Lyon 2017

*Actualités du SDRA*

# SDRA persistant : que faire ?

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Détresses Respiratoires et Infections Sévères

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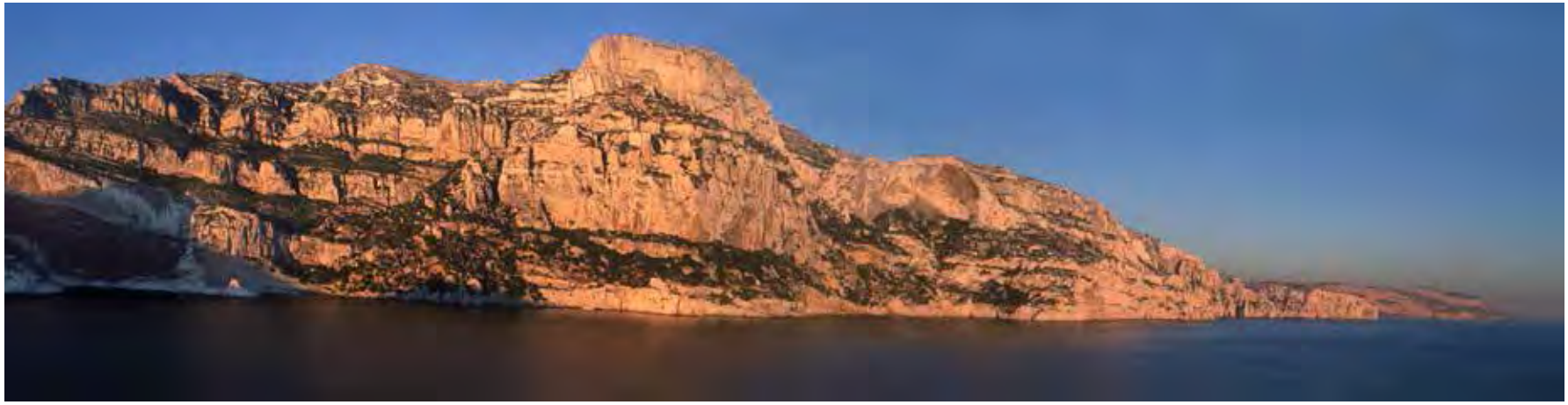
Aix*Marseille université



# Conflit d'intêret

Invitation auditeur congrès MSD – Pfizer – Astellas

Aucune rémunération

# Définition(s) du SDRA ….. Persistant (J5-J7)

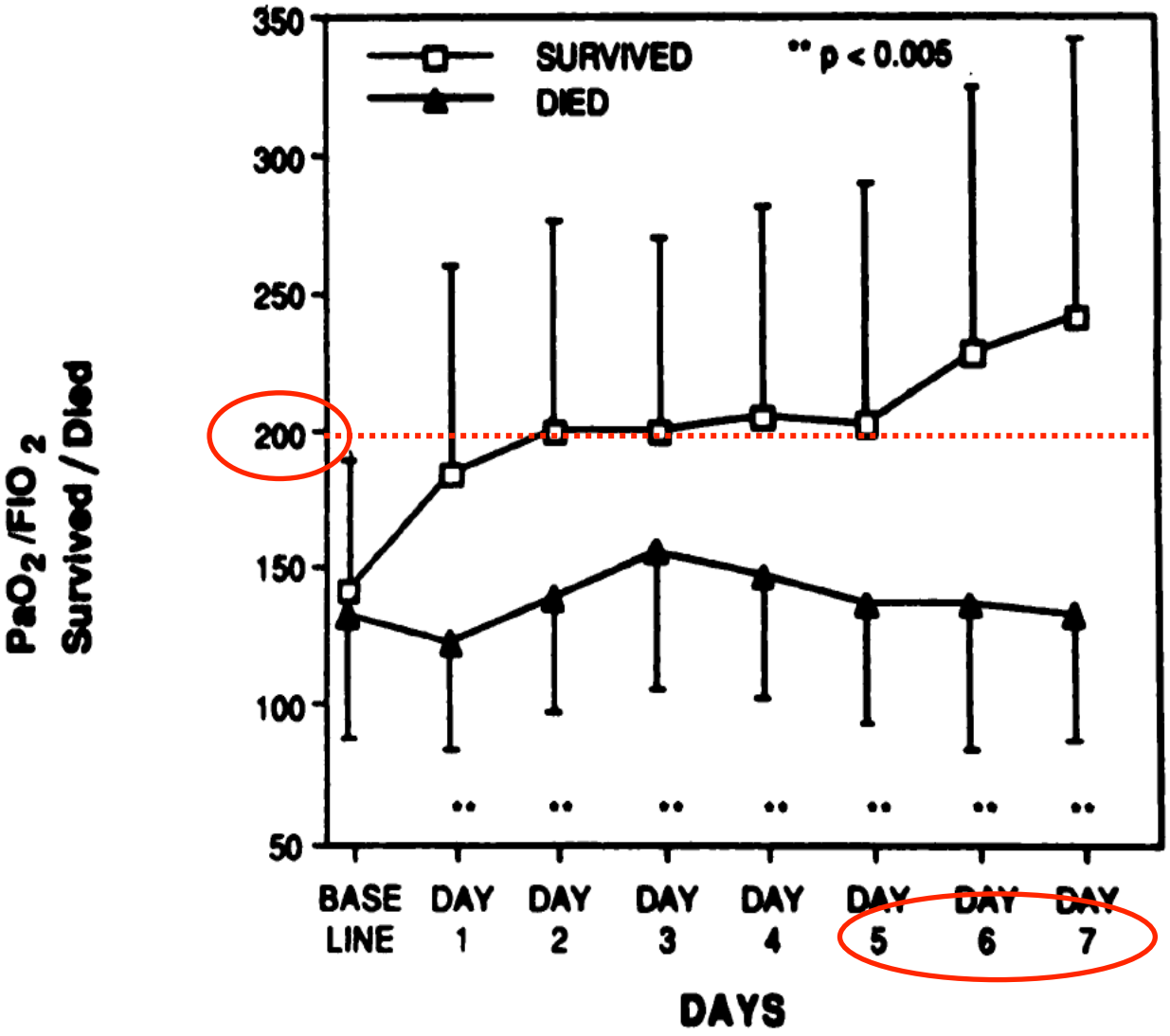
PaO2/FiO2 < 200 mmHg (?)  (PEEP >=5) (modéré – sévère)
Opacités radiologiques bilatérales
Absence d'une insuffisance cardiaque gauche

*BERLIN, JAMA 2012*

A la phase tardive
Persistant
Non résolutif

- Absence d'amélioration du PaO2/FIO2 ≥ 100 à **J5-7** /
  *Steinberg NEJM*
  *Annane, ICM*
- Absence de diminution du LIS de 1 point à **J5-7** / J1
  *Meduri JAMA*
  *Annane, ICM*

# Pas d'amélioration du $PaO_2/FIO_2 \geq 100$ à J5-7/J1




*Bone Chest 1989*

# LIS Lung Injury Score

*Murray 1*

| | |
|---|---|
| **Radiographie thoracique :** | |
| pas de syndrome alvéolaire | 0 |
| syndrome alvéolaire étendu à 1 quadrant | 1 |
| syndrome alvéolaire étendu à 2 quadrants | 2 |
| syndrome alvéolaire étendu à 3 quadrants | 3 |
| syndrome alvéolaire étendu aux 4 quadrants | 4 |
| **Rapport PaO2/FiO2 :** | |
| PaO2/FiO2 > ou = 300 | 0 |
| PaO2/FiO2 225-299 | 1 |
| PaO2/FiO2 175-224 | 2 |
| PaO2/FiO2 100-174 | 3 |
| PaO2/FiO2 < 100 | 4 |
| **Pression téléexpiratoire positive :** | |
| < ou = 5 cm d'eau | 0 |
| 6-8 cm d'eau | 1 |
| 9-11 cm d'eau | 2 |
| 12-14 cm d'eau | 3 |
| > ou = 15 cm d'eau | 4 |
| **Compliance du système respiratoire :** | |
| > ou = 80 ml/cm d'eau | 0 |
| 60-79 ml/cm d'eau | 1 |
| 40-59 ml/cm d'eau | 2 |
| 20-39 ml/cm d'eau | 3 |
| < ou = 19 ml/cm d'eau | 4 |
| **TOTAL** | /4 |

# Absence de diminution du LIS de 1 point à J5-7 / J1

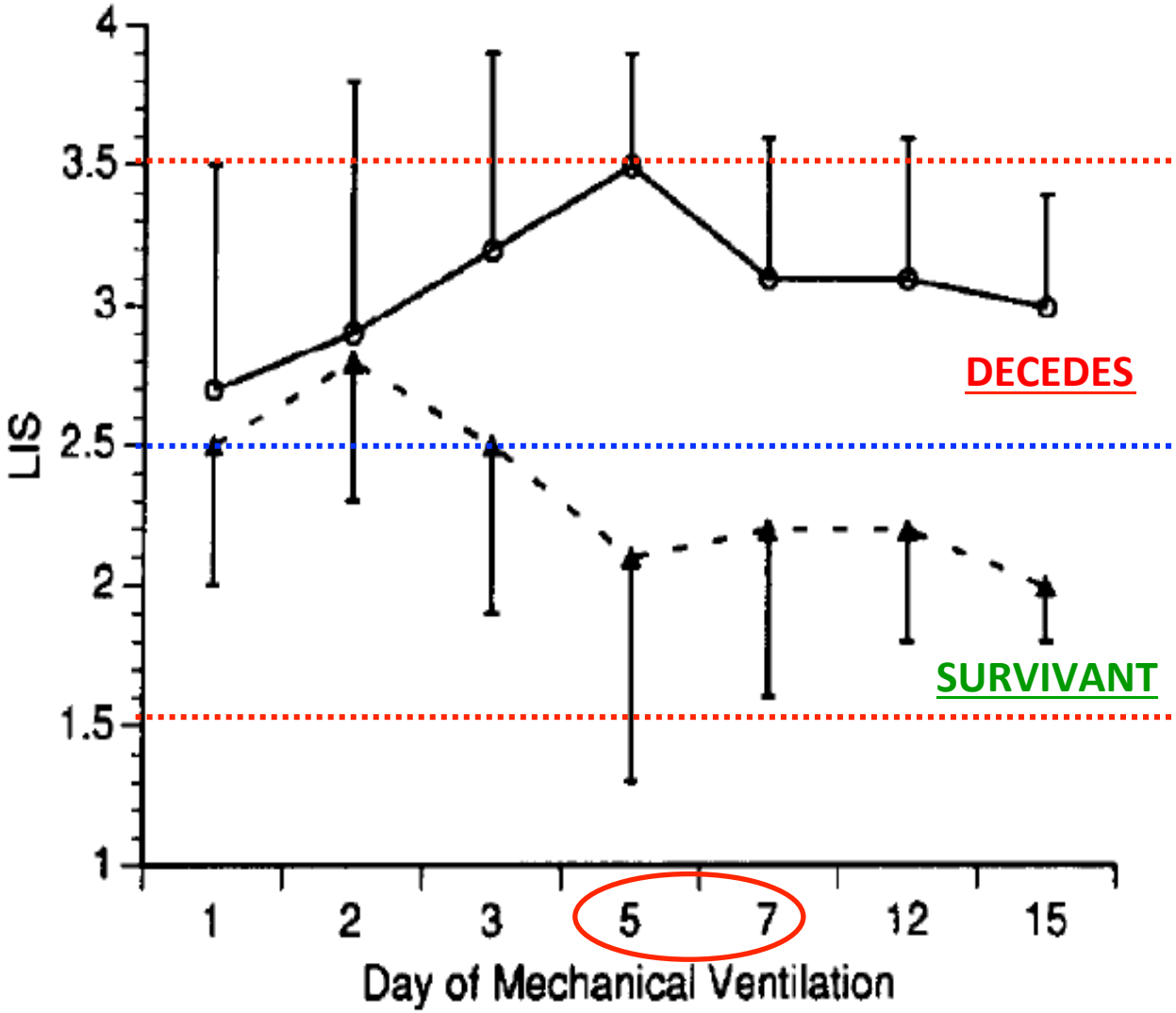
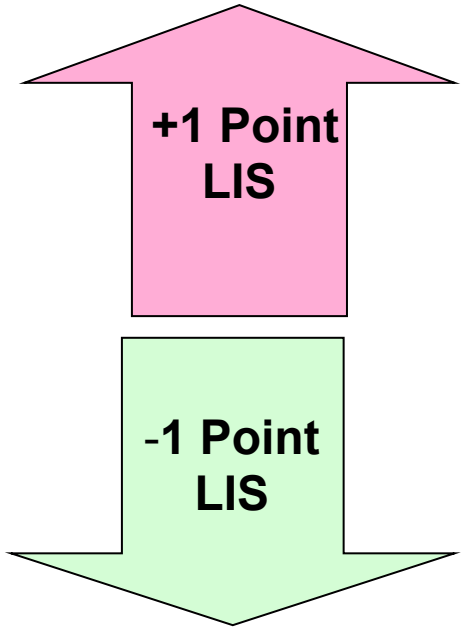



FIGURE 2. LIS in survivors (closed triangles) and nonsurvivors (open circles) during the first week of ARDS.




*Meduri Chest 1995*

# La peur du SDRA ….. persistant

- = Mortalité
- = Défaillances multiviscérales
- = Fibrose pulmonaire
- = Augmentation durée de ventilation mécanique
- = Augmentation durée de séjour en réanimation
- = Séquelles respiratoires, ψ
- = Coût

*Meduri Chest 2009*
*Roumen Ann Surg 1993*
*Baughman AJRCCM 1996*
*Parsons CCM 2005*
*Meduri Chest 2007*

# SDRA persistant : que faire ?

1. Ce que j'aurais dû faire avant (prévention)
2. Ce que je dois faire
3. Ce que je ferai « peut-être demain »

# SDRA persistant : que faire ?

1. Ce que j'aurais dû faire avant (« mieux vaut prévenir que guérir »)

# Que cache un SDRA persistant ?
# Une prise en charge antérieure inadaptée

- e non contrôle de la cause initiale (infectieuse +++)
- e « mauvais traitement » antérieur, ventilation non protectrice
- 'absence d'évaluation du ventricule droit
- Une balance hydro sodée positive (œdème hydrostatique)
- 'absence de prévention des PAVM
- Une inflammation excessive (réponse inflammatoire non-adaptée)

# J'aurais dû : Contrôler la cause initiale du SDRA

## demiology, Patterns of Care, and Mortality
## Patients With Acute Respiratory Distress Syndrome
## ntensive Care Units in 50 Countries

JAMA. 2016;315(8):788-800.

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

Table 1. Characteristics of Patients With Acute Respiratory Distress Syndrome

| Parameter | Value |
|---|---|
| No. of patients | |
| ARDS | 3022 |
| Risk factor for ARDS, No. (%)[a] | |
| Pneumonia | 1794 (59.4) |
| Extrapulmonary sepsis | 484 (16.0) |
| Aspiration | 430 (14.2) |
| Noncardiogenic shock | 226 (7.5) |
| Trauma | 127 (4.2) |

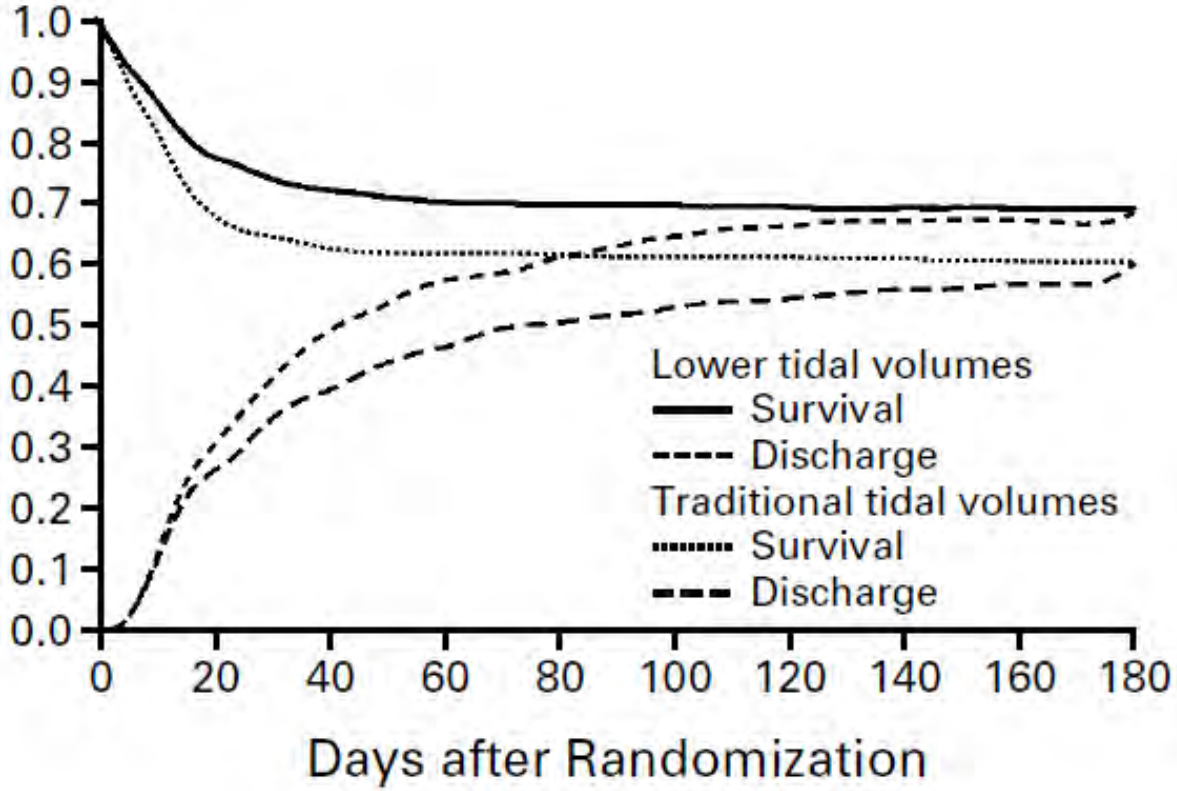
75 % = Infectio

# J'aurais dû : Ventiler de façon protectrice : Vt

## ENTILATION WITH LOWER TIDAL VOLUMES AS COMPARED WI TRADITIONAL TIDAL VOLUMES FOR ACUTE LUNG INJURY AND THE ACUTE RESPIRATORY DISTRESS SYNDROME

