



# Traitements non médicamenteux du SDRA

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# Traitements non médicamenteux du SDRA

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- Assistance ventilatoire
- Traitements non médicamenteux adjuvants à la VM
  - Manœuvres de recrutement
  - DV
  - NOi
- Gestion de l'apport liquidien
- Circulation extracorporelle

# Adjunct therapy in recent trials

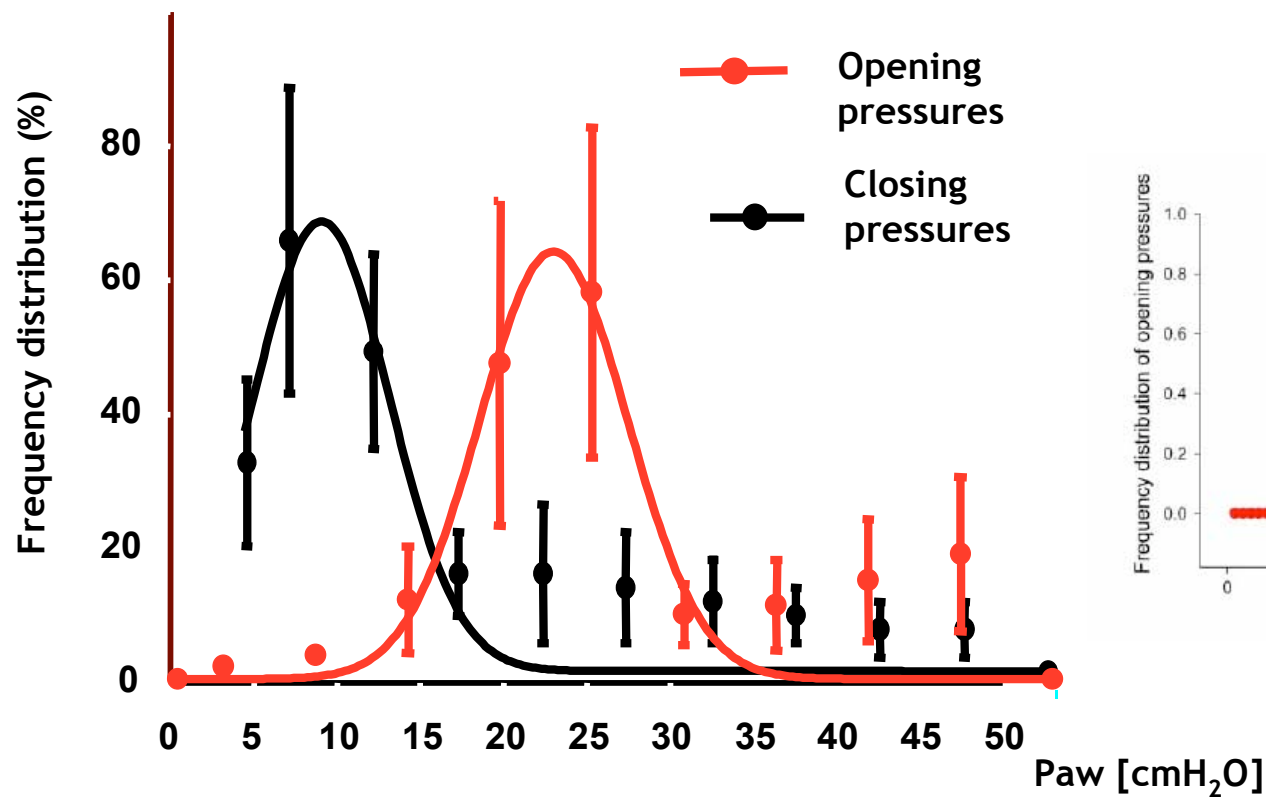
	Express study		LOVS study	
	Minimal distension	Maximal recruitment	Control	Lung Open
Prone	18.8 % N = 72	8.8 % N = 34	2.3 % N = 11	2.6 % N = 13
NO	25.7 % N = 98	14.8 % N = 57	4 %	6.9 %
HFO	0 %	0 %	2.1 %	3.4 %
ECMO	0 %	0 %	0.8 %	1.4 %



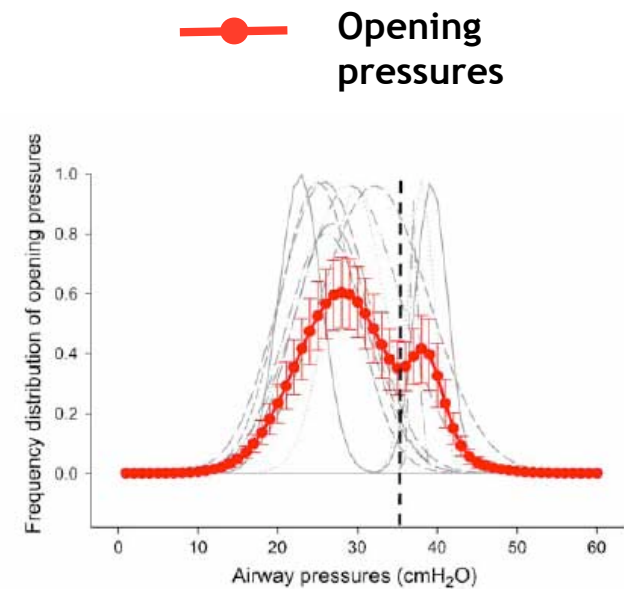
# Manœuvres de recrutement

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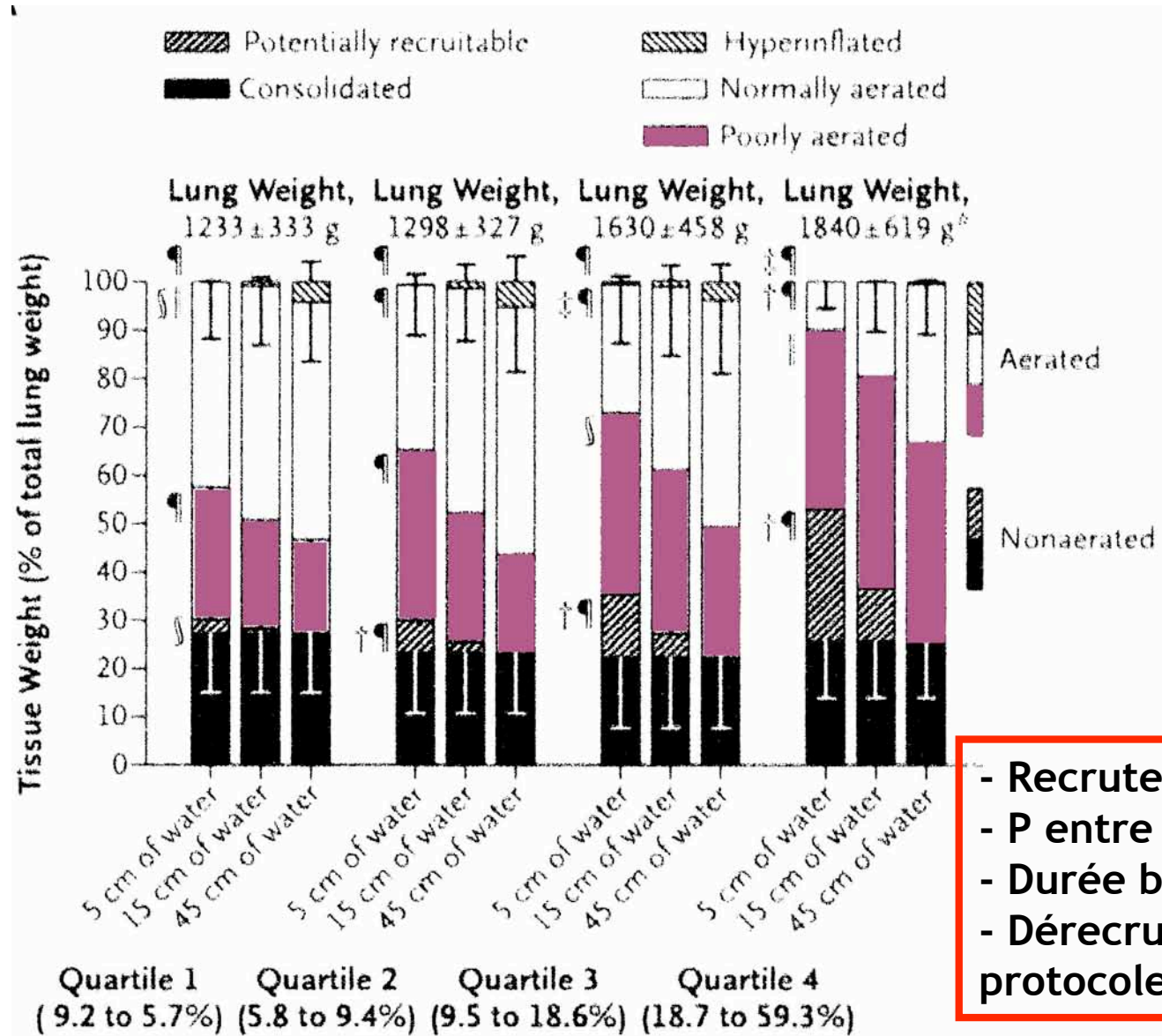
# Basic background to recruit



*Crotti AJRCCM 2001, Pelosi AJRCCM 2001*



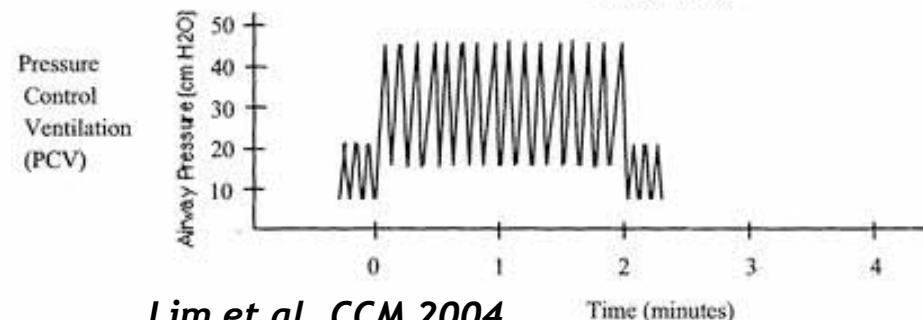
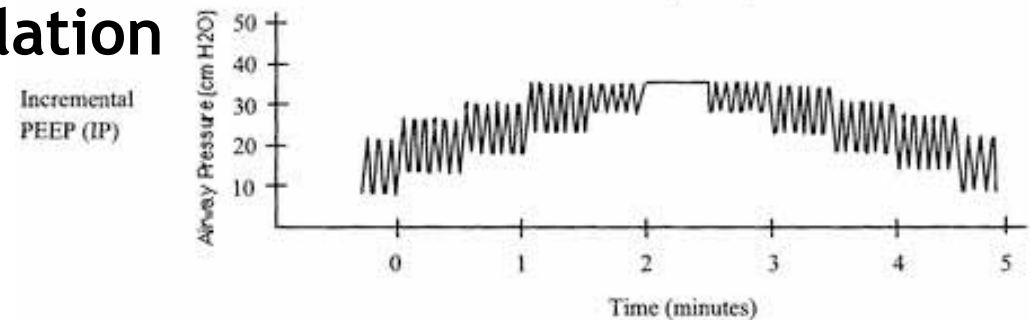
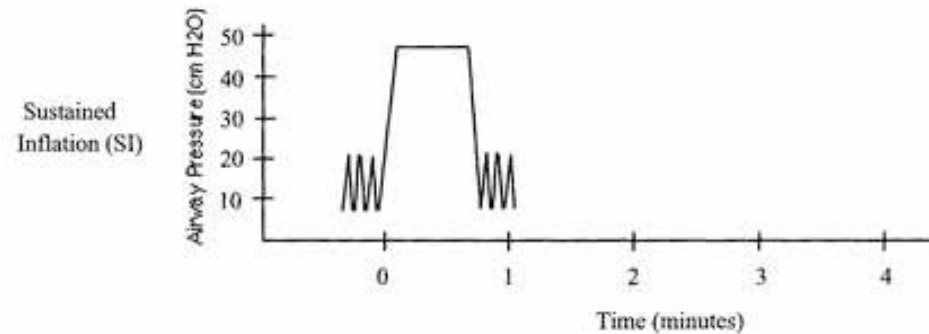
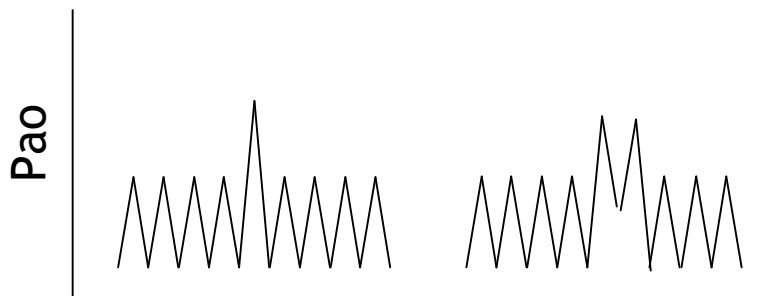
*Borges AJRCCM 2006*



