



JRUR 2024

20^{ème} Journée de Réanimation & Urgences Respiratoires

JEUDI 11 AVRIL

Faculté des Sciences Médicales et Paramédicales - Timone, Marseille



Vingt ans de SDRRA



Centre
Hospitalier
de Bastia

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Conflicts of interest

- Fees and/or travel expenses
 - Air Liquide Santé
 - Maquet
 - Drager
 - GE
 - Faron
 - GSK
 - Covidien
 - Janssen
 - Orion
 - Johnson & Johnson
 - Peninsula Pharma

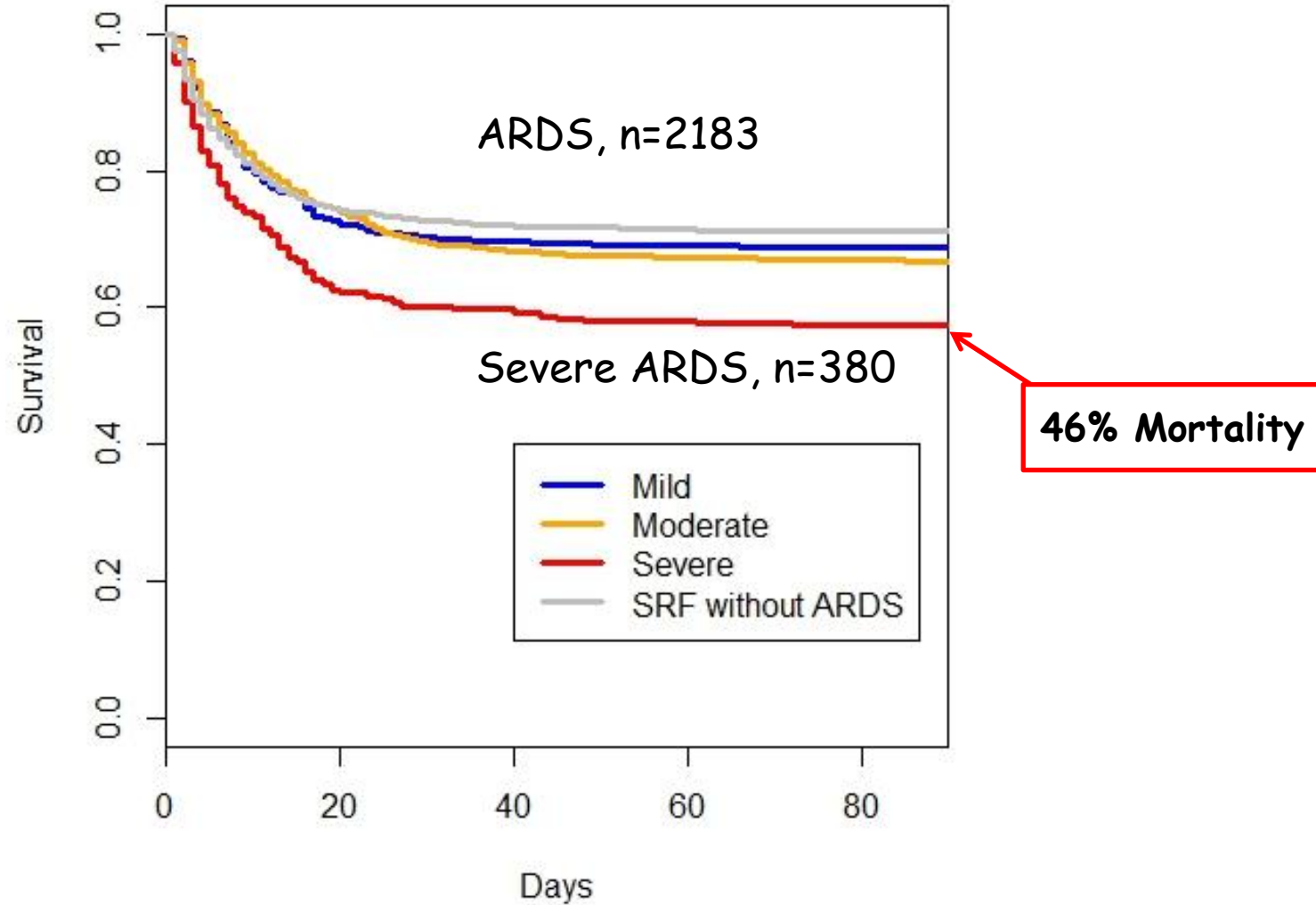
Berlin definition

Acute respiratory distress syndrome			
Timing	Within 1 week of a known clinical insult or new/worsening respiratory symptoms		
Chest imaging ^a	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		
	Mild	Moderate	Severe
Oxygenation ^b	200 < PaO ₂ /FiO ₂ ≤ 300 with PEEP or CPAP ≥5 cmH ₂ O ^c	100 < PaO ₂ /FiO ₂ ≤ 200 with PEEP ≥5 cmH ₂ O	PaO ₂ /FiO ₂ ≤100 with PEEP ≥5 cmH ₂ O

Ferguson et al. Intensive Care Med 2012

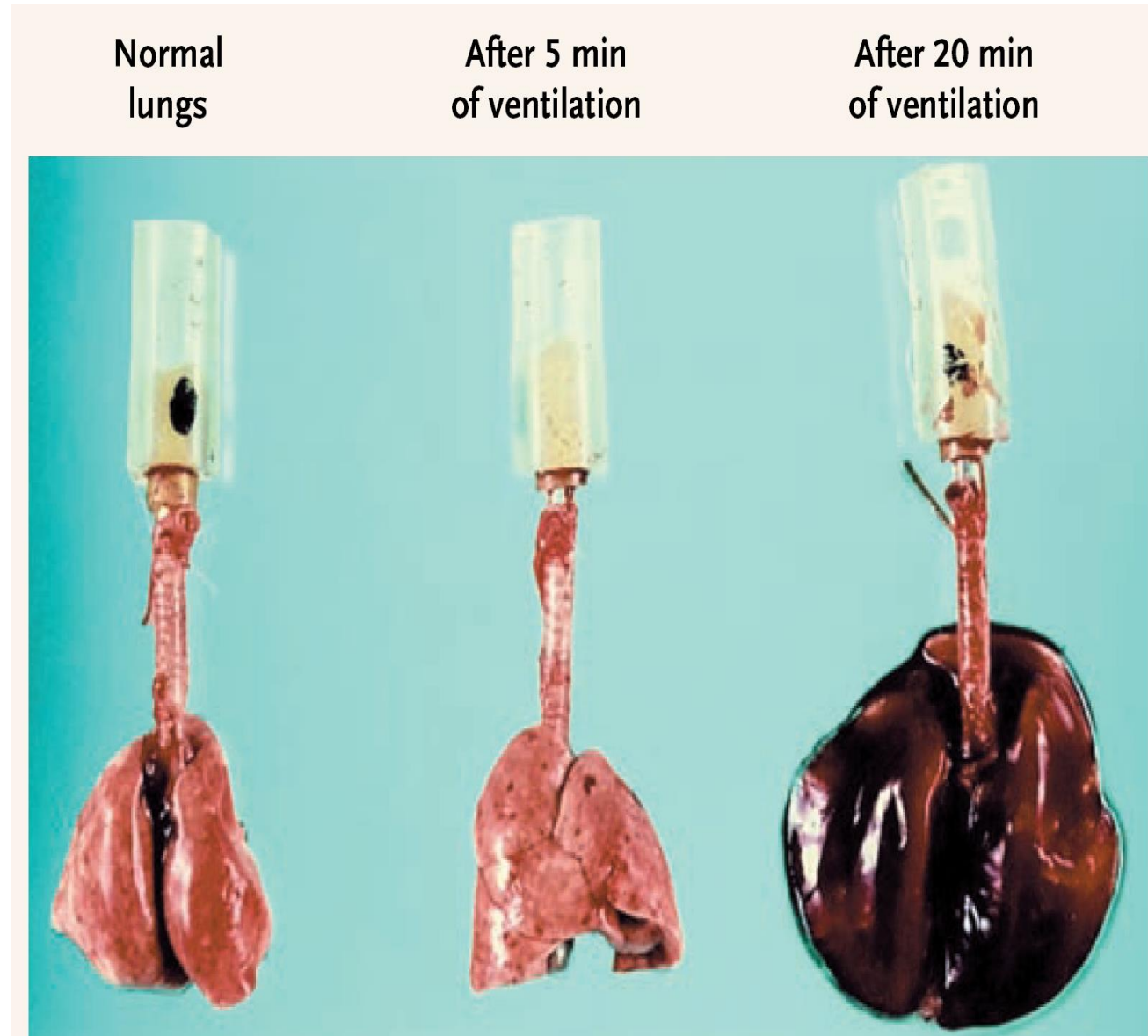


Patient Survival to Day 90



VILI prevention

Dreyfuss & Saumon AJRCCM 98



Second-hit

experimental data

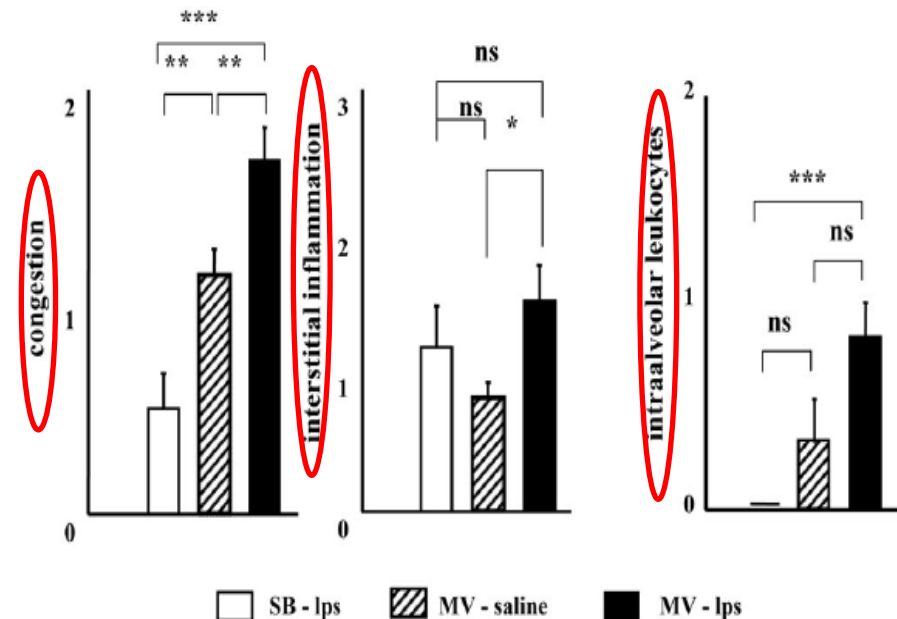
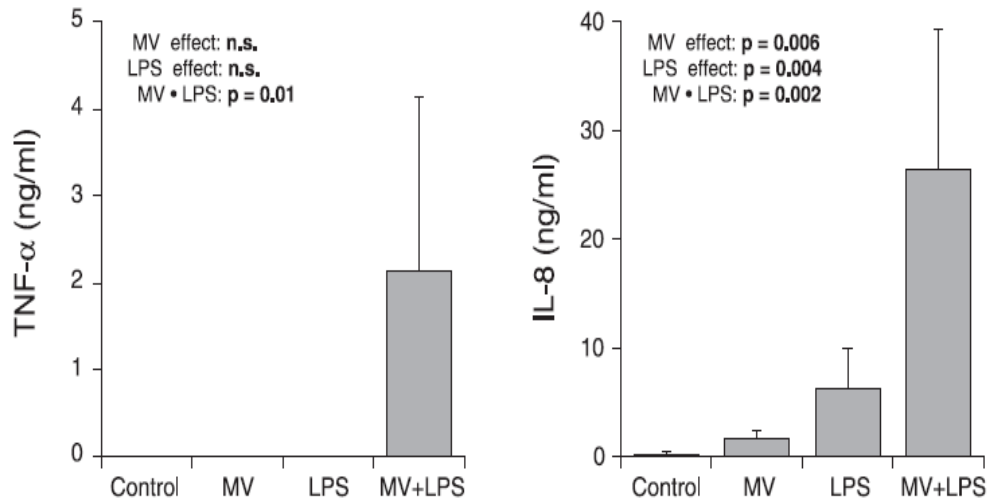
- Injured lungs
 - ↗ edema: synergy ANTU - Vt 45 ml/kg

Dreyfuss et al. AJRCCM 95

- Healthy lungs
 - LPS + MV

Brégeon et al. Anesthesiology 2005

Altemeier et al. Am J Physiol 2004



Tidal volume reduction

The New England Journal of Medicine

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VOLUME 342

MAY 4, 2000

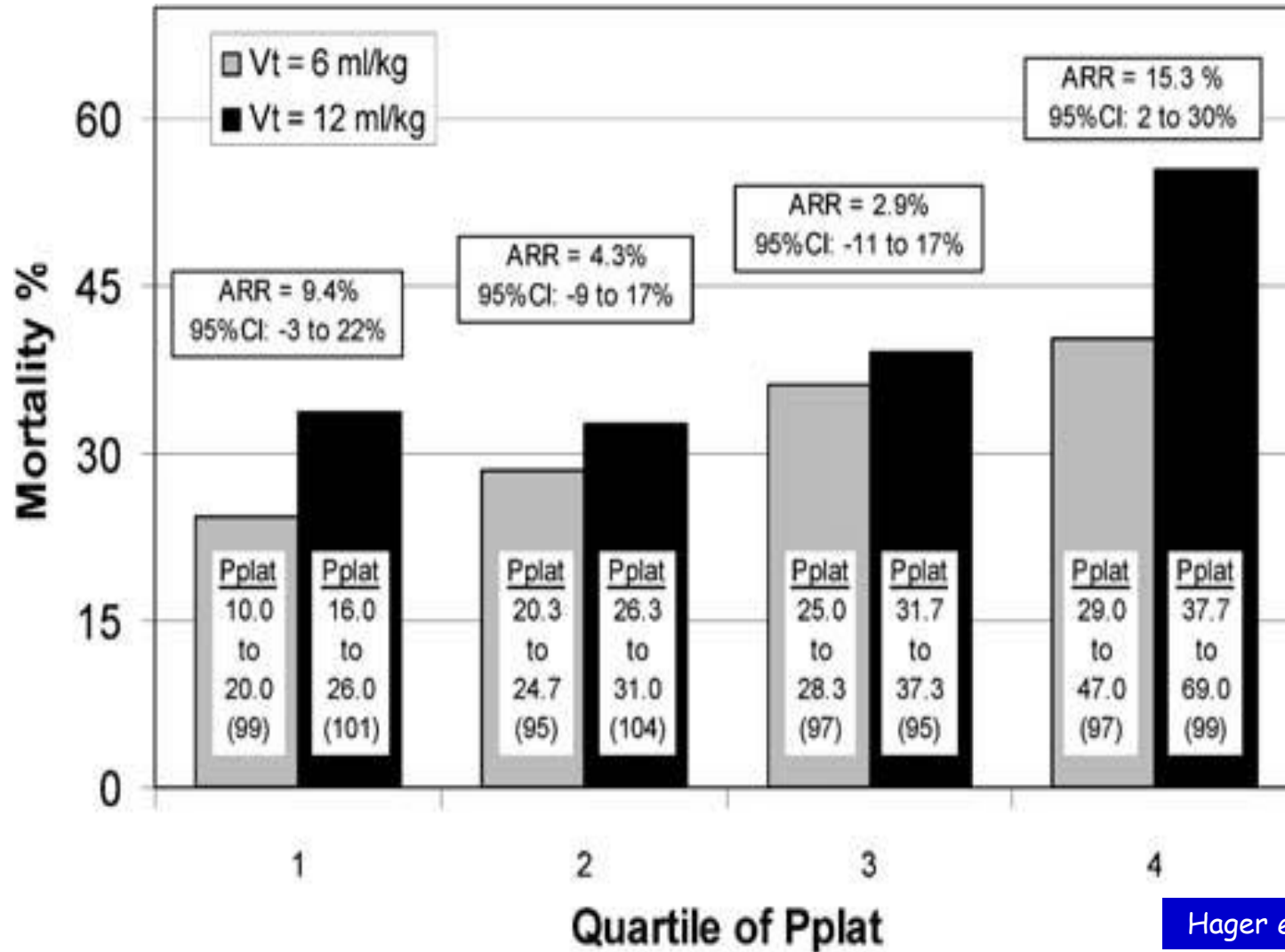
NUMBER 18



**VENTILATION WITH LOWER TIDAL VOLUMES AS COMPARED WITH
TRADITIONAL TIDAL VOLUMES FOR ACUTE LUNG INJURY
AND THE ACUTE RESPIRATORY DISTRESS SYNDROME**