THE ACUTE RESPIRATORY DISTRESS SYNDROME NETWORK*

VOLUME 342 MAY 4, 2000 NUMBER 18

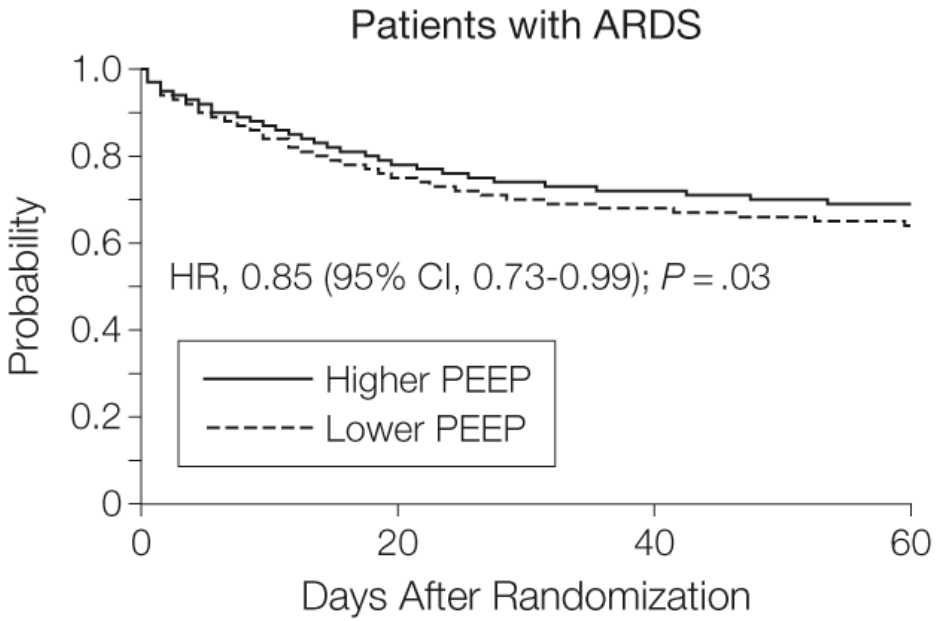



initial tidal volume of 12 ml per kilogram of pre
body weight and an airway pressure measure
a 0.5-second pause at the end of inspiration (p
pressure) of 50 cm of water or less, with ven
with a lower tidal volume, which involved ar
tidal volume of 6 ml per kilogram of predicte
weight and a plateau pressure of 30 cm of w
less. The first primary outcome was death b

# J'aurais dû : Ventiler de façon protectrice Pplat et PEEP

## Haute PEEP QSP Pplat 28

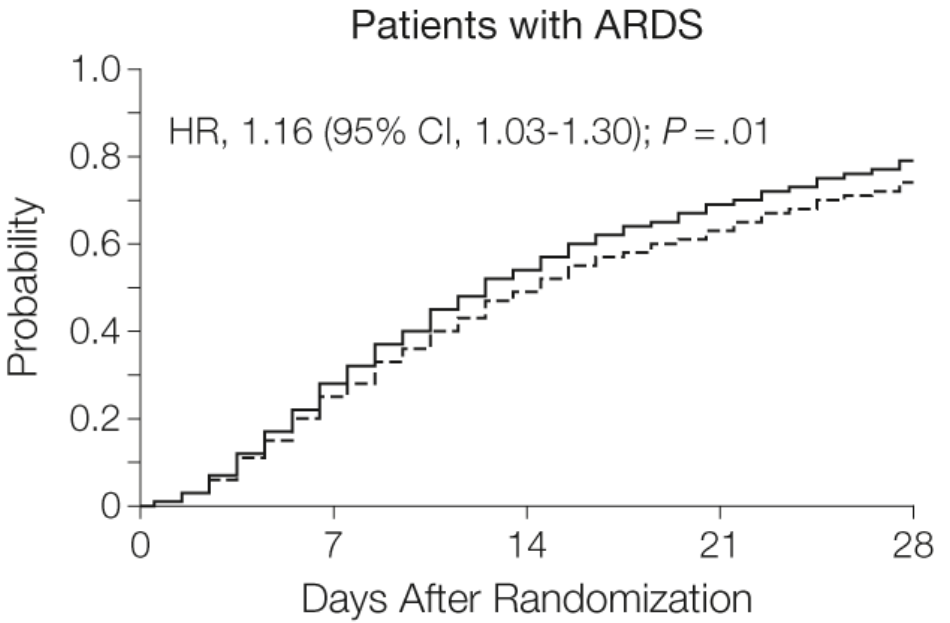
### Survie hospitalière augmentée




risk

| | | | | |
|---|---|---|---|---|
| r PEEP | 949 | 760 | 693 | 666 |
| r PEEP | 939 | 723 | 649 | 619 |

### Durée ventilation diminuée




No. at risk

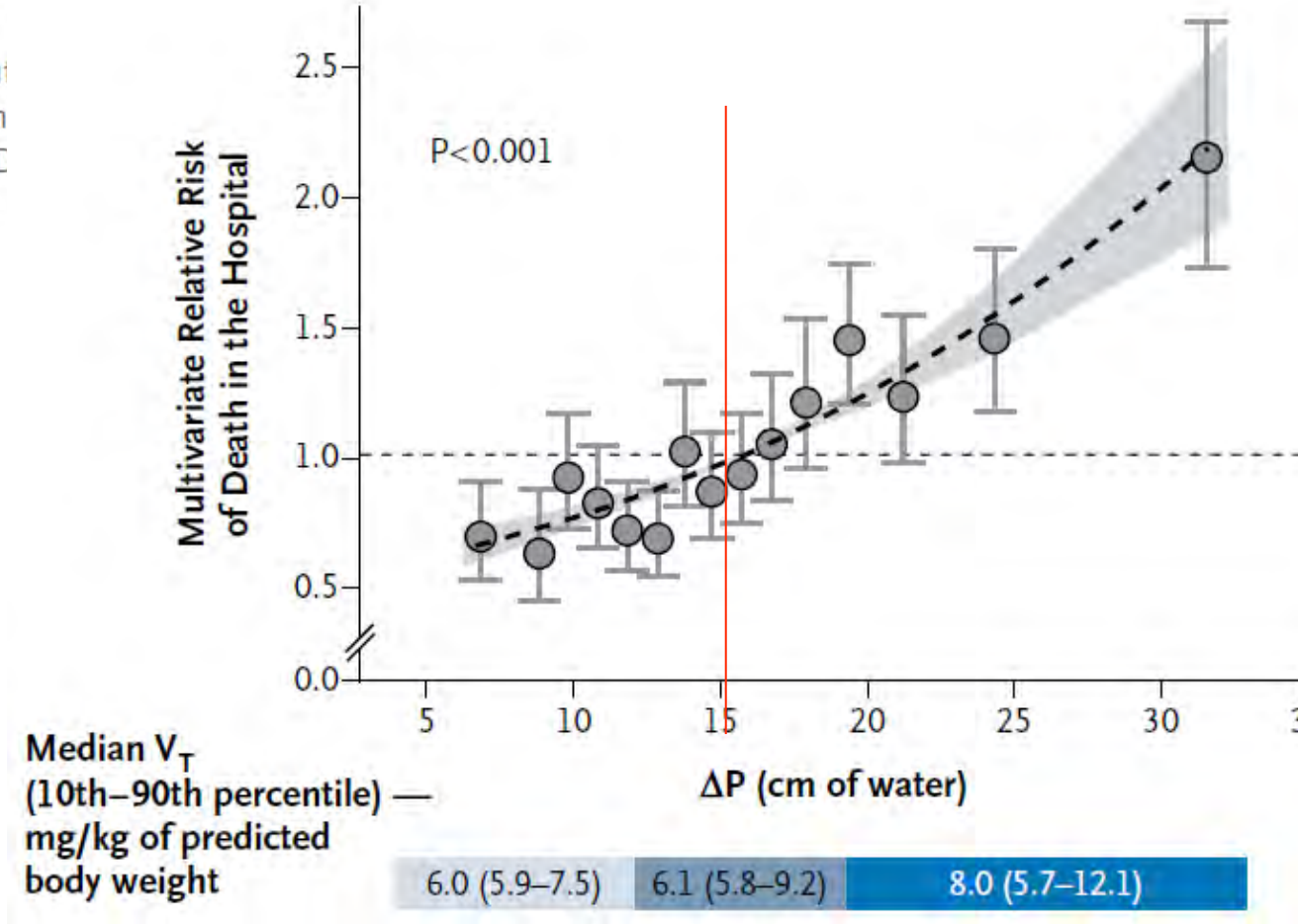
| | | | | | |
|---|---|---|---|---|---|
| Higher PEEP | 949 | 653 | 408 | 283 | 209 |
| Lower PEEP | 939 | 589 | 328 | 207 | 142 |

BRIEL JAMA. 2010;303(9):865-873

# J’aurais dû : Ventiler de façon protectrice Pression motrice

## iving Pressure and Survival in the Acute Respiratory Distress Syndrome

elo B.P. Amato, M.D., Maureen O. Meade, M.D., Arthur S. Slut
nt Brochard, M.D., Eduardo L.V. Costa, M.D., David A. Schoen
nas E. Stewart, M.D., Matthias Briel, M.D., Daniel Talmor, M.D
Alain Mercat, M.D., Jean-Christophe M. Richard, M.D.,
Carlos R.R. Carvalho, M.D., and Roy G. Brower, M.D.



Care Med (2016) 42:862–870
07/s00134-015-4141-2

SEVEN-DAY PROFILE PUBLICATION

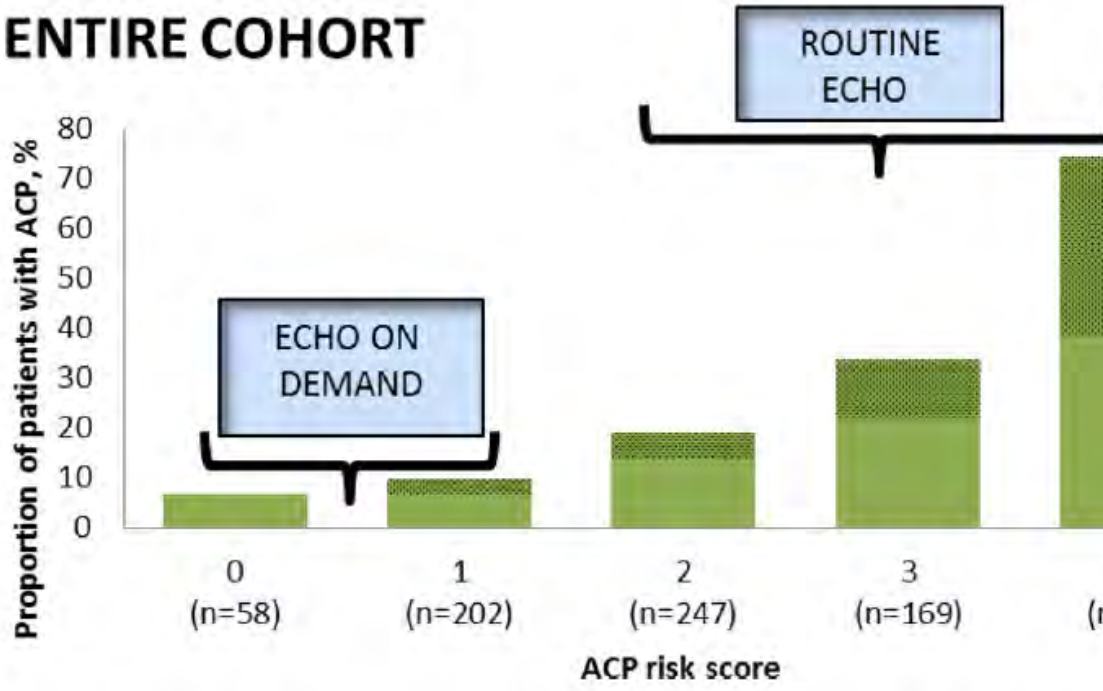
Mekontso Dessap
Boissier
arron
elle Bégot
epessé
egras
Brun-Buisson
Vignon
Vieillard-Baron

# Acute cor pulmonale during protective ventilation for acute respiratory distress syndrome: prevalence, predictors, and clinical impact

J'aurais dû : Adapter VM
Cœur pulmonaire aigu

**3** The acute cor pulmonale risk score

| eter | Score |
|---|---|
| onia as cause of ARDS | 1 |
| g pressure ≥18 $cmH_2O$[a] | 1 |
| $FiO_2$ ratio <150 mmHg | 1 |
| ≥48 mmHg | 1 |
| score | 0–4 |

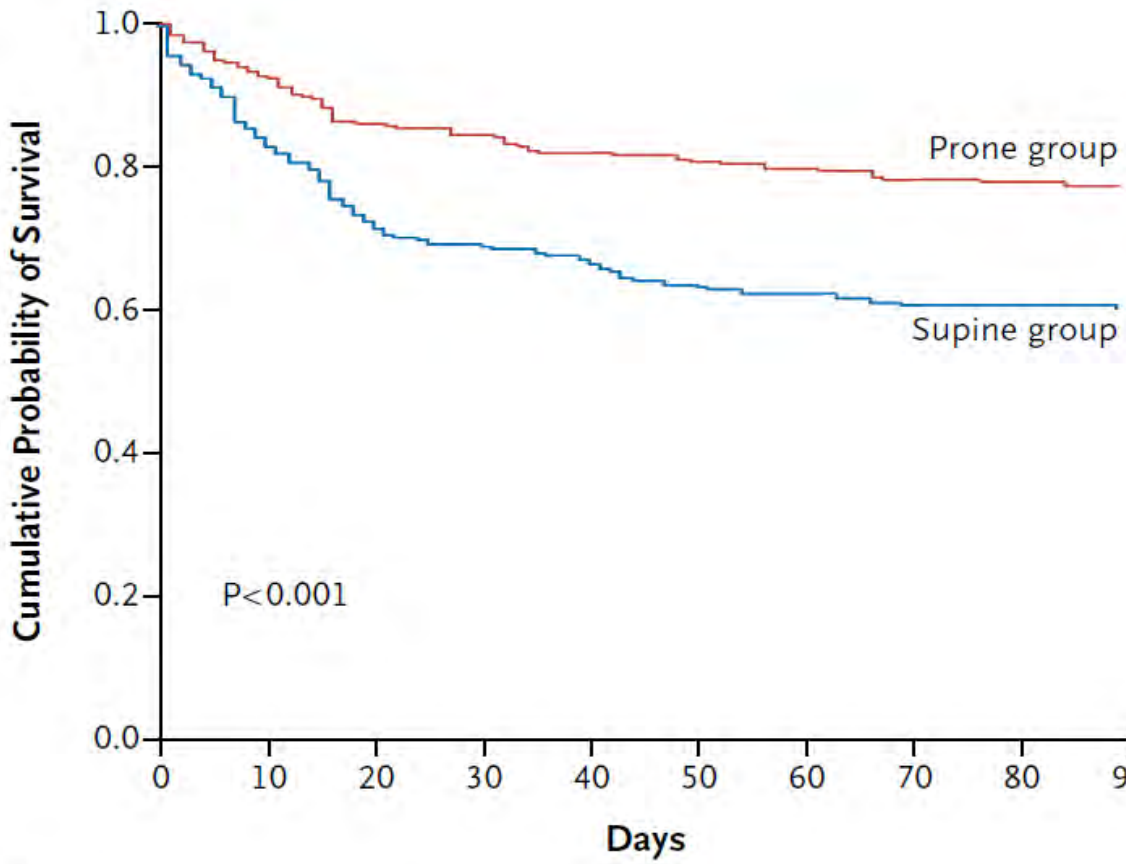


# J'aurais dû faire du DV si P/F < 150 PEP ≥ 10

## Prone Positioning in Severe Acute Respiratory Distress Syndrome

Claude Guérin, M.D., Ph.D., Jean Reignier, M.D., Ph.D.,
ristophe Richard, M.D., Ph.D., Pascal Beuret, M.D., Arnaud Gacouin, M.D.,
rry Boulain, M.D., Emmanuelle Mercier, M.D., Michel Badet, M.D.,
ain Mercat, M.D., Ph.D., Olivier Baudin, M.D., Marc Clavel, M.D.,
ine Chatellier, M.D., Samir Jaber, M.D., Ph.D., Sylvène Rosselli, M.D.,
ancebo, M.D., Ph.D., Michel Sirodot, M.D., Gilles Hilbert, M.D., Ph.D.,
an Bengler, M.D., Jack Richecoeur, M.D., Marc Gainnier, M.D., Ph.D.,
édérique Bayle, M.D., Gael Bourdin, M.D., Véronique Leray, M.D.,
haele Girard, M.D., Loredana Baboi, Ph.D., and Louis Ayzac, M.D.,
for the PROSEVA Study Group*

N Engl J Med 2013.
DOI: 10.1056/NEJMoa1214103




**No. at Risk**

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

**Figure 2. Kaplan–Meier Plot of the Probability of Survival from Randomiz tion to Day 90.**

# J'aurais dû : Assurer une balance hydro sodée neutre/négative

MATIC REVIEW

servative fluid management or
suscitation for patients with sepsis or acute
iratory distress syndrome following the
scitation phase of critical illness: a
ematic review and meta-analysis

A. Silversides[1,2*], Emmet Major[2], Andrew J. Ferguson[3], Emma E. Mann[2], Daniel F. McAuley[1,4],
arshall[5,6], Bronagh Blackwood[1] and Eddy Fan[5]

*Intensive Care Med (2017) 43:155–170*

Augmente les VFD

| Study or Subgroup | Conservative fluid Mean [Days] | SD [Days] | Total | Liberal fluid Mean [Days] | SD [Days] | Total | Weight | Mean Difference IV, Random, 95% CI [Days] |
|---|---|---|---|---|---|---|---|---|
| hen and Kollef. 2015 | 5.5 | 9.4 | 41 | 7.4 | 12.9 | 41 | 6.5% | |
| hang et al. 2015 | 9 | 17.9 | 168 | 10.3 | 18.7 | 182 | 10.3% | |
| jortrup et al. 2016 | 21.4 | 9.7 | 75 | 19.8 | 11.1 | 76 | 13.3% | |
| lartin et al. 2005 | 10.3 | 8 | 20 | 8 | 8 | 20 | 6.4% | |
| Viedemann et al. 2006 | 14.6 | 11.2 | 503 | 12.1 | 11.1 | 497 | 51.6% | |
| ichard et al. 2015 | 12.7 | 18.7 | 30 | 9.7 | 16.3 | 30 | 2.1% | |
| enakatti et al. 2014 | 15.8 | 10.8 | 54 | 12.1 | 9.4 | 47 | 9.8% | |
| **otal (95% CI)** | | | **891** | | | **893** | **100.0%** | |

eterogeneity: $Tau^2 = 0.33$; $Chi^2 = 6.63$, df = 6 (P = 0.36); $I^2 = 9\%$
est for overall effect: Z = 2.78 (P = 0.005)

10 5 0 -5 -10
Favours conservative Favours liberal

. 4 Forest plot for outcome of ventilator-free days

# J'aurai dû : Prévenir la PAVM

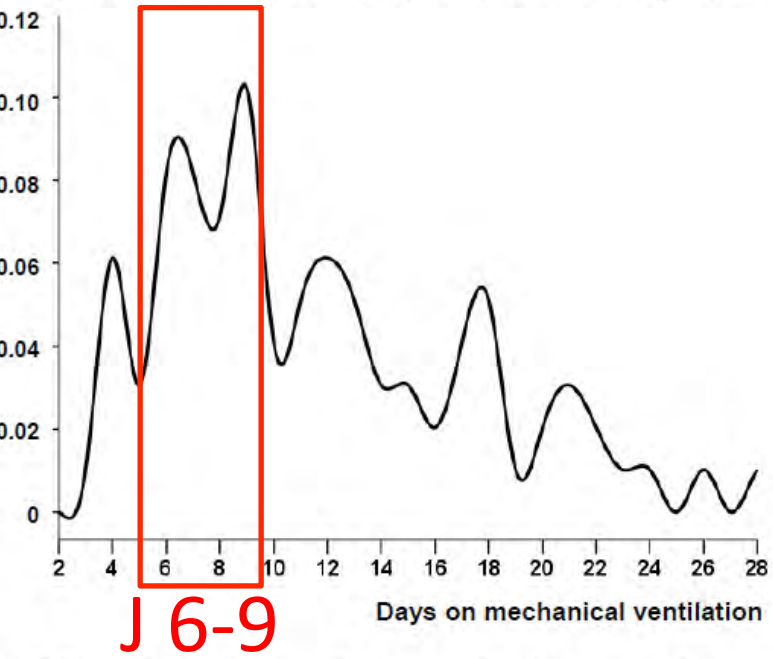
cal Care 2012, 16:R65
com/content/16/2/R65

