Traitements Pharmacologiques du SDRA

AER Lyon 2025

Jean- Marie FOREL

Médecine Intensive Réanimation, APHM, CHU Nord, Marseille

Centre d'Etudes et de Recherches sur les Services de Santé et qualité de vie (CEReSS) Aix-Marseille Université

Liens d'intérêt

- **Intérêts financiers : Aucun**

- **Liens d'intérêt : Aucun**

Ce dont nous parlerons… comment juger de l'efficacité ?

Sédation

Curarisation

Monoxyde d'azote inhalé, Prostacycline

Corticoïdes

Innovations

~~COVID-19~~

(Anti IL-6, JAK inhibiteur,…)

Sédation

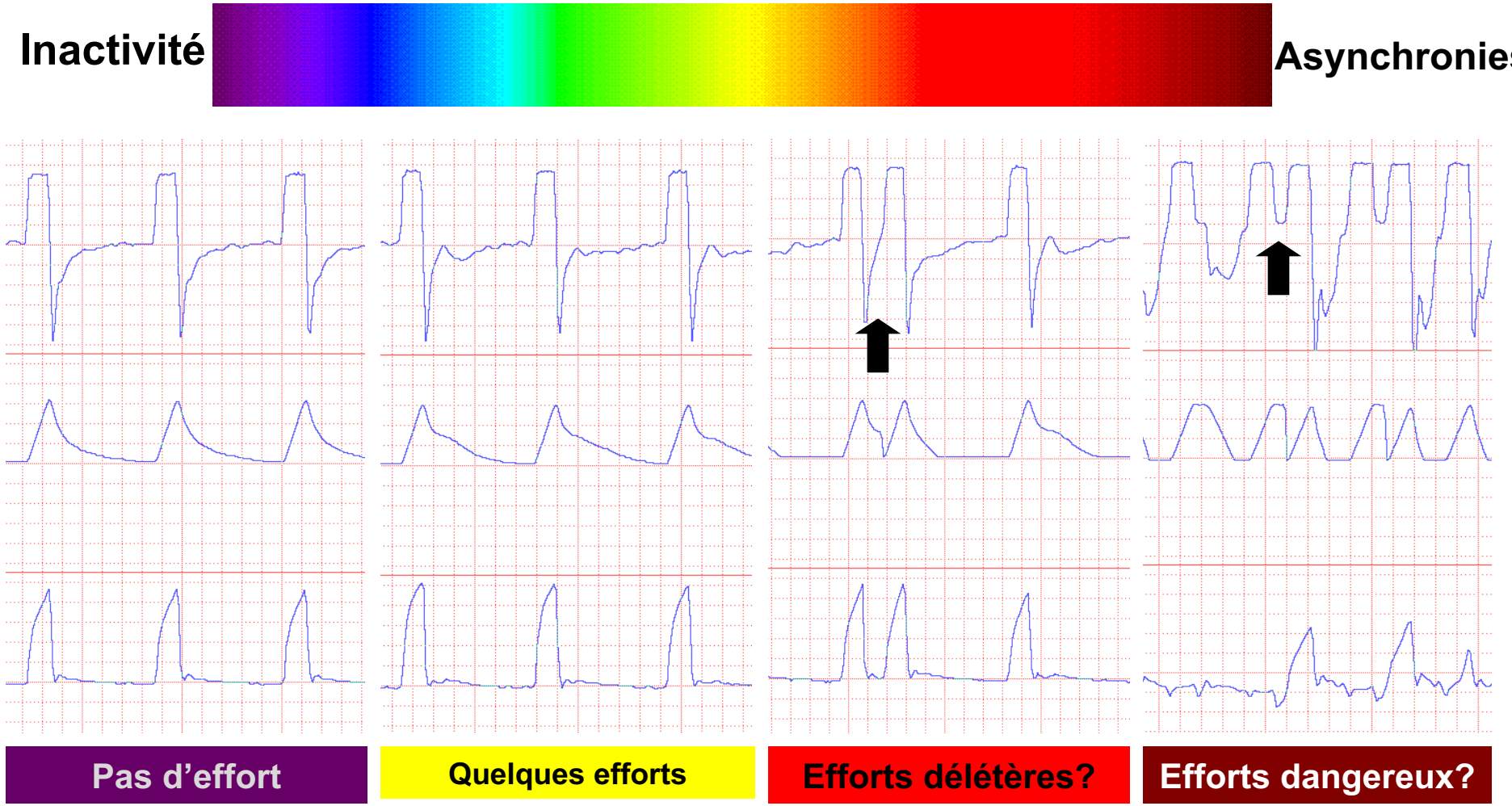

50 mg in 50 ml
Midazolam
1 mg/ml
Solution for
Injection / Infusion
50 mg in 50 ml
Midazolam 1 mg/ml
50 mg in 50 ml


PROPOFOL
INJECTABLE EMULSION, 1%
For IV Administration
1 g/100 mL
(10 mg/mL)
CONTAINS BENZYL ALCOHOL
Sterile, nonpyrogenic
SHAKE WELL BEFORE USE
Rx ONLY
PROPOFOL
INJECTABLE EMULSION, 1%
For IV Administration
200 mg/20 mL
PROPOFOL
INJECTABLE EMULSION, 1%
For IV Administration
500 mg/50 mL


50 µg / 10 ml
Sufentanil
50 µg / 10 ml
Sufentanil
50 µg / 10 ml
Sufentanil
50 µg / 10 ml
Sufentanil
50 µg / 10 ml


AnaConDa
Sevoflurane, USP
(Inhalation Anesthetic)
250 mL

Trouver le niveau adapté de sédation

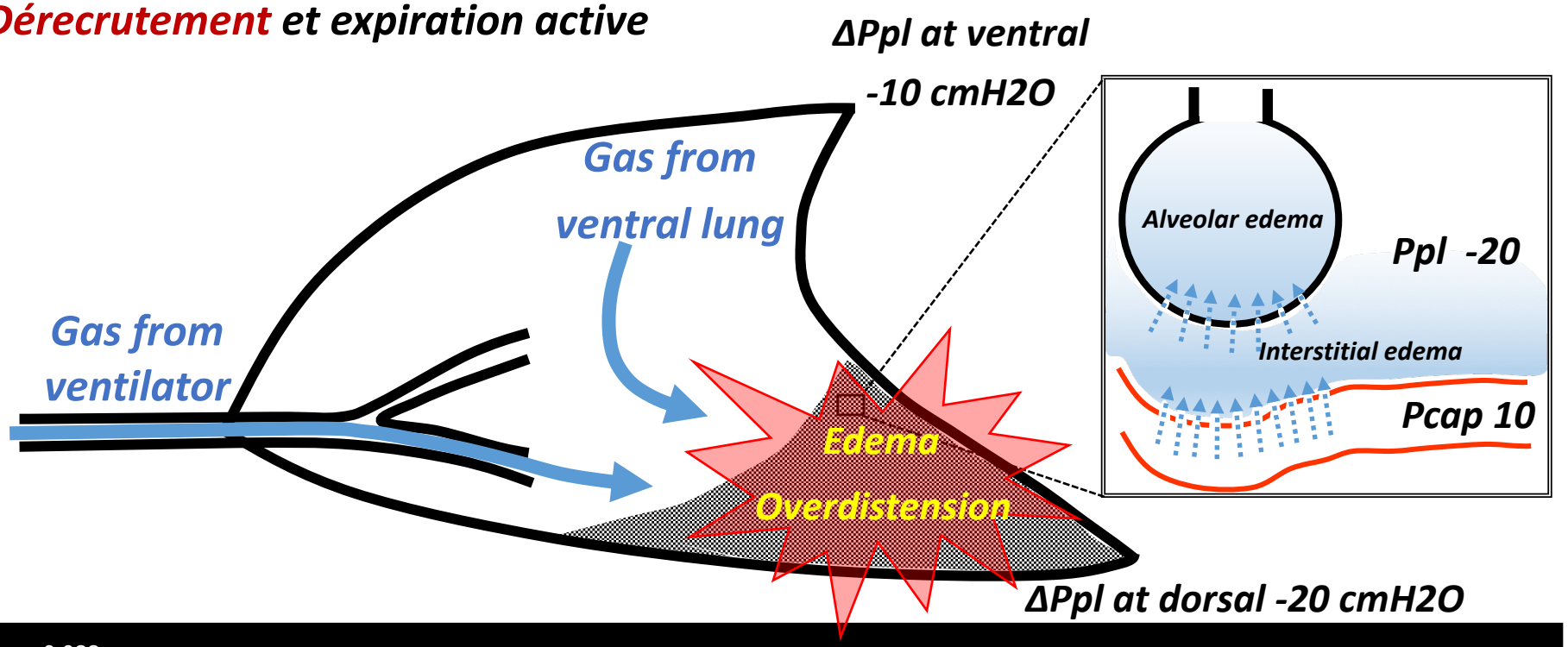


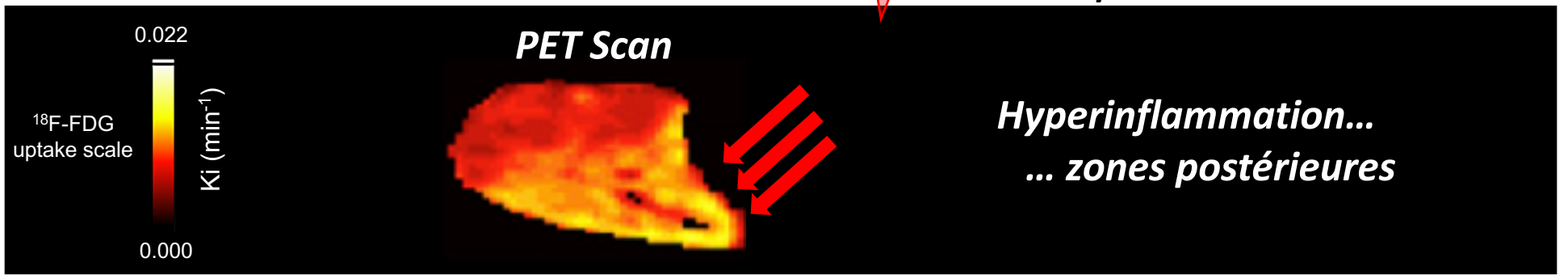
Avec la permission du Pr S Jaber

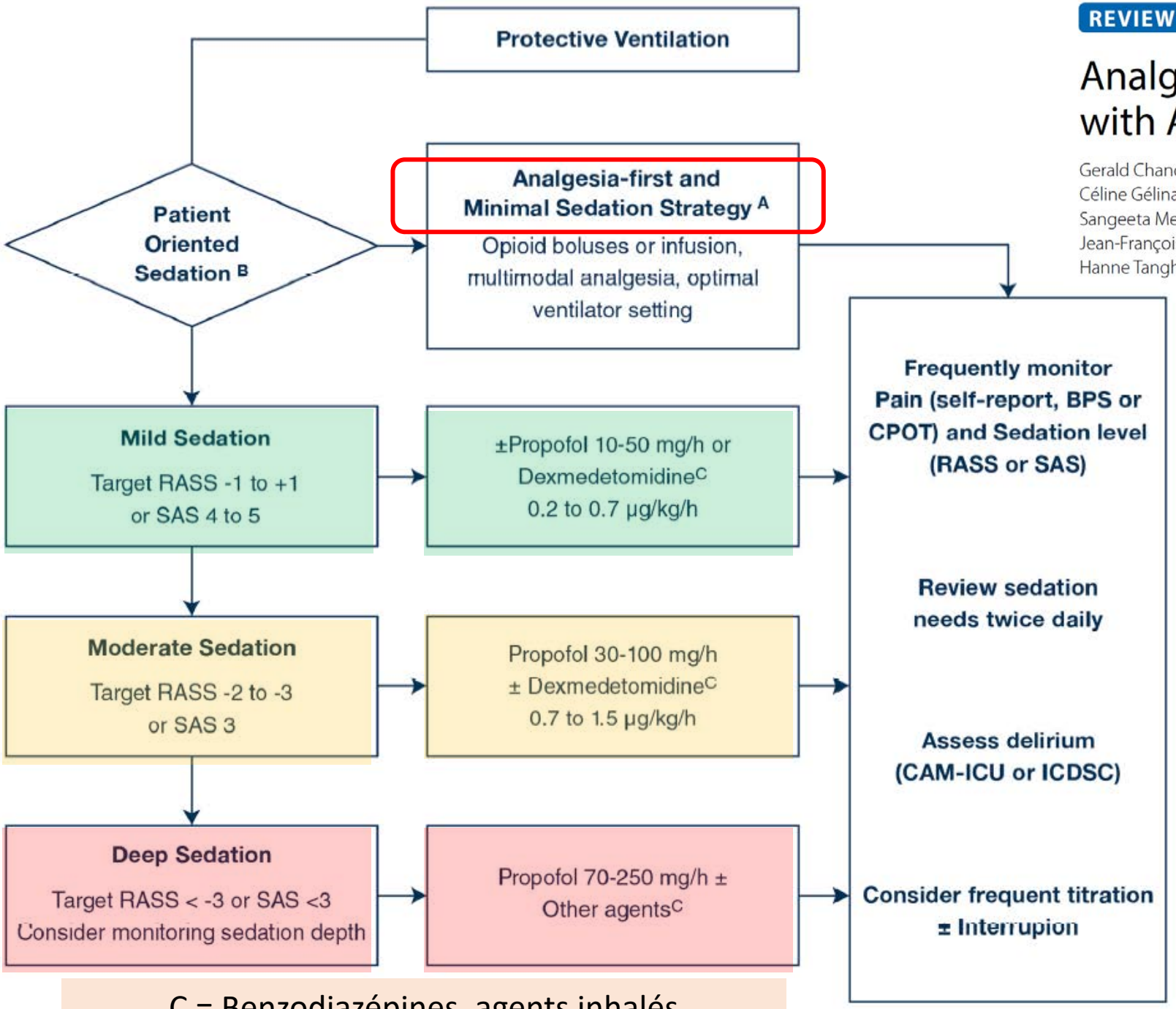
Efforts ventilatoires importants et asynchronies patient-ventilateur

With courtesy of Pr T. Yoshida, ICM 2020

- ***Surdistension*, non contrôle du Vt**
- **Distribution inhomogène du *stress pulmonaire*, elevation de la PtP à l'inspiration**
- **Augmentation de la perfusion et de *l'oedeme* pulmonaire dans les zones dépendantes**
- ***Dérecrutement* et expiration active**







REVIEW

Analgesia and sedation in patients with ARDS

Gerald Chanques[1,2*], Jean-Michel Constantin[3], John W. Devlin[4,5], E. Wesley Ely[6,7,8], Gilles L. Fraser[9], Céline Gélinas[10], Timothy D. Girard[11], Claude Guérin[12,13], Matthieu Jabaudon[14,15], Samir Jaber[1,2], Sangeeta Mehta[16], Thomas Langer[17,18], Michael J. Murray[19], Pratik Pandharipande[20], Bhakti Patel[21], Jean-François Payen[22], Kathleen Puntillo[23], Bram Rochwerg[24], Yahya Shehabi[25,26], Thomas Strøm[27,28], Hanne Tanghus Olsen[27] and John P. Kress[21]

Sufentanil
Remifentanil

Chanques et al. ICM 2020

C = Benzodiazépines, agents inhalés

Kotani et al. Critical Care (2023) 27:139
https://doi.org/10.1186/s13054-023-04431-8

2023

Critical Care

RESEARCH Open Access

Propofol and survival: an updated meta-analysis of randomized clinical trials

Yuki Kotani[1,2,3†], Alessandro Pruna[1†], Stefano Turi[1], Giovanni Borghi[1], Todd C. Lee[4], Alberto Zangrillo[1,2], Giovanni Landoni[1,2*] and Laura Pasin[5]

ICU dont peu de ARDS

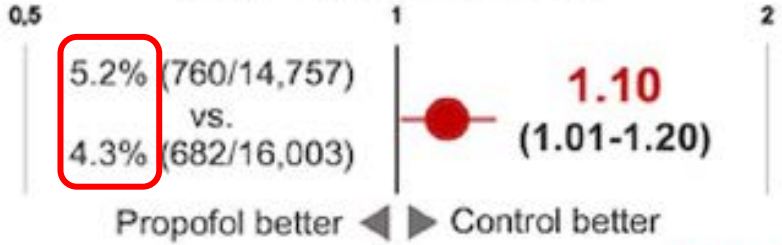
Propofol and survival: an updated meta-analysis of randomized trials

DATA SOURCE **252** RCTs with **30,757** patients

COMPARISON INTERVENTION **Propofol** CONTROL **Any comparator**

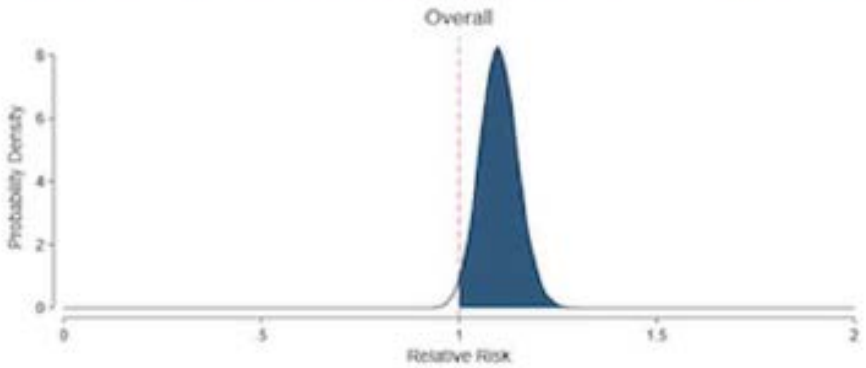
RESULTS

Risk ratio (95% confidence interval)



Number Needed to Harm = 235

Propofol vs. control
The probability of relative risk of mortality >1.0 = 98.4%



CONCLUSIONS

Propofol likely reduces survival with a number needed to harm of 235.

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Inhaled Sedation in Acute Respiratory Distress Syndrome
The SESAR Randomized Clinical Trial

2025

Matthieu Jabaudon, MD, PhD; Jean-Pierre Quenot, MD, PhD; Julio Badie, MD; Jules Audard, MD; Samir Jaber, MD, PhD; Benjamin Rieu, MD; Caroline Varillon, MD; Antoine Monsel, MD, PhD; François Thouy, MD; Julien Lorber, MD; Joël Cousson, MD; Stéphanie Bulyez, MD; Jérémy Bourenne, MD; Ghada Sboui, MD; Claire Lhommet, MD; Virginie Lemiale, MD, PhD; Belaïd Bouhemad, MD, PhD; Clément Brault, MD; Sigismond Lasocki, MD, PhD; François Legay, MD; Thomas Lebouvier, MD; Arthur Durand, MD; Julien Pottecher, MD, PhD; Alexandre Conia, MD; Delphine Brégeaud, MD; Lionel Velly, MD, PhD; Arnaud W. Thille, MD, PhD; Fabien Lambiotte, MD; Erwan L'Her, MD, PhD; Mehran Monchi, MD; Antoine Roquilly, MD, PhD; Aziz Berrouba, MD; Franck Verdonk, MD, PhD; Russell Chabanne, MD; Thomas Godet, MD, PhD; Marc Garnier, MD, PhD; Raiko Blondonnet, MD, PhD; Jérémy Vernhes, MD; Vincent Sapin, PharmD, PhD; Lucile Borao, MSc; Emmanuel Futier, MD, PhD; Bruno Pereira, PhD; Jean-Michel Constantin, MD, PhD; for the SESAR Trial Investigators

- 687 patients
- SDRA modéré à sévère
- **> 50% de COVID-19** ⚠
- > 90% en VAC curarisés
- > 90% de DV à J1
- > 70% de patients sous catécholamines
- Durée médiane de sédation **7 jours** (exposition sévo aussi longue jamais explorée auparavant)

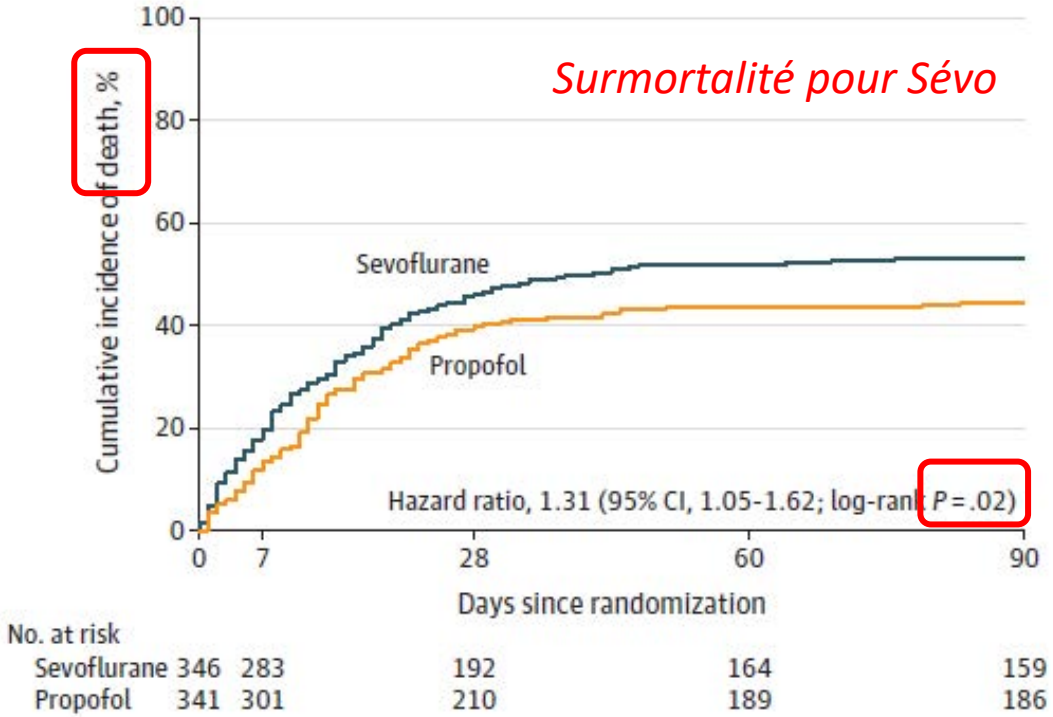
Surmortalité avec Sévoflurane

Table 2. Primary and Secondary End Points[a]

Variable	Inhaled sevoflurane (n = 346)	Intravenous propofol (n = 341)	Between-group difference (95% CI)[b]	Treatment effect (95% CI)[c]
Primary end point	*Moins de jours vivants sans VM*			
Ventilator-free days through day 28, median (IQR)	0.0 (0.0 to 11.9)	0.0 (0.0 to 18.7)	−2.1 (−3.6 to −0.7)	0.76 (0.50 to 0.97)
Key secondary end point	*Surmortalité pour Sévo*			
Death at day 90, No./total (%)	183/346 (52.9)	151/341 (44.3)	8.6 (1.2 to 16.1)	1.31 (1.05 to 1.62)
Secondary end points				
Mortality, No./total (%)[d]				
At 28 d	152/345 (44.1)	132/340 (38.8)	5.2 (-2.1 to 12.6)	1.13 (0.95 to 1.36)
At 14 d	104/345 (30.1)	90/340 (26.5)	3.7 (-3.1 to 10.4)	1.14 (0.90 to 1.45)
At 7 d	67/345 (19.4)	46/340 (13.5)	5.9 (0.4 to 11.4)	1.44 (1.02 to 2.03)
ICU-free days through day 28, median (IQR)	0.0 (0.0 to 6.0)	0.0 (0.0 to 15.0)	−2.5 (−3.7 to −1.4)	0.67 (0.52 to 0.86)
No.	345	341		

Sévoflurane
Surmortalité
2025

Figure 2. Kaplan-Meier Estimates of 90-Day Survival in the Modified Intention-to-Treat Population



Des pistes d'explications

Groupe sévoflurane:

1. Effets hémodynamiques ?

- Doses supérieures de noradrénaline de J0 à J3
- Lactatémie plus élevée de J0 à J4

2. Aggravation des VILI ?

- Effet non retrouvé sur l'oxygénation (vs. études précédentes)
- Augmentation de la PaCO2 (espace mort)
- Augmentation de la fréquence respiratoire, du ventilatory ratio et du mechanical power

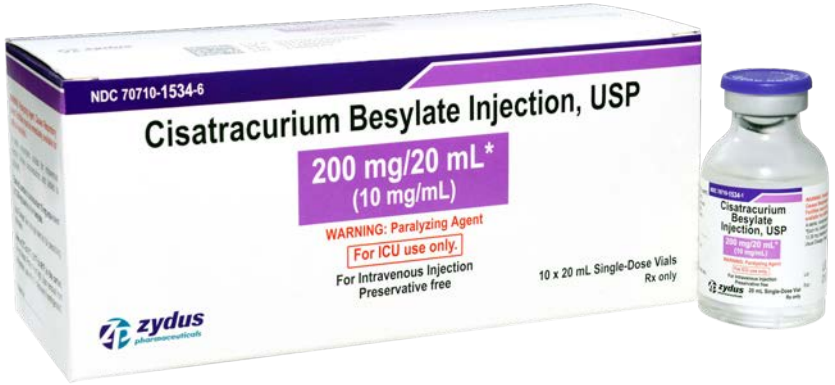
3. Effets rénaux ?