- Recrutement moyen = 9%
- P entre 5 et 45 cm H<sub>2</sub>O
- Durée brève application PEP
- Dérecrutement induit par protocole

# How to recruit the lungs ?

- Sustained inflation
- High PEEP
- Sigh
- Extended-Sigh (eSigh)
- Pressure controlled ventilation



Lim et al. CCM 2004

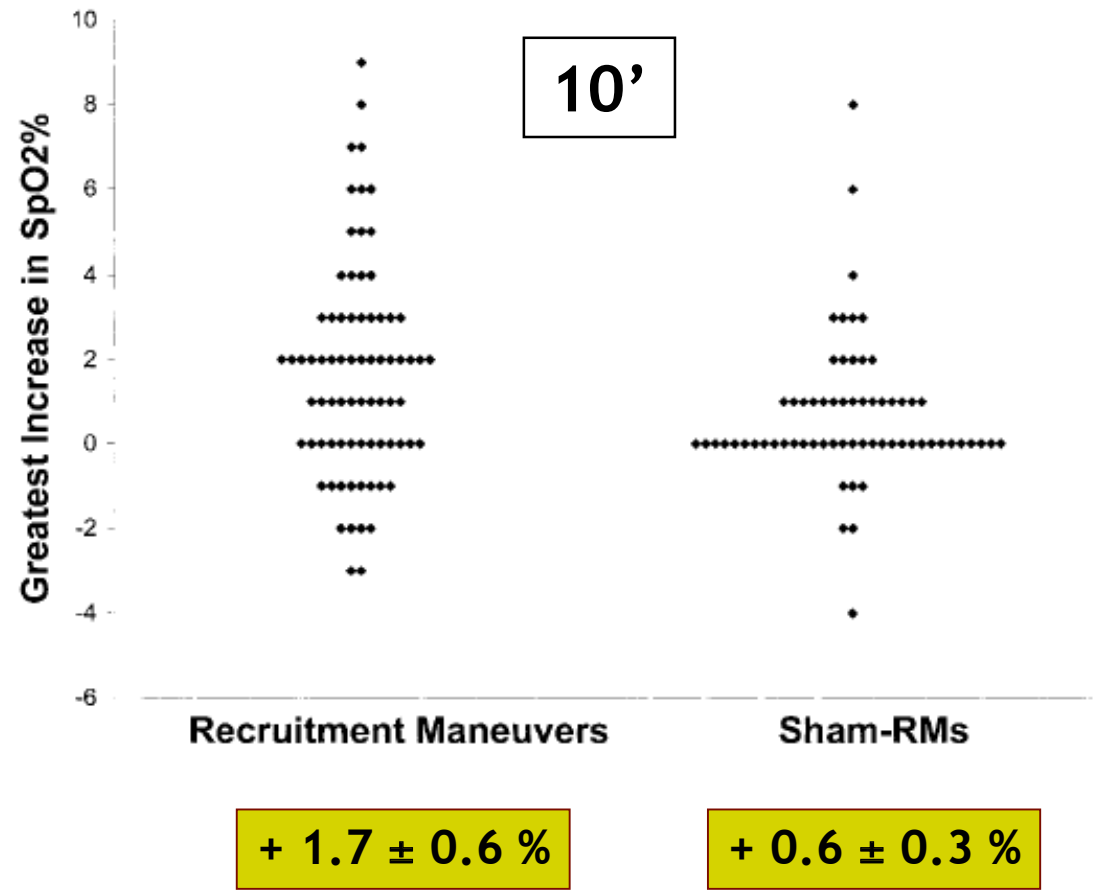
Time (minutes)



# The response to RM is VARIABLE between-patients

PEEP =  $13.8 \pm 3$  cm H<sub>2</sub>O

S.I. = 35-40 cm H<sub>2</sub>O x 30 sec



ARDSnet CCM 2003

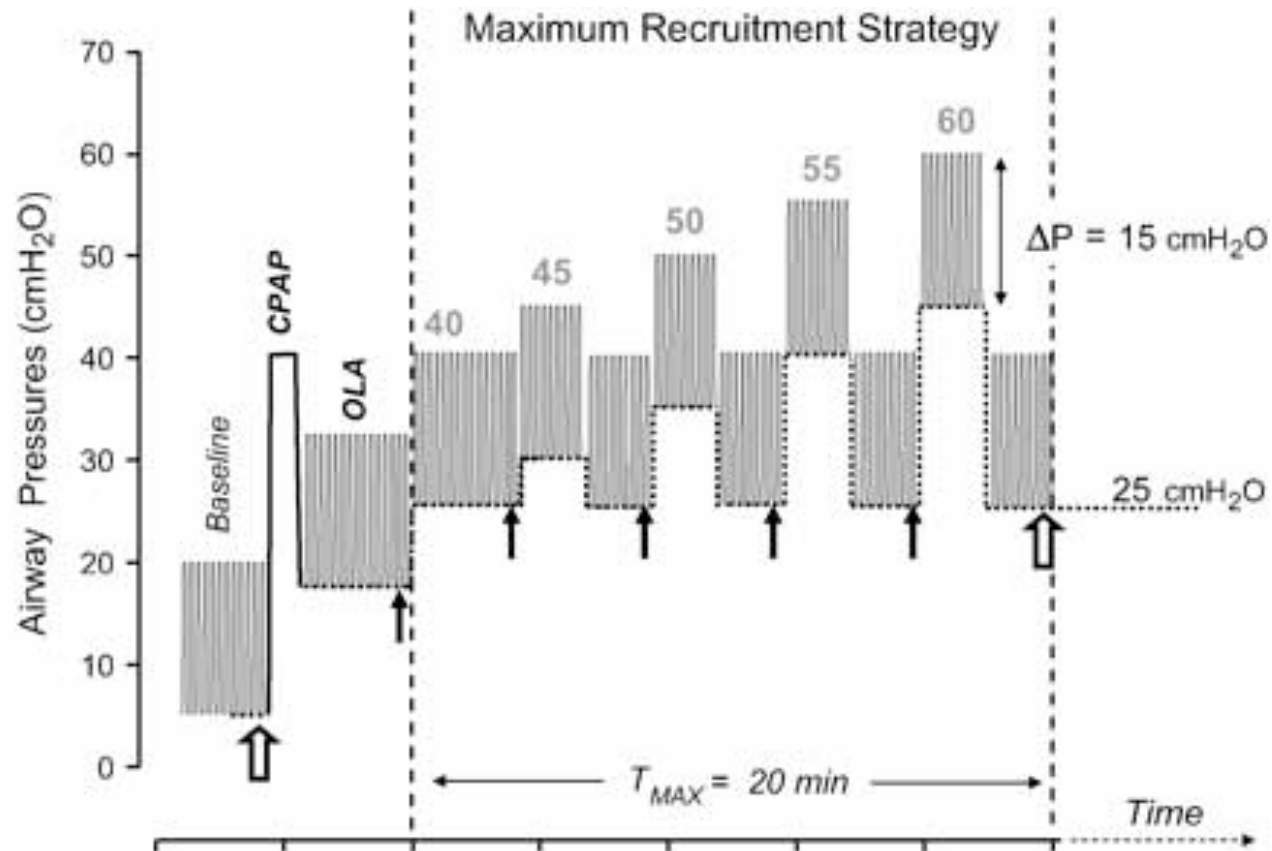


# Determinants of the response

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- Definition of the response
- Patient-related factors
  - Lung morphology
  - Chest wall
- RM-related factors
  - Lung recruitment level/status BEFORE RM
  - Targeted Pressure
  - Time Allowed for the RM
  - Strategy POST-RM

# Full recruitment strategy



Borges AJRCCM 2006

- ↑ Complete multislice CT
- ↑ Semi-complete multislice CT



# Revue systématique

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*Conclusions:* Adult patients with ALI receiving RMs experienced a significant increase in oxygenation, with few serious adverse events. Transient hypotension and desaturation during RMs is common but is self-limited without serious short-term sequelae. Given the uncertain benefit of transient oxygenation improvements in patients with ALI and the lack of information on their influence on clinical outcomes, the routine use of RMs cannot be recommended or discouraged at this time. RMs should be considered for use on an individualized basis in patients with ALI who have life-threatening hypoxemia.

*Fan AJRCCM 2008*



# Décubitus ventral

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# Impacts recherchés du D.V.

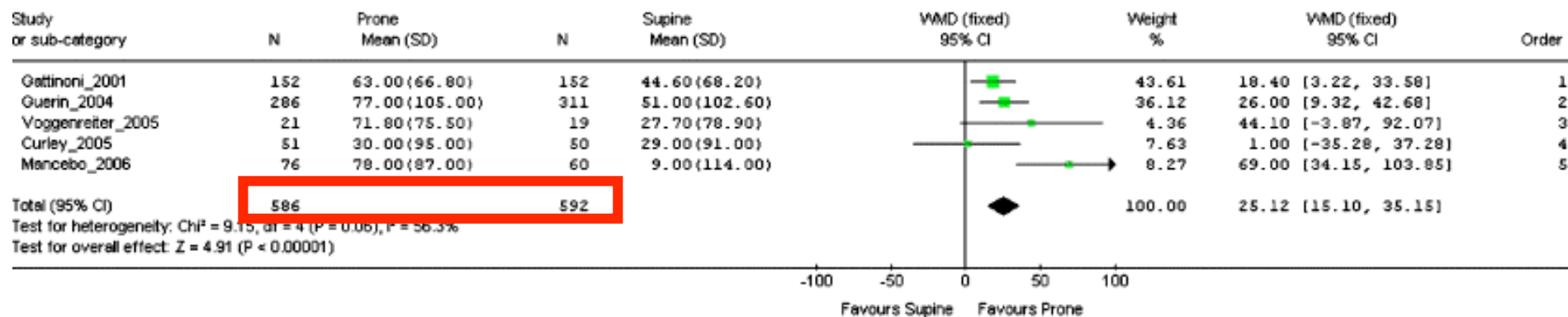
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↑ Oxygenation

# Oxygenation

↑ PaO<sub>2</sub>/FIO<sub>2</sub> 25%

Review: Prone vs Supine position in ARDS  
 Comparison: 01 Prone vs Supine Ventilation  
 Outcome: 03 PaO<sub>2</sub>/FIO<sub>2</sub> change