CRITICAL CARE

RCH Open Access

lator-associated pneumonia and ICU
ality in severe ARDS patients ventilated
rding to a lung-protective strategy

Forel[1], François Veillet[1], Daniel Pulina[1], Arnaud Gacouin[2], Gilles Perrin[3], Karine Barrau[4], Samir Jaber[5], Arnal[6], Mohamed Fathallah[7], Pascal Auquier[4], Antoine Roch[1], Elie Azoulay[8] and Laurent Papazian[1*]




J 6-9

**re 2 Hazard rate for ventilator-associated pneumonia over after the diagnosis of severe acute respiratory distress rome**. The hazard function evaluates the conditional ability of ventilator-associated pneumonia on the next day in vent-free patient. The hazard rate is the event rate per day over duration of mechanical ventilation.

| | Patients, | VAP incidenc |
|---|---|---|
| Sutherland *et al.* (8) | 105 | 15 |
| Delclaux *et al.* (6) | 30 | 60 |
| Chastre *et al.* (5) | 56 | 55 |
| Maduri *et al.* (9) | 94 | 43 |
| Markowicz *et al.* (7) | 134 | 23 |
| VAP-ACURASYS | 339 | 29 |

# PAVM prolonge la VM, le SDR

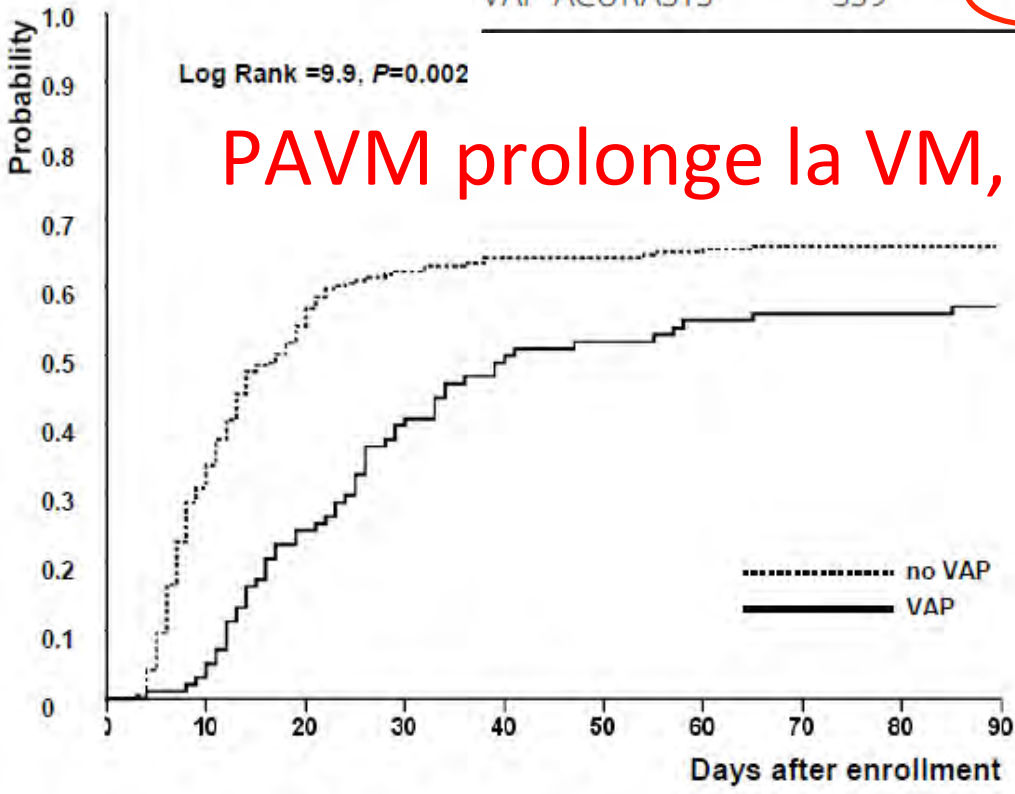



**Figure 4 Probability of breathing without assistance from the day of inclusion to day 90.**

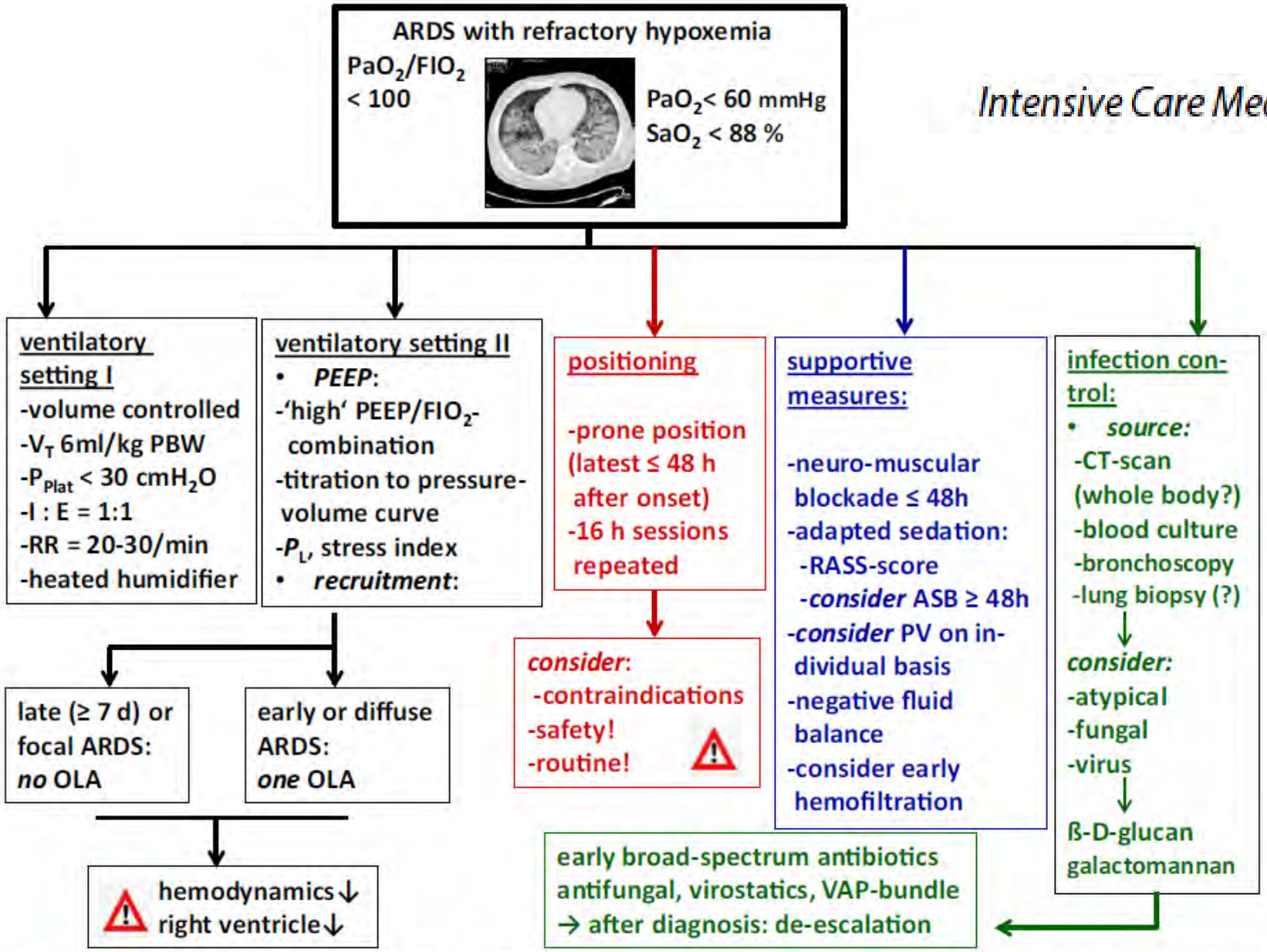
# En résumé, j'aurais dû

REVIEW

## The standard of care of patients with ARDS: ventilatory settings and rescue therapies for refractory hypoxemia

Thomas Bein[1*], Salvatore Grasso[2], Onnen Moerer[3], Michael Quintel[3], Claude Guerin[4,5], Maria Deja[6], Anita Brondani[7] and Sangeeta Mehta[7]

*Intensive Care Med (2016) 42:699–711*



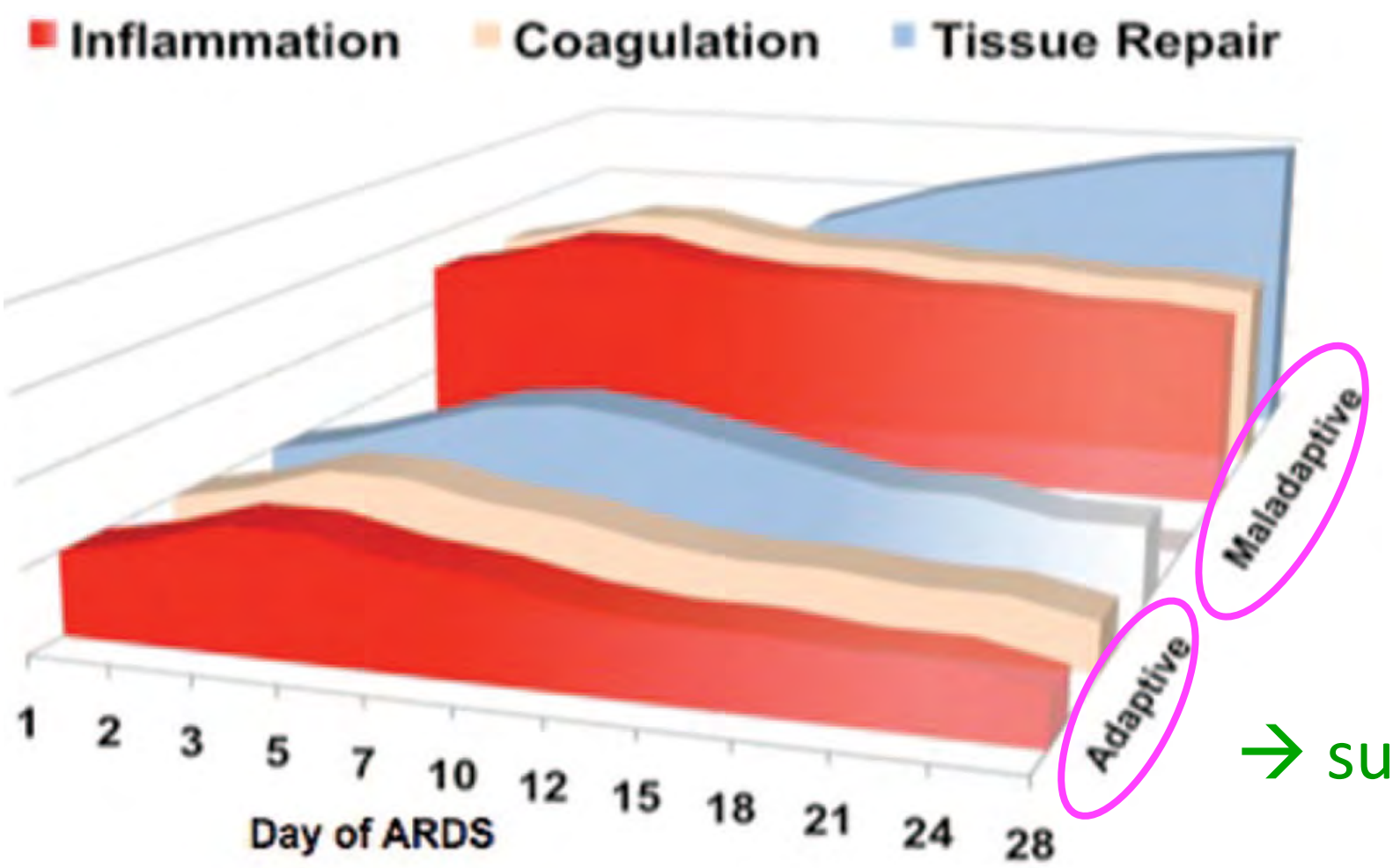

Intensive Care Med (2016) 42:699–

**Fig. 2** Algorithm for rescue therapies in ARDS patients with refractory hypoxemia. An overview of important therapeutic strategies in the management of hypoxemic (early) ARDS. *PEEP* positive end-expiratory pressure, $P_L$ transpulmonary pressure, $P_{Plat}$ plateau pressure, *OLA* open lung approach, *PBW* predicted body weight, *I:E* inspiratory/expiratory ratio, *RASS* Richmond agitation sedation scale, *ASB* augmented spontaneous breathing, *PV* pulmonary vasodilator, *VAP* ventilator-associated pneumonia

SDRA persistant = inflammation non-adaptée

→J'aurais dû Réguler tôt (< 5-7j) l'inflammation

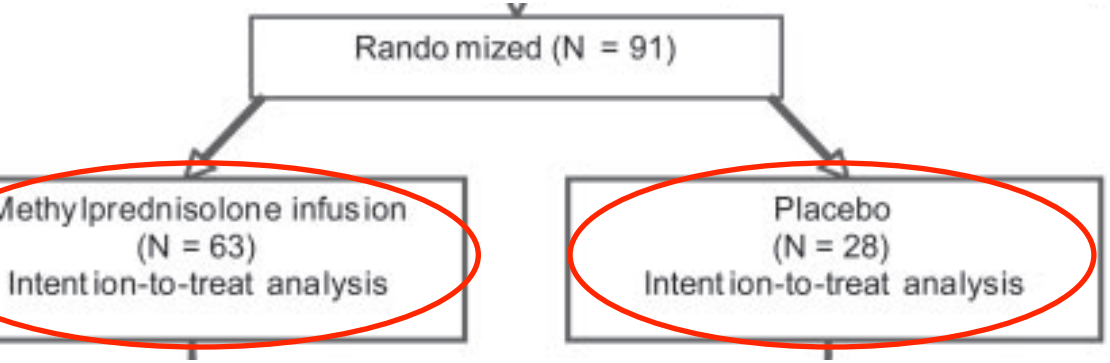
*duri Chest 1995*




→morta

→ survie

# guler l'inflammation tôt (avant J5-7)




SDRA < 72h

## Methylprednisolone Infusion in Early Sev ARDS *Results of a Randomized Controll Trial

G. Umberto Meduri, Emmel Golden, Amado X. Freire, Edwin Taylo Muhammad Zaman, Stephanie J. Carson, Mary Gibson and Reba Umberger

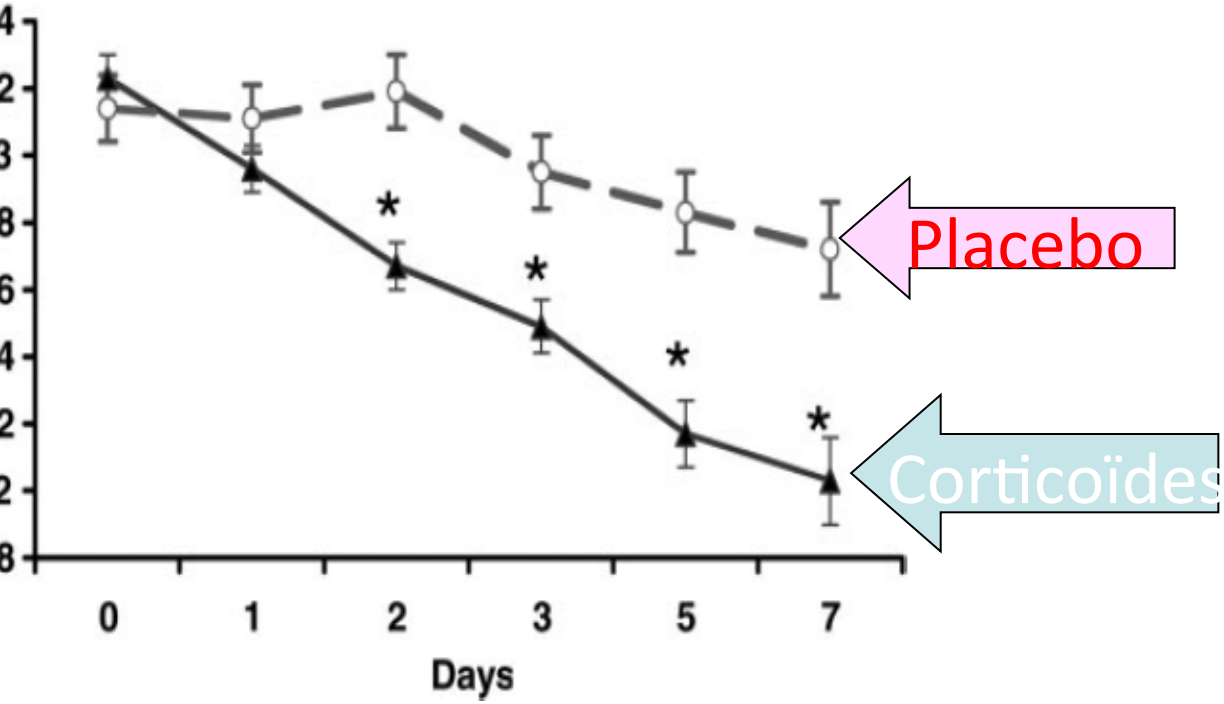
*Chest* 2007;131;954-963

*Meduri Chest 2*

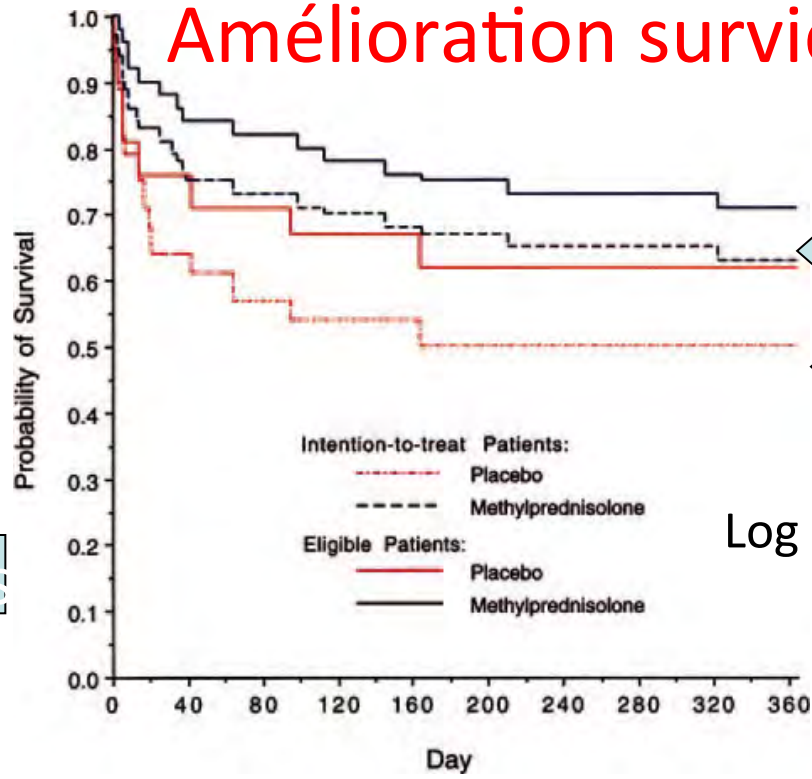
Méthylprednisolone (Solumédrol™) IV en continu

