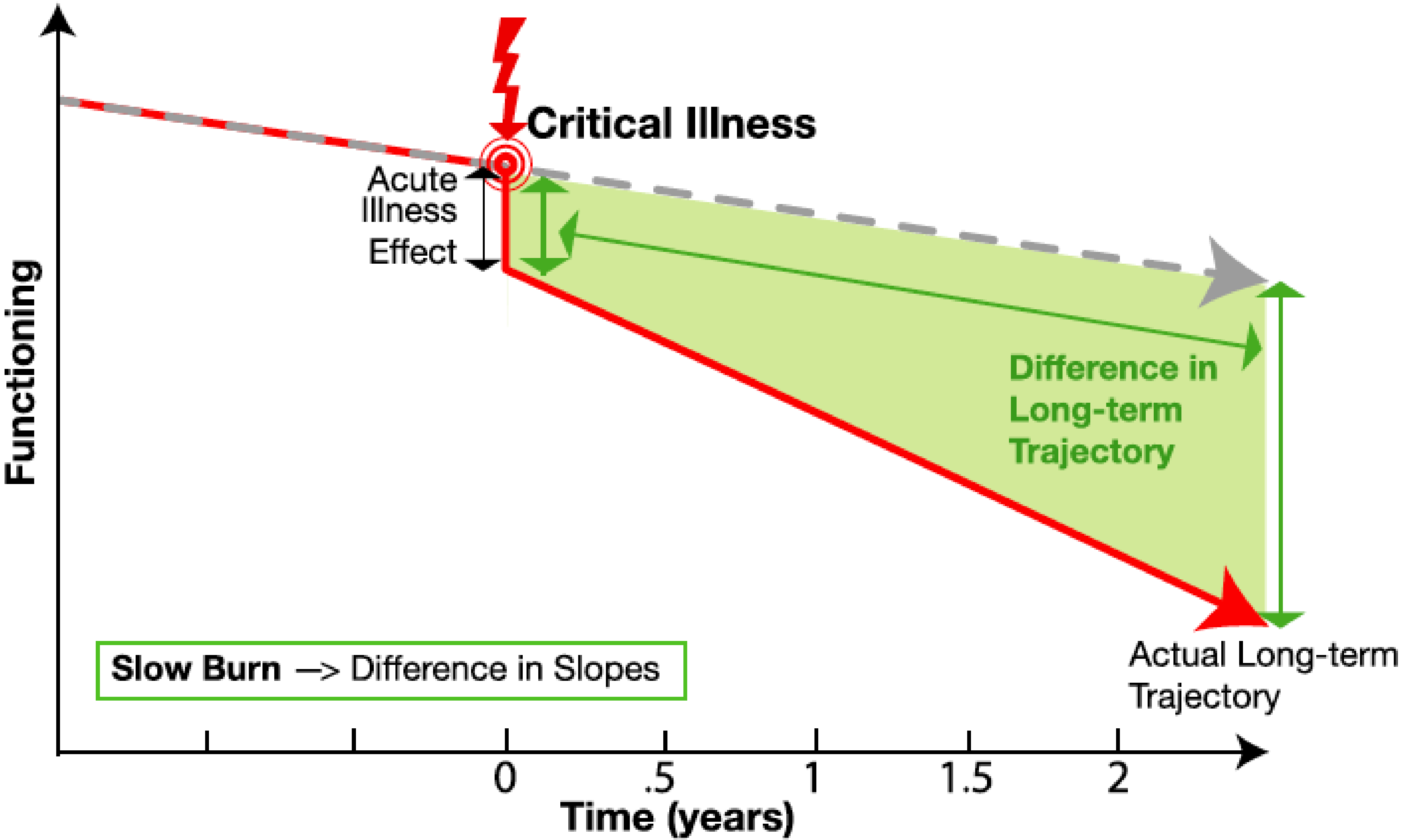

Innate
Immunity
Chronic Low Grade Inflammation
Early
MOF
Fulminant Death
Insult
CCI
Persistent Inflammation
PICS
Pro-
Inflammation
SIRS
Rapid Recovery
Anti-
Inflammation
CARS
Protein Catabolism/Cachexia
Indolent Death
Adaptive
Immunity
Progressive Immunosuppression