Abroug ICM 2008



# Impacts recherchés du D.V.

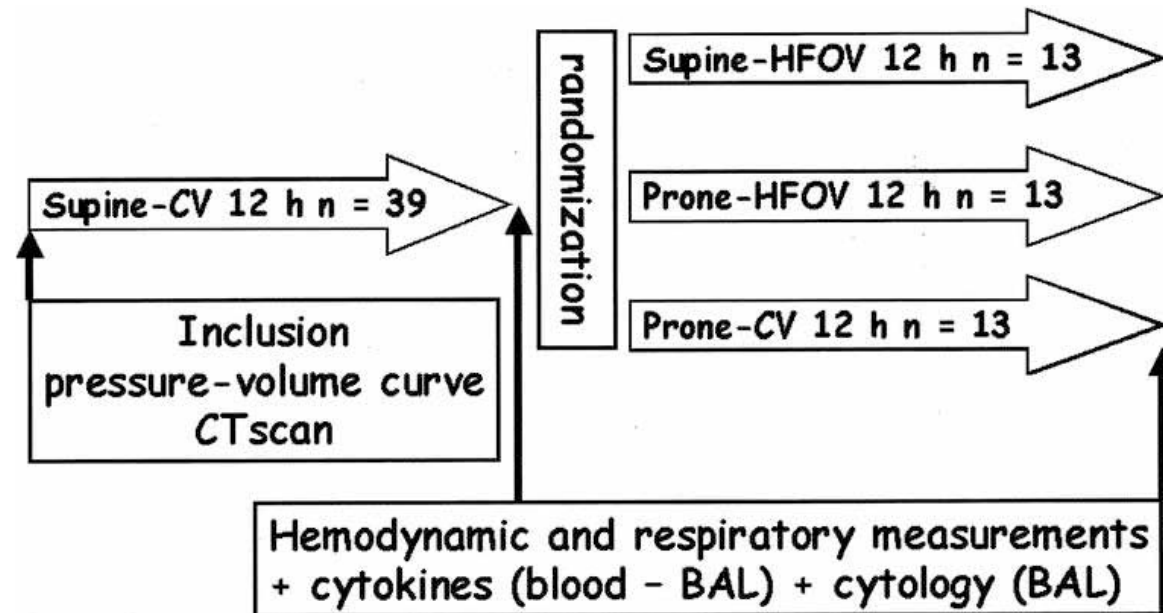
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↑ **Oxygenation**

**Oui**

↓ **VILI**

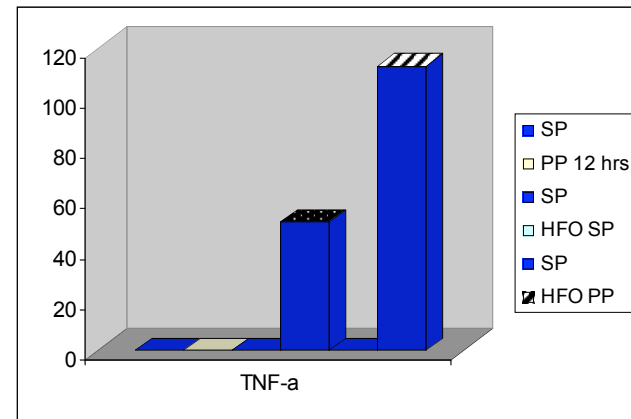
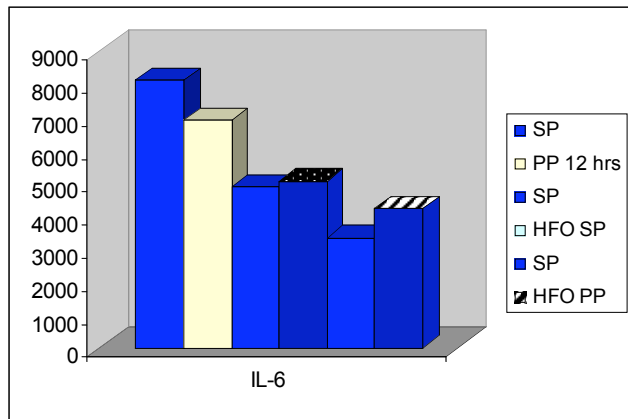
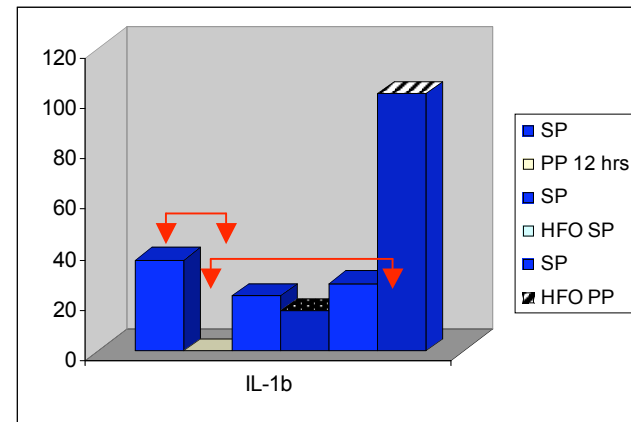
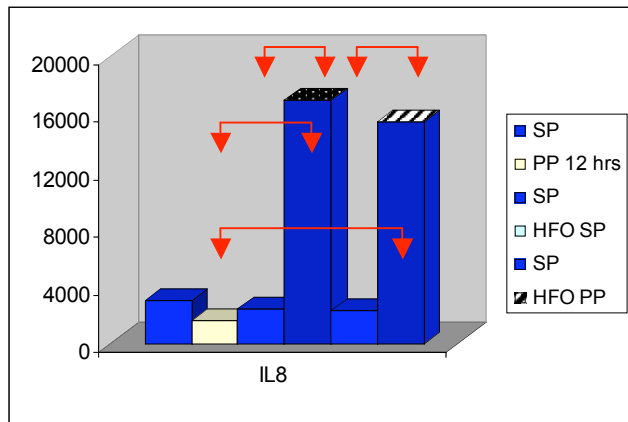
# Réduction du VILI



	Baseline Supine-CV <i>n</i> = 39
Tidal volume, mL · kg <sup>-1</sup>	6.4 ± 0.7
Respiratory rate, cycles · min <sup>-1</sup>	26 ± 6
Plateau pressure, cm H <sub>2</sub> O	25 ± 6
Mean airway pressure, cm H <sub>2</sub> O	19 ± 4 <sup>a</sup>
Applied PEEP, cm H <sub>2</sub> O	12 ± 4
Auto-PEEP, cm H <sub>2</sub> O	0.9 ± 1.3
Pressure amplitude of oscillation, cm H <sub>2</sub> O	NA
Paco <sub>2</sub> , mm Hg	50 ± 11

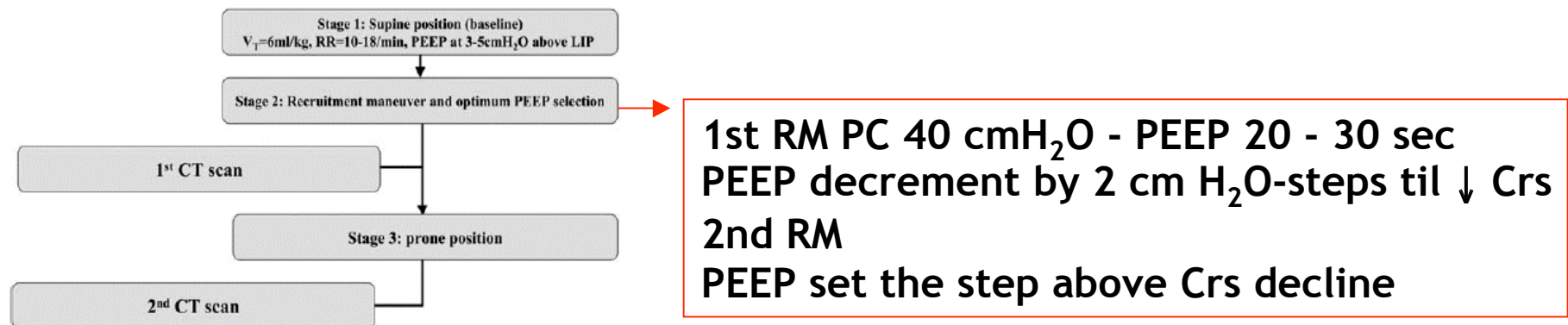
Papazian et al. CCM 2005

# BAL cytokines (pg/ml)



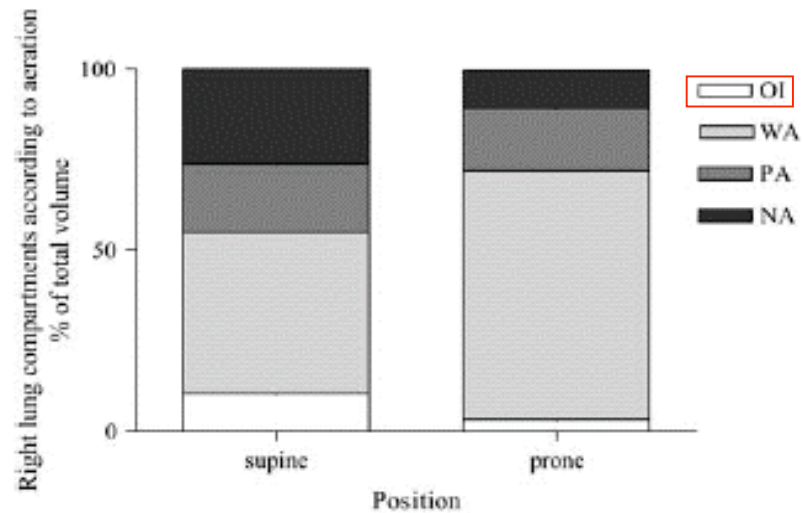
# Alveolar recruitment and reduction of hyperinflation

Age, yr	43.15 ± 12.26*
Sex	7 F/14 M
Cause of admission	
Trauma	11
Stroke	7
Sepsis	3
ARDS lobar/diffuse	15/6
Duration of ICU stay, d	13.40 ± 8.03*
Duration of mechanical ventilation, d	11.27 ± 7.64*