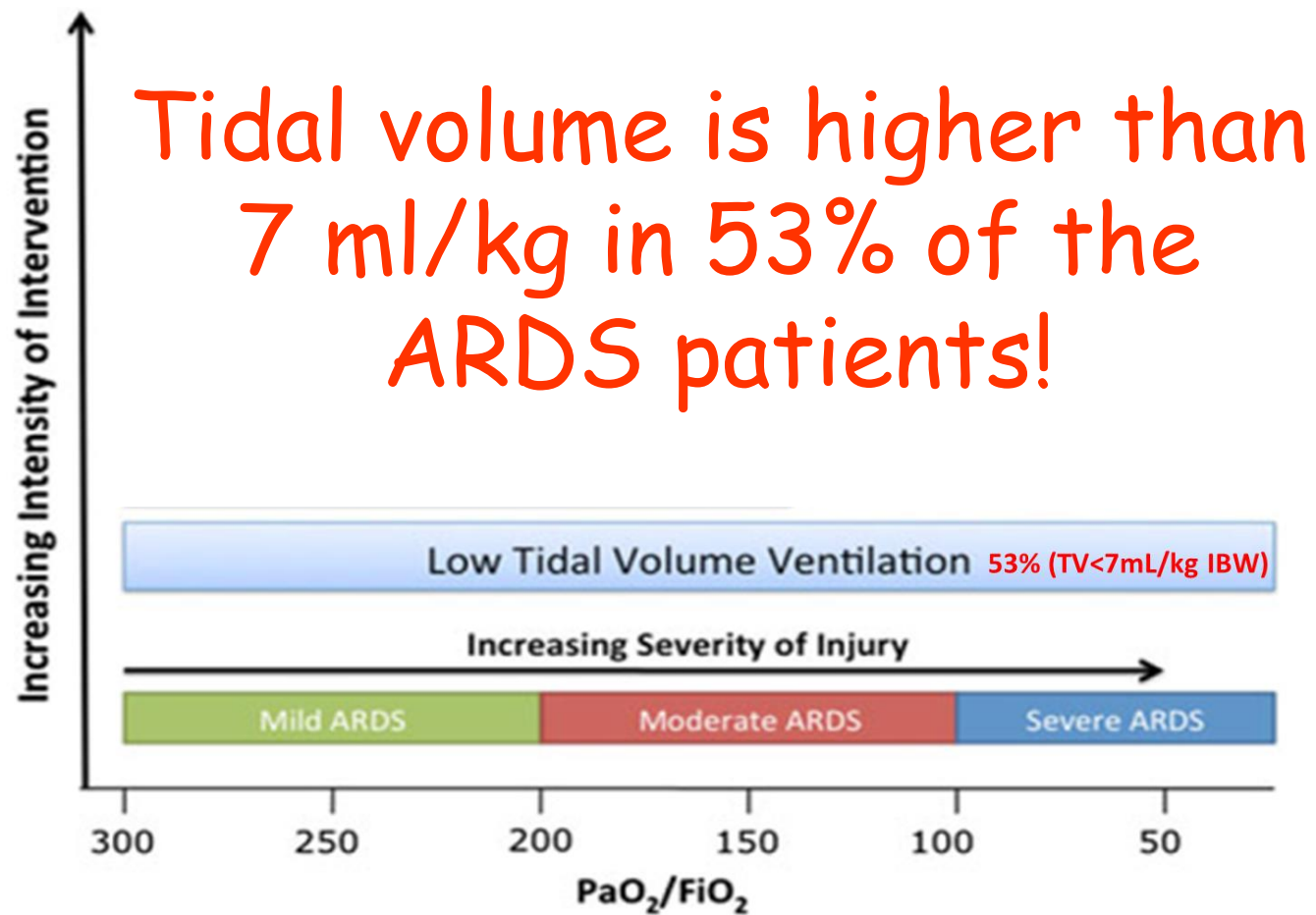
THE ACUTE RESPIRATORY DISTRESS SYNDROME NETWORK*

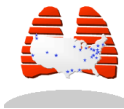
Beneficial effects





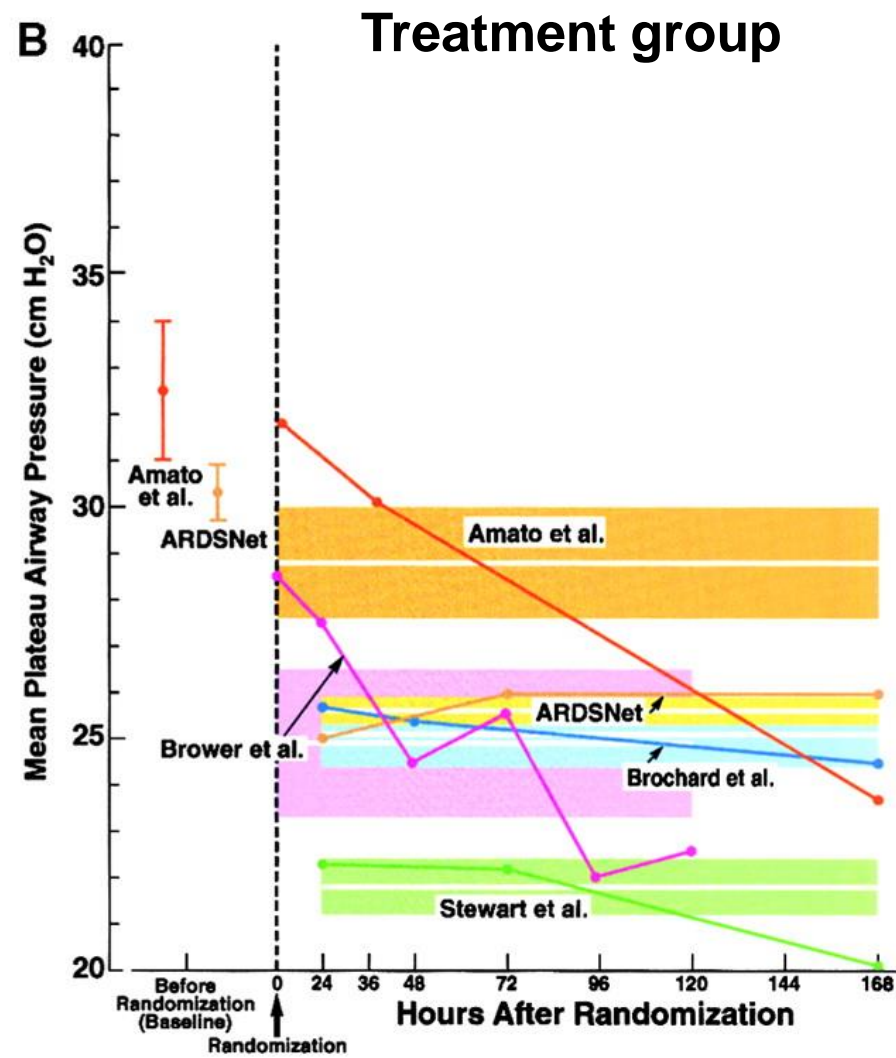
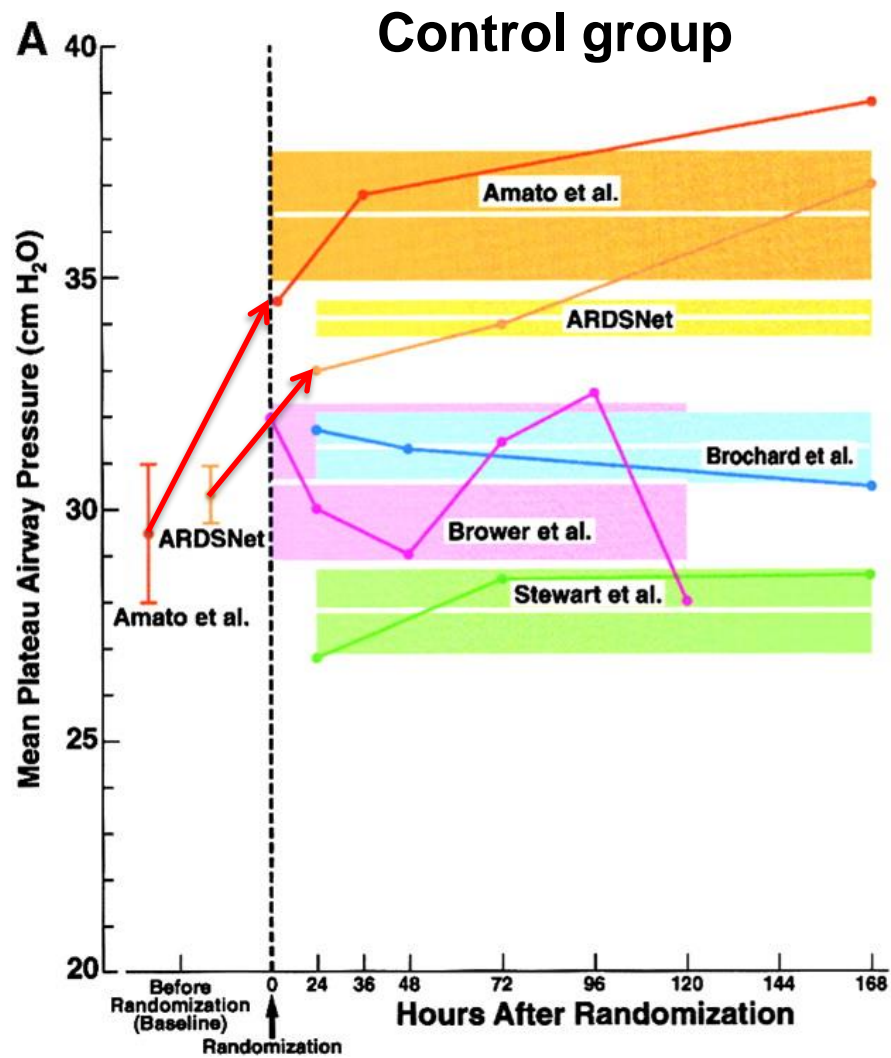
Lungsafe study





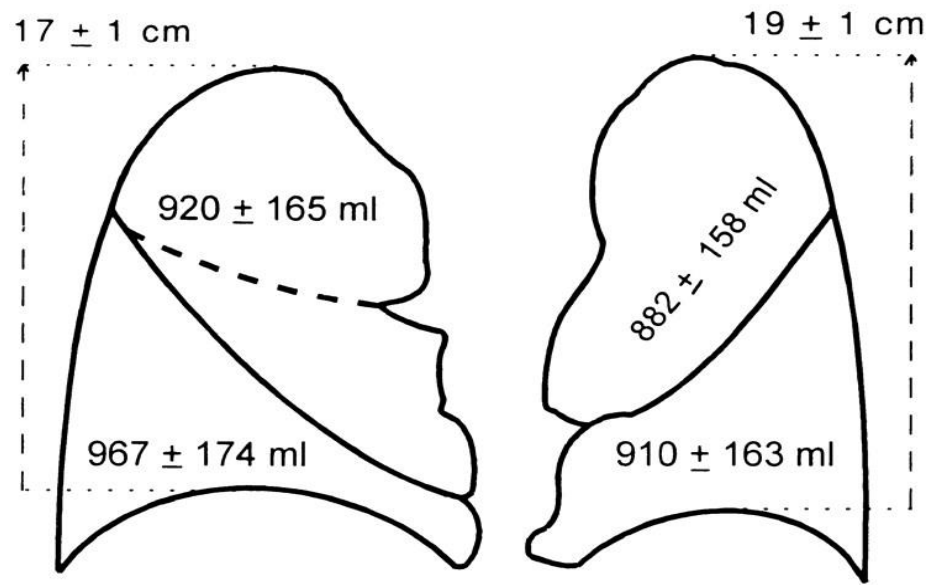
ARDSNET

	PLV	cont	PLV	cont	PLV	cont	PLV	cont	PLV	cont
n	60	60	26	26	58	58	29	24	400	400
Vt	7.0	10.7	7.5	10.2	7.1	10.5	6.0	12.0	6.2	11.8
PEEP	8.6	7.2	9.5	8.3	10.7	10.7	16.4	8.7	9.4	8.6
Pplat	22	27	28	31	26	32	30	37	25	33



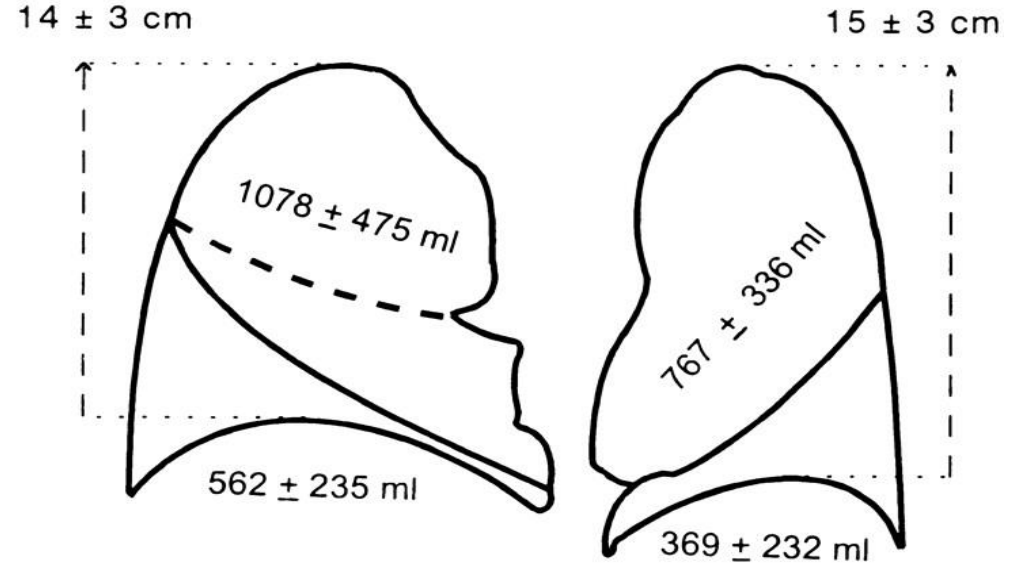
Lung volume reduction

LUNG VOLUMES IN 10 HEALTHY VOLUNTEERS

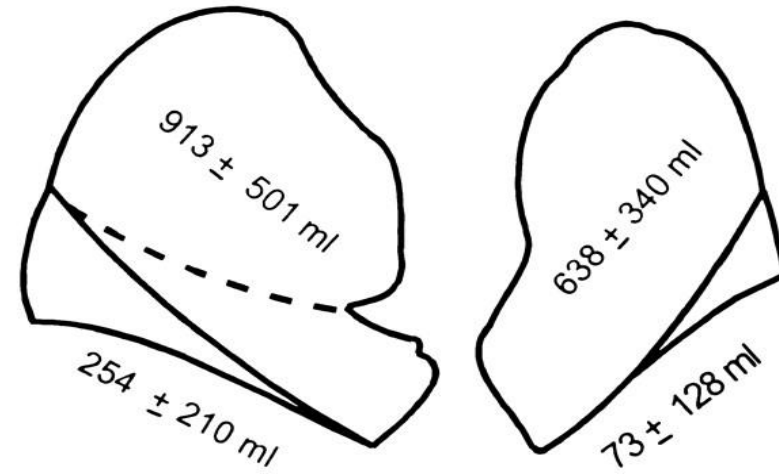


LUNG VOLUMES IN 21 PATIENTS WITH ALI

AERATED AND NON-AERATED LUNG

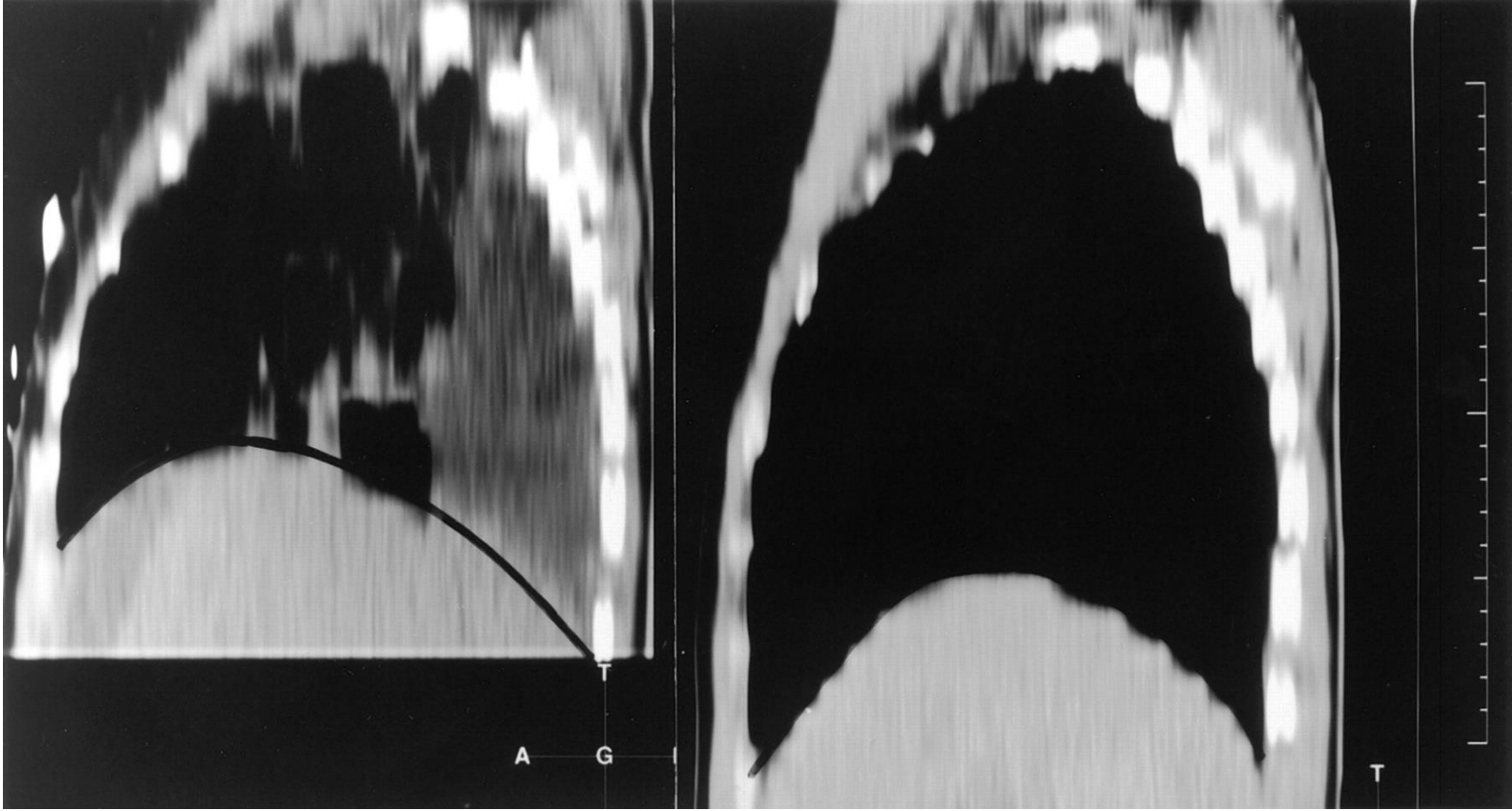


AERATED LUNG ONLY



Puybasset et al. AJRCCM 98

Lung volume reduction



Niveau de PEEP

"one-size-fits-all" approach

Higher-PEEP group (before protocol changed to use higher levels of PEEP)													
FiO ₂	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5	0.5	0.5-0.8	0.8	0.9	1.0
PEEP	5	8	10	12	14	14	16	16	18	20	22	22	22-24
Higher-PEEP group (after protocol changed to use higher levels of PEEP)													
FiO ₂	0.3	0.3	0.4	0.4	0.5	0.5	0.5-0.8	0.8	0.9	1.0			
PEEP	12	14	14	16	16	18	20	22	22	22-24			

	Fraction of Inspired Oxygen (FiO ₂)							
	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0
Control PEEP ranges, cm H ₂ O	5	5-8	8-10	10	10-14	14	14-18	18-24
Lung open ventilation PEEP ranges, cm H ₂ O								
Before protocol change	5-10	10-14	14-20	20	20	20	20	20-24
After protocol change	5-10	10-18	18-20	20	20	20-22	22	22-24

PEEP^b

Minimal distension group^c

Total PEEP between 5 and 9 cm H₂O

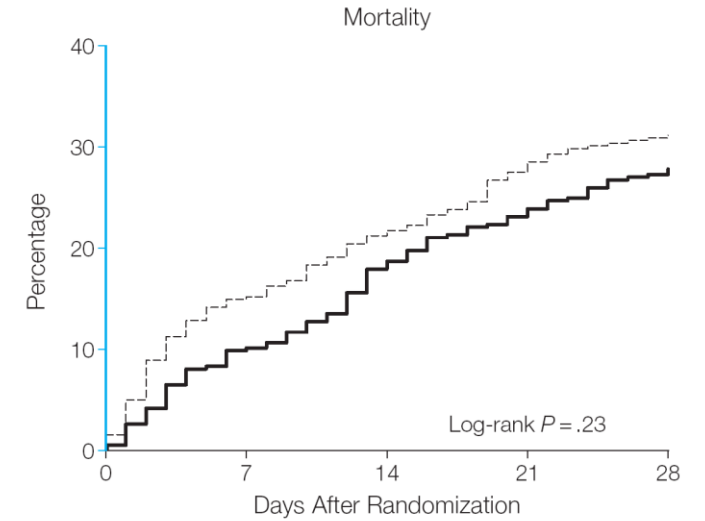
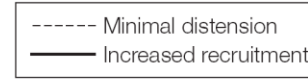
Increased recruitment group^d