The Big Hit



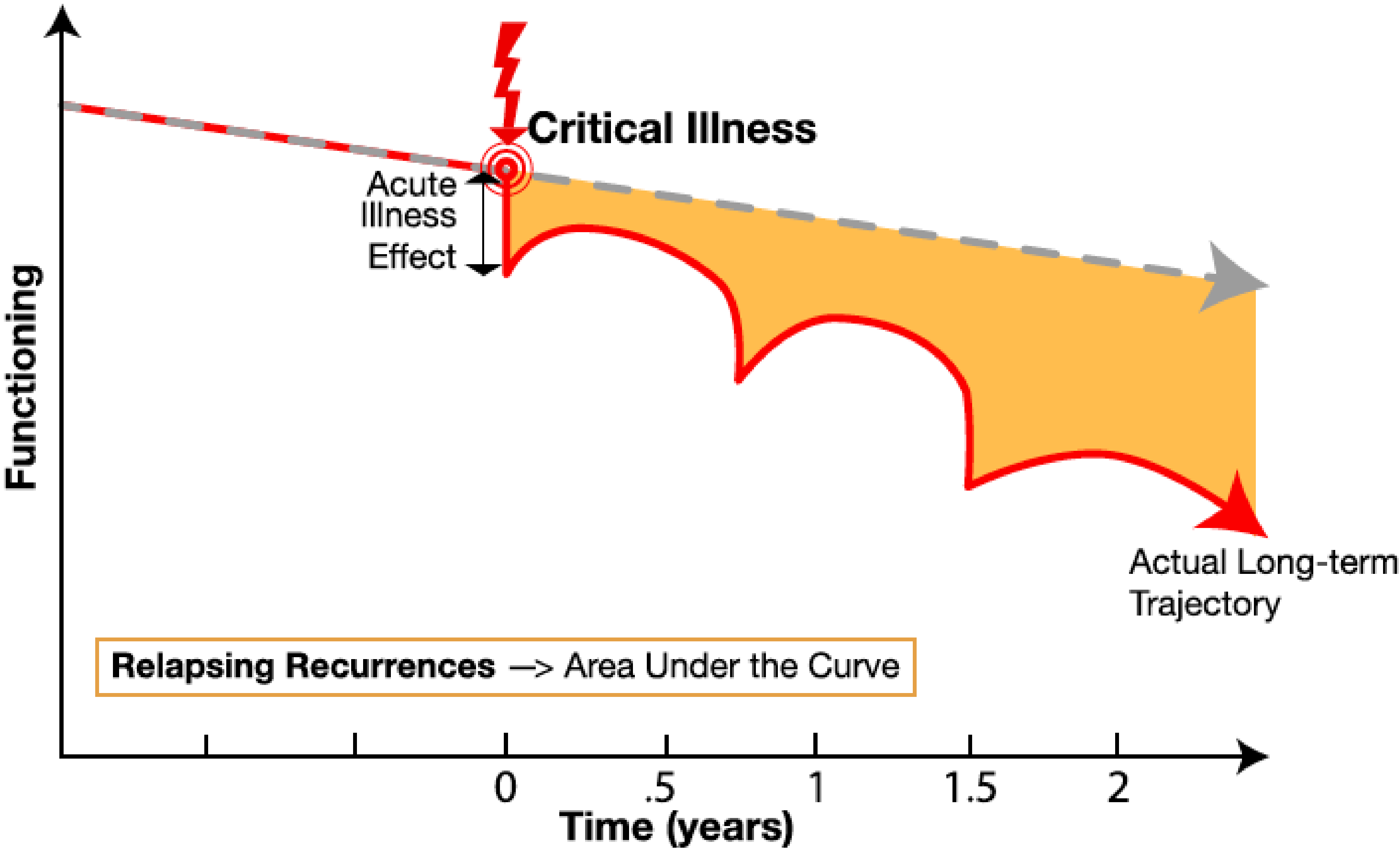
Iwashyna AJRCCM 186 2012 303-4

The Slow Burn



Iwashyna AJRCCM 186 2012 303-4

Relapsing Recurrences

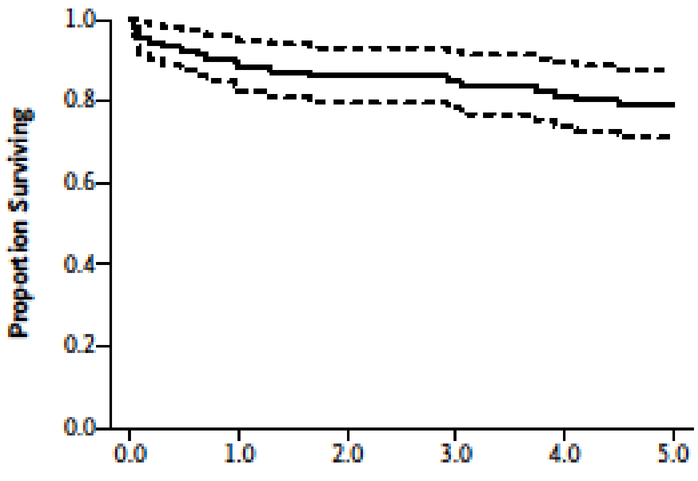


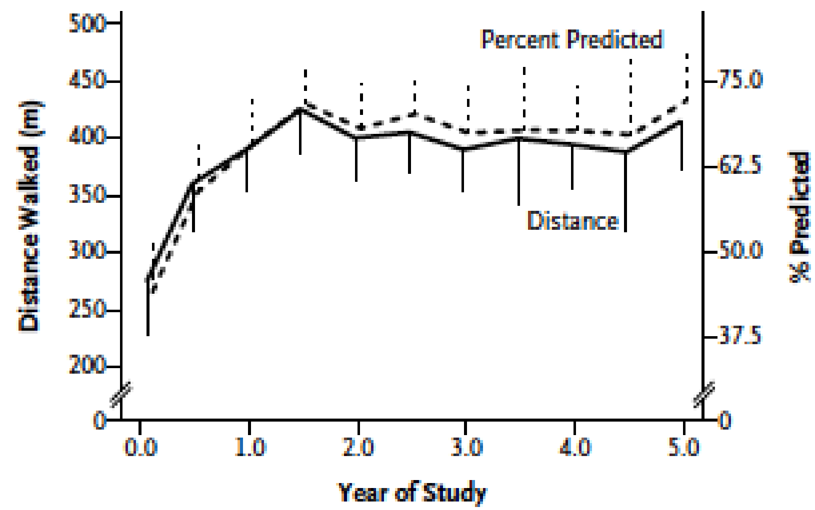
Iwashyna AJRCCM 186 2012 303-4

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 7, 2011 VOL. 364 NO. 14

Functional Disability 5 Years after Acute Respiratory Distress Syndrome





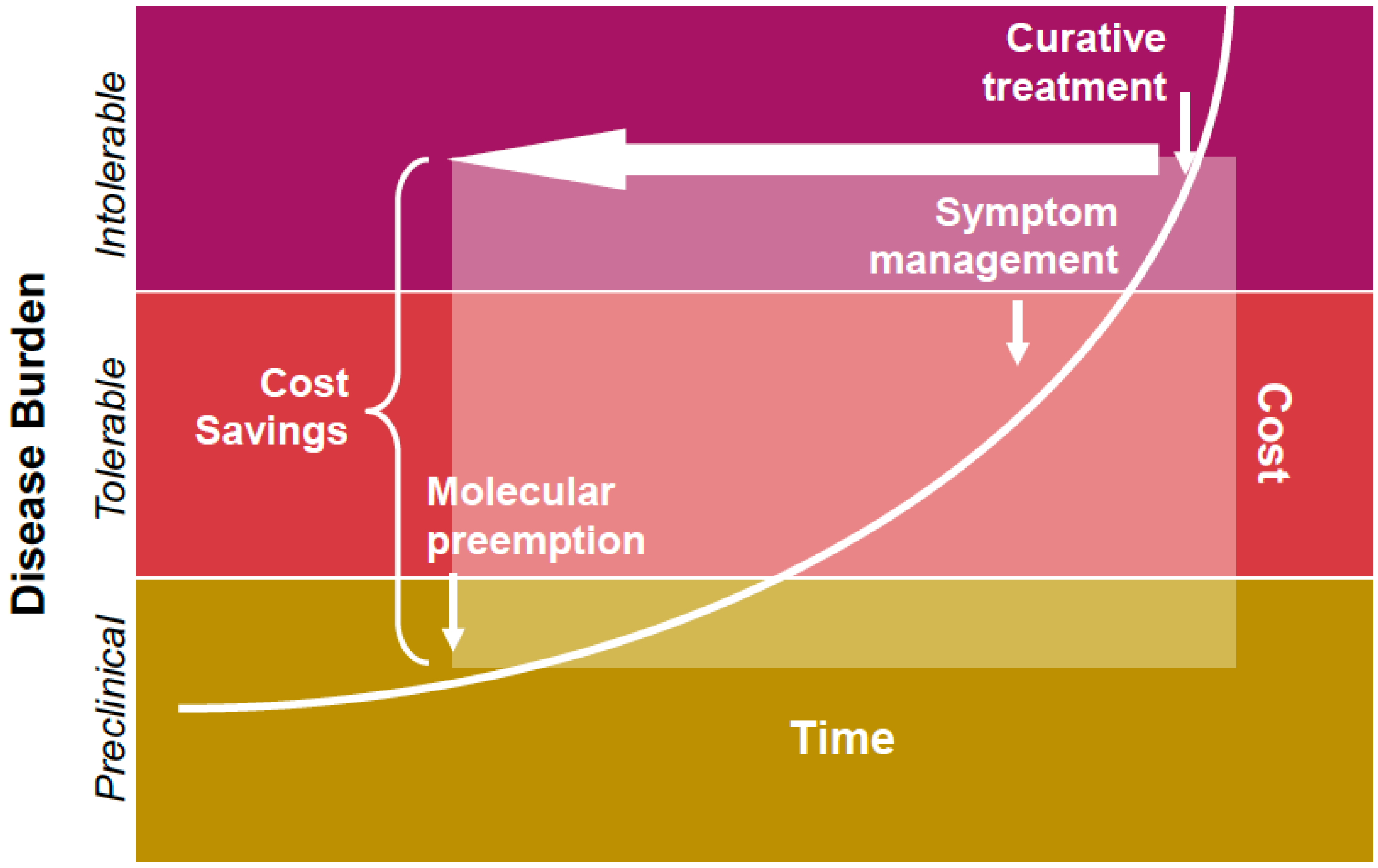
- ARDS survivors had substantial recovery at one year, but persistent deficits at 5 years for exercise tolerance, quality of life

- Focus on early intervention to prevent or reduce the severity of acute lung injury

Need to Transform Medical Research in the 21st Century

20th Century	21st Century
•Treat disease when symptoms appear and normal function is lost	•Intervene before symptoms appear and preserve normal function for as long as possible
•Did not understand the molecular and cellular events that lead to disease	•Understanding preclinical molecular events and ability to detect patients at risk
•Expensive in financial and disability costs	•Orders of magnitude more effective