Bolus 1 mg/Kg
1 mg/Kg J1-J14
0.5 mg/Kg J15-J21
0,25 mg/Kg J22-J25
0,125 mg/Kg J26-J28

# Amélioration LIS sous MP




# Amélioration survie sous




Log Rank, p = 0

| Variables | Methylprednisolone (n = 63) | Placebo (n = 28) | Relative Risk (95% Confidence Interval) [n = 91] | p Value |
|---|---|---|---|---|
| Duration of mechanical ventilation, d† | 5 (3–8) | 9.5 (6–19.5) | | 0.002 |
| Mechanical ventilation-free days to day 28‡ | 16.5 ± 10.1 | 8.7 ± 10.2 | | 0.001 |

*Meduri Chest 2007*

# Hydrocortisone
## 50 mg X4/j J1-J7

Tongyoo et al. Critical Care (2016) 20:329
DOI 10.1186/s13054-016-1511-2



RESEARCH Open Ac

# Hydrocortisone treatment in early sepsis-associated acute respiratory distress syndrome: results of a randomized controlled trial

Surat Tongyoo[1*], Chairat Permpikul[1], Wasineenart Mongkolpun[1], Veerapong Vattanavanit[1,2], Suthipol Udompanturak[1], Mehmet Kocak[3] and G. Umberto Meduri[4]

**le 2** Primary and secondary outcomes

| | Hydrocortisone ($n = 98$) | Placebo ($n = 99$) | Relative risk (95 % CI) | $p$ Va |
|---|---|---|---|---|
| ary outcome | | | | |
| ortality at 28 days, *n* (%) | 22 (22.5) | 27 (27.3) | 0.82 (0.50–1.34) | 0.51 |
| ndary outcomes | | | | |
| ortality at 60 days, *n* (%) | 34 (34.7) | 40 (40.4) | 0.86 (0.60–1.23) | 0.46 |
| uration of mechanical ventilation up to day 28, days | 11.8 ± 7.8 | 13.9 ± 9.0 | | 0.17 |
| echanical ventilation-free days to day 28 | 12.0 ± 9.7 | 9.7 ± 10.0 | | 0.17 |

DEXA-ARDS

Villar et al. Trials (2016) 17:342
DOI 10.1186/s13063-016-1456-4

Trials

STUDY PROTOCOL Open Access

# Evaluating the efficacy of dexamethasone in the treatment of patients with persistent acute respiratory distress syndrome: study protocol for a randomized controlled trial

Jesús Villar[1,23*], Javier Belda[4], José Manuel Añón[5], Jesús Blanco[1,6], Lina Pérez-Méndez[1,7], Carlos Ferrando[8], Domingo Martínez[8], Juan Alfonso Soler[9], Alfonso Ambrós[10], Tomás Muñoz[11], Rosana Rivas[12], Ruth Corpas[13], Francisco J. Díaz-Domínguez[14], Marina Soro[4], Miguel Angel García-Bello[15], Rosa Lidia Fernández[1,2], Robert M. Kacmarek[16,17] and the DEXA-ARDS Network

# Prudence avec SDRA grippal = Surmortalité

## Early Corticosteroids in Severe Influenza A/H1N1 Pneumonia and Acute Respiratory Distress Syndrome

Christian Brun-Buisson[1,2,3], Jean-Christophe M. Richard[4], Alain Mercat[5], Anne C. M. Thiébaut[3,6], and Laurent Brochard[1,2,7], for the REVA-SRLF A/H1N1v 2009 Registry Group*

Am J Respir Crit Care Med.

TABLE 5. COX REGRESSION ANALYSIS OF SURVIVAL IN 208 PATIENTS WITH ADULT RESPIRATORY DISTRESS SYNDROMEASSOCIATED WITH INFLUENZA A/H1N1V 2009 INFECTION

| Variable | aHR | 95% CI | *P* Value |
|---|---|---|---|
| Immunodepression | 2.17 | 1.15–4.09 | 0.02 |
| SAPS 3 score > 50 | 2.80 | 1.38–5.66 | 0.004 |
| Vasopressors* | 1.98 | 0.90–4.32 | 0.09 |
| Corticosteroid therapy† | 2.59 | 1.42–4.73 | 0.002 |

# elines for the diagnosis management of critical illness-related costeroid insufficiency (CIRCI) in critically ill nts (Part I): Society of Critical Care Medicine M) and European Society of Intensive Care cine (ESICM) 2017

ne[1*], Stephen M. Pastores[2*], Bram Rochwerg[3], Wiebke Arlt[4], Robert A. Balk[5], shuizen[6], Josef Briegel[7], Joseph Carcillo[8], Mirjam Christ-Crain[9], Mark S. Cooper[10], [11], Gianfranco Umberto Meduri[12], Keith M. Olsen[13], Sophia Rodgers[14], James A. Russell[15] an den Berghe[16]

*Intensive Care Med*
DOI 10.1007/s00134-017-4919-5

**Early severe ARDS ($PaO_2$:$FiO_2$ < 200 on PEEP 5 $cmH_2$**

| Time | Administration form | Dosage |
|---|---|---|
| Loading | Bolus over 30 min | 1 mg/kg |
| Days 1 to 14* † ‡ ¶ | Infusion at 10 cc/hour | 1 mg/kg/da |
| Days 15 to 21* ‡ ¶ | Infusion at 10 cc/hour | 0.5 mg/kg/ |
| Days 22 to 25* ‡ ¶ | Infusion at 10 cc/hour | 0.25 mg/kg |
| Days 26 to 28* ‡ ¶ | Infusion at 10 cc/hour | 0.125 mg/k |

summary, the task force suggested that methylpred-
lone be considered in patients with early (up to day
onset; $PaO_2/FiO_2$ of <200) in a dose of 1 mg/kg/day

# SDRA persistant : que faire ?

1. Ce que j'aurais du faire avant

2. Ce que je dois faire

3. Ce que je ferai « peut être demain »

# Que cache un SDRA persistant ?
# Je dois rechercher une complication

Persistance de la cause (ATB inadaptée, complication chirurgie, pancréatite

Une insuffisance cardiaque gauche, une EP, un atelectasie, un ep. pleural

Une surinfection (PAVM), une co-infection bactérienne, virale (CMV, HSV, Grippe nosocomiale), fongique (aspergillus)

Une dysrégulation des mécanismes inflammatoire et de réparation tissulair

L'évolution vers une fibrose pulmonaire

# Je dois rechercher une participation « hémodynamique » ?

- **ETO, ETT**, Picco, Swan …

- Œdème hydrostatique (Bilan entrée/sortie, Poids)
- Insuffisance ventriculaire gauche, droite
- Embolie pulmonaire

# Je dois rechercher une complication
# Intérêt imagerie TDM +++

Embolie pulmonaire, Œdème hydrostatique

Ep. pleuraux, baro-volotraumatismes (pneumothorax antérieur)

Trouble ventilatoire

Images spécifiques d'une étiologie (aspergillose, abcès…)

Aspect de fibrose

Orientation des prélèvements pulmonaires

Infection extra-pulmonaire (abdomen, pelvis…Chirurgie++, pancréatite)

# Je dois éliminer une PAVM +++
## (15-60% (1/3) des SDRA)

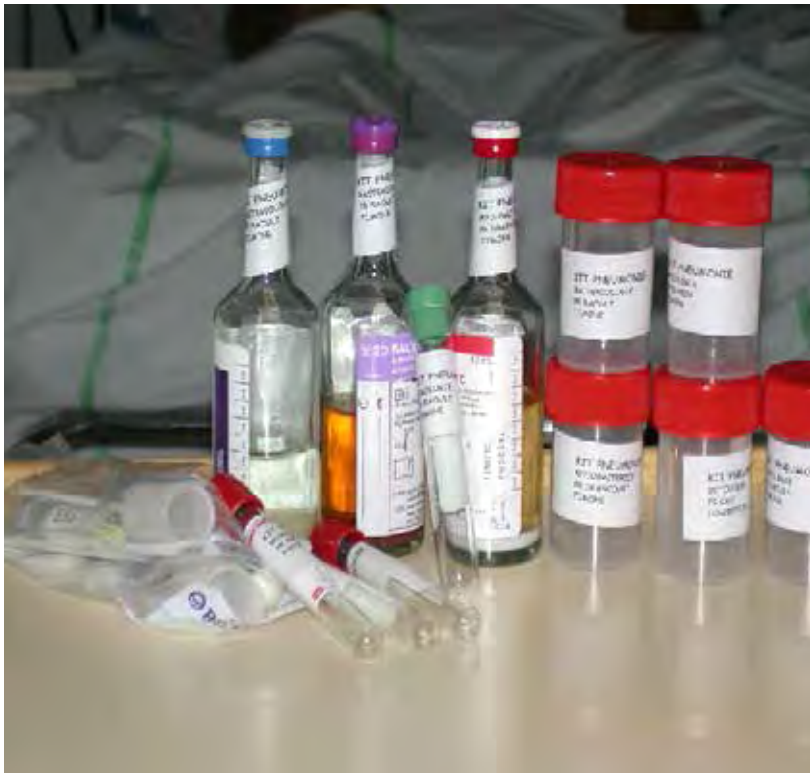
**LBA**, **PDP**, (ABR)

**bactériologie** *(standard, **moléculaire** …)*

**virologie** (CMV, HVS), **mycologie** *(idem)*

**cytologie** : PNN, éosino, sidérophage

(procollagène III ? = fibroprolifération)



# Je dois penser aux PAVM non-bactériennes

Etude retrospective : 1996-2003

- 100 biopsies (OLB)
- **30** pneumonies à **CMV** – 3 **HSV**

*Papazian CCM 2007*

**Progrès microbiologie moléculaire +++**

PCR quantitative

Antigénémie pp65

# SDRA persistant à J5-7

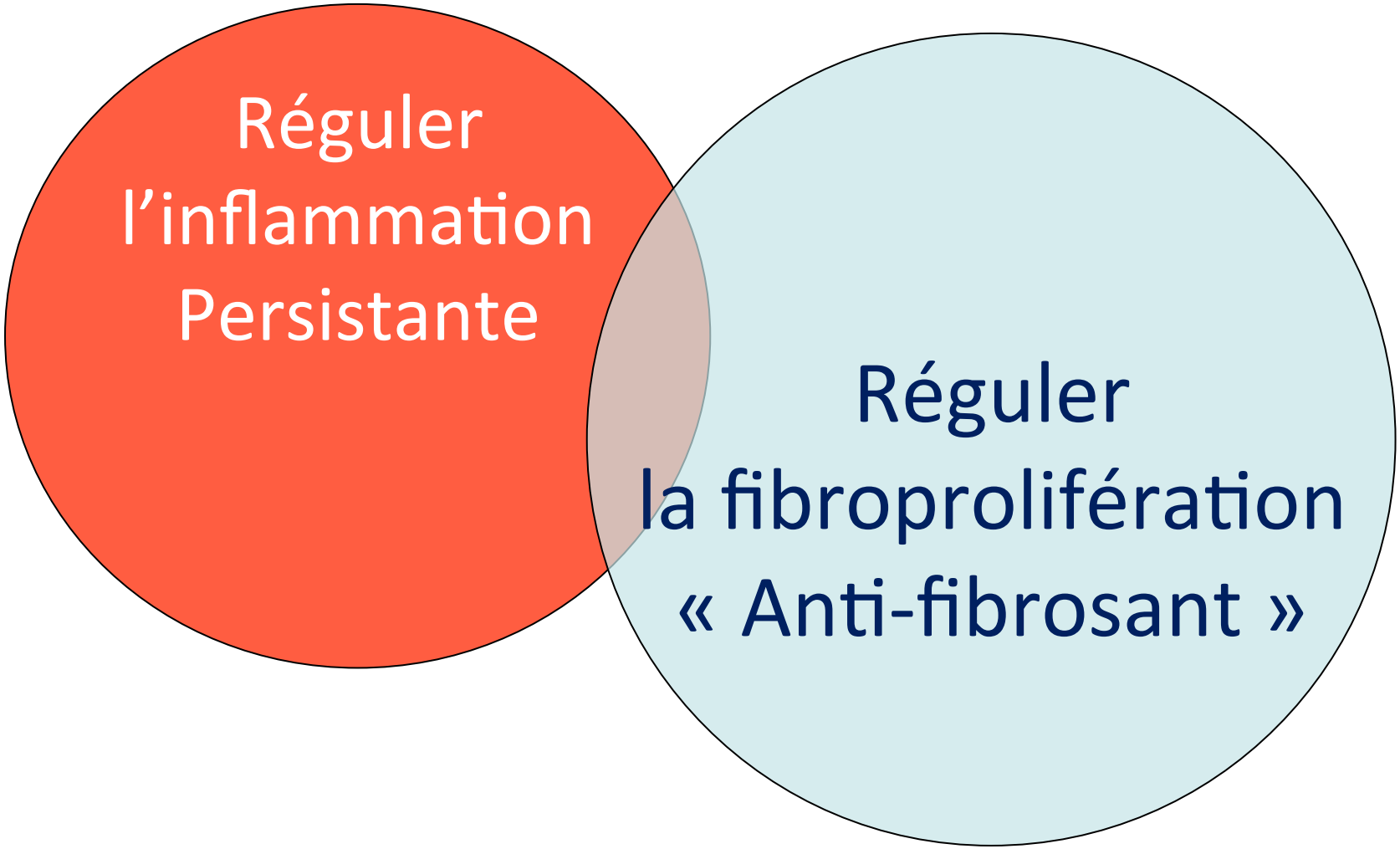
## = *après élimination d'une autre cause*

(PAVM, surcharge, Paramètres VM inadaptés)

Dysrégulation **persistante** des mécanismes inflammatoire et de réparation tissulaire ?

Evolution vers une **fibrose** pulmonaire ?

# Je dois administer un corticoïde lors du SDRA persistant **(J5-7)**



# Effect of Prolonged Methylprednisolone Therapy in Unresolving Acute Respiratory Distress Syndrome

## A Randomized Controlled Trial

G. Umberto Meduri, MD; A. Stacey Headley, MD; Emmel Golden, MD; Stephanie J. Carson, RN; Reba A. Umberger, RN; Tiffany Kelso, PharmD; Elizabeth A. Tolley, PhD

*Meduri JAMA 199*

(1) diagnosis of ARDS by consensus criteria,[17] (2) 7 days of mechanical ventilation with an LIS of 2.5 or greater and less than a 1-point reduction from day 1 of ARDS, and (3) no evidence of untreated infection.

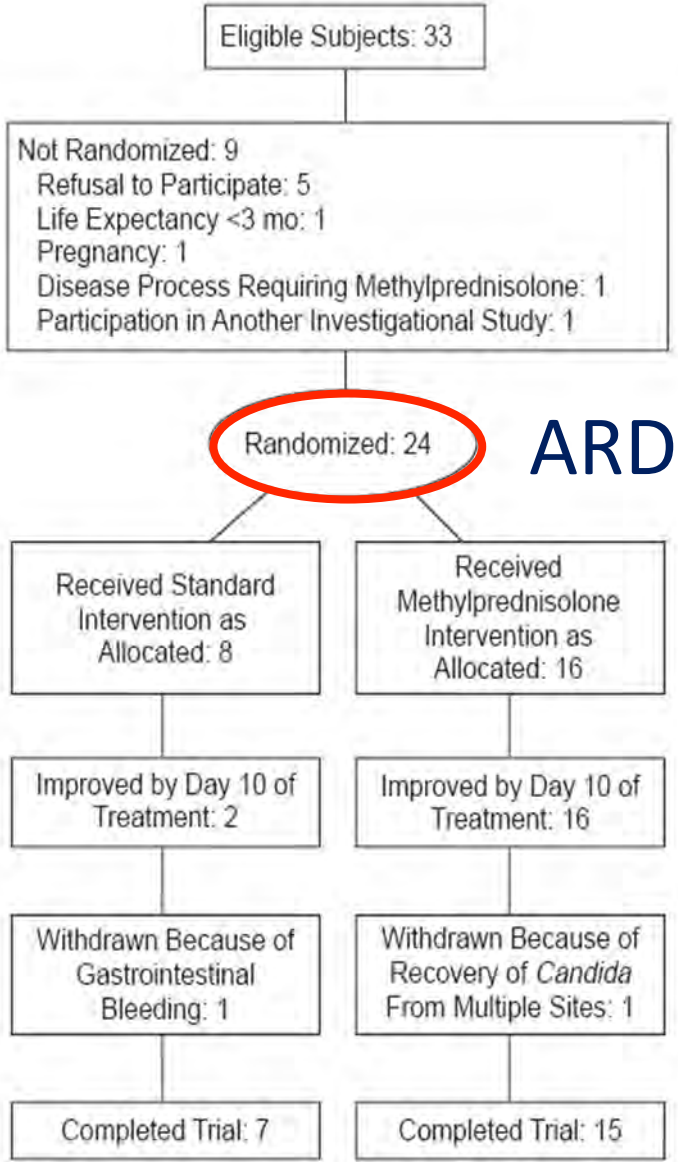
SDRA depuis 9 ± 1 jours

# Protocole « Meduri 1998»

*Meduri JAMA 1*

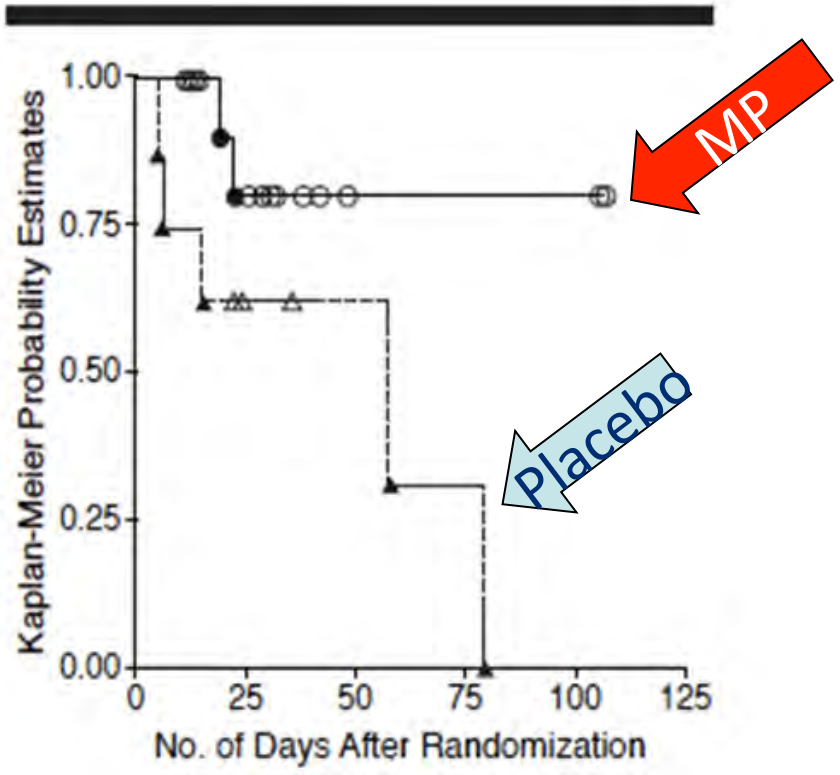
Méthylprednisolone
(Solumédrol©) IV
en 4 injections / j