Plateau pressure between 28 and 30 cm H₂O

High/Low PEEP

Mercat et al. JAMA 2008

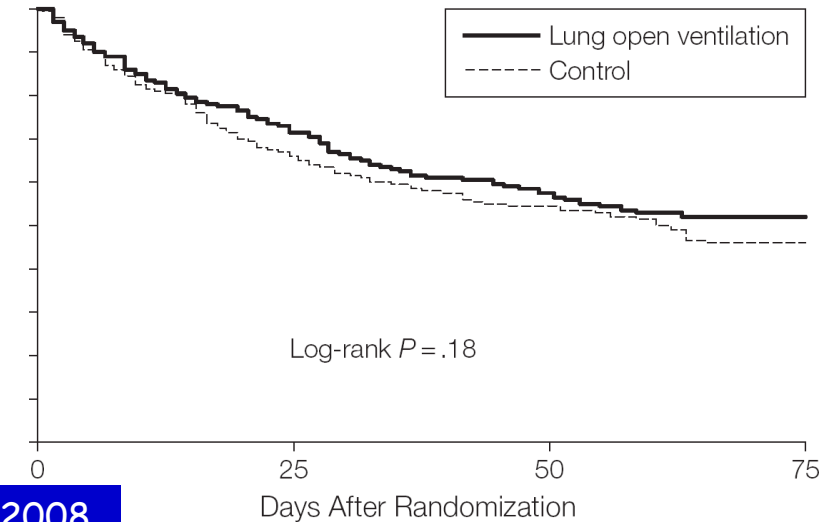
All Patients



No. at risk

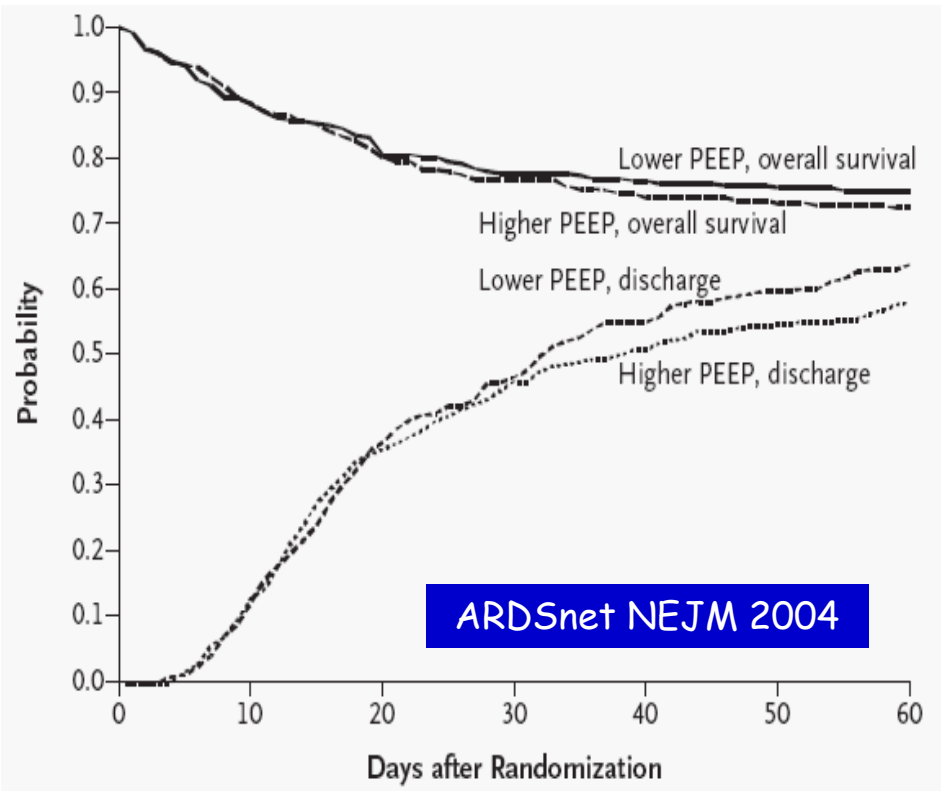
Minimal distension	382	325	301	277	264
Increased recruitment	385	347	316	296	280

All-cause mortality



O'Meade et al. JAMA 2008

475	223	91	43
508	220	97	47



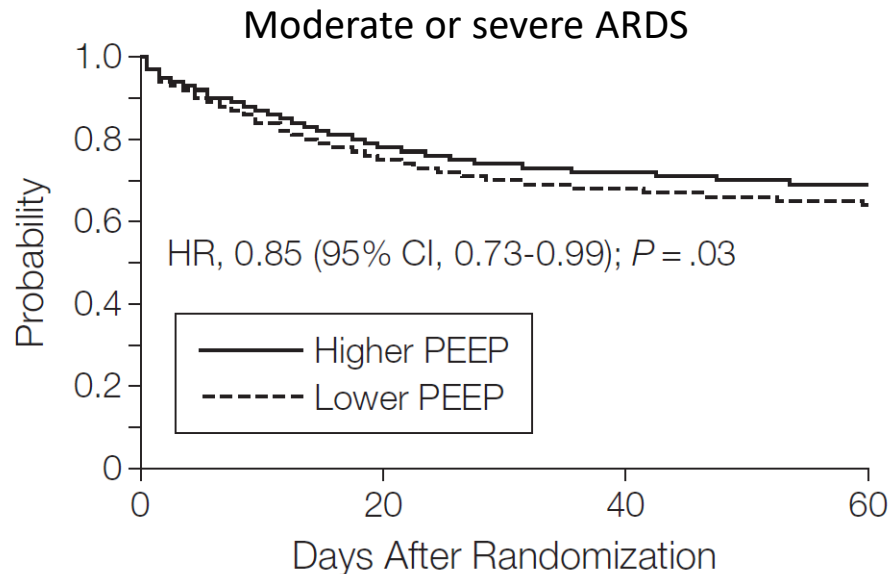
ARDSnet NEJM 2004

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

Systematic Review and Meta-analysis

Briel et al. JAMA 2010

In-hospital time to death



No. at risk

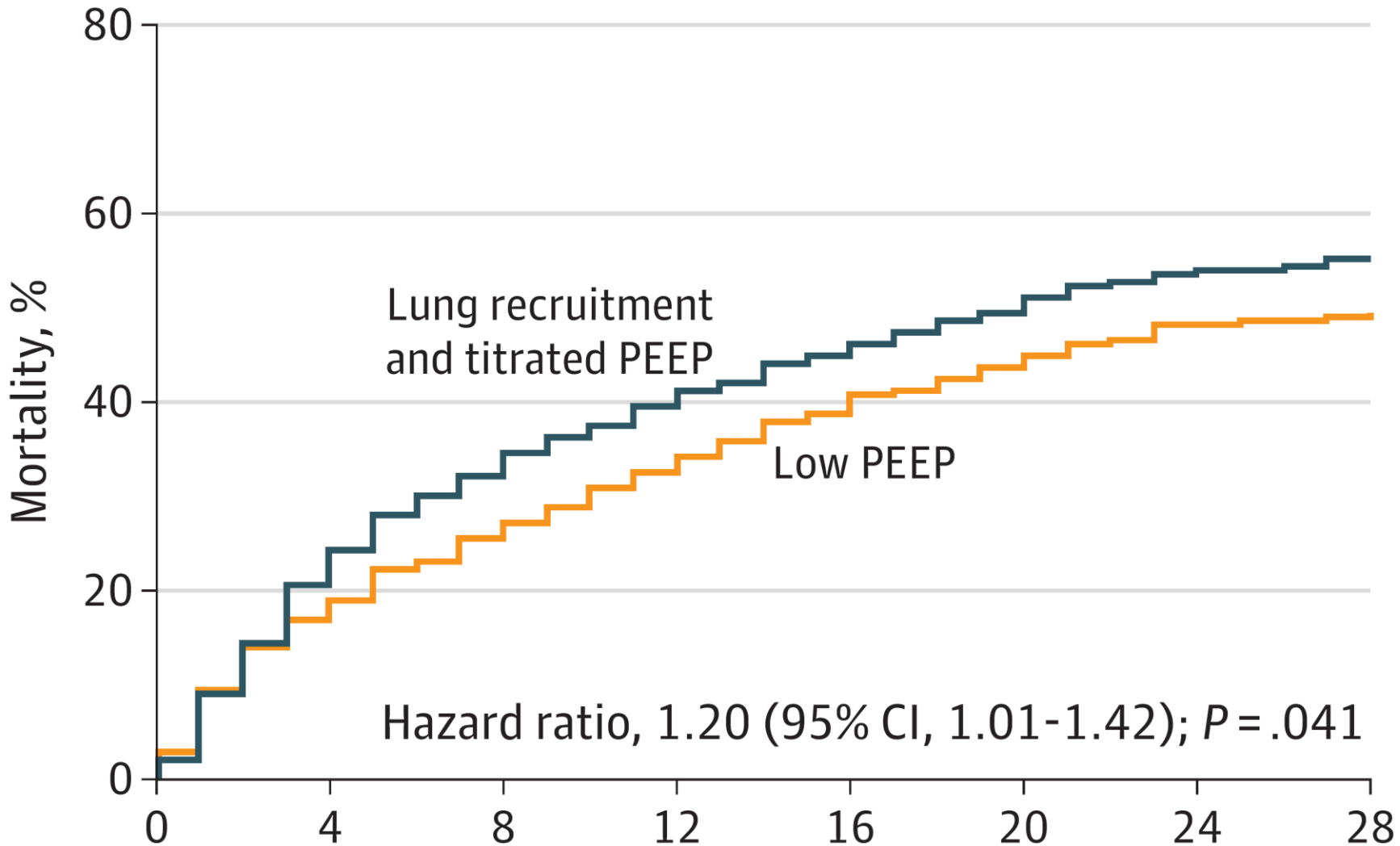
Higher PEEP	949	760	693	666	183	158	148	144
Lower PEEP	939	723	649	619	219	196	186	183

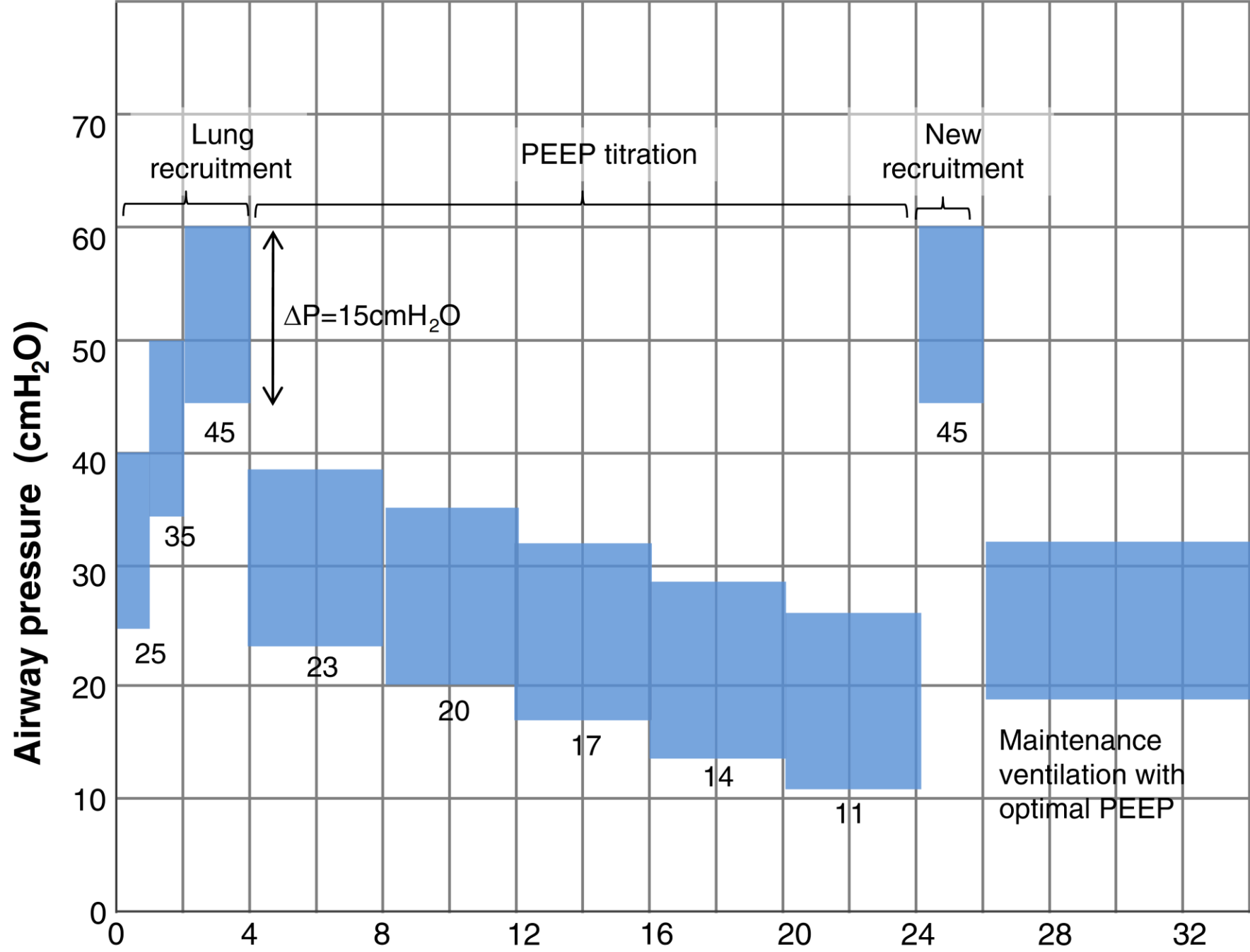
P/F ratio < 200 mmHg

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

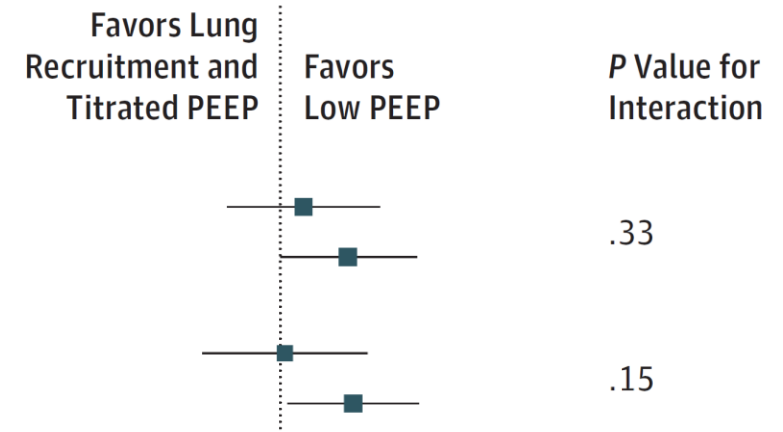
ART investigators JAMA 2017





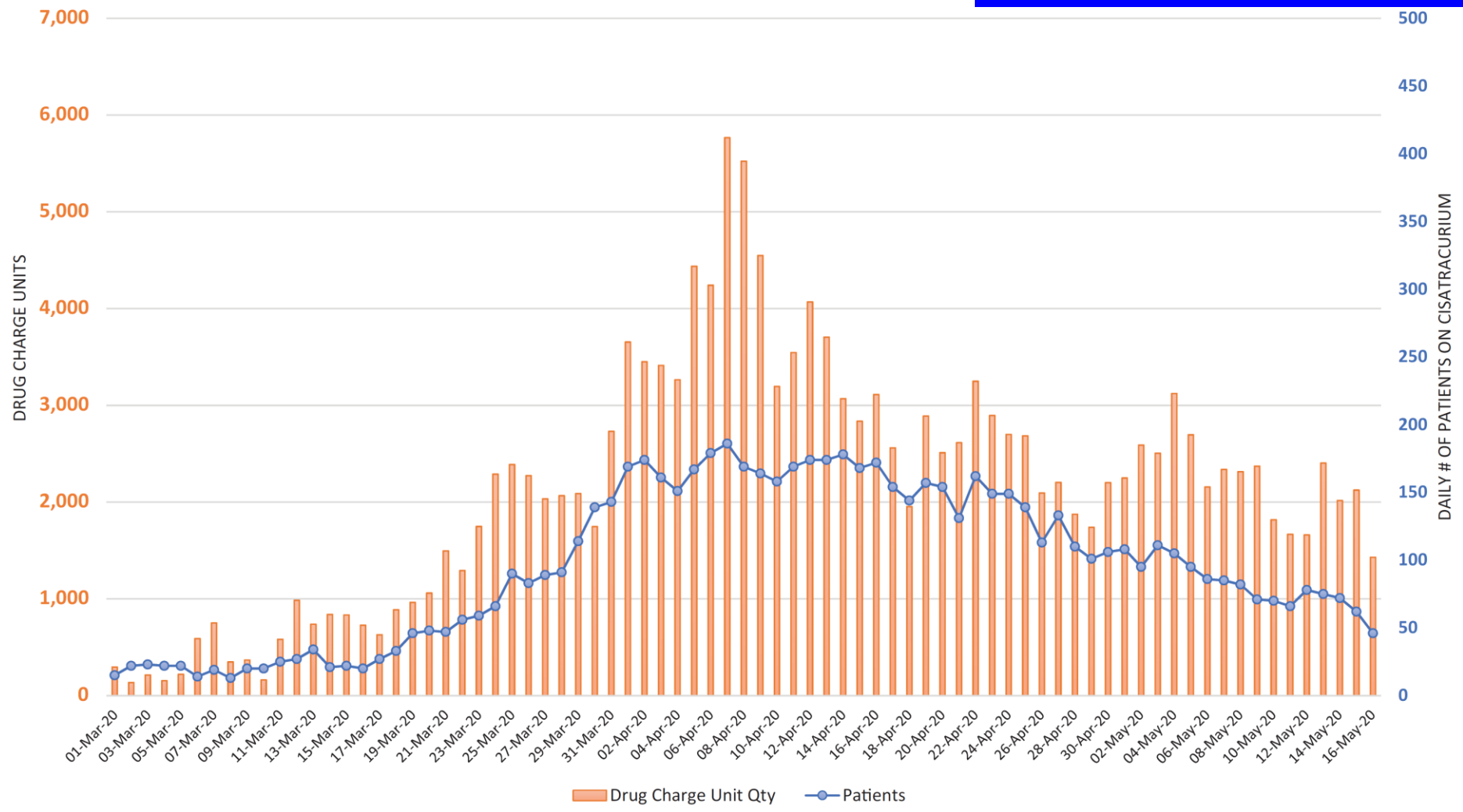
Variable	1hour			Day 1			Day 3			Day 7		
	Lung Recruitment Maneuver with PEEP Titration Group	Control Group	P Value	Lung Recruitment Maneuver with PEEP Titration Group	Control Group	P Value	Lung Recruitment Maneuver with PEEP Titration Group	Control Group	P Value	Lung Recruitment Maneuver with PEEP Titration Group	Control Group	P Value
Tidal volume, mean (95% CI), mL/kg of predicted body weight	5.4 (5.3 to 5.5)	5.5 (5.5 to 5.6)	0.004	5.6 (5.5 to 5.7)	5.7 (5.7 to 5.8)	0.006	5.8 (5.6 to 5.9)	5.8 (5.8 to 5.9)	0.20	6.1 (6.0 to 6.3)	6.2 (6.0 to 6.3)	0.67
No. of patients	500	507		482	490		418	431		296	325	
Tidal volume > 6.5 mL/kg of predicted body weight, No. of events / total No. (%)	30/500 (6.0)	36/507 (7.1)	0.56	54/482 (11.2)	49/490 (10)	0.61	64/418 (15.3)	66/431 (15.3)	>0.99	78/296 (26.4)	85/324 (26.2)	>0.99
PEEP, mean (95% CI), cmH ₂ O	16.4 (16.0 to 16.7)	13.0 (12.7 to 13.3)	<0.001	16.2 (15.9 to 16.6)	12.0 (11.7 to 12.3)	<0.001	14.2 (13.8 to 14.6)	10.5 (10.2 to 10.9)	<0.001	11.6 (11.2 to 12.1)	9.6 (9.3 to 10.0)	<0.001
No. of patients	499	507		481	490		418	432		296	326	
Plateau pressure, mean (95% CI), cmH ₂ O	27.9 (27.5 to 28.3)	25.9 (25.5 to 26.3)	<0.001	27.9 (27.5 to 28.3)	25.4 (25.0 to 25.9)	<0.001	26.3 (25.8 to 26.9)	24.0 (23.5 to 24.6)	<0.001	24.1 (23.4 to 24.8)	23.2 (22.5 to 23.8)	0.05
No. of patients	498	503		478	488		417	431		294	325	
Plateau pressure > 30 cmH ₂ O, No. of events / total No. (%)	80/498 (16.1)	45/503 (8.9)	0.001	83/478 (17.4)	52/488 (10.7)	0.004	55/417 (13.2)	37/431 (8.6)	0.04	22/294 (7.5)	25/325 (7.7)	>0.99
Driving pressure, mean (95% CI), cmH ₂ O	11.5 (11.1 to 11.8)	13.0 (12.6 to 13.3)	<0.001	11.7 (11.3 to 12.1)	13.5 (13.1 to 13.8)	<0.001	12.1 (11.7 to 12.5)	13.5 (13.1 to 13.9)	<0.001	12.5 (12.0 to 12.9)	13.6 (13.1 to 14.1)	0.001

