Giovedì 6 marzo 2014 h. 15.00 Aula didattica 2CR

EVIDENZE, RICERCA E PRATICA CLINICA: UN CIRCOLO "VIRTUOSO"

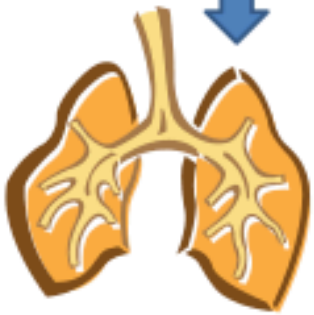
L'ESEMPIO DEL PROTOCOLLO ARDS

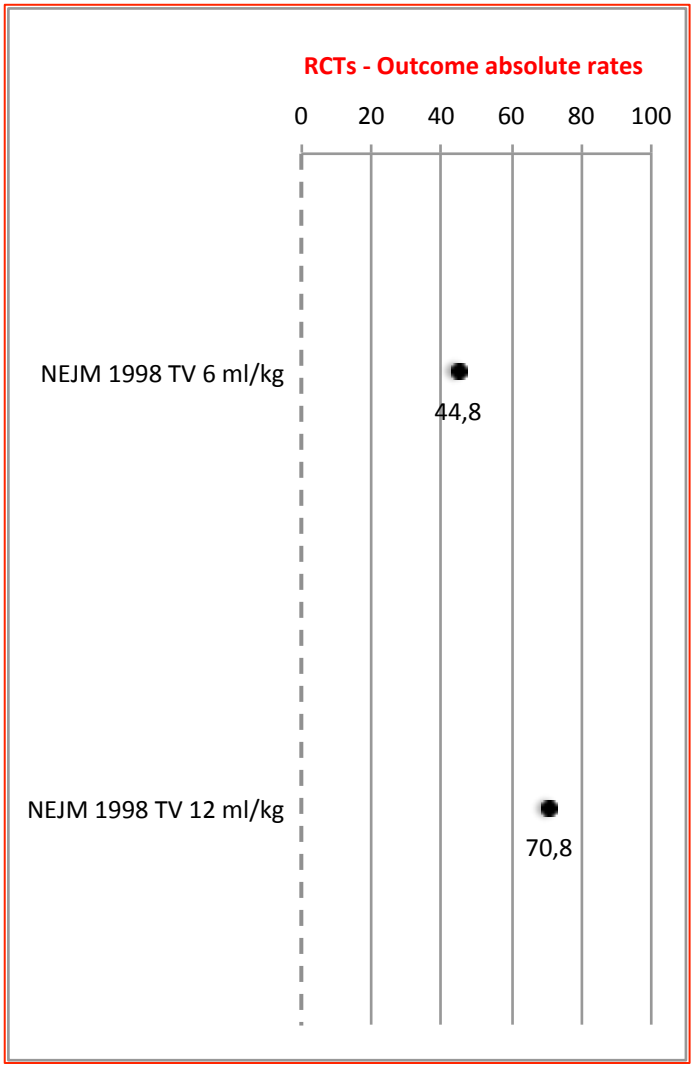
Dr. Daniele Poole

Ospedale San Martino di Belluno, Servizio di Anestesia e Rianimazione

In collaborazione con il gruppo di lavoro "ARDS e dintorni"

All'evento sono invitati medici, infermieri e studenti




RCTs - Outcome absolute rates
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NEJM 1998 TV 6 ml/kg
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NEJM 1998 TV 12 ml/kg
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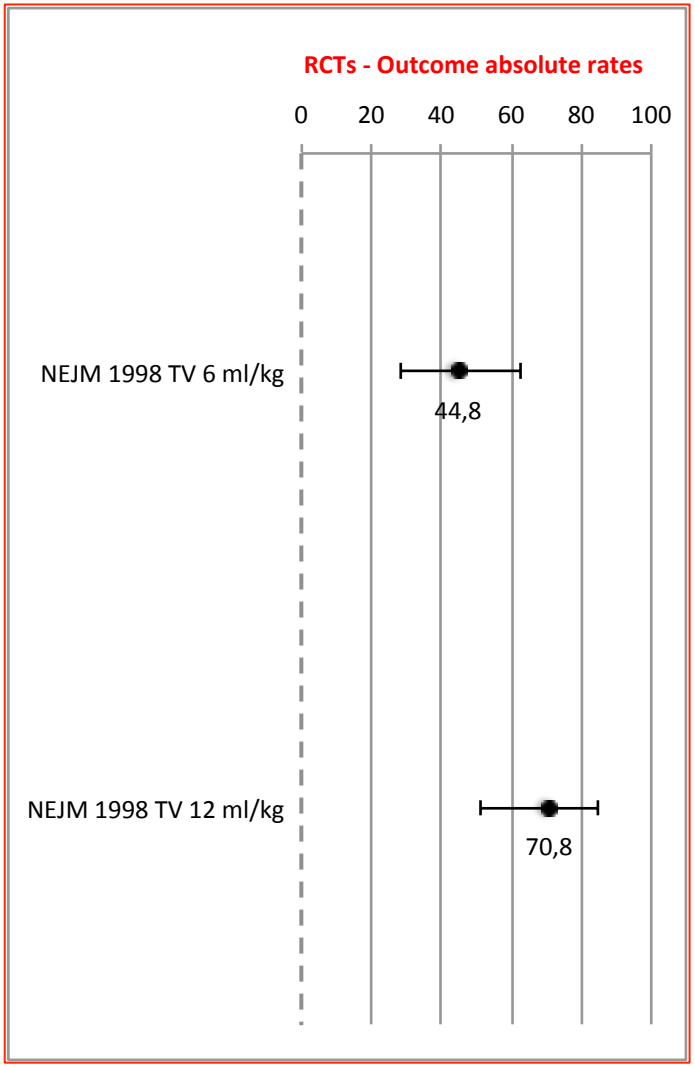
RCTs - Outcome absolute rates
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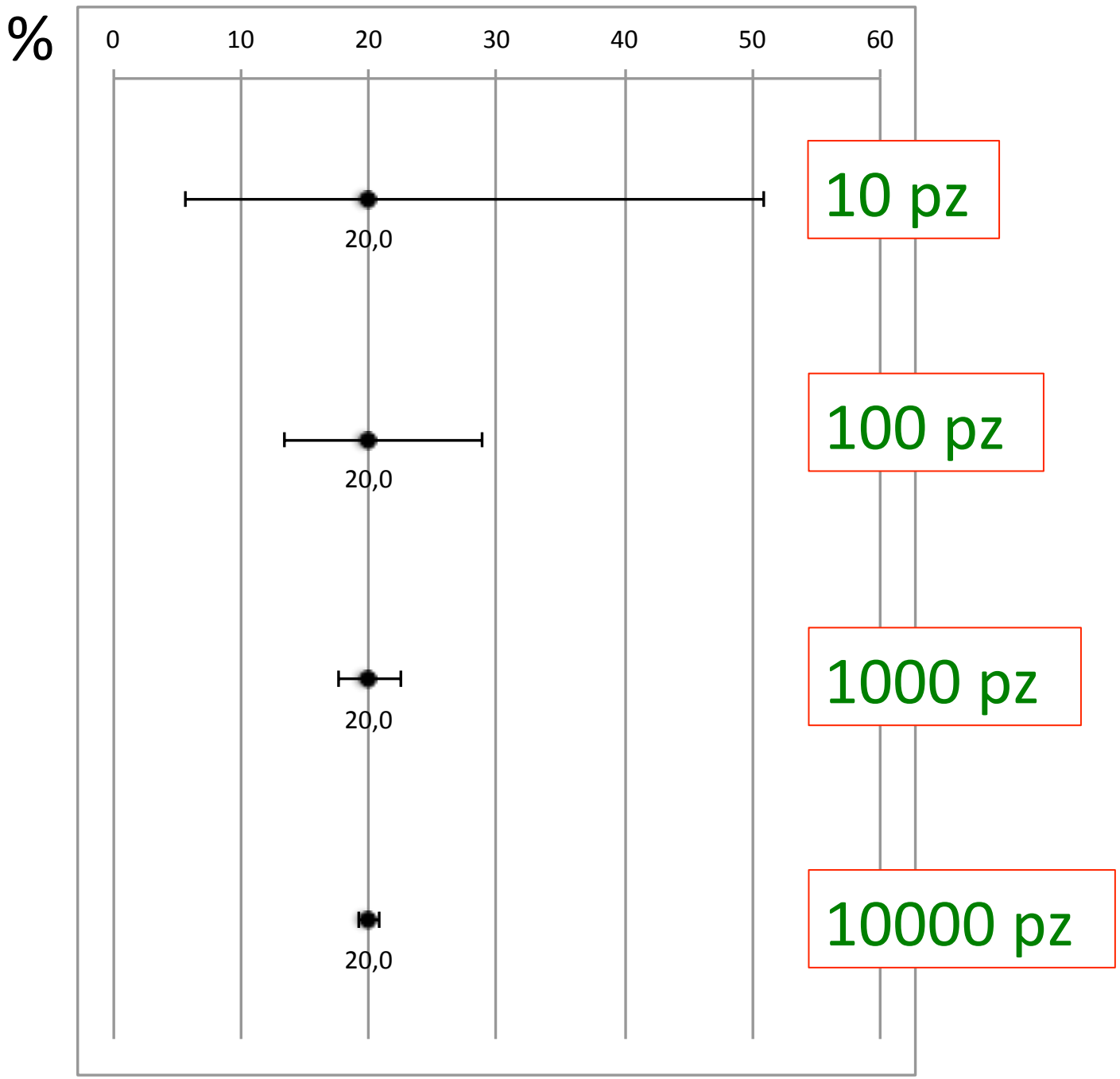
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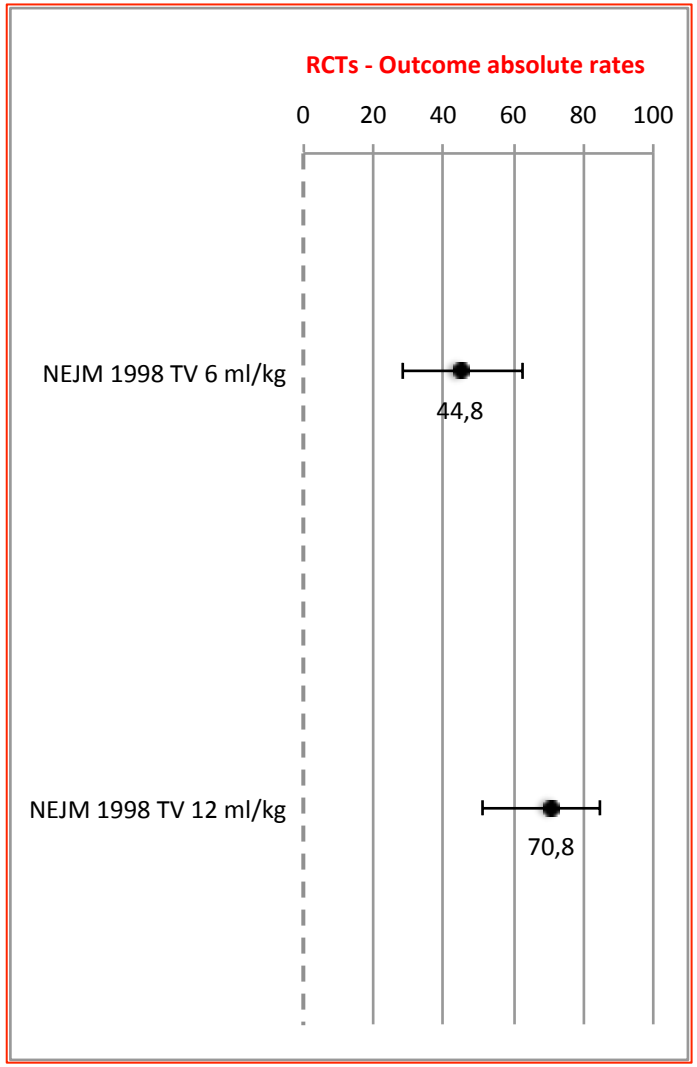
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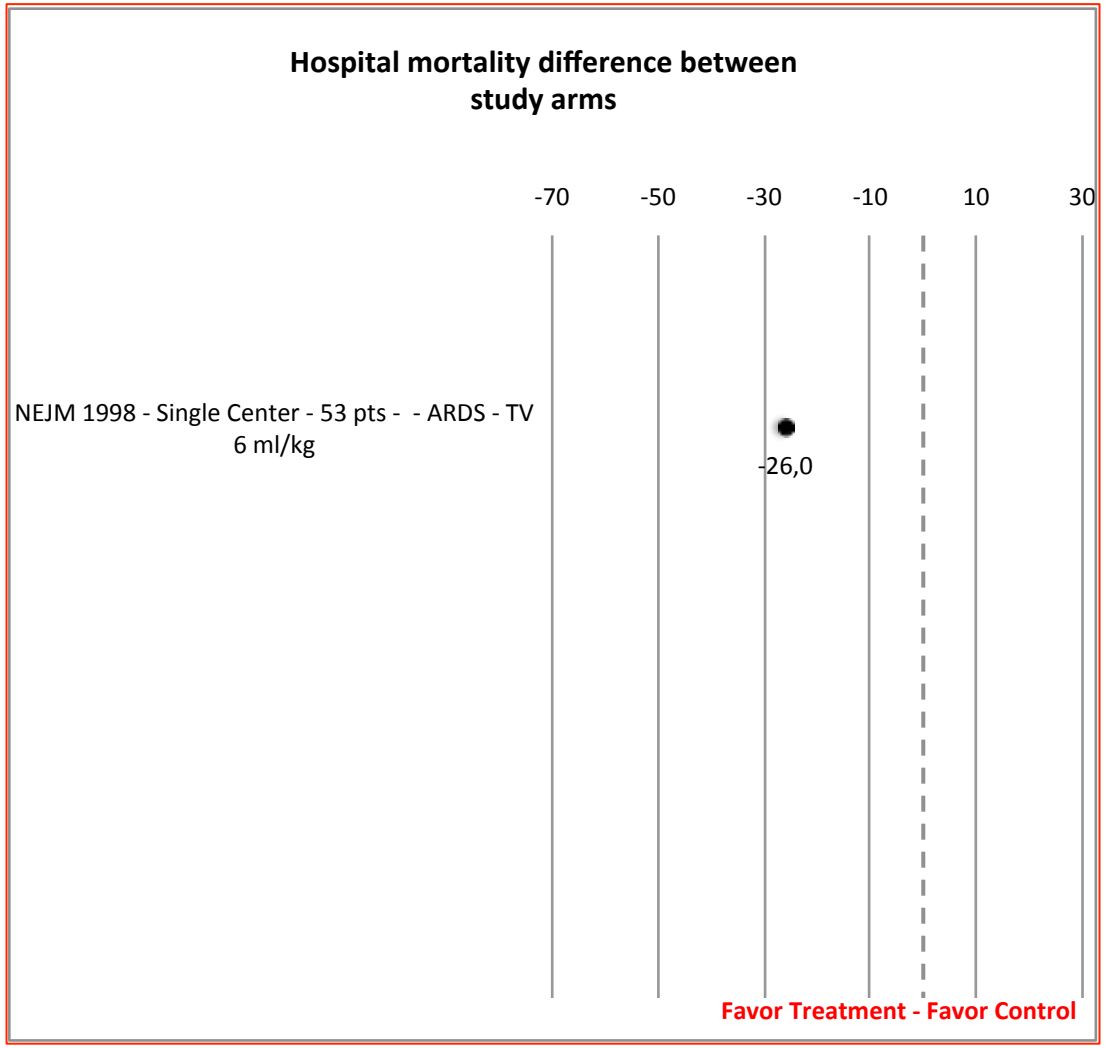
Hospital mortality difference between study arms
-70
-50
-30
-10
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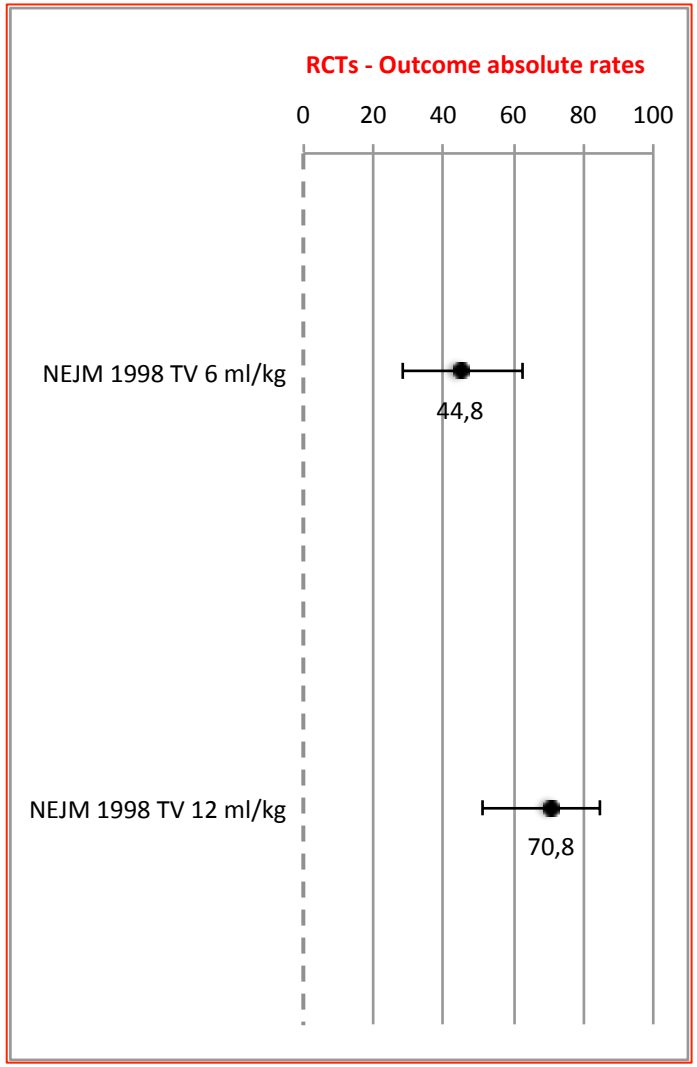
30
NEJM 1998 - Single Center - 53 pts - - ARDS - TV 6 ml/kg
-26,0
Favor Treatment - Favor Control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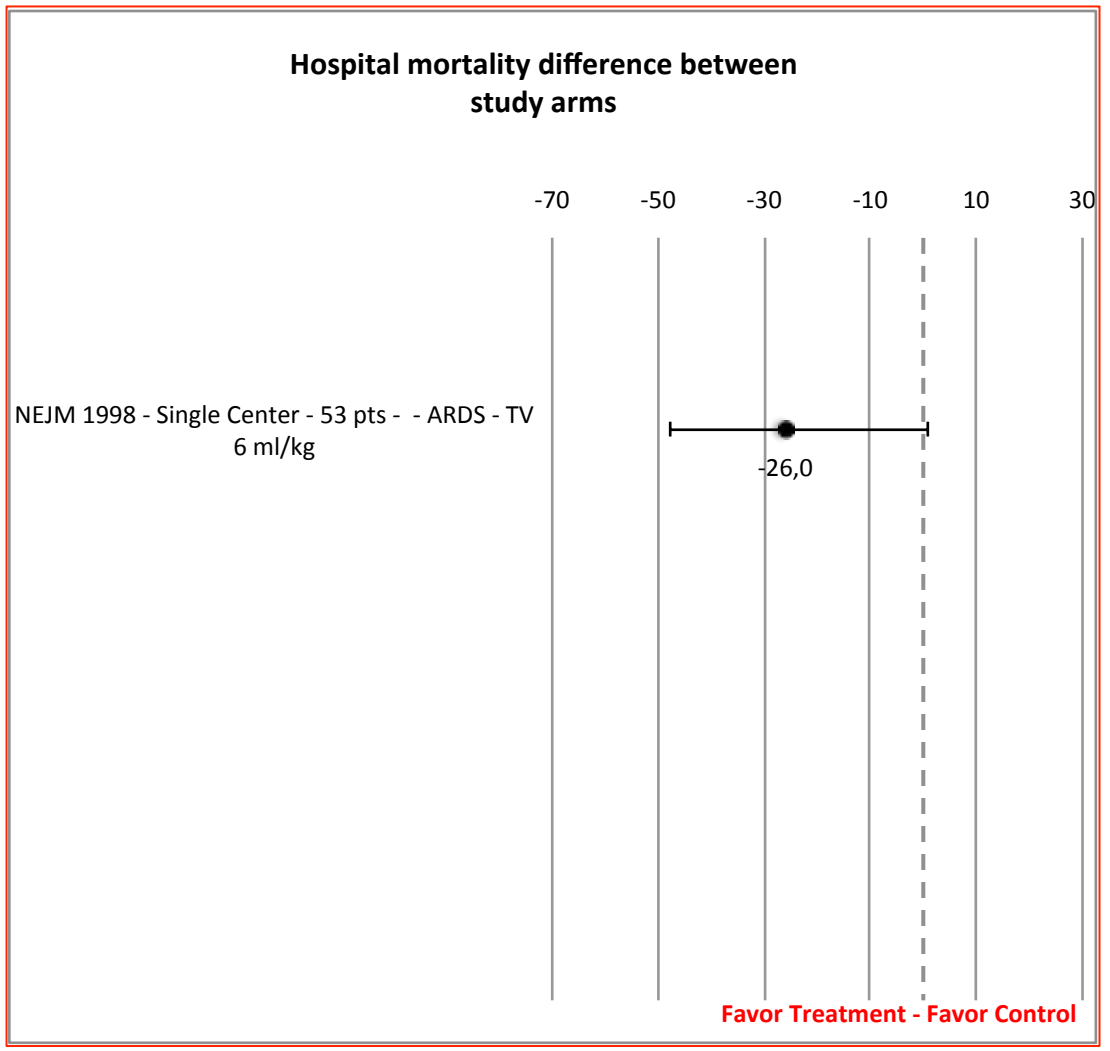
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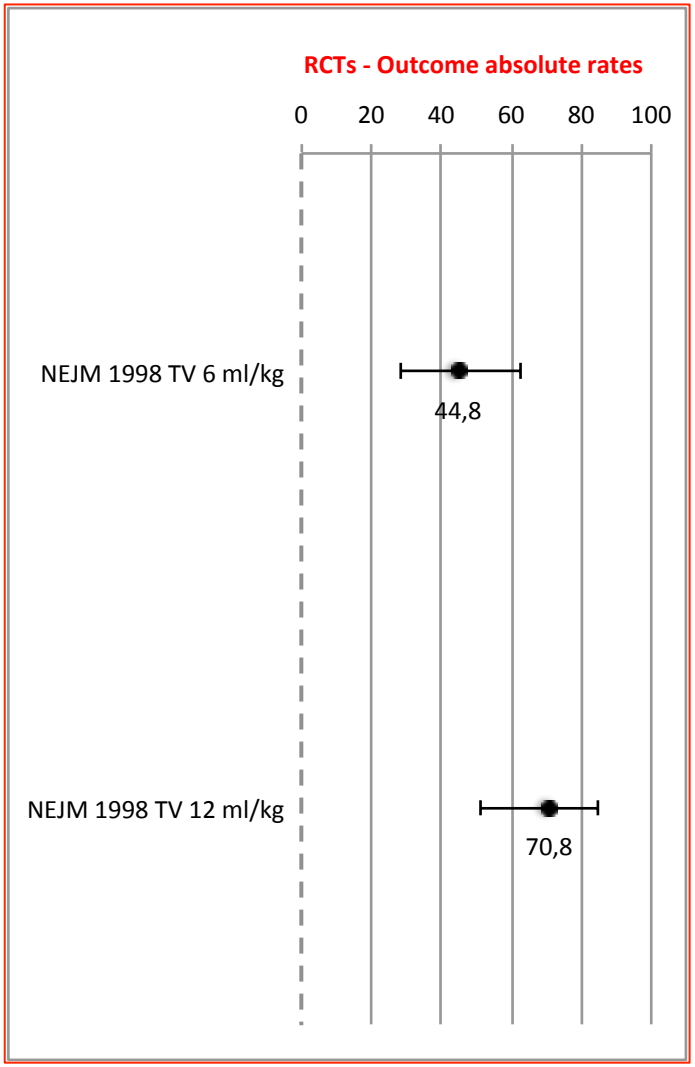
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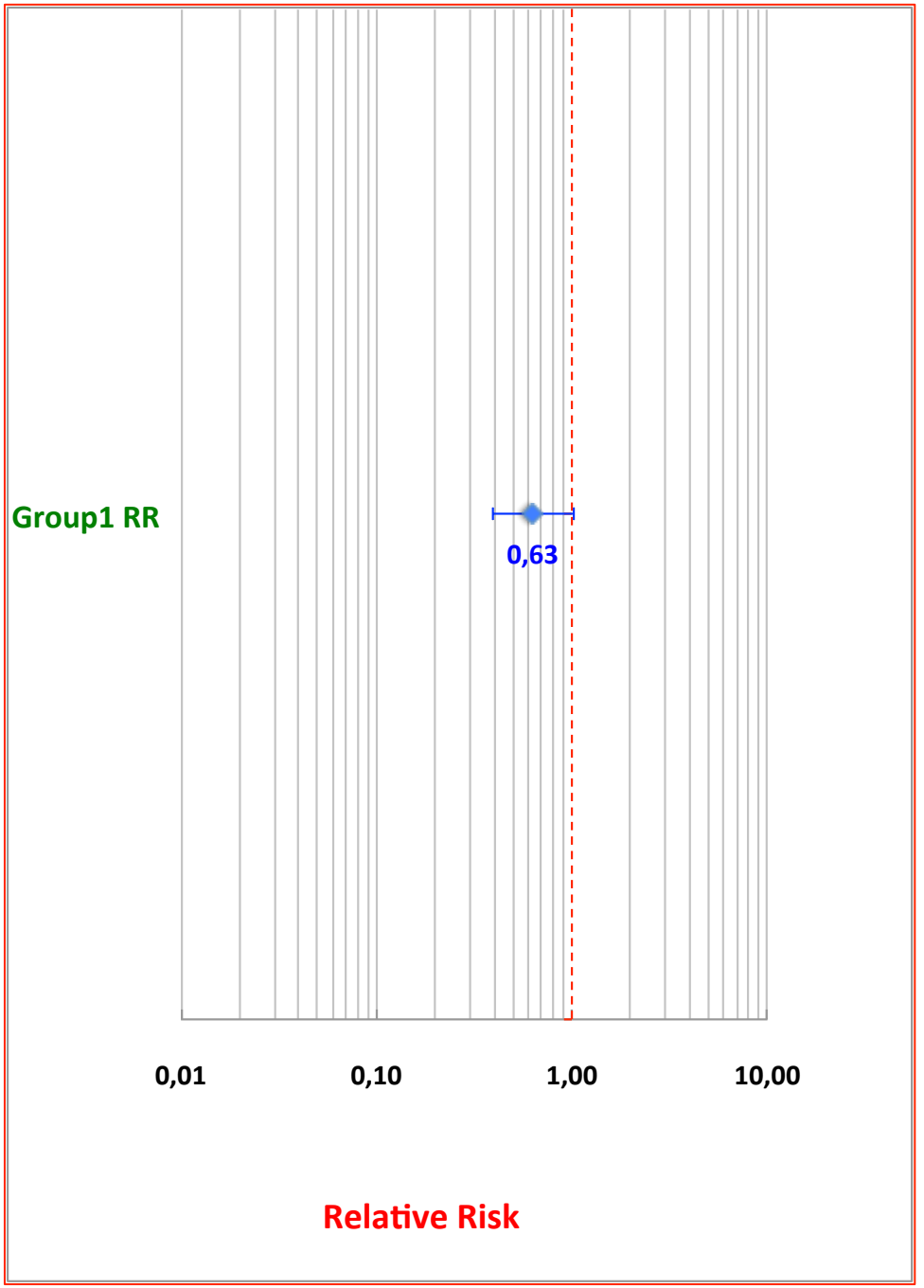

