

Aérosolthérapie dans la bronchiolite

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réanimation 2023

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Palais des Congrès de Paris
Porte Maillot

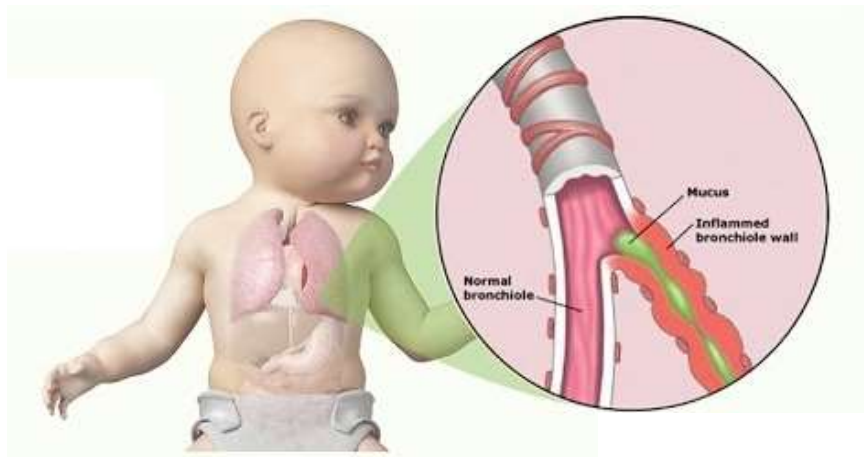
Cliniques universitaires
SAINT-LUC
UCLouvain BRUXELLES

Orateur : Damien MOERMAN, Bruxelles

Aucun lien d'intérêt potentiel à déclarer

Physiopathologie

- Atteinte virale de l'épithélium respiratoire => nécrose
- Atteinte inflammatoire :
 - Œdème de la muqueuse, exsudation, hypersécrétion bronchique
 - Obstruction des bronchioles
- Bronchospasme associé possible



Les bronchodilatateurs

Recommendation

R32—Inhaled beta2-agonists and/or inhaled epinephrine should probably not be used routinely. In some cases, a therapeutic test could be considered to avoid intubation (**GRADE 2—, strong agreement**)

D'après Milési et al, GFRUP, 2023

Short term effects of adrenaline in bronchiolitis: a randomised controlled trial

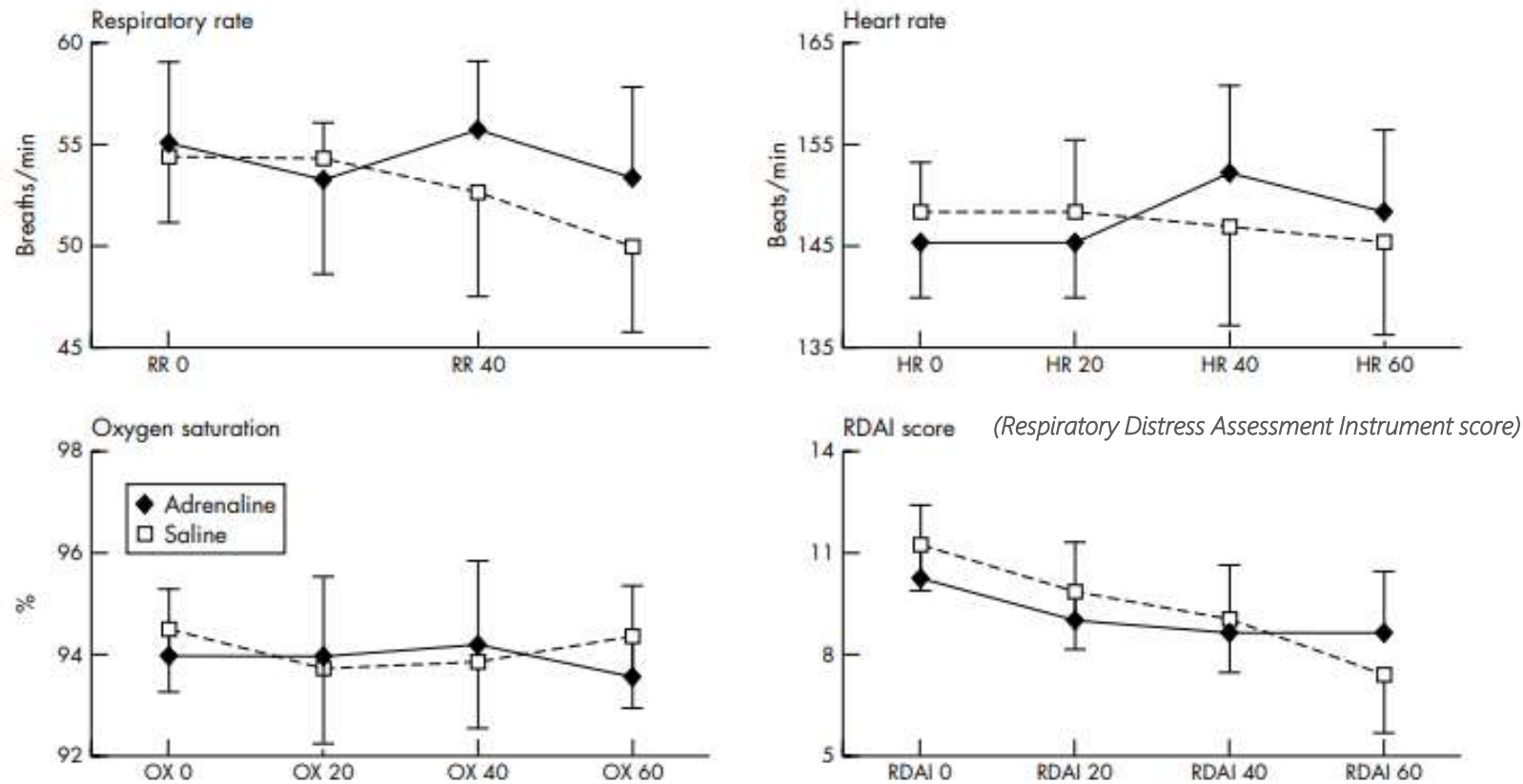


Figure 1 Mean (95% CI) for respiratory rate, heart rate, oxygen saturation, and RDAI score for infants in each group at 0, 20, 40, and 60 minutes of assessment.

Efficacy of Salbutamol and Ipratropium Bromide in the Management of Acute Bronchiolitis – A Clinical Trial

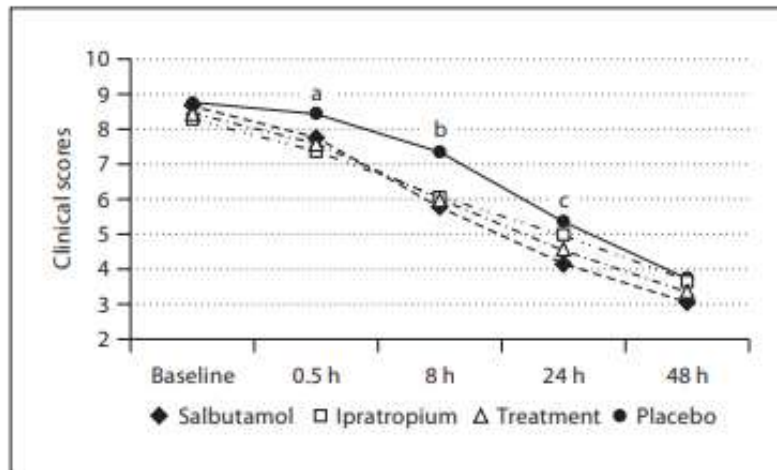


Fig. 1. Clinical scores of the treatment groups. ^aIpratropium bromide (I) vs. placebo (P), $p = 0.001$, salbutamol (S) vs. P, $p = 0.04$, S vs. I, $p > 0.05$, T vs. P, $p < 0.0001$. ^b I vs. P, $p = 0.001$, S vs. P, $p = 0.0001$, S vs. I, $p > 0.05$, T vs. P, $p < 0.0001$. ^c S vs. P, $p = 0.02$, S vs. I, I vs. P, $p > 0.05$, T vs. P, $p = 0.006$.