Subgroup	No. of Deaths/Total No. (%)		Hazard Ratio (95% CI)
	Lung Recruitment and Titrated PEEP (n = 501)	Low PEEP (n = 509)	
PaO₂: FIO₂			
≤100 mm Hg	117/197 (59.4)	120/214 (56.1)	1.09 (0.82-1.46)
>100 mm Hg	160/304 (52.6)	131/295 (44.4)	1.30 (1.00-1.69)
Type of ARDS			
Extrapulmonary	98/188 (52.1)	102/196 (52)	1.02 (0.74-1.40)
Pulmonary	179/313 (57.2)	149/313 (47.6)	1.32 (1.03-1.69)

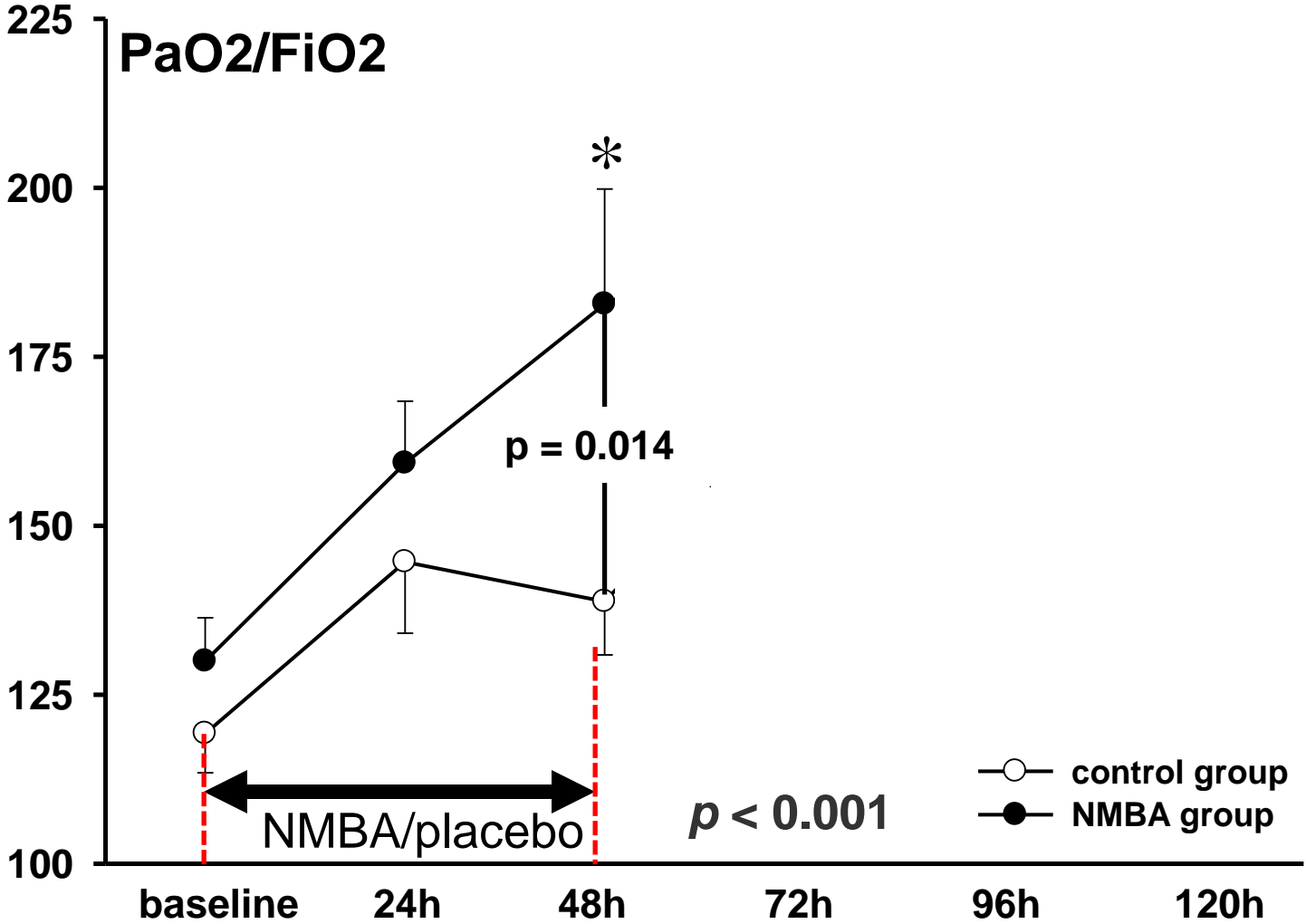


Daily count of patients who received cisatracurium and corresponding net charge-unit quantities from March 1 through May 16, 2020

Dabestani et al. Am J Health Syst Pharm 2020

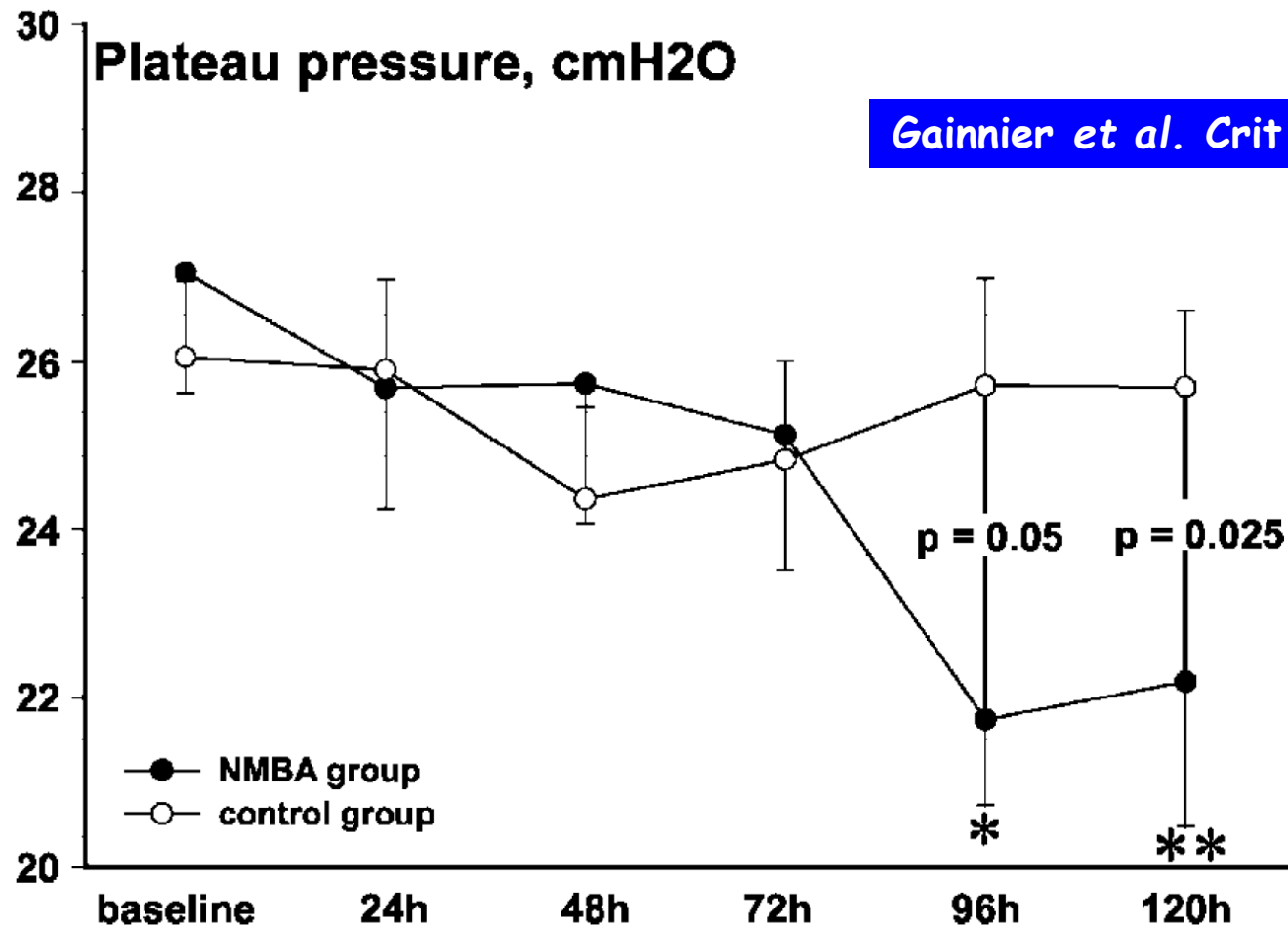


Effect of cisatracurium on oxygenation



4 ICUs - 56 patients

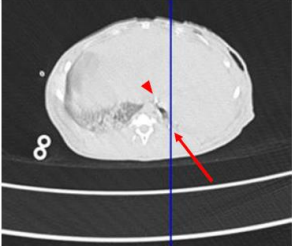
Gainnier et al. Crit Care Med 2004



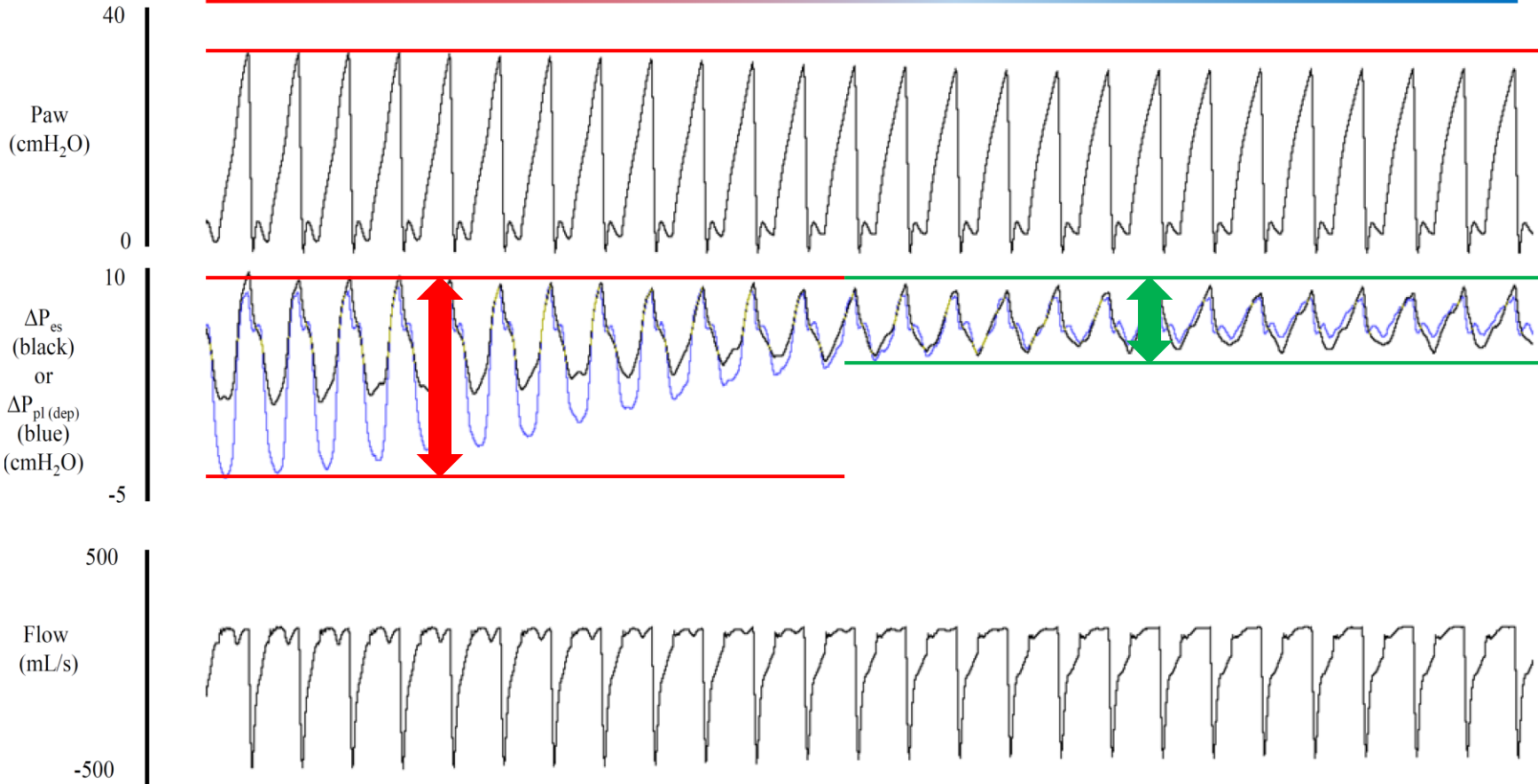
V_T, mL/kg IBW

	baseline	24h	48h	72h	96h	120h
NMBA	7.1 ± 1.1	7.0 ± 1.1	7.0 ± 1.0	7.2 ± 1.0	7.5 ± 1.8	7.0 ± 2.3
Control	7.5 ± 1.9	7.4 ± 1.4	7.6 ± 1.5	7.4 ± 1.6	7.8 ± 1.9	7.7 ± 1.4

Regional lung stress

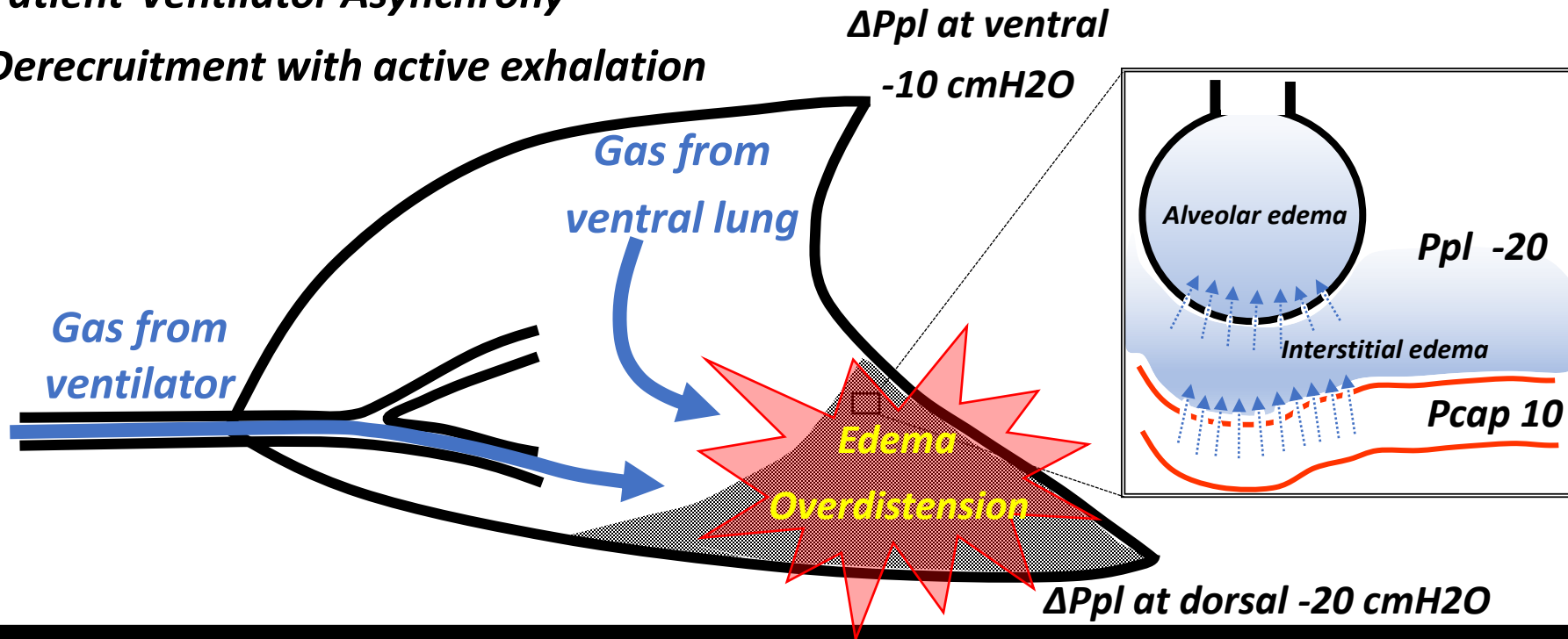


I.V. of Neuromuscular blocking agent

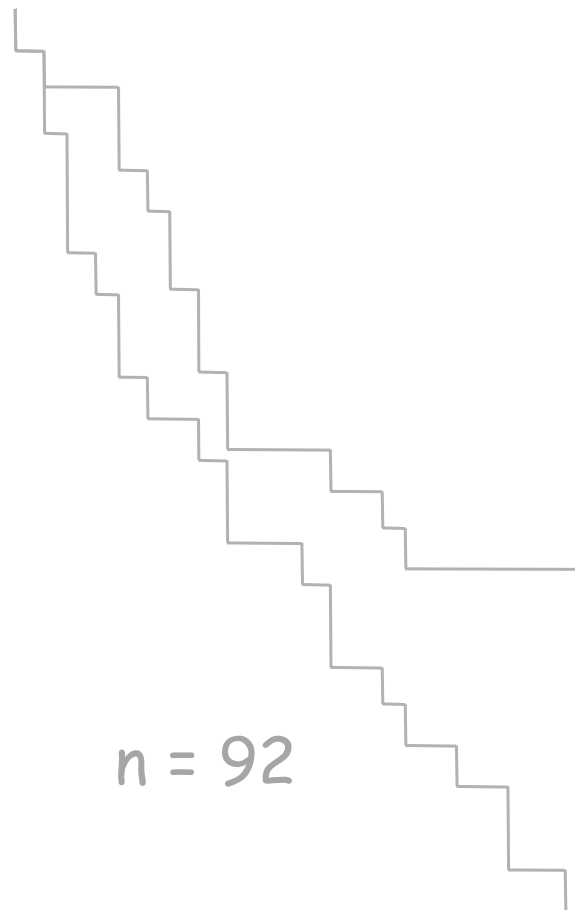


Vigorous Spontaneous Effort Causes...