Group1 RR
0,63
0,01
0,10
1,00
10,00
Relative Risk

The American-European Consensus Conference on ARDS

Definitions, Mechanisms, Relevant Outcomes, and Clinical Trial Coordination

GORDON R. BERNARD, ANTONIO ARTIGAS, KENNETH L. BRIGHAM, JEAN CARLET, KONRAD FALKE, LEONARD HUDSON, MAURICE LAMY, JEAN ROGER LEGALL, ALAN MORRIS, ROGER SPRAGG, and the Consensus Committee

RECOMMENDED CRITERIA FOR ACUTE LUNG INJURY (ALI) AND ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS)

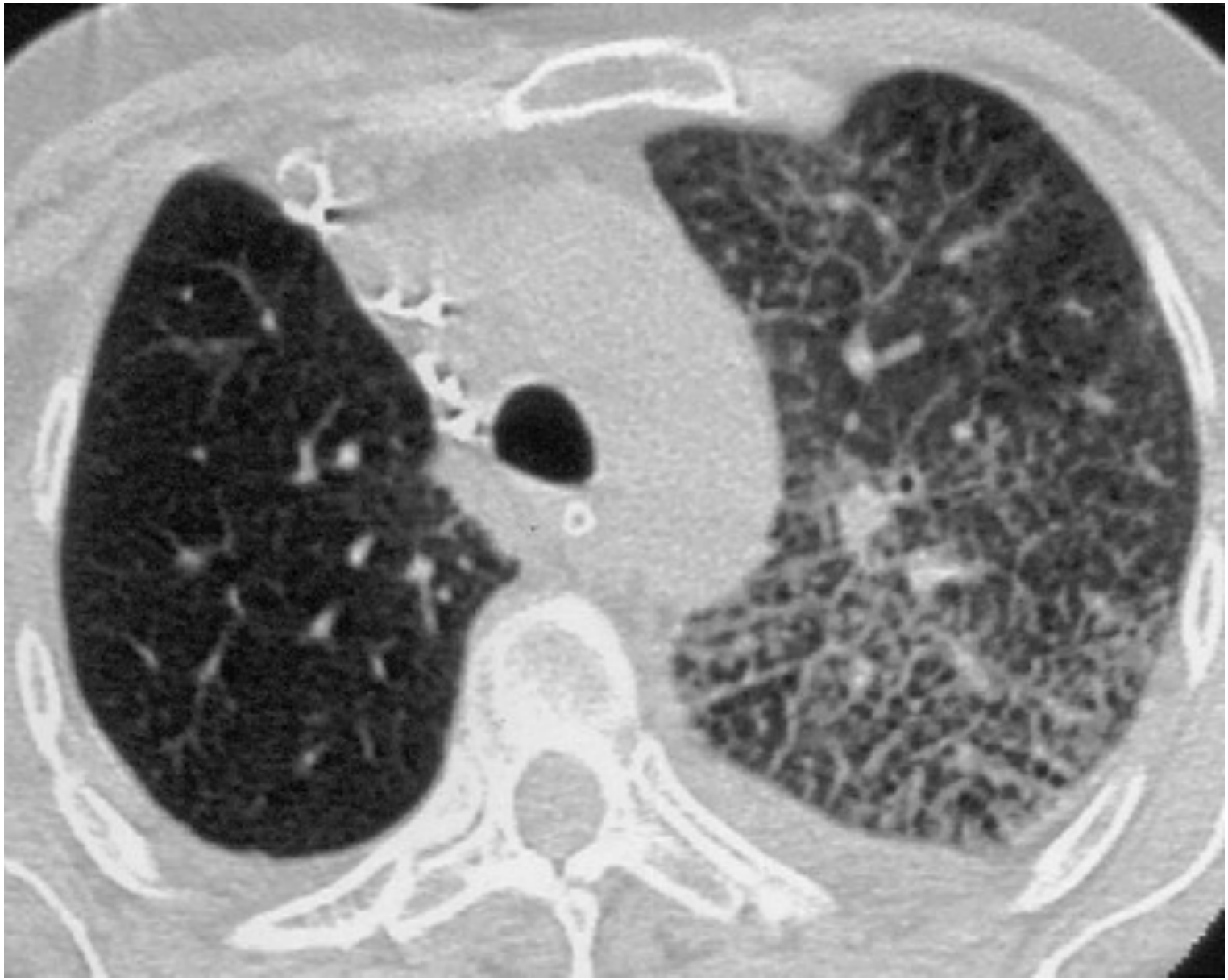
	Timing	Oxygenation	Chest Radiograph	Pulmonary Artery Wedge Pressure
ALI criteria	Acute onset	$Pa_{O_2}/FI_{O_2} \leq 300$ mm Hg (regardless of PEEP level)	Bilateral infiltrates seen on frontal chest radiograph	$\leq$ 18 mm Hg when measured or no clinical evidence of left atrial hypertension
ARDS criteria	Acute onset	$Pa_{O_2}/FI_{O_2} \leq 200$ mm Hg (regardless of PEEP level)	Bilateral infiltrates seen on frontal chest radiograph	$\leq$ 18 mm Hg when measured or no clinical evidence of left atrial hypertension

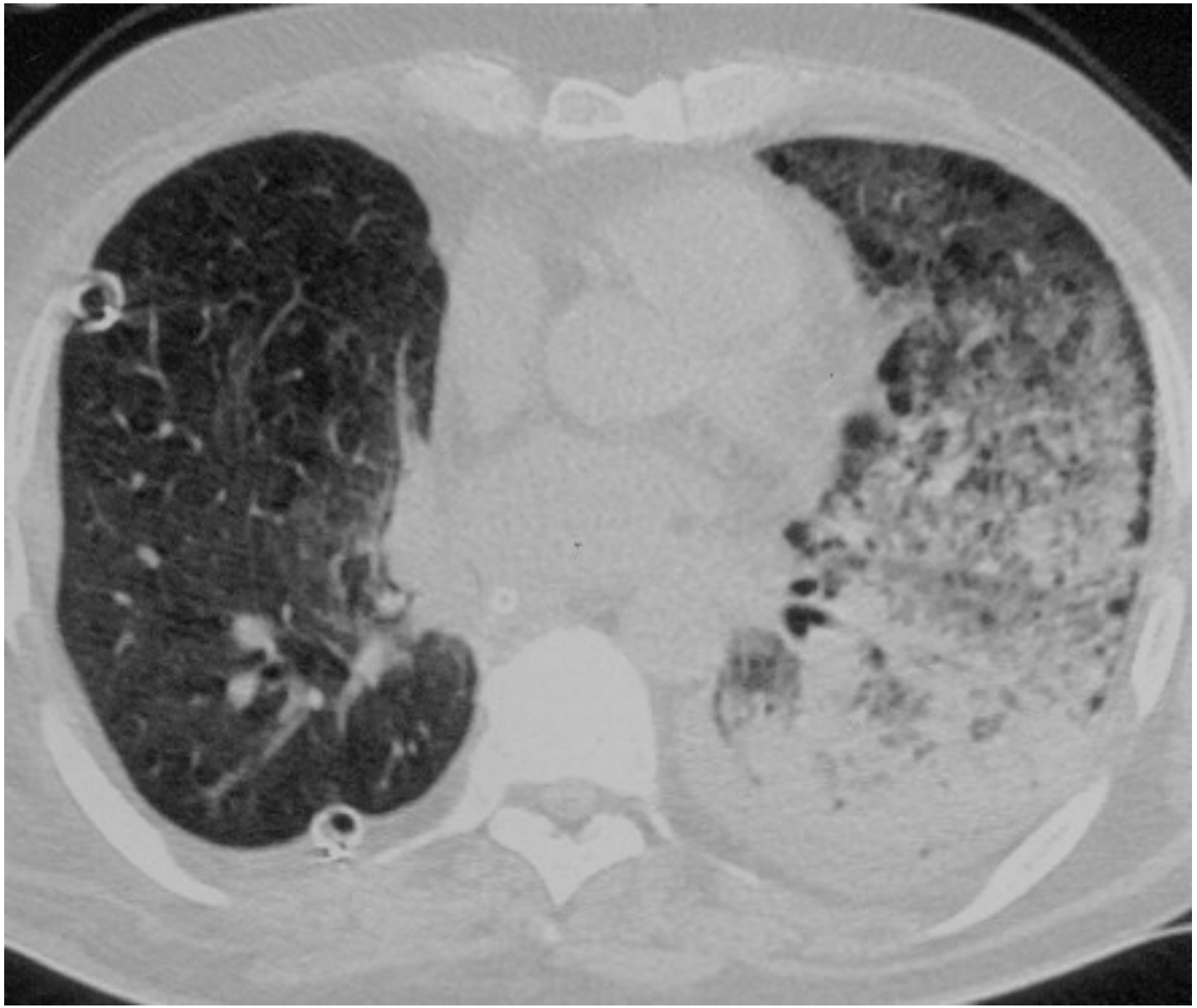
Acute Respiratory Distress Syndrome
The Berlin Definition

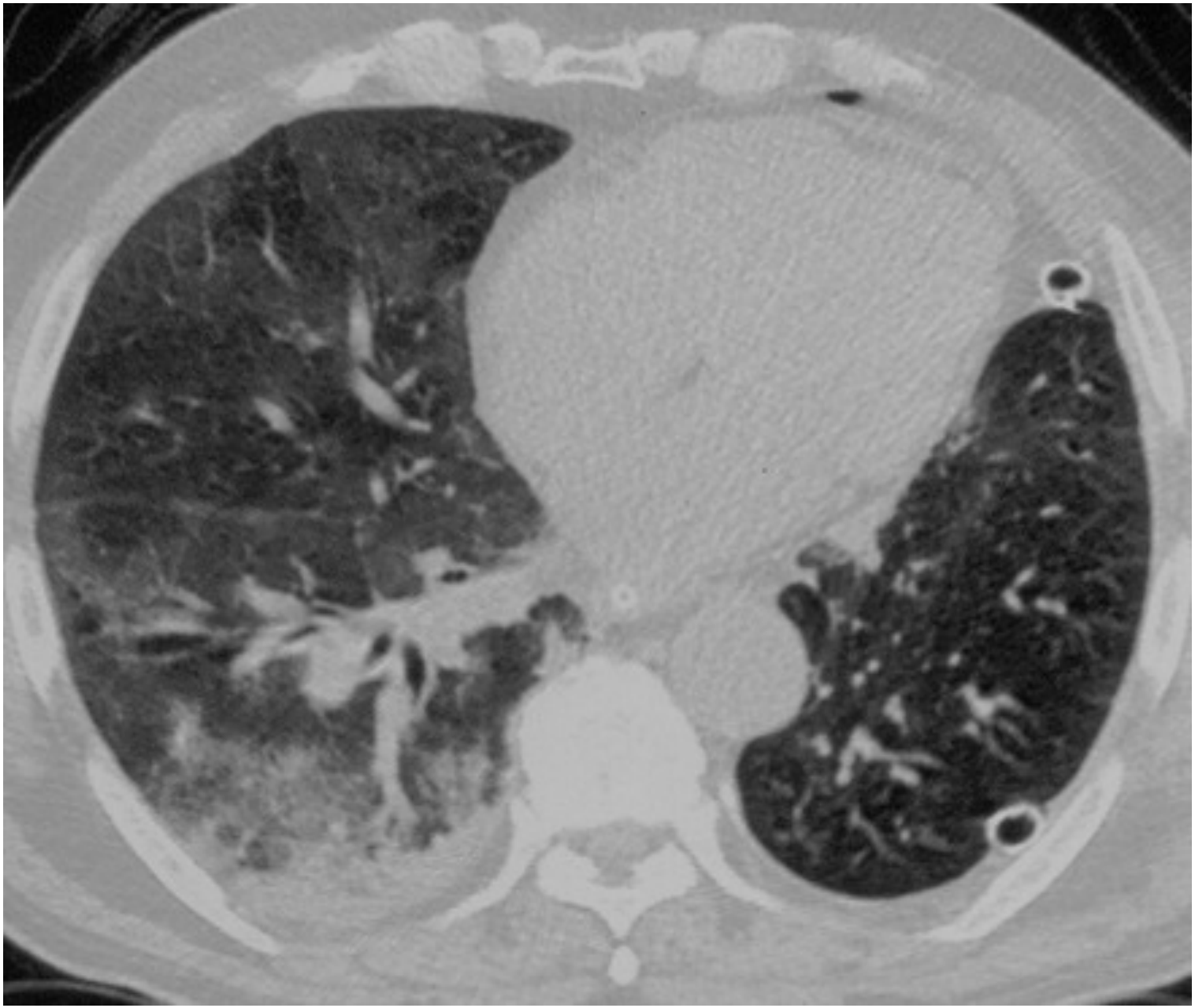
JAMA. 2012;307(23):doi:10.1001/jama.2012.5669