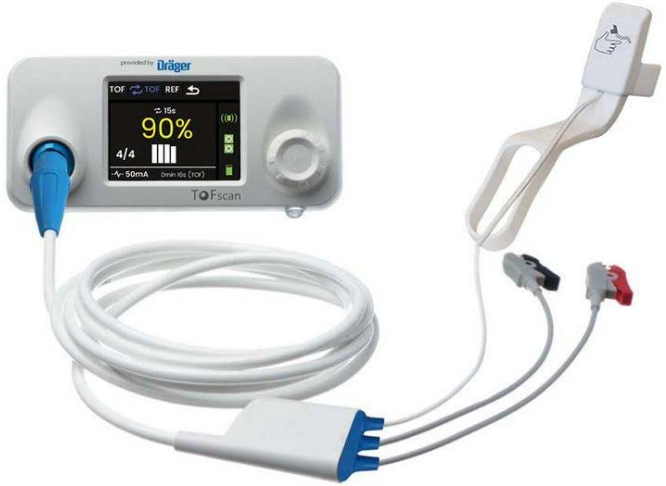
- Plus d'insuffisance rénale à J7
- Plus de diabètes insipides néphrogéniques

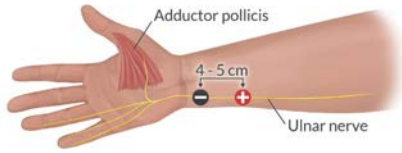
Limites

- Pas d'information sur la Fe sévoflurane (effet dose ?)
- Majorité de **COVID-19** (effets sur l'oxygénation non retrouvés dans cette population dans autres travaux)
- Médiane de **curarisation** = **5 jours (!)** dans les 2 groupes

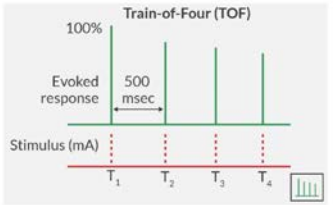
Curarisation







Supramaximal stimulation
2 Hz x 2 seconds



Loss of:
4th twitch = 75-80% receptors blocked
3rd twitch = 80-85% blocked
2nd twitch = 85-95% blocked
1st twitch = 100% blocked

Curares au cours du SDRA

ACURASYS

Papazian et al. NEJM 2010

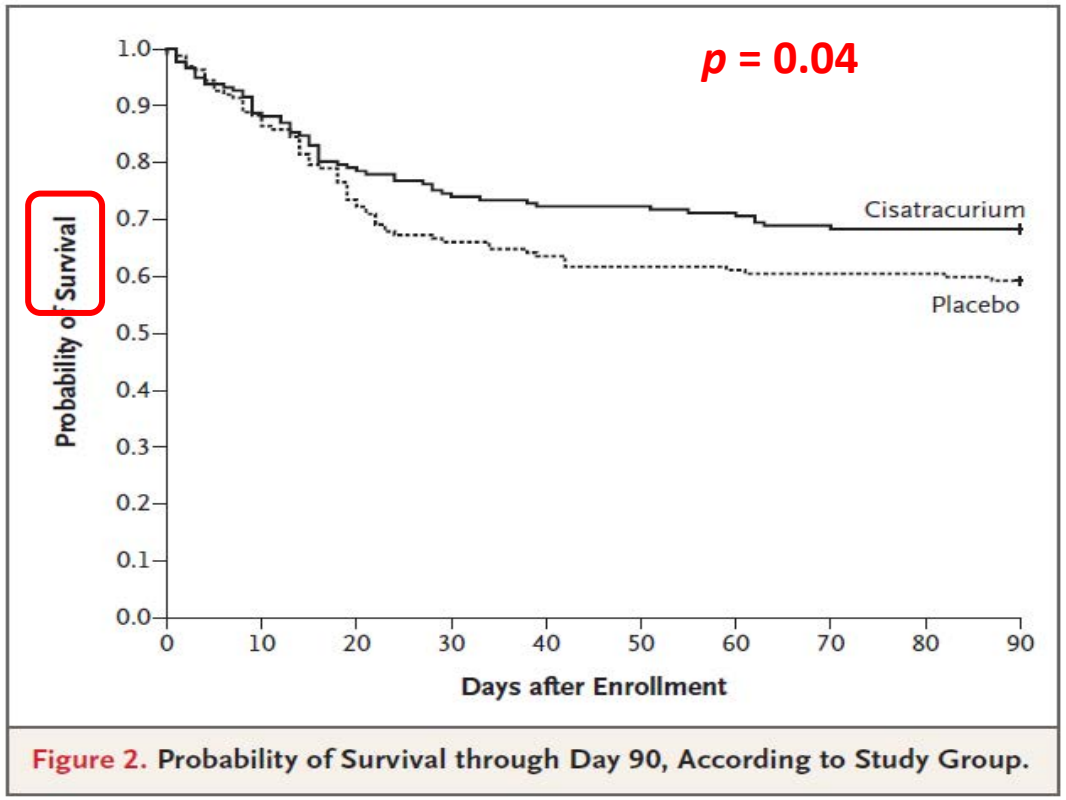


Figure 2. Probability of Survival through Day 90, According to Study Group.

P/F<150 et PEP≥5 cm H2O
Cisatracurium 48h vs. placebo (sédation profonde)

ROSE

Moss et al. NEJM 2019

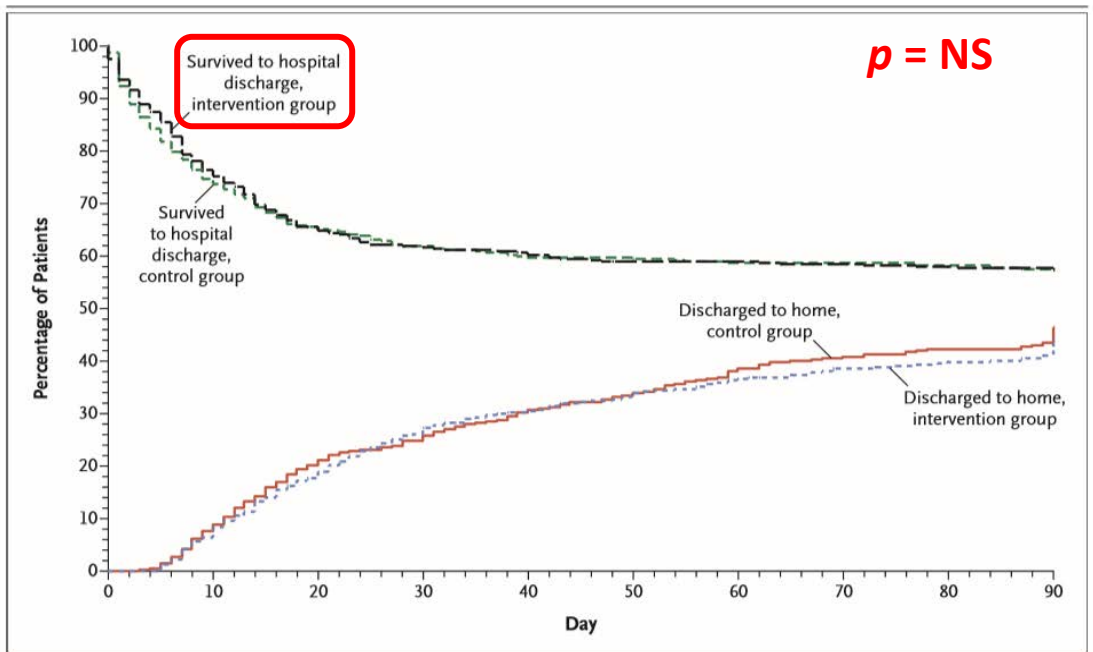


Figure 3. Patients Who Survived to Hospital Discharge and Were Discharged Home during the First 90 Days after Randomization.
The period of hospitalization included transfer to other health care facilities.

P/F<150 et PEP≥8 cm H2O
Cisatracurium 48h vs. sédation légère

ACURASYS et ROSE: différences méthodologiques

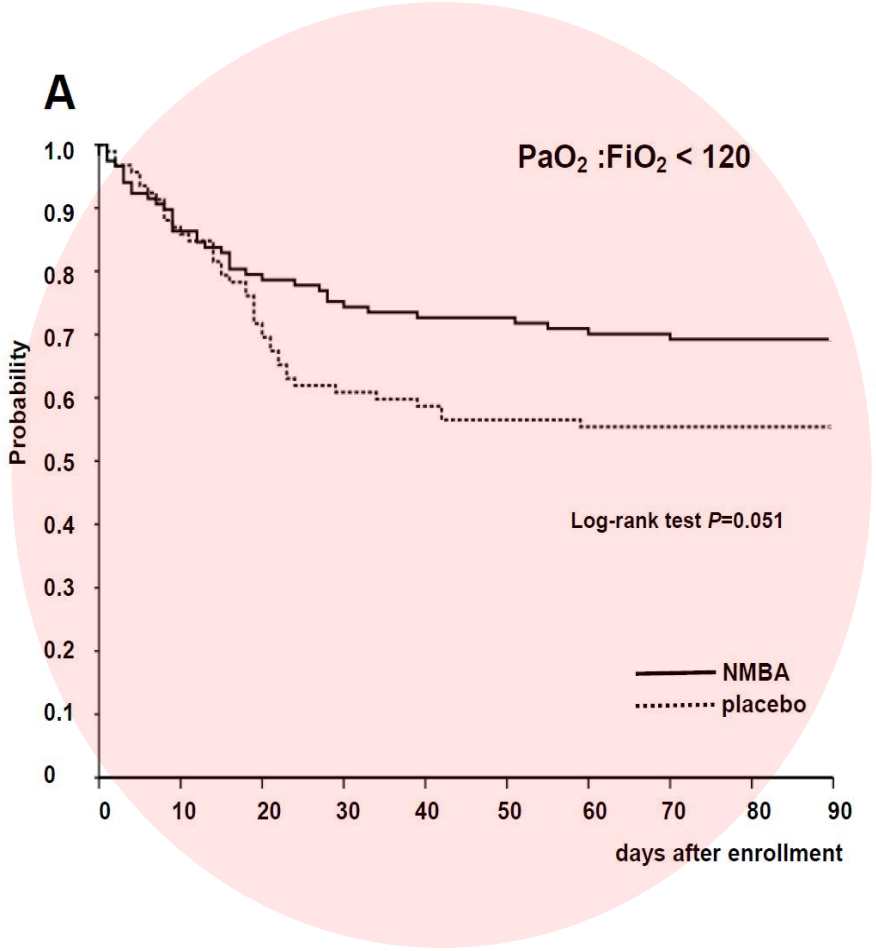
	ACURASYS	ROSE
Sédation contrôle	Sédation profonde	Sédation légère
Délai avant curarisation	16h	7h optimisation VM ?
PEEP	Modérée (ARMA)	Haute (EXPRESS)
DV	28% (avant PROSEVA)	16 % (après PROSEVA)

Mortalité moindre si PaO2/FiO2 < 120

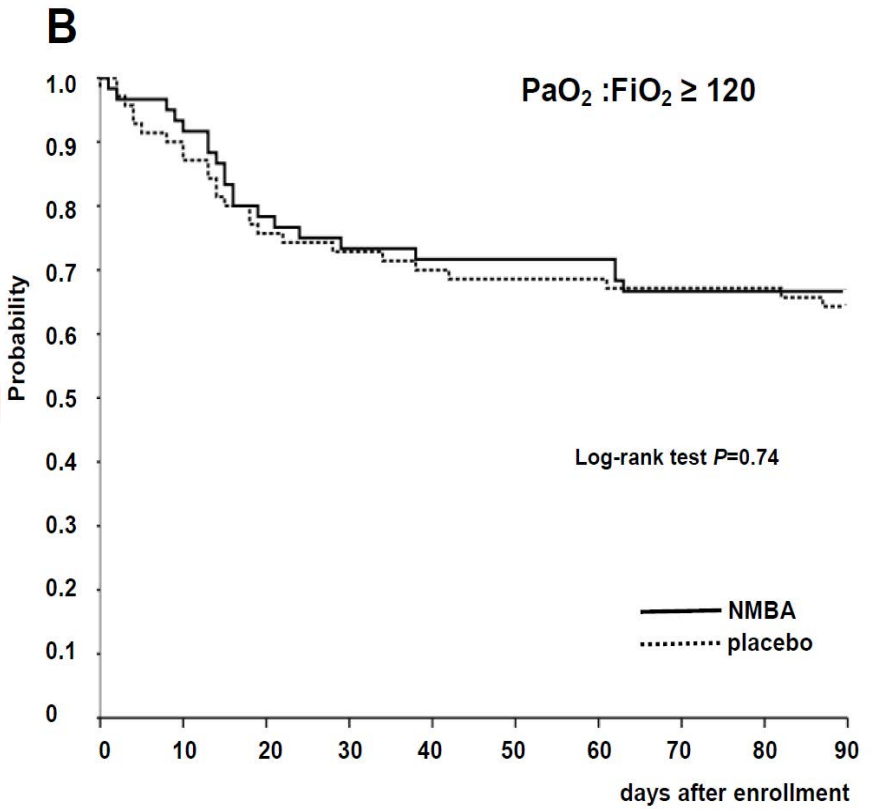
ACURASYS

Papazian et al. NEJM 2010

PaO2/FiO2 < 120



PaO2/FiO2 ≥ 120



Synergie DV- Curares ?

PROSEVA

91% des patients du groupe DV ont une perfusion continue de cisatracurium

Guérin et al. NEJM 2013

DV et curares permettent (séparément):

- Homogénéisation PTP
- Réduction des VILI

Intensive Care Med (2015) 41:2195–2197
DOI 10.1007/s00134-015-3918-7

EDITORIAL

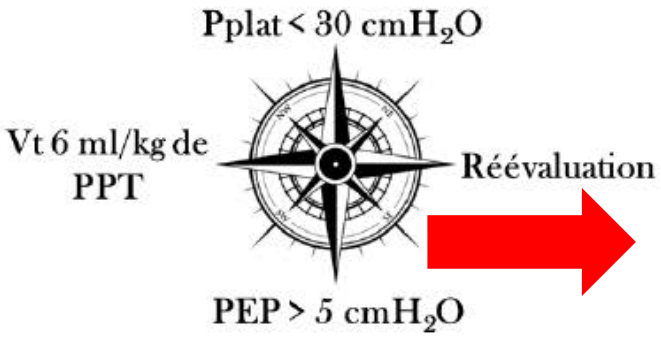
Claude Guérin
Jordi Mancebo

Prone positioning and neuromuscular blocking agents are part of standard care in severe ARDS patients: yes

PHRC PEPER (DV avec ou sans curarisation) : Les Inclusions débutent…

Prise en charge initiale du SDRA en 2019

Avant ROSE



P/F < 80 — Discuter ECMO VV

P/F < 150 — Curarisation, Décubitus ventral

P/F < 200 — PEP élevée si améliore oxygénation

SDRA confirmé

Vt autour de 6 ml/kg de PPT
Pplateau < 30 cmH2O
PEP > 5 cmH2O
Surveiller hypercapnie

Toute initiation de ventilation invasive avec sédation en réanimation

Vt autour de 6 ml/kg de PPT à la phase initiale en l'absence d'acidose métabolique profonde

Recherche systématique des critères diagnostiques de SDRA

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

Sévérité du SDRA

Poids prédit par la taille
- Tableau

ECMO veino-veineuse
- ❑ Si hypoxémie réfractaire ou ventilation protectrice non applicable
- ❑ A discuter avec un centre expert

Modalités de la curarisation : IVSE
- ❑ Précocement, dans les 48h du diagnostic

Modalités du décubitus ventral (DV) : VIDEO
- ❑ séance ≥ 16 heures, plusieurs séances

SDRA modéré ou sévère → Test PEP élevée (> 12 cmH2O)
Utilisation PEP élevée si :
- ❑ Amélioration de l'oxygénation
- ❑ Sans dégradation significative de la compliance du système respiratoire et de l'hémodynamique
- ❑ Maintien Pplateau < 30 cmH2O, monitorage continu

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

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

Pas de recommandation possible
- ➢ ECCO2R
- ➢ Pression motrice
- ➢ Ventilation spontanée à la phase aiguë

Probablement ne pas faire
- ➢ Manœuvres de recrutement systématiques

Ne pas faire
- ➢ HFOV

Intensive Care Med (2023) 49:727–759
https://doi.org/10.1007/s00134-023-07050-7

2023

CONFERENCE REPORTS AND EXPERT PANEL

ESICM guidelines on acute respiratory distress syndrome: definition, phenotyping and respiratory support strategies

NEUROMUSCULAR BLOCKING AGENTS

Q1 **Does the *routine* use of a continuous infusion of neuromuscular blocking agents (NMBA) in patients with moderate to severe ARDS not due to COVID-19 or moderate to severe ARDS due to COVID-19 reduce mortality?**

1 We **recommend against** the *routine* use of continuous infusions of NMBA to reduce mortality in patients with moderate to severe ARDS not due to COVID-19. — MODERATE LEVEL OF EVIDENCE

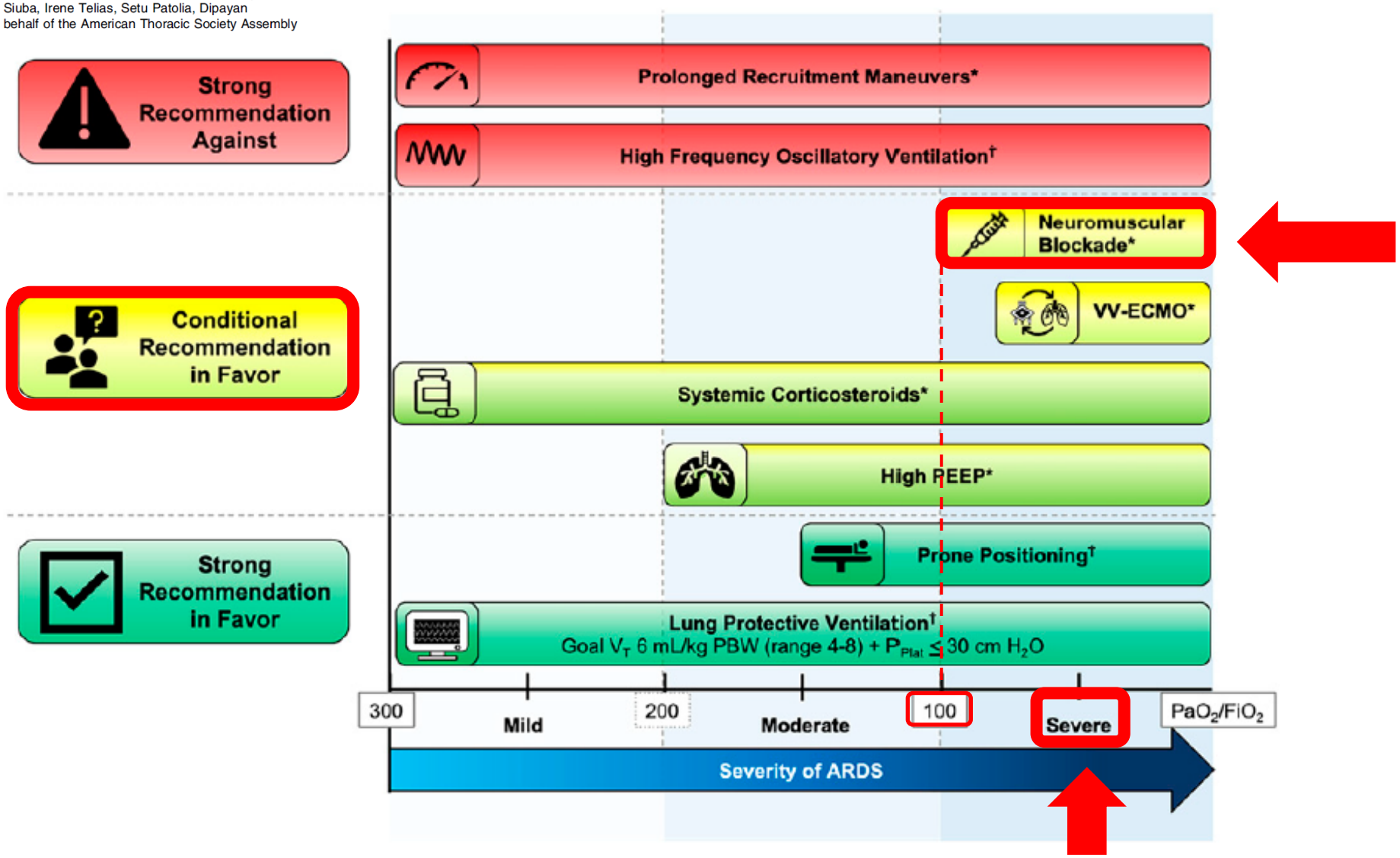
2 We are **unable to make a recommendation** for or against the *routine* use of continuous infusions of NMBA to reduce mortality in patients with moderate to severe ARDS due to COVID-19. — NO EVIDENCE

An Update on Management of Adult Patients with Acute Respiratory Distress Syndrome

An Official American Thoracic Society Clinical Practice Guideline

Nida Qadir*, Sarina Sahetya*, Laveena Munshi*, Charlotte Summers*, Darryl Abrams, Jeremy Beitler, Giacomo Bellani, Roy G. Brower, Lisa Burry, Jen-Ting Chen, Carol Hodgson, Catherine L. Hough, Francois Lamontagne, Anica Law, Laurent Papazian, Tai Pham, Eileen Rubin, Matthew Siuba, Irene Telias, Setu Patolia, Dipayan Chaudhuri, Allan Walkey‡, Bram Rochwerg‡, and Eddy Fan‡; on behalf of the American Thoracic Society Assembly on Critical Care