- **Global Overdistension**
- **Maldistribution of Lung stress & Local Overdistension**
- **Increased Lung Perfusion & Lung Edema**
- **Patient-Ventilator Asynchrony**
- **Derecruitment with active exhalation**



Mortality

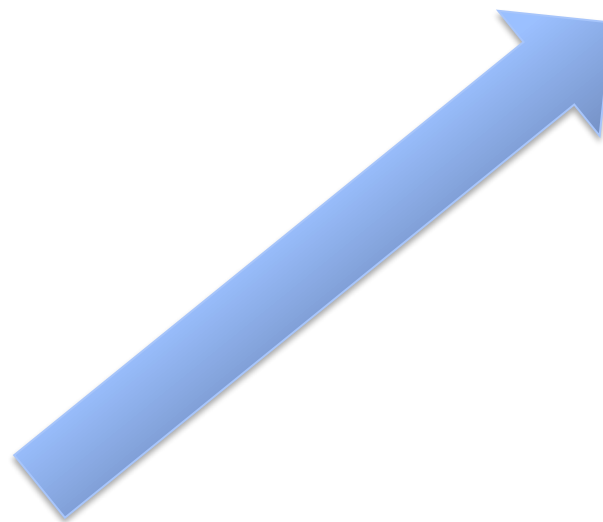


Gainnier et al. CCM 2004

+

Forel et al. CCM 2006

ACURASYS



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 Seghboyen, 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., Gwenaél Prat, M.D., Sophie Morange, M.D., and Antoine Roch, M.D., Ph.D.,
for the ACURASYS Study Investigators*

Important methodological aspects

- Prospective, randomized, double-blind study

cisatracurium vs. placebo

- Vt 6-8 ml/kg, Pplat \leq 32 cmH₂O

- Inclusion criteria:

$\text{PaO}_2:\text{FiO}_2 < 150$ (PEEP ≥ 5) for < 48 h

EARLY IN THE COURSE OF ARDS

ACURASYS strategy

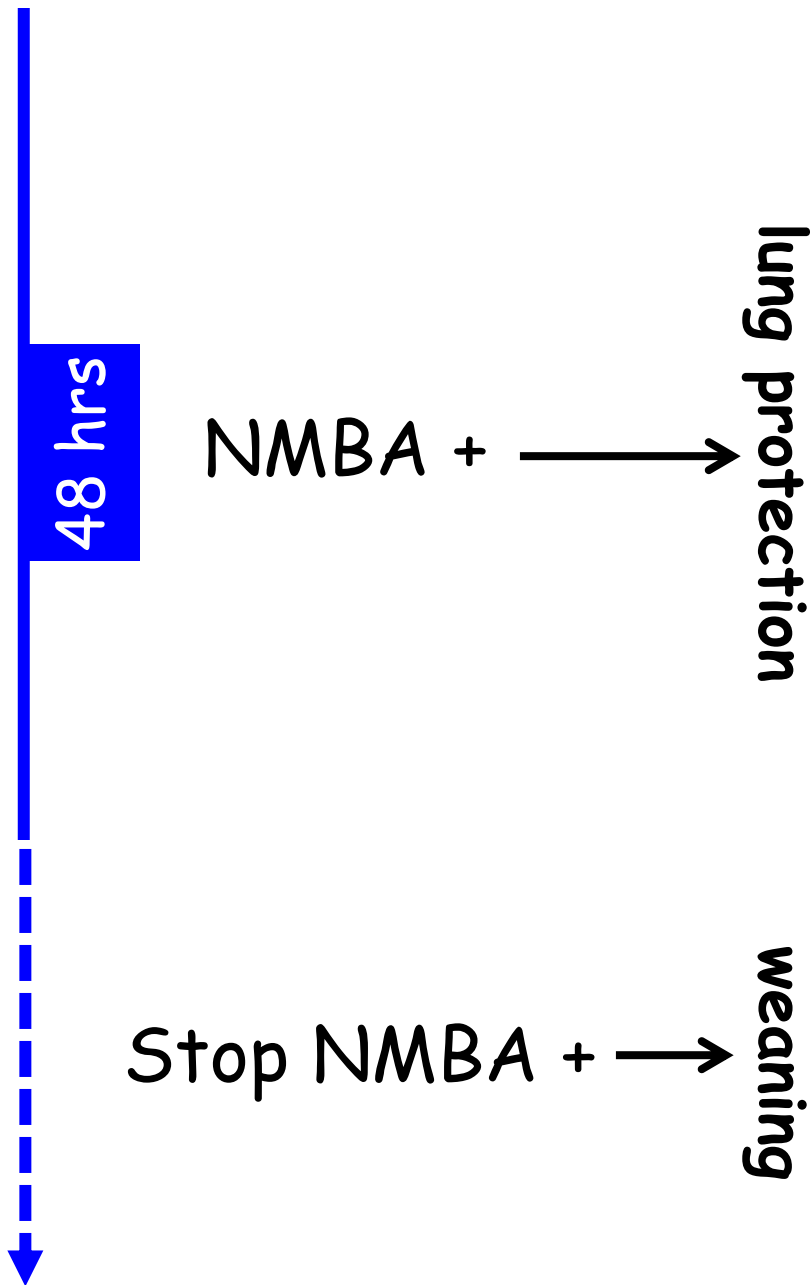


Table 1. Summary of the Ventilation Procedure.*

Variable

Ventilator mode: volume assist-control

Initial tidal volume: 6–8 ml/kg of predicted body weight

Plateau pressure: ≤32 cm of water

Plateau pressure limitation

ARMA PEEP/FiO₂ Table «low PEEP»

iNO, almitrine, prone position

Control hypercapnia

Injection of cisatracurium in a bolus of 20 mg (not to be given again if plateau pressure decreased by <2 cm of water because further doses would probably be futile, but permitted if the drug had its intended effect)

Procedure to correct hypercapnia when pH is <7.20 (in the following order, as needed): connect Y-piece directly to endotracheal tube, increase respiratory rate to a maximum of 35 cycles per min, and increase tidal volume to a maximum of 8 ml/kg

Weaning attempt: starting on day 3 if FiO₂ <0.6

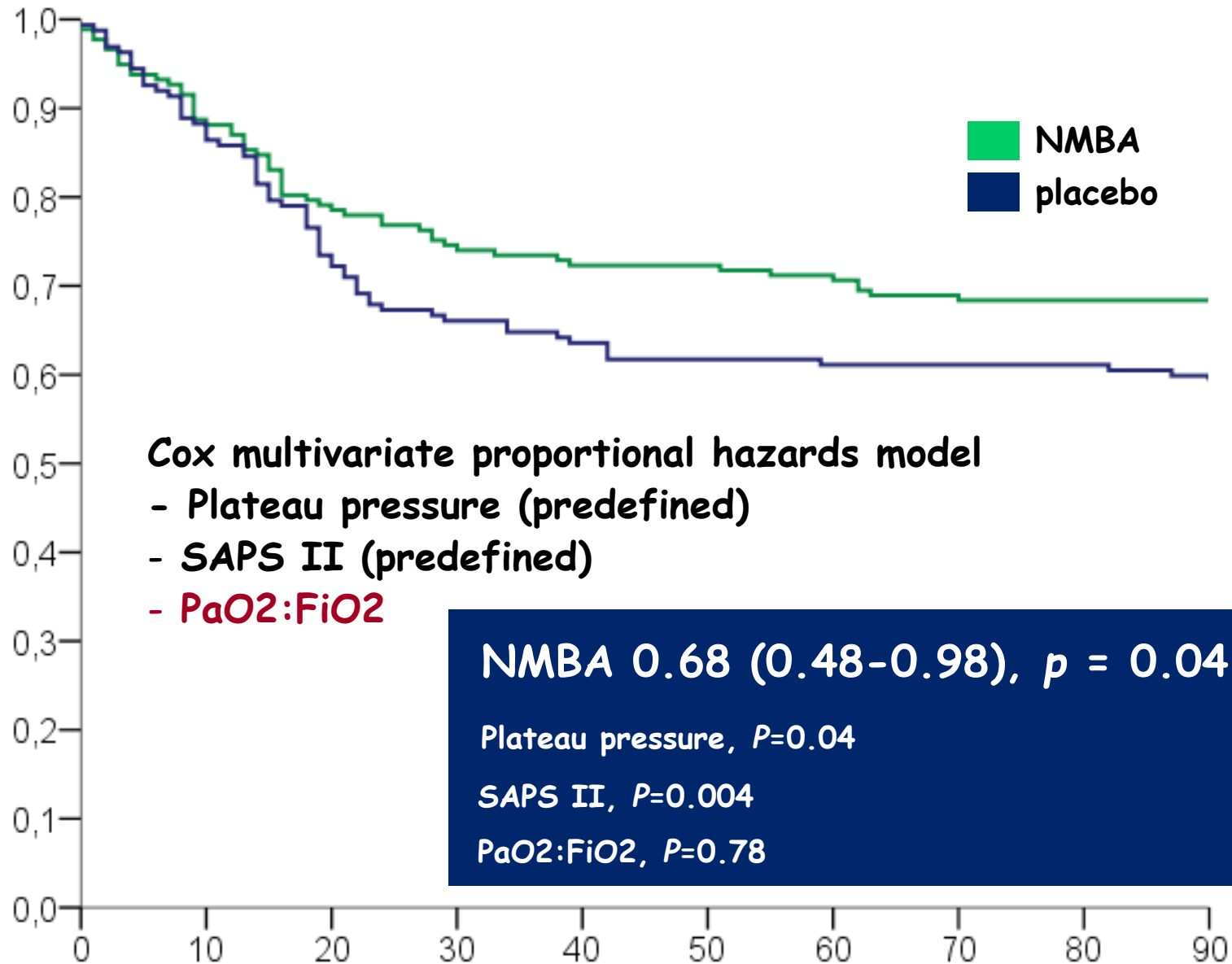
3rd day: ↘ PEEP

PS 20-15-10-5

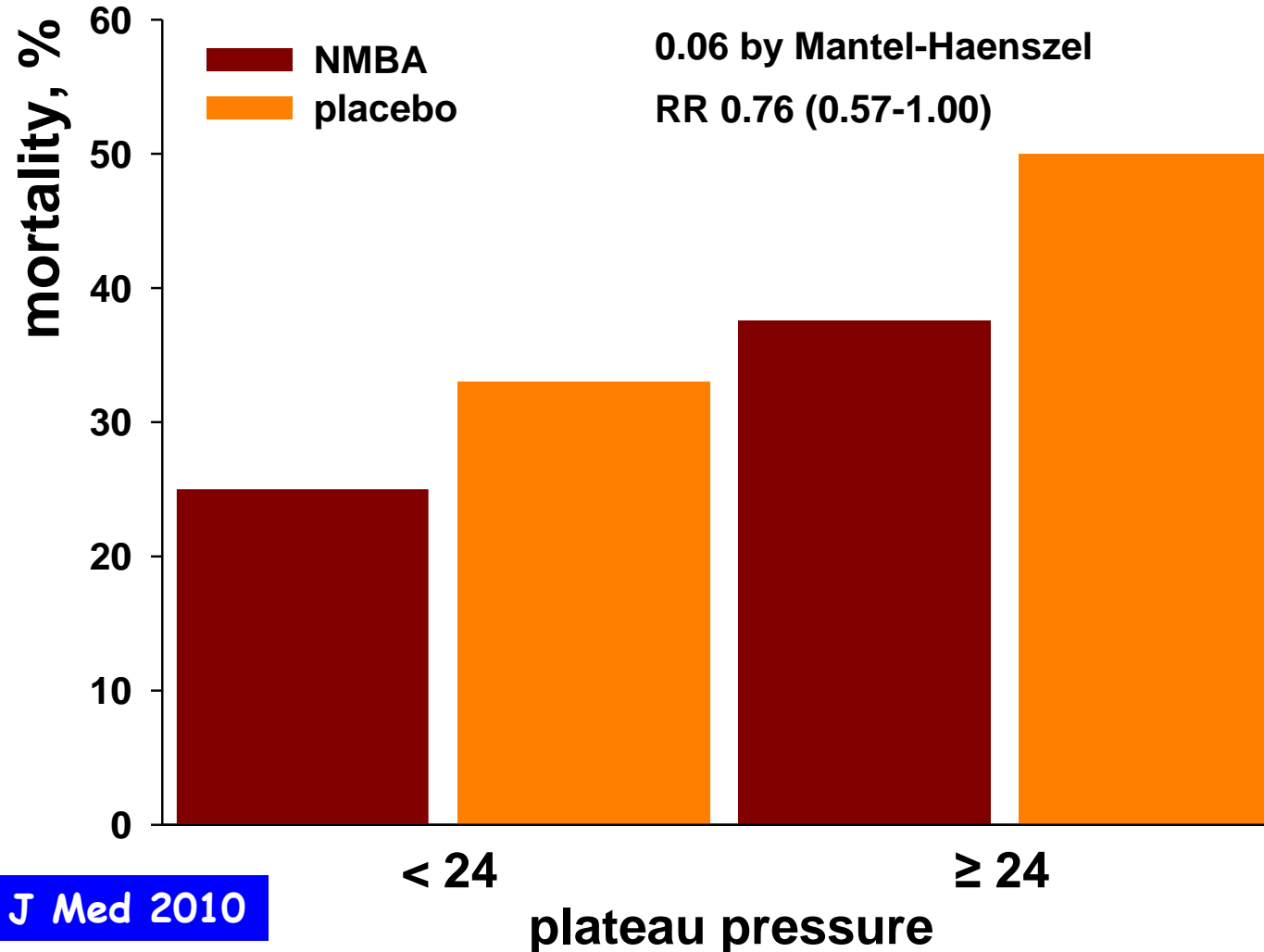
SV

Survival curve

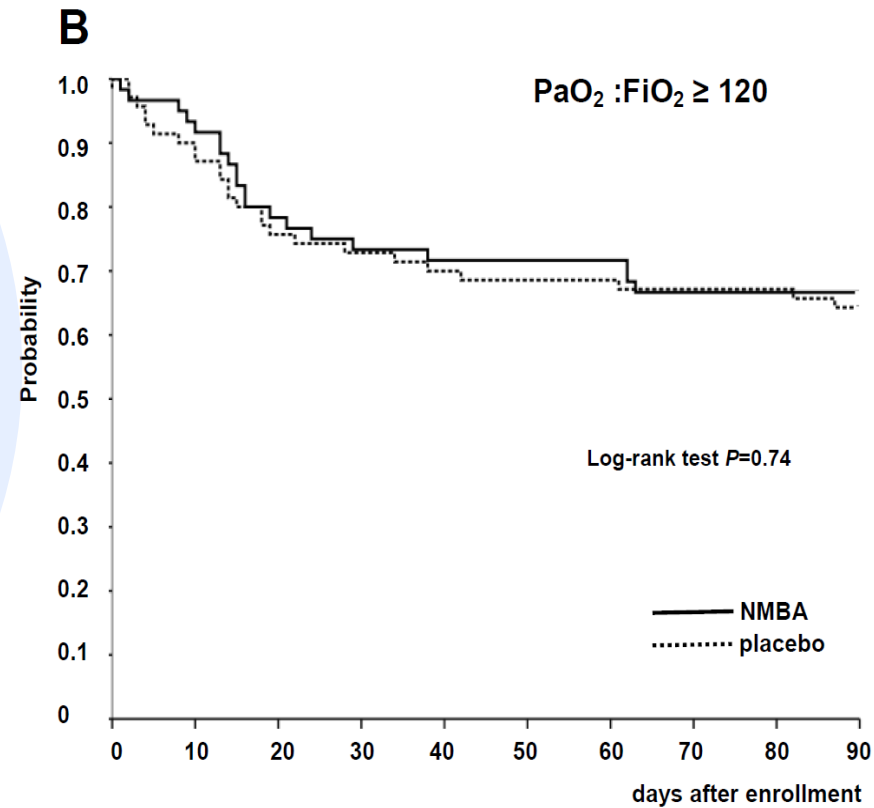
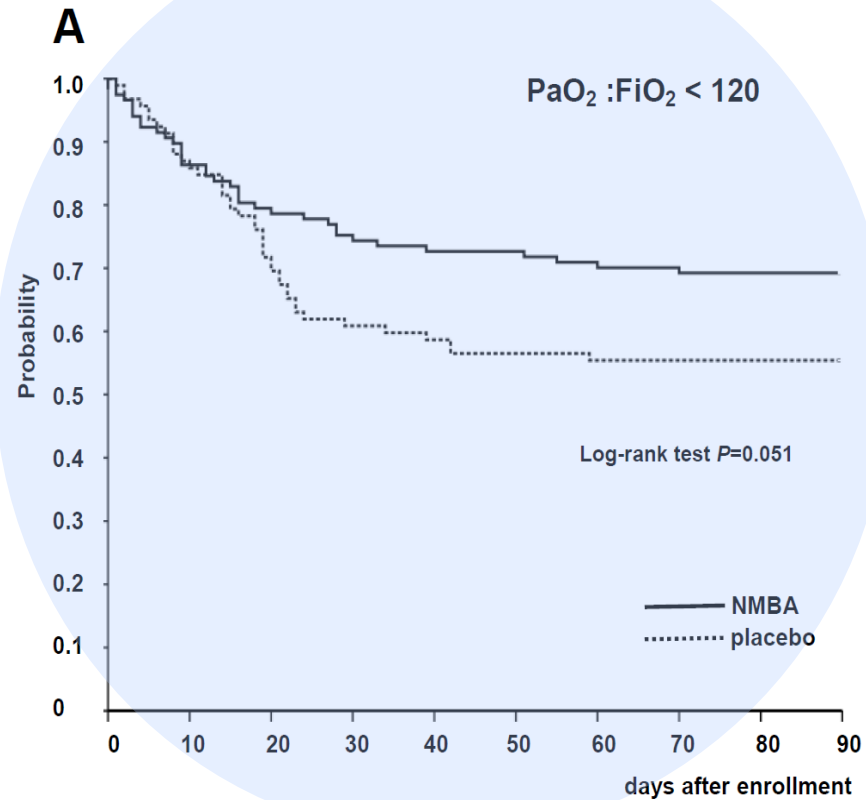
ACURASYS