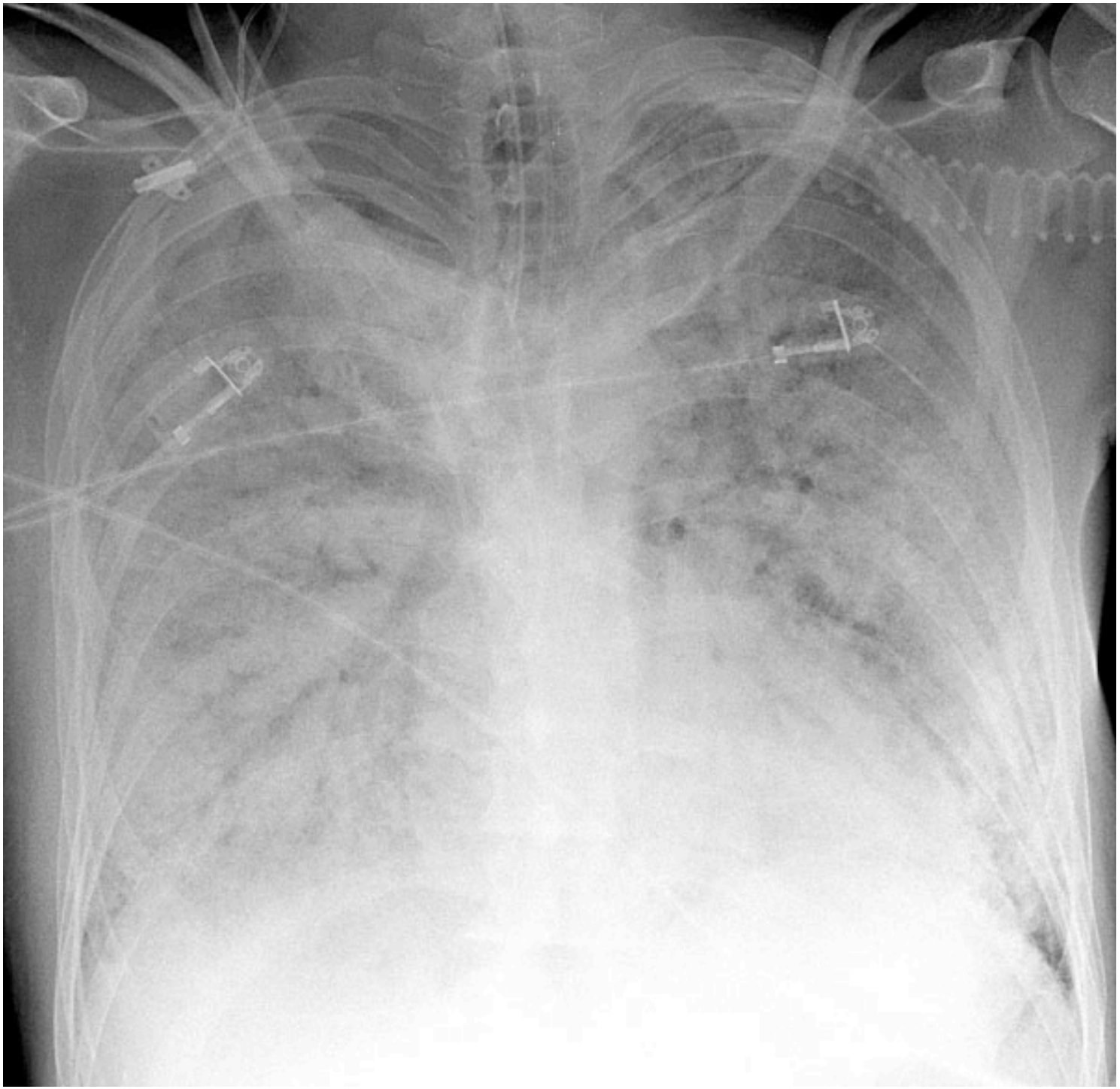
Table 3. The Berlin Definition of Acute Respiratory Distress Syndrome

	Acute Respiratory Distress Syndrome
Timing	Within 1 week of a known clinical insult or new or 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 (eg, echocardiography) to exclude hydrostatic edema if no risk factor present
Oxygenation[b]	
Mild	200 mm Hg < PaO_2/FIO_2 ≤ 300 mm Hg with PEEP or CPAP ≥5 cm H_2O[c]
Moderate	100 mm Hg < PaO_2/FIO_2 ≤ 200 mm Hg with PEEP ≥5 cm H_2O
Severe	PaO_2/FIO_2 ≤ 100 mm Hg with PEEP ≥5 cm H_2O









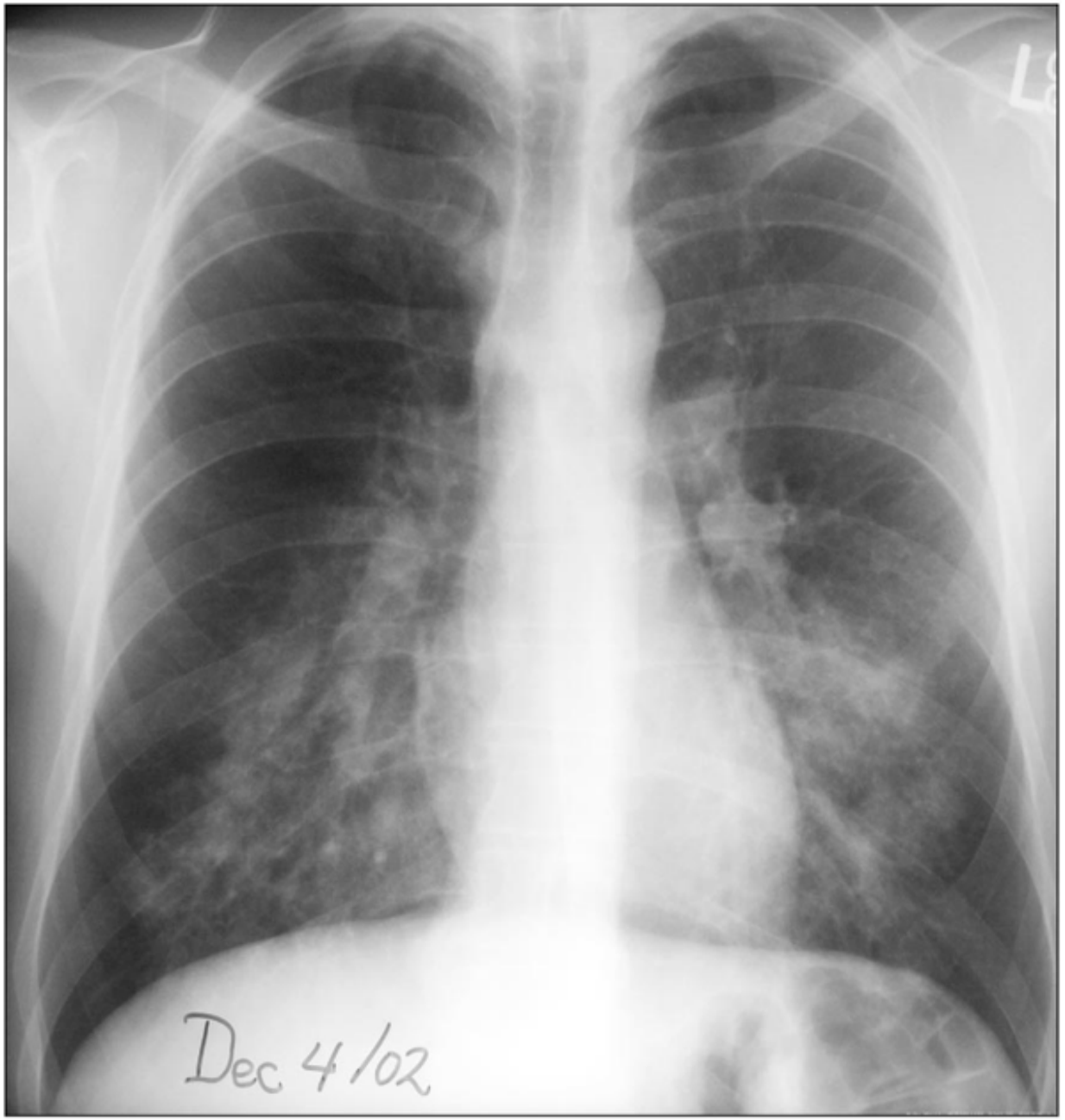
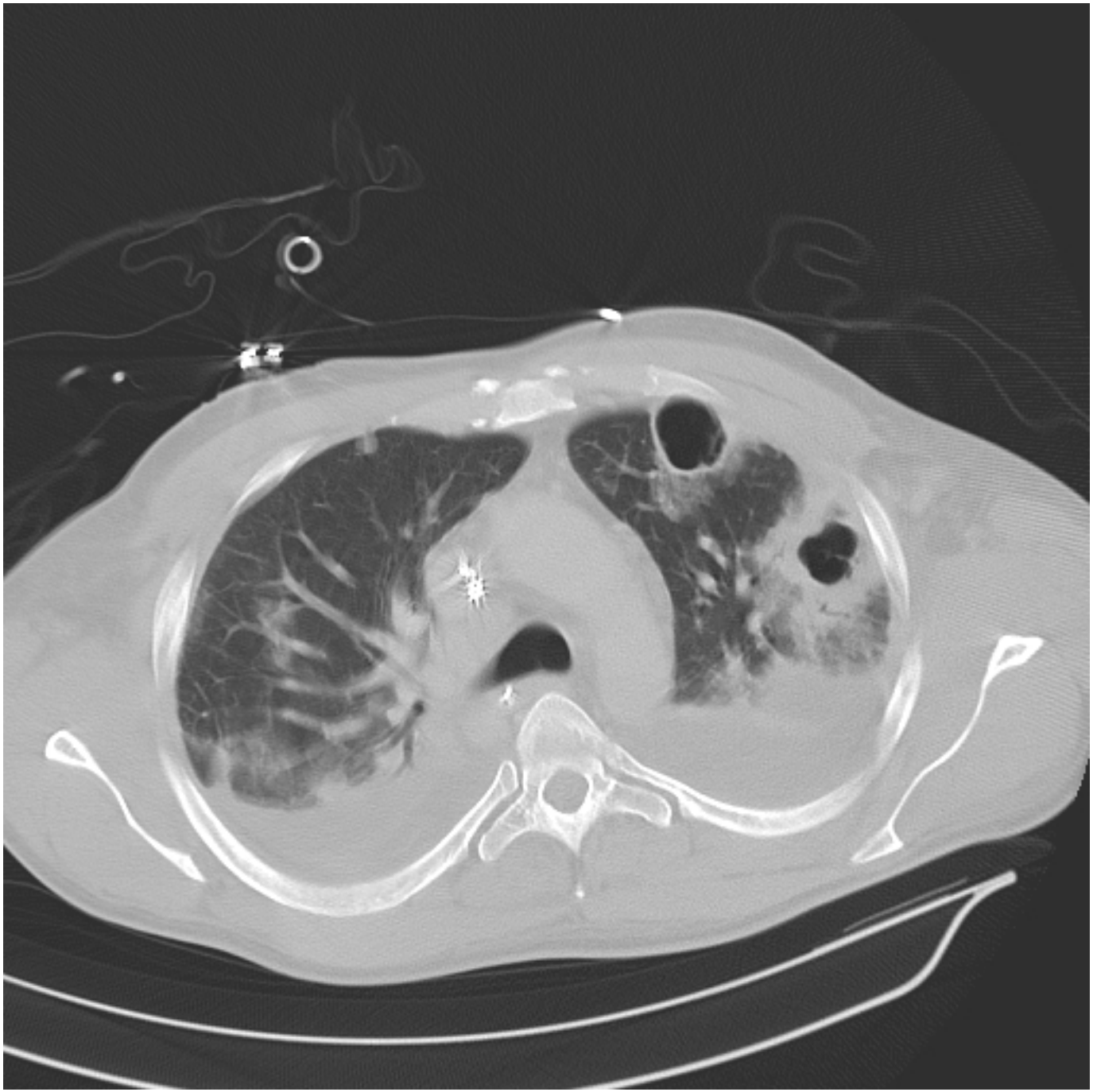
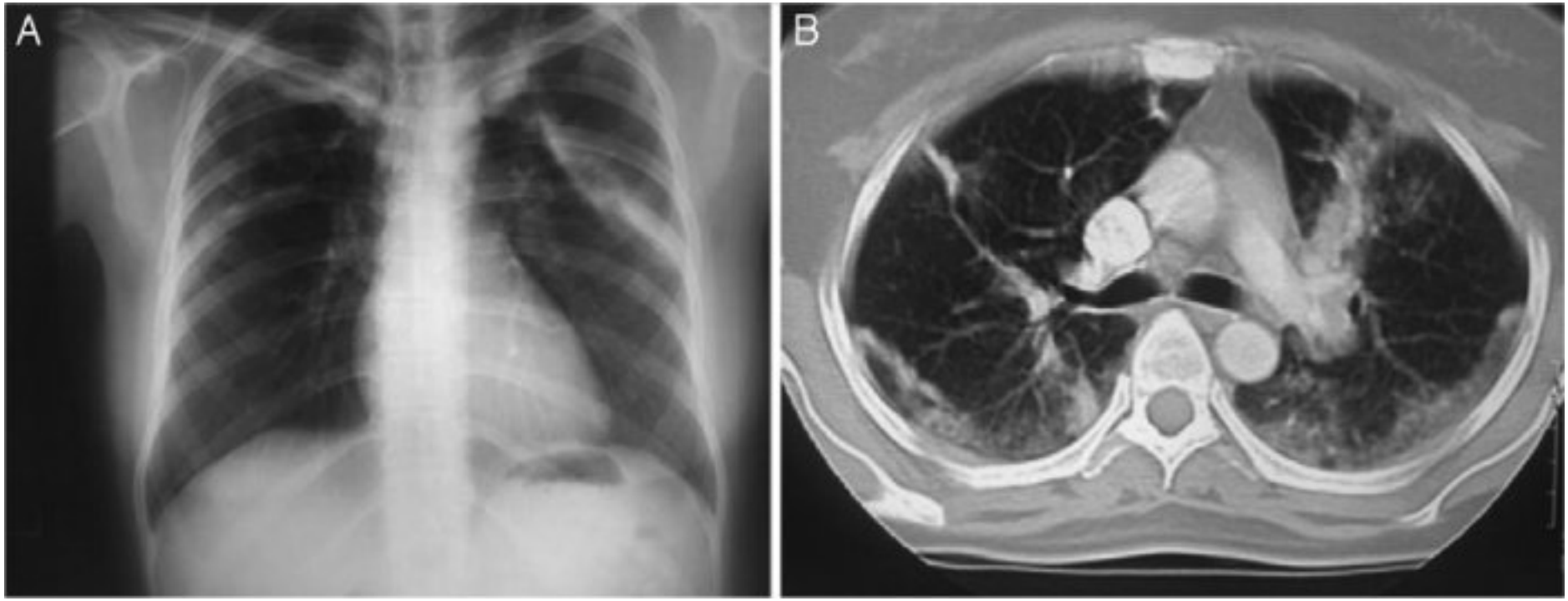
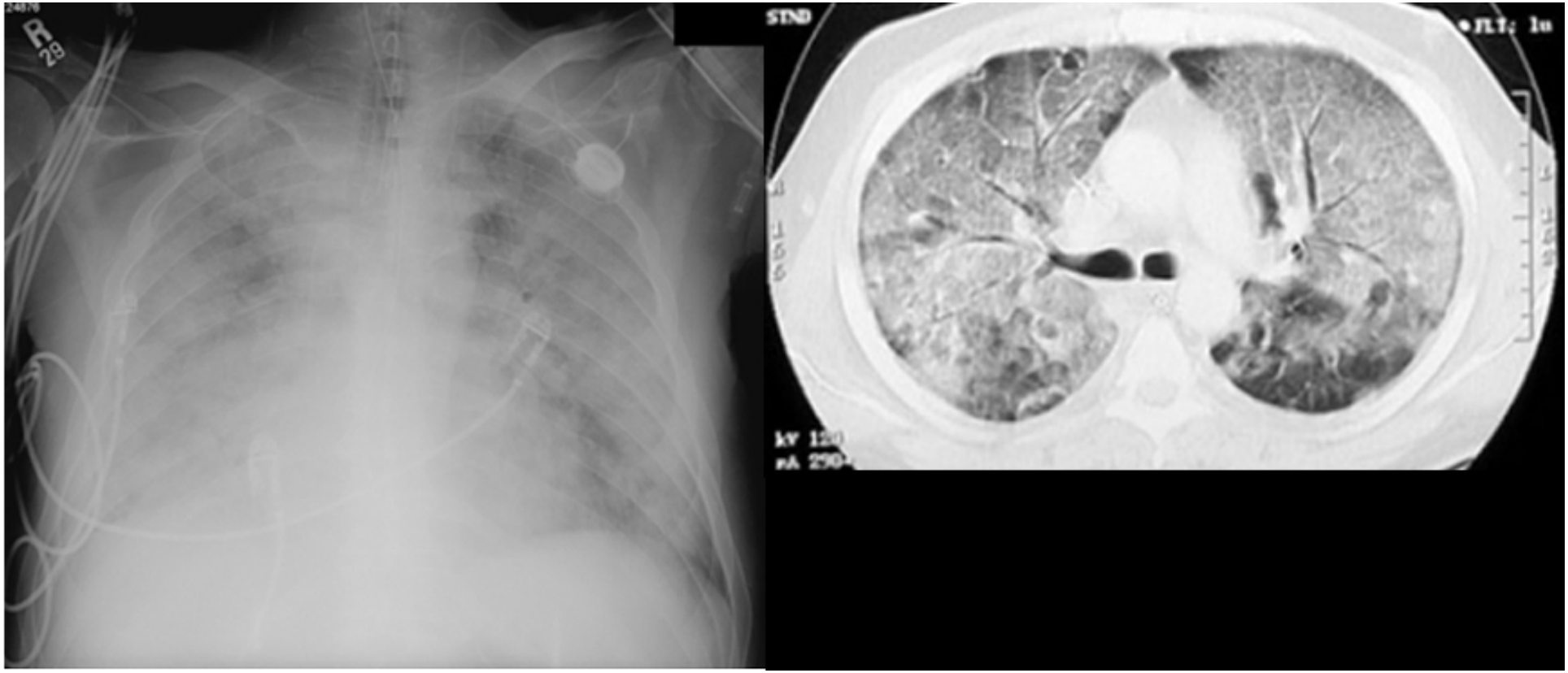


Figure 1. Chest X-ray on admission showing bilateral lower lobe patchy consolidations.