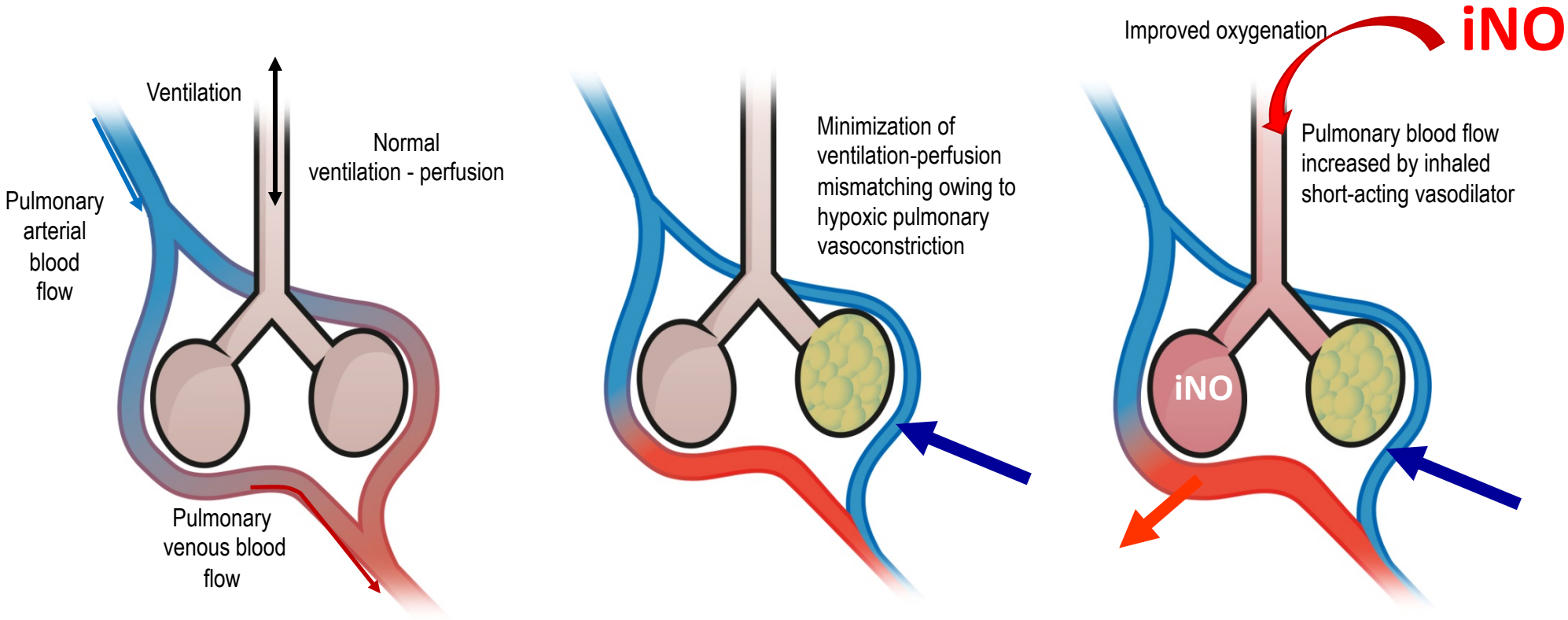
2024



Vasodilatateurs pulmonaires
NO inhalé
Prostaglandines inhalées (epoprostenol, iloprost)

Effet du NO inhalé = Vasodilatation pulmonaire

Redistribution du flux sanguin vers les territoires les mieux ventilés
Diminue le shunt intrapulmonaire



Baisse transitoire des PAP à H24

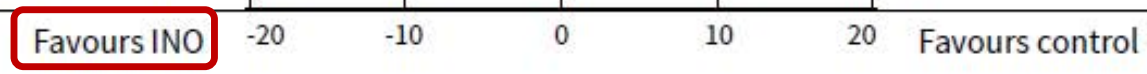
Gebistorf et al. Cochrane Database Syst Rev 2016

Cochrane Library
Cochrane Database of Systematic Reviews

Study or subgroup	Experimental N	Experimental Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Day 1997	4	42.5 (7.1)	2	33.5 (6.4)		2.14%	9[-2.25,20.25]
Dellinger 1998	81	29.8 (5.9)	47	32.1 (5.8)		61.46%	-2.3[-4.4,-0.2]
Gerlach 2003	20	25 (6)	20	26 (7)		16.56%	-1[-5.04,3.04]
Mehta 2001	8	31 (6)	6	32 (5)		8.12%	-1[-6.77,4.77]
Park 2003	11	27 (4.5)	6	29.5 (5)		11.72%	-2.5[-7.3,2.3]
Total ***	**124**		**81**			**100%**	**-1.76[-3.41,-0.12]**

Heterogeneity: $Tau^2=0$; $Chi^2=4.06$, df=4(P=0.4); $I^2=1.48\%$

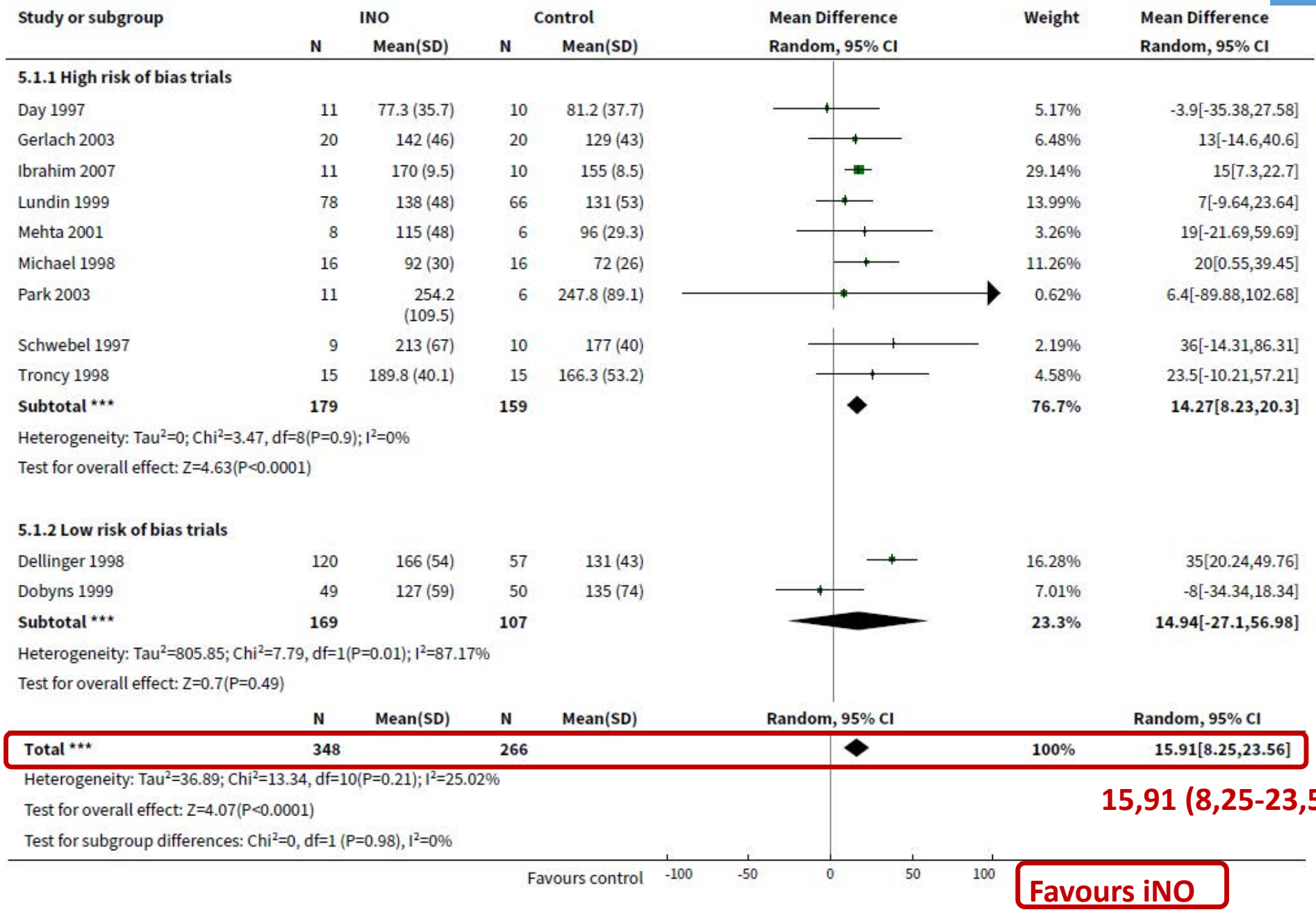
Test for overall effect: Z=2.1(P=0.04)



Effet non retrouvé au-delà de la 24ème heure (population de SDRA)

Amélioration du PaO2/FiO2 à 24H

Gebistorf et al. Cochrane Database Syst Rev 2016



Study or subgroup	INO N	INO Mean(SD)	Control N	Control Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
5.1.1 High risk of bias trials							
Day 1997	11	77.3 (35.7)	10	81.2 (37.7)		5.17%	-3.9[-35.38,27.58]
Gerlach 2003	20	142 (46)	20	129 (43)		6.48%	13[-14.6,40.6]
Ibrahim 2007	11	170 (9.5)	10	155 (8.5)		29.14%	15[7.3,22.7]
Lundin 1999	78	138 (48)	66	131 (53)		13.99%	7[-9.64,23.64]
Mehta 2001	8	115 (48)	6	96 (29.3)		3.26%	19[-21.69,59.69]
Michael 1998	16	92 (30)	16	72 (26)		11.26%	20[0.55,39.45]
Park 2003	11	254.2 (109.5)	6	247.8 (89.1)		0.62%	6.4[-89.88,102.68]
Schwebel 1997	9	213 (67)	10	177 (40)		2.19%	36[-14.31,86.31]
Troncy 1998	15	189.8 (40.1)	15	166.3 (53.2)		4.58%	23.5[-10.21,57.21]
Subtotal ***	**179**		**159**			**76.7%**	**14.27[8.23,20.3]**
Heterogeneity: Tau^2=0; Chi^2=3.47, df=8(P=0.9); I^2=0%							
Test for overall effect: Z=4.63(P<0.0001)							
5.1.2 Low risk of bias trials							
Dellinger 1998	120	166 (54)	57	131 (43)		16.28%	35[20.24,49.76]
Dobyns 1999	49	127 (59)	50	135 (74)		7.01%	-8[-34.34,18.34]
Subtotal ***	**169**		**107**			**23.3%**	**14.94[-27.1,56.98]**
Heterogeneity: Tau^2=805.85; Chi^2=7.79, df=1(P=0.01); I^2=87.17%							
Test for overall effect: Z=0.7(P=0.49)							
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
Total ***	**348**		**266**			**100%**	**15.91[8.25,23.56]**
Heterogeneity: Tau^2=36.89; Chi^2=13.34, df=10(P=0.21); I^2=25.02%							
Test for overall effect: Z=4.07(P<0.0001)							
Test for subgroup differences: Chi^2=0, df=1 (P=0.98), I^2=0%							

15,91 (8,25-23,56)

Pas d'effet sur la Mortalité du iNO

Inhaled nitric oxide for acute respiratory distress syndrome (ARDS) in children and adults (Review)

Gebistorf F, Karam O, Wetterslev J, Afshari A 2016

Cochrane Library
Cochrane Database of Systematic Reviews

Study or subgroup	INO n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Dellinger 1998	35/120	17/57		10.18%	0.98[0.6,1.59]
Dobyns 1999	22/53	24/55		10.41%	0.95[0.61,1.47]
Gerlach 2003	3/20	4/20		1.77%	0.75[0.19,2.93]
Lundin 1999	48/93	38/87		17.35%	1.18[0.87,1.61]
Mehta 2001	4/8	3/6		1.51%	1[0.35,2.88]
Michael 1998	11/20	9/20		3.98%	1.22[0.65,2.29]
Park 2003	8/17	2/6		1.31%	1.41[0.41,4.87]
Payen 1999	53/98	53/105		22.61%	1.07[0.82,1.39]
Schwebel 1997	0/9	0/10			Not estimable
Taylor 2004	54/165	53/167		23.27%	1.03[0.75,1.41]
Troncy 1998	9/15	8/15		3.53%	1.13[0.6,2.11]
Total (95% CI)	**654**	**589**		**100%**	**1,04 (0,9 – 1,19)**

Total events: 250 (INO), 221 (Control)

Heterogeneity: $Tau^2=0$; $Chi^2=4.92$, df=11(P=0.93); $I^2=0\%$

Test for overall effect: Z=0.48(P=0.63)

Favours experimental 0.01 0.1 1 10 100 Favours control

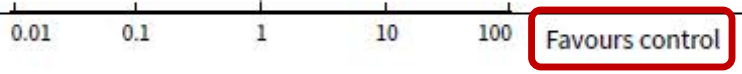
Toxicité rénale du iNO

Cochrane Library 2016

Cochrane Database of Systematic Reviews

Analysis 4.1. Comparison 4 Complications during the in-patient stay: INO versus control, Outcome 1 Renal impairment: INO vs control.

Study or subgroup	INO n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
4.1.1 Trials with overall high risk of bias					
Lundin 1999	28/93	12/87		23.41%	2.18[1.19,4.02]
Subtotal (95% CI)	**93**	**87**		**23.41%**	**2.18[1.19,4.02]**
Total events: 28 (INO), 12 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.51(P=0.01)					
4.1.2 Trials with overall low risk of bias					
Dellinger 1998	20/120	7/57		17.92%	1.36[0.61,3.02]
Payen 1999	33/98	26/105		47.38%	1.36[0.88,2.1]
Taylor 2004	10/192	6/193		11.3%	1.68[0.62,4.52]
Subtotal (95% CI)	**410**	**355**		**76.59%**	**1.41[0.98,2.01]**
Total events: 63 (INO), 39 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.15, df=2(P=0.93); I^2=0%					
Test for overall effect: Z=1.86(P=0.06)					
Total (95% CI)	**503**	**442**		**100%**	**1.59[1.17,2.16]**
Total events: 91 (INO), 51 (Control)					
Heterogeneity: Tau^2=0; Chi^2=1.69, df=3(P=0.64); I^2=0%					
Test for overall effect: Z=2.94(P=0)					
Test for subgroup differences: Chi^2=1.48, df=1 (P=0.22), I^2=32.64%					



Journal of Clinical Medicine 2022 MDPI

Brief Report

Impact of Dexamethasone and Inhaled Nitric Oxide on Severe Acute Kidney Injury in Critically Ill Patients with COVID-19

Mickaël Bobot [1,2,3,*], David Tonon [4], Noémie Peres [3], Christophe Guervilly [3], Flora Lefèvre [1], Howard Max [5], Youri Bommel [5], Maxime Volff [5], Marc Leone [6], Alexandre Lopez [6], Pierre Simeone [5,7], Julien Carvelli [8], Sophie Chopinet [9,10], Sami Hraiech [3], Laurent Papazian [3], Lionel Velly [5,7], Jérémy Bourenne [8] and Jean-Marie Forel [3] on behalf of the GRAM+ (Groupe de Recherche en Réanimation et Anesthésie deMarseille)

Durée médiane de NOi 6 jours

Analyse multivariée facteurs associés de survenue d'IRA KDIGO 3 SDRA COVID

Traitement	Odds ratio	P value
IEC	4.238 (1.307–13.736)	0.016
DV	0.234 (0.057–0.967)	0.045
NOi	**5.694 (1.953–16.606)**	**0.001**
Dexamethasone	0.194 (0.053–0.713)	0.014

Al Sulaiman *et al. Critical Care* (2022) 26:304
https://doi.org/10.1186/s13054-022-04158-y

2022

Critical Care

RESEARCH Open Access

Evaluation of inhaled nitric oxide (iNO) treatment for moderate-to-severe ARDS in critically ill patients with COVID-19: a multicenter cohort study

Khalid Al Sulaiman[1,2,3,4,18*], Ghazwa B. Korayem[4], Ali F. Altebainawi[5], Shmeylan Al Harbi[1,2,3], Abdulrahman Alissa[6], Abdullah Alharthi[7], Raed Kensara[1,2,3], Amjaad Alfahed[4], Ramesh Vishwakarma[8], Hussain Al Haji[9], Naif Almohaimid[9], Omar Al Zumai[9], Fahad Alrubayan[3,10,11], Abdulmajid Asiri[3,10], Nasser Alkahtani[11], Abdulaziz Alolayan[11], Samiah Alsohimi[12,17], Nawal Melibari[16], Alaa Almagthali[12], Seba Aljahdali[16], Abeer A. Alenazi[13], Alawi S. Alsaeedi[3,10,11], Ghassan Al Ghamdi[3,10,11], Omar Al Faris[9], Joud Alqahtani[15], Jalal Al Qahtani[9], Khalid A. Alshammari[5], Khalil I. Alshammari[14] and Ohoud Aljuhani[16]

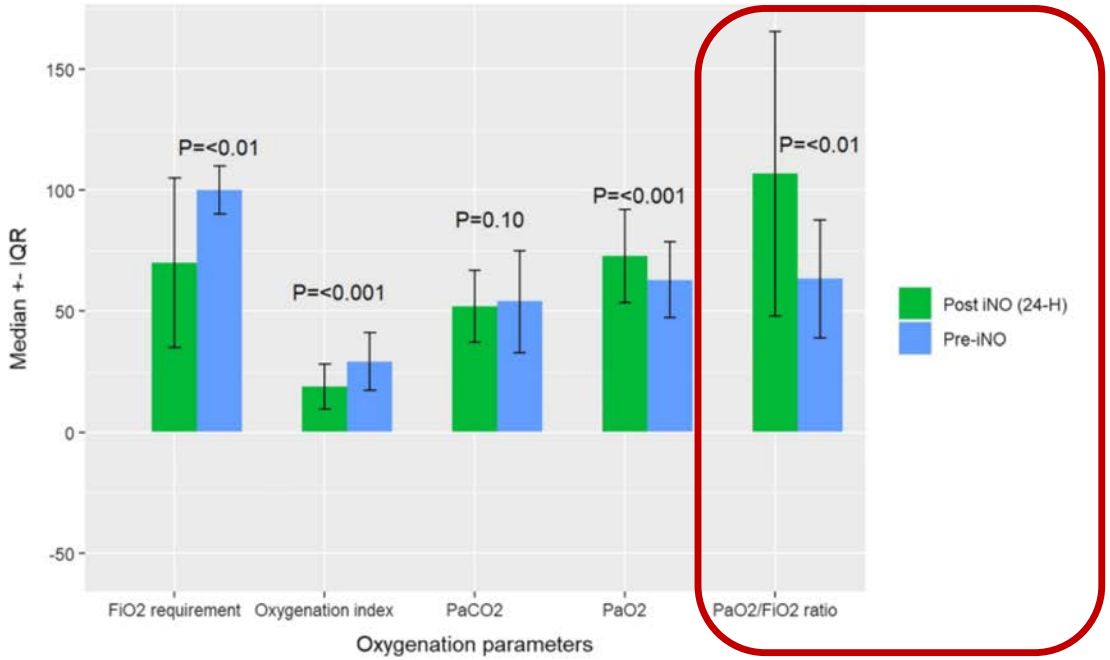


Fig. 2 Oxygenation parameters pre-and 24-h post inhaled nitric oxide administration

Table 2 The clinical outcomes of critically ill patients with COVID-19 after Propensity score matching

Outcomes	Number of outcomes/Total number of patients			Hazard Ratio (HR) (95%CI)	*p*-value$
	Control	iNO	*p*-value		
30-day mortality, *n* (%)Δ	44 (36.1)	41 (73.2)	< 0.0001^^	1.18 (0.77, 1.82)	0.45
In-hospital mortality, *n* (%)Δ	52 (41.6)	44 (78.6)	< 0.0001^^	1.40 (0.94, 2.11)	0.10
				Beta coefficient (estimates) (95%CI)	***p*-value $***
Ventilator-free days, mean (SD)	12.0 (11.23)	3.8 (7.38)	< 0.001*	− 1.17 (− 1.79, − 0.54)	< 0.001
ICU length of stay (days), median (Q1,Q3)∞	12.0 (8.0, 19.0)	26.0 (19.0, 35.5)	< 0.001^	0.63 (0.32, 0.95)	< 0.001
Hospital length of stay (days), median (Q1,Q3)∞	21.0 (13.0, 31.0)	36.0 (28.0, 65.5)	0.002^	0.45 (0.04, 0.87)	0.03

SDRA COVID – 19

Effet sur le PaO2/FiO2 à H24
Plus de VFD30
Pas d'effet sur la mortalité

Parameters	Control	iNO	OR (95% CI)	Pvalue
New onset A fib., n (%)	15/140 (10.7)	10/70 (14.3)	1.39 (0.58, 3.27)	0.45
Acute kidney injury, n(%)	57/140 (40.7)	43/70 (61.4)	2.35 (1.30, 4.26)	0.005
Liver injury, n(%)	9/140 (6.4)	13/70 (18.6)	3.32 (1.34, 8.22)	0.009
Venous/arterial thrombosis, n(%)	12/140 (8.6)	5/62 (7.9)	0.92 (0.31, 2.73)	0.88
Hospital/Ventilator acquired pneumonia, n(%)	43/140 (30.7)	41/70 (58.6)	3.2 (1.76, 5.83)	0.0001
Secondary fungal infection, n(%)	24/137 (17.5)	17/70 (24.3)	1.51 (0.75, 3.05)	0.25

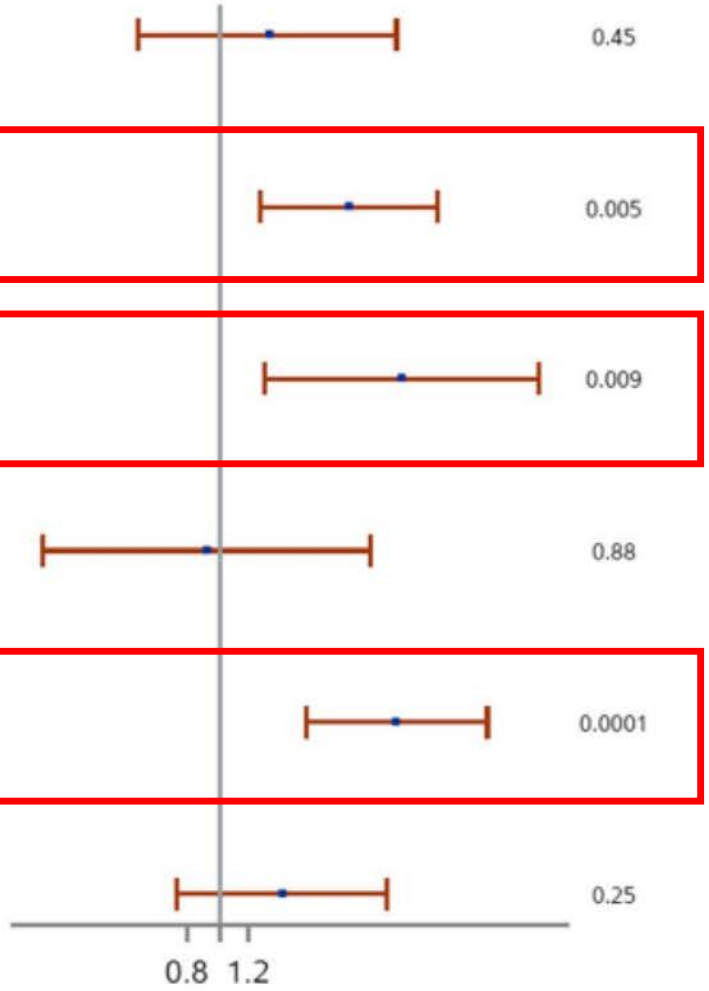


Fig. 3 Forest plot of the ICU-acquired complications during stay

Al Sulaiman *et al. Critical Care* (2022) 26:304
https://doi.org/10.1186/s13054-022-04158-y