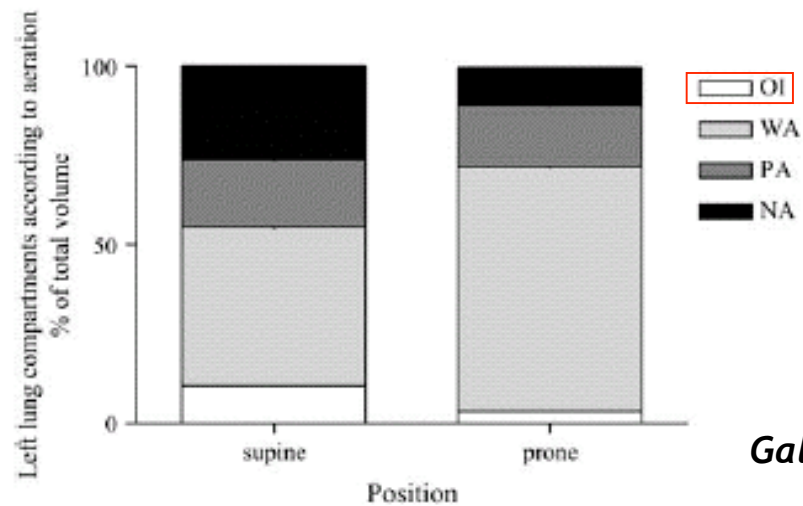


# Alveolar recruitment and reduction of hyperinflation

Right Lung

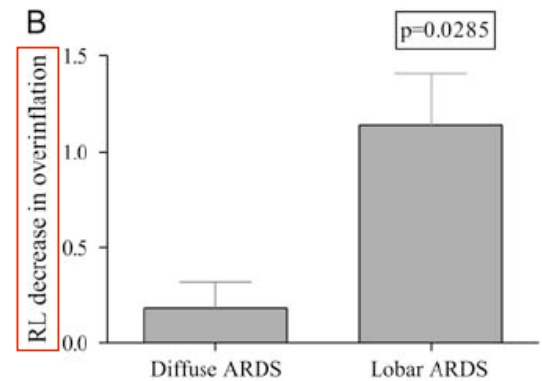
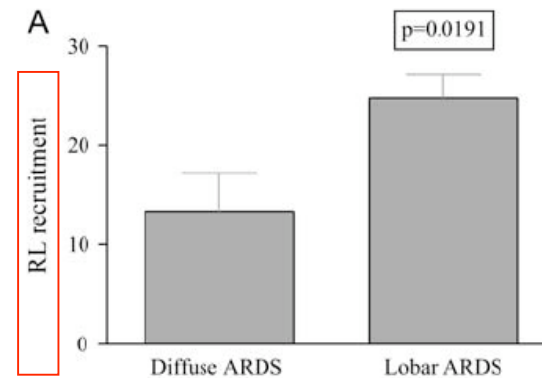
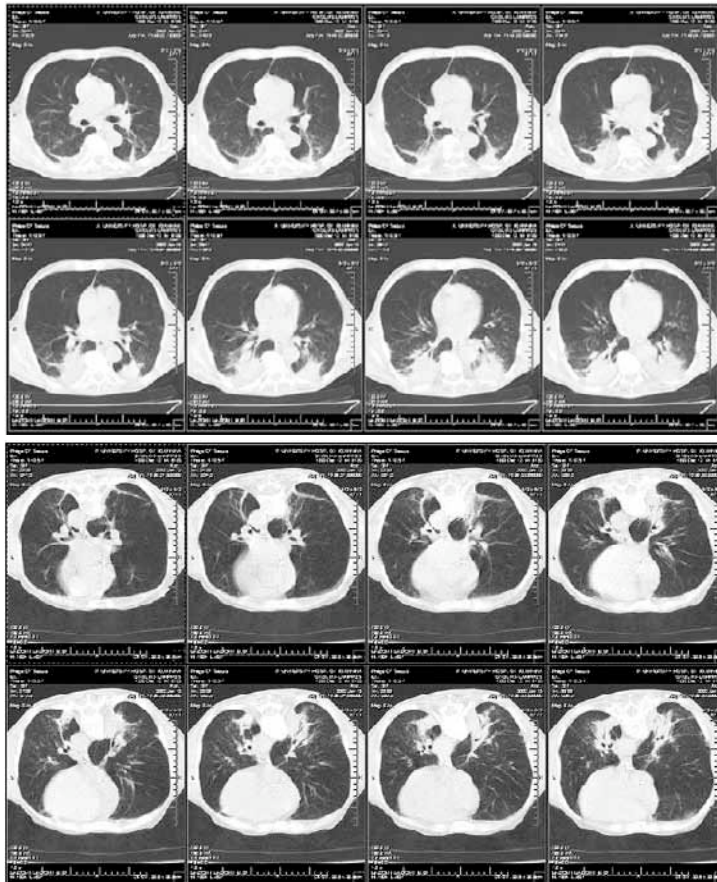


Left Lung



# Alveolar recruitment and reduction of hyperinflation

## Alveolar recruitment



## Decrease in hyperinflation

# Préserver le V.D.

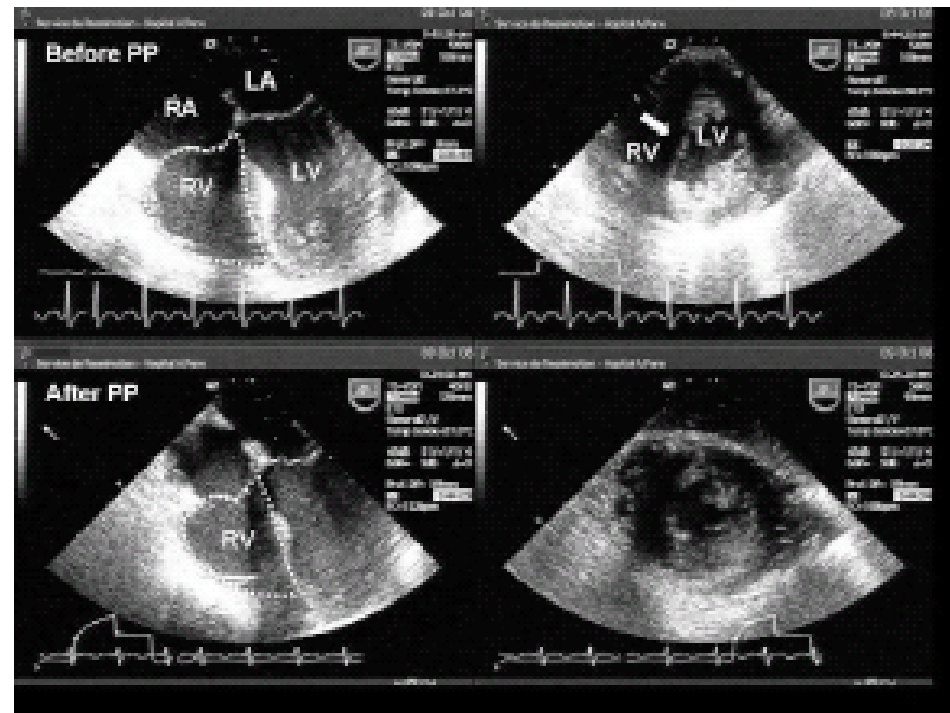


FIGURE 1. An illustrative example of echocardiographic changes observed before PE (top) and after 18 h of PE (bottom). The RV at ED (underlined by a broken contour) was observed in the long axis, whereas the LV at ES was observed in the short axis. The arrow shows septal dyskinesia. LA = left atrium; RA = right atrium.

Viellard-Baron  
Chest 2005

# Impacts attendus du D.V.

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↑ **Oxygenation**

**Oui**

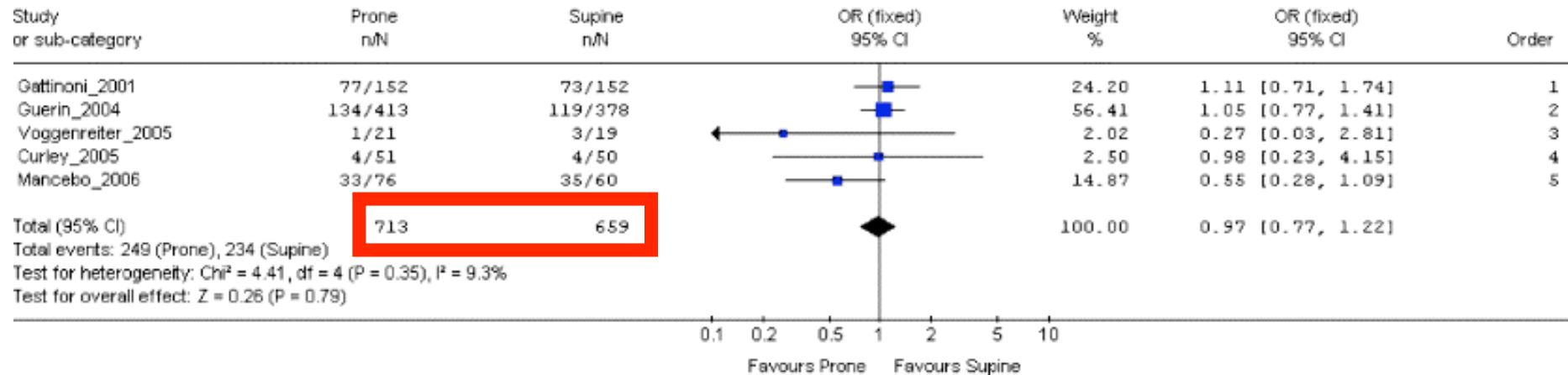
↓ **VILI**

**Oui**

↓ **Mortality**

# ICU mortality

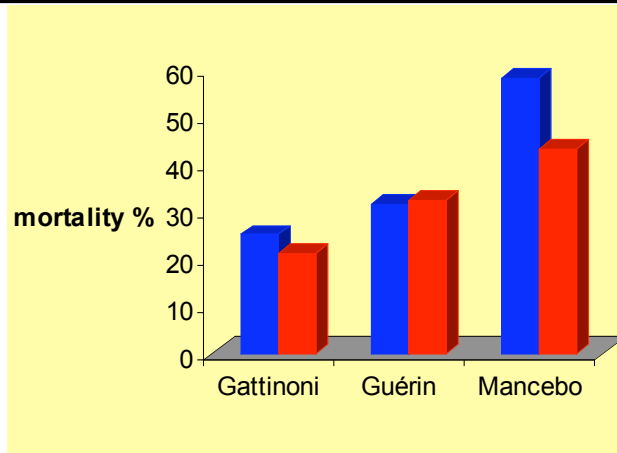
Review: Prone vs Supine position in ARDS  
 Comparison: 01 Prone vs Supine Ventilation  
 Outcome: 01 ICU Mortality ←



Abroug ICM 2008



	NEJM 2001	JAMA 2004	AJRCCM 2006
Population	ALI	Hypoxemic ARF	ARDS
SP/PP n	152 / 152	378 / 413	60 / 76
Hours PP/day	7	8	17
Weaknesses	Lack of power	Heterogenous case mix	Lack of power
<b>Lung protection</b>	<b>no</b>	<b>no</b>	<b>no</b>



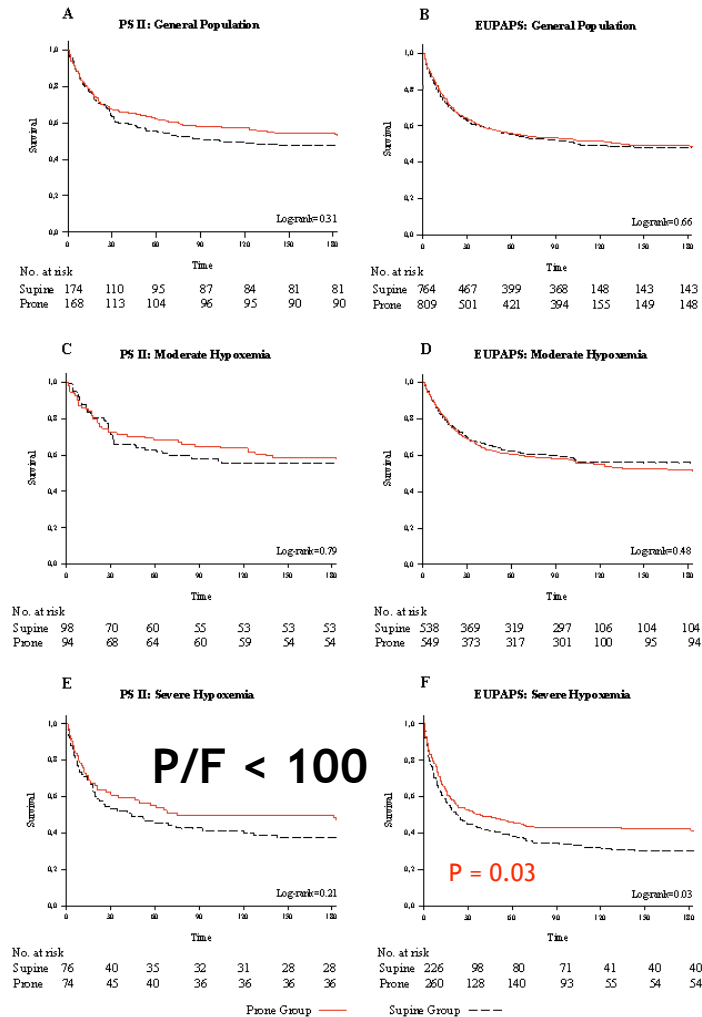
**ETUDES COMPLEMENTAIRES  
NECESSAIRES**