A
B


STND

Improved Survival of Patients With Acute Respiratory Distress Syndrome (ARDS): 1983-1993

John A. Milberg, MPH; Donna R. Davis, RN; Kenneth P. Steinberg, MD; Leonard D. Hudson, MD

JAMA. 1995;273(4):306-309. doi:10.1001/jama.1995.03520280052039.

The North American group examined yearly ARDS mortality from 1983 to 1993. Overall mortality was constant up to 1988 (approximately 60%) but then showed a marked and significant decline to 36% in 1993.

Thorax; 1998;**53**:292–294

Reduced mortality in association with the acute respiratory distress syndrome (ARDS)

S J C Abel, S J Finney, S J Brett, B F Keogh, C J Morgan, T W Evans

1990 – 1993 vs. 1993 - 1997 …[t]here was a marked reduction in mortality between groups 1 and 2 (66% versus 34%)

PROTOCOLLO PER LA GESTIONE

DIAGNOSTICO-TERAPEUTICA DELL'ARDS

- **Inapplicabilità per ventilazione non compatibile con la definizione (si veda lo schema riportato nella sezione 2a.):**
  - La diagnosi di ARDS (come descritto nella Sezione 2.) prevede che i pazienti siano in trattamento, almeno nella fase iniziale, con tecniche di Ventilazione Meccanica (anche Non Invasiva), compresa la sola CPAP:
    - la diagnosi di ARDS LIEVE è possibile (alle condizioni indicate nella Sezione 2.) nei pazienti sottoposti a Ventilazione Meccanica Invasiva o NIMV;
    - le diagnosi di ARDS MODERATA e ARDS SEVERA sono possibili soltanto nei pazienti sottoposti a Ventilazione Meccanica Invasiva.

PROTOCOLLO PER LA GESTIONE

DIAGNOSTICO-TERAPEUTICA DELL'ARDS

- **Impostazioni iniziali del Ventilatore Meccanico (T0):**
  - OBIETTIVO: $SpO_2 > 90\%$
  - Garantire un piano analgosedativo (ed eventualmente di miorisoluzione; si veda eventualmente la sezione 6a.) adeguato al fine di massimizzare la tolleranza del paziente alla Ventilazione Meccanica;
  - Impostare una modalità di Ventilazione Controllata Totale: VCV o PCV;
  - Mantenere Vt = 4-6 ml/Kg;
  - Impostare FR 18-30 atti/minuto;
  - Impostare il Rapporto I:E a valori compresi tra 1:1,5 e 1:2;

EFFECT OF A PROTECTIVE-VENTILATION STRATEGY ON MORTALITY IN THE ACUTE RESPIRATORY DISTRESS SYNDROME

MARCELO BRITTO PASSOS AMATO, M.D., CARMEN SILVIA VALENTE BARBAS, M.D., DENISE MACHADO MEDEIROS, M.D., RICARDO BORGES MAGALDI, M.D., GUILHERME DE PAULA PINTO SCHETTINO, M.D., GERALDO LORENZI-FILHO, M.D., RONALDO ADIB KAIRALLA, M.D., DANIEL DEHEINZELIN, M.D., CARLOS MUNOZ, M.D., ROSELAINE OLIVEIRA, M.D., TERESA YAE TAKAGAKI, M.D., AND CARLOS ROBERTO RIBEIRO CARVALHO, M.D.

(N Engl J Med 1998;338:347-54.)

The New England
Journal of Medicine

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*

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

Background Traditional approaches to mechanical ventilation use tidal volumes of 10 to 15 ml per kilogram of body weight and may cause stretch-induced

Valore mediano VT nell'ARDS: 8,5 ml/kg (ARMA trial + 361 ICU da 20 nazioni)

J Crit Care 1996;11:9–18

Survey 1992: più di 1000 intensivisti, 50% ventila ARDS con VT 8-9 ml/kg, 96% decide il VT anche sulla base delle Paw.

Crit Care Med 2005; 33:21 – 30

Take-home message:

1. La letteratura non è vangelo e i “nomi famosi” non sono evangelisti

	N° of centers	study period	Patients	TV	total	dead in the ICU - N	dead in the ICU %	dead in the H - N	dead in the H %
NEJM 1998	2	1990-1995			29	11	38	13	45
					24	17	71	17	71
NEJM 2000	10	996-1999			4[illegible]2	na	na	134	31
					429	[illegible]a	na	171	40

5 pz/anno

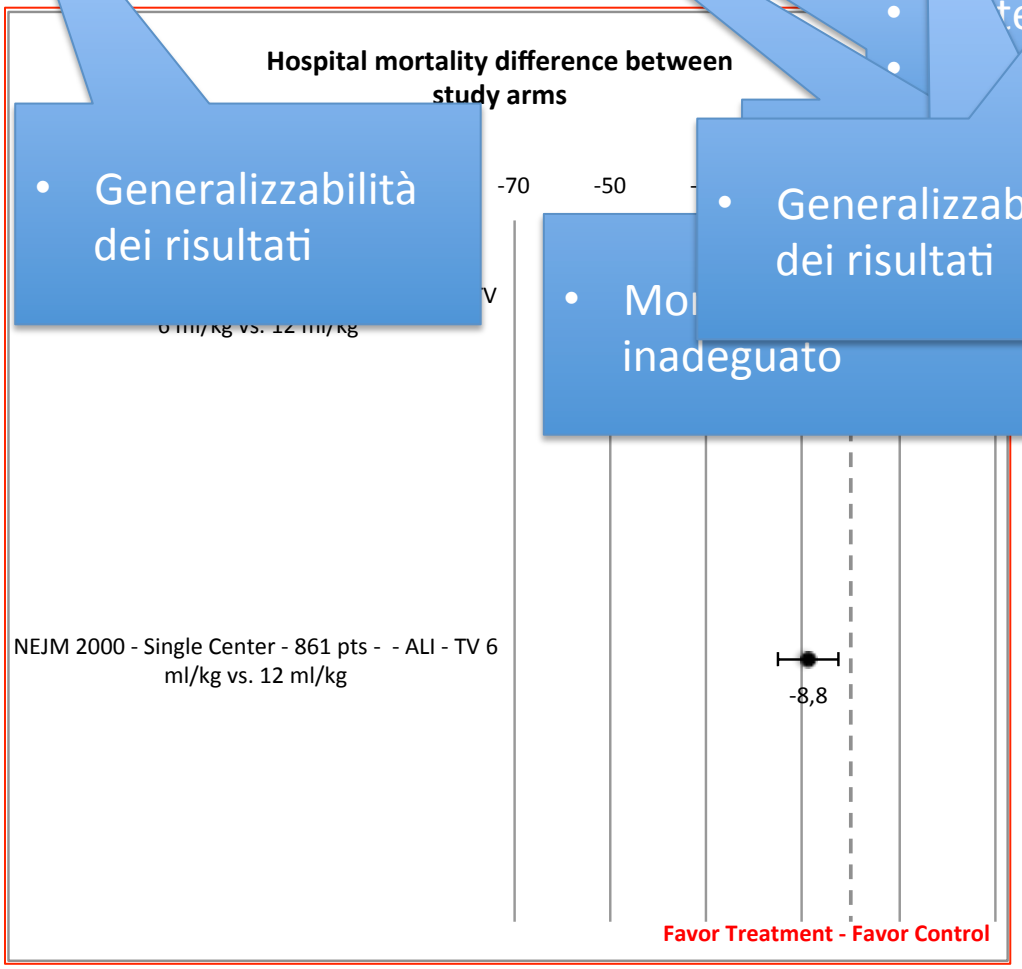
29 pz/anno

- Generalizzabilità dei risultati

- Generalizzabilità dei risultati

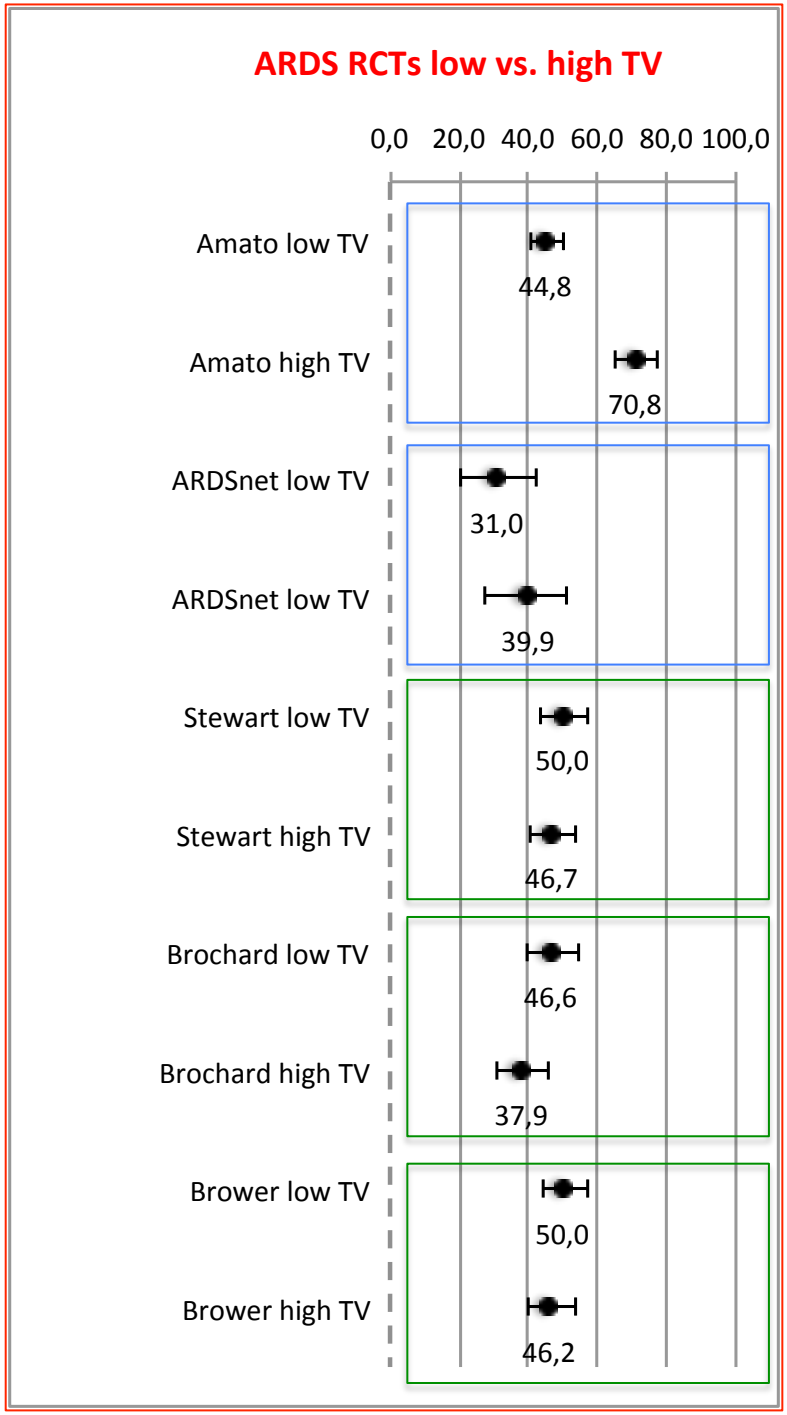
- Mo[illegible] inadeguato

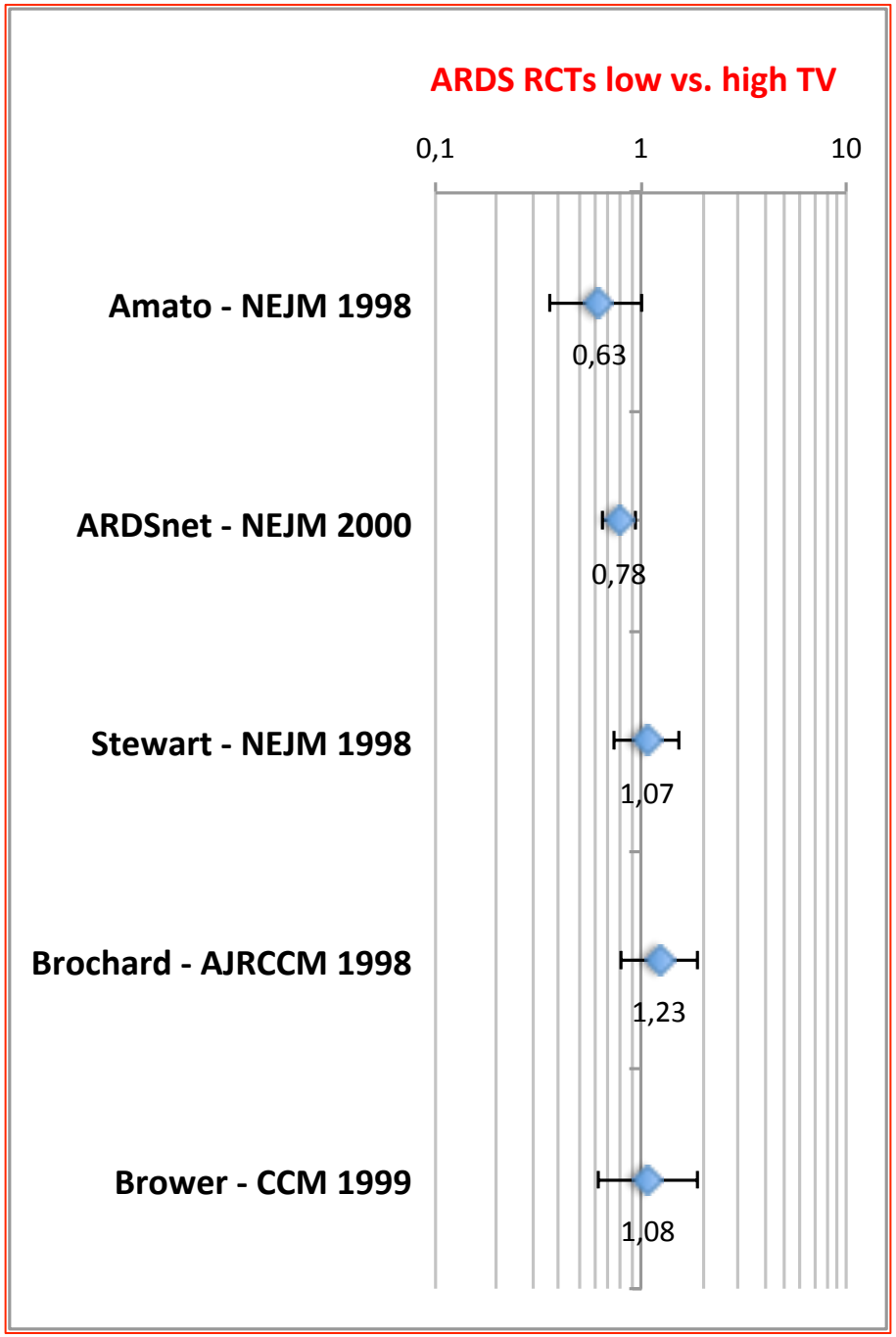
- [illegible]ter
- [illegible] della [illegible]one



Take-home message:

1. La letteratura non è vangelo e i “nomi famosi” non sono evangelisti
2. Attenzione alla generalizzabilità (numero e tipo di centri, paragonabilità delle popolazioni)
3. Verificare se c’è una forte selezione dei pz reclutati (bias potenziale)
4. Verificare se il controllo è adeguato
5. Verificare se l’outcome è adeguato
6. Verificare la numerosità del campione


ARDS RCTs low vs. high TV
0,0
20,0
40,0
60,0
80,0
100,0
Amato low TV
44,8
Amato high TV
70,8
ARDSnet low TV
31,0
ARDSnet low TV
39,9
Stewart low TV
50,0
Stewart high TV
46,7
Brochard low TV
46,6
Brochard high TV
37,9
Brower low TV
50,0
Brower high TV
46,2


ARDS RCTs low vs. high TV
0,1
1
10
Amato - NEJM 1998
0,63
ARDSnet - NEJM 2000
0,78
Stewart - NEJM 1998
1,07
Brochard - AJRCCM 1998
1,23
Brower - CCM 1999
1,08

Meta-Analysis of Acute Lung Injury and Acute Respiratory Distress Syndrome Trials Testing Low Tidal Volumes

Peter Q. Eichacker, Eric P. Gerstenberger, Steven M. Banks, Xizhong Cui, and Charles Natanson

Critical Care Medicine Department, Clinical Center, National Institutes of Health, Bethesda, Maryland

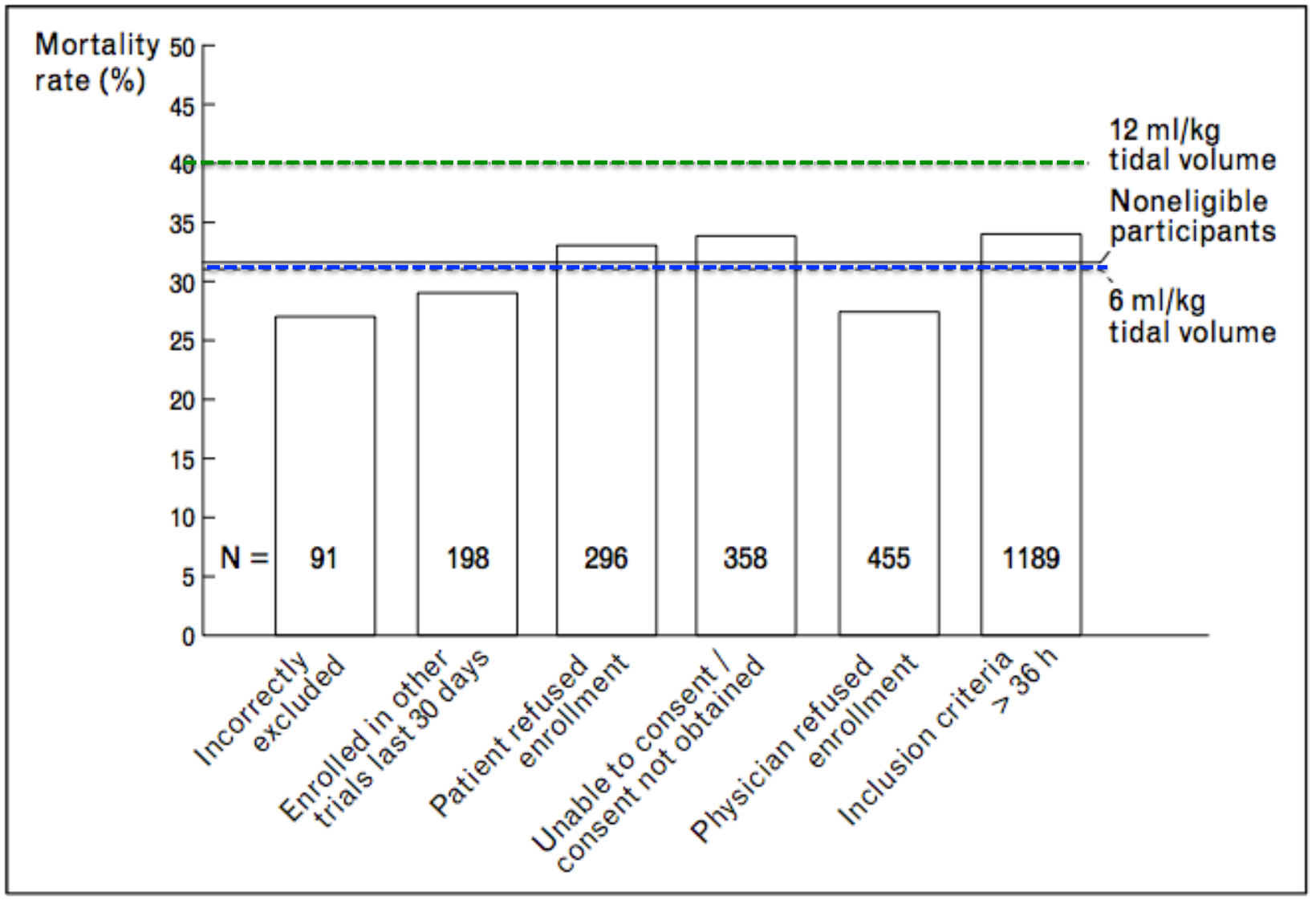
trials (Figure 3) to explain the discrepant results (Figure 1). The three nonbeneficial trials used control tidal volumes that resulted in lower airway pressures (28 to 32 cm H_2O), consistent with routine care at the time of the studies (29 to 31 cm H_2O) (10). Compared with these control pressures, low tidal volumes did not improve outcomes. However, the two beneficial trials compared low tidal volume ventilation with control arms with airway pressures high enough (34 to 37 cm H_2O) to potentially increase control mortality rates. In this setting, low tidal volumes may

Author (Ref.)	orted Mortality Difference (*p Value*)
Amato and co	< 0.001
Stewart and cc	0.72
Brochard and	0.38
Brower and co	0.60
ARDSNet (4)	0.007

Limitations of clinical trials in acute lung injury and acute respiratory distress syndrome

John J. Marini

Current Opinion in Critical Care 2006, 12:25–31



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produced a worse outcome and they clearly showed that high tidal volumes (e.g., 12 ml/kg based on predicted or measured body weight) associated with high airway pressures (34 cm H_2O or more) were harmful and should be avoided (3, 4). In contrast, the three nonbeneficial trials (5–7) employed control arms that closely reflected current practice of physicians studying and treating patients with ALI and ARDS (3, 4, 10–13). These trials established that, as long as tidal volumes produce airway pressures between 28 and 32 cm H_2O, there is no benefit from using low tidal volumes (i.e., 6 to 7 ml/kg based on either ideal [5], predicted [7], or dry [6] body weight), and it may be harmful.