Inh. Prostacyclines

Améliore le P/F

[Original Research **Critical Care**]

Study or Subgroup	Mean Difference	SE	Prostaglandin Total	No therapy Total	Weight	Mean Difference IV, Random, 95% CI	Year
Walmrath, 1993	53.5	6.9	3	3	7.0%	53.50 [39.98, 67.02]	1993
Pappert, 1995	15	4.7	3	3	7.3%	15.00 [5.79, 24.21]	1995
Walmrath, 1996	21	3.9	16	16	7.4%	21.00 [13.36, 28.64]	1996
Meyer, 1998	140	27.4	15	15	3.1%	140.00 [86.30, 193.70]	1998
van Heerden, 2000	15	4	9	9	7.4%	15.00 [7.16, 22.84]	2000
Domenighetti, 2001	2	5	15	15	7.3%	2.00 [-7.80, 11.80]	2001
Siobal, 2003	20	4.5	11	11	7.3%	20.00 [11.18, 28.82]	2003
Rovira, 2004	51	15.8	5	5	5.1%	51.00 [20.03, 81.97]	2004
Camamo, 2005	7.8	13	27	27	5.7%	7.80 [-17.68, 33.28]	2005
Raheem, 2009	48	8.3	15	15	6.7%	48.00 [31.73, 64.27]	2009
McMillen, 2011	26.2	14.1	4	4	5.5%	26.20 [-1.44, 53.84]	2011
Ross, 2012	68.4	11.7	12	12	6.0%	68.40 [45.47, 91.33]	2012
Pacheo, 2013	97.7	7.8	216	216	6.8%	97.70 [82.41, 112.99]	2013
Dunkley, 2013	50.7	24.4	16	16	3.5%	50.70 [2.88, 98.52]	2013
Torbic, 2013	33.3	7	32	32	7.0%	33.30 [19.58, 47.02]	2013
Singh, 2014	42.9	7.7	98	98	6.8%	42.90 [27.81, 57.99]	2014
Total (95% CI)			**497**	**497**	**100.0%**	**39.00 [26.68, 51.31]**	

Heterogeneity: Tau² = 518.51; Chi² = 188.60, df = 15 (P < 0.00001); I² = 92%
Test for overall effect: Z = 6.21 (P < 0.00001)

Mean Difference IV, Random, 95% CI

-100 -50 0 50 100
Favours no therapy Favours prostaglandin

The Use of Inhaled Prostaglandins in Patients With ARDS

A Systematic Review and Meta-analysis

Brian M. Fuller, MD, MSCI; Nicholas M. Mohr, MD; Lee Skrupky, Marin H. Kollef, MD, FCCP; and Christopher R. Carpenter, MD

CHEST 2015; 147(6):1510-1522

C

Study or Subgroup	Mean Difference	SE	Prostaglandin Total	No therapy Total	Weight	Mean Difference IV, Random, 95% CI	Year
Walmrath, 1993	-8.3	3.7	3	3	5.1%	-8.30 [-15.55, -1.05]	1993
zwissler, 1996	-7.1	0.7	8	8	15.7%	-7.10 [-8.47, -5.73]	1996
Walmrath, 1996	-3.1	0.6	16	16	16.1%	-3.10 [-4.28, -1.92]	1996
Putensen, 1998	-8	0.8	10	10	15.4%	-8.00 [-9.57, -6.43]	1998
Meyer, 1998	-6	1.1	15	15	14.1%	-6.00 [-8.16, -3.84]	1998
van Heerden, 2000	-1	0.3	9	9	16.8%	-1.00 [-1.59, -0.41]	2000
Domenighetti, 2001	-3	0.3	15	15	16.8%	-3.00 [-3.59, -2.41]	2001
Total (95% CI)			**76**	**76**	**100.0%**	**-4.79 [-6.75, -2.83]**	

Heterogeneity: Tau² = 5.87; Chi² = 127.05, df = 6 (P < 0.00001); I² = 95%
Test for overall effect: Z = 4.79 (P < 0.00001)

Mean Difference IV, Random, 95% CI

-100 -50 0 50 100
Favours prostaglandin Favours no therapy

Baisse les PAP

Inh. Prostacyclines

Cochrane Library

Cochrane Database of Systematic Reviews

Afshari A, Bastholm Bille A, Allingstrup M.
Aerosolized prostacyclins for acute respiratory distress syndrome (ARDS).
Cochrane Database of Systematic Reviews 2017, Issue 7. Art. No.: CD007733.
DOI: 10.1002/14651858.CD007733.pub3.

Aerosolized prostacyclin for acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) (Review)

2017

Afshari A, Brok J, Møller AM, Wetterslev J

Pas d'effet sur la mortalité

Mortality for Acute lung injury (ALI) and acute respiratory distress syndrome (ARDS)

Patient or population: patients with Acute lung injury (ALI) and acute respiratory distress syndrome (ARDS)
Settings: Critical Care
Intervention: Mortality

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Control	Mortality			
28 days mortality, paediatric, low bias trial	Study population		RR 1.5 (0.17 to 12.94)	14 (1 study)	⊕⊕⊖⊖ low [1,2,3,4]
	167 per 1000	251 per 1000 (28 to 1000)			

Recommandation iNO SRLF SDRA 2019

R7.1 – Les experts suggèrent que le NO inhalé puisse être utilisé en cas de SDRA avec hypoxémie profonde malgré l'implémentation d'une stratégie de ventilation protectrice et mise en décubitus ventral et avant d'envisager le recours à l'ECMO veino-veineuse.

NO inhalé

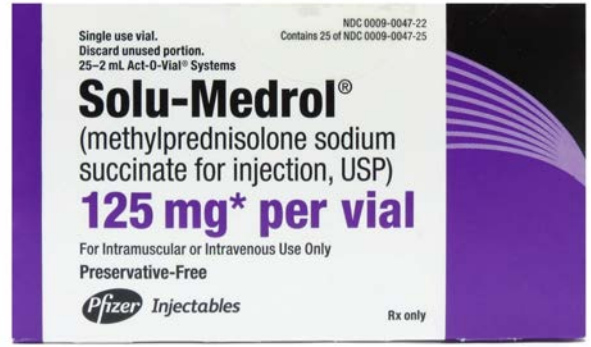
HYPOXÉMIE RÉFRACTAIRE EN DV

- Avant l'ECMO

- Attention au rein

- Limiter la durée

Corticoïdes



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

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

Lancet Respir Med 2020

Published online February 7, 2020 https://doi.org/10.1016/S2213-2600(19)30417-5

AVANT COVID

DEXA-ARDS

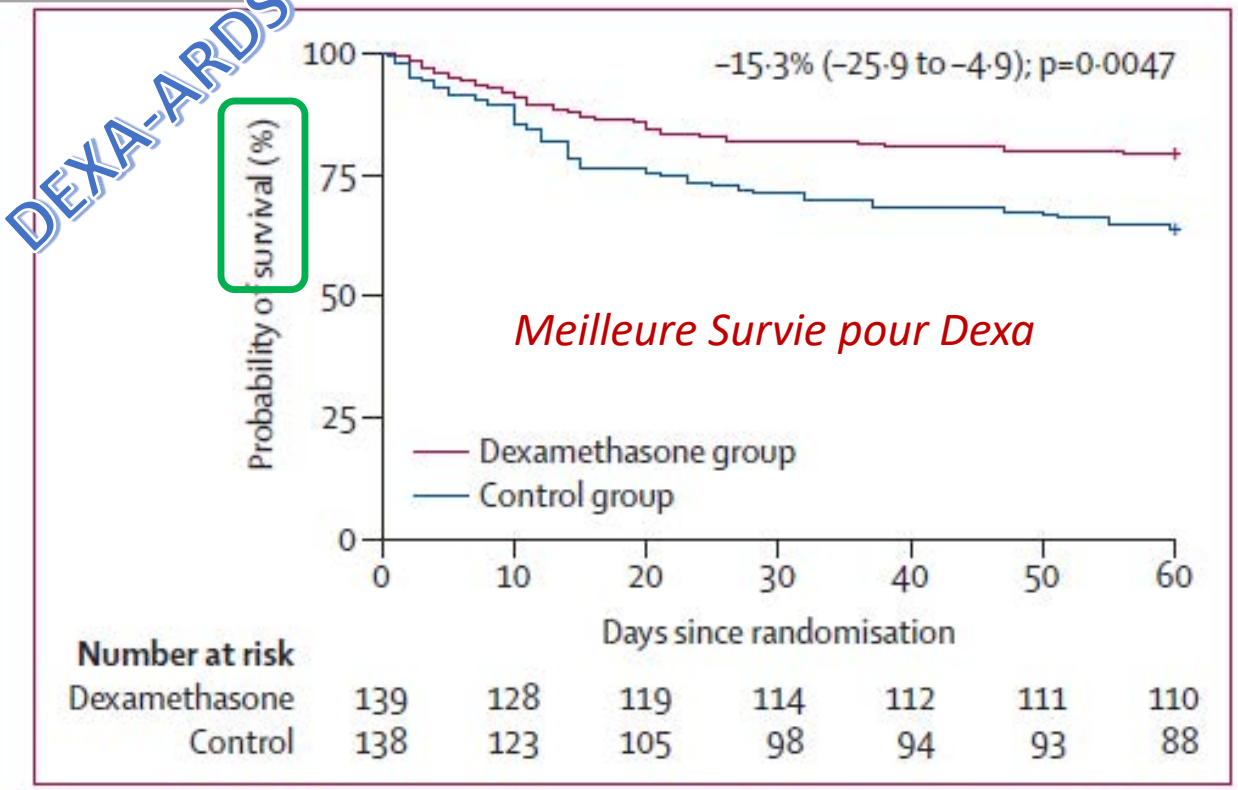


Figure 2: Kaplan-Meier survival estimates during the first 60 days of trial

Dexamethasone in Hospitalized Patients with Covid-19 — Preliminary Report

The RECOVERY Collaborative Group*

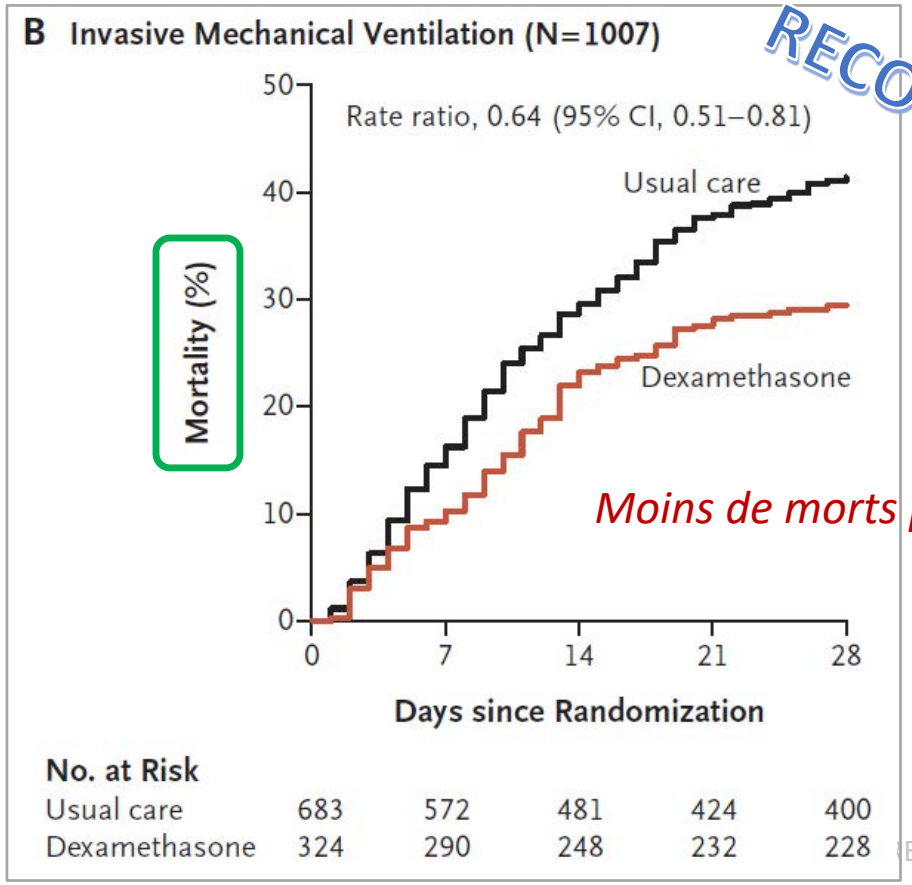
The NEW ENGLAND JOURNAL of MEDICINE

This article was published on July 17, 2020, at NEJM.org.

DOI: 10.1056/NEJMoa2021436

PENDANT COVID

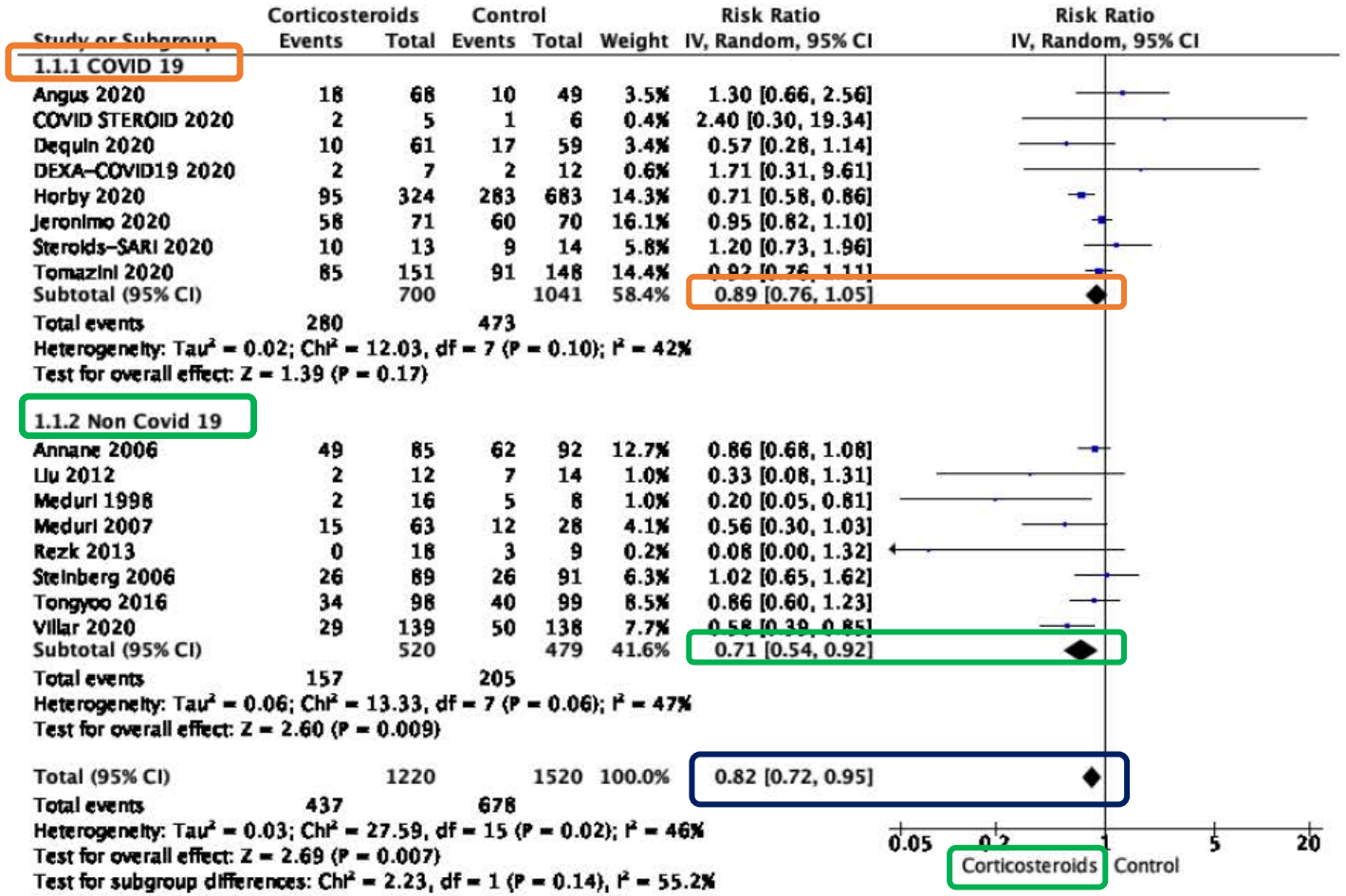
RECOVERY



Corticoïdes + SDRA = Moins de mort

Moderate certainty

Forest plot: Corticosteroids versus placebo or no corticosteroids in patients with ARDS. Grouped by COVID-19 Status. 28 day Mortality.
Df = degrees of freedom



SDRA COVID 19
RR 0,89 (0,76-1,05)

SDRA NON COVID 19
RR 0,71 (0,54-0,92)

SDRA TOUS
RR 0,82 (0,72-0,95)

2024 Focused Update: Guidelines on Use of Corticosteroids in Sepsis, Acute Respiratory Distress Syndrome, and Community-Acquired Pneumonia

Chaudhuri D et al. Crit Care Med. 2024 May 1;52(5):e219-e233
doi: 10.1097/CCM.0000000000006172.

Corticoïdes + SDRA = Moins de mort

Moderate certainty

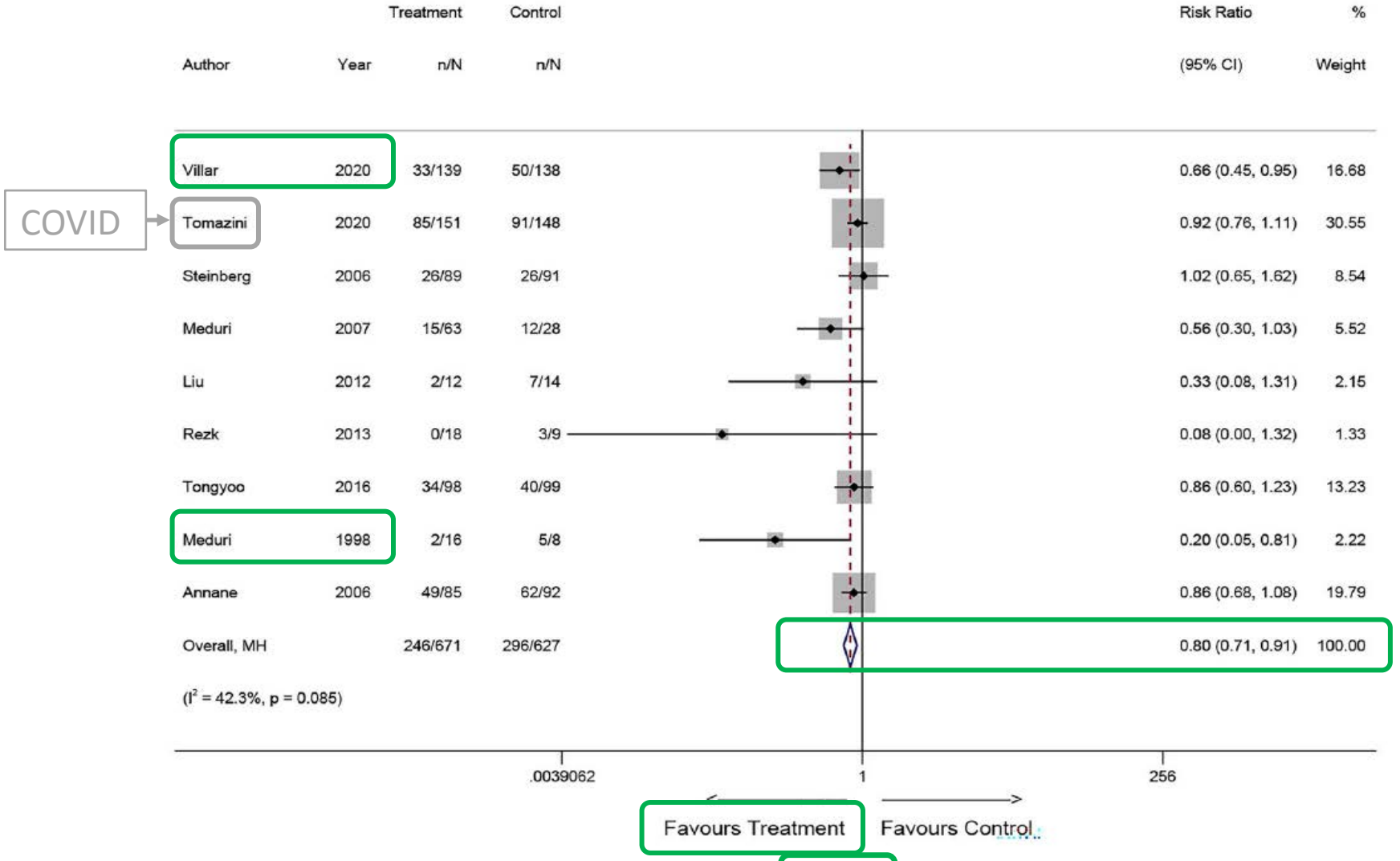


Figure 2. Forest plot illustrating the effects of corticosteroids on mortality of patients with ARDS in RCTs.