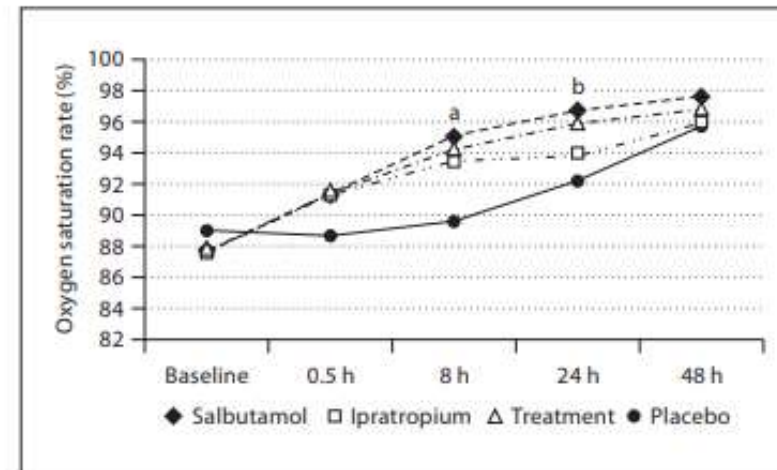


Fig. 2. Oxygen saturation measurements of the treatment groups. ^a Ipratropium bromide (I) vs. placebo (P), $p = 0.005$, salbutamol (S) vs. P, $p = 0.0001$, S vs. I, $p > 0.05$, T vs. P, $p < 0.0001$. ^b S vs. P, $p = 0.001$, I vs. P, $p = 0.05$, S vs. I, $p > 0.05$, T vs. P, $p < 0.0001$.

Bronchodilatateurs et SpO2

Analysis 1.1. Comparison 1 Bronchodilators compared to placebo for treatment of acute bronchiolitis, Outcome 1 Oxygen saturation measured by pulse oximetry: inpatient and outpatient settings.

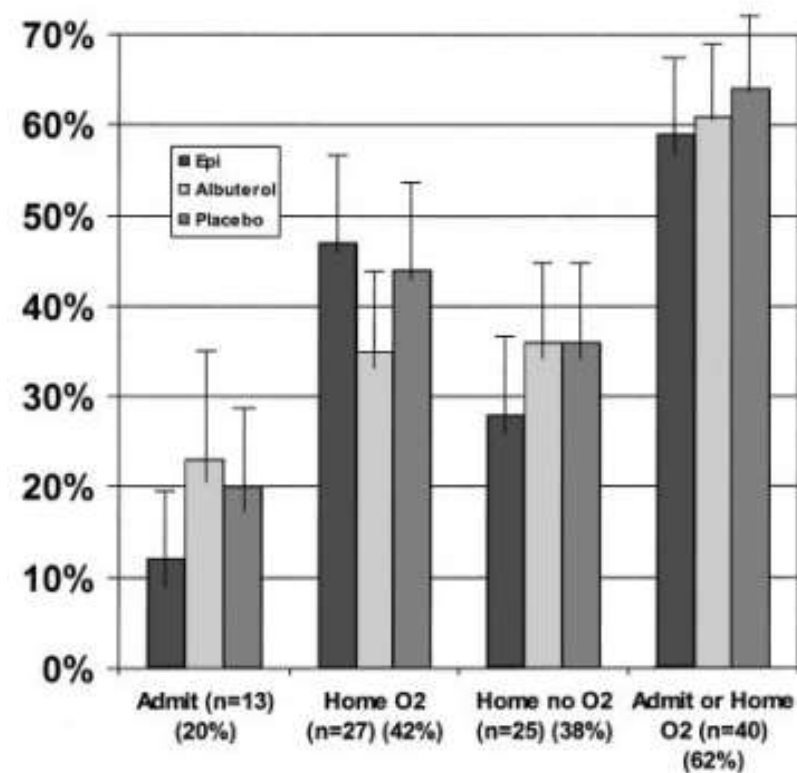
Study or subgroup	Placebo		Bronchodilator		Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)			
1.1.1 Inpatient studies							
Chevallier 1995	17	93.2 (0.4)	16	94.4 (0.4)		6.47%	-1.2[-1.47,-0.93]
Dobson 1998	29	93.5 (6)	23	93.2 (7.8)		1.28%	0.3[-3.58,4.18]
Gurkan 2004	12	95.6 (1.2)	18	95.8 (1.4)		5.32%	-0.2[-1.14,0.74]
Ho 1991	8	97.6 (0.7)	13	95.4 (0.8)		5.91%	2.2[1.55,2.85]
Karadag 2005 - IPR	11	92.2 (2.6)	22	93.8 (4)		2.73%	-1.6[-3.87,0.67]
Karadag 2005 - SAL	12	92.2 (2.6)	24	96.7 (4.1)		2.83%	-4.5[-6.7,-2.3]
Lines 1990	23	95.6 (2)	26	95.8 (1.9)		4.96%	-0.2[-1.3,0.9]
Lines 1992	14	93 (0.4)	17	94 (0.6)		6.39%	-1[-1.35,-0.65]
Patel 2002	48	96.2 (3.3)	51	95.8 (4.1)		4.16%	0.46[-1.19,1.92]
Tinsa 2009	19	97 (1.3)	16	97.2 (1.5)		5.31%	-0.2[-1.14,0.74]
Totapally 2002	9	94 (2.4)	10	95 (3.1)		2.45%	-1[-3.48,1.48]
Wang 1992	17	95.1 (2.7)	40	97.2 (1.8)		4.29%	-2.1[-3.5,-0.7]
Subtotal ***	219		276			52.11%	-0.62[-1.4,0.16]
Heterogeneity: Tau ² =1.36; Chi ² =112.89, df=11(P<0.0001); I ² =90.26%							
Test for overall effect: Z=1.57(P=0.12)							

Bronchodilatateurs et scores cliniques

Comparison 1. Bronchodilators compared to placebo for treatment of acute bronchiolitis

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4 Average clinical score after treatment: by treatment setting (continuous)	21	1086	Std. Mean Difference (IV, Random, 95% CI)	-0.30 [-0.54, -0.05]
4.1 Inpatient studies	9	416	Std. Mean Difference (IV, Random, 95% CI)	-0.14 [-0.41, 0.12]
4.2 Outpatient studies	12	670	Std. Mean Difference (IV, Random, 95% CI)	-0.42 [-0.79, -0.06]
Subtotal ***	249	167		40.51% -0.14[-0.41,0.12]
Subtotal ***	349	321		59.49% -0.42[-0.79,-0.06]
Total ***	598	488		100% -0.3[-0.54,-0.05]
Heterogeneity: Tau ² =0.23; Chi ² =73.62, df=20(P<0.0001); I ² =72.83%				
Test for overall effect: Z=2.4(P=0.02)				
Test for subgroup differences: Chi ² =1.46, df=1 (P=0.23), I ² =31.59%				
Favours treatment -4 -2 0 2 4 Favours placebo				

Randomized, Placebo-Controlled Trial of Albuterol and Epinephrine at Equipotent Beta-2 Agonist Doses in Acute Bronchiolitis