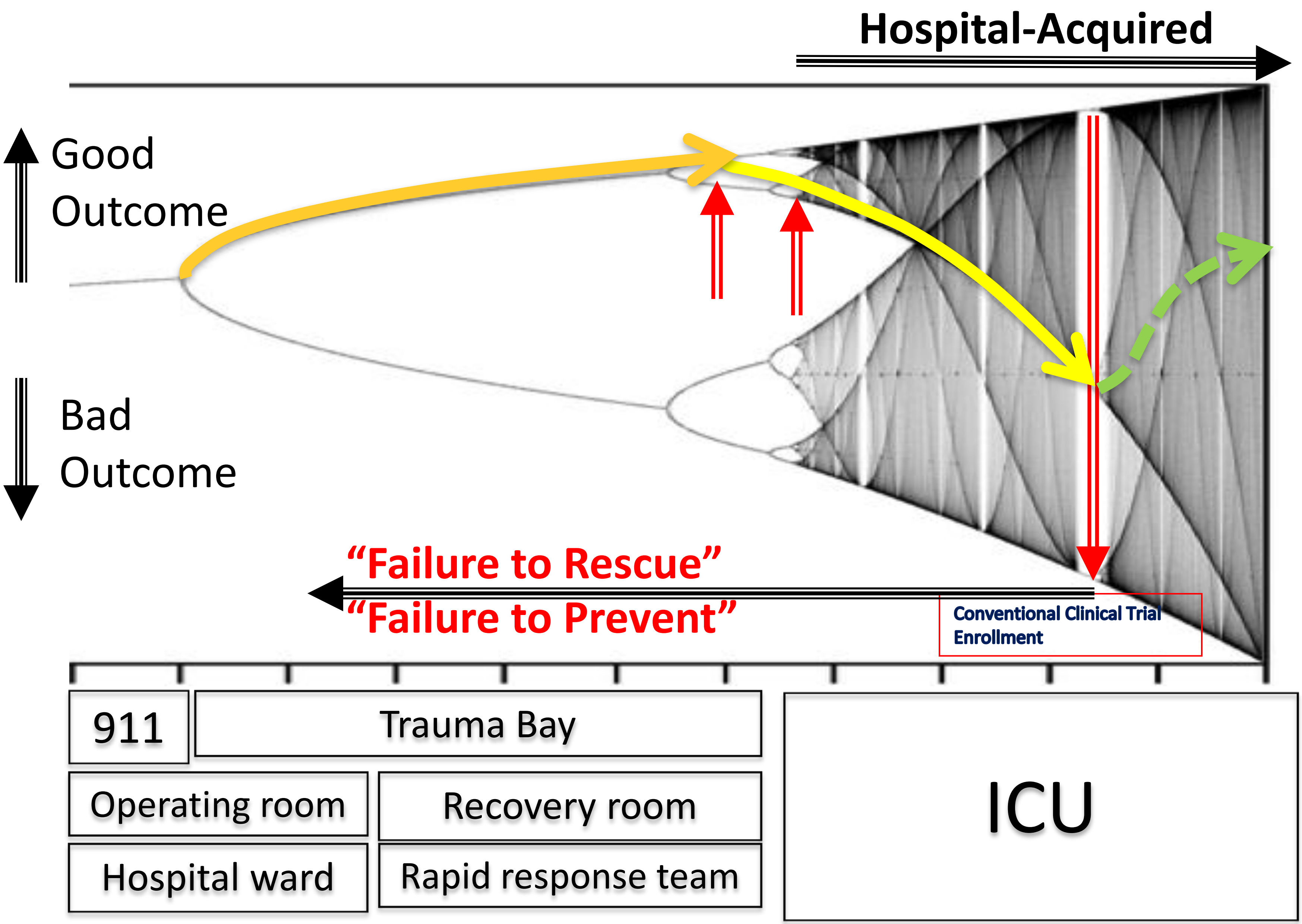
The Future Paradigm: Preempt Disease



National Heart Lung and Blood Institute

MAYO CLINIC

"Chaos" of Critical Illness



❖ Prevention

- Never as exciting……
- But *always* makes more sense

Prevention and Personalized Medicine for ARDS

The New England Journal of Medicine

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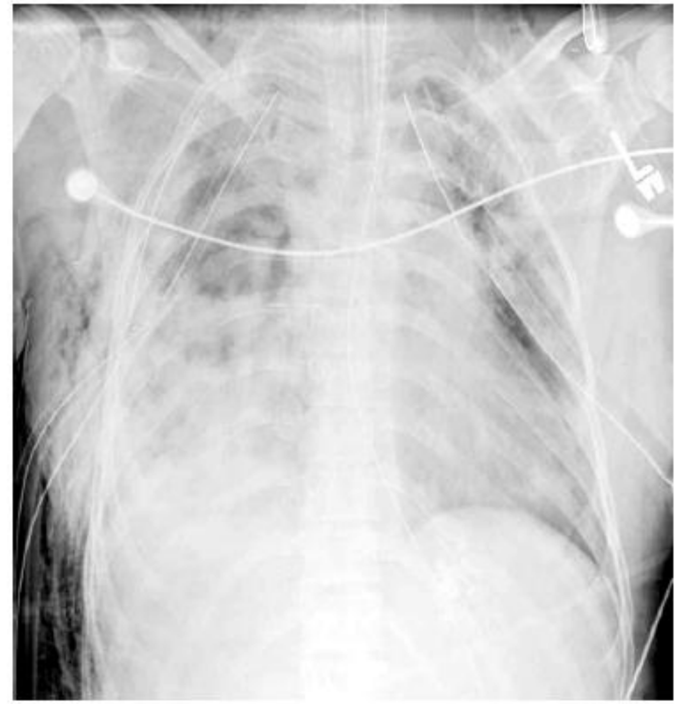