Mortality d90 and plateau pressure on inclusion



Mortality according to P/F ratio

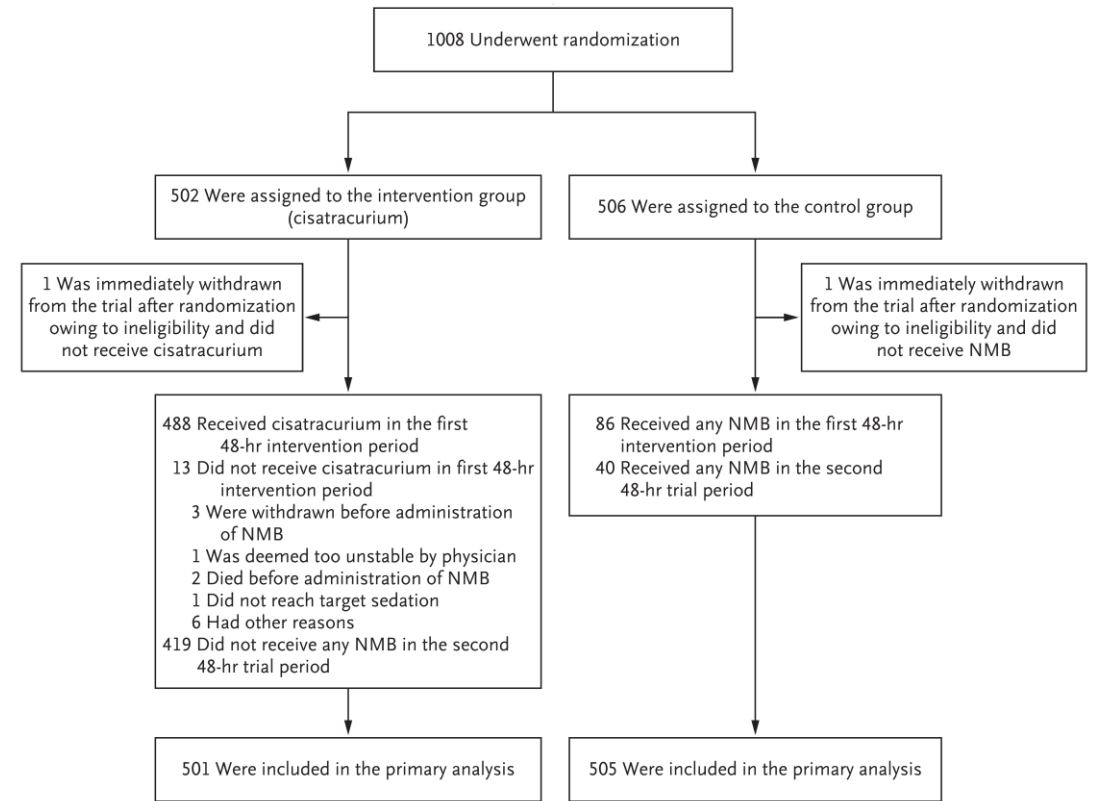
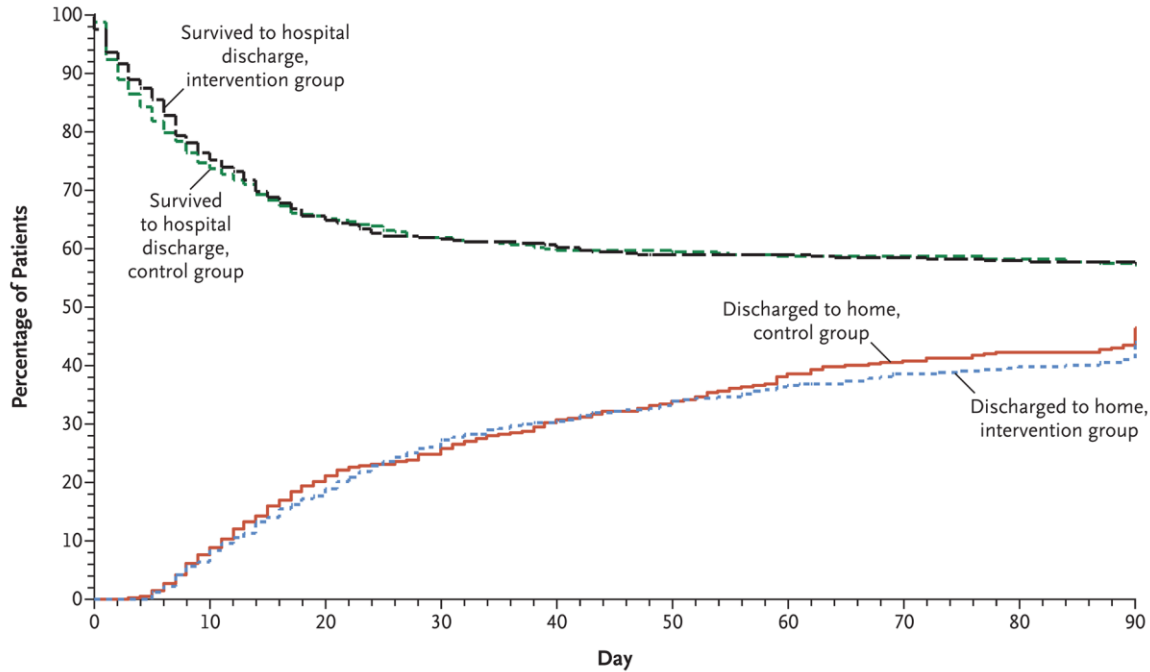


ACURASYS

ORIGINAL ARTICLE

Early Neuromuscular Blockade in the Acute Respiratory Distress Syndrome

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



ACURASYS

- Median time from the diagnosis of ARDS to inclusion
 - 16 hrs (6-29)
- Median time from initiation of MV to inclusion
 - Cis 22 hrs (9-41)
 - Placebo 21 hrs (10-42)

ROSE

- Median of 7.6 hrs (3.7-15.6) after diagnosis of moderate-to-severe ARDS
- ?

Sedation/paralysis

ACURASYS

1. Sedation -> Ramsay 6
2. Ventilator settings
3. Cisatracurium/placebo
4. Stop at 48 hr

ROSE

4848 Patients were assessed for eligibility

3840 Were excluded

658 Had $\text{PaO}_2:\text{FiO}_2 >200$ mm Hg at time of randomization

655 Were receiving continuous NMB at enrollment

394 Declined to participate or had surrogate who declined

384 Were not expected to survive 24 hr

307 Were withdrawn by physician

270 Did not have surrogate available

245 Had been receiving mechanical ventilation for >120 hr

237 Had severe chronic liver disease

209 Had inclusion criteria for >48 hr

159 Decided to withhold life-sustaining treatment

124 Had body weight >1 kg/cm of height

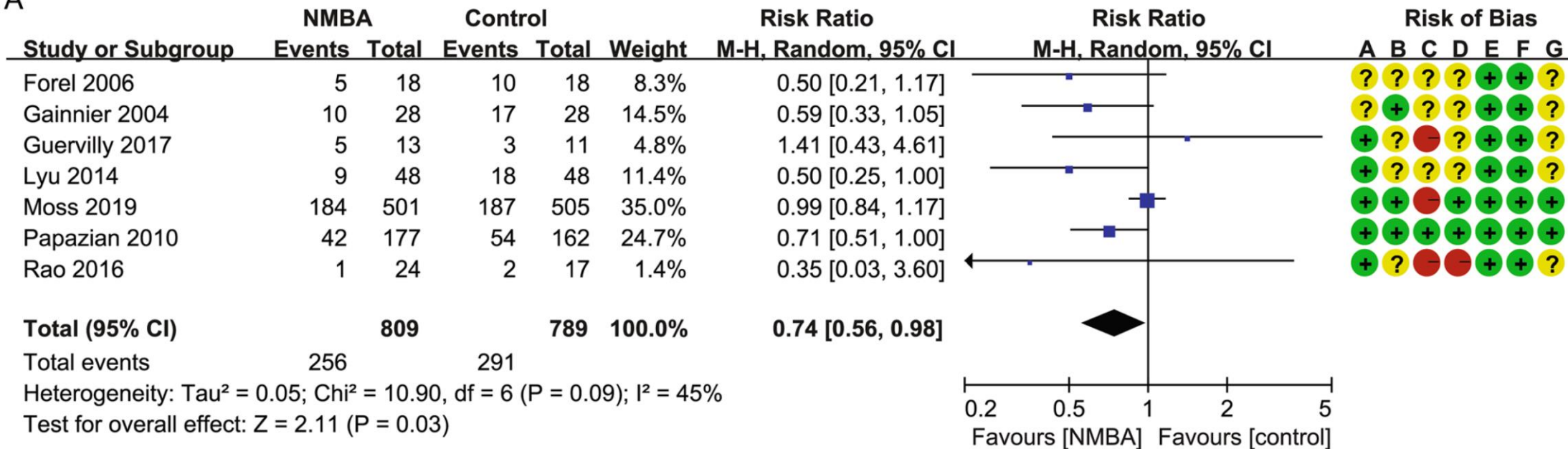
113 Were receiving extracorporeal membrane oxygenation

109 Were expected to receive mechanical ventilation for <48 hr

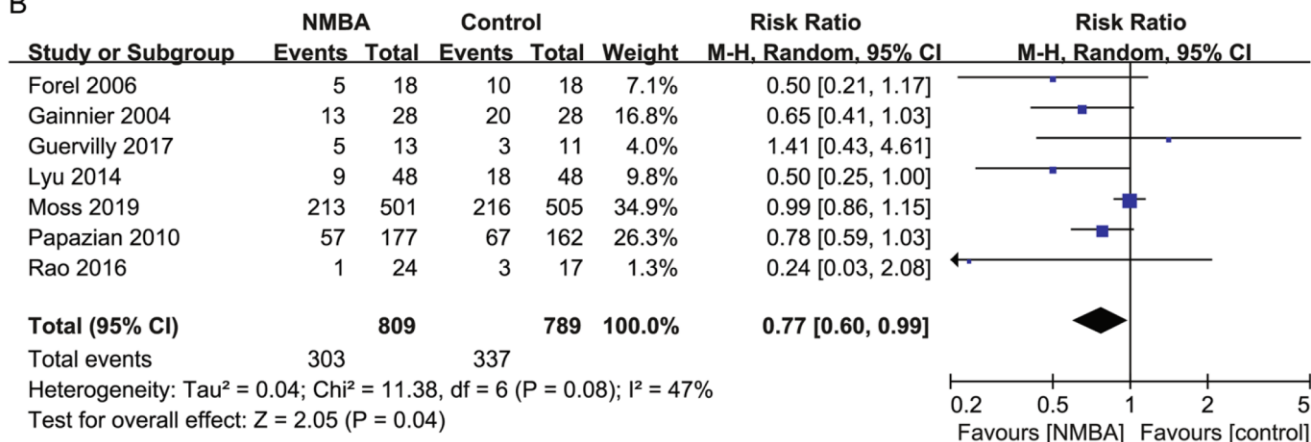
561 Had other reason

1008 Underwent randomization

A



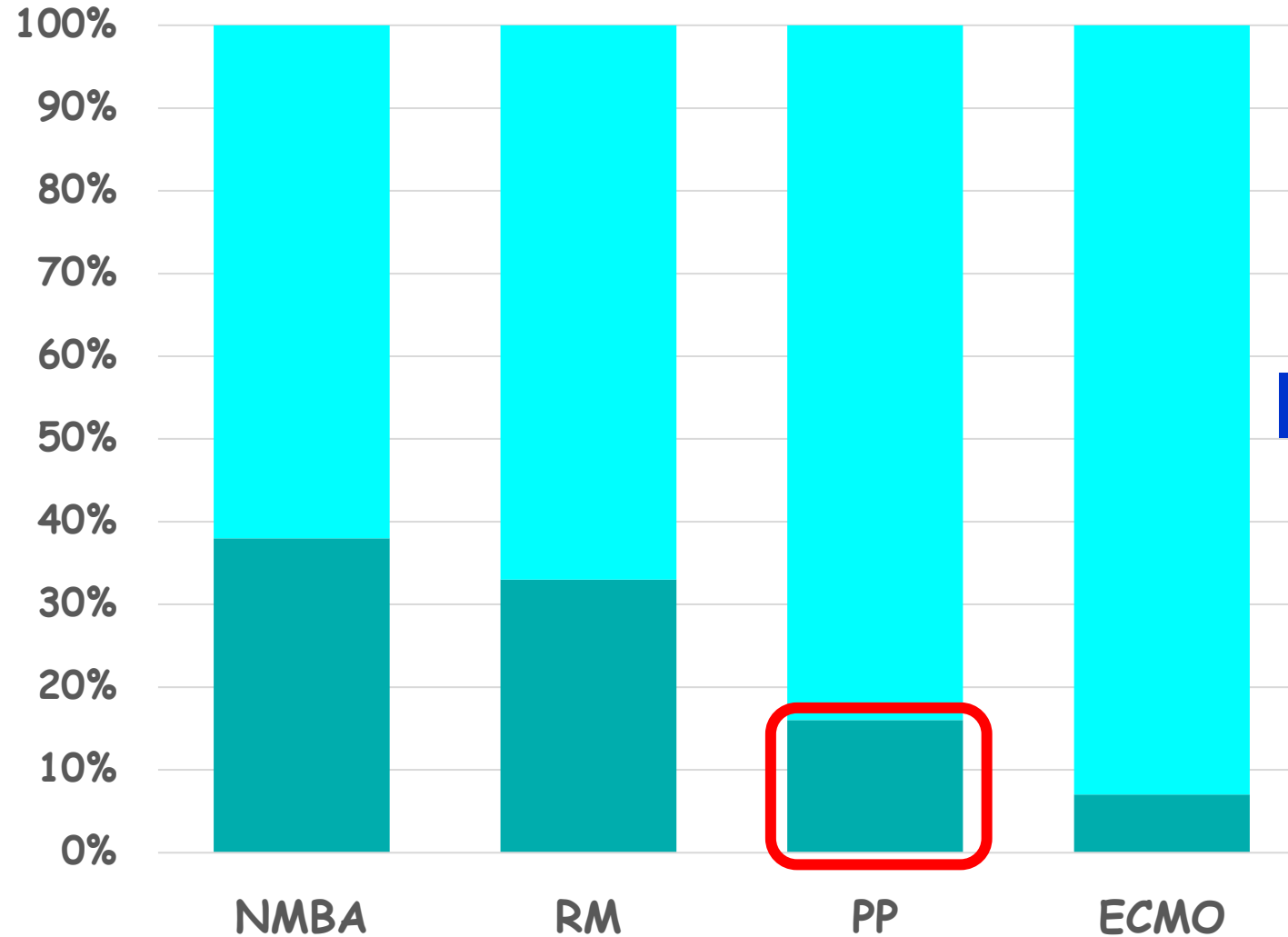
B



Décubitus ventral

LUNG SAFE

Severe ARDS patients



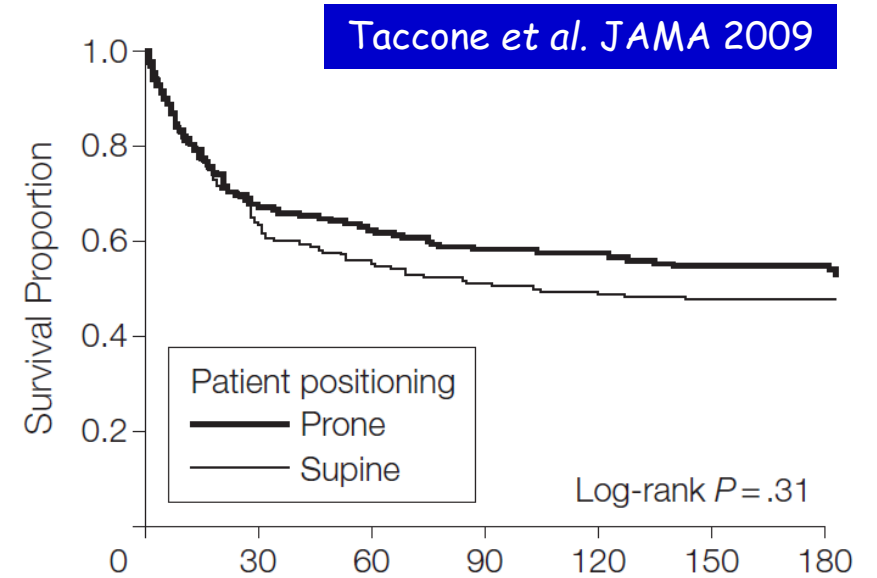
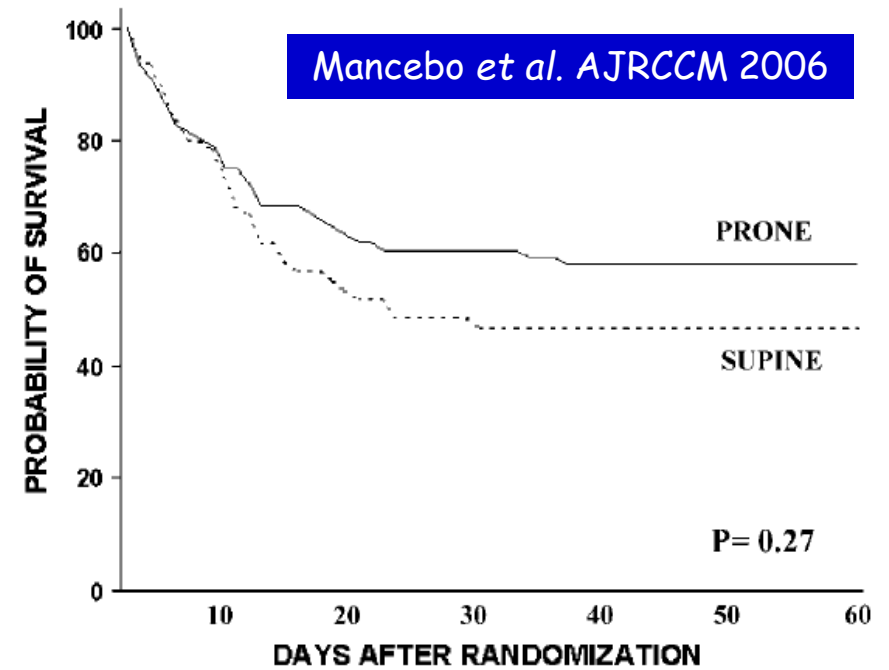
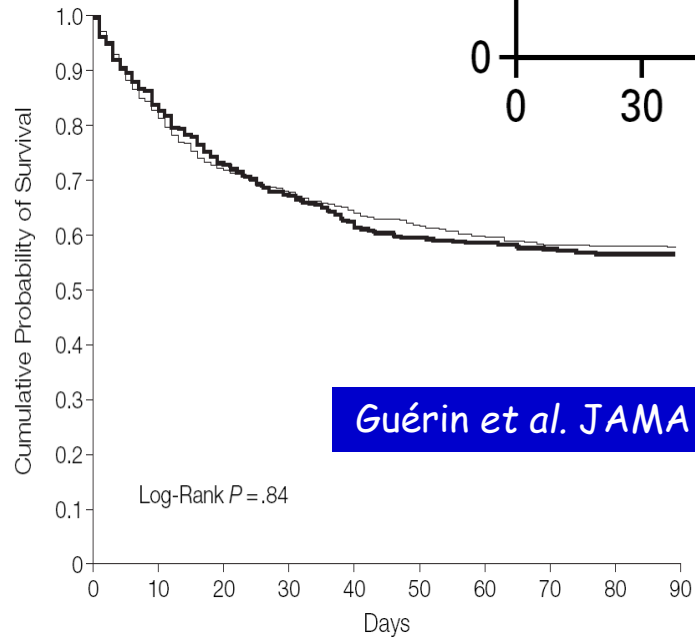
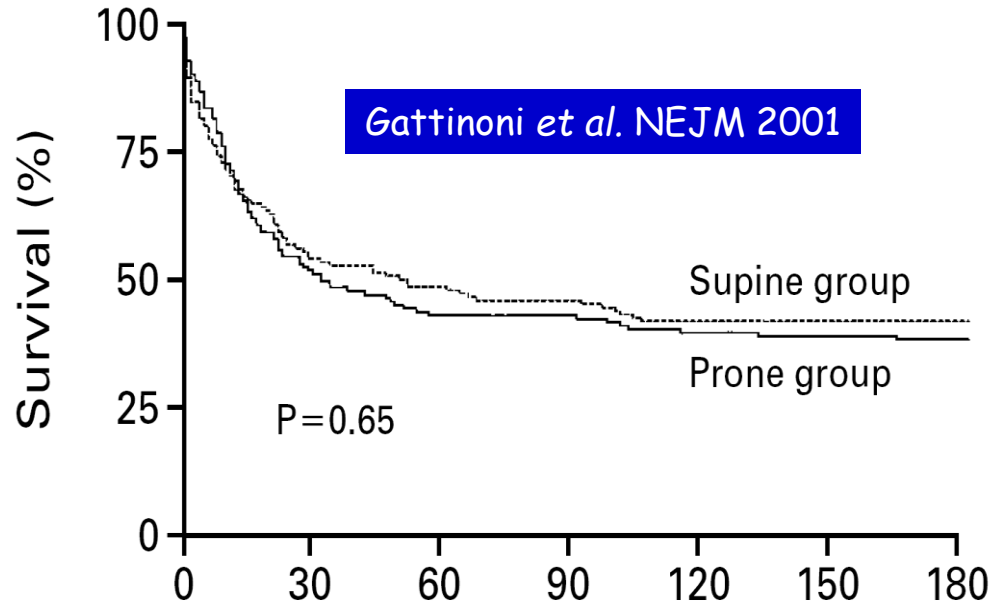
Bellani *et al.* JAMA 2016