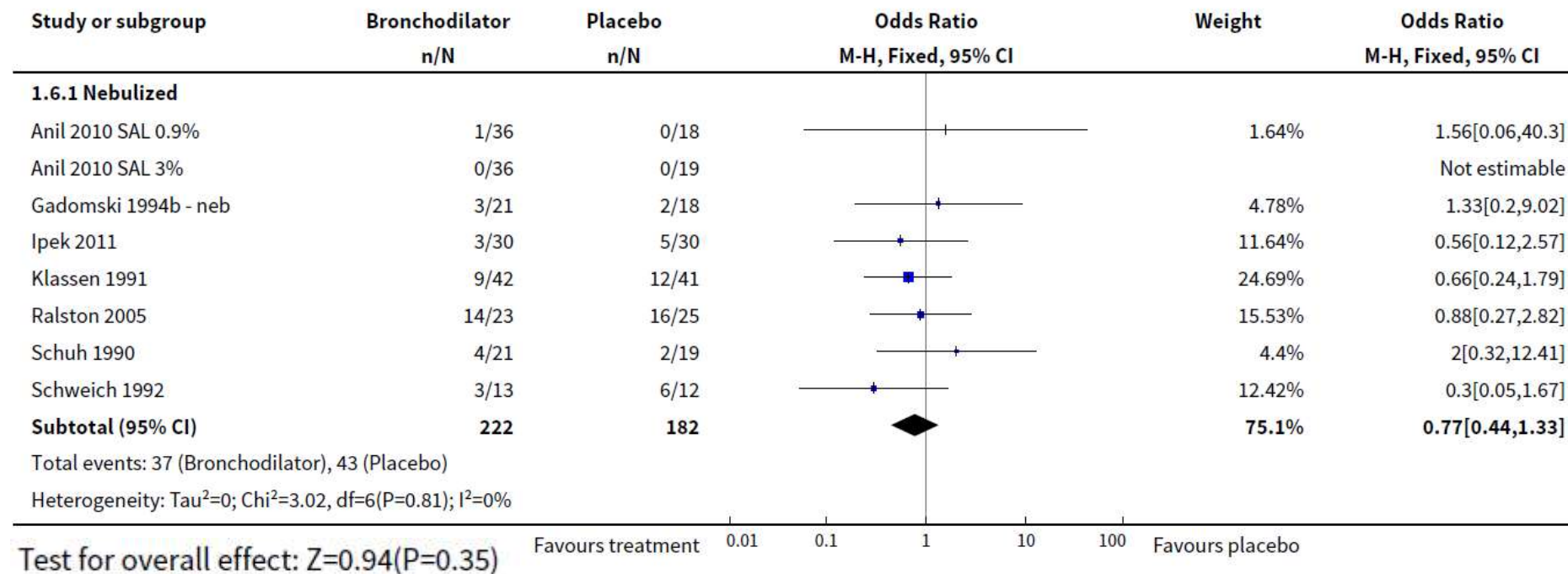


D'après Ralston et al, 2005



Bronchodilatateurs et admission

Analysis 1.6. Comparison 1 Bronchodilators compared to placebo for treatment of acute bronchiolitis, Outcome 6 Hospital admission after treatment (outpatients treated with albuterol or salbutamol).

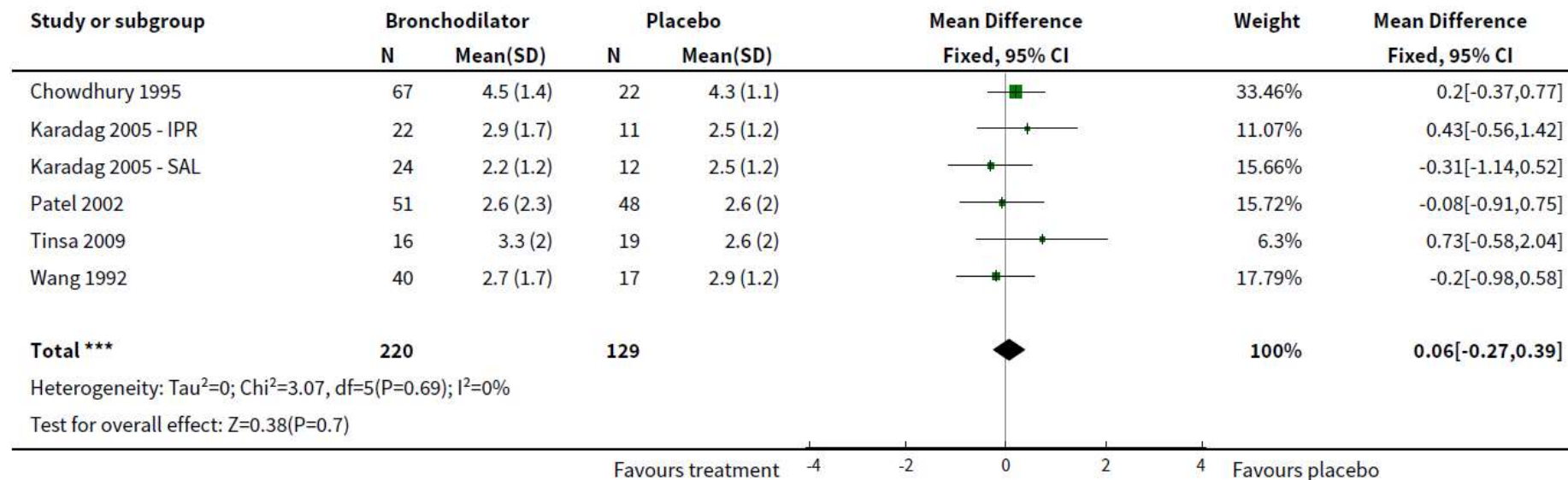


A randomized, controlled trial of the effectiveness of nebulized therapy with epinephrine compared with albuterol and saline in infants hospitalized for acute viral bronchiolitis

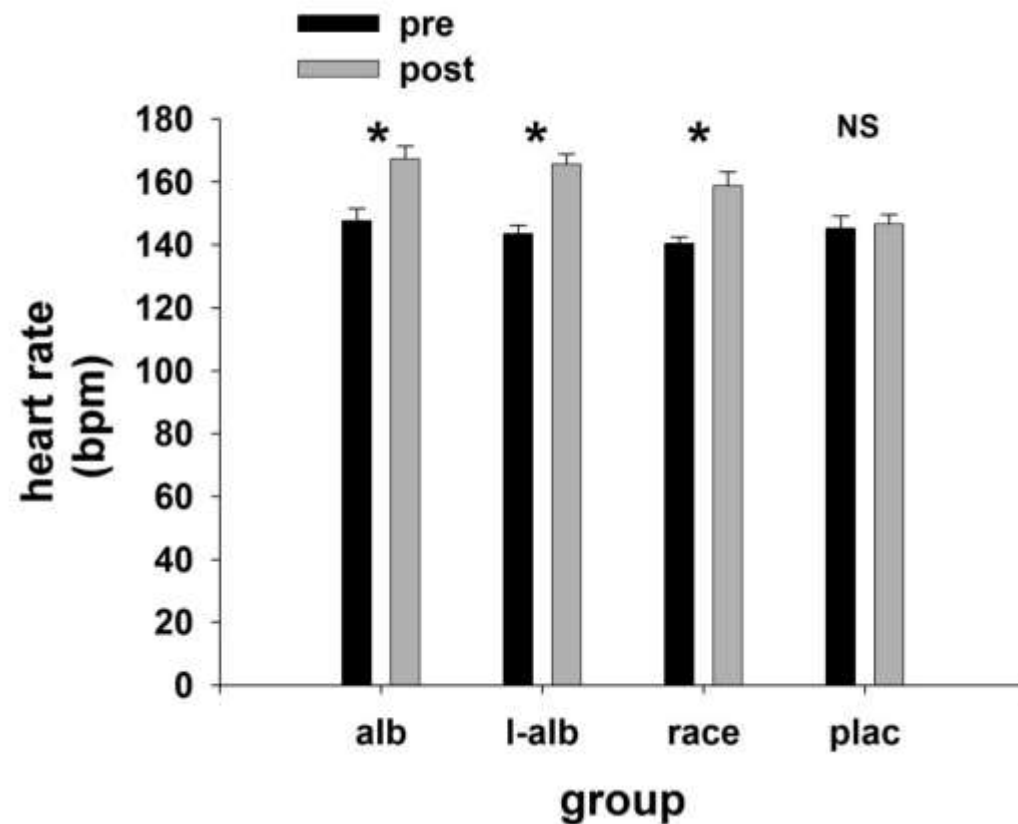
Outcomes (h)(SD)	EPI (n = 50)	ALB (n = 51)	PLAC (n = 48)	P value
Mean LOS	59.8 (62)	61.4 (54)	63.3 (47)	.95
Mean time to normal oxygenation (hemoglobin oxygen saturation of $\geq 95\%$ in room air)	25.0 (37)	33.0 (55)	36.6 (56)	.5
Mean time to adequate fluid intake	35.1 (44)	38.4 (42)	47.6 (48)	.4
Mean time to RDAI ≤ 4	34.6 (34)	45.7 (55)	36.8 (44)	.4
Mean time to infrequent nebulizations (every 4 h or less often)	16.3 (30)	31.1 (48)	34.3 (46)	.08

Bronchodilatateurs et LOS

Analysis 1.7. Comparison 1 Bronchodilators compared to placebo for treatment of acute bronchiolitis, Outcome 7 Duration of hospitalization (inpatients).