Bolus 2 mg/Kg
2 mg/Kg J1-J14
1 mg/Kg J15-J21
0,5 mg/Kg J22-J28
0,25 mg/Kg J29-J30
0,125 mg/Kg J31-J32




ARDS >D7 (m

*ri JAMA 1998*




# Cortico = MP = Meilleure survie

MP

Placebo

| Outcome Measures | Methylprednisolone | Placebo | *P* Value |
|---|---|---|---|
| Survivors of ICU admission, No. (%) | 16 (100) | 3 (37) | .002 |
| Survivors of hospital admission, No. (%) | 14 (87) | 3 (37) | .03 |
| Death associated with unresolving ARDS, No.† | 0 of 2 | 5 of 5 | NA |
| MODS-free days by study day 28, mean (SEM)‡ | 16 (2) | 6 (2) | .005 |
| Duration of mechanical ventilation, median, d | 11.5 | 23 | .001 |

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 20, 2006 VOL. 354 NO. 16

*Steinberg NEJM 2006*

# Efficacy and Safety of Corticosteroids for Persistent Acute Respiratory Distress Syndrome

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network*

180 (5%) Enrolled while receiving assisted ventilation
91 Assigned to placebo
89 Assigned to methylprednisolone

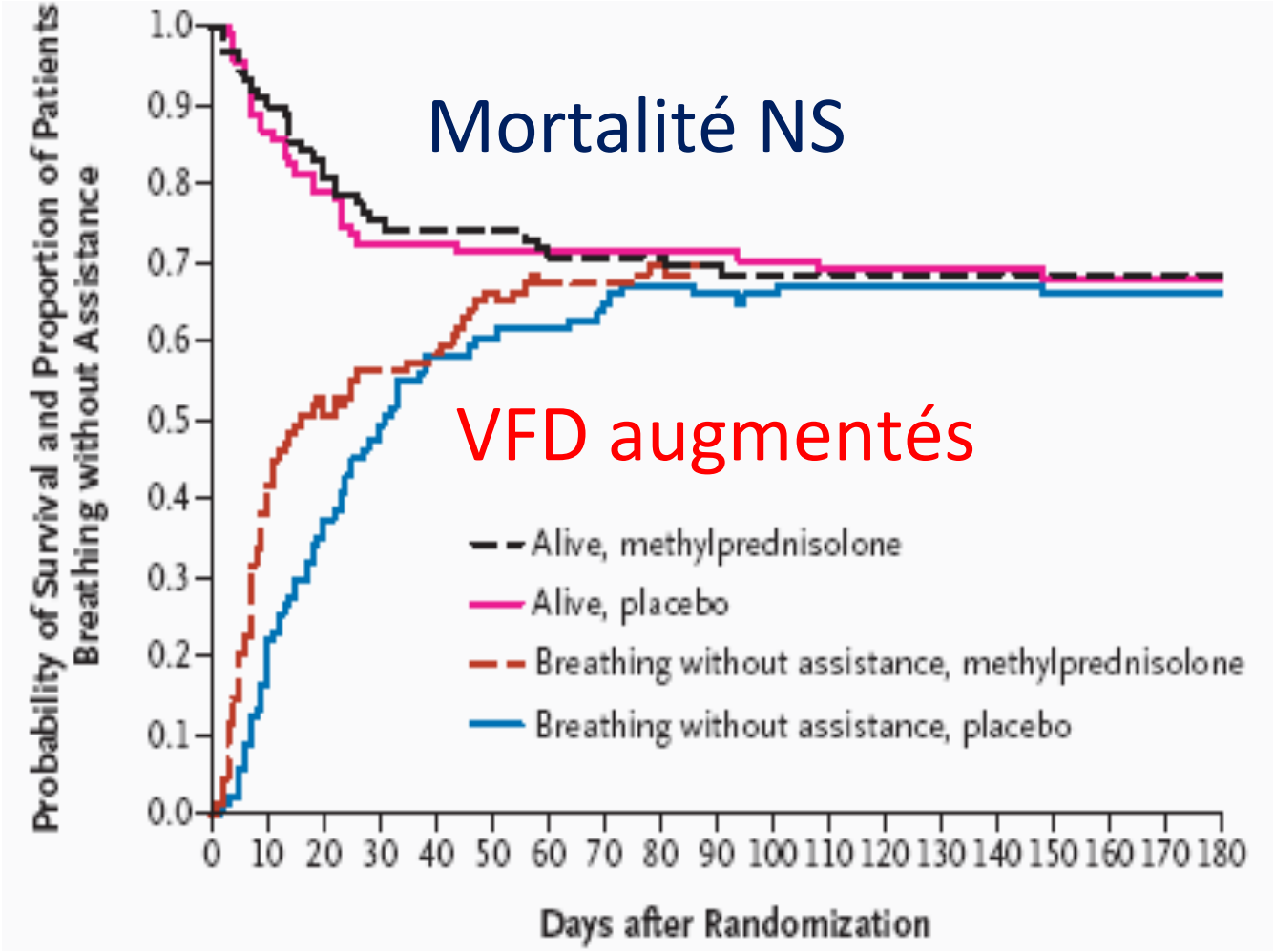
- P/F < 200
- ARDS D7-D28 (mD11)
- MethylPrednisolone
  - 2 mg/kg
  - 4x0.5 mg/kg /D/14D
  - 2x0.5 mg/kg /D/7D
  - ↘ /4D (sevrage rapide)

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 20, 2006 VOL. 354 NO. 16

# Efficacy and Safety of Corticosteroids for Persistent Acute Respiratory Distress Syndrome

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network*




*Steinberg NEJM 2*

# Surmortalité si cortico après J 14

Table 3. Post Hoc Analyses of Outcomes and Adverse Events at 180 Days.*

| Variable | Placebo (N=91) | Methylprednisolone (N=89) | P Value |
|---|---|---|---|
| >14 Days — %† | 12 | 44 | 0.01 |
| No. of patients | 25 | 23 | |

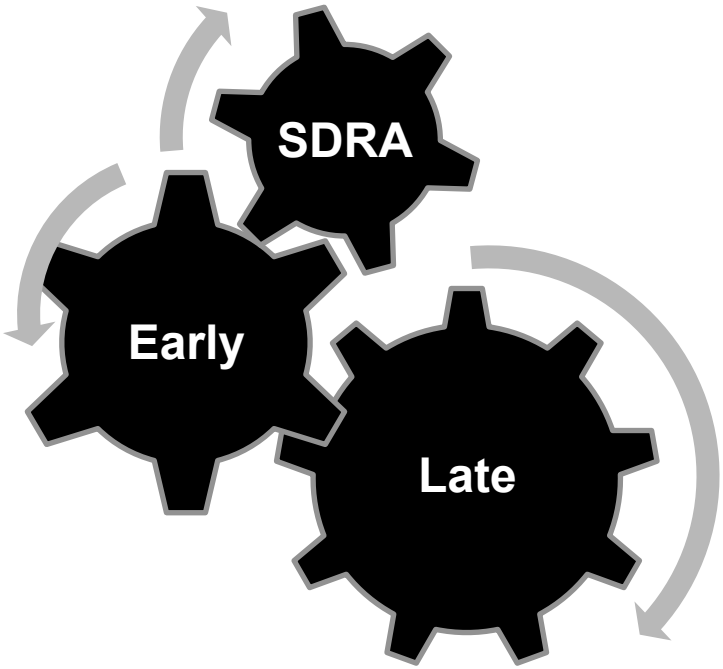
**SDRA persistant =**

**Agir avant J14**

**Pas de corticoïde après J14** **(exclu connectivite)**

# SDRA et corticoïdes

## 15 Méta-analyses…
## (9 RCT, 760 patients !)




Meduri 2016
Data individuelles

Annane 2017
Experts / Guidelines

# Corticoïdes pour SDRA

## *Méta-analyses des data individuelles*

G. Umberto Meduri
Lisa Bridges
Mei-Chiung Shih
Paul E. Marik
Reed A. C. Siemieniuk
Mehmet Kocak

**Prolonged glucocorticoid treatment is associated with improved ARDS outcomes: analysis of individual patients' data from four randomized trials and trial-level meta-analysis of the updated literature**

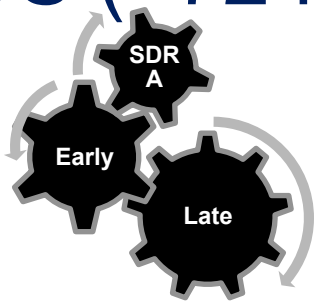
Intensive Care Med. 2016;42(5):82

RCTs investigating prolonged methylprednisolone treatmen

early ARDS (<72 h; n = 118)

Meduri *et al.* Chest 2007

Rezk *et al.* Egypt J Chest Dis Tuberc 2013



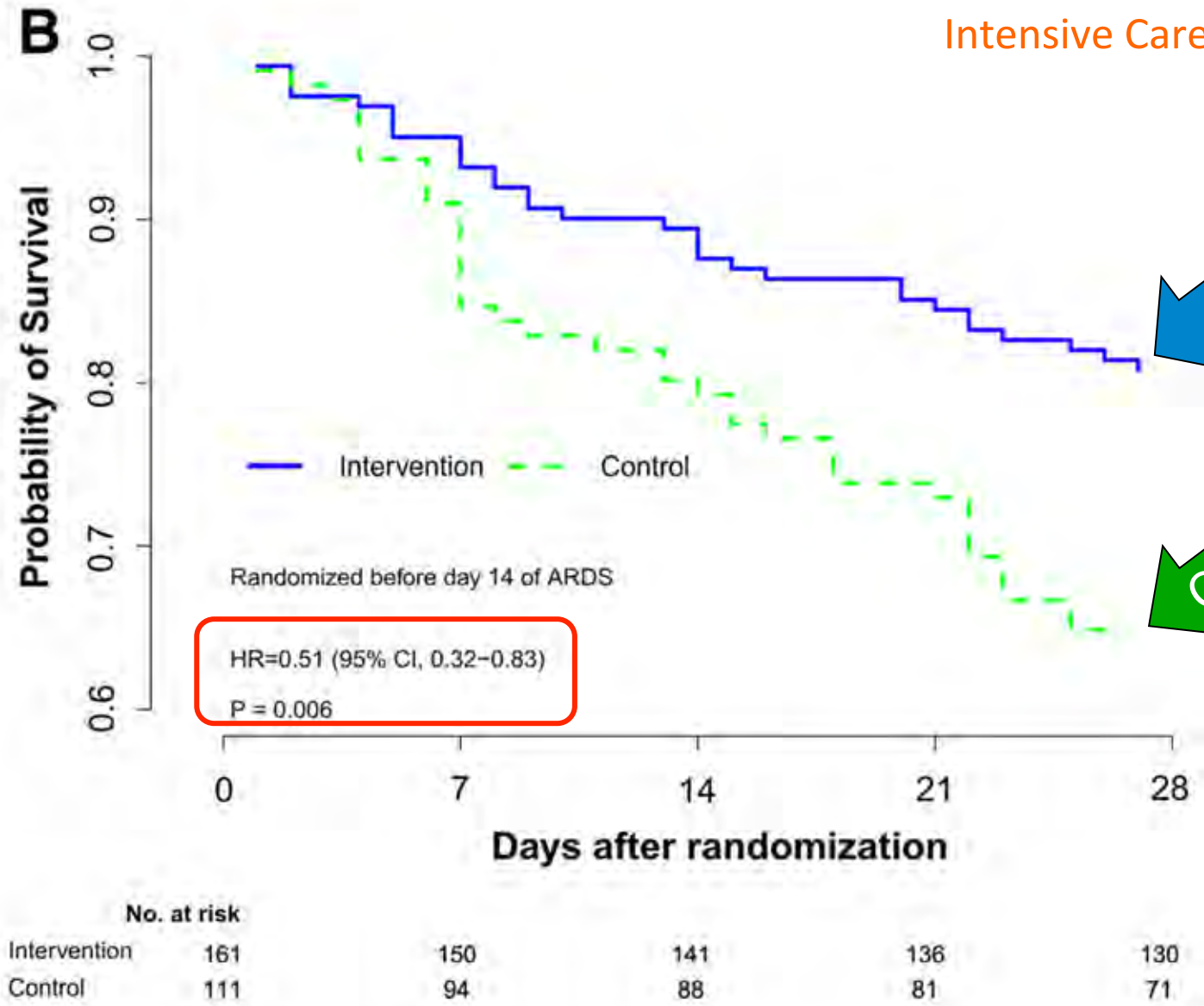

late ARDS (after 7 days; n = 204)

Meduri *et al.* JAMA 1998

Steinberg *et al.* NEJM 2006

# Methylprednisolone avant J14 = meilleure survie

Intensive Care Med. 2016;42(5):82



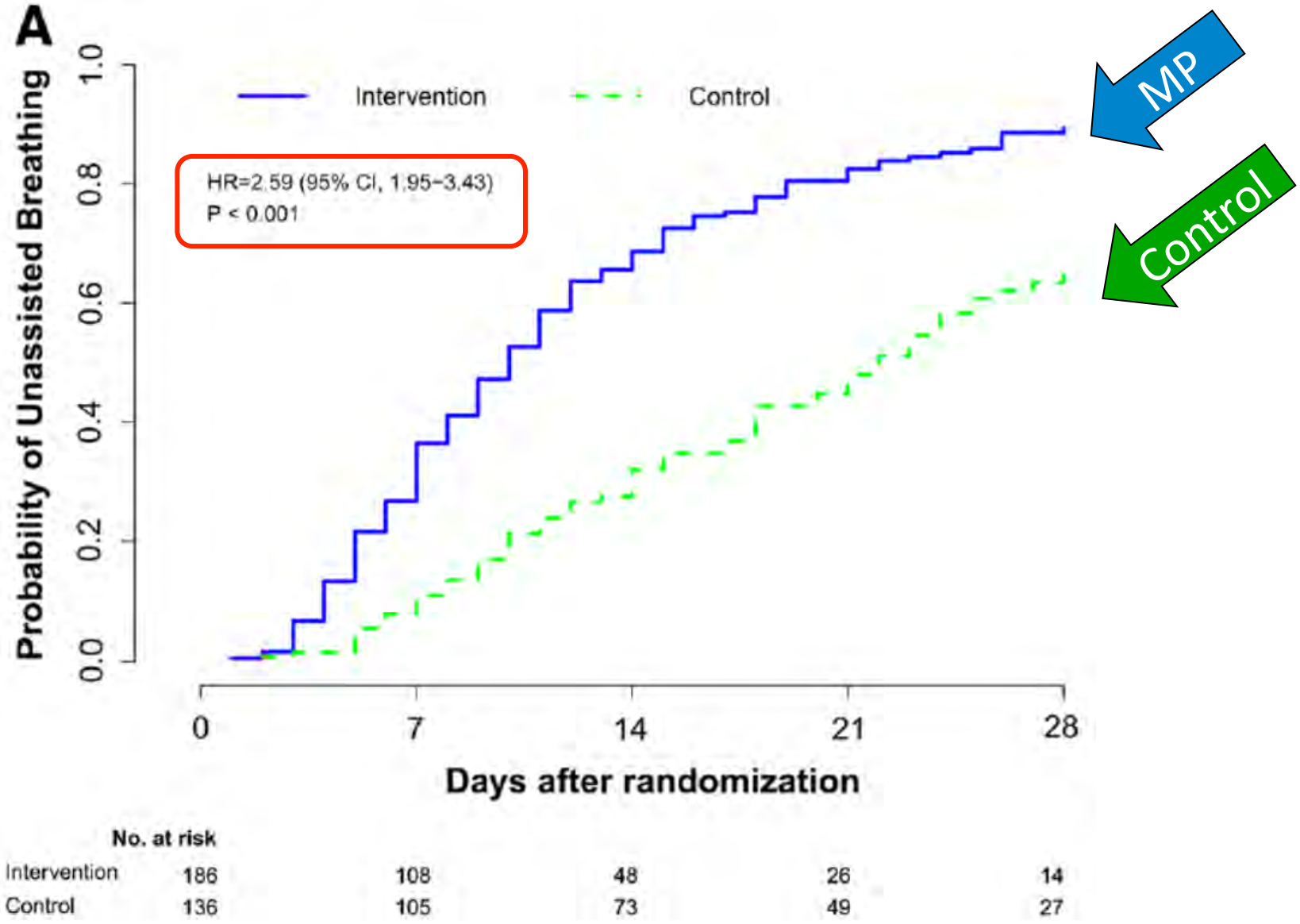

MP

Control

SURVIE

# Plus rapidement sevré de la VM

Intensive Care Med. 2016;42(5):82

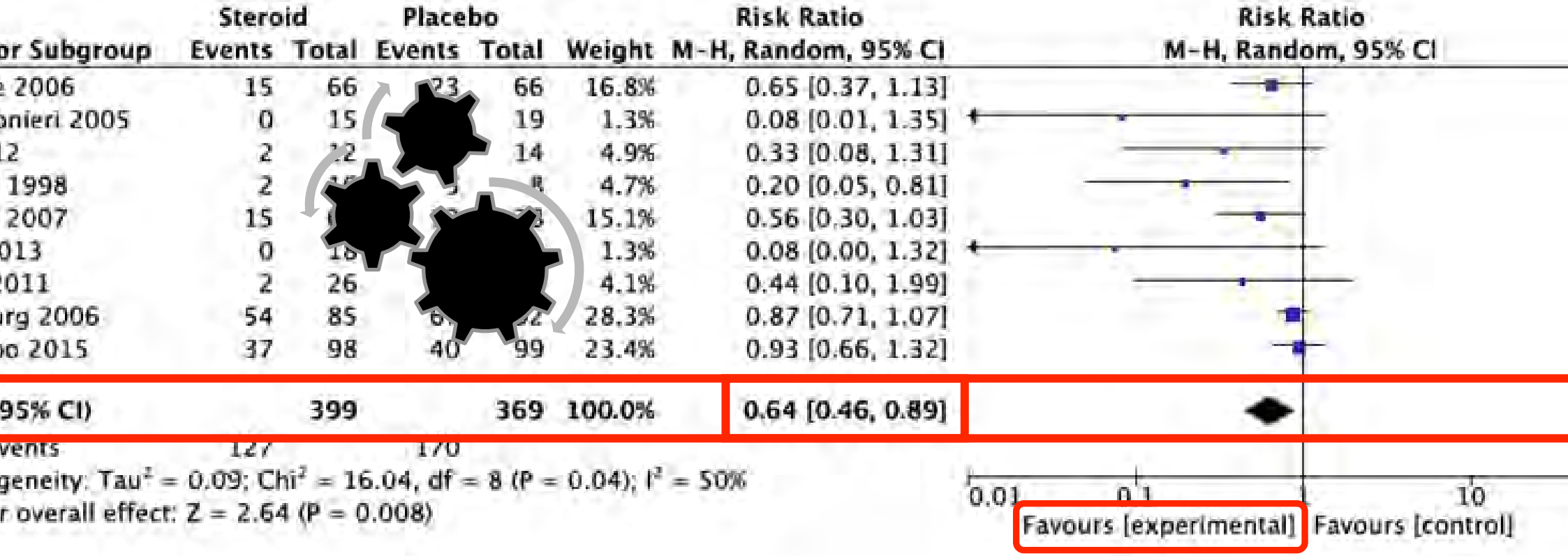


# delines for the diagnosis management of critical illness-related ticosteroid insufficiency (CIRCI) in critically ill ents (Part I): Society of Critical Care Medicine CM) and European Society of Intensive Care dicine (ESICM) 2017