	Supine (n = 19)	Prone (n = 21)	p-value
60-day mortality	10 (53%)	8 (38%)	0.3
ICU length of stay (days)	17.5 ± 16.1	14.7 ± 9.7	0.5
Survivors	11.3 ± 7.6	15.9 ± 11.1	0.3
Nonsurvivors	23.0 ± 19.9	12.6 ± 7.2	0.2
Mechanical ventilation length (days)	15.7 ± 16.9	11.9 ± 9.2	0.5
Survivors	7.6 ± 7.6	12.0 ± 10.6	0.3
Nonsurvivors	23.0 ± 19.9	11.9 ± 6.9	0.2
Hospital stay (days)	25.5 ± 17.4	31.3 ± 26.4	0.4
Pneumothorax	1 (5%)	0 (0%)	0.5
Unplanned extubation	1 (5%)	1 (5%)	1.0
Ventilator associated pneumonia	1 (5%)	3 (14%)	0.6

*Fernandez ICM 2008*

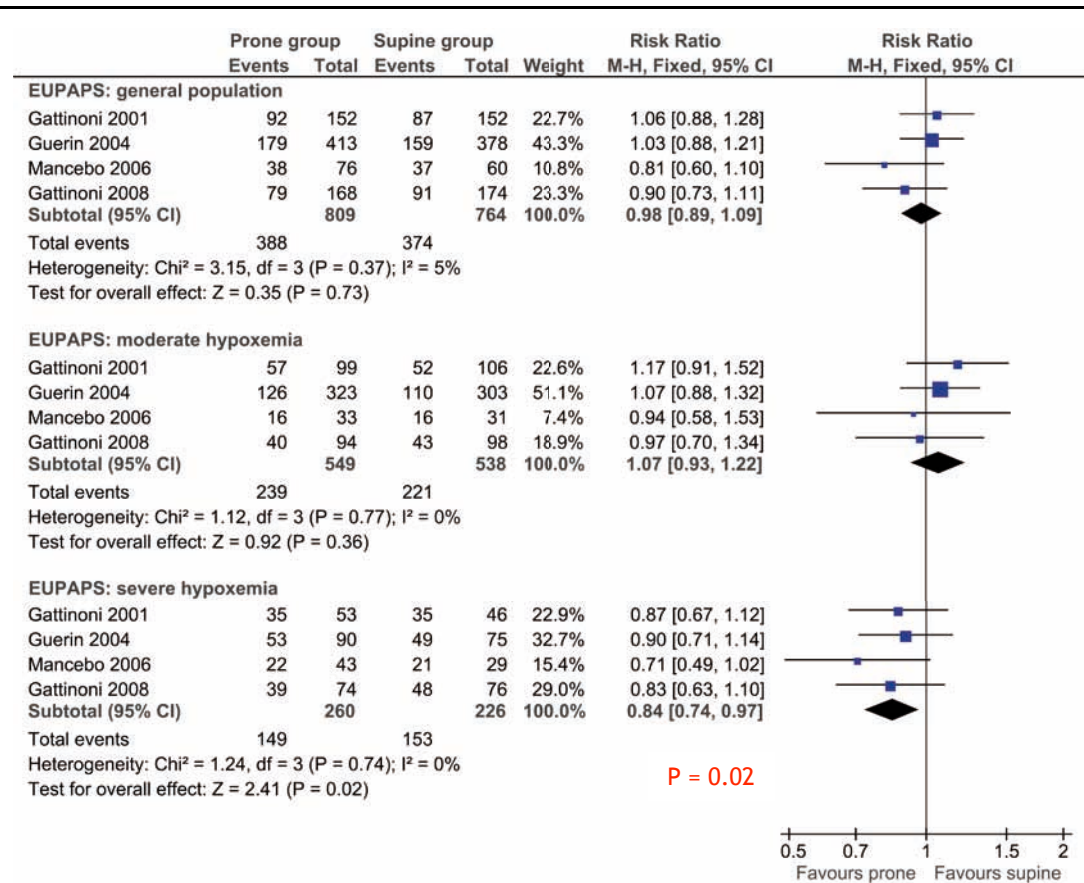
## PS II

## Méta-analyse



**P/F < 100**

**P = 0.03**

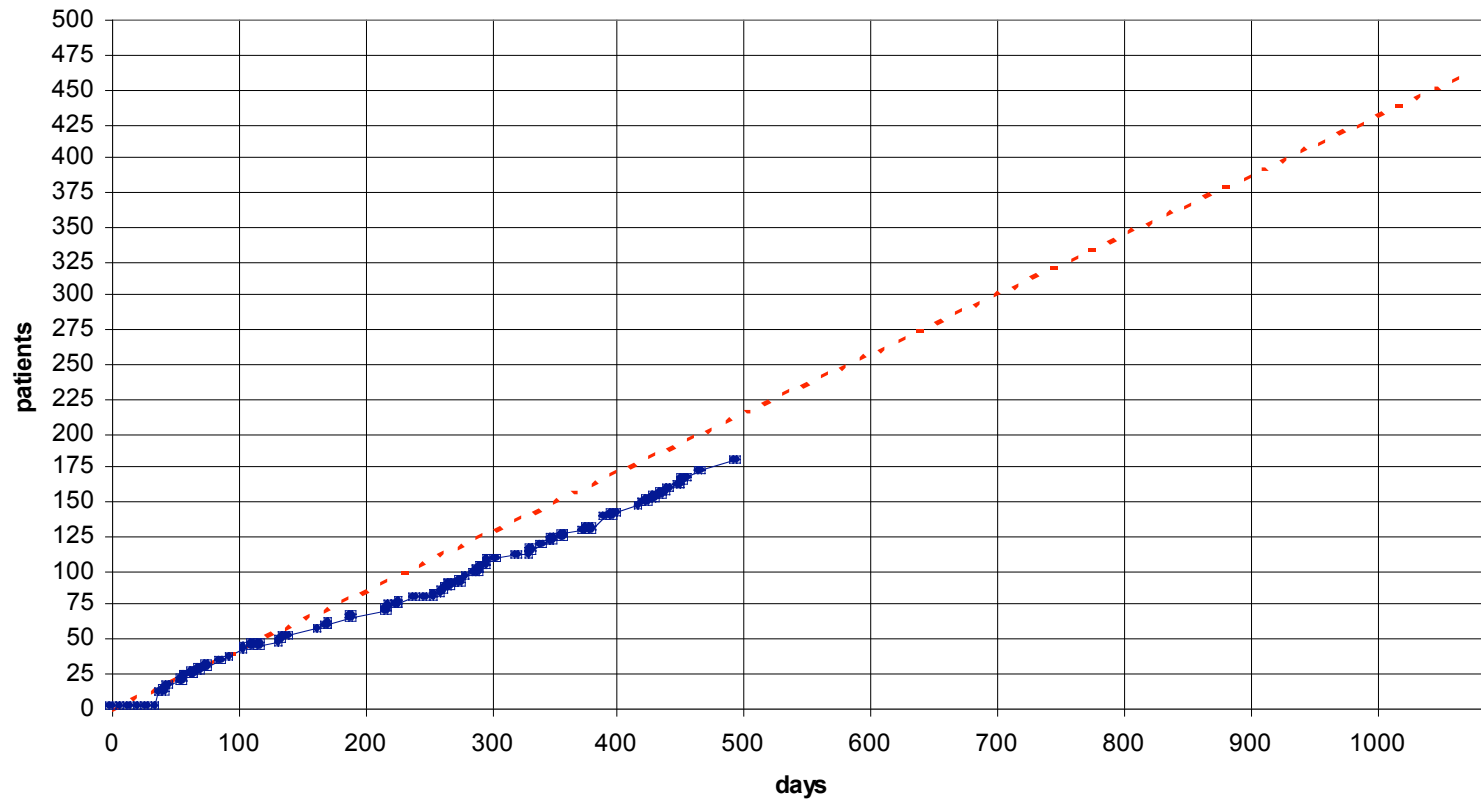


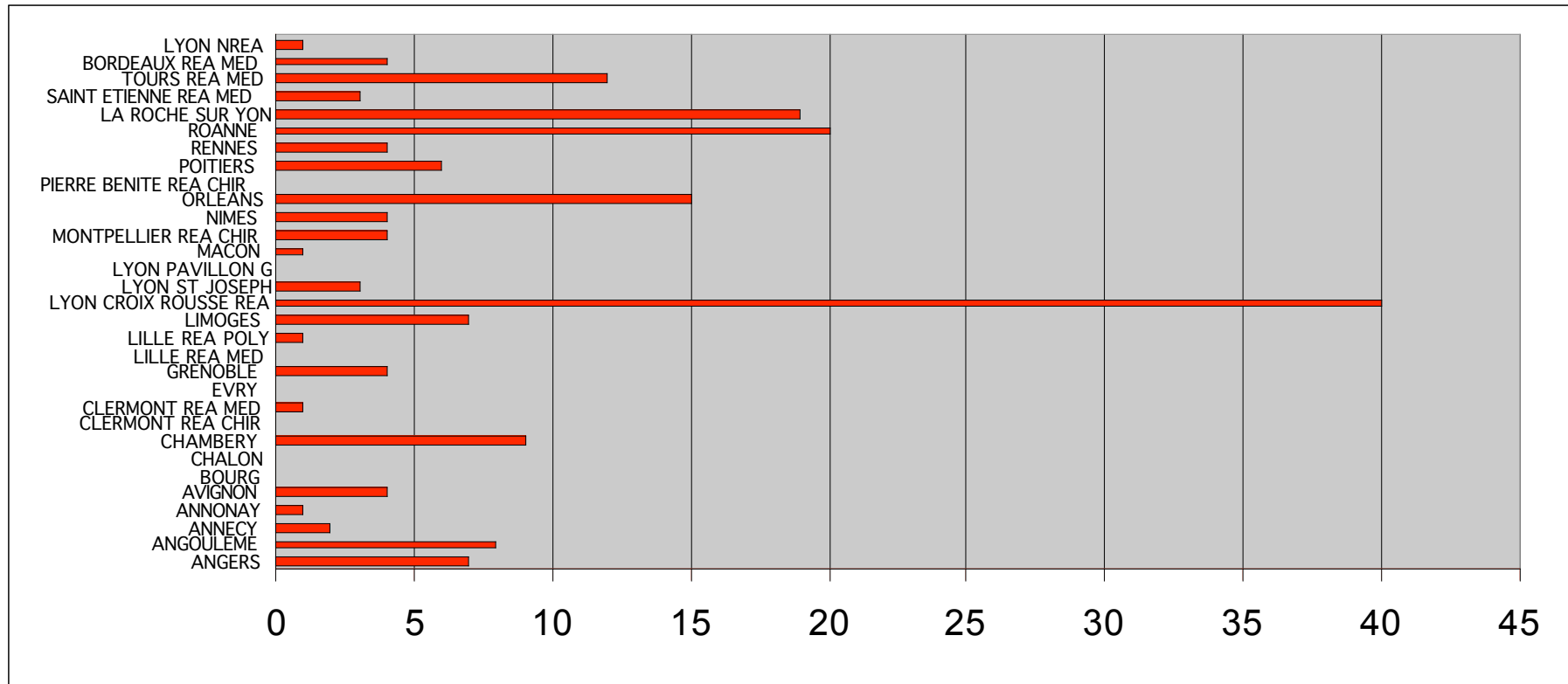
# PROSEVA trial

- Multicenter RCT in France
- Severe and persistent ARDS
  - Mechanical ventilation for < 36 hours for ARDS
  - Persistent after 12-24 hrs
  - Severe
    - $\text{PaO}_2/\text{F}_i\text{O}_2 < 150$
    - $\text{PEEP} \geq 5 \text{ cm H}_2\text{O}$
    - $\text{F}_i\text{O}_2 \geq 60\%$
    - $\text{VT} 6 \text{ ml/kg PBW}$
- Two arms
  - Prone position for  $\geq 16 \text{ hrs/day}$
  - vs. Supine position
- Mortality at D 28