SDRA (70% NON COVID 19)
RR 0,80 (0,71-0,91)

Efficacy of corticosteroids in patients with acute respiratory distress syndrome: a meta-analysis

Guowei Li, Dunfan Chen, Feng Gao, Wei Huang, Jin Wang, Yonglin Li, Baijian Chen, Yuejia Zhong, Rui Chen and Manhua Huang

ANNALS OF MEDICINE
2024, VOL. 56, NO. 1, 2381086
https://doi.org/10.1080/07853890.2024.2381086

Corticoïdes + SDRA = Sevré plus vite

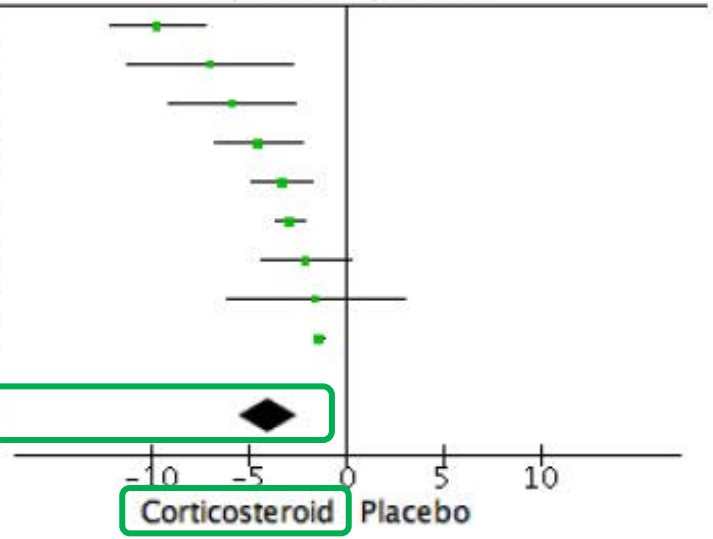
Low certainty

Forest plot: Corticosteroids versus placebo or no corticosteroids in all patients with ARDS (COVID-19 and non-COVID-19). Duration of mechanical ventilation Df = degrees of freedom

	Corticosteroids			Control				Mean Difference	Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**	**IV, Random, 95% CI**
Rezk 2013	10.56	4.61	18	20.33	1.86	9	11.0%	-9.77 [-12.22, -7.32]	
Steinberg 2006	11	11.85	89	18	17	91	6.8%	-7.00 [-11.27, -2.73]	
Villar 2020	14.3	13.3	139	20.2	14	138	9.0%	-5.90 [-9.12, -2.68]	
Meduri 2007	5	3.7	63	9.5	10	91	11.5%	-4.50 [-6.75, -2.25]	
Zhifang 2016	5.6	2.7	20	8.9	2.3	20	13.4%	-3.30 [-4.85, -1.75]	
Zhou 2014	4.21	1.18	23	7.11	1.51	23	15.0%	-2.90 [-3.68, -2.12]	
Tongyoo 2016	11.8	7.8	98	13.9	9	99	11.3%	-2.10 [-4.45, 0.25]	
Steroids-SARI 2020	8.8	5.9	13	10.4	6.2	14	6.3%	-1.60 [-6.16, 2.96]	
Tomazini 2020	12.5	1.3	151	13.9	1.2	148	15.6%	-1.40 [-1.68, -1.12]	
Total (95% CI)			**614**			**633**	**100.0%**	**-4.04 [-5.53, -2.55]**	

Heterogeneity: $Tau^2 = 3.68$; $Chi^2 = 76.93$, df = 8 ($P < 0.00001$); $I^2 = 90\%$

Test for overall effect: $Z = 5.32$ ($P < 0.00001$)

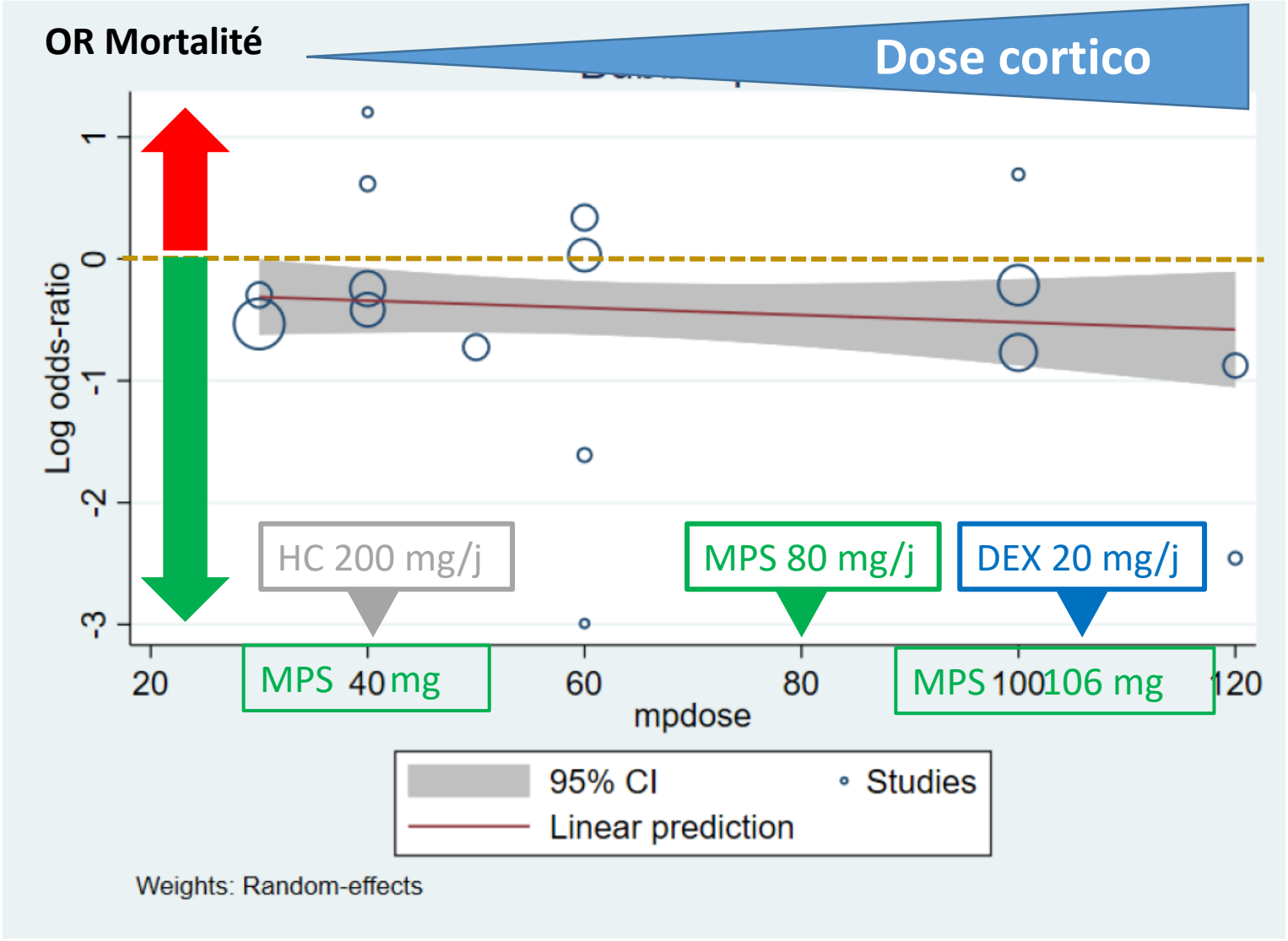


2024 Focused Update: Guidelines on Use of Corticosteroids in Sepsis, Acute Respiratory Distress Syndrome, and Community-Acquired Pneumonia

Chaudhuri D et al. Crit Care Med. 2024 May 1;52(5):e219-e233
doi: 10.1097/CCM.0000000000006172.

Quelle dose ?

Metaregression for mortality based on average daily steroid dose. CI = confidence interval



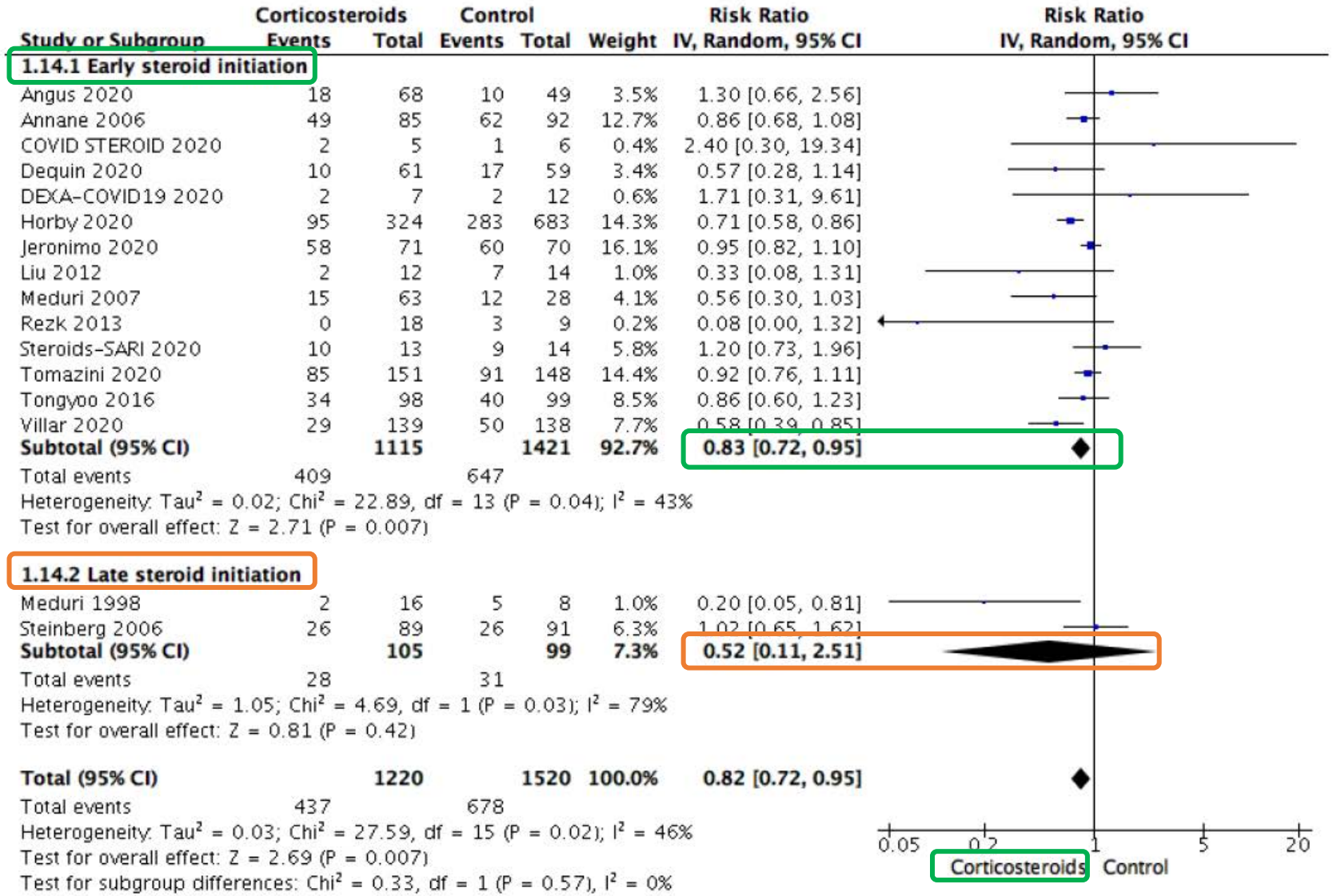
0,5 à 1,5 mg/Kg
d'Eq. Methylprednisolone

2024 Focused Update: Guidelines on Use of Corticosteroids in Sepsis, Acute Respiratory Distress Syndrome, and Community-Acquired Pneumonia

Chaudhuri D et al. Crit Care Med. 2024

Quand = Tôt (1-7 premiers jours du SDRA)

Forest Plot: Effect of corticosteroids on mortality. Studies are grouped by steroid initiation time. Df = degrees of freedom.



Study or Subgroup	Corticosteroids Events	Total	Control Events	Total	Weight	Risk Ratio IV, Random, 95% CI
1.14.1 Early steroid initiation						
Angus 2020	18	68	10	49	3.5%	1.30 [0.66, 2.56]
Annane 2006	49	85	62	92	12.7%	0.86 [0.68, 1.08]
COVID STEROID 2020	2	5	1	6	0.4%	2.40 [0.30, 19.34]
Dequin 2020	10	61	17	59	3.4%	0.57 [0.28, 1.14]
DEXA-COVID19 2020	2	7	2	12	0.6%	1.71 [0.31, 9.61]
Horby 2020	95	324	283	683	14.3%	0.71 [0.58, 0.86]
Jeronimo 2020	58	71	60	70	16.1%	0.95 [0.82, 1.10]
Liu 2012	2	12	7	14	1.0%	0.33 [0.08, 1.31]
Meduri 2007	15	63	12	28	4.1%	0.56 [0.30, 1.03]
Rezk 2013	0	18	3	9	0.2%	0.08 [0.00, 1.32]
Steroids-SARI 2020	10	13	9	14	5.8%	1.20 [0.73, 1.96]
Tomazini 2020	85	151	91	148	14.4%	0.92 [0.76, 1.11]
Tongyoo 2016	34	98	40	99	8.5%	0.86 [0.60, 1.23]
Villar 2020	29	139	50	138	7.7%	0.58 [0.39, 0.85]
Subtotal (95% CI)		**1115**		**1421**	**92.7%**	**0.83 [0.72, 0.95]**
Total events	409		647			
Heterogeneity: Tau² = 0.02; Chi² = 22.89, df = 13 (P = 0.04); I² = 43%						
Test for overall effect: Z = 2.71 (P = 0.007)						
1.14.2 Late steroid initiation						
Meduri 1998	2	16	5	8	1.0%	0.20 [0.05, 0.81]
Steinberg 2006	26	89	26	91	6.3%	1.02 [0.65, 1.62]
Subtotal (95% CI)		**105**		**99**	**7.3%**	**0.52 [0.11, 2.51]**
Total events	28		31			
Heterogeneity: Tau² = 1.05; Chi² = 4.69, df = 1 (P = 0.03); I² = 79%						
Test for overall effect: Z = 0.81 (P = 0.42)						
Total (95% CI)		**1220**		**1520**	**100.0%**	**0.82 [0.72, 0.95]**
Total events	437		678			
Heterogeneity: Tau² = 0.03; Chi² = 27.59, df = 15 (P = 0.02); I² = 46%						
Test for overall effect: Z = 2.69 (P = 0.007)						
Test for subgroup differences: Chi² = 0.33, df = 1 (P = 0.57), I² = 0%						

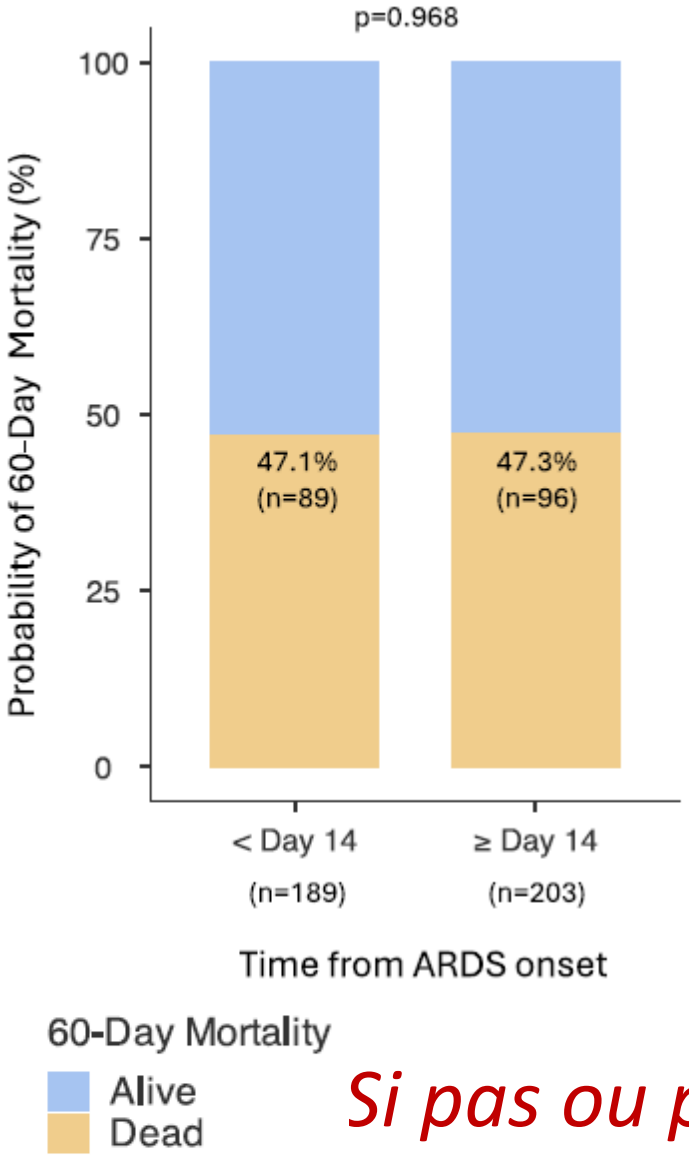
< J7

≥ J7

2024 Focused Update: Guidelines on Use of Corticosteroids in Sepsis, Acute Respiratory Distress Syndrome, and Community-Acquired Pneumonia

Chaudhuri D et al. Crit Care Med. 2024

Dangereux après J14 ?



Early versus late 2 mg/kg methylprednisolone therapy in ARDS

Justine Verchère[1,10]✉, Damien Barrau[1,8,10], Jonathan Chelly[2], Julien Carvelli[3,8,10], Lionel Velly[4,10], Nicolas Bruder[5,10], David Lagier[6,10], Antoine Bianchi[7,10], Christophe Guervilly[1,8,10], Anderson Loundou[8,9], Noémie Peres[2] & Jean-Marie Forel[1,8,10]

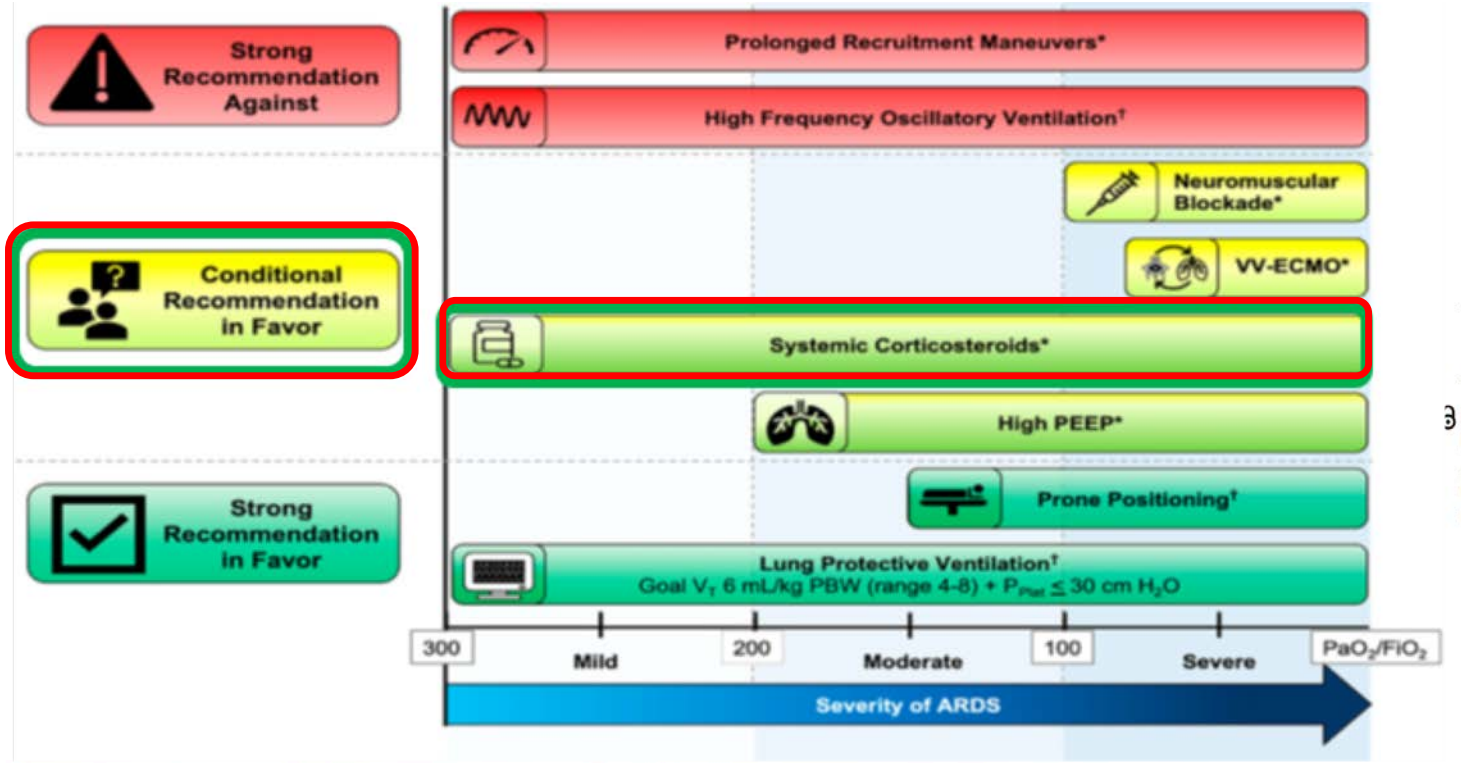
Scientific Reports | (2025) 15:38167

	Alive (n = 188)	Dead (n = 204)	Univariate *p* value	Odd ratio	Multivariate *p* value	VIF
Age (years)	59 (± 11)	64 (± 11)	< 0.001	1.05 [1.03–1.08]	< 0.001	1.52
Chronic cardiac insufficiency	21 (11.2%)	36 (17.6%)	0.069	1.16 [0.61–2.22]	0.66	1.10
Hypertension	77 (41%)	100 (49%)	0.109	0.97 [0.60–1.56]	0.90	1.21
Diabetes	43 (22.9%)	63 (30.9%)	0.074	1.32 [0.78–2.25]	0.31	1.18
Chronic immune suppression	33 (17.6%)	63 (30.9%)	0.002	2.39 [1.39–4.11]	0.002	1.08
COVID-19 ARDS	164 (87.2%)	168 (82.4%)	0.180	0.85 [0.44–1.64]	0.62	1.14
SAPS II at admission	38 (± 12)	42 (± 13)	0.003	1.01 [0.99–1.03]	0.54	1.29
ECMO	68 (36.2%)	80 (39.2%)	0.534	1.45 [0.83–2.51]	0.19	1.49
Septic shock	70 (37.2.5%)	130 (63.7%)	< 0.001	3.33 [2.10–5.27]	< 0.001	1.12
2 mg/kg MTP initiation < day 14 from ARDS onset	91 (48.4%)	98 (48%)	0.942	1.08 [0.69–1.71]	0.73	1.09

Table 3. Variables associated with 6-month mortality: univariate and multivariate analysis. Results are

85 % SDRA COVID – 19

Si pas ou peu de corticoïdes avant J14, pas trop tard après J14



An Update on Management of Adult Patients with Acute Respiratory Distress Syndrome

An Official American Thoracic Society Clinical Practice Guideline

Nida Qadir*, Sarina Sahetya*, Laveena Munshi*, Charlotte Summers*, Darryl Abrams, Jeremy Beitler, Giacomo Bellani, Roy G. Brower, Lisa Burry, Jen-Ting Chen, Carol Hodgson, Catherine L. Hough, Francois Lamontagne, Anica Law, Laurent Papazian, Tai Pham, Eileen Rubin, Matthew Siuba, Irene Telias, Setu Patolia, Dipayan Chaudhuri, Allan Walkey‡, Bram Rochwerg‡, and Eddy Fan‡; on behalf of the American Thoracic Society Assembly on Critical Care

Intervention	Population	Precautions	Practical considerations
Corticosteroids	$PaO_2/FiO_2 \leq 300$	• May be associated with increased risk of harm when initiated after > 14 days of mechanical ventilation • Monitor more closely for adverse effects in patients with immunosuppressed conditions, metabolic syndrome, or known or increased risk of fungal, parasitic, or mycobacterial infections	• Optimal regimen, including type of corticosteroid, is unknown • For patients with corticosteroid-responsive etiologies, regimen should be tailored to the specific condition • For other patients, regimens used in prior RCTs may be used • For patients that improve rapidly, consider discontinuation at time of extubation

American Journal of Respiratory and Critical Care Medicine Volume 209 Number 1 | January 1 2024

2024 Focused Update: Guidelines on Use of Corticosteroids in Sepsis, Acute Respiratory Distress Syndrome, and Community-Acquired Pneumonia

Chaudhuri D et al. Crit Care Med. 2024 May 1;52(5):e219-e233
doi: 10.1097/CCM.0000000000006172.