Effets secondaires



Si nébulisation :

- Adrénaline : 0,1 mL/kg (max 5 mL) d'une solution de 1mg/1mL
- Salbutamol : 0,01 à 0,03 mL/kg (max 1mL) d'une solution de 5mg/1mL

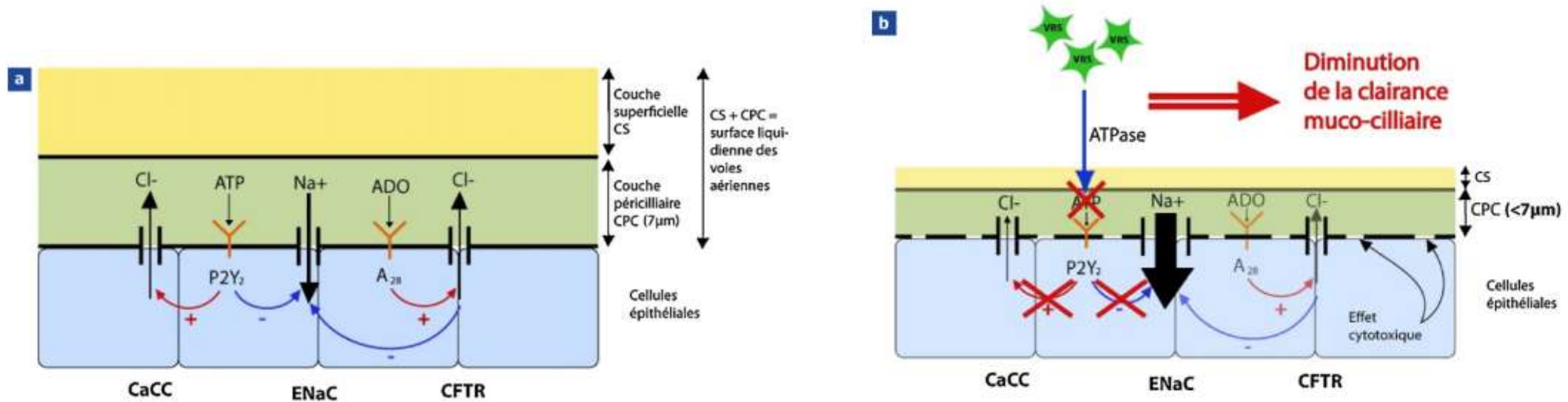
La nébulisation de sérum salé hypertonique

Recommendation

R38—Nebulization of hypertonic saline should probably not be used routinely (**GRADE 2—, strong agreement**)

D'après Milési et al, GFRUP, 2023

Mécanisme



D'après Sauvaget et al, 2012

Nebulized hypertonic saline in infants hospitalized with moderately severe bronchiolitis due to RSV infection: A multicenter randomized controlled trial

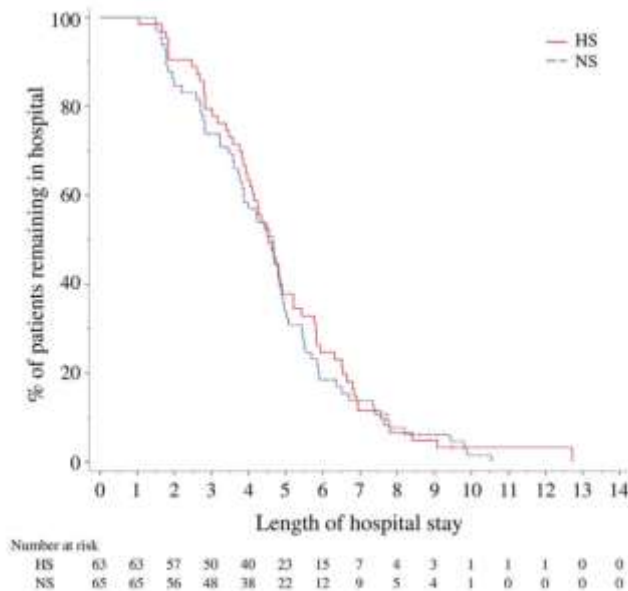


FIGURE 2 The percentage of infants remaining in hospital per group

TABLE 2 Clinical outcomes in HS and NS groups

Variable	HS (n = 63)	NS (n = 65)	P-value
Length of hospital stay in days (mean ± SD)	4.81 ± 2.14	4.61 ± 2.18	0.62
Duration of O2 administration in days (mean ± SD)	2.77 ± 2.68	2.50 ± 2.50	0.55
Improvement in CSS (admission–72 h), (mean ± SD)	–3.63 ± 2.30	–3.58 ± 2.56	0.91

HS, hypertonic saline; NS, normal saline; SD, standard deviation; CSS, clinical severity score.

SABRE: a multicentre randomised control trial of nebulised hypertonic saline in infants hospitalised with acute bronchiolitis



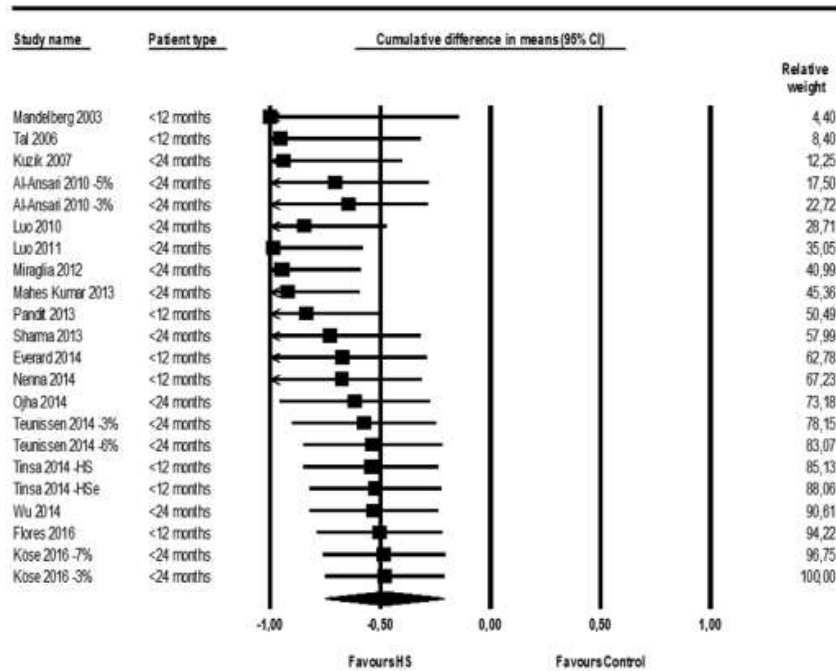
Figure 2 Cumulative survival plot for time to being declared fit for discharge.



Figure 3 Cumulative survival plot for actual time to discharge.