# PHRC national 2006

- Ongoing since January 1<sup>st</sup> 2008
- 180 Patients included to date





# Impacts attendus du D.V.

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↑ **Oxygenation**

**Oui**

↓ **VILI**

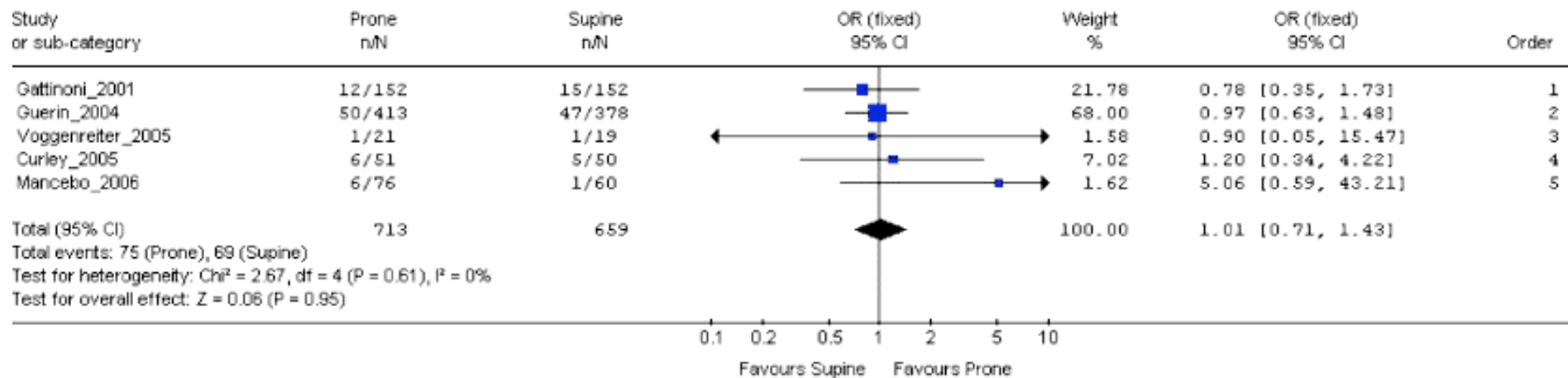
**Oui**

↓ **Mortality**

**Non**

# Safety Concern

Review: Prone vs Supine position in ARDS  
 Comparison: 01 Prone vs Supine Ventilation  
 Outcome: 04 Major respiratory complications



Abroug ICM 2008

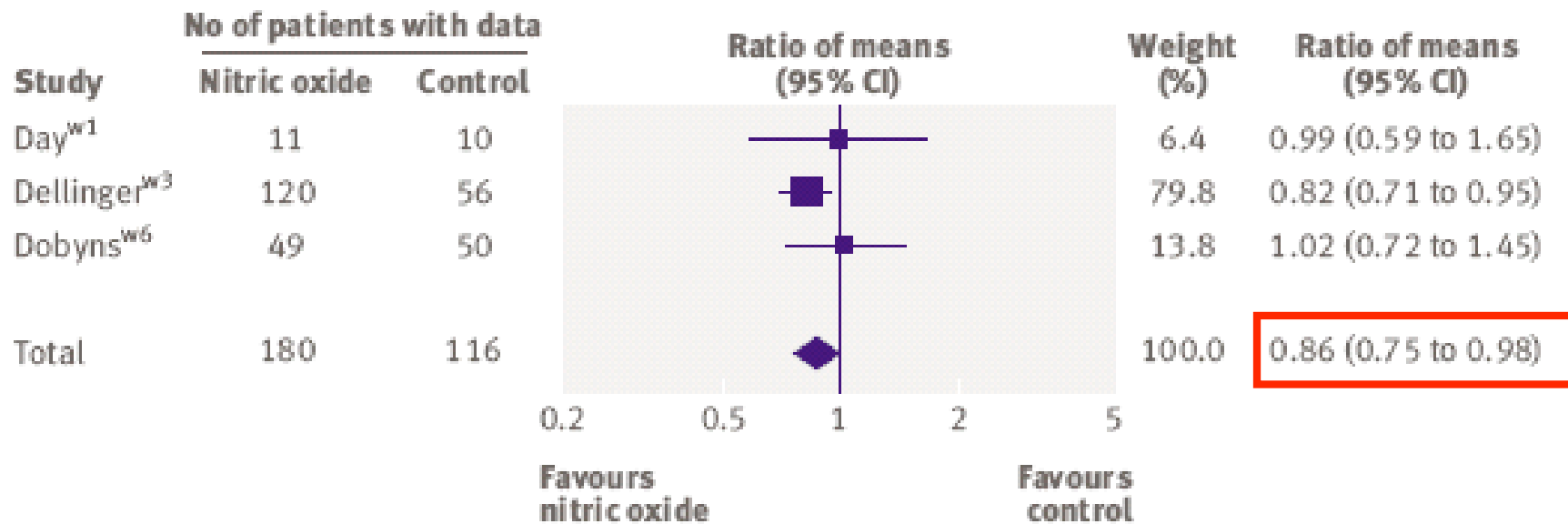


# NOi

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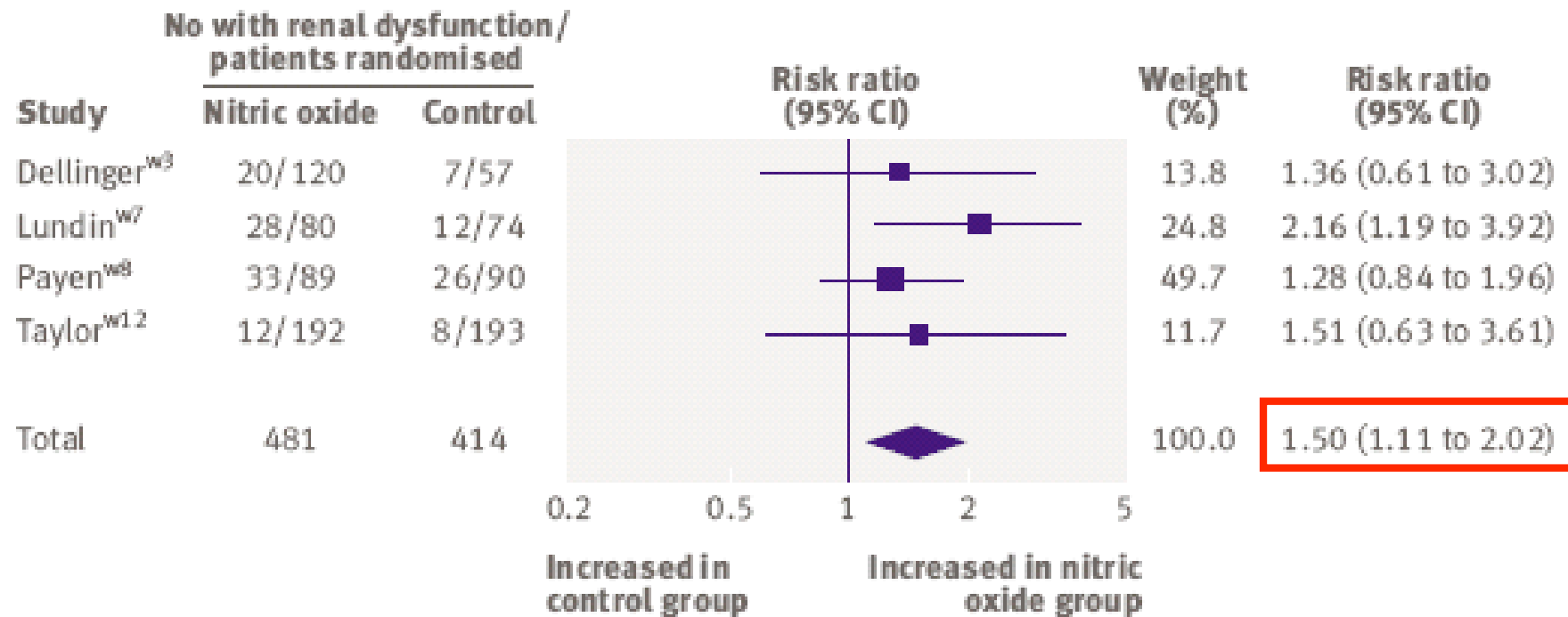
# NOi