Djillali Annane[1*], Stephen M. Pastores[2*], Bram Rochwerg[3], Wiebke Arlt[4], Robert A. Balk[5], Albertus Beishuizen[6], Josef Briegel[7], Joseph Carcillo[8], Mirjam Christ-Crain[9], Mark S. Cooper Paul E. Marik[11], Gianfranco Umberto Meduri[12], Keith M. Olsen[13], Sophia Rodgers[14], James and Greet Van den Berghe[16]

*Intensive Care Med*
DOI 10.1007/s00134-017-4

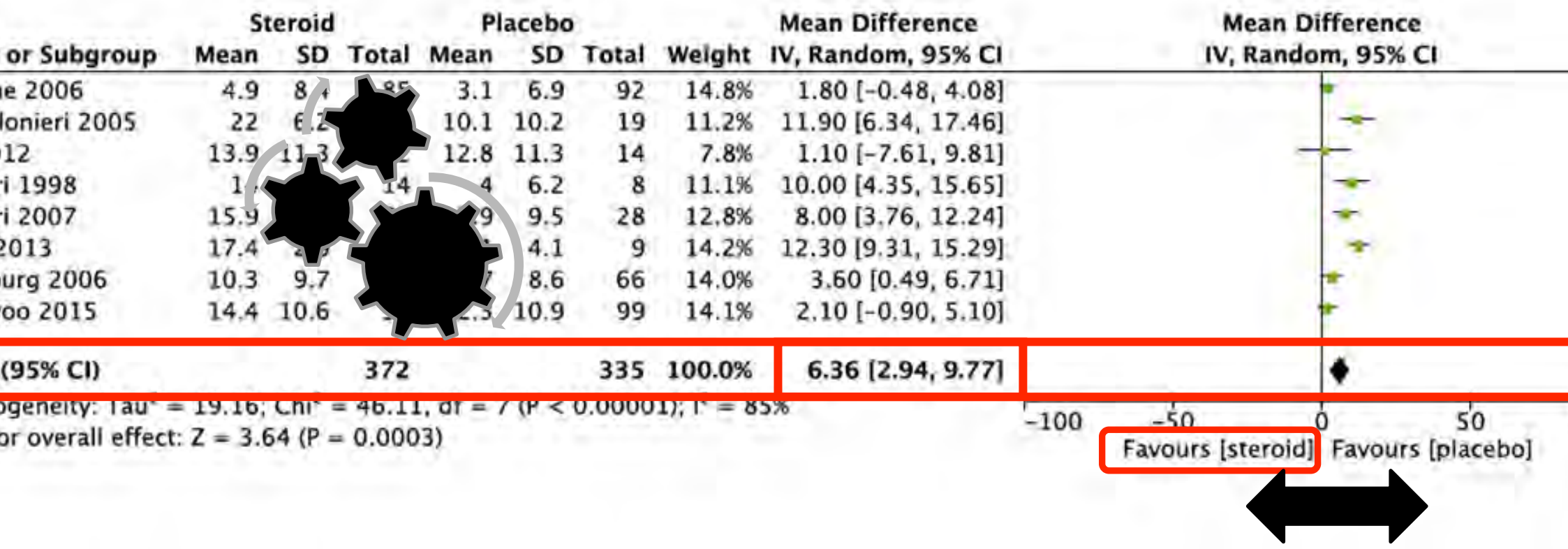
Cortico diminuent mortal



# delines for the diagnosis management of critical illness-related icosteroid insufficiency (CIRCI) in critically ill ents (Part I): Society of Critical Care Medicine CM) and European Society of Intensive Care licine (ESICM) 2017

*Intensive Care Med*
DOI 10.1007/s00134-017-4919-

Cortico augmentent Ventilator free days at da



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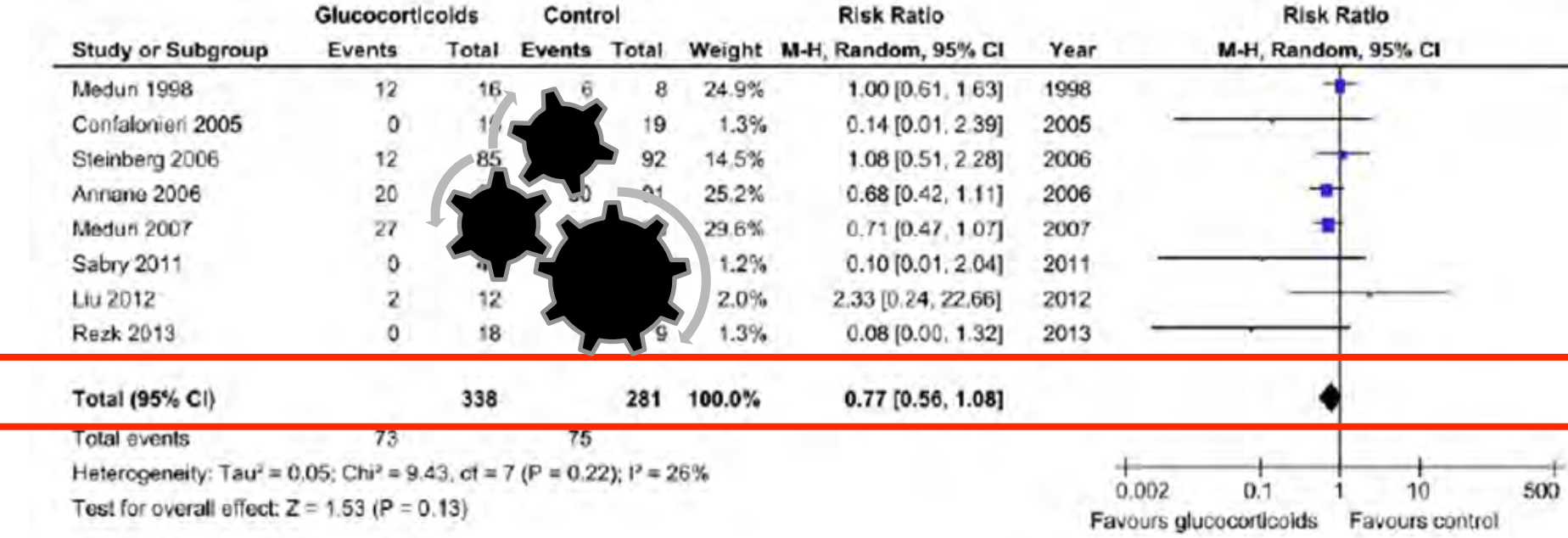
*Intensive Care Med*
DOI 10.1007/s00134-017-4919

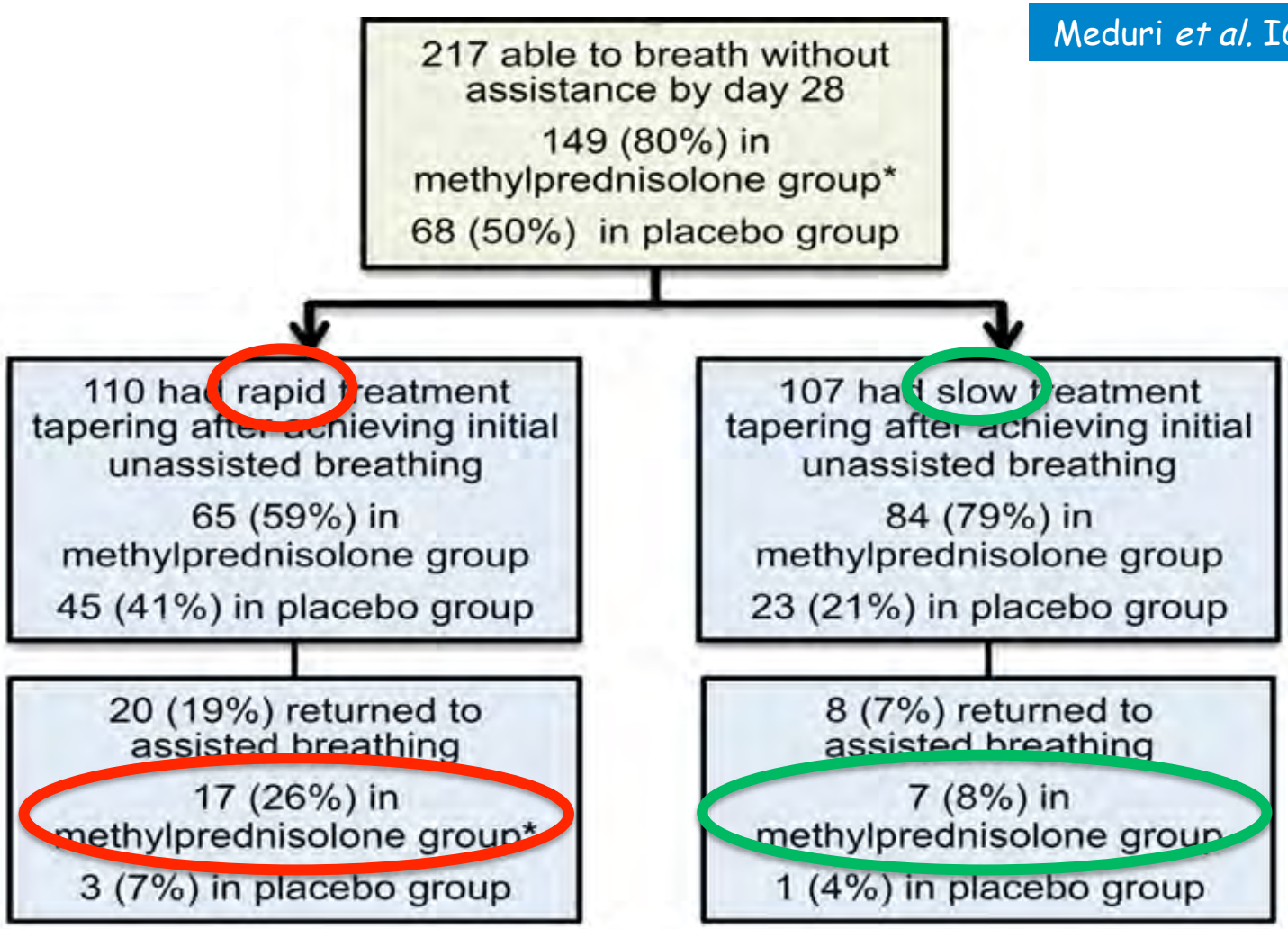
**Figure S5.** Effects of prolonged glucocorticoid treatment on development of nosocomial infections; data from eight randomized trials (n=619).

Cortico n'augmentent pas les infections nosocomiales (SDR



# Sevrage des corticoïdes = lent et prolongé (28j)

Meduri *et al.* ICM 2016




sse sevrage

reventilé

RENCE REPORTS AND EXPERT PANEL

# elines for the diagnosis management of critical illness-related costeroid insufficiency (CIRCI) in critically ill nts (Part I): Society of Critical Care Medicine M) and European Society of Intensive Care cine (ESICM) 2017

ne[1*], Stephen M. Pastores[2*], Bram Rochwerg[3], Wiebke Arlt[4], Robert A. Balk[5], ishuizen[6], Josef Briegel[7], Joseph Carcillo[8], Mirjam Christ-Crain[9], Mark S. Cooper[10], [11], Gianfranco Umberto Meduri[12], Keith M. Olsen[13], Sophia Rodgers[14], James A. Russell[15] an den Berghe[16]

*Intensive Care Med*
DOI 10.1007/s00134-017-4919-5

summary, the task force suggested that methylpred-
one be considered in patients
$PaO_2/FiO_2$ of <200)
late (after day 6 of onset) persistent ARDS in a dose
mg/kg/day followed by slow tapering over 13 days

**Unresolving ARDS = less than**

**(a) 1-point reduction in lung injury score**

**(b) or 100 improvement of in $PaO_2$:$FiO_2$**

- **By day 7 of ARDS in patients not receiving methylprednisolone for early ARDS.**
- **By day 5-7 of ARDS in patients receiving methylprednisolone (above) for early ARDS.**

| Time | Administration form | Dosage |
|---|---|---|
| Loading | Bolus over 30 min | 2 mg/kg |
| Days 1 to 14*† ‡ ¶ | Infusion at 10 cc/hour | **2 mg/kg/day** |
| Days 15 to 21* ‡ ¶ | Infusion at 10 cc/hour | 1 mg/kg/day |
| Days 22 to 25* ‡ ¶ | Infusion at 10 cc/hour | 0.5 mg/kg/day |
| Days 26 to 28* ‡ ¶ | Infusion at 10 cc/hour | 0.25 mg/kg/day |
| Days 29 to 28* ‡ ¶ | Bolus over 30 min | 0.125 mg/kg/day |

# SDRA persistant

Faut il faire une biopsie pulmonaire ?

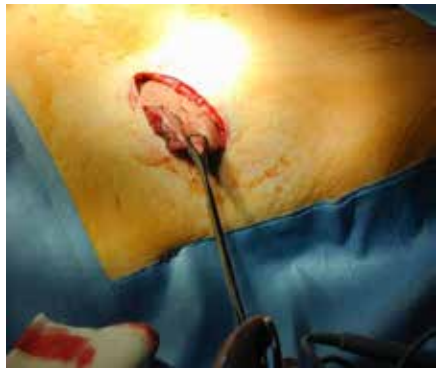
# TransBronchial Lung Biopsy

- Hemoptysis ( ≅ 12%)
  - 3 of 14 — Papin *et al.* Chest 1986
  - 1 of 13 — Pincus *et al.* CCM 1987
  - 3 of 25 — Martin *et al.* Chest 1995
  - 4 of 38 — Bulpa *et al.* Eur Respir J 2003
- Pneumothorax (≅ 17%)
  - 1 of 14 — Papin *et al.* Chest 1986
  - 2 of 13 — Pincus *et al.* CCM 1987
  - 8 of 38 — Bulpa *et al.* Eur Respir J 2003
- Insufficient lung sample for histological analysis
  - 3 of 25 (≅ 12%) — Martin *et al.* Chest 1995

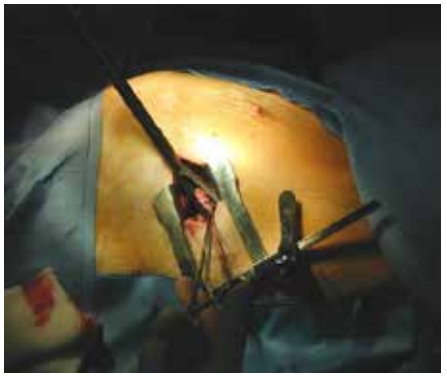
PAS de BTB

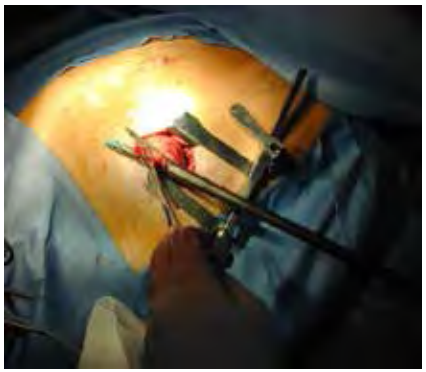
# opsie pulmonaire chirurgicale (open lung biopsy OLB

(au mieux guidée par une TDM préalable)

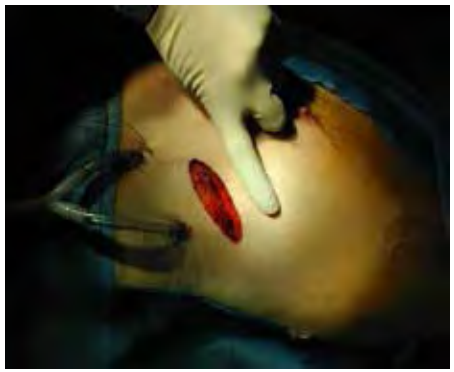


Incision de thoracotomie latérale 10 cm - 5èm EIC





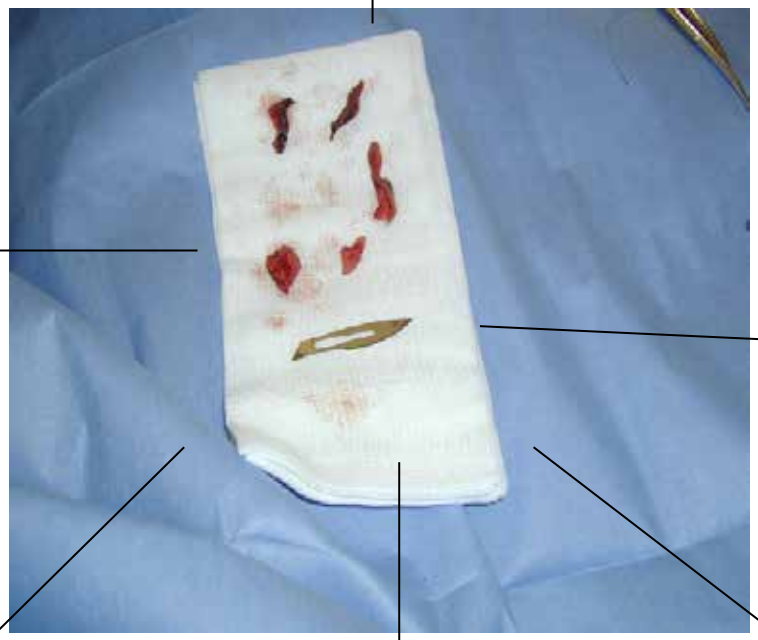
1 biopsie zones dépendantes pince à agrafes (pause expiratoire)



Double drainage pleural antérieur et postérieur

# 1 biopsie principale secondairement fractionnée

Expérience +++

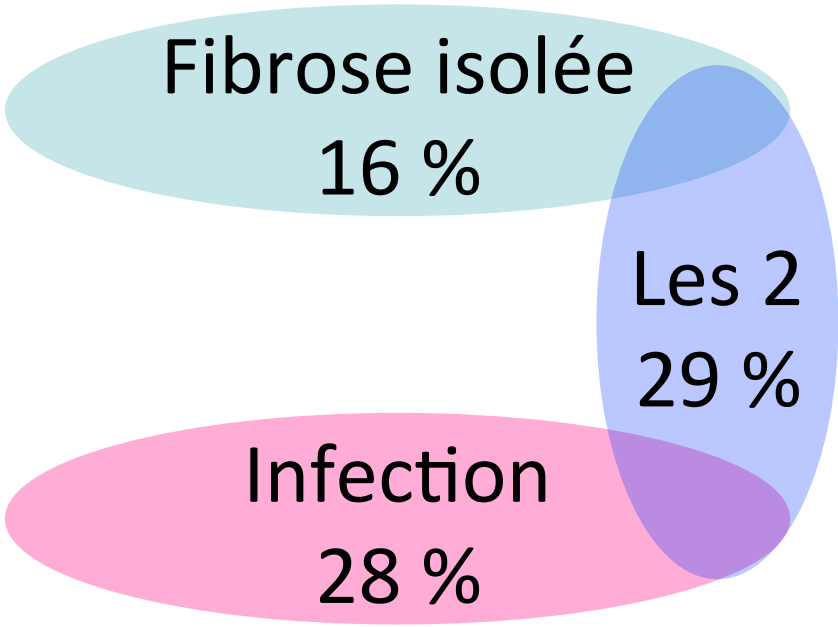


# A contributive result of open-lung biopsy improves survival in acute respiratory distress syndrome patients

Laurent Papazian, MD; Christophe Doddoli, MD; Bruno Chetaille, MD; Yaël Gernez, MD; Xavier Thirion, MD; Antoine Roch, MD; Yannis Donati, MD; Marilyne Bonnety, MD; Christine Zandotti, MD; Pascal Thomas, MD

| Result of OLB | No. |
|---|---|
| Fibrosis | 16 |
| Fibrosis and infection | 29 |
| Infection | 28 |
| Diffuse alveolar damage | 13 |
| Miscellaneous | |
| Systemic lupus erythematosus | 2 |
| Bronchioloalveolar carcinoma | 1 |
| Amiodarone toxicity | 2 |
| Intra-alveolar hemorrhage | 1 |
| Allograft rejection | 1 |
| Drug toxicity | 2 |
| Rheumatoid lung and mycobacterial infection | 1 |
| Acute eosinophilic pneumonia | 1 |
| Carcinomatous lymphangitis | 2 |
| Microangiitis | 1 |