PROTOCOLLO PER LA GESTIONE

DIAGNOSTICO-TERAPEUTICA DELL'ARDS

Sezione 5c. Posizione prona

- **Indicazioni:**
  - Indicazione salvavita (immediata): $PaO_2 < 55$ mmHg con ventilazione ottimale e $FiO_2 = 1$;
  - ARDS SEVERA dopo 12 ore di ventilazione ottimizzata;
  - ARDS MODERATA nei casi in cui $PaO_2/FiO_2 \leq 150$ mmHg dopo 12 ore di ventilazione ottimizzata.

The New England Journal of Medicine

EFFECT OF PRONE POSITIONING ON THE SURVIVAL OF PATIENTS WITH ACUTE RESPIRATORY FAILURE (ALI 5% & ARDS 95%)

LUCIANO GATTINONI, M.D., GIANNI TOGNONI, M.D., ANTONIO PESENTI, M.D., PAOLO TACCONE, M.D., DANIELE MASCHERONI, M.D., VIOLETA LABARTA, M.S., ROBERTO MALACRIDA, M.D., PAOLA DI GIULIO, R.N., M.S.C., ROBERTO FUMAGALLI, M.D., PAOLO PELOSI, M.D., LUCA BRAZZI, M.D., AND ROBERTO LATINI, M.D., FOR THE PRONE–SUPINE STUDY GROUP*

(N Engl J Med 2001;345:568-73.)

In the case of 12 patients (43 maneuvers) in the supine group, a decision was made, despite randomization, to use the prone position because of the severity of arterial hypoxemia. In the prone group, lo-

Take-home message:

1. La letteratura non è vangelo e i “nomi famosi” non sono evangelisti
2. Attenzione alla generalizzabilità (numero e tipo di centri, paragonabilità delle popolazioni)
3. Verificare se c’è una forte selezione dei pz reclutati (bias potenziale)
4. Verificare se il controllo è adeguato
5. Verificare se l’outcome è adeguato
6. Verificare la numerosità del campione
7. Attenzione ai RCT in cui non sia possibile il cieco e vi sia una propensione per il trattamento oggetto di studio

The New England Journal of Medicine

EFFECT OF PRONE POSITIONING ON THE SURVIVAL OF PATIENTS WITH ACUTE RESPIRATORY FAILURE

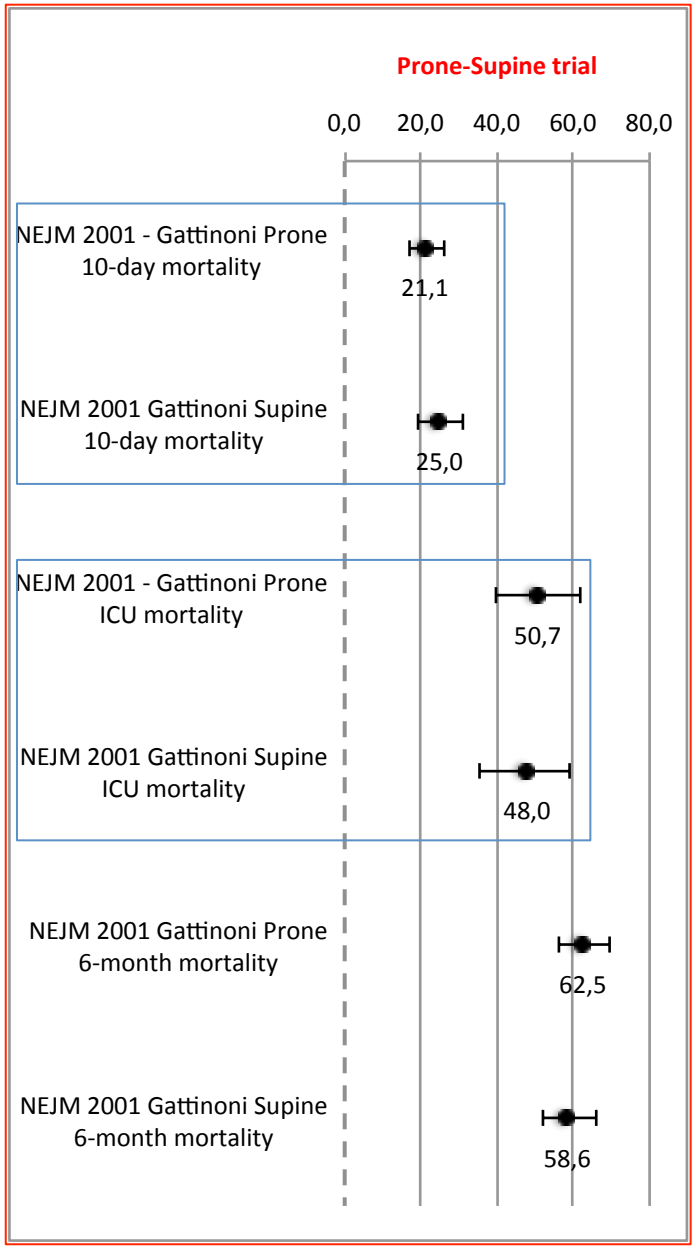
LUCIANO GATTINONI, M.D., GIANNI TOGNONI, M.D., ANTONIO PESENTI, M.D., PAOLO TACCONE, M.D., DANIELE MASCHERONI, M.D., VIOLETA LABARTA, M.S., ROBERTO MALACRIDA, M.D., PAOLA DI GIULIO, R.N., M.S.C., ROBERTO FUMAGALLI, M.D., PAOLO PELOSI, M.D., LUCA BRAZZI, M.D., AND ROBERTO LATINI, M.D., FOR THE PRONE–SUPINE STUDY GROUP*

- **30 centri**
- **Periodo circa 3 anni**

304 pz randomizzati
Circa 3,5 pz/anno/centro

- **Monitoraggio idonei non arruolati**
- **21 centri**
- **Periodo circa 1,5 anni**

214 idonei non arruolati
Circa 7 pz/anno/centro



Prone Positioning in Patients With Moderate and Severe Acute Respiratory Distress Syndrome

A Randomized Controlled Trial

JAMA. 2009;302(18):1977-1984

Paolo Taccone, MD
Antonio Pesenti, MD
Roberto Latini, MD
Federico Polli, MD
Federica Vagginelli, MD
Cristina Mietto, MD
Luisa Caspani, MD
Ferdinando Raimondi, MD
Giovanni Bordone, MD
Gaetano Iapichino, MD
Jordi Mancebo, MD
Claude Guérin, MD
Louis Ayzac, MD
Lluis Blanch, MD
Roberto Fumagalli, MD
Gianni Tognoni, MD
Luciano Gattinoni, MD, FRCP
for the Prone-Supine II Study Group

Almeno 20 ore di pronazione al giorno rispetto alle 6 dello studio precedente

Prone Positioning in Patients With Moderate and Severe Acute Respiratory Distress Syndrome

A Randomized Controlled Trial

JAMA. 2009;302(18):1977-1984

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Lluis Blanch, MD
Roberto Fumagalli, MD
Gianni Tognoni, MD
Luciano Gattinoni, MD, FRCP
for the Prone-Supine II Study Group

tocol in both study groups. In particular, it was required that tidal volumes be limited to a maximum of 8 mL/kg of ideal body weight and airway plateau pressures be limited to 30 cm H_2O.

Prone Positioning in Patients With Moderate and Severe Acute Respiratory Distress Syndrome

A Randomized Controlled Trial

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Jordi Mancebo, MD
Claude Guérin, MD
Louis Ayzac, MD
Lluis Blanch, MD
Roberto Fumagalli, MD
Gianni Tognoni, MD
Luciano Gattinoni, MD, FRCP
for the Prone-Supine II Study Group

The primary outcome measure was death from any cause, assessed 28 days after enrollment in the study. Second-

Prone Positioning in Patients With Moderate and Severe Acute Respiratory Distress Syndrome

A Randomized Controlled Trial

JAMA. 2009;302(18):1977-1984

Paolo Taccone, MD
Antonio Pesenti, MD
Roberto Latini, MD
Federico Polli, MD
Federica Vagginelli, MD
Cristina Mietto, MD
Luisa Caspani, MD
Ferdinando Raimondi, MD
Giovanni Bordone, MD
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Roberto Fumagalli, MD
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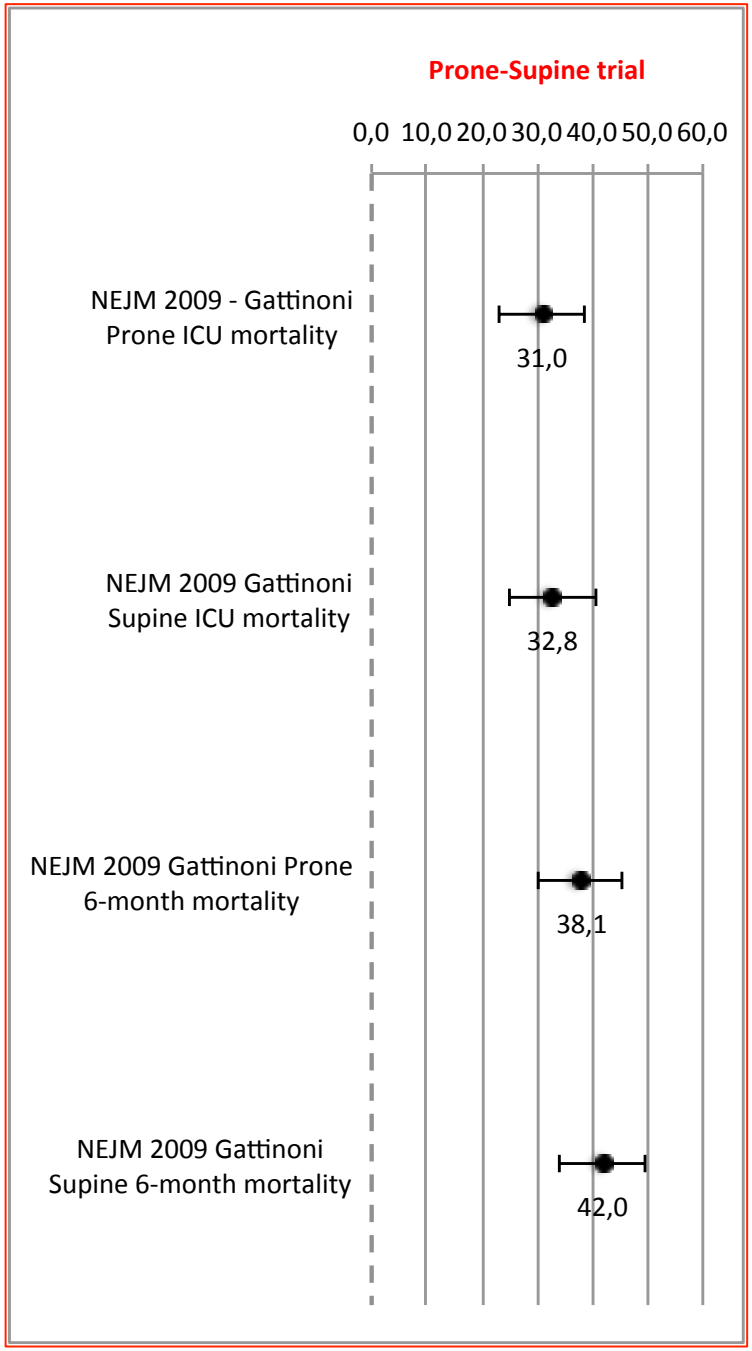
Luciano Gattinoni, MD, FRCP
for the Prone-Supine II Study Group

- **25 centri**
- **Periodo circa 3,5 anni**

342 pz randomizzati
Circa 4 pz/anno/centro



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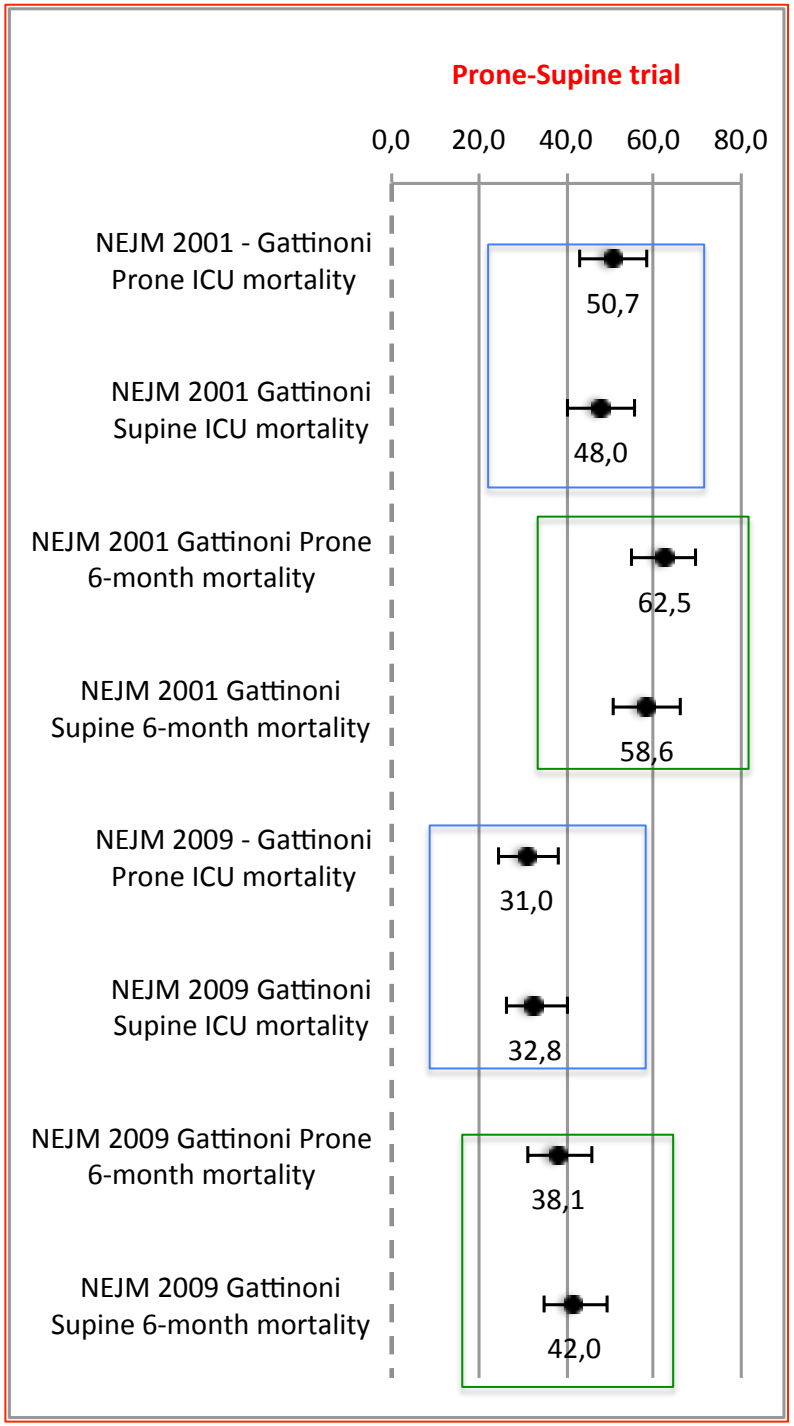
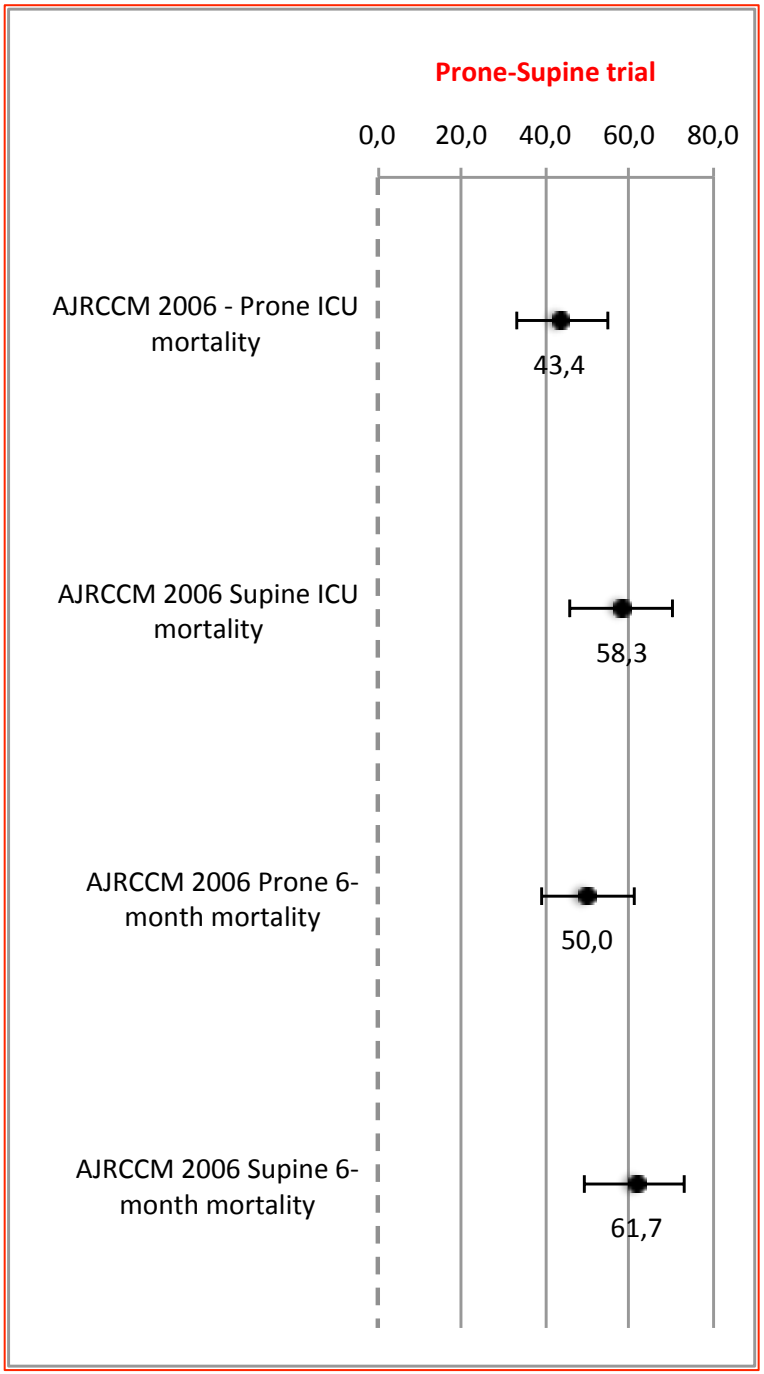