## oxygénation



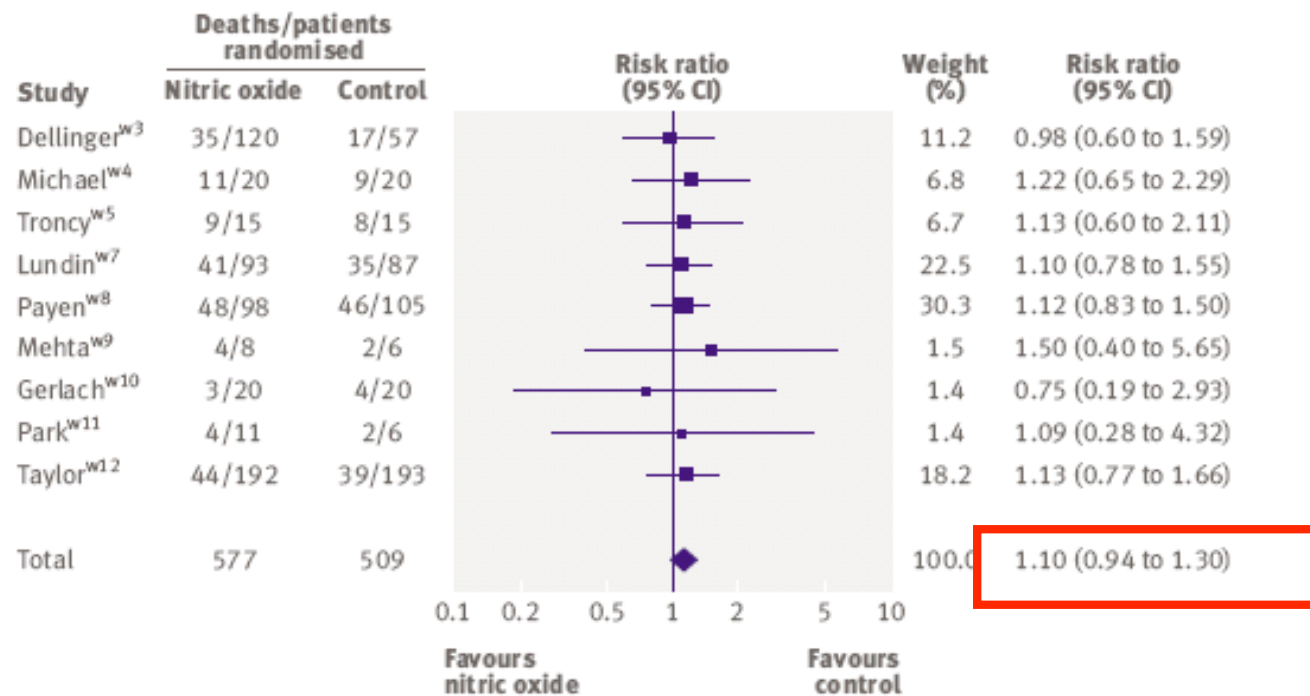
# NOi

## AKI



# NOi

## Mortalité





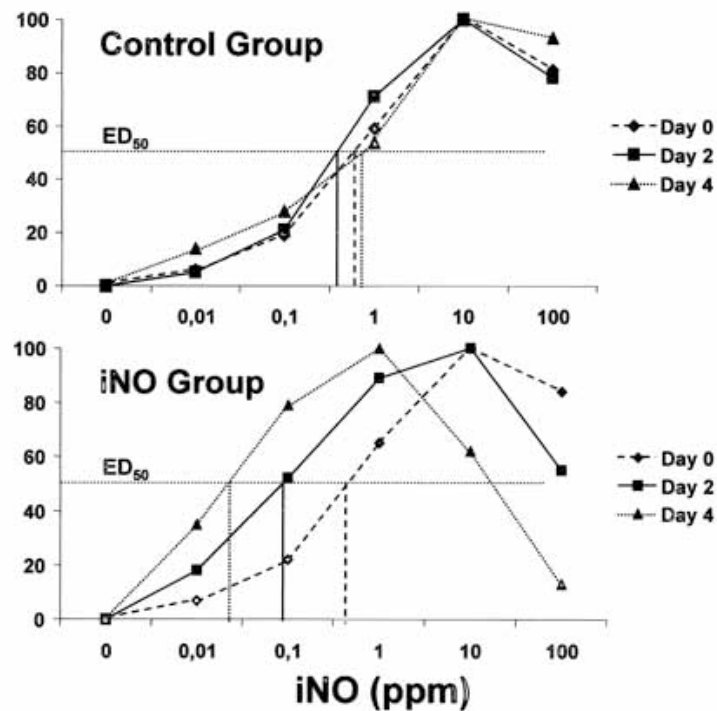
# NOi

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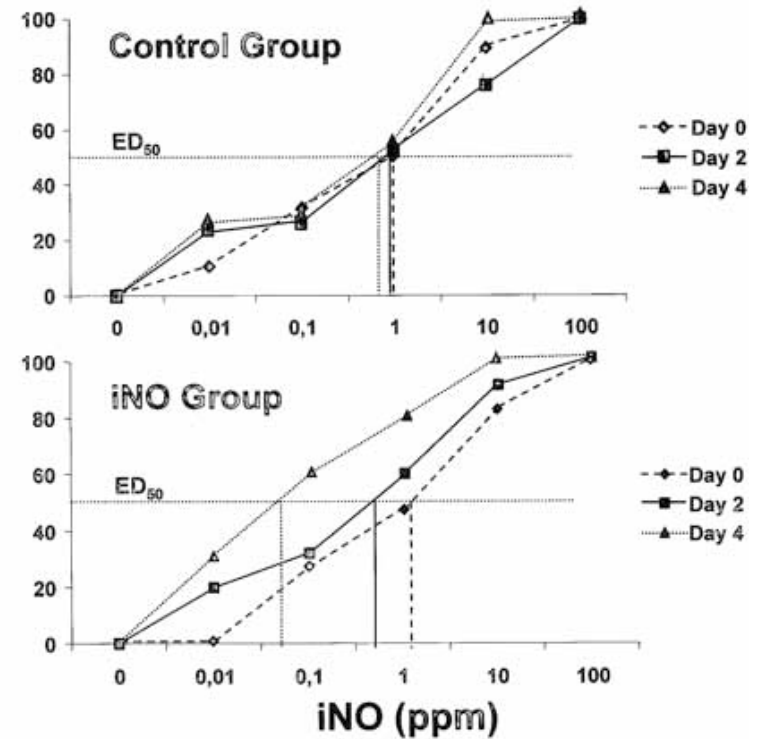
- Hypoxémie
- CPA
- FOP
- 0,5 - 5 ppm (2 ppm en moyenne)
- Ré-évaluation de la dose
- Sevrage progressif plutôt que brutal

# NOi : Ré-évaluation de la dose

Effect (%) on PaO<sub>2</sub>/FIO<sub>2</sub>



Effect (%) on MPAP





# Gestion de l'apport liquidien

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## Albumine + diurétiques vs placebo Martin et al. CCM 2002

RCT double aveugle  
ALI, protidémie  $\leq 50\text{g/l}$ , VM  $> 48\text{h}$

Contrôle (n=18)

NaCl 0.9%  
isovolume

Groupe traité (n=19)

- Furosémide QSP  
perte poids = 1 kg
- Albumine 25 g/8 h si  
protidémie  $< 60\text{ g/l}$
- 5 jours

## Albumine + diurétiques vs placebo + diurétiques Martin et al. CCM 2005

RCT double aveugle  
ALI, protidémie  $\leq 60\text{g/l}$ , VM  $> 24\text{h}$

Contrôle (n=20)

- Furosémide : QSP  
perte poids = 1 kg
- Placebo : NaCl  
0.9% isovolume

Groupe traité (n=20)

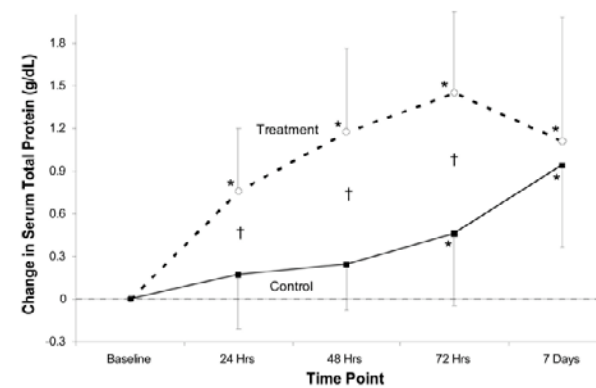
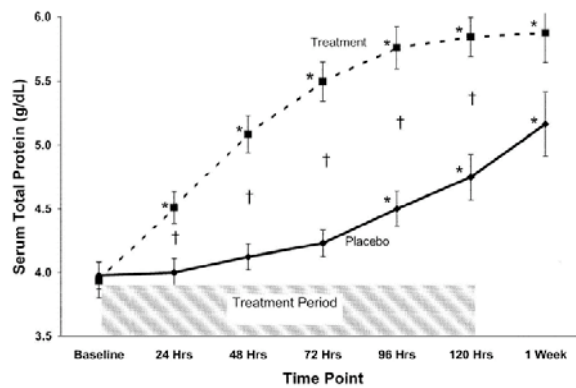
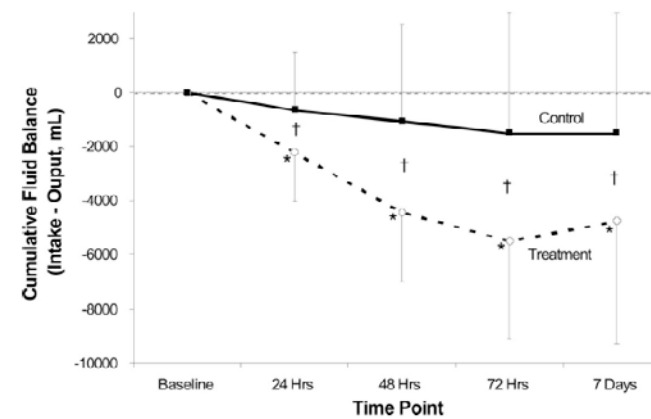
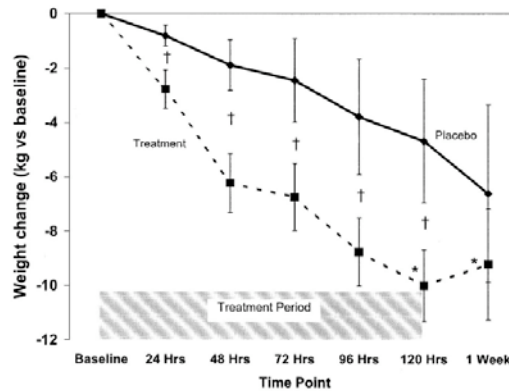
- Furosémide : QSP perte  
poids = 1 kg
- Albumine : 25 g/8h si  
protidémie  $< 80\text{ g/l}$

### Exclusion

- Instabilité hémodynamique
- Défaillance rénale
- Défaillance hépatique
- $\text{K}^+ < 2,5$  ou  $\text{Na}^+ > 150\text{ mmol/l}$

## Albumine + diurétiques vs placebo Martin et al. CCM 2002

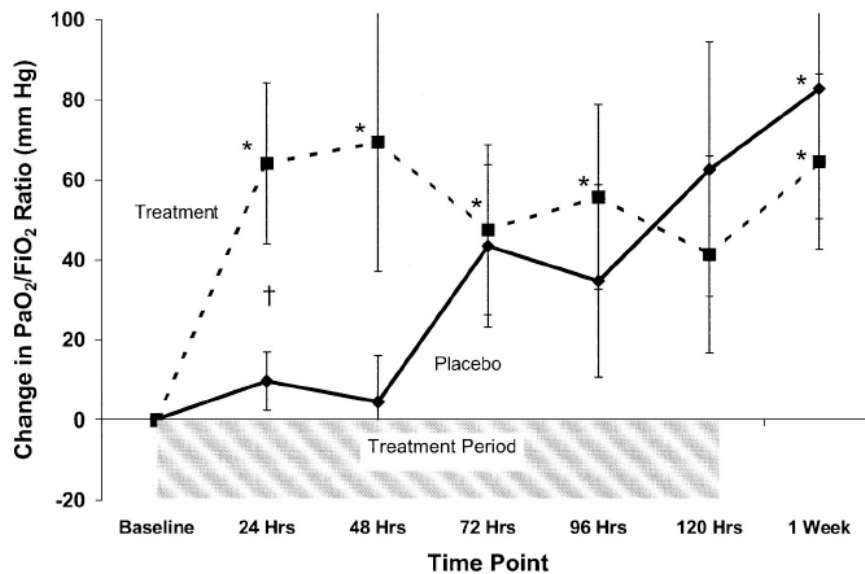
## Albumine + diurétiques vs placebo + diurétiques Martin et al. CCM 2005



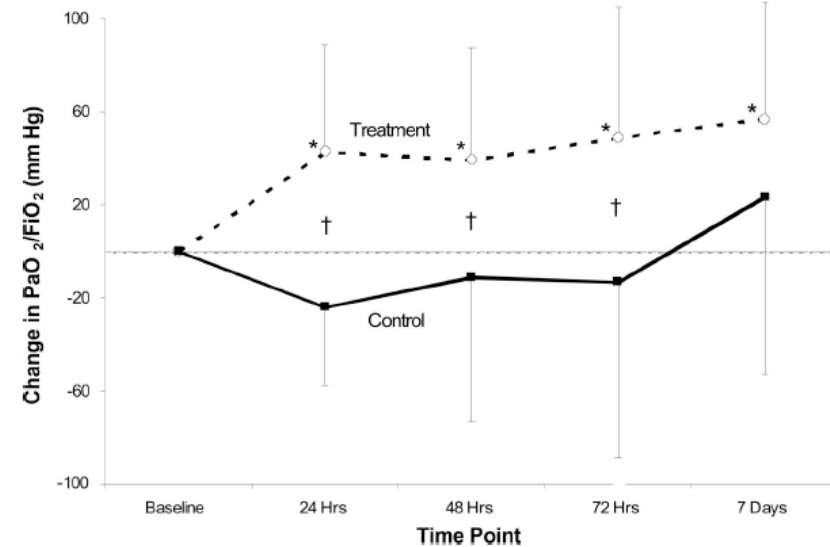
†  $p < 0,05$  placebo vs. traitement (albumine+furosémide)

\*  $P < 0,05$  vs baseline

## Albumine + diurétiques vs placebo Martin et al. CCM 2002



## Albumine + diurétiques vs placebo + diurétiques Martin et al. CCM 2005



- ❑ Jours vivants sans VM : NS
- ❑ Durée de séjour hospitalière : NS
- ❑ Mortalité à 30 jours : NS (16 vs 17%) (35 vs 45%)

†  $p < 0,05$  placebo vs. traitement (albumine+furosémide)  
\*  $P < 0,05$  vs base



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# Comparison of Two Fluid-Management Strategies in Acute Lung Injury