OLB
6 (6-13,5) jours SDRA



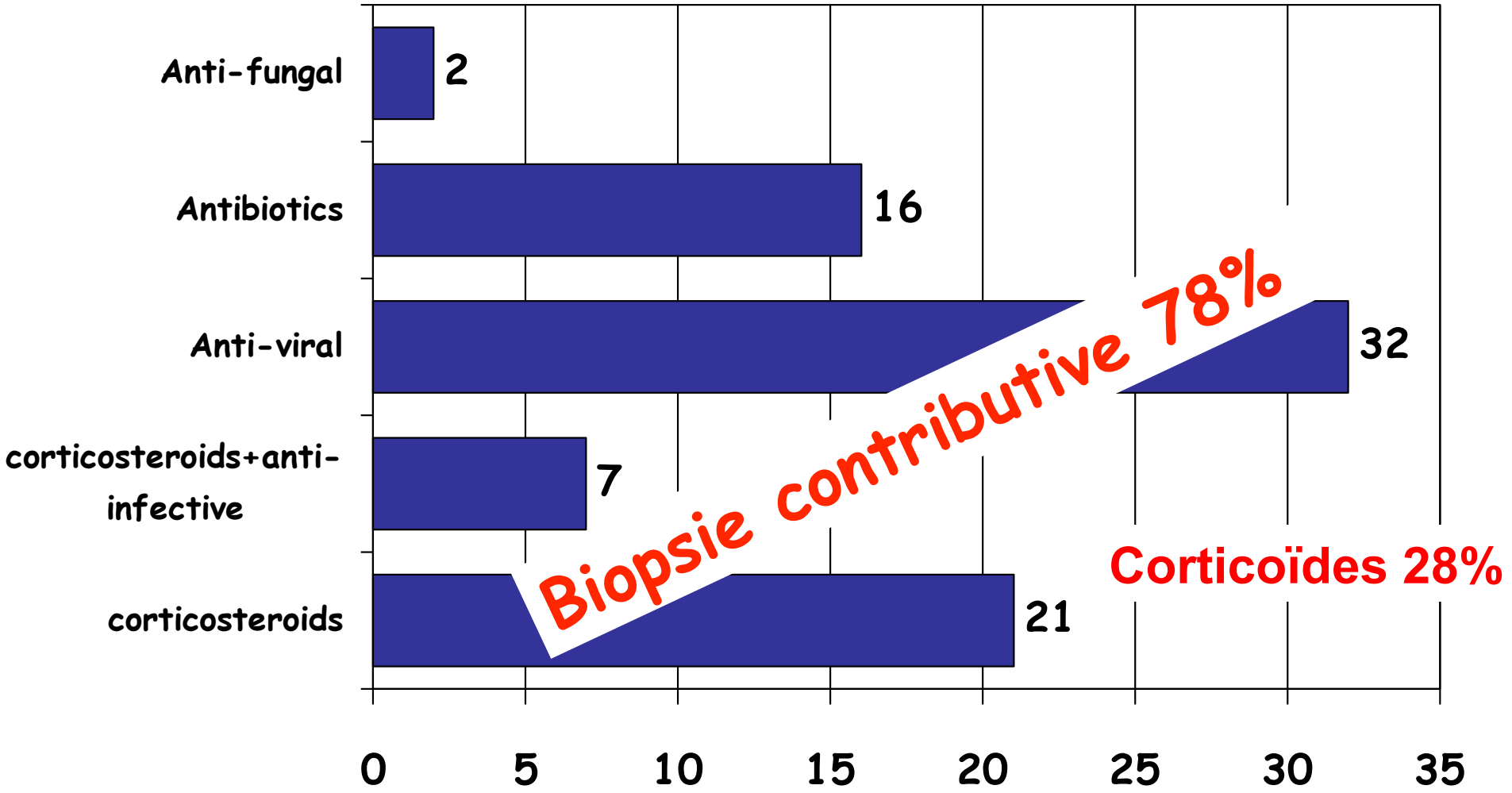

**Diag. rares 14% !!!!!**

*Papazian CCM 2007*

# Adjonction nouveau traitement après OLB

## 100 OLB → 78 OLB Contributives

Papazian *et al.* CCM 2007

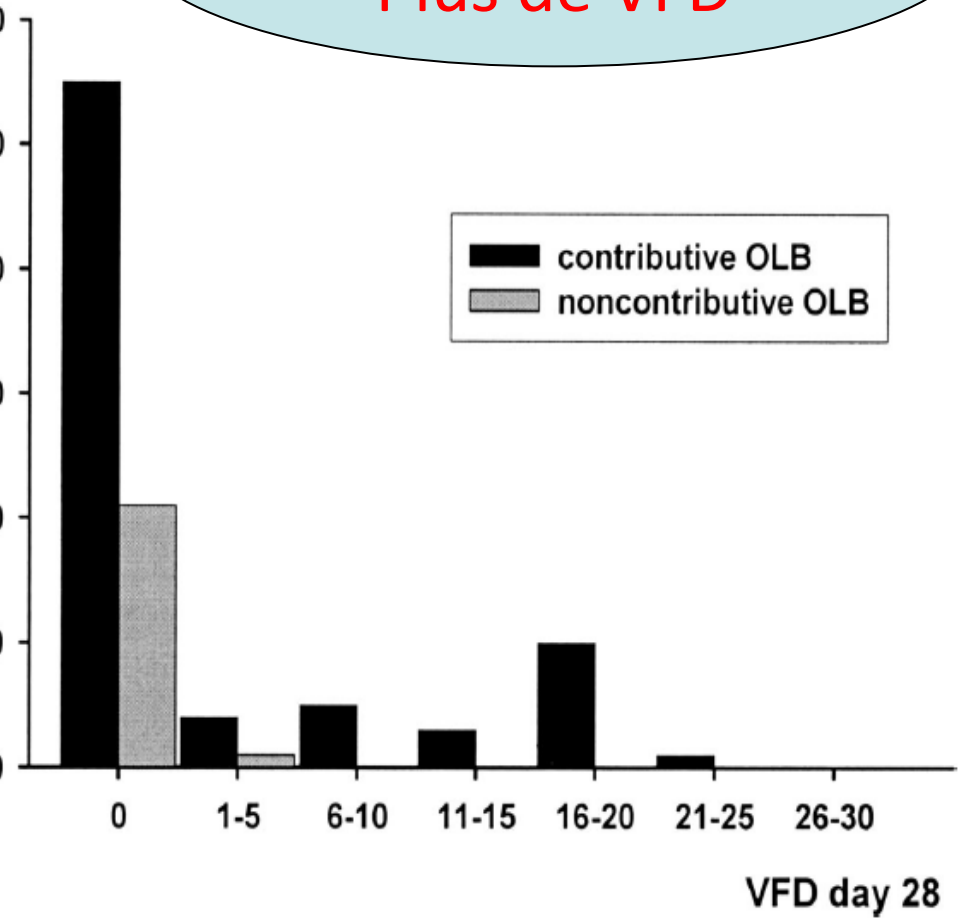


ontributive result of open-lung biopsy improves survival in
te respiratory distress syndrome patients

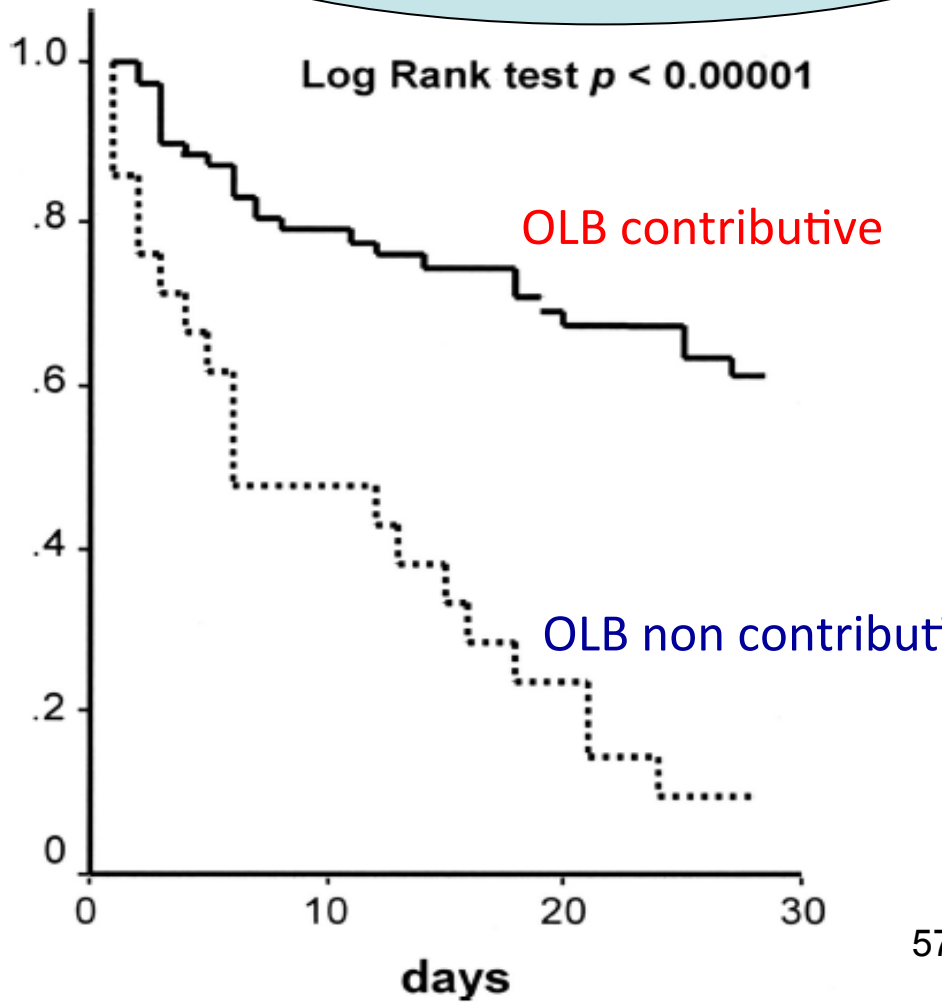
*Papazian CCM 2007*

nt Papazian, MD; Christophe Doddoli, MD; Bruno Chetaille, MD; Yaël Gernez, MD; Xavier Thirion, MD;
ne Roch, MD; Yannis Donati, MD; Marilyne Bonnety, MD; Christine Zandotti, MD; Pascal Thomas, MD

Biopsie contributive =
Plus de VFD




Biopsie contributive =
Meilleur survie



# urgical Lung Biopsy in Adult Respiratory Distress yndrome: A Meta-Analysis

ura J. Libby, MD, Brian D. Gelbman, MD, Nasser K. Altorki, MD,
ul J. Christos, DPH, MS, and Daniel M. Libby, MD

(Ann Thorac Surg 2014;98:1254–6

*Results.* OLB in ARDS provided a specific diagnosis in 84% of patients and altered management in 73%. Hospital mortality was 43%. The complication rate for OLB in ARDS was 22%, but death from OLB was rare.

# urgical Lung Biopsy in Adult Respiratory Distress yndrome: A Meta-Analysis

ura J. Libby, MD, Brian D. Gelbman, MD, Nasser K. Altorki, MD,
ul J. Christos, DPH, MS, and Daniel M. Libby, MD

(Ann Thorac Surg 2014;98:1254–6

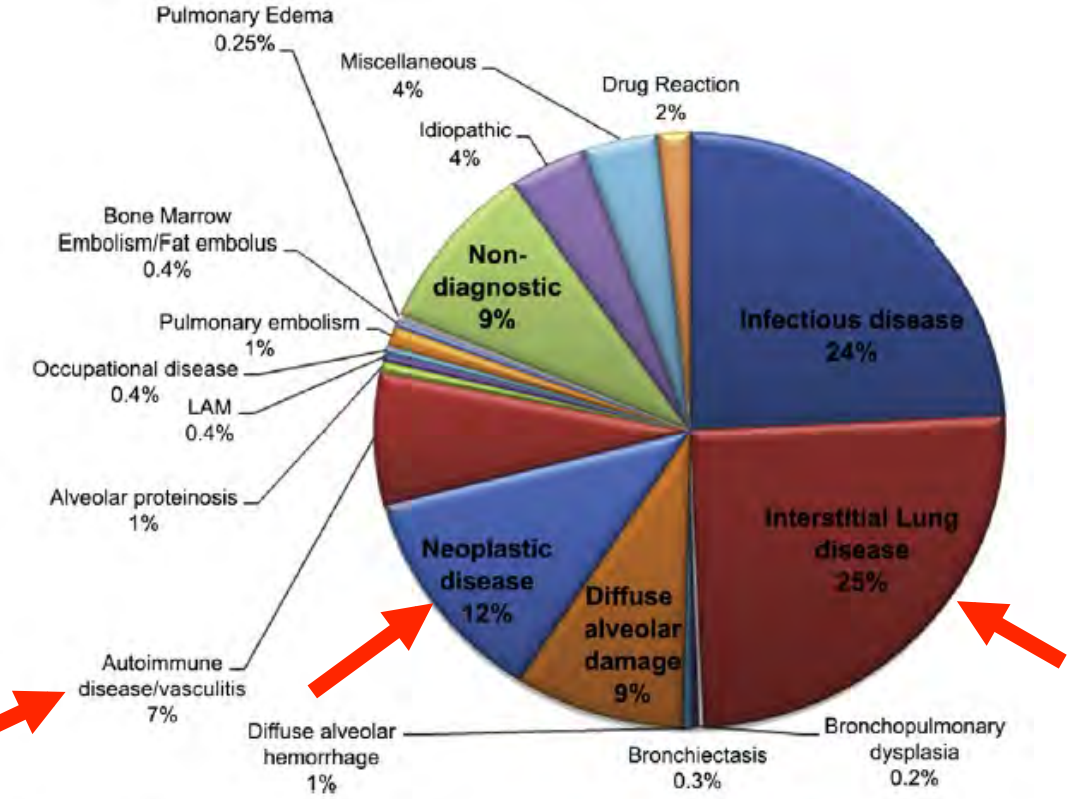



*Fig 3. Pathologic diagnoses made by open lung biopsy. (LAM = lymphangioleiomyomatosis.)*

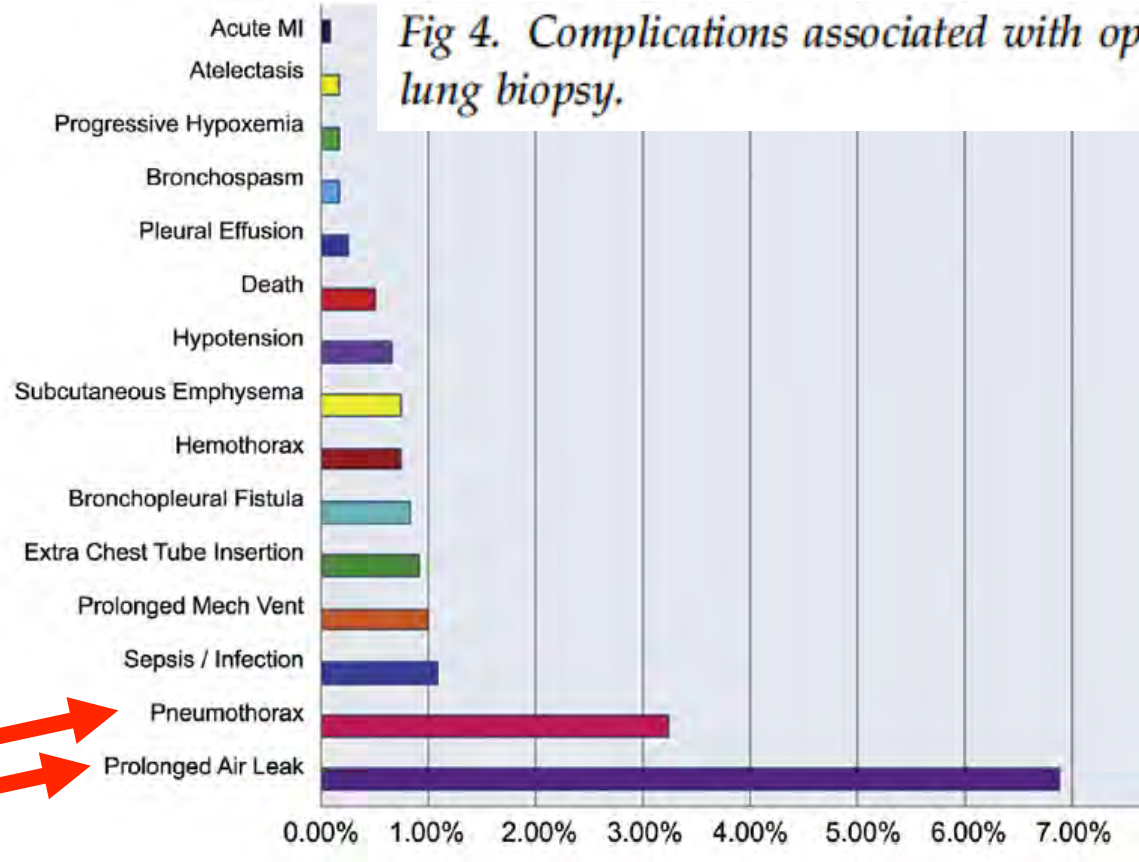



*Fig 4. Complications associated with op lung biopsy.*

# Recommandation française SRLF 2005

9.3.3. La biopsie pulmonaire peut apporter des informations diagnostiques utiles au cours du SDRA. Néanmoins, sa pratique doit être réservée à des situations de SDRA non résolutif ou présentant des incertitudes diagnostiques pouvant conduire à un traitement spécifique *(accord faible)*.