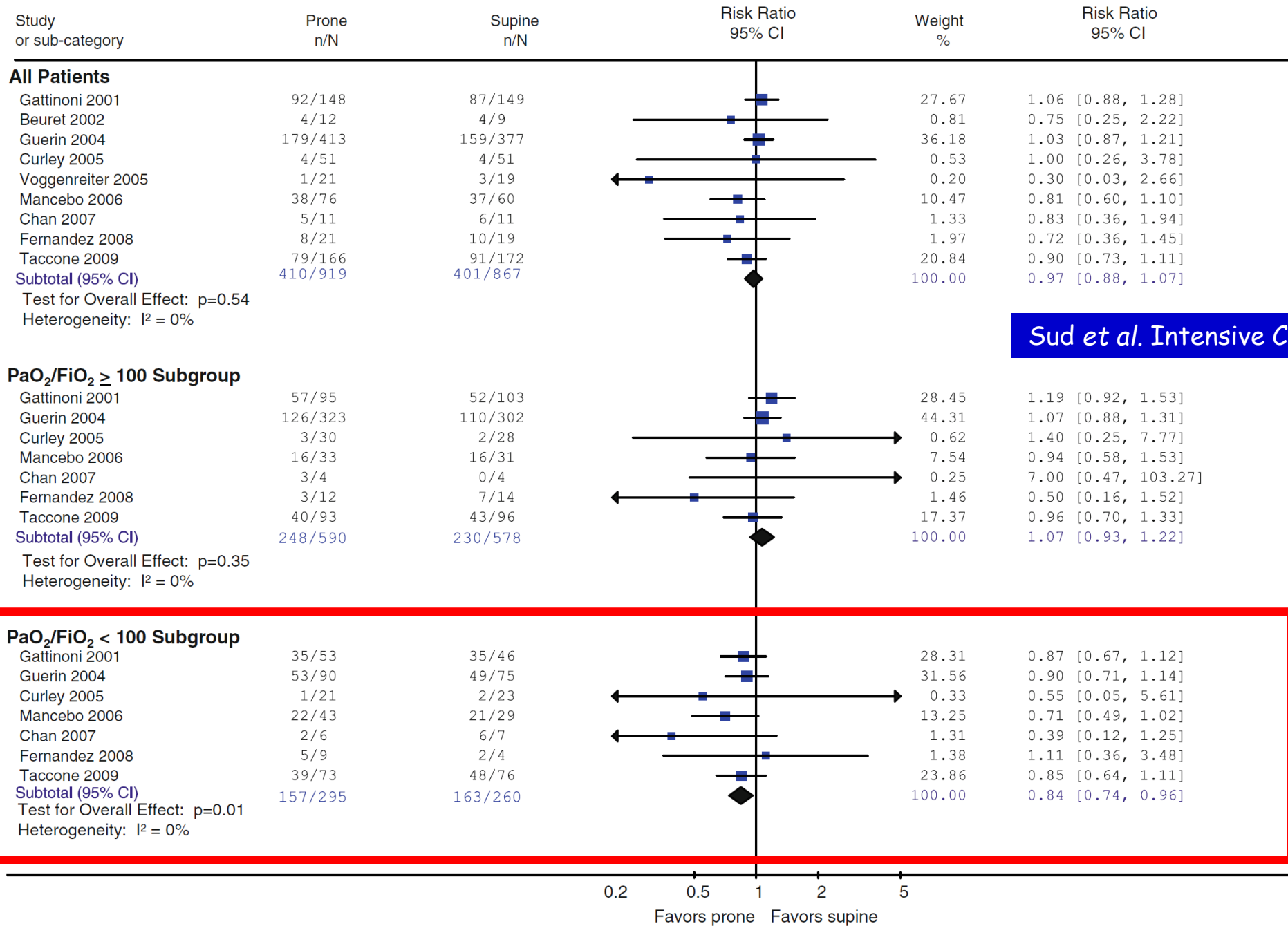
Adjunct measures according to ARDS severity on ICU day 1

Parameter	No.	All ^a (n=2233)	Mild ARDS ^b (n=539)	Moderate ARDS ^c (n=1154)	Severe ARDS ^d (n=540)	P value
Prone position	2223	1556 (70)	308 (57)	822 (71)	426 (79)	<0.001
Number of session	1553	3 (2-6)	3 (2-6)	3 (2-6)	3 (2-6)	0.585
Continuous neuromuscular blockers	2224	1966 (88)	441 (82)	1025 (89)	500 (93)	<0.001
Nitric oxide	2224	425 (19)	74 (14)	206 (18)	145 (27)	<0.001
Corticosteroids ^h	2224	888 (41)	192 (37)	458 (41)	238 (46)	0.012
ECMO	2153	235 (11)	41 (8)	111 (10)	83 (15)	<0.001

For all ARDS patients?

Prone position for all ARDS patients





Sud et al. Intensive Care Med 2010

PaO₂/FiO₂ < 100 Subgroup

0.2 0.5 1 2 5
Favors prone Favors supine

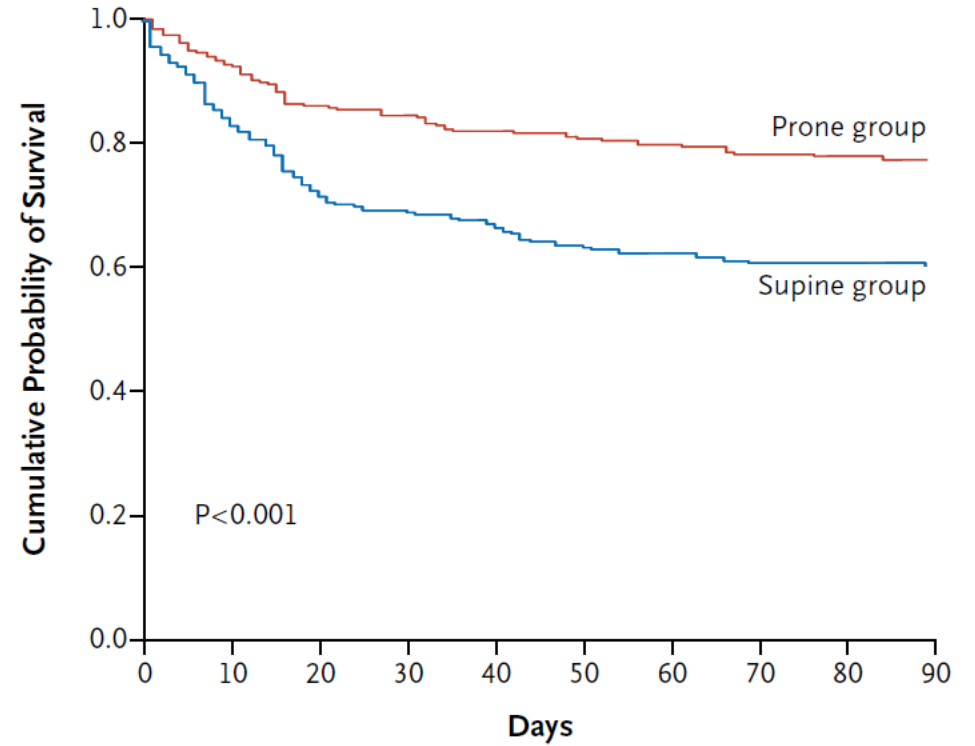
ORIGINAL ARTICLE

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 Richcoeur, M.D., Marc Gainnier, M.D., Ph.D.,
 Frédérique Bayle, M.D., Gael Bourdin, M.D., Véronique Leray, M.D.,
 Raphaelle Girard, M.D., Loredana Baboi, Ph.D., and Louis Ayzac, M.D.,
 for the PROSEVA Study Group*

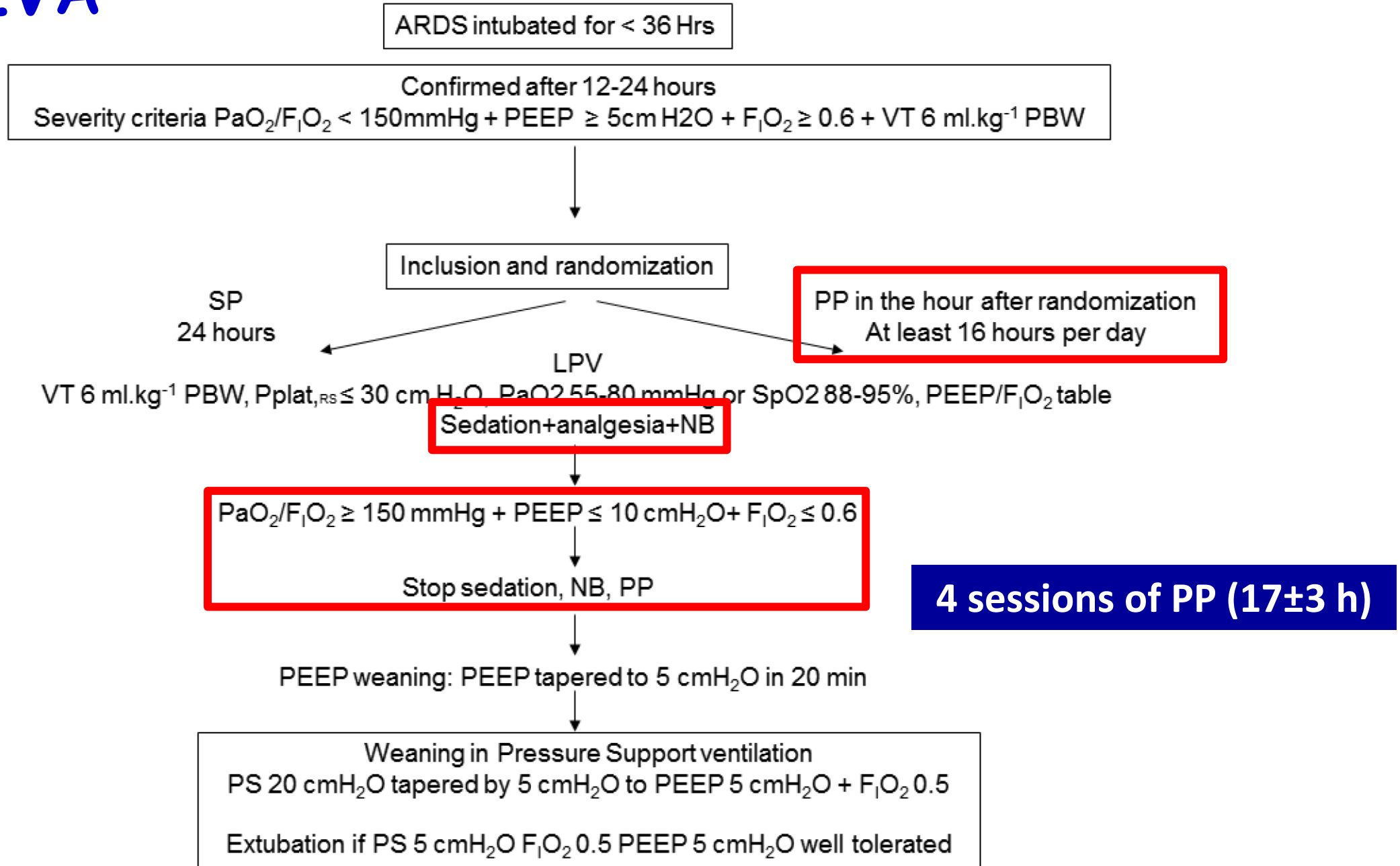
P/F ratio < 150 mmHg

Mean P/F ratio, 100 mmHg

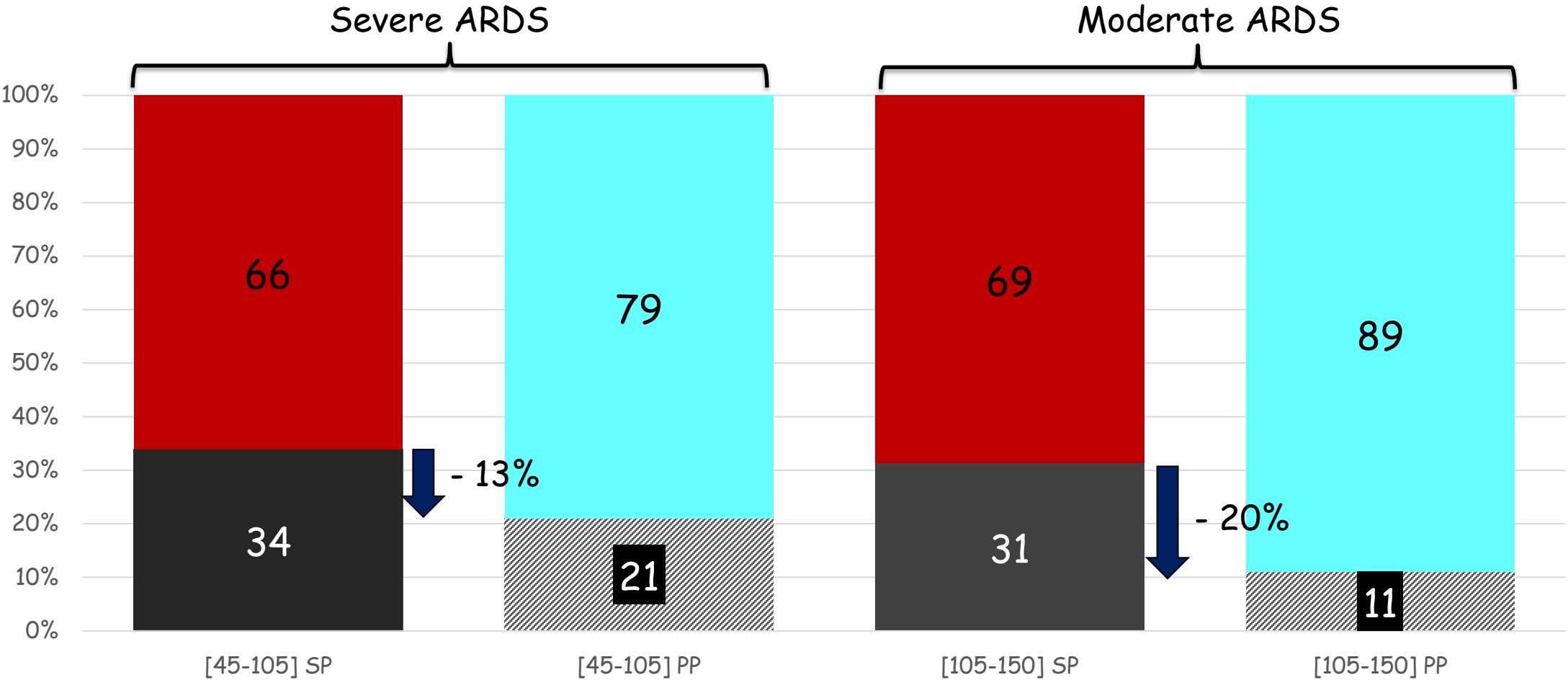


		Supine group (n=229)	Prone group (n=237)
ARDS main origin	Pneumonia	133 (58.1)	148 (62.4)
	Aspiration	41 (17.9)	45 (19.0)
	Extra-pulmonary sepsis	28 (12.2)	17 (7.2)
	Other	27 (11.8)	27 (11.4)

PROSEVA



PROSEVA - D28 mortality according to P/F on inclusion



Corticosteroids

Corticosteroids for patients with acute respiratory distress syndrome: a systematic review and meta-analysis of randomized trials

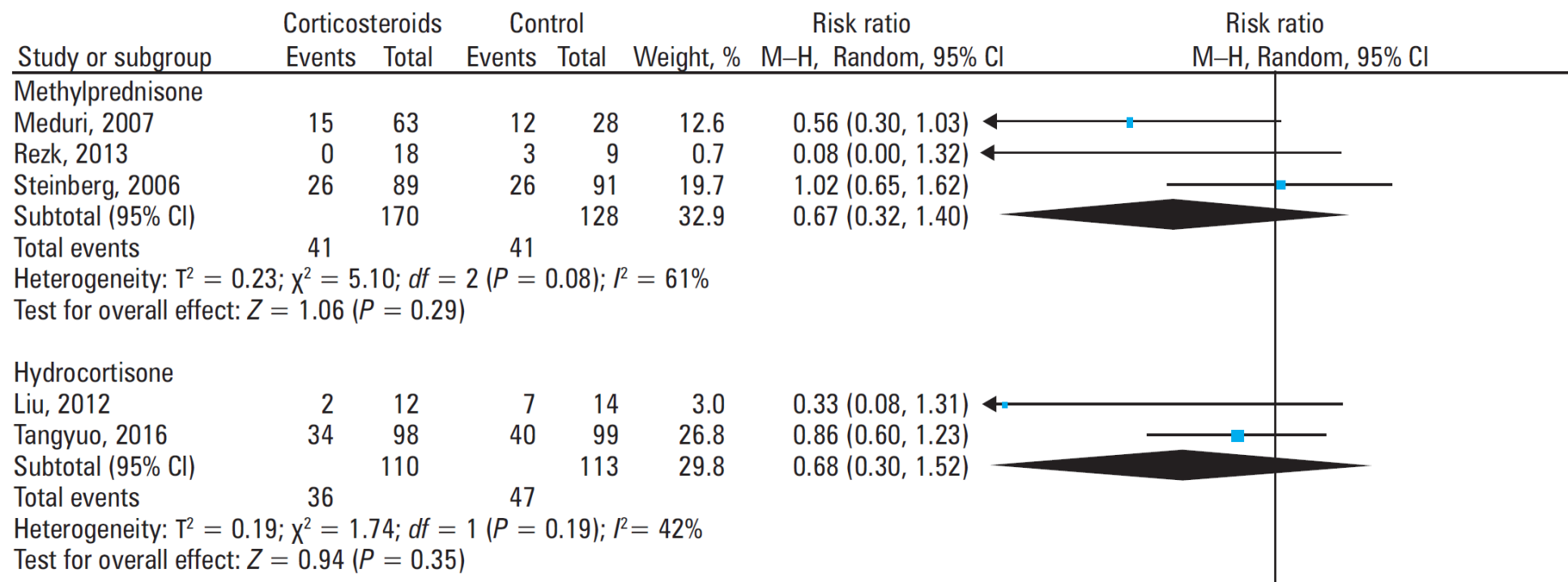
Manoj J. Mammen¹, Komal Aryal², Waleed Alhazzani^{2,3}, Paul E. Alexander²