Summary of Recommendations[a]

Recommendation 2024	Recommendation Strength, Quality of Evidence
Acute respiratory distress syndrome	
2A. We "suggest" administering corticosteroids to adult hospitalized patients with acute respiratory distress syndrome	Conditional recommendation, moderate certainty evidence

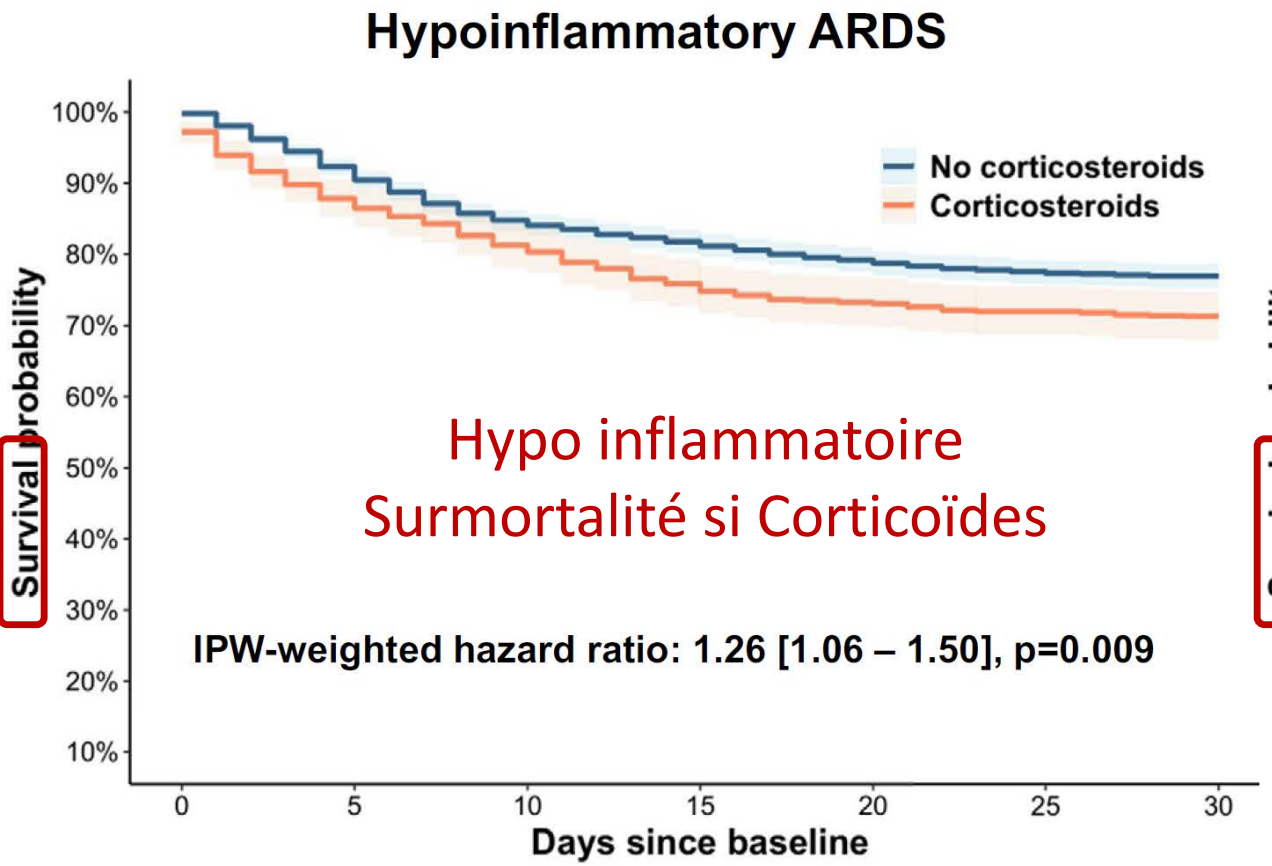
Corticoïdes **Phénotypes** SDRA Hyper vs. Hypo inflammatoires

Intensive Care Med
https://doi.org/10.1007/s00134-025-08089-4

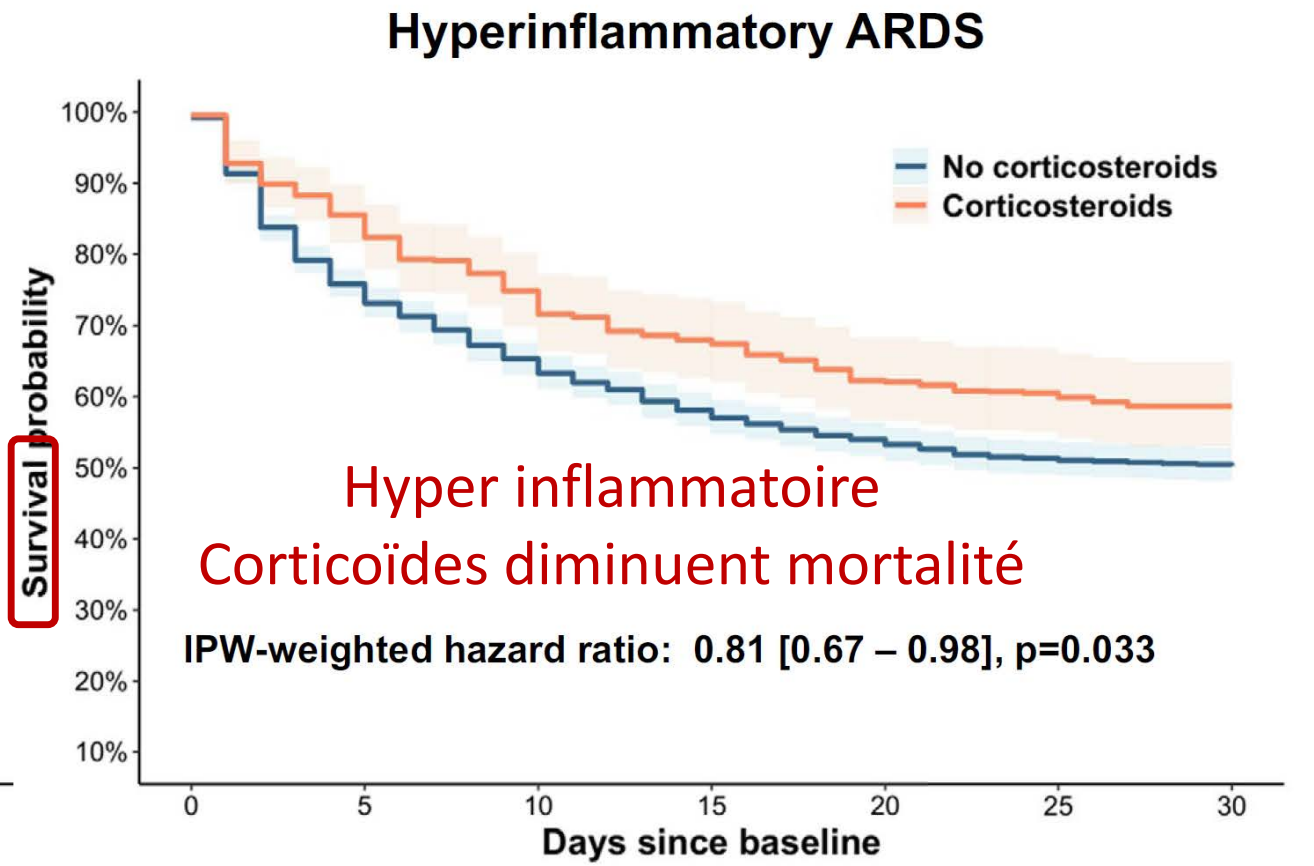
2025

Temporal stability of phenotypes of acute respiratory distress syndrome: clinical implications for early corticosteroid therapy and mortality

Joris Pensier[1,2], Maxime Fosset[2,3], Béla-Simon Paschold[2], Dario von Wedel[2,4], Simone Redaelli[2], Ben L. P. Braeuer[2], Victor Novack[5], Felix Balzer[4], Boris Jung[2,3,6], Marcelo B. P. Amato[7], Samir Jaber[1], Daniel Talmor[2], Elias Baedorf-Kassis[2,6] and Maximilian S. Schaefer[2,8*]



Hypo inflammatoire
Surmortalité si Corticoïdes

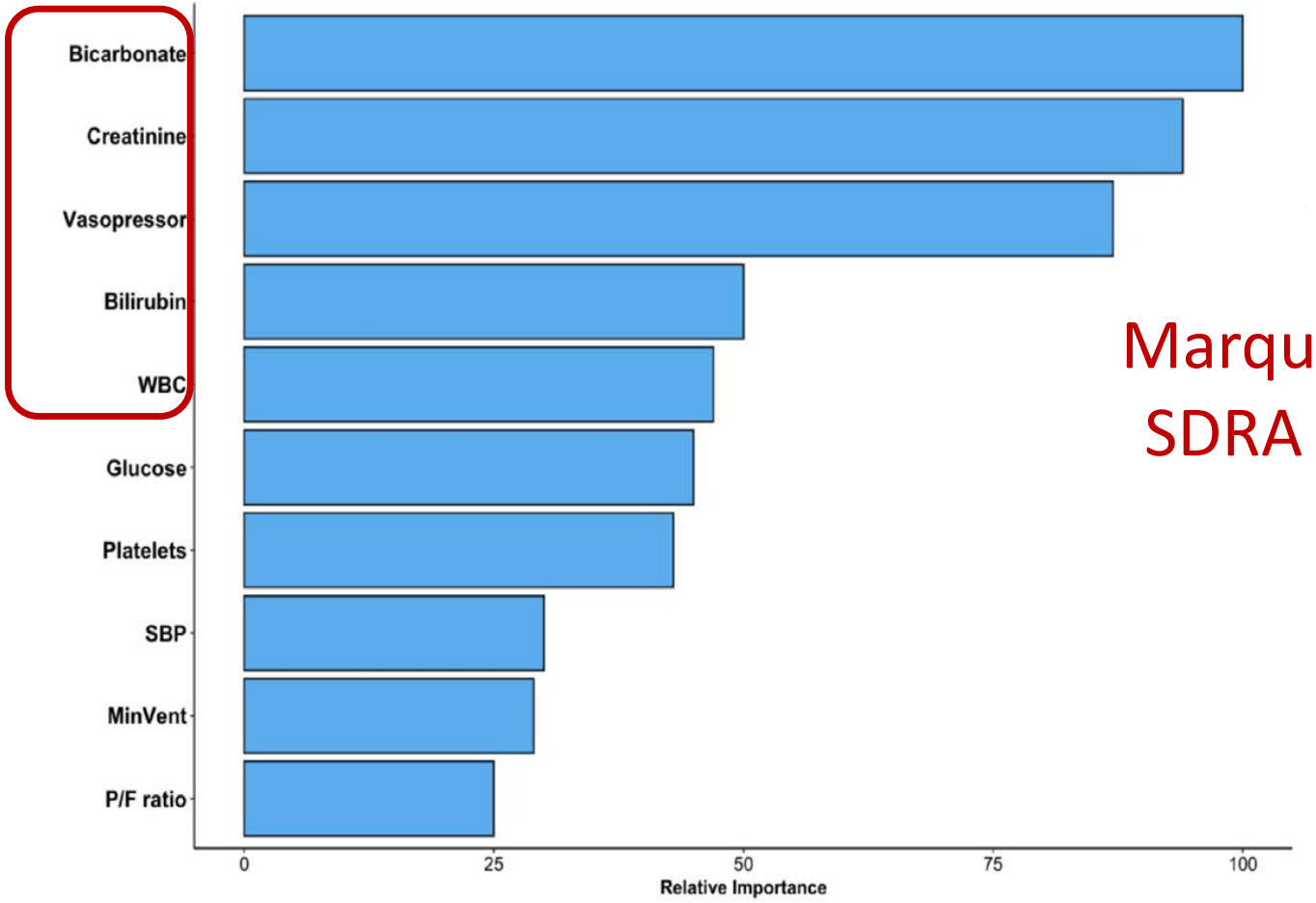


Hyper inflammatoire
Corticoïdes diminuent mortalité

Temporal stability of phenotypes of acute respiratory distress syndrome: clinical implications for early corticosteroid therapy and mortality

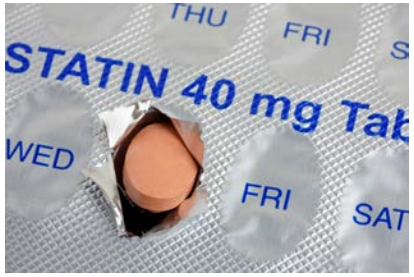
Intensive Care Med
https://doi.org/10.1007/s00134-025-08089-4

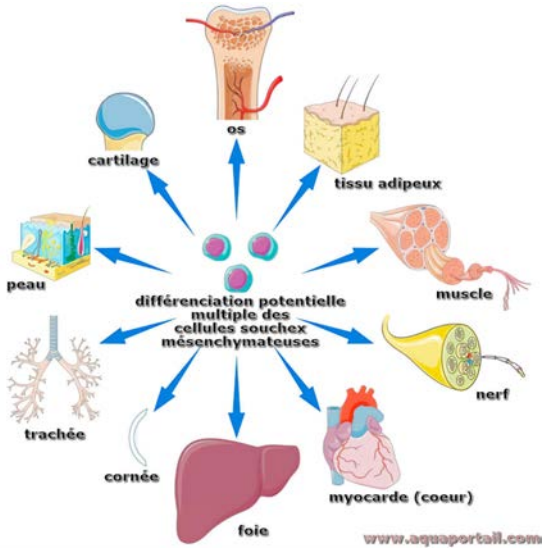
Joris Pensier[1,2], Maxime Fosset[2,3], Béla-Simon Paschold[2], Dario von Wedel[2,4], Simone Redaelli[2], Ben L. P. Braeuer[2], Victor Novack[5], Felix Balzer[4], Boris Jung[2,3,6], Marcelo B. P. Amato[7], Samir Jaber[1], Daniel Talmor[2], Elias Baedorf-Kassis[2,6] and Maximilian S. Schaefer[2,8*]



Marqueurs « cliniques » du SDRA Hyperinflammatoire

Innovations et ...





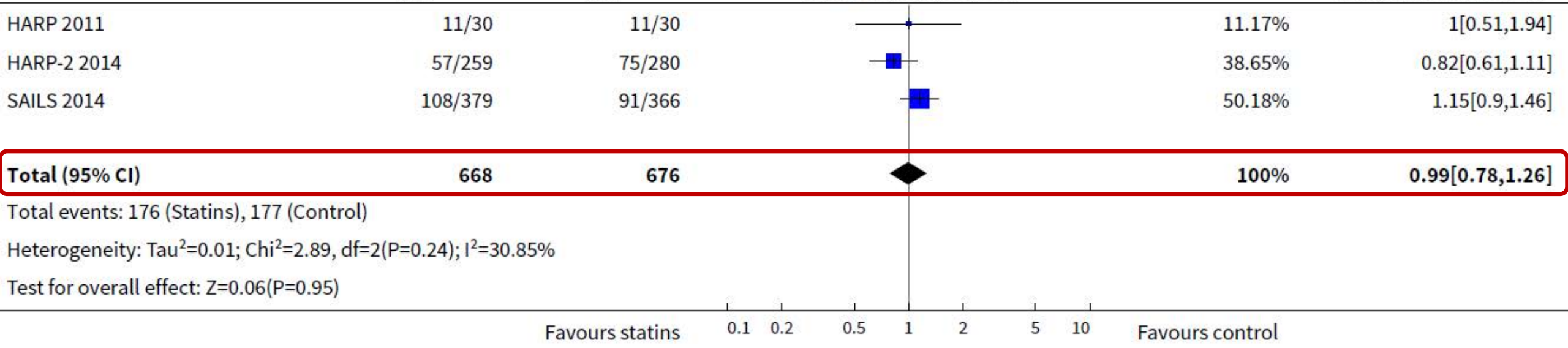
Statines

2019

Pharmacological agents for adults with acute respiratory distress syndrome (Review)

Pas d'effet sur la survie

Analysis 3.1. Comparison 3 Statins versus control, Outcome 1 Early mortality.



Study or subgroup	Statins n/N	Control n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
HARP 2011	11/30	11/30		11.17%	1[0.51,1.94]
HARP-2 2014	57/259	75/280		38.65%	0.82[0.61,1.11]
SAILS 2014	108/379	91/366		50.18%	1.15[0.9,1.46]
Total (95% CI)	**668**	**676**		**100%**	**0.99[0.78,1.26]**

Total events: 176 (Statins), 177 (Control)

Heterogeneity: Tau^2=0.01; Chi^2=2.89, df=2(P=0.24); I^2=30.85%

Test for overall effect: Z=0.06(P=0.95)

Lewis SR, Pritchard MW, Thomas CM, Smith AF.
Pharmacological agents for adults with acute respiratory distress syndrome.
Cochrane Database of Systematic Reviews 2019, Issue 7. Art. No.: CD004477.
DOI: 10.1002/14651858.CD004477.pub3.

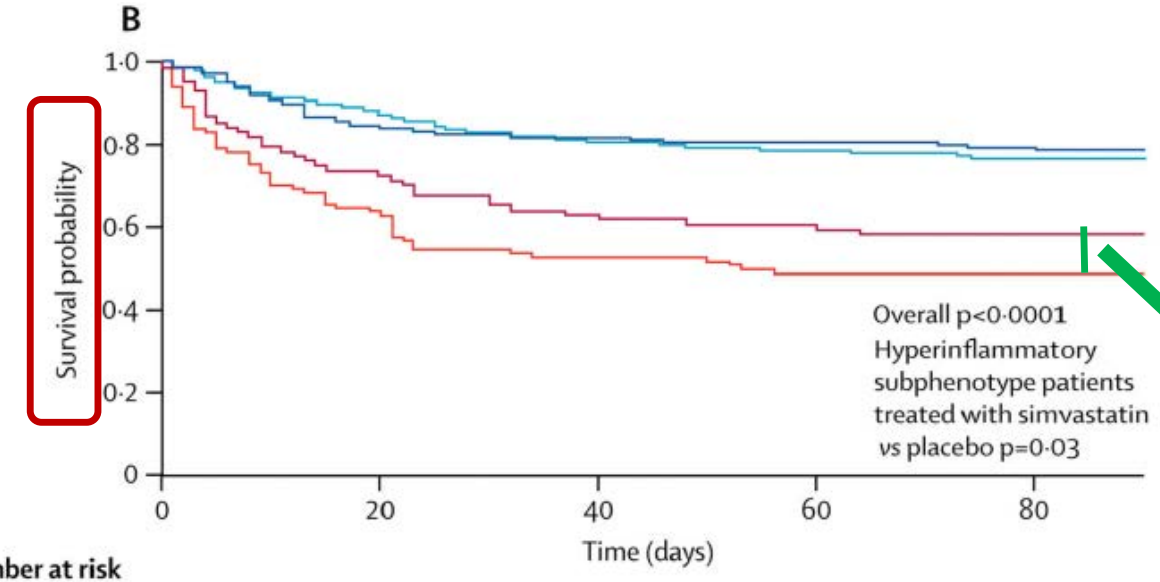
Cochrane Library
Cochrane Database of Systematic Reviews

Statines
Post hoc HARP2 2018

Lancet Respir Med. 2018 September ; 6(9): 691–698. doi:10.1016/S2213-2600(18)30177-2.

ARDS Subphenotypes and Differential Response to Simvastatin: Secondary Analysis of a Randomized Controlled Trial

Carolyn S. Calfee, MD[1,2,3], Kevin L. Delucchi, PhD[4] [Professor], Pratik Sinha, PhD[1], Michael A. Matthay, MD[1,2,3] [Professor], Jonathan Hackett, MBBCh[5], Manu Shankar-Hari, PhD[6,7], Cliona McDowell, MSc[8], John G. Laffey, MD[9,10,11] [Professor], Cecilia M. O'Kane, PhD[5], Daniel F. McAuley, MD[5,12] [Professor], and Irish Critical Care Trials Group



Number at risk					
Hypoinflammatory subphenotype, placebo	178	157	144	140	137
Hypoinflammatory subphenotype, simvastatin	175	148	143	141	139
Hyperinflammatory subphenotype, simvastatin	84	62	53	51	49
Hyperinflammatory subphenotype placebo	102	65	54	50	50

Hypoinflammatory subphenotype, placebo
Hypoinflammatory subphenotype, simvastatin
Hyperinflammatory subphenotype, simvastatin
Hyperinflammatory subphenotype, placebo

P = 0.03

Meilleure survie avec simvastatine SI SDRA HYPERINFLAMMATOIRE

Figure 2:
Kaplan-Meier survival curves to 28 days (Figure 3A) and 90 days (Figure 3B) for patients in HARP-2, stratified by ARDS subphenotype and treatment (simvastatin vs placebo).

Héparine (aérosol) 2021

	Heparin group (n=128)	Placebo group (n=124)	Effect estimate (95% CI)	p value
Primary outcome				
SF-36 physical function score of survivors at day 60*	53·6 (31·6); n=97	48·7 (35·7); n=94	MD 4·9 (−4·8 to 14·5)	0·32
Secondary outcomes				
Day 5				
Developed new ARDS†	9 (15%); n=62	21 (30%); n=71	HR 0·46 (0·22 to 0·98)	0·0431
Deterioration in Murray Lung Injury Score‡	−0·05 (0·49); n=124	0·09 (0·48); n=123	MD −0·14 (−0·26 to −0·02)	0·0215
Day 28				
New respiratory therapies				
Neuromuscular blocker	16 (24%); n=67	18 (29%); n=63	OR 0·78 (0·36 to 1·72)	0·54
Recruitment manoeuvre	14 (12%); n=115	10 (9%); n=114	OR 1·44 (0·61 to 3·39)	0·40
Nitric oxide or nebulised prostacyclin	7 (6%); n=117	10 (9%); n=114	OR 0·66 (0·24 to 1·80)	0·42
Prone positioning	3 (2%); n=127	3 (2%); n=122	OR 0·96 (0·19 to 4·85)	0·96
ECMO	0	1 (1%)	OR 0·97 (0 to 37·78)	0·98
Tracheotomy	13 (10%)	22 (18%)	OR 0·52 (0·25 to 1·09)	0·09
Time to ventilator separation, days§	9·9 (9·8)	10·2 (10·1); n=123	HR 1·01 (0·77 to 1·33)	0·92
Time to ventilator separation of survivors, days	6·0 (5·5); n=106	7·5 (7·8); n=107	HR 1·23 (0·93 to 1·62)	0·14
Time to ICU separation, days§	11·9 (9·3)	12·6 (9·7); n=123	HR 1·08 (0·82 to 1·42)	0·59
Time to ICU separation of survivors, days	8·5 (6·0); n=106	10·2 (8·1); n=107	HR 1·31 (0·99 to 1·74)	0·06
ICU readmission¶	1 (1%); n=103	9 (9%); n=101	OR 0·10 (0·01 to 0·81)	0·0306
Deceased	22 (17%)	16 (13%); n=123	OR 1·39 (0·69 to 2·79)	0·36
Day 60				
Survivors residing at home	86 (87%); n=99	73 (73%); n=100	OR 2·45 (1·18 to 5·08)	0·0165
Place of residence				
Home	86 (70%); n=122	73 (62%); n=118	OR 1·47 (0·86 to 2·52)	0·16
Rehabilitation	4 (3%); n=122	11 (9%); n=118	OR 0·33 (0·10 to 1·07)	0·06
Hospital ward	9 (7%); n=122	11 (9%); n=118	OR 0·77 (0·31 to 1·94)	0·59
ICU or long-term ventilation	0; n=122	5 (4%); n=118	OR 0·14 (0 to 1·04)	0·06
Deceased	23 (18%); n=127	18 (15%); n=123	OR 1·29 (0·66 to 2·53)	0·46
Day 180				
Survivors residing at home	89 (94%); n=95	87 (93%); n=94	OR 1·19 (0·39 to 3·69)	0·76
Deceased	28 (22%); n=126	24 (20%); n=120	HR 1·15 (0·67 to 1·99)	0·61

Nebulised heparin for patients with or at risk of acute respiratory distress syndrome: a multicentre, randomised, double-blind, placebo-controlled phase 3 trial

*Barry Dixon, Roger J Smith, Duncan J Campbell, John L Moran, Gordon S Doig, Thomas Rechnitzer, Christopher M MacIsaac, Nicholas Simpson, Frank M P van Haren, Angajendra N Ghosh, Sachin Gupta, Emma J C Broadfield, Timothy M E Crozier, Craig French, John D Santamaria on behalf of the CHARLI Study Group**

Lancet Respir Med 2021; 9: 360–72

Pas d'effet sur la survie

Vitamine C

Meilleure survie

2019

JAMA | Preliminary Communication | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Vitamin C Infusion on Organ Failure and Biomarkers of Inflammation and Vascular Injury in Patients With Sepsis and Severe Acute Respiratory Failure

The CITRIS-ALI Randomized Clinical Trial

Alpha A. Fowler III, MD; Jonathon D. Truwit, MD; R. Duncan Hite, MD; Peter E. Morris, MD; Christine DeWilde, RN, PhD; Anna Priday, BS, MS;

JAMA Network

QUESTION Can intravenous administration of high-dose vitamin C reduce organ failure scores and biomarkers of inflammation and vascular injury in patients with sepsis and acute respiratory distress syndrome (ARDS)?