VOLUME 342 — MAY 4, 2000 — NUMBER 18

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*

•Will earlier alterations in ventilation *prevent* ARDS?

Gajic and colleagues



•Can ventilation settings be *personalized*?

Marini and others

National Heart Lung and Blood Institute

LIPS
A

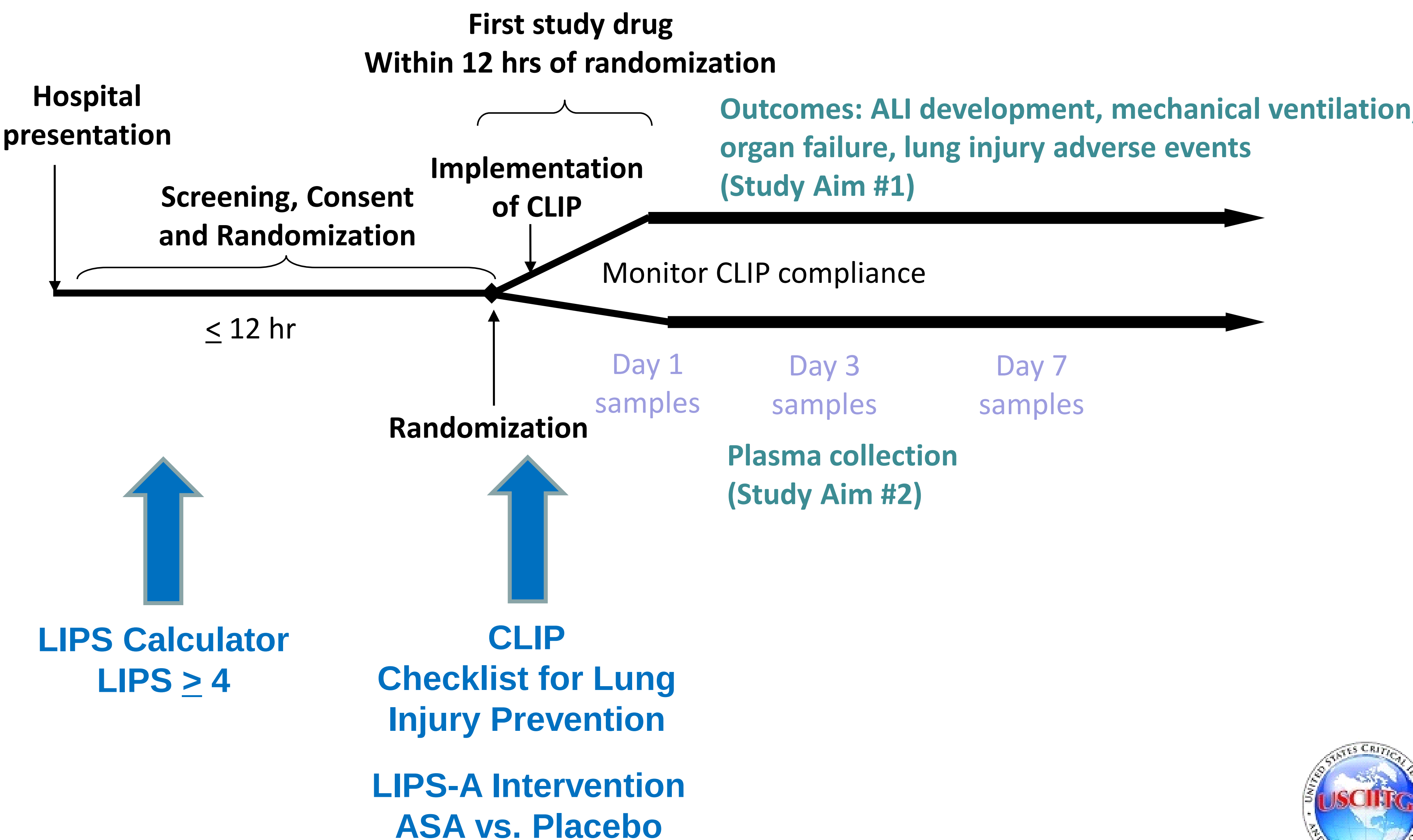
Lung Injury Prevention Study with Aspirin