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POLISH ARCHIVES OF INTERNAL MEDICINE 2020; 130 (4)



Dexamethasone treatment for the acute respiratory distress syndrome: a multicentre, randomised controlled trial

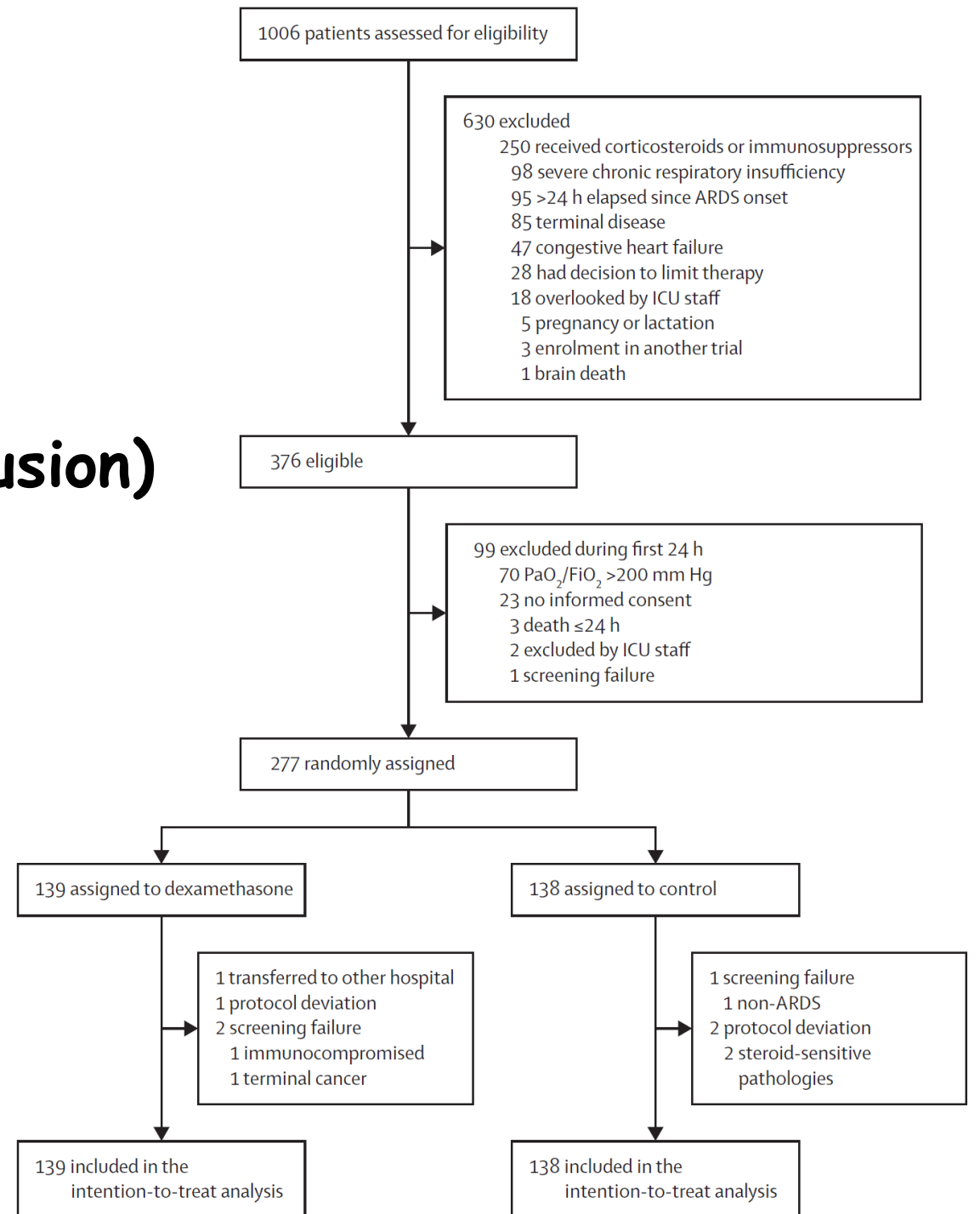


*Jesús Villar, Carlos Ferrando, Domingo Martínez, Alfonso Ambrós, Tomás Muñoz, Juan A Soler, Gerardo Aguilar, Francisco Alba, Elena González-Higueras, Luís A Conesa, Carmen Martín-Rodríguez, Francisco J Díaz-Domínguez, Pablo Serna-Grande, Rosana Rivas, José Ferreres, Javier Belda, Lucía Capilla, Alec Tallet, José M Añón, Rosa L Fernández, Jesús M González-Martín for the dexamethasone in ARDS network**

Lancet Respir Med 2020

- **17 ICUs in teaching hospitals across Spain**
- **ARDS** ($\text{PaO}_2/\text{FiO}_2 < 200$ mm Hg, $\text{PEEP} \geq 10$ and $\text{FiO}_2 \geq 0.5$ at 24 h after ARDS onset)
- **Dexamethasone (<30h after ARDS onset) or routine care (control)**
- **Dexamethasone**
 - IV dose of 20 mg once daily from day 1 to day 5
 - 10 mg once daily from day 6 to day 10 (stop if extubation)
- **Primary outcome: number of ventilator-free days at 28 days**

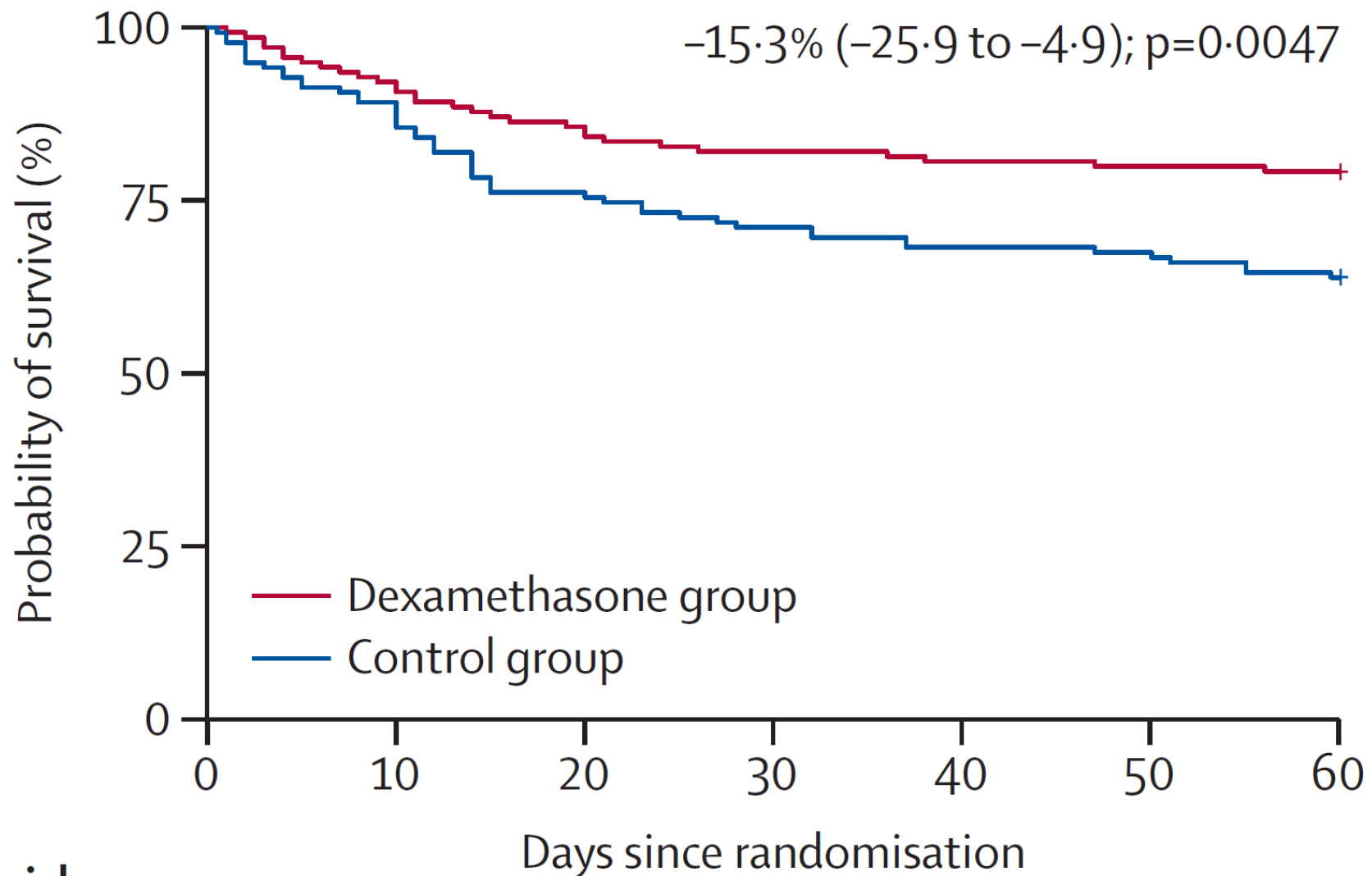
- 2013-2018
- Arrêté par DSMB (rythme d'inclusion)
- > 88% (277/314) de l'effectif



	Dexamethasone group (n=139)	Control group (n=138)	Between-group difference (95% CI)	p value
Ventilator-free days at 28 days	12.3 (9.9)	7.5 (9.0)	4.8 (2.57 to 7.03)	<0.0001
All-cause mortality at day 60	29 (21%)	50 (36%)	-15.3% (-25.9 to -4.9)	0.0047
ICU mortality	26 (19%)	43 (31%)	-12.5% (-22.4 to -2.3)	0.0166
Hospital mortality	33 (24%)	50 (36%)	-12.5% (-22.9 to -1.7)	0.0235
Actual duration of mechanical ventilation in ICU survivors, days	14.2 (13.2)	19.5 (13.2)	-5.3 (-8.4 to -2.2)	0.0009
Actual duration of mechanical ventilation in survivors at day 60, days	14.3 (13.3)	20.2 (14.0)	-5.9 (-9.1 to -2.7)	0.0004
Adverse events and complications*				
Hyperglycaemia in ICU	105 (76%)	97 (70%)	5.2% (-5.2 to 15.6)	0.33
New infections in ICU	33 (24%)	35 (25%)	1.6% (-8.5 to 11.7)	0.75
Barotrauma	14 (10%)	10 (7%)	2.8% (-4.0 to 9.8)	0.41

Data are n (%) or mean (SD). ICU=intensive care unit. *Data included the period from randomisation to day 10 (for hyperglycaemia) and from randomisation to ICU discharge (for new infections and barotrauma).

Table 2: Outcomes, adverse events, and complications



Number at risk

Dexamethasone	139	128	119	114	112	111	110
Control	138	123	105	98	94	93	88

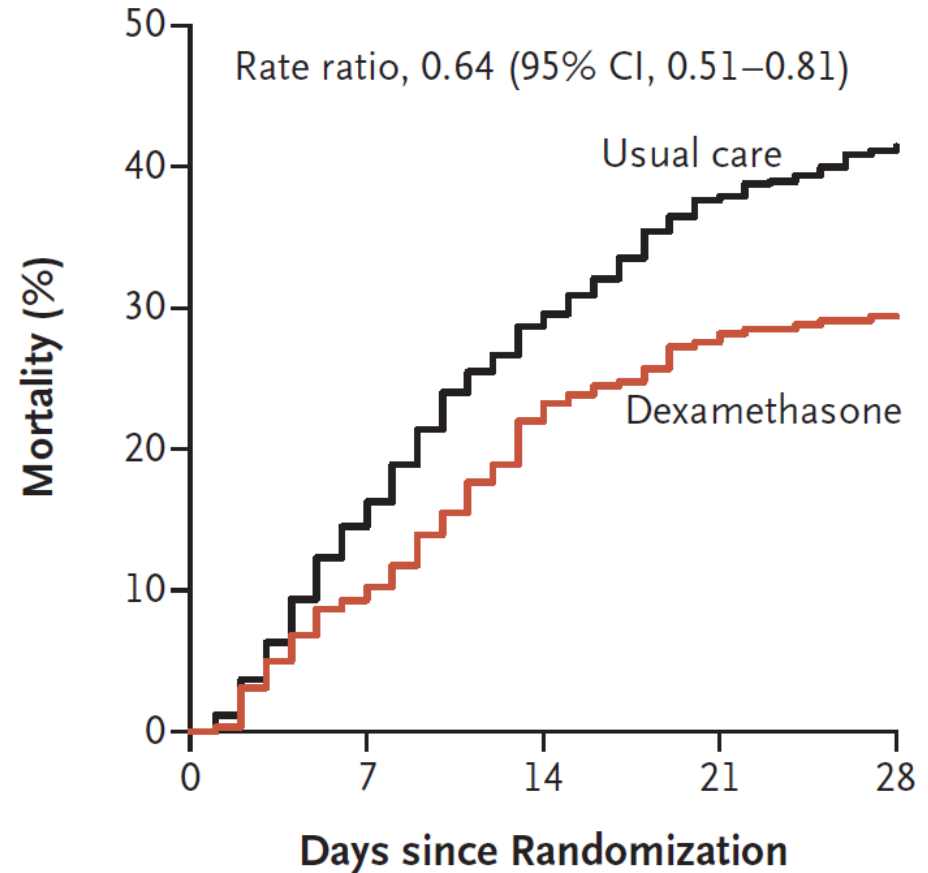
ORIGINAL ARTICLE

Dexamethasone in Hospitalized Patients with Covid-19 — Preliminary Report

The RECOVERY Collaborative Group*

Dexa: IV dose of 6 mg once daily from day 1 to day 10

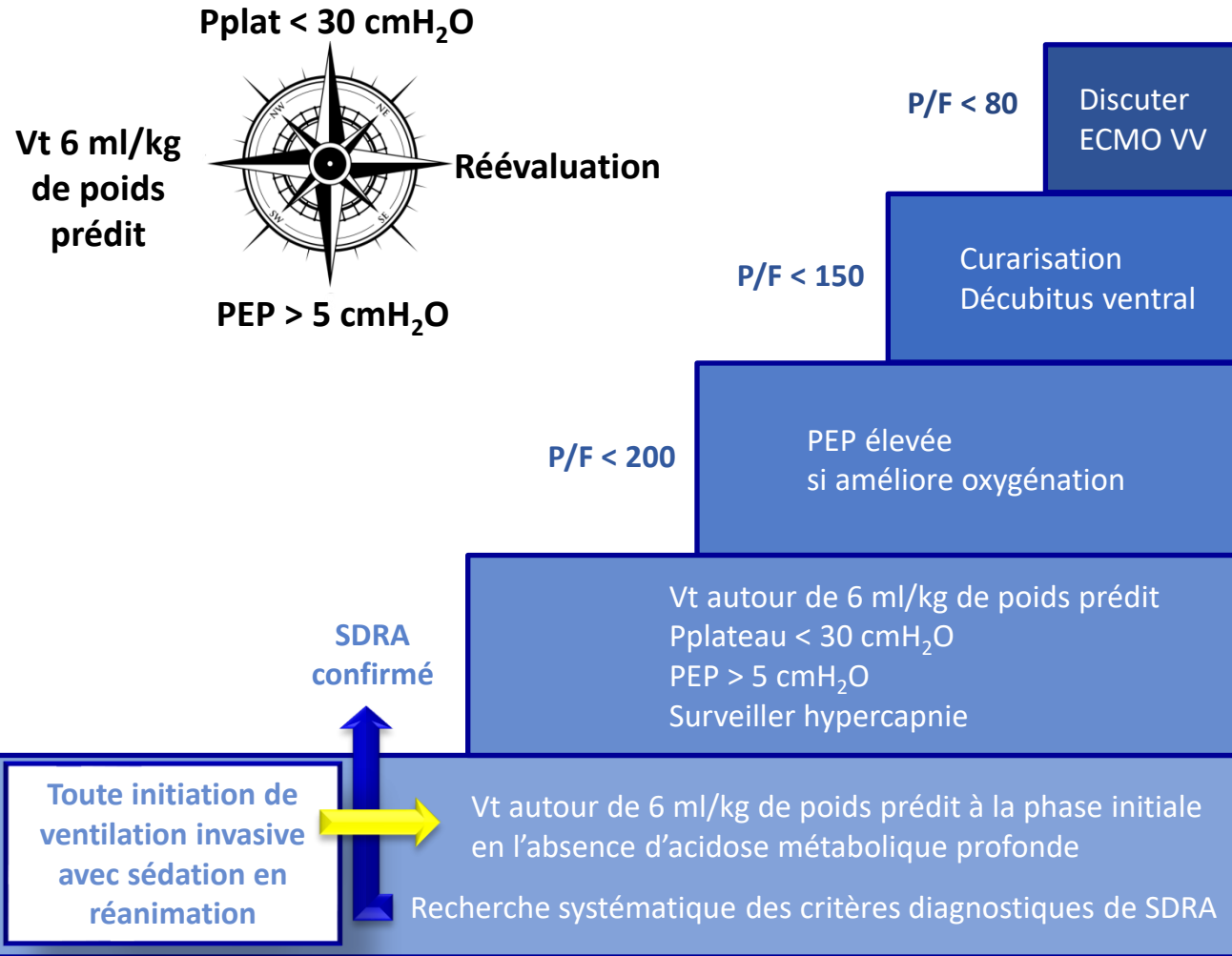
Invasive Mechanical Ventilation (N=1007)



No. at Risk

Usual care	683	572	481	424	400
Dexamethasone	324	290	248	232	228

Prise en charge initiale du SDR A



S É V É R I T É S D R A

ECMO veino-veineuse

- Si hypoxémie réfractaire ou ventilation protectrice non applicable
- A discuter avec un centre expert

Modalités de la curarisation : IVSE

- Précocement, dans les 48h du diagnostic

Modalités du décubitus ventral (DV)

- séance ≥ 16 heures, plusieurs séances

SDRA modéré ou sévère → Test PEP élevée (> 12 cmH₂O)

Utilisation PEP élevée si :

- Amélioration de l'oxygénation
- Sans dégradation significative de la compliance du système respiratoire et de l'hémodynamique
- Maintien Pplateau < 30 cmH₂O, monitoring continu

Critères du SDR A

- PaO₂/FiO₂ ≤ 300 mmHg
- PEP ≥ 5 cmH₂O
- Opacités bilatérales sur l'imagerie thoracique
- Non expliquées par défaillance ventriculaire gauche
- Évolution depuis moins de 7 jours

Traitement possible

- Monoxyde d'azote inhalé (iNO), si hypoxémie persistante en DV avant discussion de l'ECMO VV
- Ventilation spontanée après la phase aiguë avec Vt généré autour de 6 ml/kg sans dépasser 8 ml/kg

Pas de recommandation possible

- ECCO₂R
- Pression motrice
- Ventilation spontanée à la phase aiguë

Probablement ne pas faire

- Manœuvres de recrutement systématiques

Ne pas faire

- HFOV

Réévaluation des réglages et de la stratégie de prise en charge au moins toutes les 24h