CONCLUSION This randomized clinical trial found that in patients with sepsis and ARDS, high-dose vitamin C compared with placebo did not significantly reduce organ failure scores or improve biomarker levels.

© AMA

POPULATION

90 Men
77 Women

Adults in the intensive care unit (ICU) with sepsis and ARDS for <24 hours

Mean age: 55 years

INTERVENTION

167 Patients analyzed

84

Vitamin C
Intravenous vitamin C infusion, 50 mg/kg every 6 hours for 96 hours total

83

Placebo
Dextrose infusion every 6 hours for 96 hours total

FINDINGS

Change in mSOFA score, points (range 0-20)

Vitamin C	3 points	Placebo	3.5 points

C-reactive protein at 168 hours, μg/mL

Vitamin C	54.1 μg/mL	Placebo	46.1 μg/mL

Thrombomodulin at 168 hours, ng/mL

Vitamin C	14.5 ng/mL	Placebo	13.8 ng/mL

Between-group differences were not significant:

mSOFA, **-0.10** (95% CI, −1.23 to 1.03)

C-reactive protein, **7.94 μg/mL** (95% CI, −8.2 to 24.11)

Thrombomodulin, **0.69 ng/mL** (95% CI, −2.8 to 4.2)

LOCATIONS

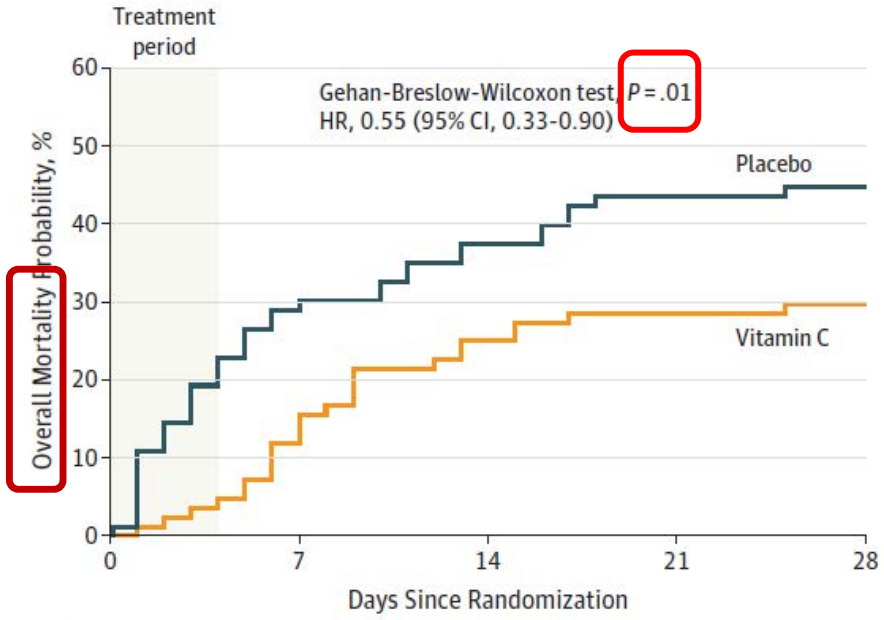
7 ICUs in the United States

PRIMARY OUTCOME

Change in organ failure assessment (mSOFA), biomarkers of inflammation (C-reactive protein), and vascular injury (thrombomodulin)

Fowler III AA, Truwit JD, Hite RD, et al. Effect of vitamin C infusion on organ failure and biomarkers of inflammation and vascular injury in patients with sepsis and severe acute respiratory failure: the CITRIS-ALI randomized clinical trial [published October 1, 2019]. *JAMA*. doi:10.1001/jama.2019.11825

Figure 3. All-Cause Mortality From Randomization (Day 0) to Day 28 Among Patients With Sepsis-Associated Acute Respiratory Distress Syndrome



No. at risk

Placebo	83	59	53	47	45
Vitamin C	84	74	65	61	59

Vitamine C

Meilleure survie

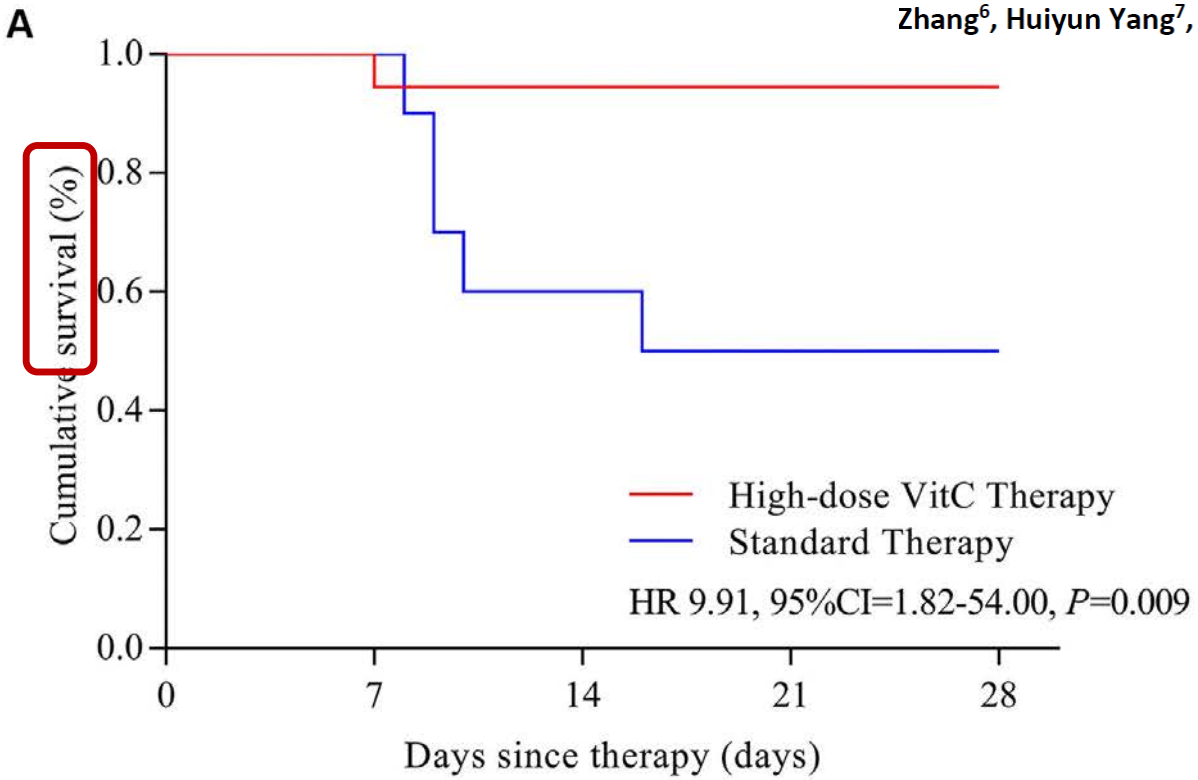
2021

www.aging-us.com AGING 2021, Vol. 13, No. 5

Research Paper

The efficiency and safety of high-dose vitamin C in patients with COVID-19: a retrospective cohort study

Dengfeng Gao[1,*], Min Xu[1,*], Gang Wang[2], Jianrui Lv[3], Xiaorong Ma[4], Yonghong Guo[5], Dexin Zhang[6], Huiyun Yang[7], Wei Jiang[1], Fuxue Deng[1], Guozhi Xia[1], Ziwei Lu[1], Lv Lv[1], Shouping Gong[8]



Number at risk

High-dose VitC Therapy	18	18	18	12	6
Standard Therapy	10	10	10	10	2

COVID-19

ARDS ?

Forte dose Vit C

6g intravenous infusion per 12 hr on the first day, and 6g once for the following 4 days

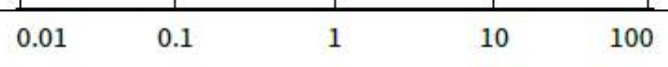
Bêta-agoniste

Pas d'effet sur la survie 2019

Lewis SR, Pritchard MW, Thomas CM, Smith AF.
Pharmacological agents for adults with acute respiratory distress syndrome.
Cochrane Database of Systematic Reviews 2019, Issue 7. Art. No.: CD004477.
DOI: 10.1002/14651858.CD004477.pub3.

Analysis 4.1. Comparison 4 Beta-agonist versus control, Outcome 1 Early mortality.

Study or subgroup	Beta-agonists n/N	Control n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
ALTA 2011	34/152	22/130		21.5%	1.32[0.82,2.14]
BALTI 2006	11/19	14/21		20.98%	0.87[0.53,1.42]
BALTI-2 2013	62/161	53/163		57.52%	1.18[0.88,1.59]
Total (95% CI)	**332**	**314**		**100%**	**1.14[0.91,1.42]**
Total events: 107 (Beta-agonists), 89 (Control)					
Heterogeneity: $Tau^2=0$; $Chi^2=1.7$, df=2(P=0.43); $I^2=0\%$					
Test for overall effect: Z=1.12(P=0.26)					



Favours beta-agonists — Favours control

Arrest RESpiraTory Failure from PNEUMONIA (AR- REST) trial, which examines whether inhaled beta-agonists and corticosteroids can prevent acute respiratory failure in patients with hypoxemia and pneumonia (NCT04193878)

Surfactant Adulte

Pas d'effet sur la survie 2019

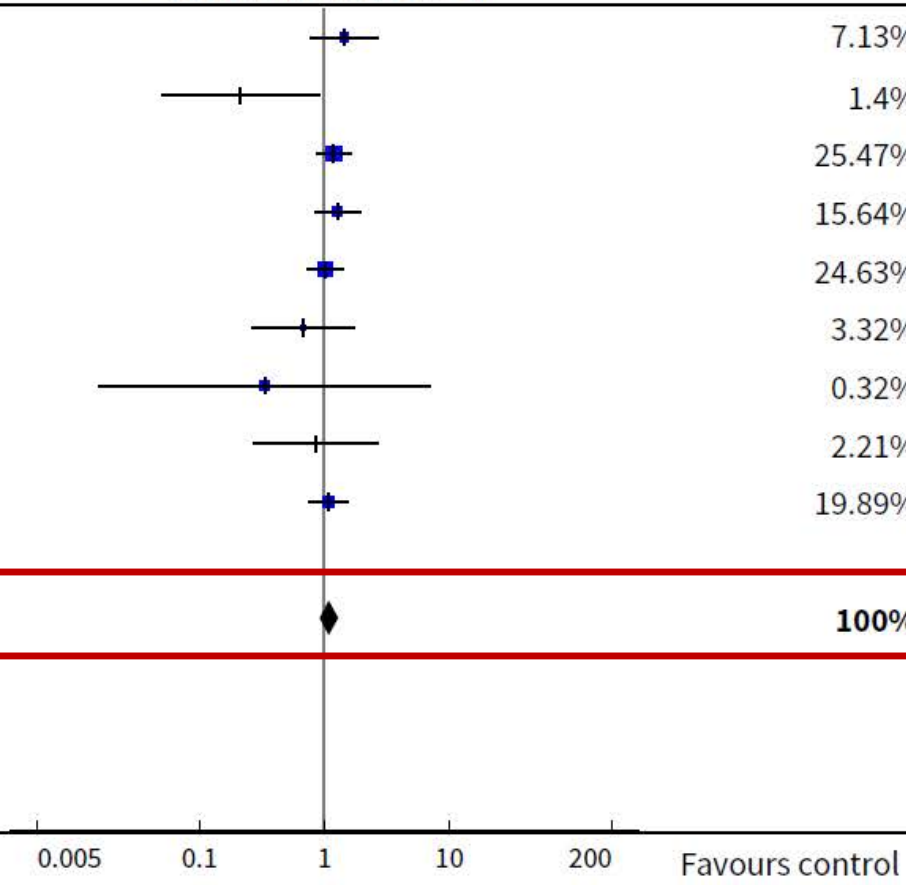
Pharmacological agents for adults with acute respiratory distress syndrome (Review)

Lewis SR, Pritchard MW, Thomas CM, Smith AF.
Pharmacological agents for adults with acute respiratory distress syndrome.
Cochrane Database of Systematic Reviews 2019, Issue 7. Art. No.: CD004477.
DOI: 10.1002/14651858.CD004477.pub3.

Lewis SR, Pritchard MW, Thomas CM,

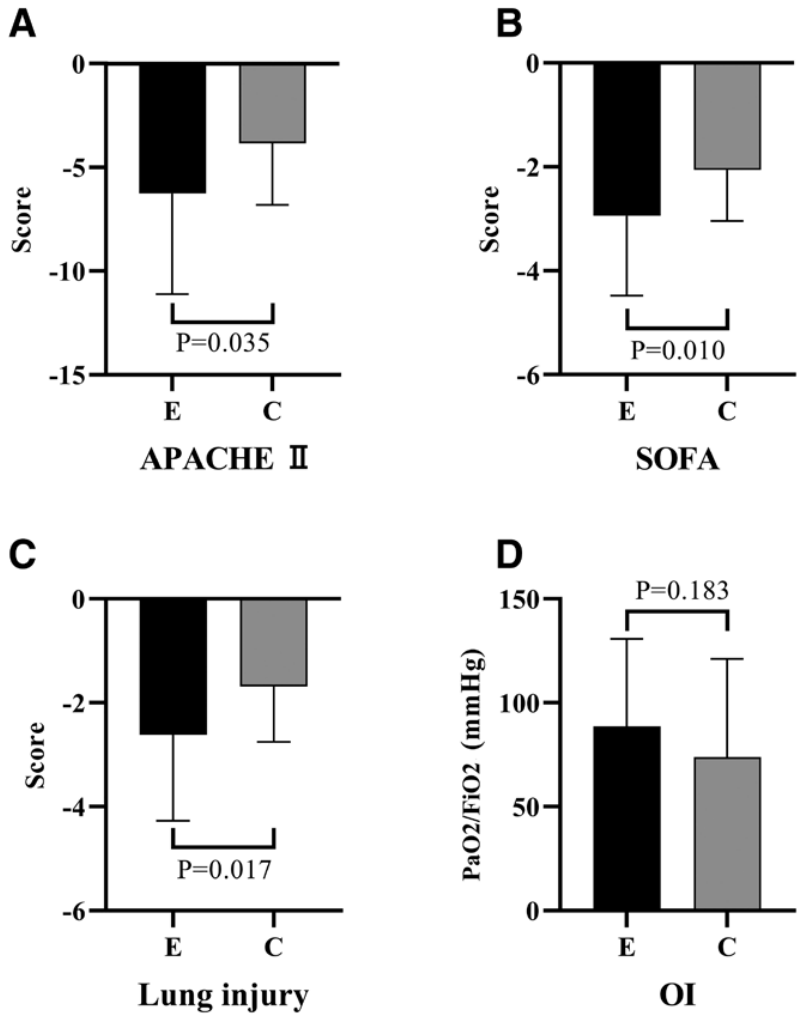
Analysis 2.1. Comparison 2 Surfactant versus control, Outcome 1 Early mortality.

Study or subgroup	Surfactants n/N	control n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Barrese-Perez 2015	13/24	9/24		7.13%	1.44[0.77,2.72]
Kesecioglu 2001	2/22	6/14		1.4%	0.21[0.05,0.91]
Kesecioglu 2009	60/208	51/210		25.47%	1.19[0.86,1.64]
Spragg 2002a	34/106	29/115		15.64%	1.27[0.84,1.93]
Spragg 2002b	46/117	42/108		24.63%	1.01[0.73,1.4]
Spragg 2003	7/27	5/13		3.32%	0.67[0.26,1.72]
Tsangaris 2007	0/8	1/8		0.32%	0.33[0.02,7.14]
Walmrath 2000	4/14	4/12		2.21%	0.86[0.27,2.71]
Willson 2015	42/151	41/157		19.89%	1.07[0.74,1.54]
Total (95% CI)	**677**	**661**		**100%**	**1.08[0.91,1.29]**
Total events: 208 (Surfactants), 188 (control)					
Heterogeneity: Tau^2=0; Chi^2=8.41, df=8(P=0.39); I^2=4.89%					
Test for overall effect: Z=0.93(P=0.35)					



GM-CSF

Pas d'effet sur la survie 2023



Clinical Trial/Experimental Study

Medicine

OPEN

Clinical study of rhGM-CSF for the treatment of pulmonary exogenous acute respiratory distress syndrome by modulating alveolar macrophage subtypes

A randomized controlled trial

Jie Sun, MM[a,*], Xiaokun Zhang, MD[b], Liliang Ma, MM[a], Yong Yang, MM[a], Xia Li, MD[a]

Sun et al. • Medicine (2023) 102:19

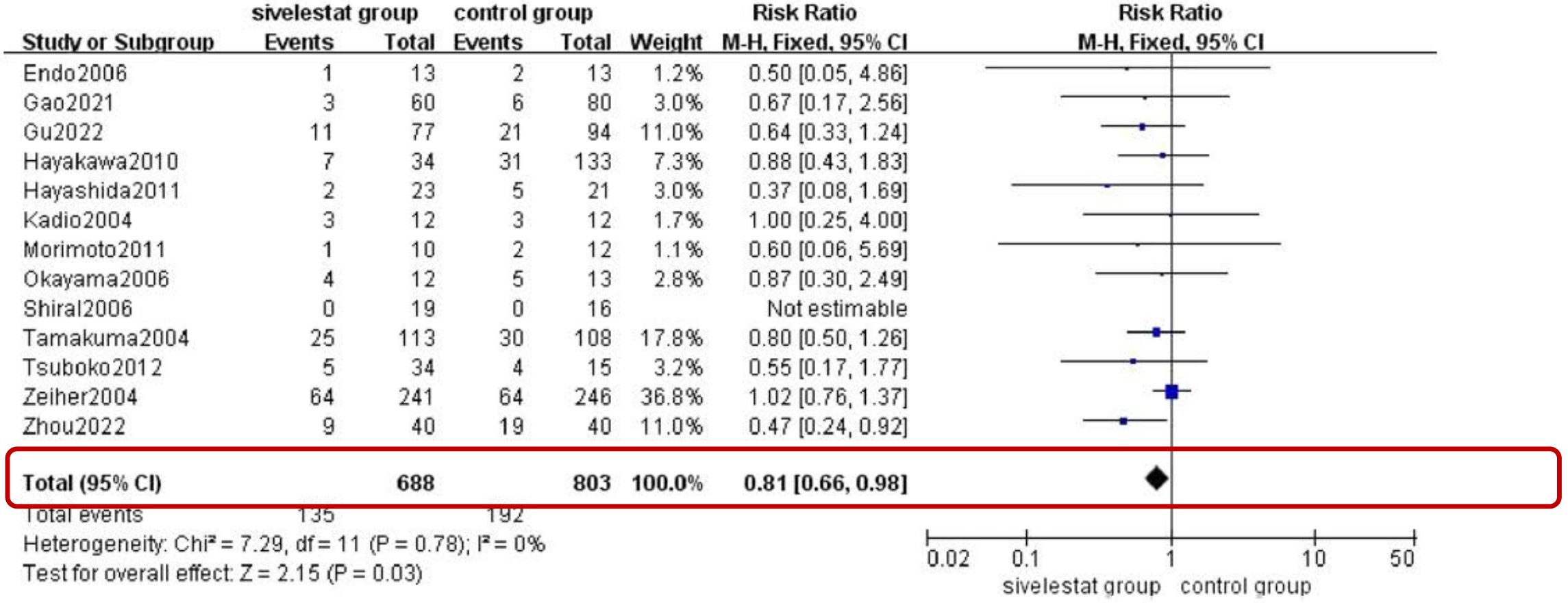
No notable difference in mortality between the 2 groups (P > .05)
No COVID ARDS

Granulocyte Macrophage-Colony Stimulating Factor (GM-CSF) Inhalation to Improve Host Defense and Pulmonary Barrier Restoration (GI-HOPE) NCT02595060

Sivelestat
Inhibiteur Elastase PNN
2023
Meilleure survie

Effect of Sivelestat in the Treatment of Acute Lung Injury and Acute Respiratory Distress Syndrome: A Systematic Review and Meta-Analysis

Qiongli Ding[1,2] · Yi Wang[1,2,3] · Chunbo Yang[1,2,3] · Dilireba Tuerxun[1,2] · Xiangyou Yu[1,2,3]



Study or Subgroup	sivelestat group Events	Total	control group Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Endo2006	1	13	2	13	1.2%	0.50 [0.05, 4.86]
Gao2021	3	60	6	80	3.0%	0.67 [0.17, 2.56]
Gu2022	11	77	21	94	11.0%	0.64 [0.33, 1.24]
Hayakawa2010	7	34	31	133	7.3%	0.88 [0.43, 1.83]
Hayashida2011	2	23	5	21	3.0%	0.37 [0.08, 1.69]
Kadio2004	3	12	3	12	1.7%	1.00 [0.25, 4.00]
Morimoto2011	1	10	2	12	1.1%	0.60 [0.06, 5.69]
Okayama2006	4	12	5	13	2.8%	0.87 [0.30, 2.49]
Shiral2006	0	19	0	16		Not estimable
Tamakuma2004	25	113	30	108	17.8%	0.80 [0.50, 1.26]
Tsuboko2012	5	34	4	15	3.2%	0.55 [0.17, 1.77]
Zeiher2004	64	241	64	246	36.8%	1.02 [0.76, 1.37]
Zhou2022	9	40	19	40	11.0%	0.47 [0.24, 0.92]
Total (95% CI)		**688**		**803**	**100.0%**	**0.81 [0.66, 0.98]**
Total events	135		192			

Heterogeneity: Chi² = 7.29, df = 11 (P = 0.78); I² = 0%
Test for overall effect: Z = 2.15 (P = 0.03)