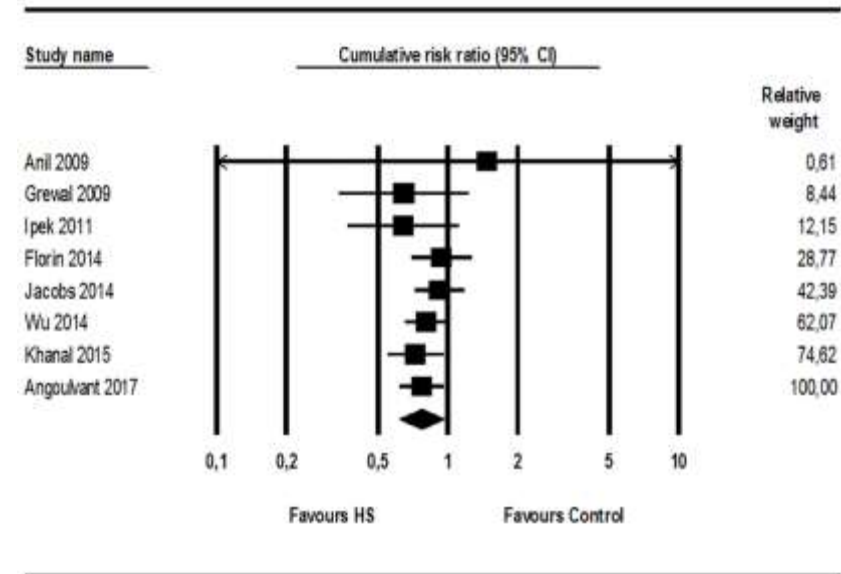
Hypertonic saline inhalations in bronchiolitis—A cumulative meta-analysis

Durée d'hospitalisation



$I^2 = 66,4\%$

Risque d'hospitalisation

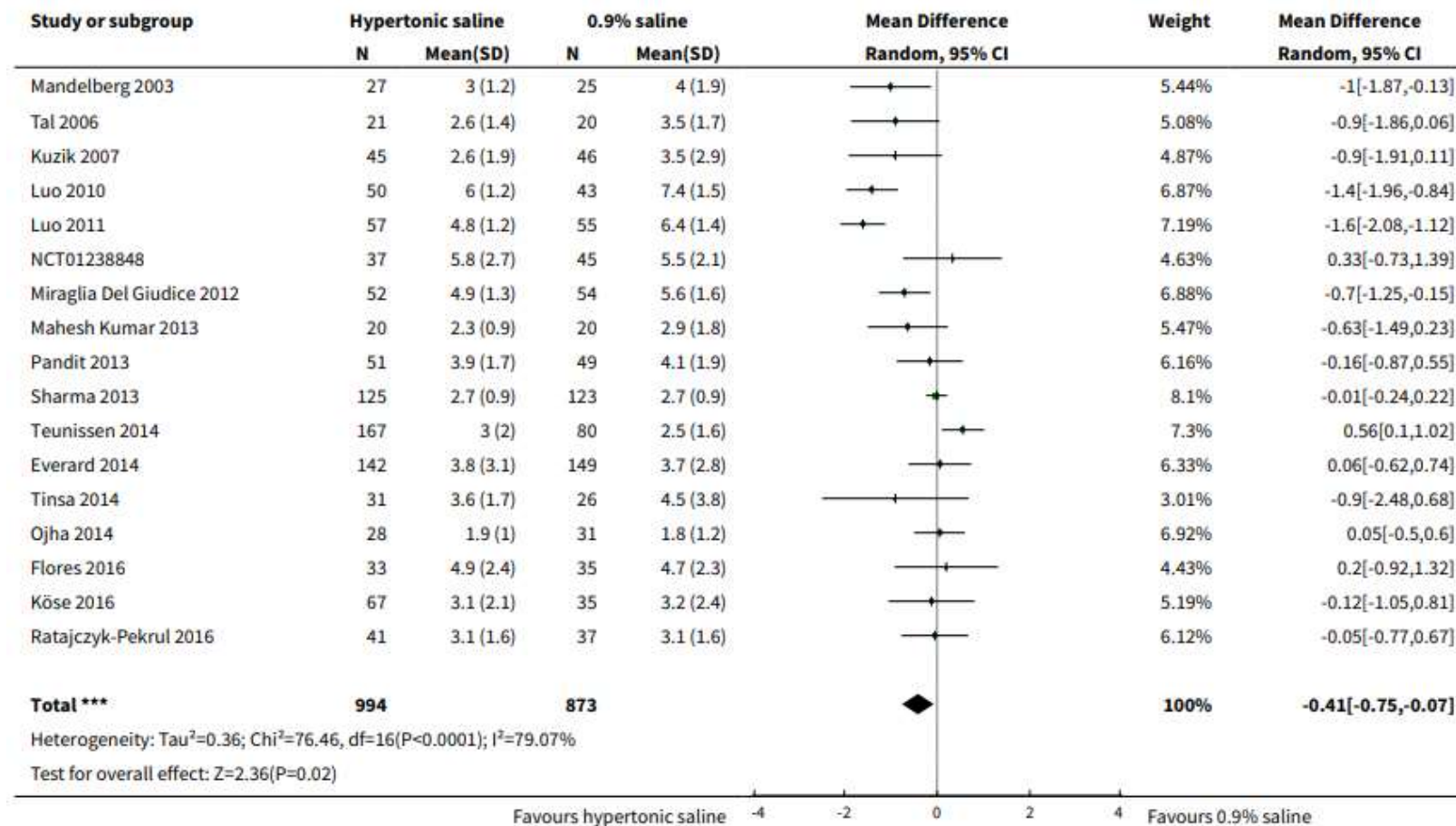


$I^2 = 55,8\%$

- Fréquence d'administration : 6h, 8h, 2x/j
- Concentration : 3%, 6% ou 7%

Sel hypertonique et LOS

Analysis 1.1. Comparison 1 Hypertonic saline versus normal saline (0.9%), Outcome 1 Length of hospital stay (days).



Les corticoïdes

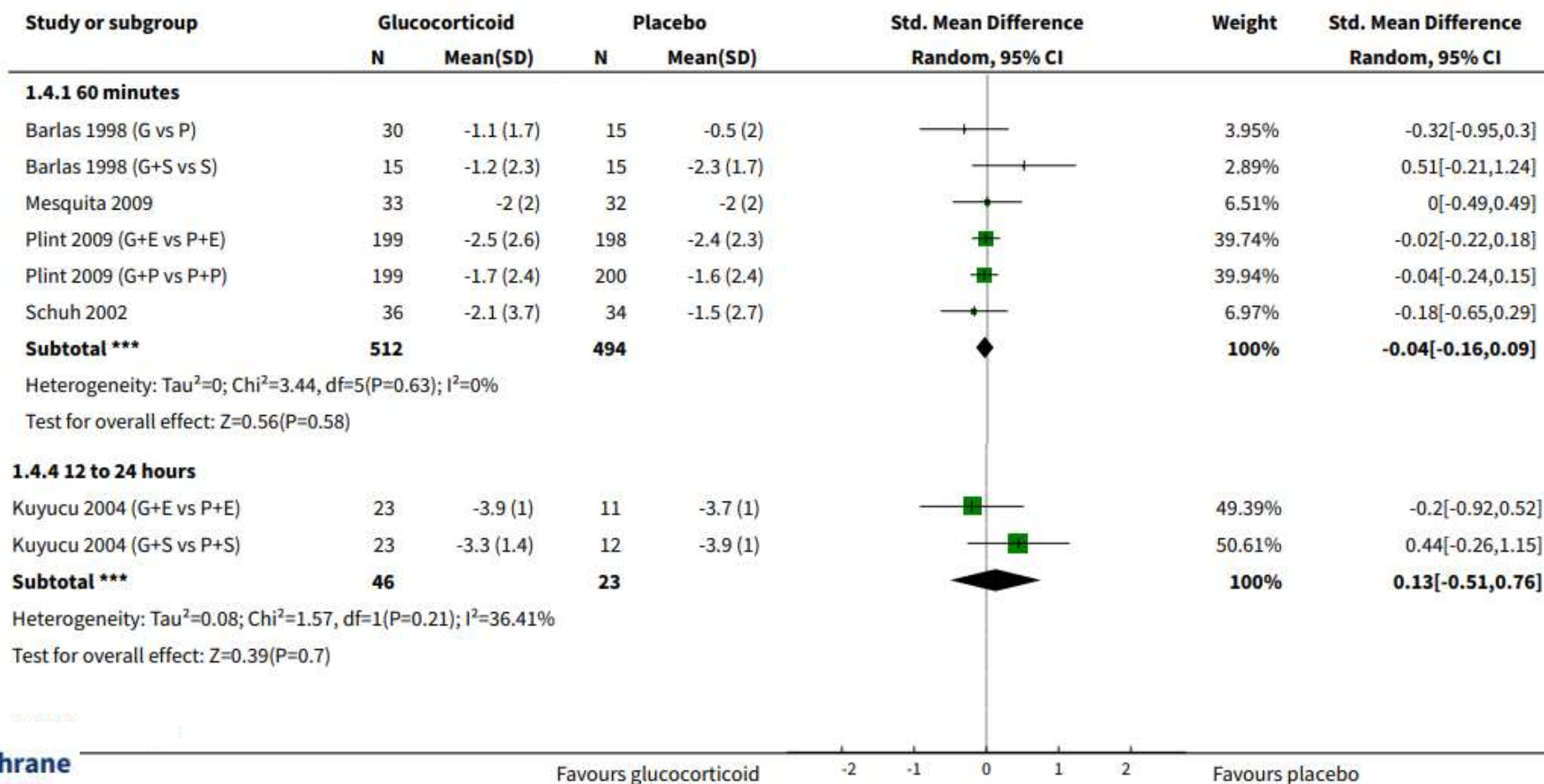
Recommendation

R31—Corticosteroids, whether inhaled or systemic, should probably not be used (**GRADE 2, strong agreement**)