LIPS-A Kick-off Meeting

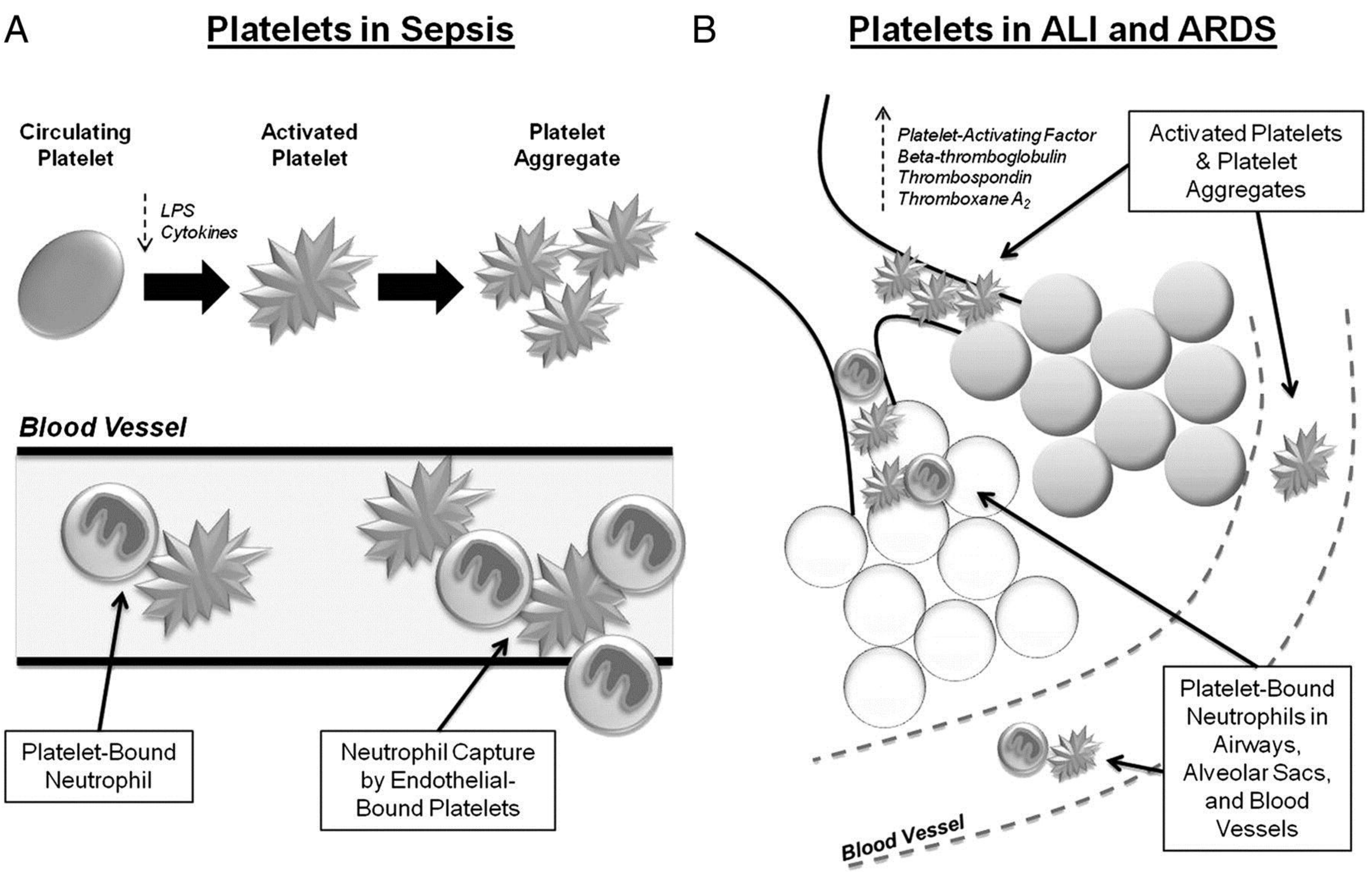
NIH, Bethesda, MD

Nov. 8, 2011

LIPS-A Study Schematic

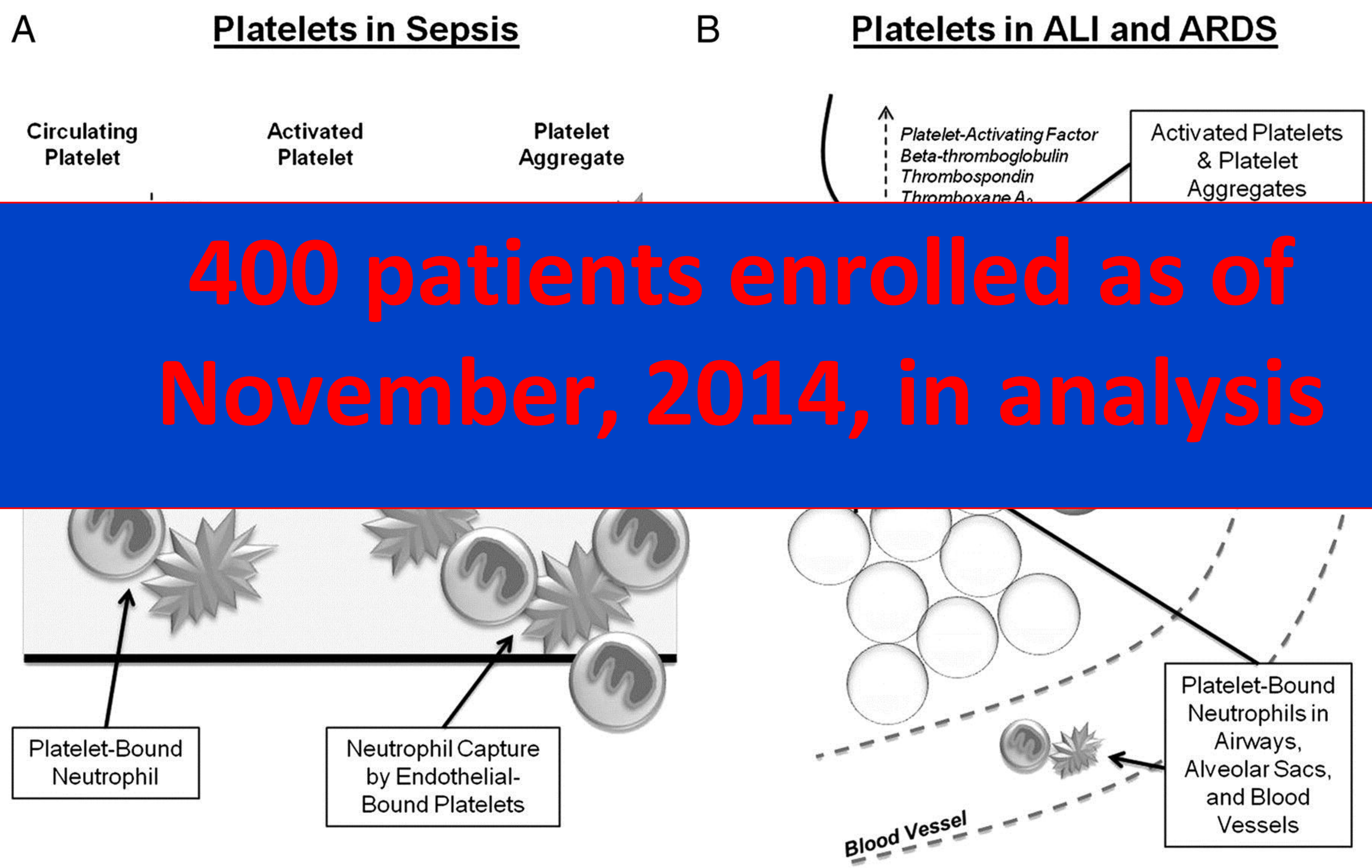


Platelets and platelet-neutrophil interactions in sepsis and ALI



Katz J N et al. Chest 2011;139:658-668

Platelets and platelet-neutrophil interactions in sepsis and ALI

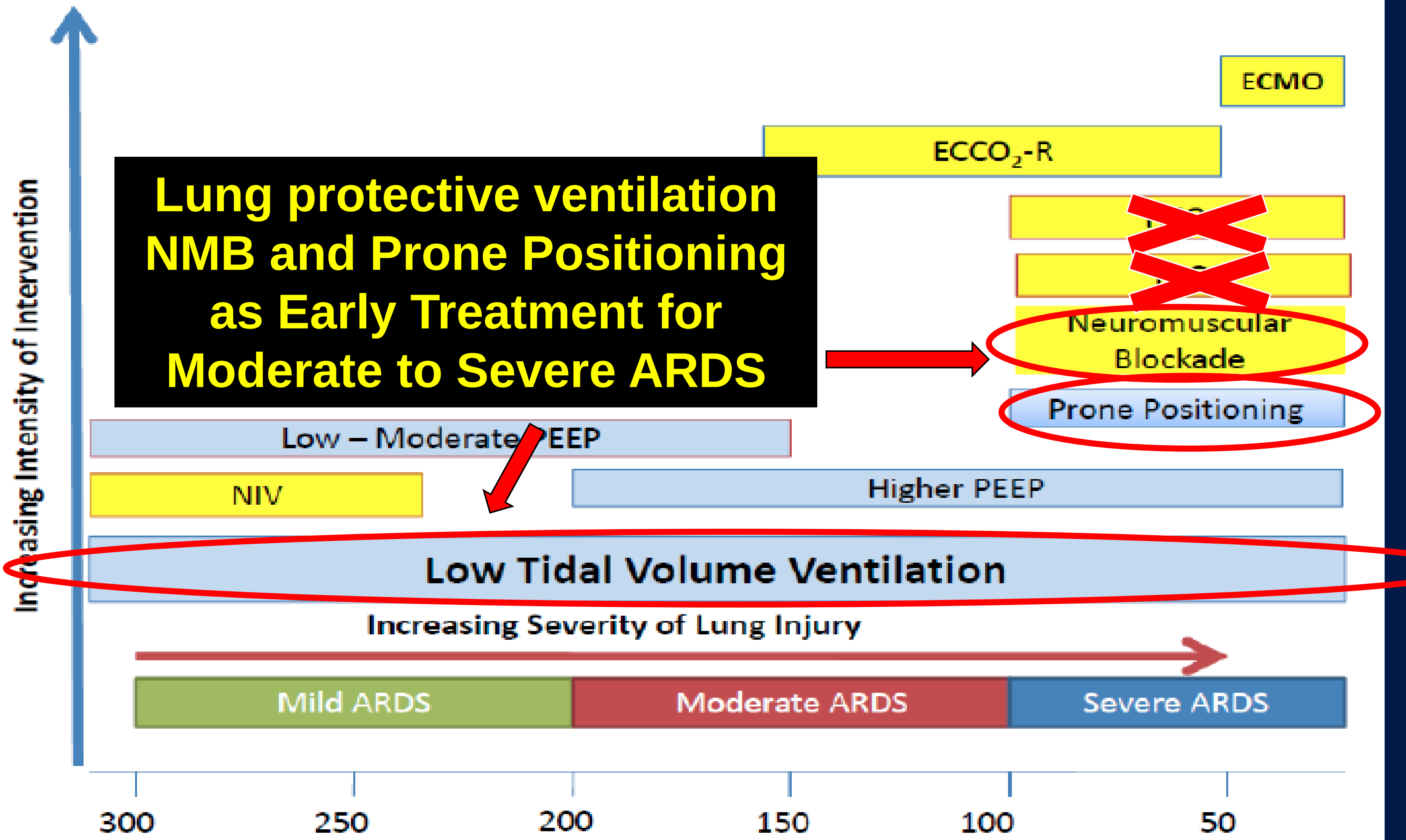