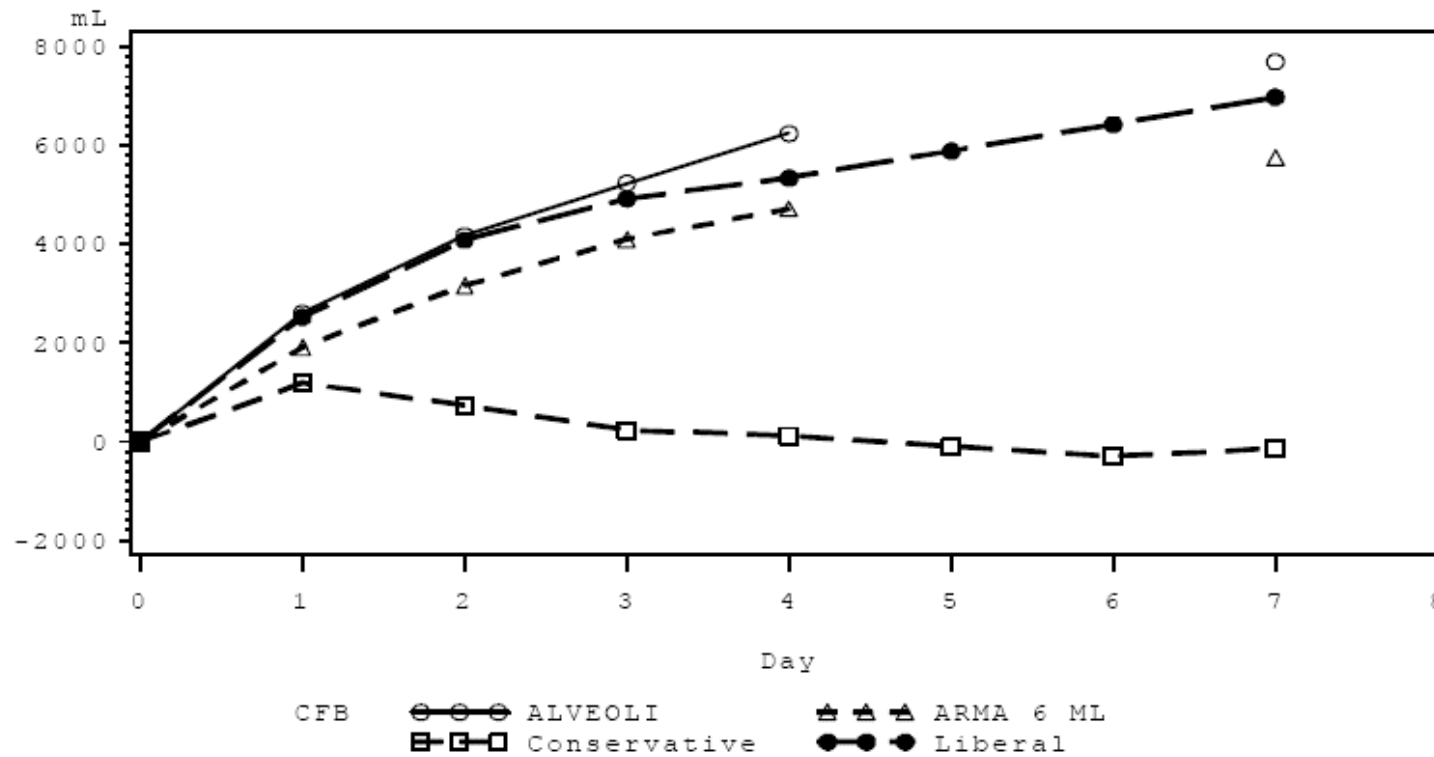
The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network\*

N Engl J Med 2006;354:2564-75

# Gestion du bilan hydrique guidé par la mesure des pressions de remplissage au cours de l'ALI

Measured intravascular pressure (mm Hg)				MAP <60 mm Hg or a need for any vasopressor (except dopamine $\leq 5 \mu\text{g/kg/min}$ ); consider correctable causes of shock first	MAP $\geq 60$ mm Hg without vasopressors <b>except dopamine <math>\leq 5 \mu\text{g/kg/min}</math></b>			
CVP		PAOP <sup>G</sup>			Average urinary output <0.5 ml/kg/hr		Average urinary output $\geq 0.5$ ml/kg/hr	
Conservative strategy	Liberal strategy	Conservative strategy	Liberal strategy		<b>Ineffective Circulation</b> Cardiac index <2.5 liters/min/m <sup>2</sup> or cold, mottled skin with capillary-refilling time >2 sec	<b>Effective Circulation</b> Cardiac index $\geq 2.5$ liters/min/m <sup>2</sup> or absence of criteria for ineffective circulation	<b>Ineffective Circulation</b> Cardiac index <2.5 liters/min/m <sup>2</sup> or cold, mottled skin with capillary-refilling time >2 sec	<b>Effective Circulation</b> Cardiac index $\geq 2.5$ liters/min/m <sup>2</sup> or absence of criteria for ineffective circulation
Range 1				1 Vasopressor <sup>F</sup> Fluid bolus <sup>F</sup>	3 KVO IV Dobutamine <sup>A</sup> Furosemide <sup>B,1,2,4</sup>	7 KVO IV Furosemide <sup>B,1,2,4</sup>	11 KVO IV Dobutamine <sup>A</sup> Furosemide <sup>B,1,3,4</sup>	15 KVO IV Furosemide <sup>B,1,3,4</sup>
>13	>18	>18	>24					
Range 2				2 Fluid bolus <sup>F</sup> Vasopressor <sup>F</sup>	4 KVO IV Dobutamine <sup>A</sup>	8 KVO IV Furosemide <sup>B,1,2,4</sup>	12 KVO IV Dobutamine <sup>A</sup>	16 KVO IV Furosemide <sup>B,1,3,4</sup>
9–13	15–18	13–18	19–24					
Range 3				5 Fluid bolus <sup>C</sup>	9 Fluid bolus <sup>C</sup>	13 Fluid bolus <sup>C</sup>	17 Liberal KVO IV	18 Conservative Furosemide <sup>B,1,3,4</sup>
4–8	10–14	8–12	14–18					
Range 4				6 Fluid bolus <sup>C</sup>	10 Fluid bolus <sup>C</sup>	14 Fluid bolus <sup>C</sup>	19 Liberal fluid bolus	20 Conservative KVO IV
<4	<10	<8	<14					

## Supplemental Figure 1. Cumulative Fluid Balance



**Table 3. Main Outcome Variables.\***

Outcome	Conservative Strategy	Liberal Strategy	P Value
Death at 60 days (%)	25.5	28.4	0.30
Ventilator-free days from day 1 to day 28 †	14.6±0.5	12.1±0.5	<0.001
ICU-free days †			
Days 1 to 7	0.9±0.1	0.6±0.1	<0.001
Days 1 to 28	13.4±0.4	11.2±0.4	<0.001
Organ-failure-free days † ‡			
Days 1 to 7			
Cardiovascular failure	3.9±0.1	4.2±0.1	0.04
CNS failure	3.4±0.2	2.9±0.2	0.02
Renal failure	5.5±0.1	5.6±0.1	0.45
Hepatic failure	5.7±0.1	5.5±0.1	0.12
Coagulation abnormalities	5.6±0.1	5.4±0.1	0.23
Days 1 to 28			
Cardiovascular failure	19.0±0.5	19.1±0.4	0.85
CNS failure	18.8±0.5	17.2±0.5	0.03
Renal failure	21.5±0.5	21.2±0.5	0.59
Hepatic failure	22.0±0.4	21.2±0.5	0.18
Coagulation abnormalities	22.0±0.4	21.5±0.4	0.37
Dialysis to day 60			
Patients (%)	10	14	0.06
Days	11.0±1.7	10.9±1.4	0.96

# FACTT Algorithme simplifié

## Used in the FACTT\*

CVP, mm Hg (Recommended)	PAOP, mm Hg (Optional)	MAP $\geq$ 60 mm Hg and Not Receiving Vasopressors for $\geq$ 12 h	
		Average Urine Output $<$ 0.5 mL/kg/h	Average Urine Output $\geq$ 0.5 mL/kg/h
$>$ 8	$>$ 12	Furosemide <sup>†</sup> ; reassess in 1 h	Furosemide; reassess in 4 h
4-8	8-12	Fluid bolus as fast as possible <sup>‡</sup> ; reassess in 1 h	Furosemide; reassess in 4 h
$<$ 4	$<$ 8	Fluid bolus as fast as possible <sup>‡</sup> ; reassess in 1 h	No intervention; reassess in 4 h

\*CVP = central venous pressure; PAOP = pulmonary artery occlusion pressure; MAP = mean arterial pressure. Reprinted with the courtesy of the NHLBI Acute Respiratory Distress Syndrome Network. Patients must have had a MAP of  $>$  60 mm Hg without requiring vasopressors for at least 12 h before this protocol is initiated.

<sup>†</sup>Furosemide dosing: begin with a 20-mg bolus, 3 mg/h infusion, or last known effective dose. Double each subsequent dose until the goal is achieved (oliguria reversal or intravascular pressure target), with a maximal dose of 160-mg bolus or 24 mg/h. Do not exceed 620 mg/d. If the patient has heart failure, treatment with dobutamine may be considered. Diuretic therapy should be withheld for patients with renal failure, which is defined as dialysis dependence, oliguria with a serum creatinine level of  $>$  2 mg/dL, or oliguria with a serum creatinine level of  $<$  2 mg/dL but with urinary indices indicative of acute renal failure.

<sup>‡</sup>Fluid bolus: 15 mL/kg crystalloid (round to nearest 250 mL) or 1 unit of packed RBCs or 25 g of albumin.



# Circulation extracorporelle

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# Assistance circulatoire extracorporelle

- Objectifs PaO<sub>2</sub>
  - ECMO
- Objectifs PaCO<sub>2</sub>
  - ECCO<sub>2</sub>R
- Veino-veineux
  - ECLA
  - ECMO
  - ECCO2R
- Veino-artériel
  - ECLS
  - ECMO
  - ECCO2R
- Artério-veineux
  - iLA

# CESAR

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- **Juillet 2001 - août 2006 - 70 ICUs en Grande-Bretagne**
- **Inclusion**
  - **Malades avec IRA potentiellement réversible**
  - **Murray score  $\geq 3$  OU Hypercapnie OU pH  $< 7.20$**
  - **Ventilation mécanique invasive avec pressions et/ou FIO<sub>2</sub> élevées depuis 7 Jours ou moins**
  - **Adultes 18-65 ans**
  - **Pas de limitation thérapeutique**
  - **Pas de contre-indication à l'Héparine**
  - **Pas de saignement intra-crânien**

# CESAR

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- **Groupe VM conventionnelle**
  - Il est recommandé d'utiliser la stratégie du NIH (Pression < 30 cm H<sub>2</sub>O et VT 4-8 ml/kg bw)
  - il n'y a pas de recueil systématique des réglages mais un document proforma à signer par l'investigateur comme preuve d'engagement à suivre cette stratégie
- **Groupe ECMO**
  - CEC veino-veineuse par canulation percutanée JID ou VF → VF
  - Débit sang 120 ml/kg/min
  - Un ou deux poumons avec O<sub>2</sub> pur
  - VM pour P<sub>max</sub> < 30, PEEP 10, FR 10, FIO<sub>2</sub> 30%
  - Cibles : Hb 14, Plaquettes > 100 000

# CESAR

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- Critère de jugement principal
  - à 6 mois : décès ou handicap majeur (ne peut se lever du lit, s'habiller et se laver seul)
- Puissance
  - $\alpha = 5\%$ ,  $\beta = 20\%$ , formulation bilatérale, réduction de 33% du risque de survenue du critère de jugement principal, survenue dans le groupe de contrôle 65%
  - N = 180 patients au total

# CESAR

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- 766 patients « screenés » et 180 randomisés
- 90 ECMO vs 90 conventionnelle
- 90 ECMO = 68 ECMO + 22 ECMO -
- Transport groupe ECMO
  - Air 24
  - Terre 24
  - Pas de transport 6
- 22 ECMO -
  - 16 = amélioration dont 3 décès
  - 3 = décès avant transport
  - 2 = décès pendant transport
  - 1 = amputation

# CESAR

(P=0.03)

	ECMO	CONV
Age (ans)	40	40
PNEUMONIE (n)	56	53
TRAUMA (n)	5	7
DUREE VM (HEURES)	35	37
PAO2	85	87
LIS	3.5	3.4
APACHE II	20	20
HFO (n)	6	13
NO (n)	9	6
DV (n)	32	38
<b>DECES OU INCAPACITE SEVERE à 6 mois (n)</b>	<b>33</b>	<b>46</b>