# ch Patients With ARDS Benefit From Lung
# sy?

CHEST 2015; 148(4):1073-1082

Palakshappa, MD; and Nuala J. Meyer, MD, FCCP

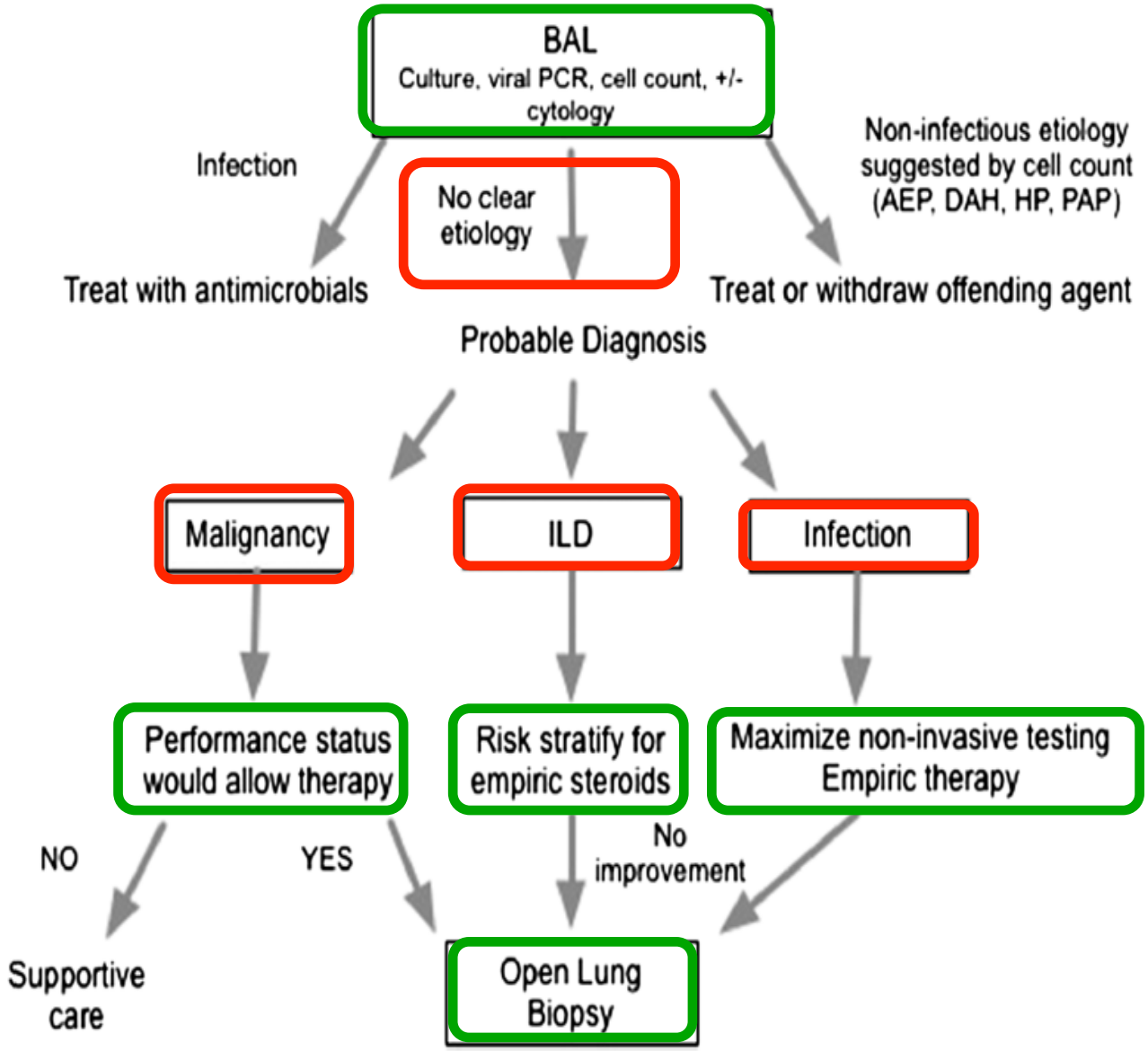



Figure 1 – *Decision-making algorithm for open lung biopsy. *Pneumonia, sepsis, trauma, aspiration, pancreatitis. AEP = acute eosinophilic pneumonia; DAH = diffuse alveolar hemorrhage; HP = hypersensitivity pneumonitis; ILD = interstitial lung disease; PAP = pulmonary alveolar proteinosis; PCR = polymerase chain reaction.*

# SDRA persistant : que faire ?

1. Ce que j'aurais du faire avant
2. Ce que je dois faire
3. Ce que je ferai « peut-être demain »

# ntilator-related causes of lung injury: e mechanical power

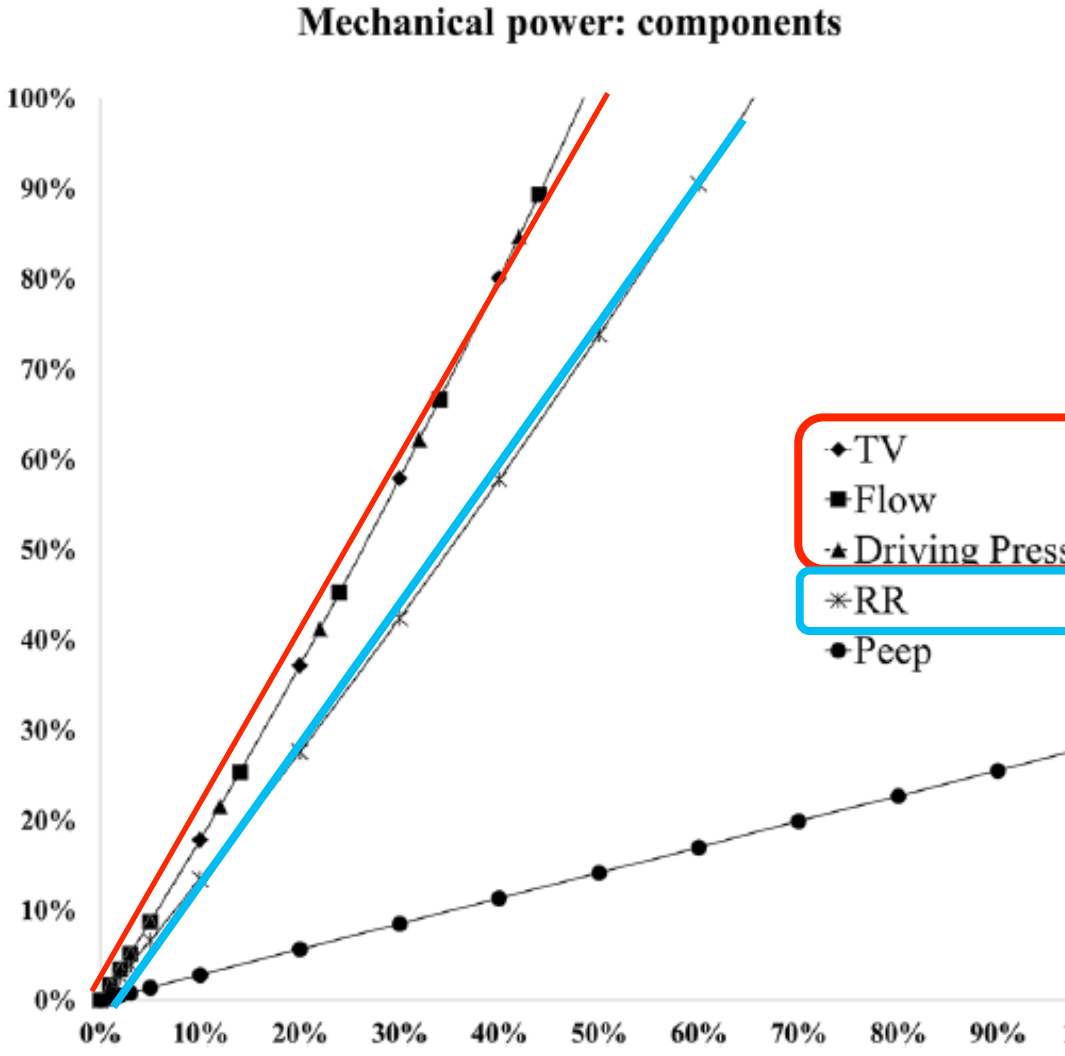
VM ultra-protectrice
Prevention SDRA persis

inoni[1*], T. Tonetti[1], M. Cressoni[2], P. Cadringher[3], P. Herrmann[1], O. Moerer[1], A. Protti[3], M. Gotti[2], urazzi[2], E. Carlesso[2], D. Chiumello[4] and M. Quintel[1]

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

e mechanical power increases exponentially with TV, $\Delta P_{aw}$, flow (exponent = 2) as well as with RR (exponent = 1.4)

*Intensive Care Med (2016) 42:1567–1575*



Anesthesiology 2009; 111:826–35 

# *Tidal Volume Lower than 6 ml/kg Enhances Lung Protection*

## *Role of Extracorporeal Carbon Dioxide Removal*

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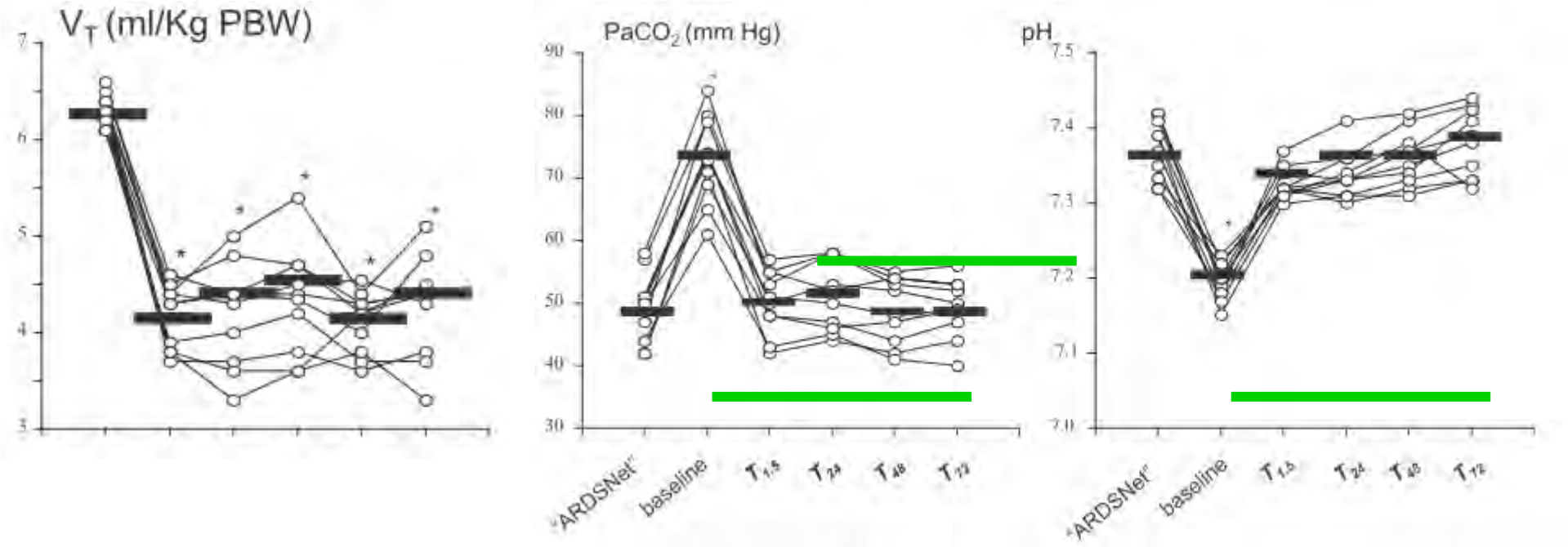


Prévention SDRA persistant

Attente éfficacité trt cortico/spécifique

# ersonnaliser le traitement = Traiter si BAL PCIII élevés

**Table 3. Post Hoc Analyses of Outcomes and Adverse Events at 180 Days.***

| Variable | Placebo (N=91) | Methylprednisolone (N=89) | P Value |
|---|---|---|---|
| 180-Day mortality according to baseline BAL procollagen peptide type III level | | | |
| ≤ Median — % | 13 | 39 | 0.04 |
| No. of patients | 23 | 23 | |
| > Median — %‡ | 24 | 4 | 0.05 |
| No. of patients | 21 | 24 | |

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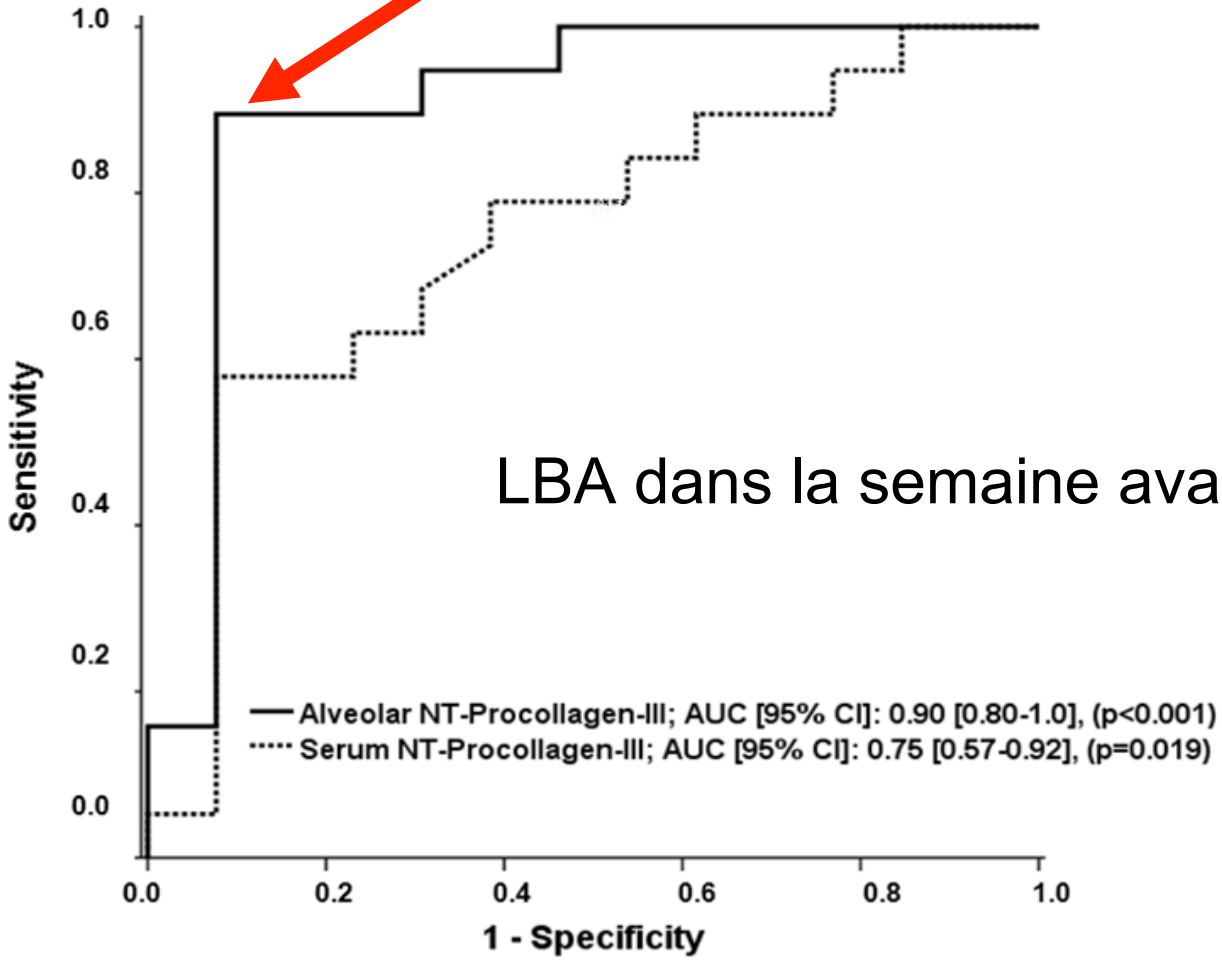
ORIGINAL

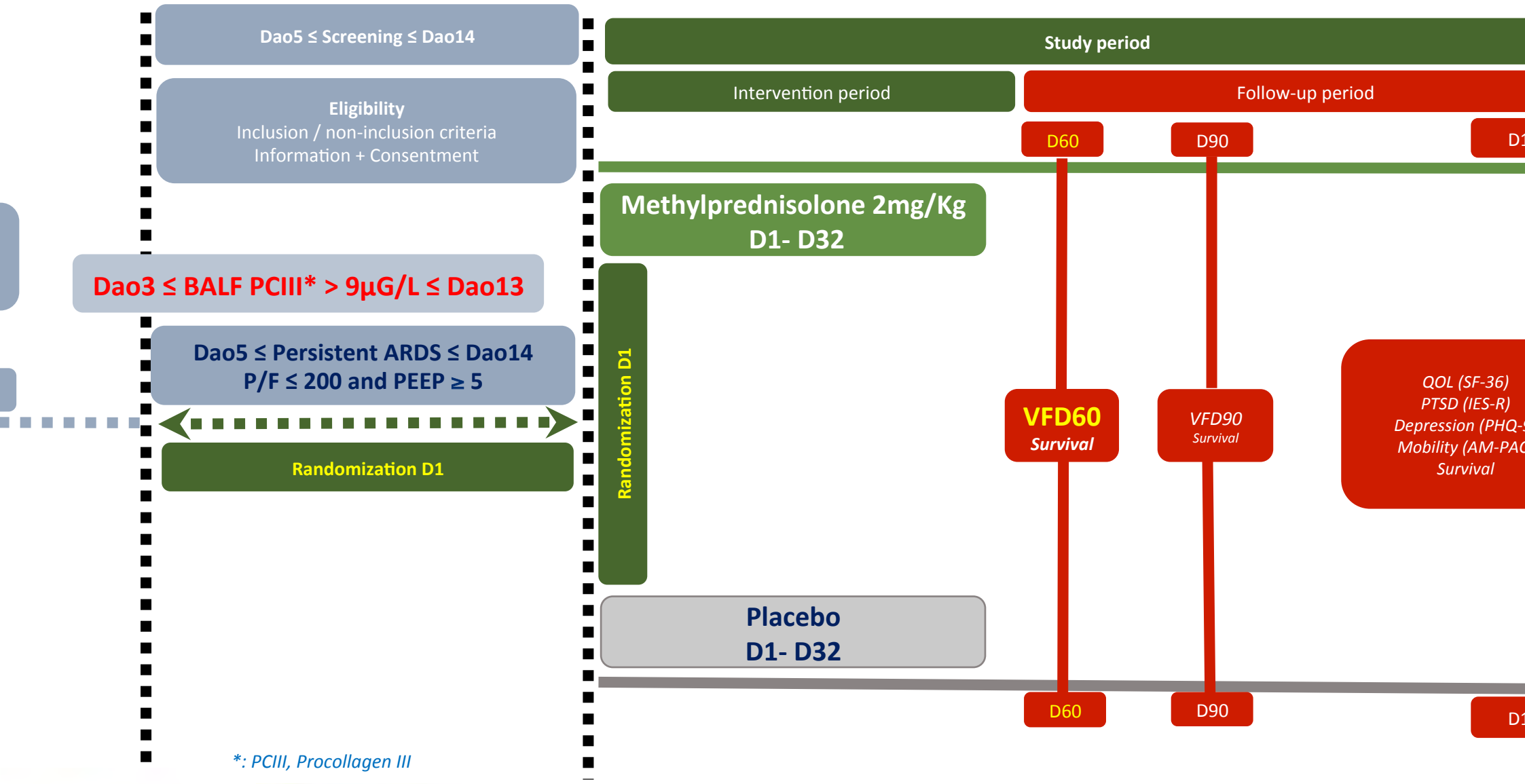
Marie Forel
phe Guervilly
Iraiech
is Voillet
nette Thomas
Somma
que Secq
ine Farnarier
Josée Payan
nie-Yannis Donati
Perrin
ne Trousse
nie Dizier
t Chiche
Baumstarck
e Roch
t Papazian

# Type III procollagen is a reliable marker of ARDS-associated lung fibroproliferation

LBA procollagène III > 9 µG
= fibroprolifération histologi




LBA dans la semaine avant la biopsie




# Design diagram of ProCoCo study

# Conclusion provisoire