400 patients enrolled as of November, 2014, in analysis

Katz J N et al. Chest 2011;139:658-668

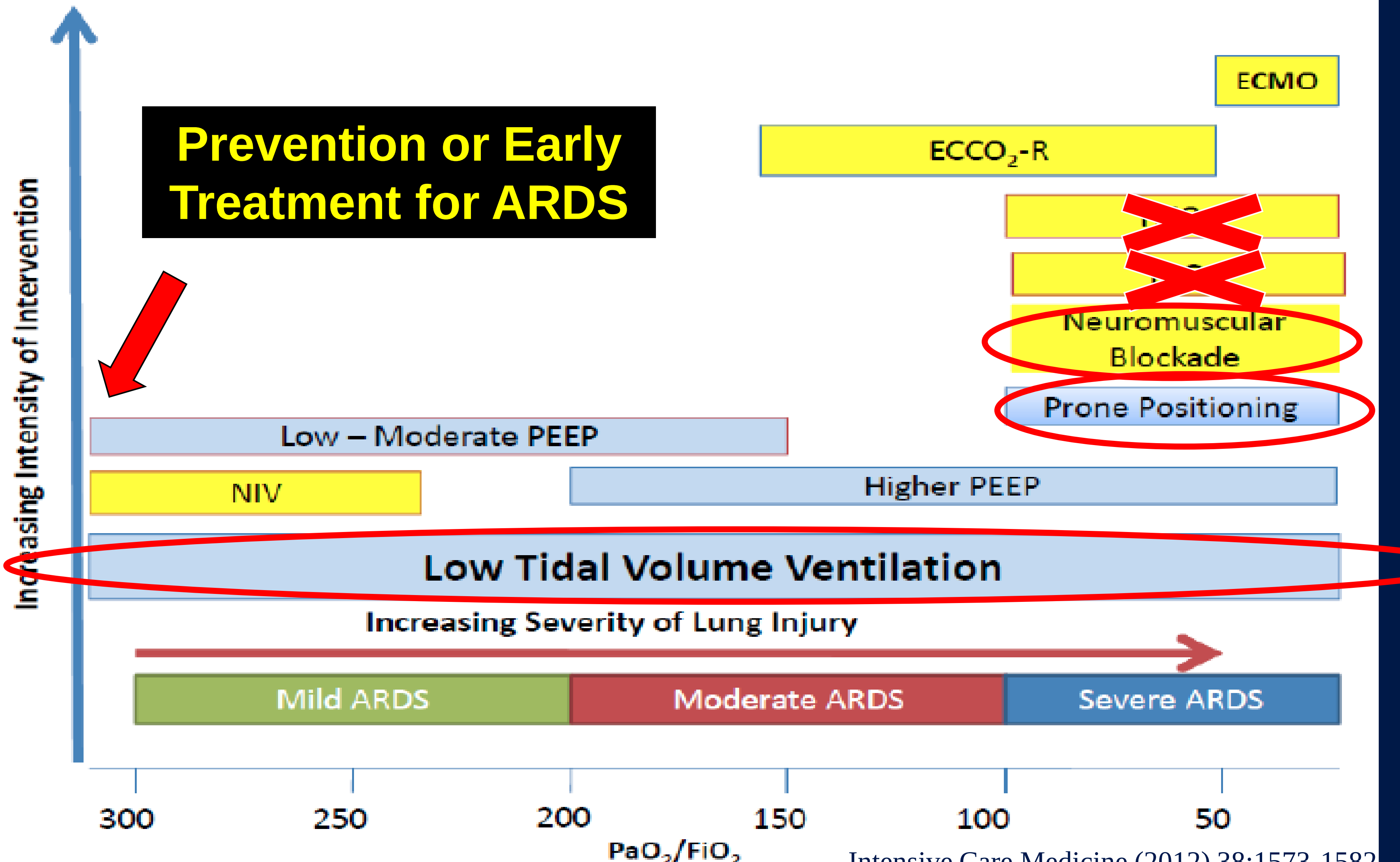
- 12 Clinical Centers, 1 Coordinating Center (Michigan Center – UMich and Henry Ford)
- Focus on trials of prevention and early intervention in lung injury
- Multidisciplinary focus: Pulmonary, ED, Surgery to address continuum of care