D'après Milési et al, GFRUP, 2023

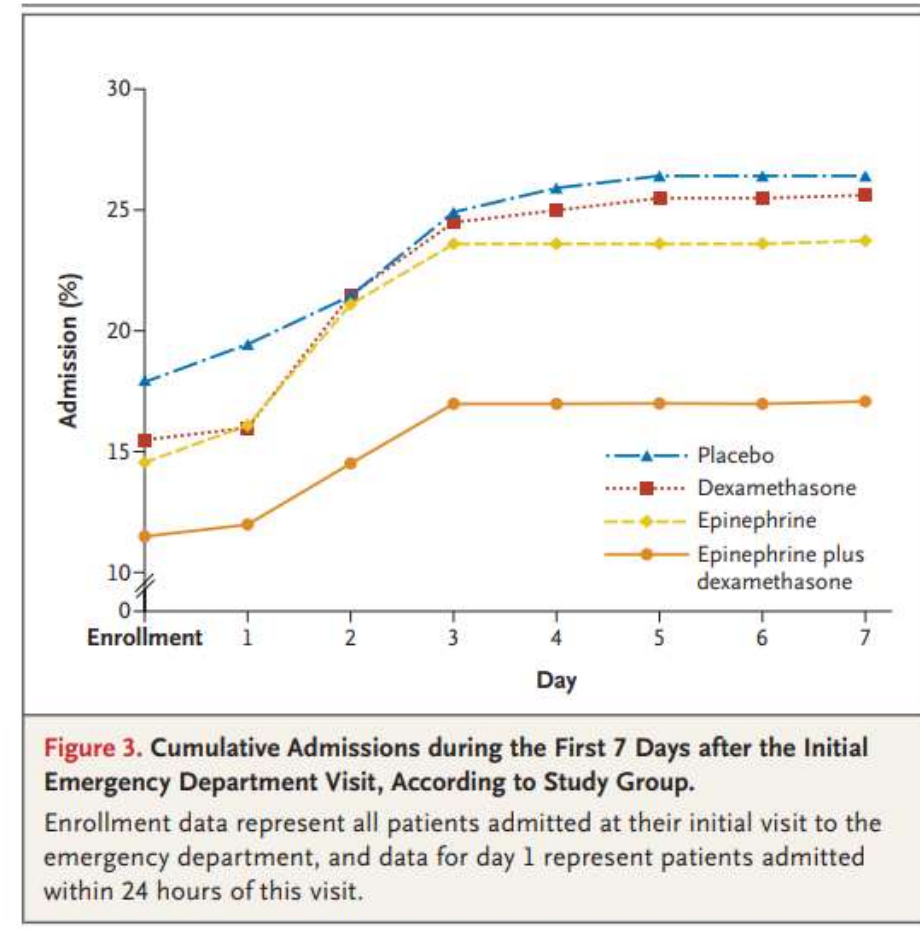
Les corticoïdes et scores cliniques

Analysis 1.4. Comparison 1 Glucocorticoid versus placebo, Outcome 4 Clinical scores (outpatients).



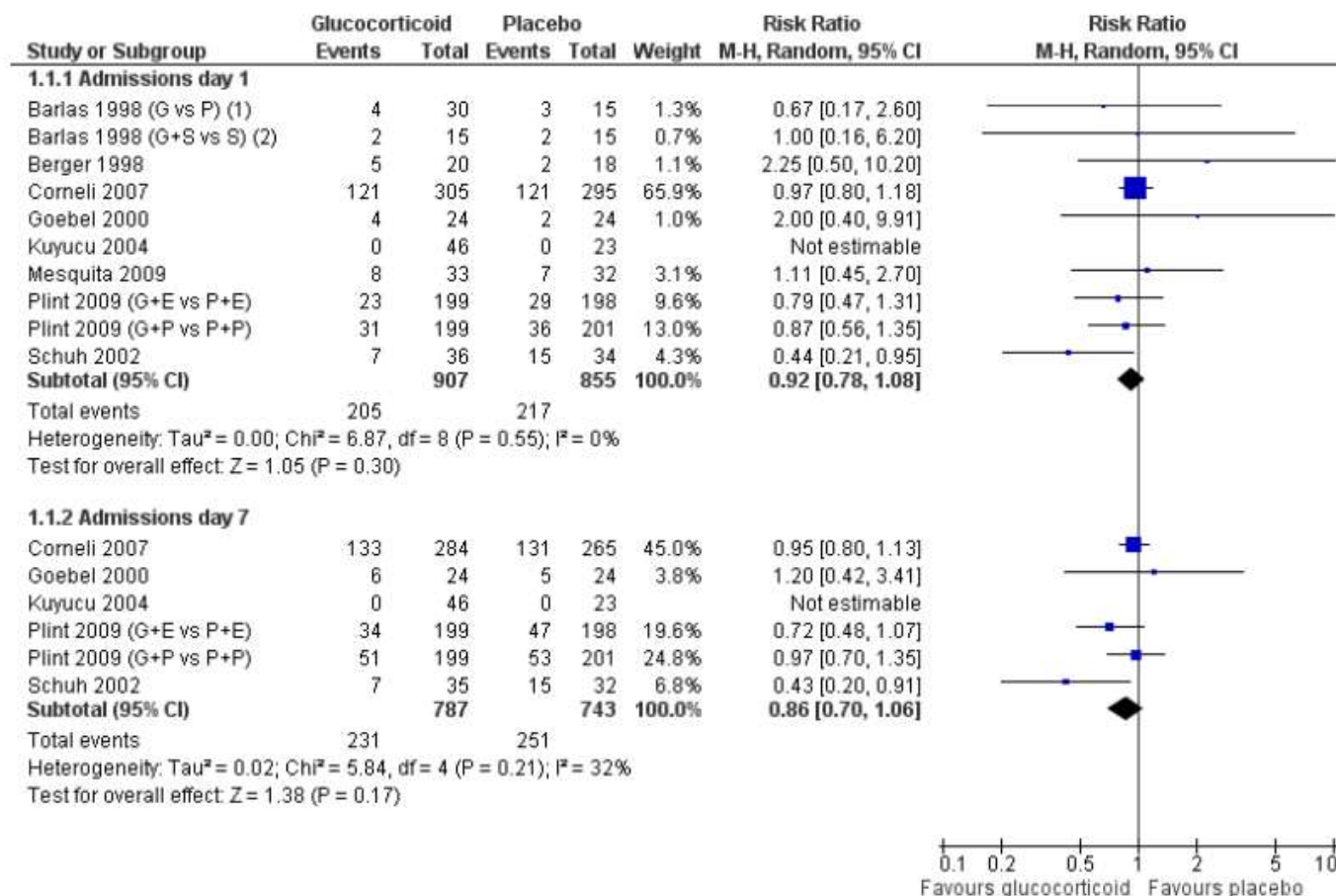
Les corticoïdes et admission

- RCT double aveugle multicentrique (Canada)
- 800 enfants (6 sem – 12 mois)
- Outpatients
- 4 groupes :
 - Aérosol Adrénaline (3mL) + dexaméthasone PO (1 mg/kg puis 5 x 0,6 mg/kg)
 - Aérosol Adrénaline + placebo PO
 - Aérosol placebo + dexta PO
 - Aérosol placebo + placebo PO