Prone-Supine trial
0,0
20,0
40,0
60,0
80,0
NEJM 2001 - Gattinoni
Prone ICU mortality
50,7
NEJM 2001 Gattinoni
Supine ICU mortality
48,0
NEJM 2001 Gattinoni Prone
6-month mortality
62,5
NEJM 2001 Gattinoni
Supine 6-month mortality
58,6
NEJM 2009 - Gattinoni
Prone ICU mortality
31,0
NEJM 2009 Gattinoni
Supine ICU mortality
32,8
NEJM 2009 Gattinoni Prone
6-month mortality
38,1
NEJM 2009 Gattinoni
Supine 6-month mortality
42,0

A Multicenter Trial of Prolonged Prone Ventilation in Severe Acute Respiratory Distress Syndrome

Jordi Mancebo, Rafael Fernández, Lluis Blanch, Gemma Rialp, Federico Gordo, Miquel Ferrer, Fernando Rodríguez, Pau Garro, Pilar Ricart, Immaculada Vallverdú, Ignasi Gich, José Castaño, Pilar Saura, Guillermo Domínguez, Alfons Bonet, and Richard K. Albert

Am J Respir Crit Care Med Vol 173. pp 1233–1239, 2006

The treatment guidelines, including mechanical ventilation settings (maximal V_T = 10 ml/kg and maximal plateau airway pressure = 35 cm H_2O, or up to 40 cm H_2O when chest wall stiffness was clinically suspected), weaning (using T-piece trials or pressure support ventila-



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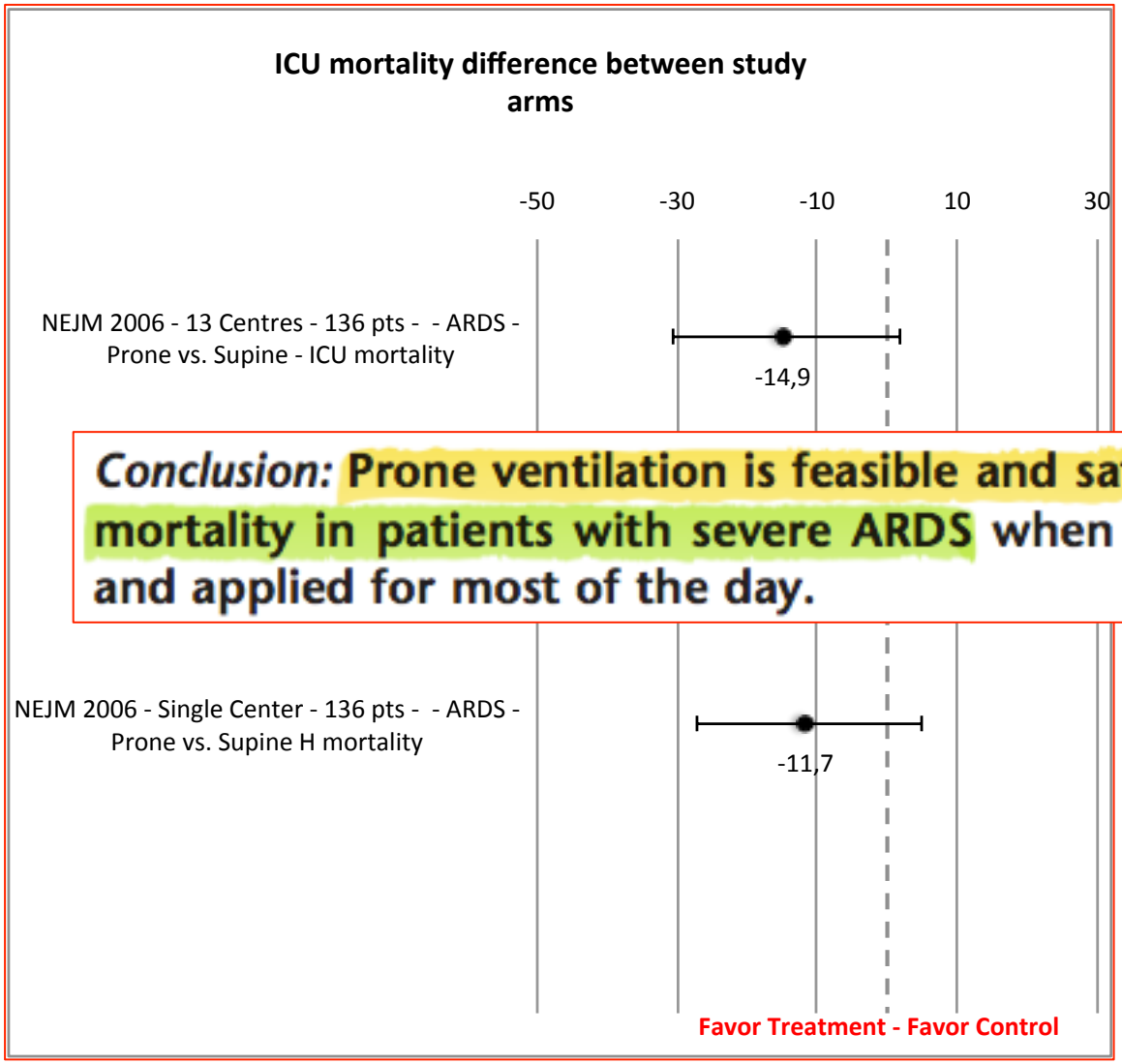
- **13 centri**
- **Periodo circa 4 anni**

136 pz randomizzati
Circa 2,5 pz/anno/centro

A Multicenter Trial of Prolonged Prone Ventilation in Severe Acute Respiratory Distress Syndrome

Jordi Mancebo, Rafael Fernández, Lluis Blanch, Gemma Rialp, Federico Gordo, Miquel Ferrer, Fernando Rodríguez, Pau Garro, Pilar Ricart, Immaculada Vallverdú, Ignasi Gich, José Castaño, Pilar Saura, Guillermo Domínguez, Alfons Bonet, and Richard K. Albert



Conclusion: Prone ventilation is feasible and safe, and may reduce mortality in patients with severe ARDS when it is initiated early and applied for most of the day.

Take-home message:

1. La letteratura non è vangelo e i “nomi famosi” non sono evangelisti
2. Attenzione alla generalizzabilità (numero e tipo di centri, paragonabilità delle popolazioni)
3. Verificare se c’è una forte selezione dei pz reclutati (bias potenziale)
4. Verificare se il controllo è adeguato
5. Verificare se l’outcome è adeguato
6. Verificare la numerosità del campione
7. Attenzione ai RCT in cui non sia possibile il cieco e vi sia una propensione per il trattamento oggetto di studio
8. Verificare la fondatezza delle conclusioni

The NEW ENGLAND JOURNAL of MEDICINE

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 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*

N Engl J Med 2013; 368:2159-2168

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- **27 centri**
- **Periodo circa 2,5 anni**

466 pz randomizzati
Circa 7 pz/anno/centro

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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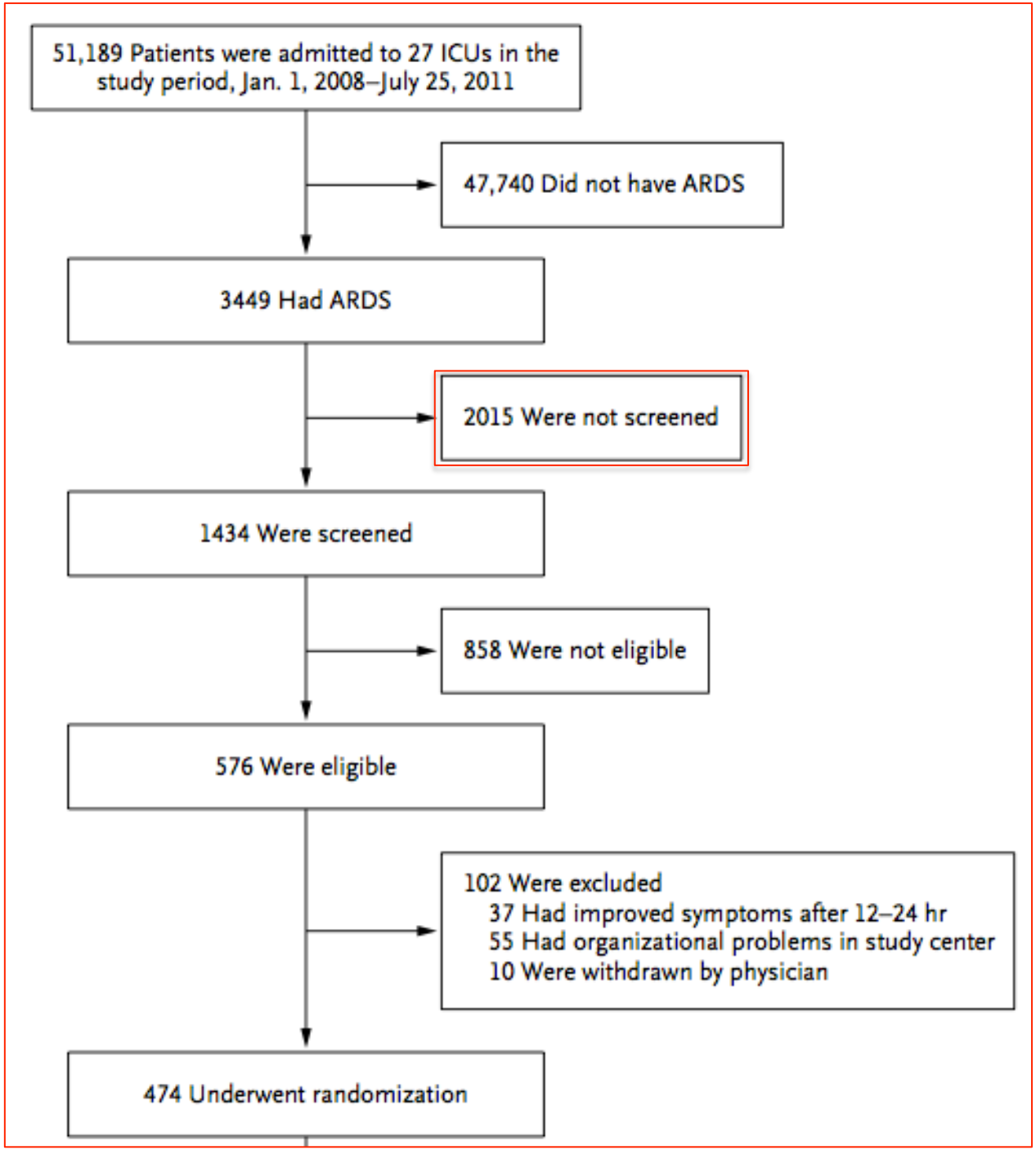
Patients were recruited from 26 ICUs in France and 1 in Spain, all of which have used prone positioning in daily practice for more than 5 years.


51,189 Patients were admitted to 27 ICUs in the study period, Jan. 1, 2008–July 25, 2011
47,740 Did not have ARDS
3449 Had ARDS
2015 Were not screened
1434 Were screened
858 Were not eligible
576 Were eligible
102 Were excluded
37 Had improved symptoms after 12–24 hr
55 Had organizational problems in study center
10 Were withdrawn by physician
474 Underwent randomization

The NEW ENGLAND JOURNAL of MEDICINE

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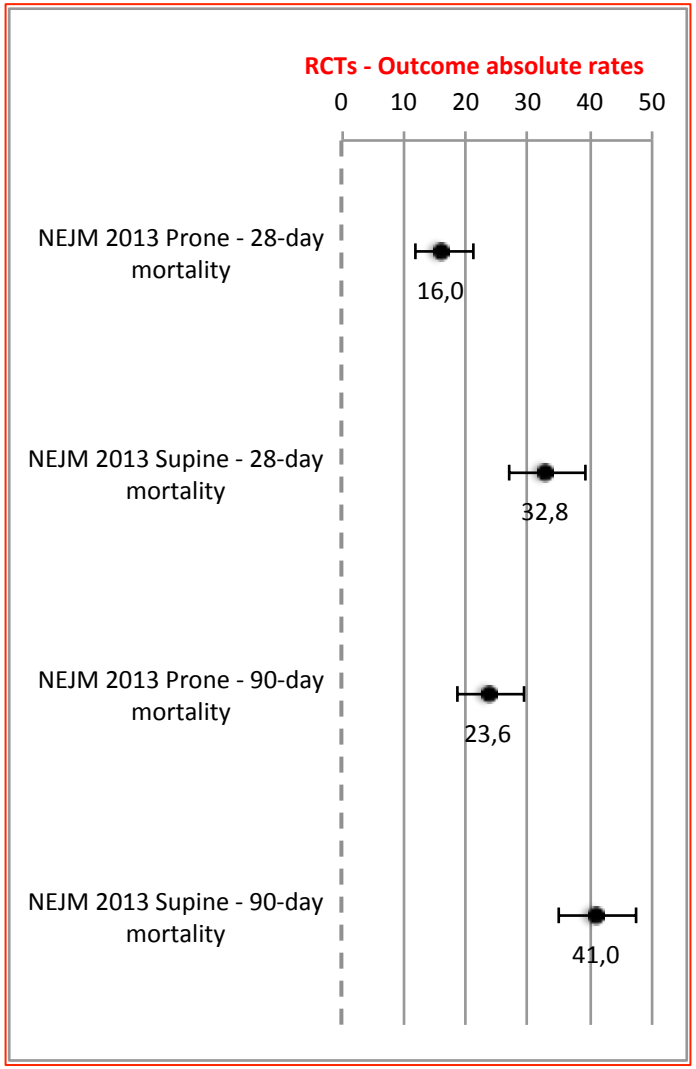
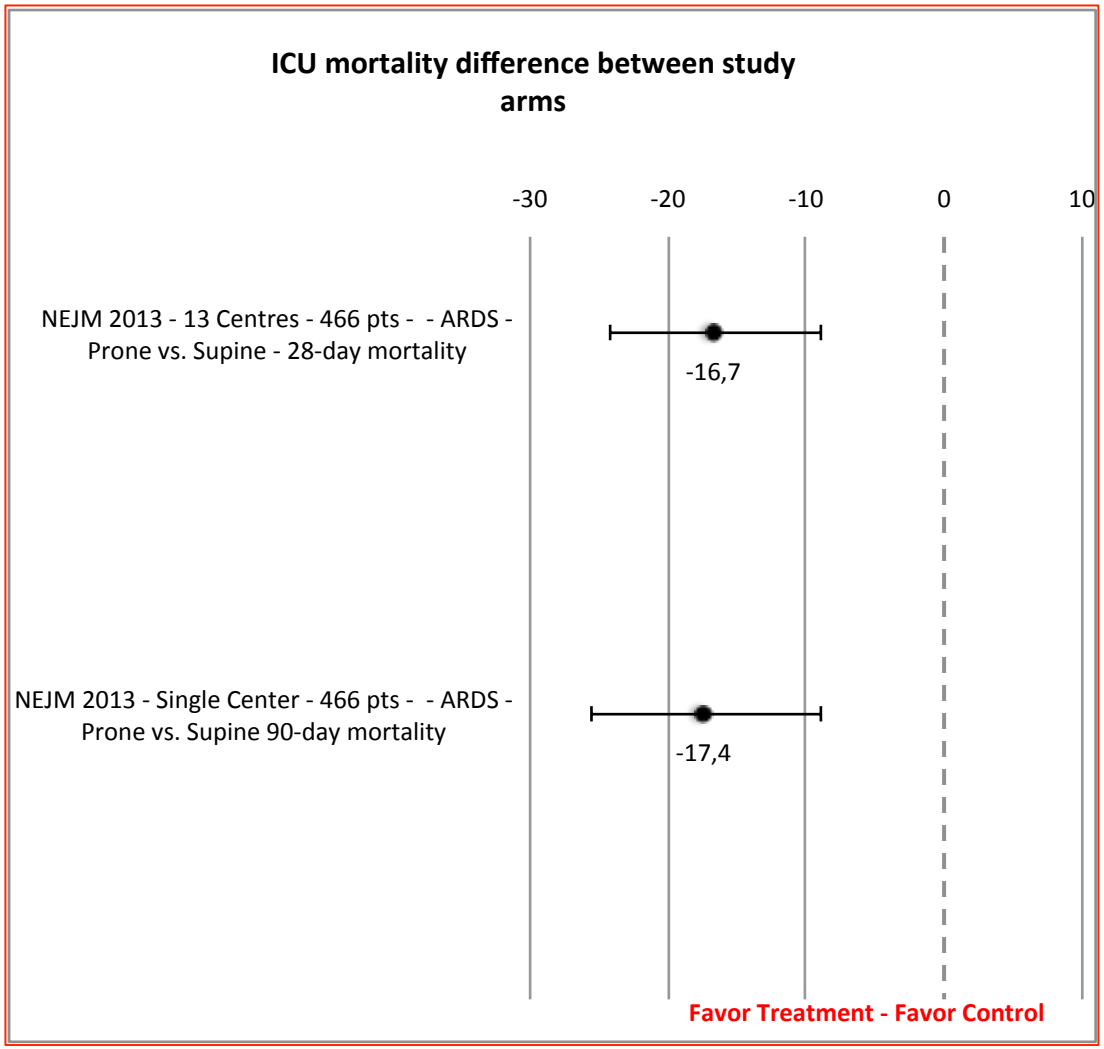
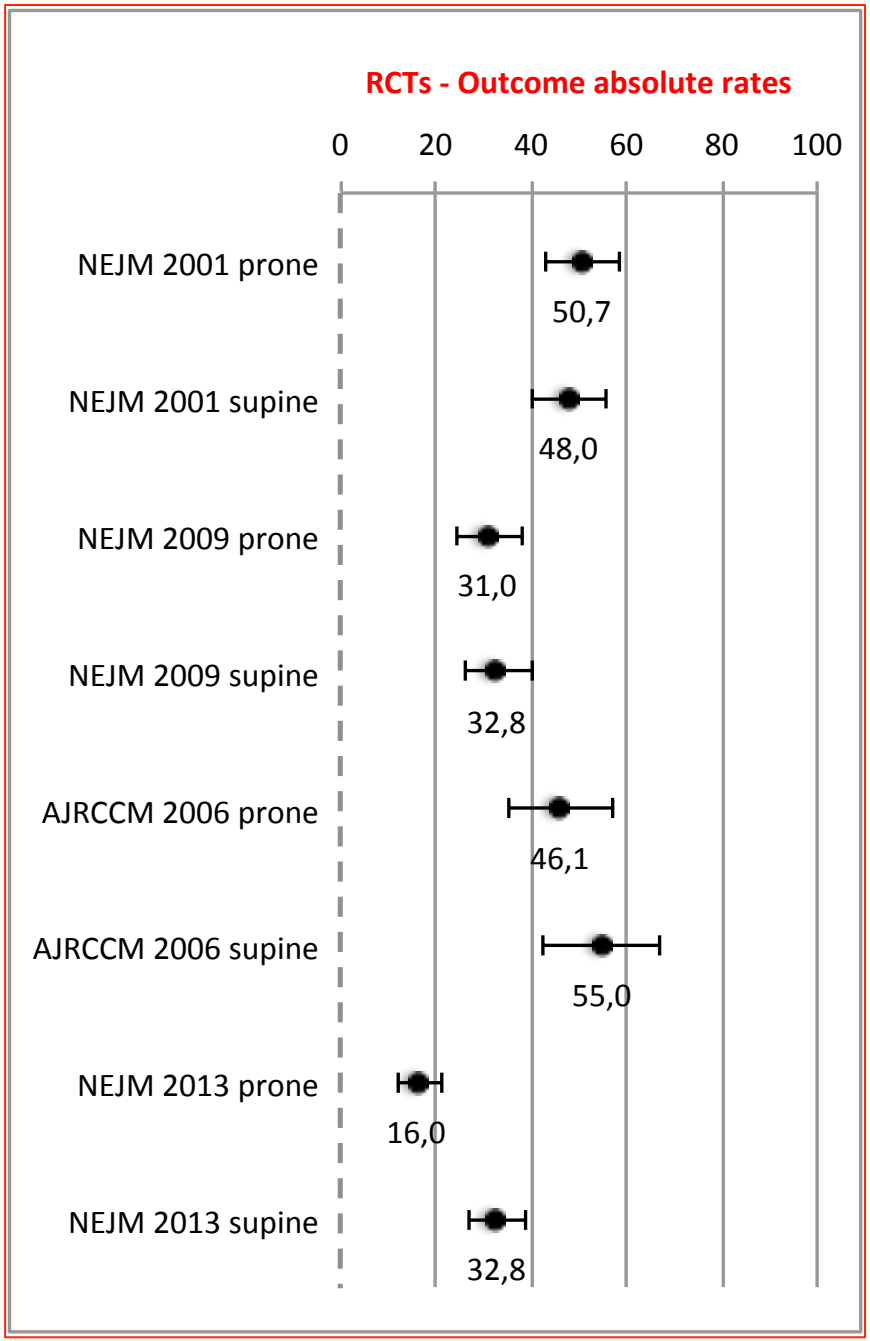
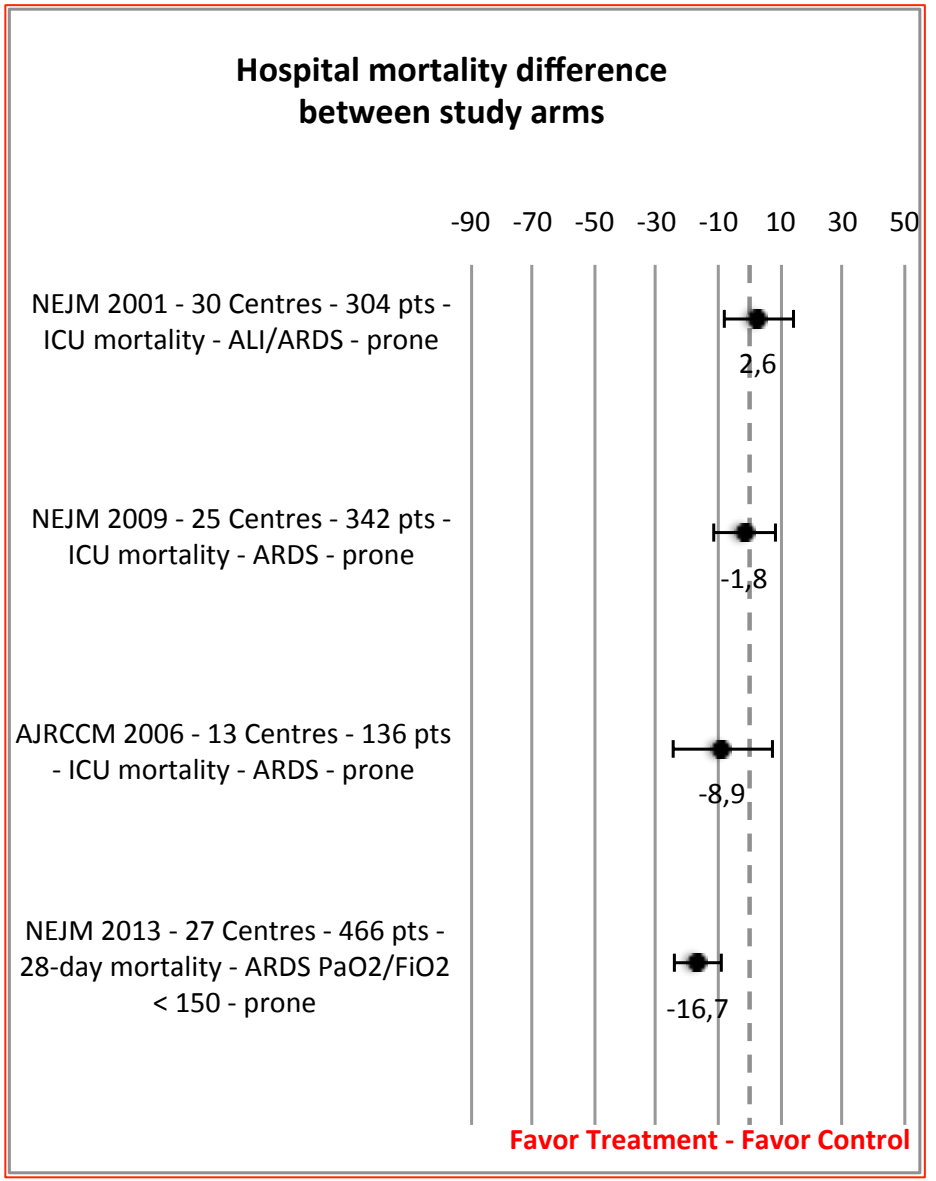