Fig. 4 Forest plot for the mortality of 28–30 days

Intensive Care Research
https://doi.org/10.1007/s44231-023-00032-9

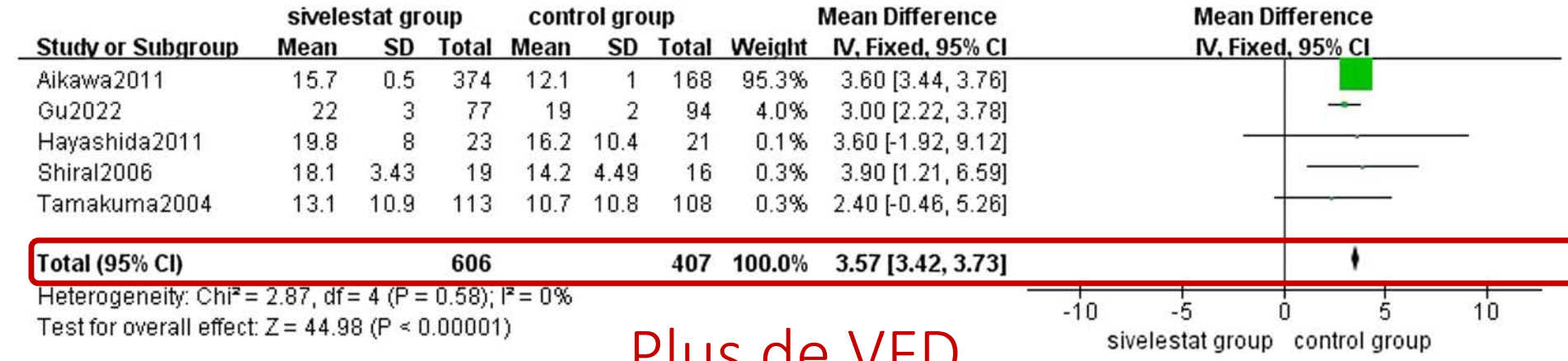


Fig. 7 Forest plot for ventilation free days

Plus de VFD

Sivelestat

Plus de ICUFD

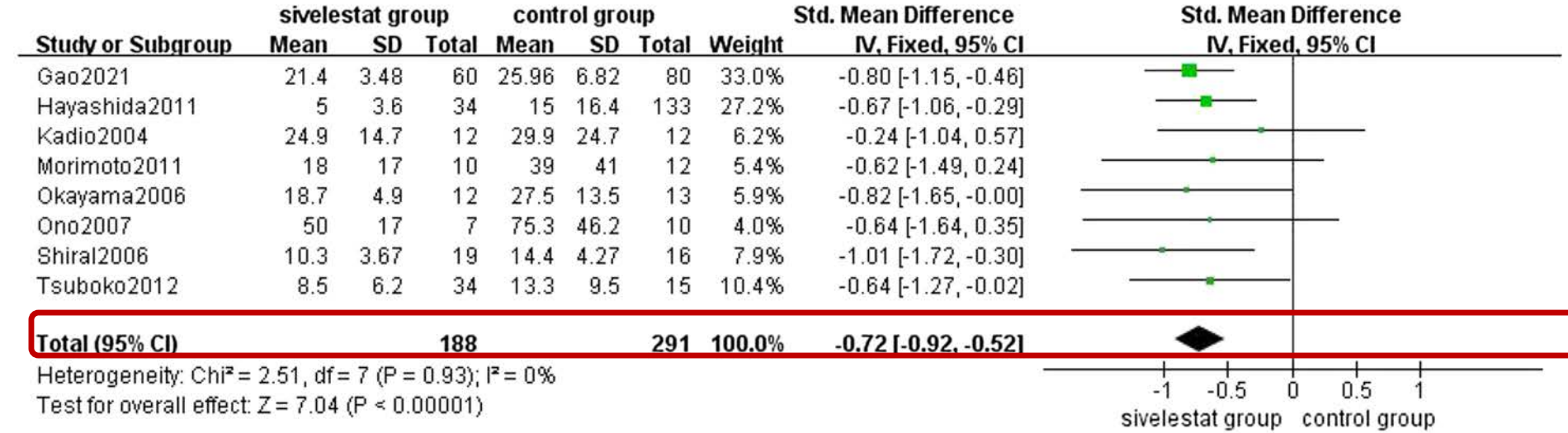


Fig. 8 Forest plot for ICU stays

Intensive Care Research
https://doi.org/10.1007/s44231-023-00032-9

N-Acétylcysteine

Pas d'effet sur la survie

2025

Pas de grosses séries

N-Acetylcysteine in the Treatment of Acute Lung Injury: Perspectives and Limitations

Daniela Mokra [1,*], Igor Porvaznik [2] and Juraj Mokry [3]

Int. J. Mol. Sci. **2025**, *26*, 2657

Subtype of ARDS	No. of Patients	NAC Dose/Way of Delivery	Major Findings/Outcomes	Ref.
ARDS requiring mechanical ventilation	NAC n = 22, placebo n = 20	NAC (190 mg/kg/d) or placebo, continuous i.v. infusion, for the first 3 days	↓ lung injury score, no improvement in oxygenation, and no reduction in the need for ventilation	[114]
ARDS requiring mechanical ventilation	NAC n = 17, NAC-nontreated n = 10	NAC (150 mg/kg i.v. on the first day followed by 50 mg/kg/day for 3 days) and controls obtained the standard therapy	↑ extracellular total antioxidant power, ↑ total thiols, ↑ GSH, and improved outcome	[115]
Community-acquired pneumonia	NAC n = 37, NAC-nontreated n = 24	NAC (600 mg tablets, a dose of 1200 mg/d p.o., for 10 days) + conventional therapy and controls treated by conventional therapy	↓ plasma MDA and TNFα, ↑ total antioxidant capacity, no effect on SOD, and no improvement in CT	[116]
Ventilator-associated pneumonia	NAC n = 30, NAC-nontreated n = 30	NAC (600 mg) given twice daily via nasogastric tube in addition to routine care	↓ development of clinically confirmed pneumonia, shorter stay in ICU, and more patients with complete recovery	[117]
ARDS requiring mechanical ventilation	NAC n = 30, NAC-nontreated n = 30	NAC (150 mg/kg on the day 1 of admission, then 50 mg/kg up to day 4 of admission) and control group given routine care without NAC	Improved level of consciousness, oxygenation, and PEEP within 3–4 days of intervention	[118]

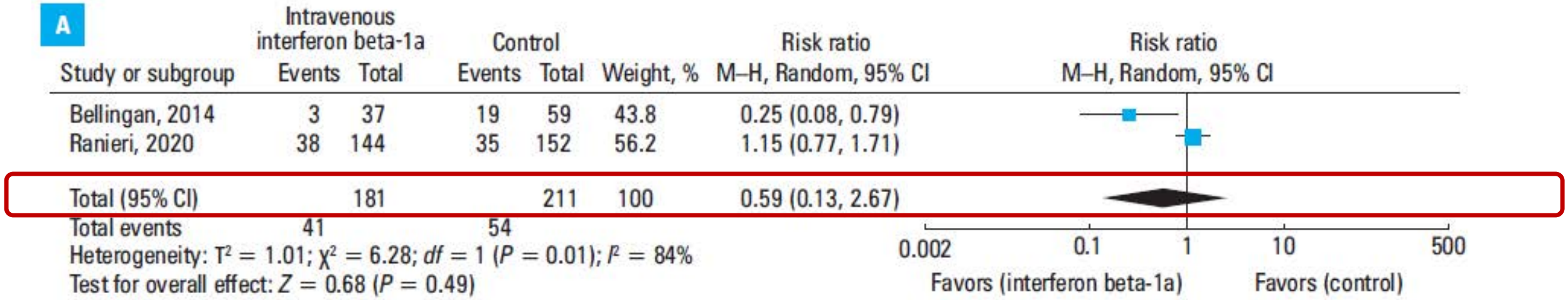
Interferon - ß1a

Pas d'effet sur la survie 2020

Interferon beta-1a for patients with moderate to severe acute respiratory distress syndrome: a systematic review and meta-analysis of randomized trials

Manoj J. Mammen[1], Komal Aryal[2], Waleed Alhazzani[2,3], Dianna Y. Deng[4], Paul E. Alexander[2]

POLISH ARCHIVES OF INTERNAL MEDICINE 2020; 130 (4)



28-day hospital mortality

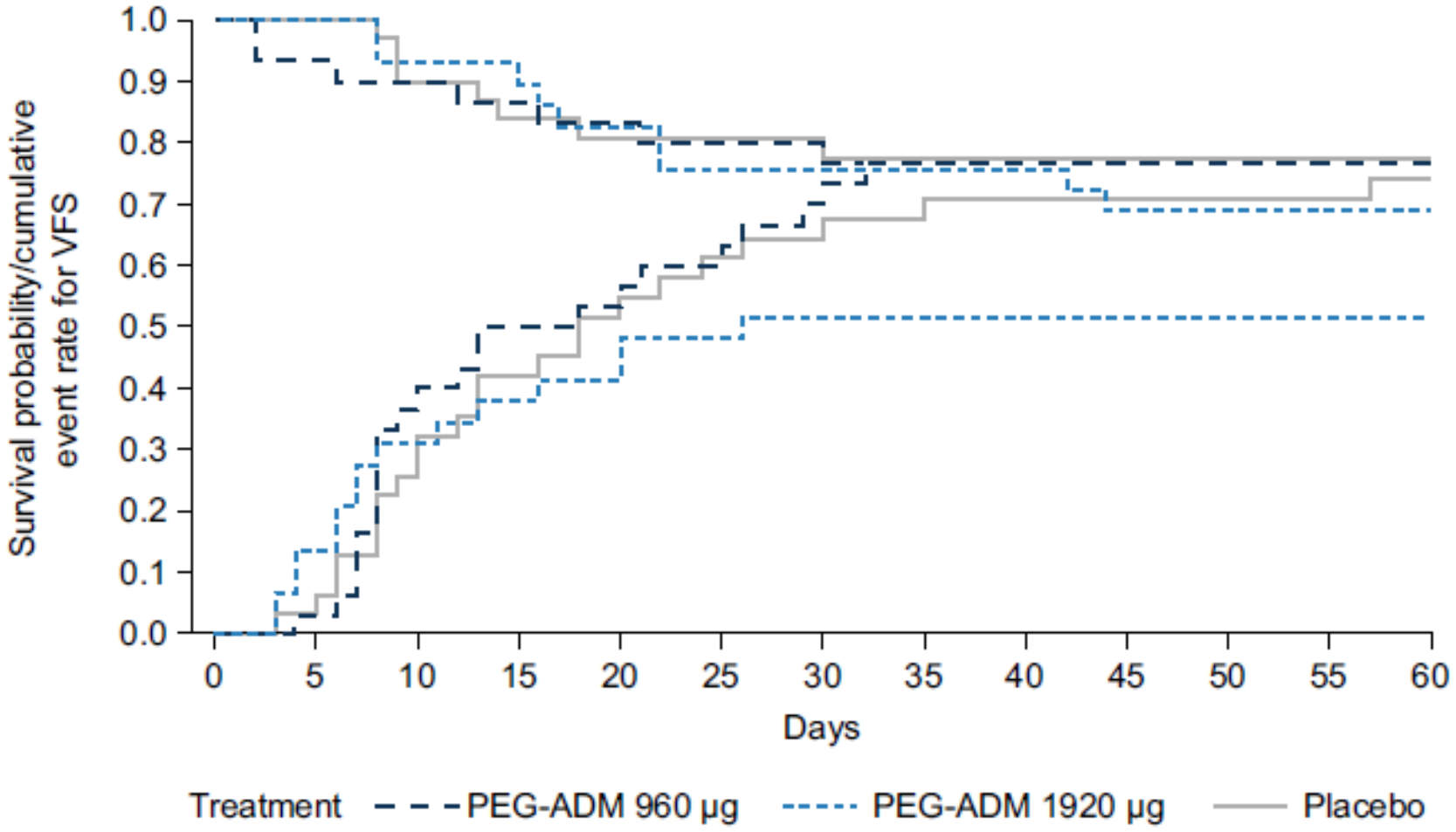
Adrénomédulline

2025

Pas d'effet sur la survie

Adrenomedullin (ADM) is an endogenous peptide hormone associated with enhanced barrier function and reduced hyperpermeability of endothelial cells [6], with receptors highly expressed in lung endothelium [7,

Karagiannidis *et al. Critical Care* (2025) 29:448
https://doi.org/10.1186/s13054-025-05617-y



Deaths

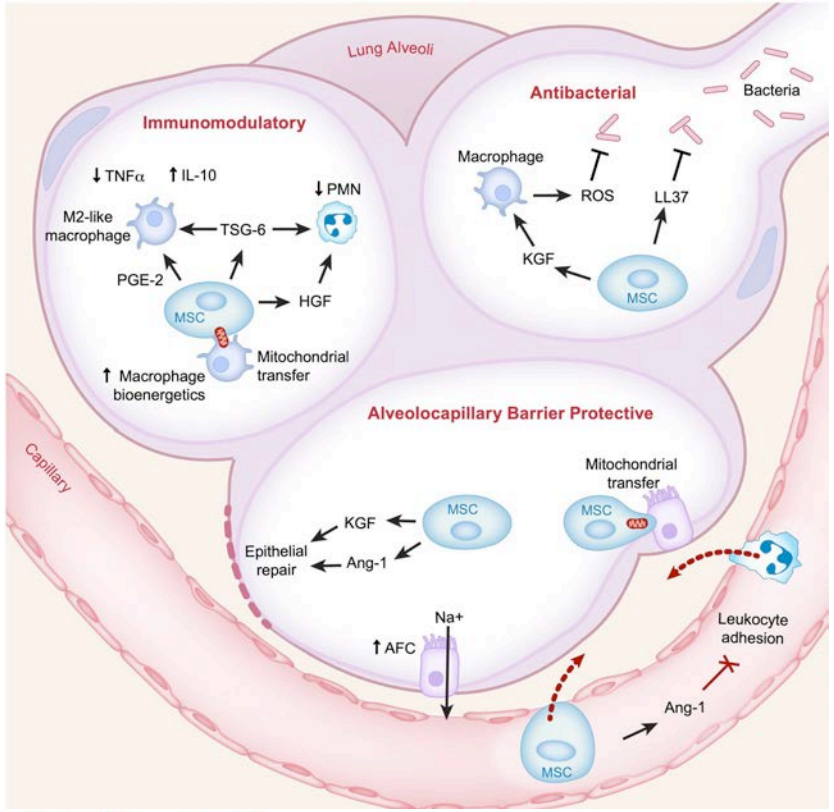
Alive but ventilated

Onset of ventilator-free survival

Safety and efficacy of inhaled PEG-ADM in ARDS patients: a randomised controlled trial

Christian Karagiannidis[1*], Danny F. McAuley[2], B. Taylor Thompson[3], Thomas Reimer[4], Kaweh Shakery[4], Sebastian Schmitz[4], Manuel Núñez Cortés[4], Roman Ullrich[5], Ferhat Meziani[6], Alain Mercat[7], Davide Chiumello[8,9,10], Frantisek Duska[11], Alain Combes[12,13] and for the SEAL Trial Investigators

Cellules Souches Mésenchymateuses



Wick et al. Critical Care (2021) 25:404
https://doi.org/10.1186/s13054-021-03822-z

Critical Care

REVIEW Open Access

Promises and challenges of personalized medicine to guide ARDS therapy

Katherine D. Wick[1*], Daniel F. McAuley[2], Joseph E. Levitt[3], Jeremy R. Beitler[4], Djillali Annane[5,6], Elisabeth D. Riviello[7], Carolyn S. Calfee[1,8] and Michael A. Matthay[1,8]

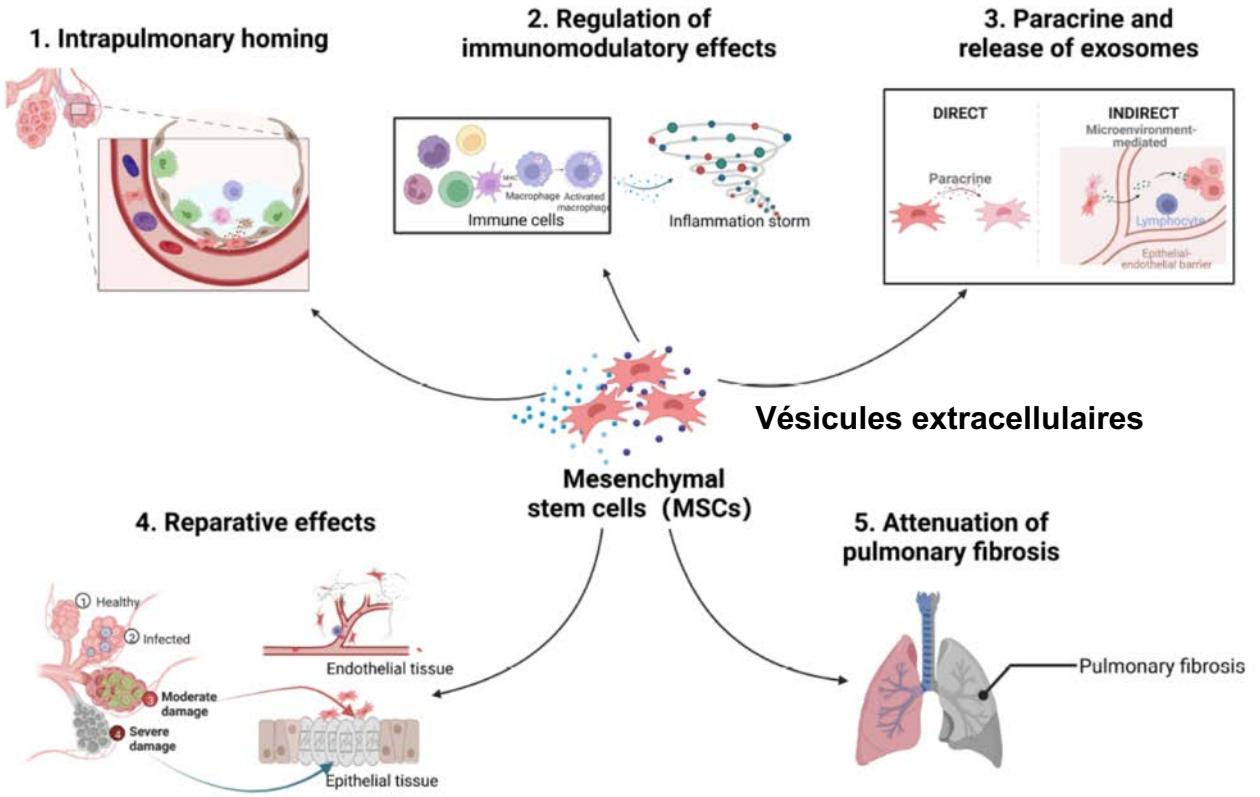
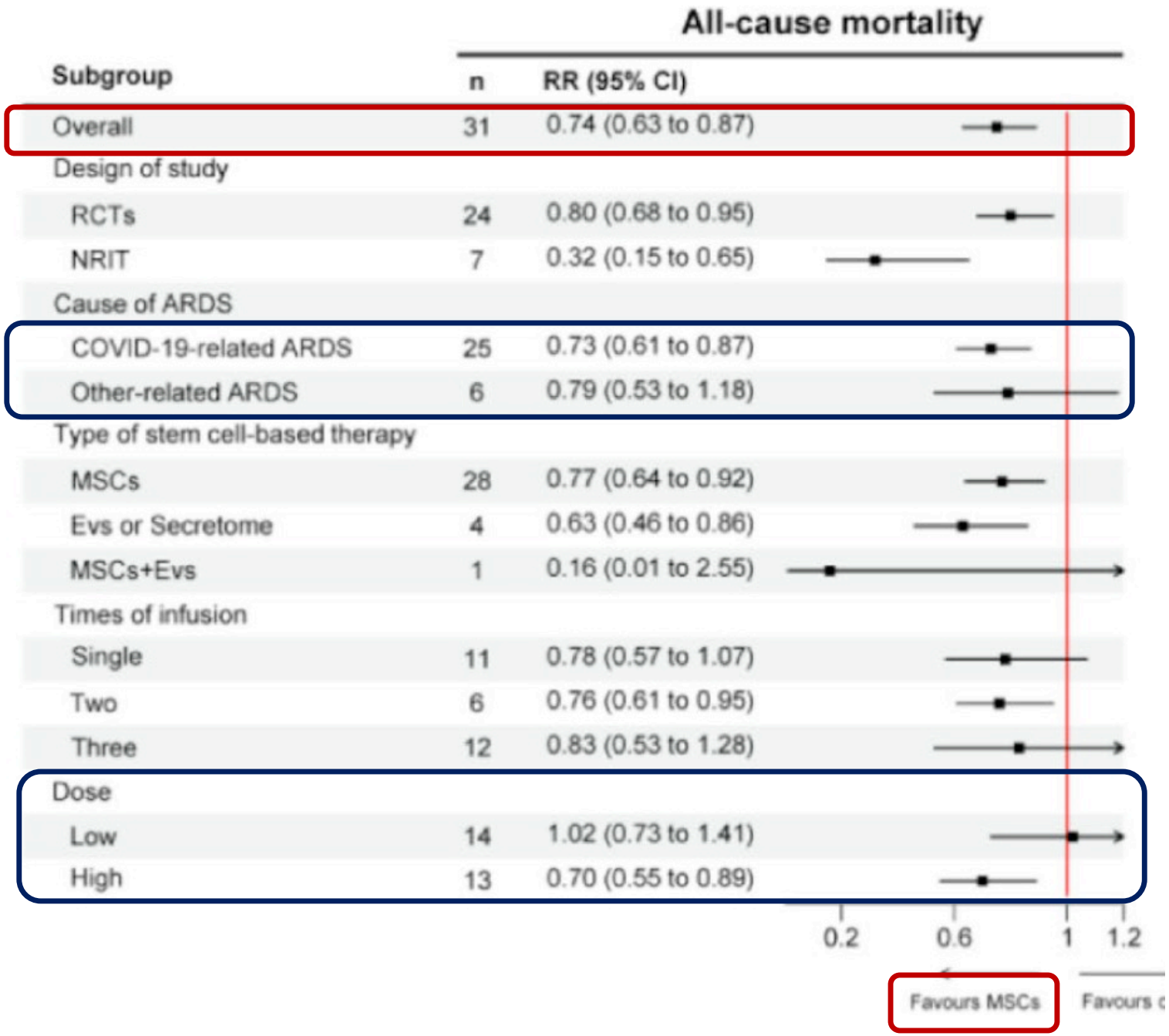


Figure 3 The mechanisms by which mesenchymal stem cell therapy improves acute respiratory distress syndrome. Several mechanisms by which mesenchymal stem cells are used to treat acute respiratory distress syndrome, including homing to the intrapulmonary injury site, regulation of immune and inflammatory cells, repair of damaged tissues, and inhibition of lung fibrosis. (Created using BioRender.com).

Therapeutic Benefits of Mesenchymal Stem Cells in Acute Respiratory Distress Syndrome: Potential Mechanisms and Challenges

Chao Cao[1–4], Lin Zhang[2,3], Fuli Liu[2,3], Jie Shen[1–4]

Journal of Inflammation Research 2022:15 5235–5246



Efficacy and safety of mesenchymal stem/stromal cells and their derived extracellular vesicles for acute respiratory distress syndrome: a systematic review and meta-analysis

Wu *et al. Stem Cell Research & Therapy* (2025) 16:522
https://doi.org/10.1186/s13287-025-04644-4

Cellules Souches Mésenchymateuses Vésicules Extracellulaires

85% COVID-19

Meilleure survie

2025

A retenir :Traitements pharmacologiques du SDRA

Sédation : Sévoflurane → surmortalié

Curarisation : SDRA sévère (P/F<100), 24-48h→ survie

Monoxyde d'azote : Avant (attente) ECMO → neutre (rein !)

Corticoïdes : Tôt (1-7 jours), 0,5-1,5 mg/Kg, sevrage → survie

Hyper vs Hypo ?

Inflammatoire

Innovations :

- Statines : SDRA hyperinflammatoires → survie
- Vitamine C : SDRA + sepsis → survie
- Sivelestat : → survie
- Cellules souches mésenchymateuses → survie