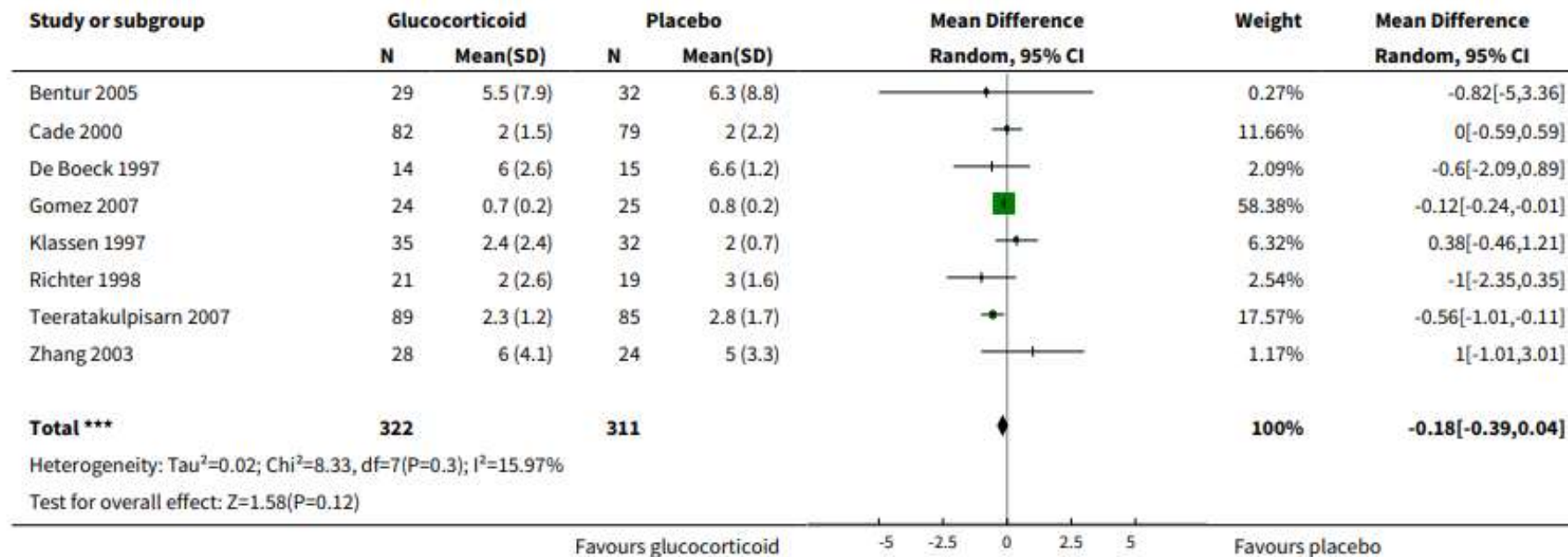
Les corticoïdes et admission

Figure 6. Forest plot of comparison: 1 Steroid versus placebo, outcome: 1.1 Admissions (days 1 and 7) (outpatients) - review primary outcome.



Les corticoïdes et LOS

**Analysis 1.2. Comparison 1 Glucocorticoid versus placebo,
Outcome 2 Length of stay (inpatients) - review primary outcome.**



Et le nébuliseur...



Masque vs Hood



Hood

2,6%



Mask

2,4%



D'après Amirav, 2003

Aerosol Deposition in Neonatal Ventilation

JEAN C. DUBUS, LAURENT VECELLIO, MICHELE DE MONTE, JAMES B. FINK,
DANIEL GRIMBERT, JEROME MONTHARU, CHANTAL VALAT, NEIL BEHAN, AND PATRICE DIOT

INSERM U618 [J.C.D., L.V., M.d.M., D.G., J.M., C.V., P.D.], 37044, Tours, France; Department of
Pediatrics [J.C.D.], Timone-Enfants Hospital, 13385, Marseille, France; and Aerogen, Inc. [J.B.F., N.B.],
Mountain View, California 94043

Table 1. Deposition of ^{99m}Tc -DTPA using APN-S, APN-C, and the MistyNeb in a macaque model of neonatal ventilation

	APN-S	APN-C	MistyNeb
Nebulizer	2.7 (1.8–3.7)*	9.9 (8.7–11.3)*	22.4 (19.7–23.7)*
T-piece	0.9 (0.7–2.0)*	9.8 (2.3–15.9)*	6.5 (2.1–10.0)*
	0.9 (0.7–2.1)†	9.8 (2.6–18)†	8.4 (2.0–12.5)†
Inspiratory limb	8.2 (0.5–9.5)*	8.4 (0.7–17.3)*	7.9 (3.7–11.3)*
	8.4 (0.6–9.8)†	9.3 (0.8–19.0)†	10.2 (3.6–14.1)†
Y-piece	3.3 (1.9–5.7)*	10.5 (5.6–17.1)*	3.5 (0.0–6.9)*
	3.4 (2.0–5.9)†	11.6 (6.3–19.3)†	4.4 (0.0–6.7)†
ETT	9.0 (3.1–9.8)*	4.4 (2.1–6.8)*	1.0 (0.5–2.1)*
	9.3 (3.1–14.0)†	4.8 (2.4–7.7)†	1.3 (0.5–2.8)
Lungs	14.0 (12.2–23.7)*	12.6 (9.6–20.6)*	0.5 (0.4–1.3)*
Expiratory limb	3.0 (1.4–4.2)*	3.3 (2.7–4.8)*	1.6 (0.6–2.3)*
	3.1 (1.4–4.3)†	3.7 (3.1–5.2)†	1.9 (0.7–2.6)†
Expiratory filter	20.1 (19.0–22.3)*	9.5 (7.7–11.1)*	10.6 (8.2–12.7)*
	20.6 (19.7–22.8)†	10.5 (8.5–12.4)†	12.0 (10.2–16.4)†