Treatment paradigm in ARDS



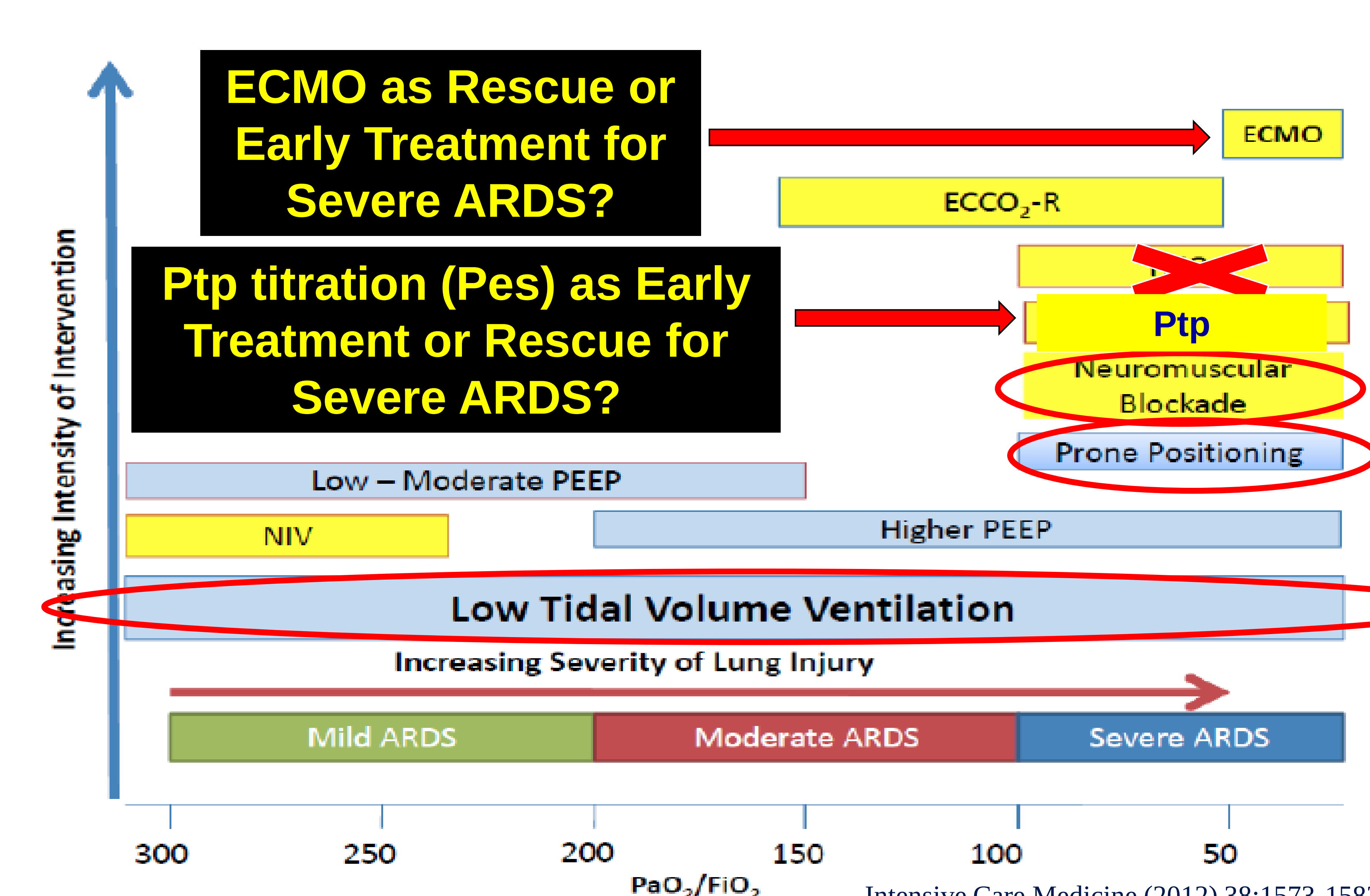
Intensive Care Medicine (2012) 38:1573-1582

Treatment paradigm in ARDS



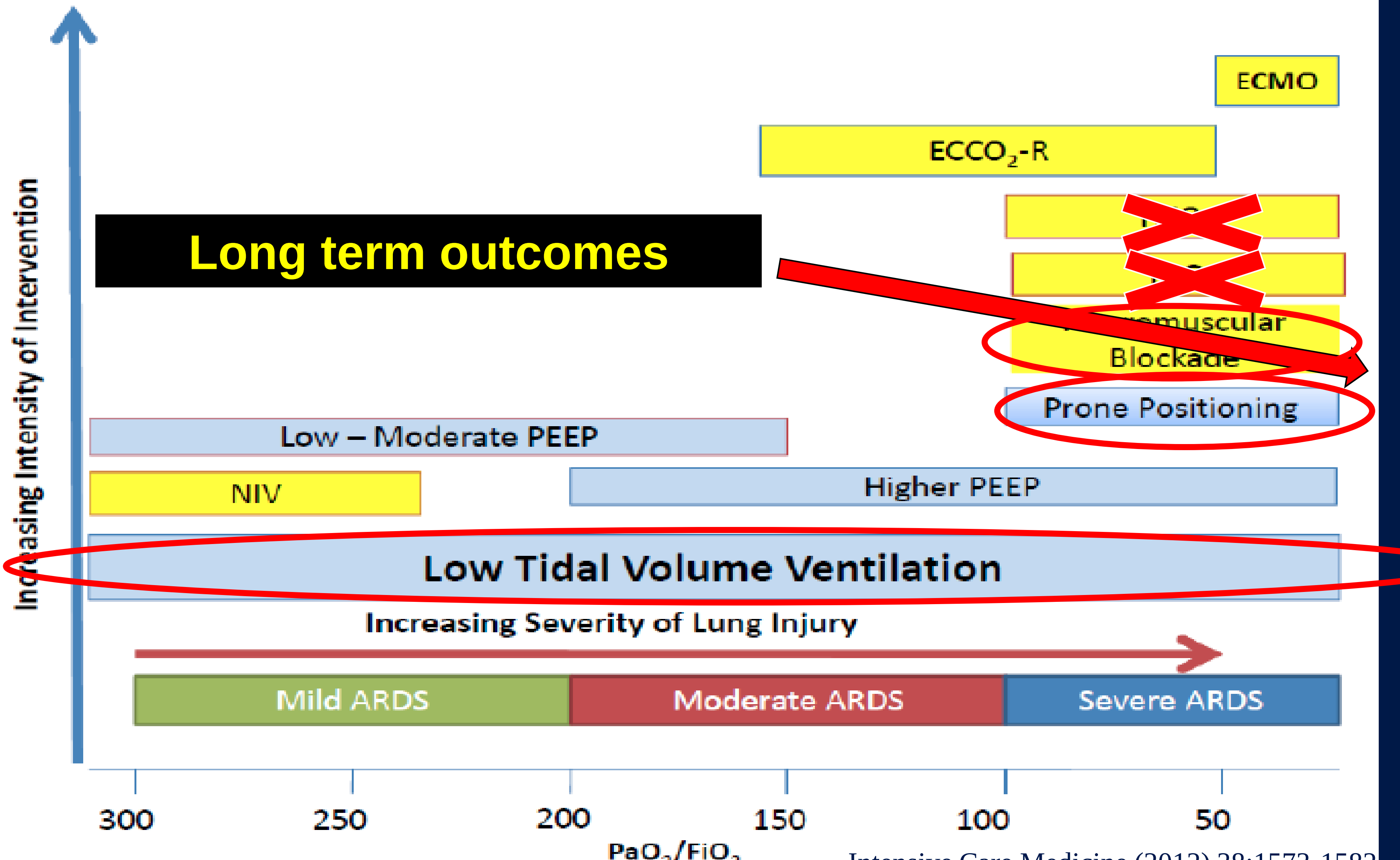
Intensive Care Medicine (2012) 38:1573-1582

Treatment paradigm in ARDS



Intensive Care Medicine (2012) 38:1573-1582

Treatment paradigm in ARDS



Intensive Care Medicine (2012) 38:1573-1582

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Ann Arbor, MI