RCTs - Outcome absolute rates
0
20
40
60
80
100
NEJM 2001 prone
50,7
NEJM 2001 supine
48,0
NEJM 2009 prone
31,0
NEJM 2009 supine
32,8
AJRCCM 2006 prone
46,1
AJRCCM 2006 supine
55,0
NEJM 2013 prone
16,0
NEJM 2013 supine
32,8


Hospital mortality difference between study arms
-90
-70
-50
-30
-10
10
30
50
NEJM 2001 - 30 Centres - 304 pts - ICU mortality - ALI/ARDS - prone
2,6
NEJM 2009 - 25 Centres - 342 pts - ICU mortality - ARDS - prone
-1,8
AJRCCM 2006 - 13 Centres - 136 pts - ICU mortality - ARDS - prone
-8,9
NEJM 2013 - 27 Centres - 466 pts - 28-day mortality - ARDS PaO2/FiO2 < 150 - prone
-16,7
Favor Treatment - Favor Control

Take-home message:

1. La letteratura non è vangelo e i “nomi famosi” non sono evangelisti
2. Attenzione alla generalizzabilità (numero e tipo di centri, paragonabilità delle popolazioni)
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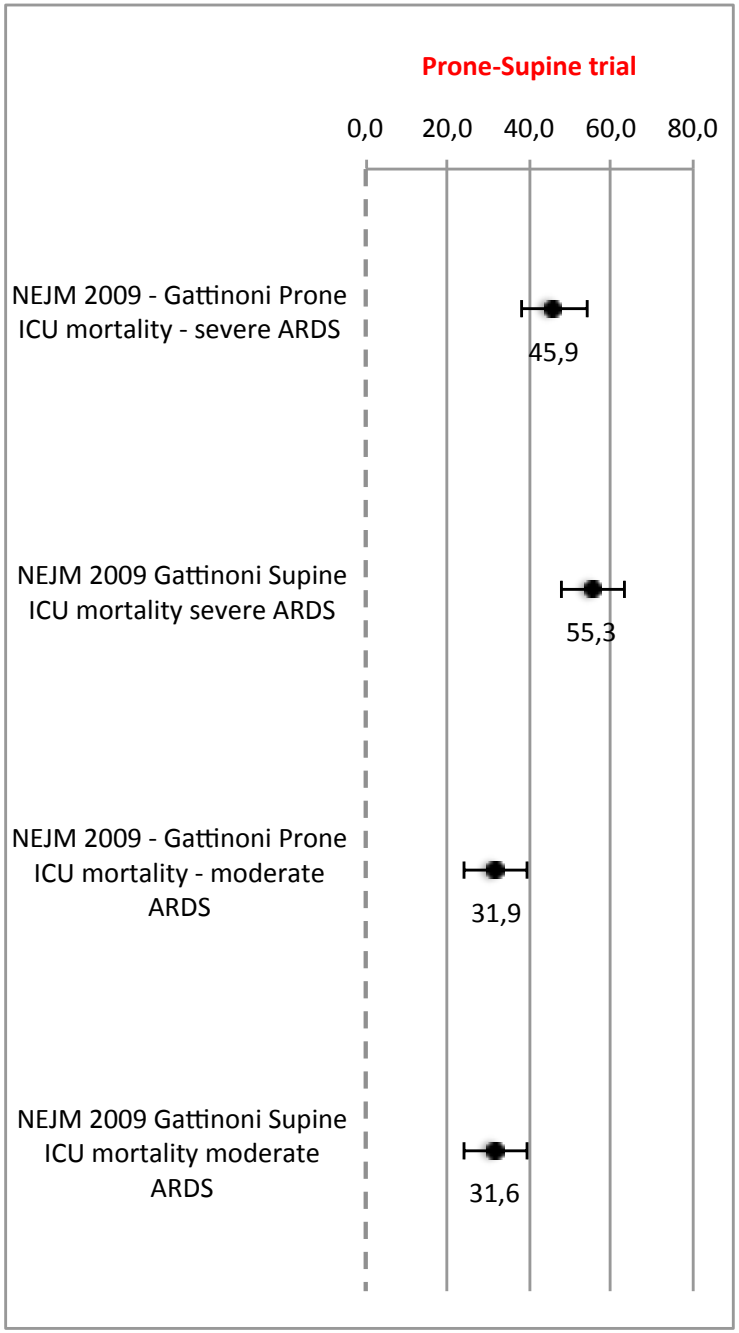
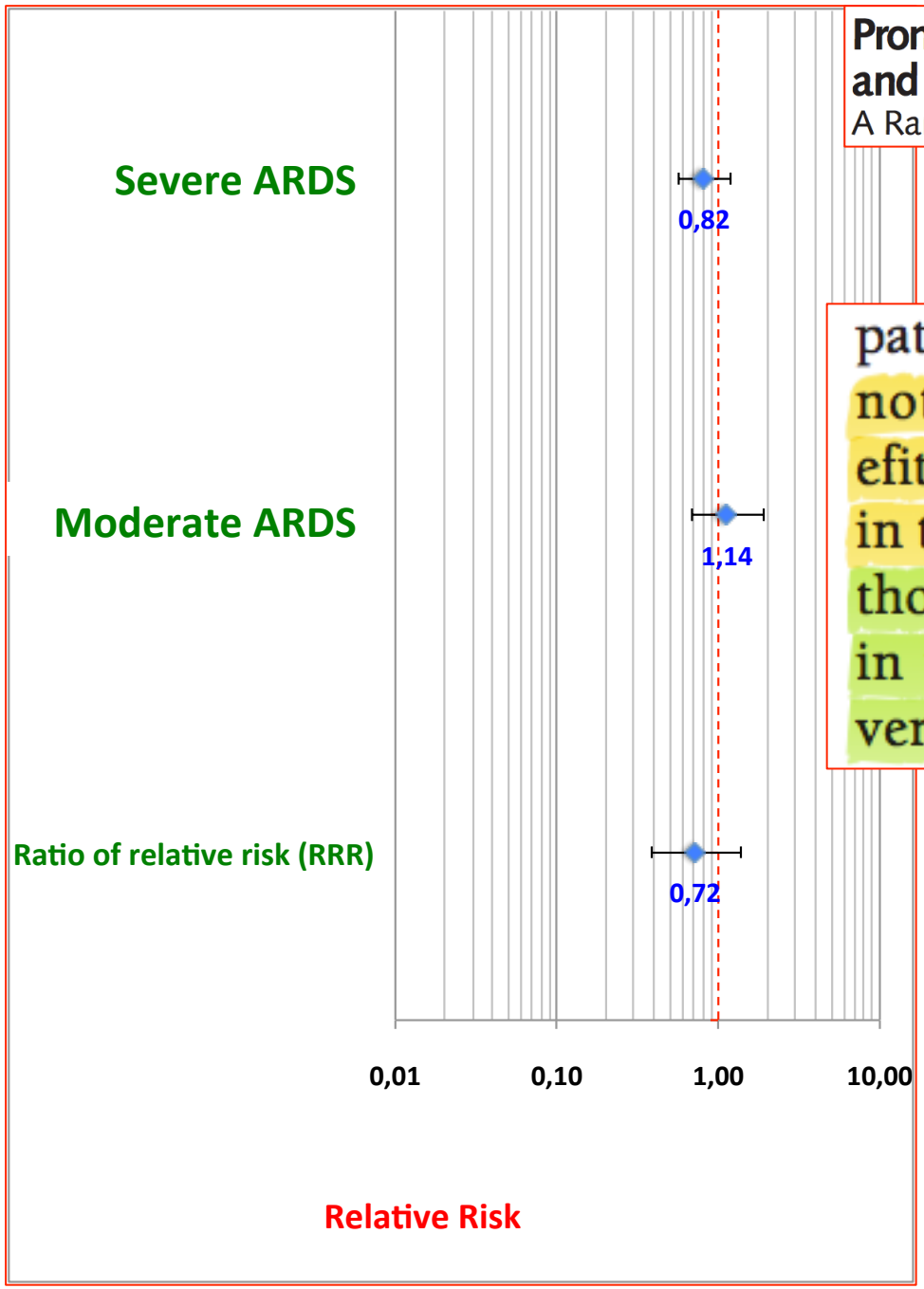
6. Verificare la numerosità del campione
7. Attenzione ai RCT in cui non sia possibile il cieco e vi sia una propensione per il trattamento oggetto di studio
8. Verificare la fondatezza delle conclusioni
9. Porsi il problema dei risultati discrepanti in letteratura e non innamorarsi dei risultati positivi



Prone Positioning in Patients With Moderate and Severe Acute Respiratory Distress Syndrome
A Randomized Controlled Trial

patient severity. Despite that, we could not show a significant survival benefit, either in the general population or in the predefined study subgroups, although a favorable trend was detected in the subgroup of patients with severe hypoxemia.



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Treating Individuals 2

Subgroup analysis in randomised controlled trials: importance, indications, and interpretation

Lancet 2005; 365: 176–86 Peter M Rothwell

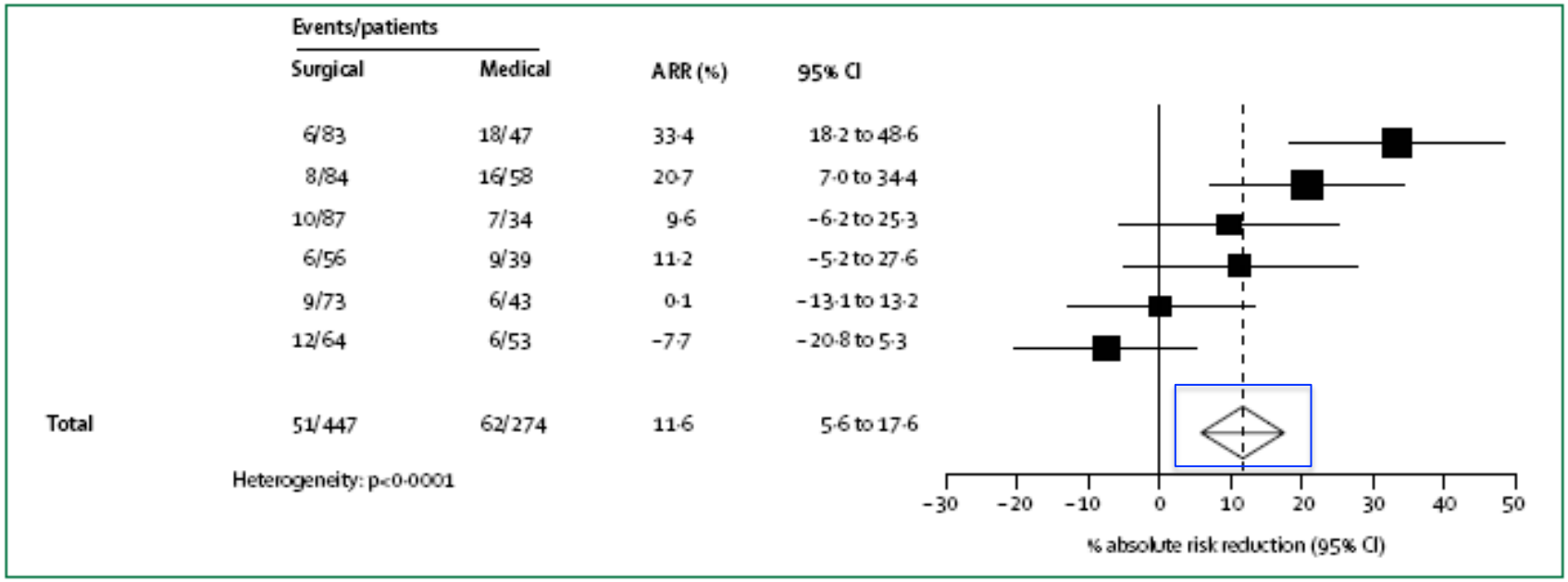

Figure 3: Effect of carotid endarterectomy in patients with ≥70% symptomatic stenosis in ECST[21]

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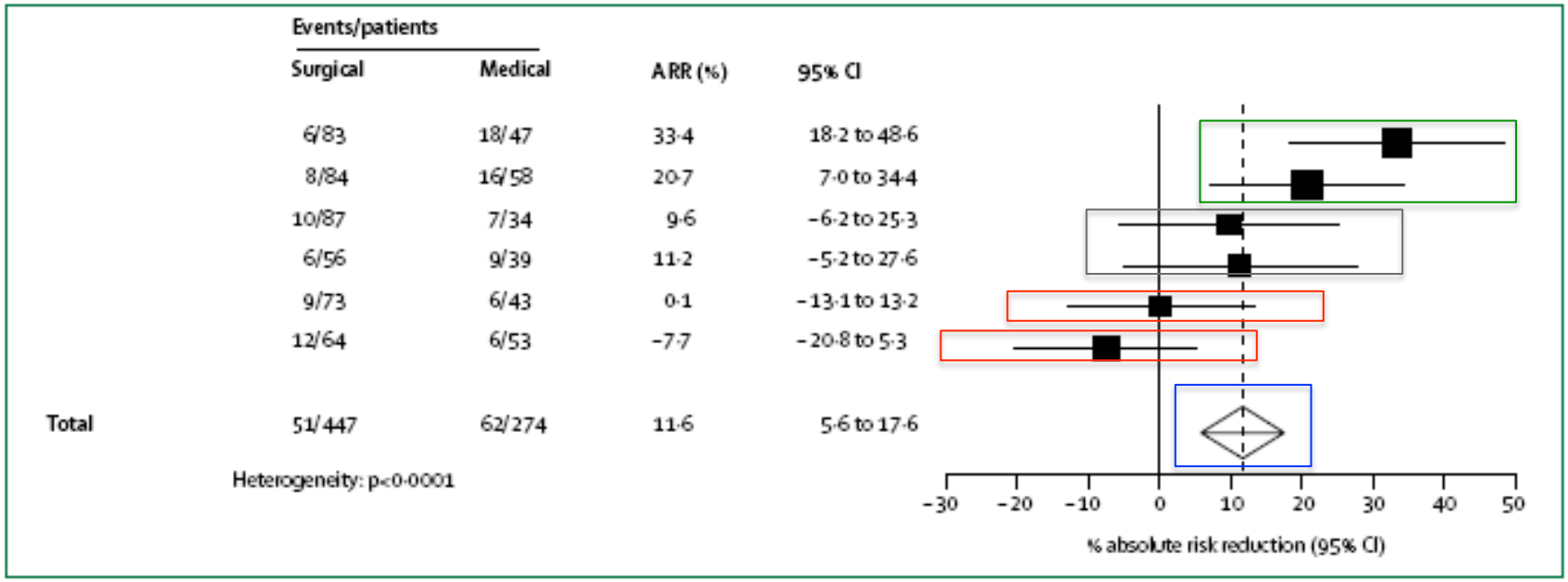