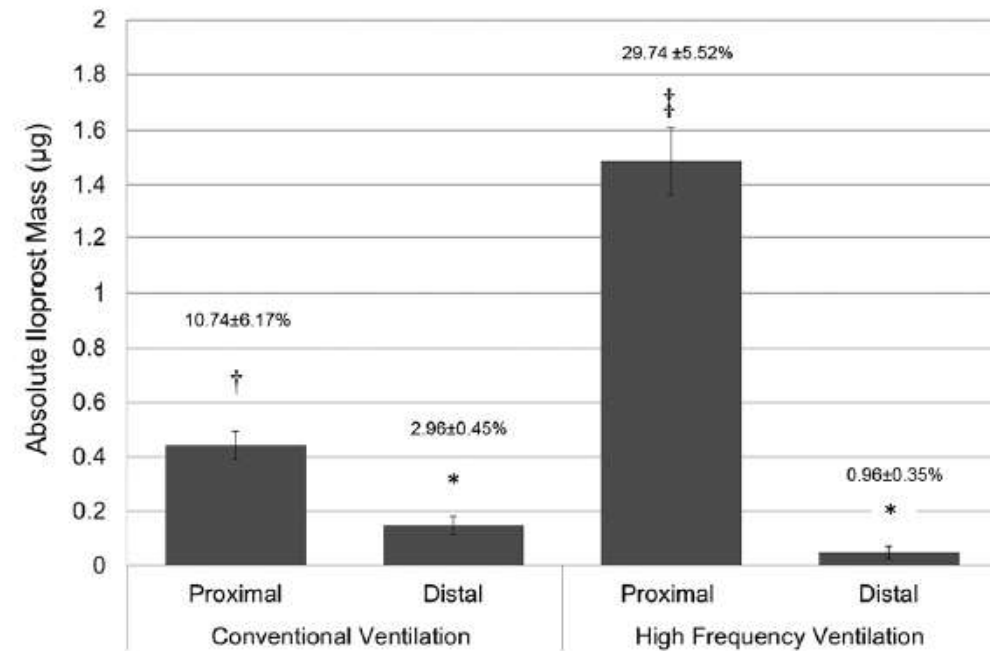
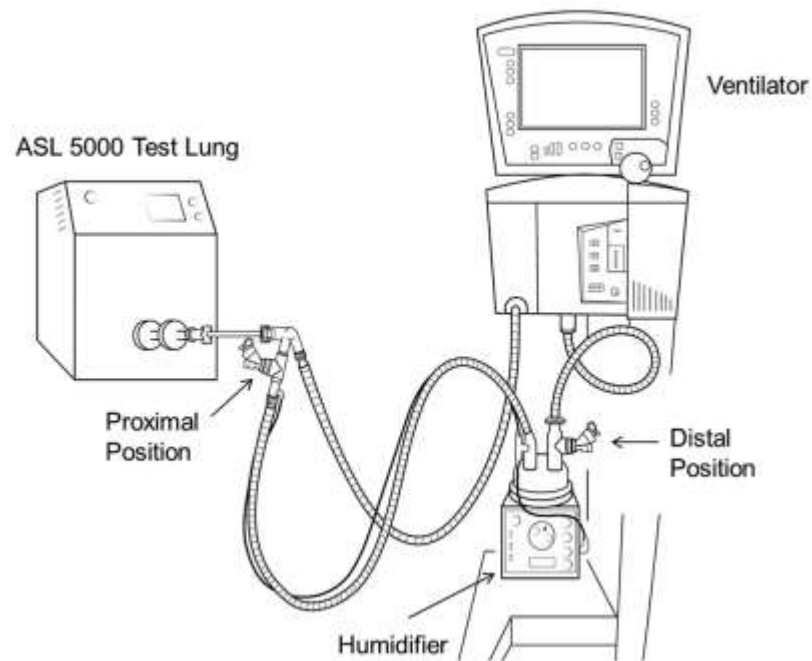
Results are expressed in percentage of the nebulizer charge (median and range)* and in percentage of the aerosol nebulized (median and range)† in the case of the circuit components.



Iloprost drug delivery during infant conventional and high-frequency oscillatory ventilation

Robert M. DiBlasi,^{1,2} Dave N. Crotwell,¹ Shuijie Shen,² Jiang Zheng,² James B. Fink,³ Delphine Yung⁴

¹Respiratory Therapy Department, Seattle Children's Hospital, Seattle, Washington, USA; ²Seattle Children's Hospital Research Institute, Seattle, Washington, USA; ³James B. Fink, LLC, San Mateo, California, USA; ⁴Department of Cardiology, Seattle Children's Hospital, Seattle, Washington, USA



Influence of Nebulizer Type, Position, and Bias Flow on Aerosol Drug Delivery in Simulated Pediatric and Adult Lung Models During Mechanical Ventilation

Arzu Ari PhD RRT PT CPFT, Orcin Telli Atalay PhD PT, Robert Harwood MSA RRT, Meryl M Sheard MSc RRT, Essam A Aljamhan MSc RRT, and James B Fink PhD RRT FAARC

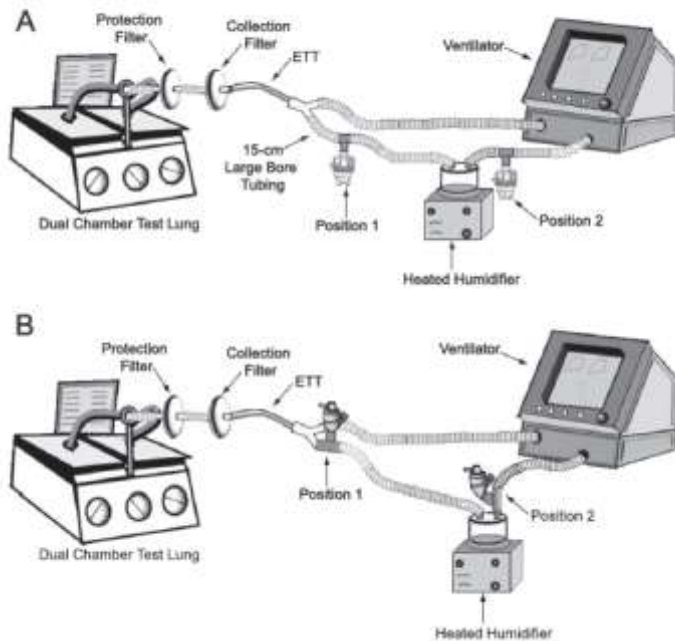


Table 1. Albuterol Sulfate Deposited Distal to the Endotracheal Tube

	Percent of Nominal or Emitted Dose (mean $\pm$ SD %)							
	Adult Lung Model				Pediatric Lung Model			
	Position 1		Position 2		Position 1		Position 2	
	Bias flow 2 L/min	Bias flow 5 L/min	Bias flow 2 L/min	Bias flow 5 L/min	Bias flow 2 L/min	Bias flow 5 L/min	Bias flow 2 L/min	Bias flow 5 L/min
Jet nebulizer	4.7 $\pm$ 0.1*	4.0 $\pm$ 0.1*	5.2 $\pm$ 0.2*	4.7 $\pm$ 0.4*	4.2 $\pm$ 0.2*	3.8 $\pm$ 0.3*	5.2 $\pm$ 0.3*	4.1 $\pm$ 0.4*
Vibrating-mesh nebulizer	13.4 $\pm$ 1.1	9.7 $\pm$ 0.6	23.8 $\pm$ 1.0	21.4 $\pm$ 0.4	11.4 $\pm$ 0.7	8.4 $\pm$ 0.2	13.6 $\pm$ 1.3	10.6 $\pm$ 0.3

* Significant difference between jet nebulizer and vibrating-mesh nebulizer ($p < .05$).

High-Percentage Lung Delivery in Children From Detergent-Treated Spacers

Johannes H. Wildhaber, MD,* Hettie M. Janssens, MD, Frédéric Piérart, MD, Nigel D. Dore, FRACP, Sunalene G. Devadason, PhD, and Peter N. LeSouëf, MD



	Group A	Group B	Group C
Actuator	12.3‰ (5.2)	12.4‰ (4.3)	8.5‰ (2.7)
Spacer	36.9‰ (2.6)	42.4‰ (10.3)	32.9‰ (2.7)
Filter	8.7‰ (3.9)	0.2‰ (0.1)	0.3‰ (0.2)
Mask	4.7‰ (2.8)		
Gastrointestinal deposition	20.9‰ (5.1)	16.8‰ (3.7)	16.5‰ (3.0)
Lung deposition	16.4‰ (5.5)	28.2‰ (6.7)	41.8‰ (3.8)

< 48 months

48 - 96 months

> 96 months

Babyhaler + mask

Volumatic + embout buccal

Take home messages

Bronchodilatateurs

- C** Il n'est pas recommandé d'administrer des bêta-2mimétiques (salbutamol, terbutaline) dans la prise en charge de BA en raison de l'absence de données suffisantes sur les profils répondeurs. L'administration peut être mal tolérée chez le nourrisson de moins de 2 mois.

Adrénaline

- A** Il n'est pas recommandé d'administrer de l'adrénaline en nébulisation dans la prise en charge de la BA.

Nébulisation de sérum salé hypertonique

- A** La nébulisation de sérum salé hypertonique n'est pas recommandée dans la prise en charge de la bronchiolite aiguë aux urgences.
La nébulisation de sérum salé hypertonique n'est pas recommandée dans la prise en charge de la bronchiolite aiguë en hospitalisation.

Corticoïdes

- C** Il n'est pas recommandé d'administrer des corticoïdes systémiques dans la prise en charge du nourrisson avec une BA.
- B** Il n'est pas recommandé d'administrer des corticoïdes inhalés dans la prise en charge du nourrisson avec une BA, ni en prévention d'un asthme ou atonie, ni en prévention de rechute de dyspnée sifflante.

HAS

HAUTE AUTORITÉ DE SANTÉ

CNP
de Pédiatrie
Conseil National Professionnel de Pédiatrie

D'après recommandations HAS, 2019