Figure 3: Effect of carotid endarterectomy in patients with ≥70% symptomatic stenosis in ECST[21]

Treating Individuals 2

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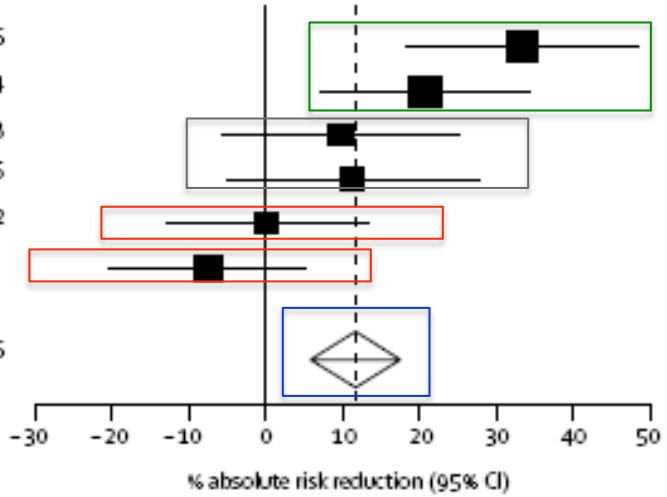
Month of birth	Events/patients: Surgical	Medical	ARR (%)	95% CI
May–Jun	6/83	18/47	33·4	18·2 to 48·6
Jul–Aug	8/84	16/58	20·7	7·0 to 34·4
Sept–Oct	10/87	7/34	9·6	−6·2 to 25·3
Nov–Dec	6/56	9/39	11·2	−5·2 to 27·6
Jan–Feb	9/73	6/43	0·1	−13·1 to 13·2
Mar–Apr	12/64	6/53	−7·7	−20·8 to 5·3
Total	51/447	62/274	11·6	5·6 to 17·6

Heterogeneity: p<0·0001



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Take-home message:

1. La letteratura non è vangelo e i “nomi famosi” non sono evangelisti
2. Attenzione alla generalizzabilità (numero e tipo di centri, paragonabilità delle popolazioni)
3. Verificare se c’è una forte selezione dei pz reclutati (bias potenziale)
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7. Attenzione ai RCT in cui non sia possibile il cieco e vi sia una propensione per il trattamento oggetto di studio
8. Verificare la fondatezza delle conclusioni
9. Porsi criticamente rispetto ai risultati discrepanti in letteratura e non innamorarsi dei risultati positivi
10. Le analisi per sottogruppi possono generare solo ipotesi

PROTOCOLLO PER LA GESTIONE

DIAGNOSTICO-TERAPEUTICA DELL'ARDS

03

- **Corticosteroidi:**
  - Non vi è attualmente evidenza che l'impiego dei corticosteroidi sia benefico in tutti pazienti con ARDS.
  - NON sono raccomandabili nelle fasi tardive dell'ARDS (oltre i 14 giorni dall'esordio).
  - Nei pazienti che NON ricevono corticosteroidi per altre ragioni e che NON presentano controindicazioni al loro impiego: valutare, secondo giudizio clinico, l'impiego di Metilprednisolone 1 mg/kg/die da iniziare entro 72 ore dalla diagnosi e proseguire fino al 14° giorno successivo alla stessa.

Use of corticosteroids in acute lung injury and acute respiratory distress syndrome: A systematic review and meta-analysis*

Benjamin M. P. Tang, PhD; Jonathan C. Craig, PhD; Guy D. Eslick, PhD; Ian Seppelt, MBBS; Anthony S. McLean, MBBS

Crit Care Med 2009; 37:1594 –1603

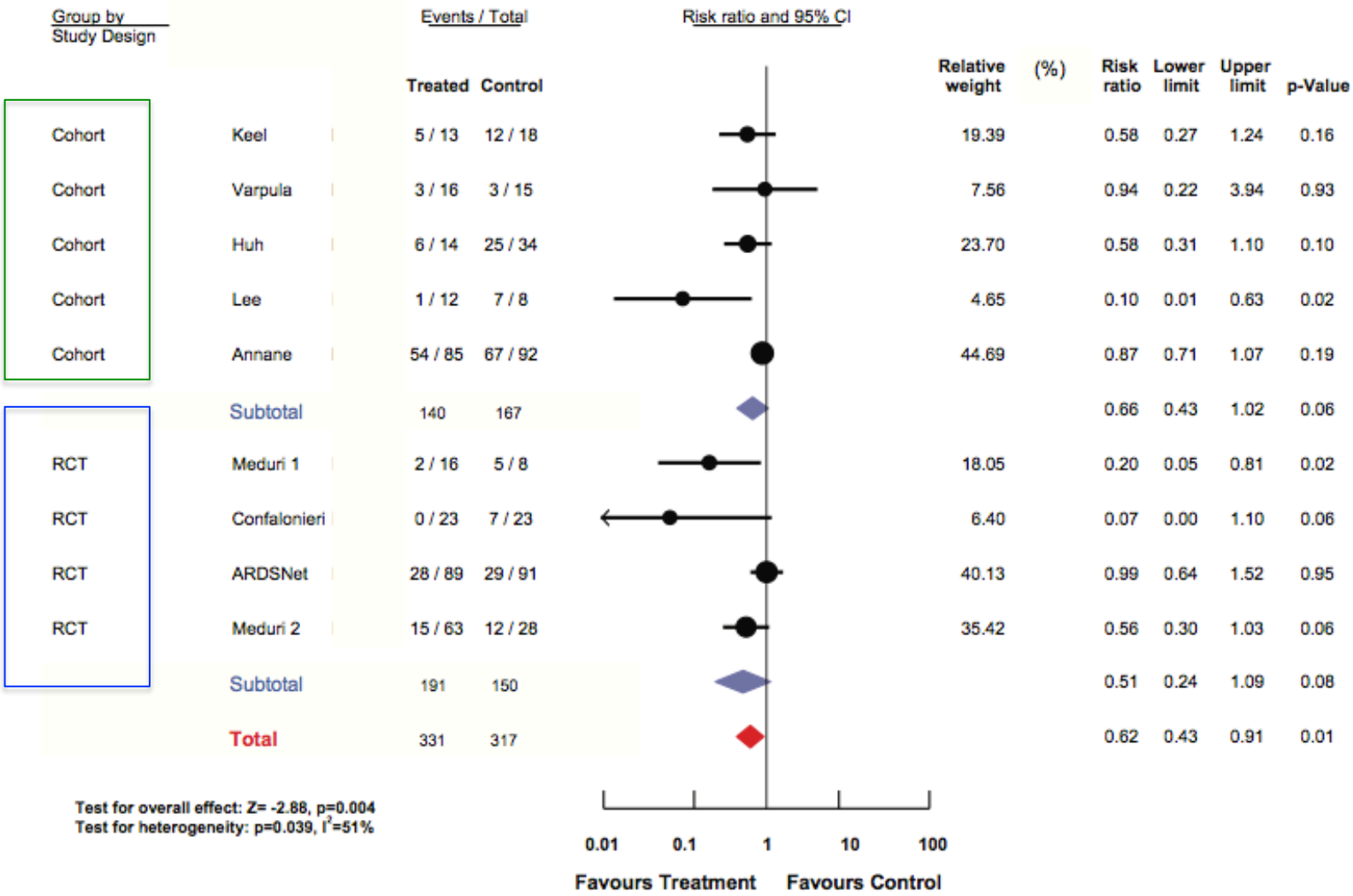
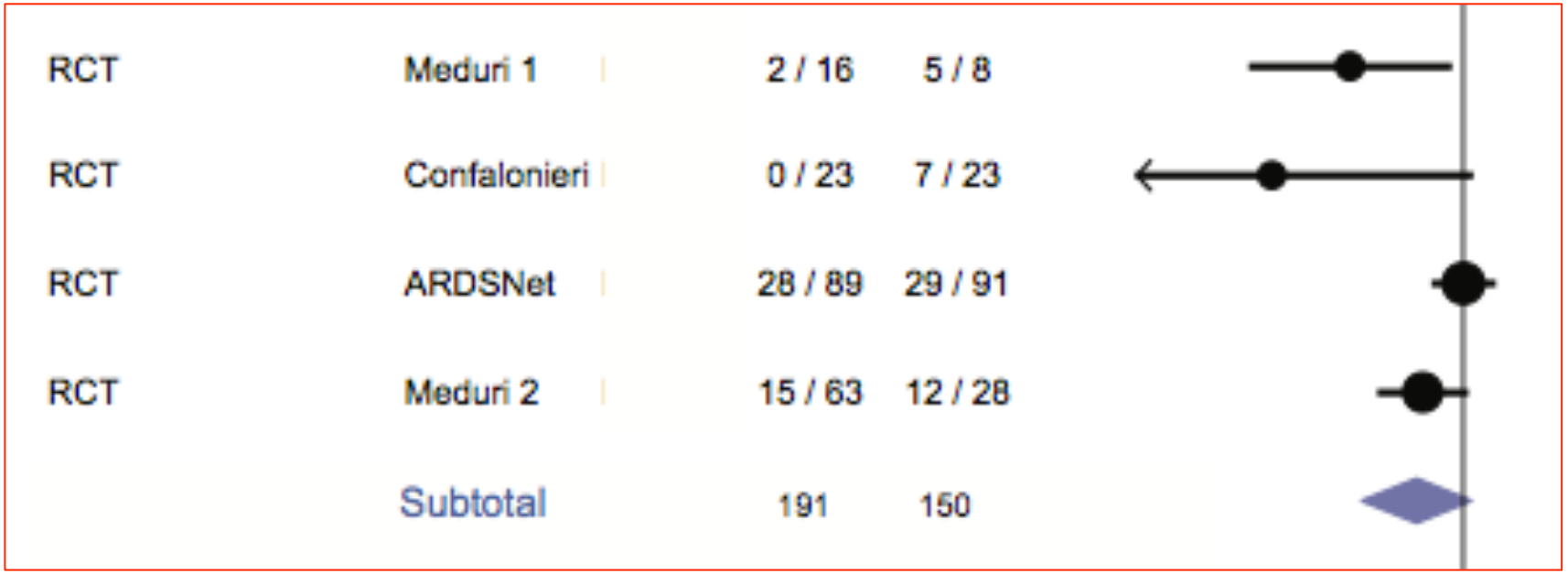
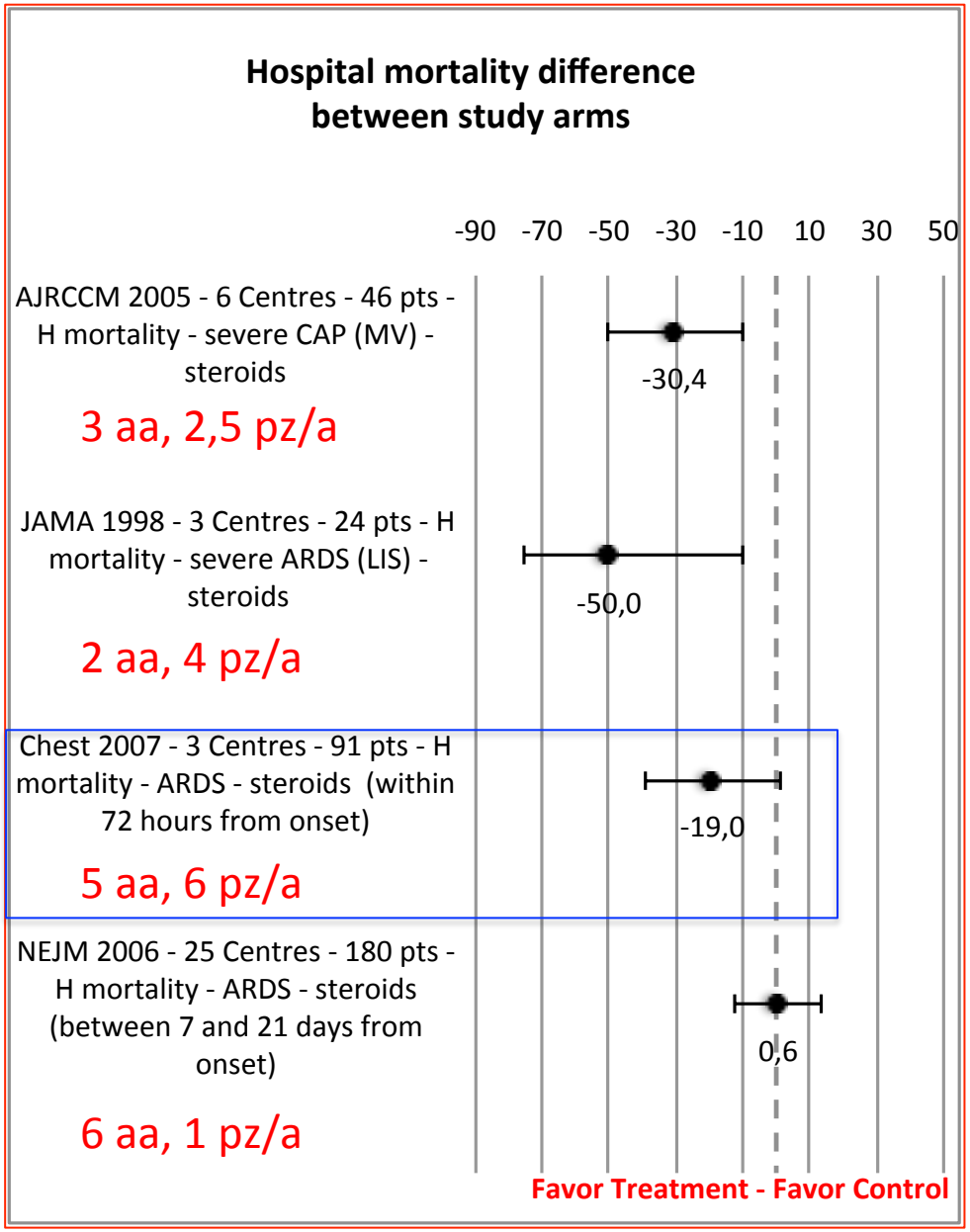


Figure 2. Effect of steroid on mortality. Size of data markers is proportional to the weight of each study in the forest plot. *RCT*, randomized controlled trial; *CI*, confidence interval.


RCT
Meduri 1
2 / 16
5 / 8
RCT
Confalonieri
0 / 23
7 / 23
RCT
ARDSNet
28 / 89
29 / 91
RCT
Meduri 2
15 / 63
12 / 28
Subtotal
191
150


Hospital mortality difference between study arms
-90 -70 -50 -30 -10 10 30 50
AJRCCM 2005 - 6 Centres - 46 pts - H mortality - severe CAP (MV) - steroids
3 aa, 2,5 pz/a
-30,4
JAMA 1998 - 3 Centres - 24 pts - H mortality - severe ARDS (LIS) - steroids
2 aa, 4 pz/a
-50,0
Chest 2007 - 3 Centres - 91 pts - H mortality - ARDS - steroids (within 72 hours from onset)
5 aa, 6 pz/a
-19,0
NEJM 2006 - 25 Centres - 180 pts - H mortality - ARDS - steroids (between 7 and 21 days from onset)
6 aa, 1 pz/a
0,6
Favor Treatment - Favor Control

Take-home message:

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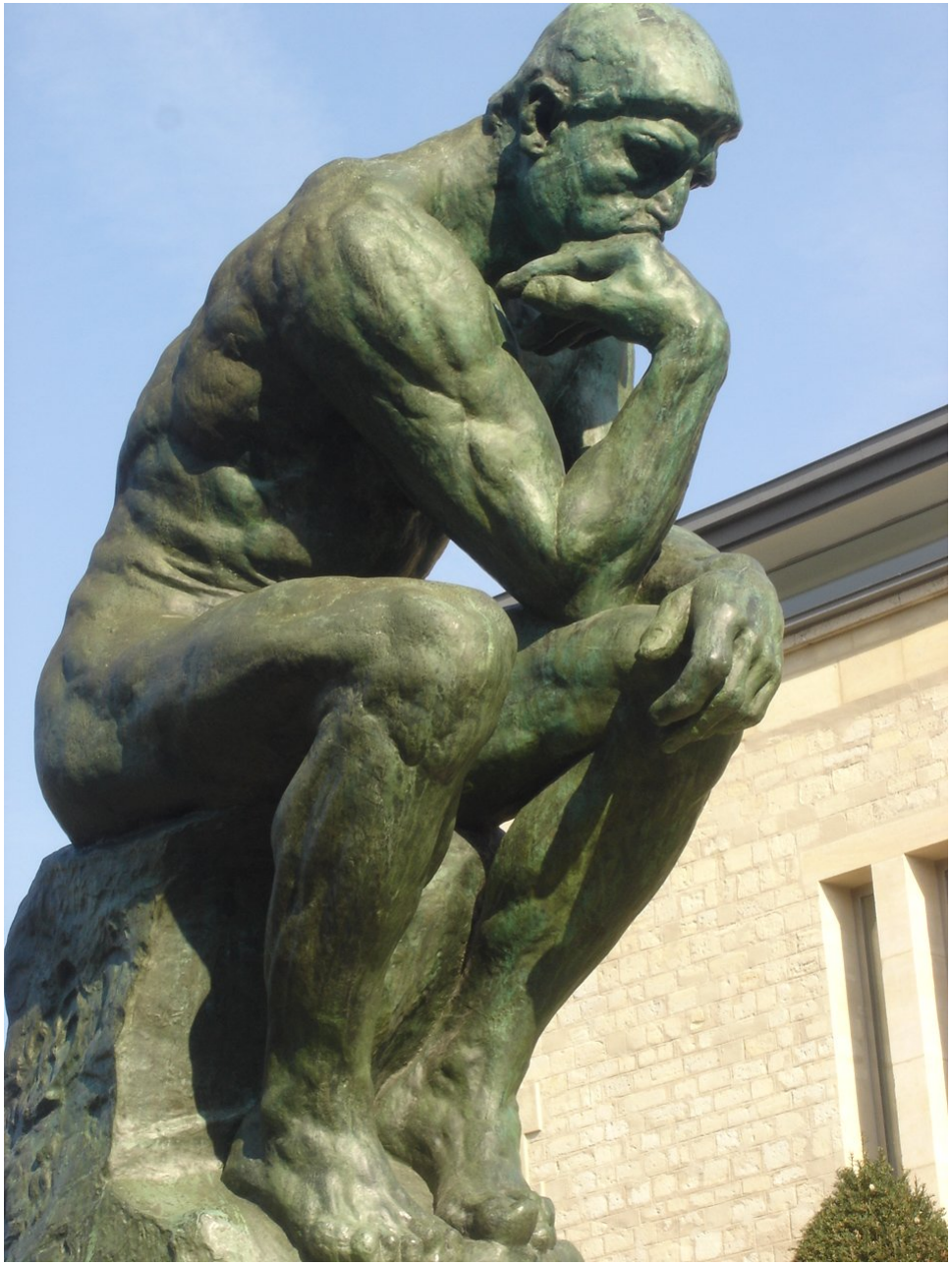
9. Porsi criticamente rispetto ai risultati discrepanti in letteratura e non innamorarsi dei risultati positivi
10. Le analisi per sottogruppi possono generare solo ipotesi
11. Diffidare dalle metanalisi

Take-home message:

Come faccio a trasferire i risultati della letteratura sul singolo paziente?



Grazie