L'aérosolthérapie, comment faire au mieux

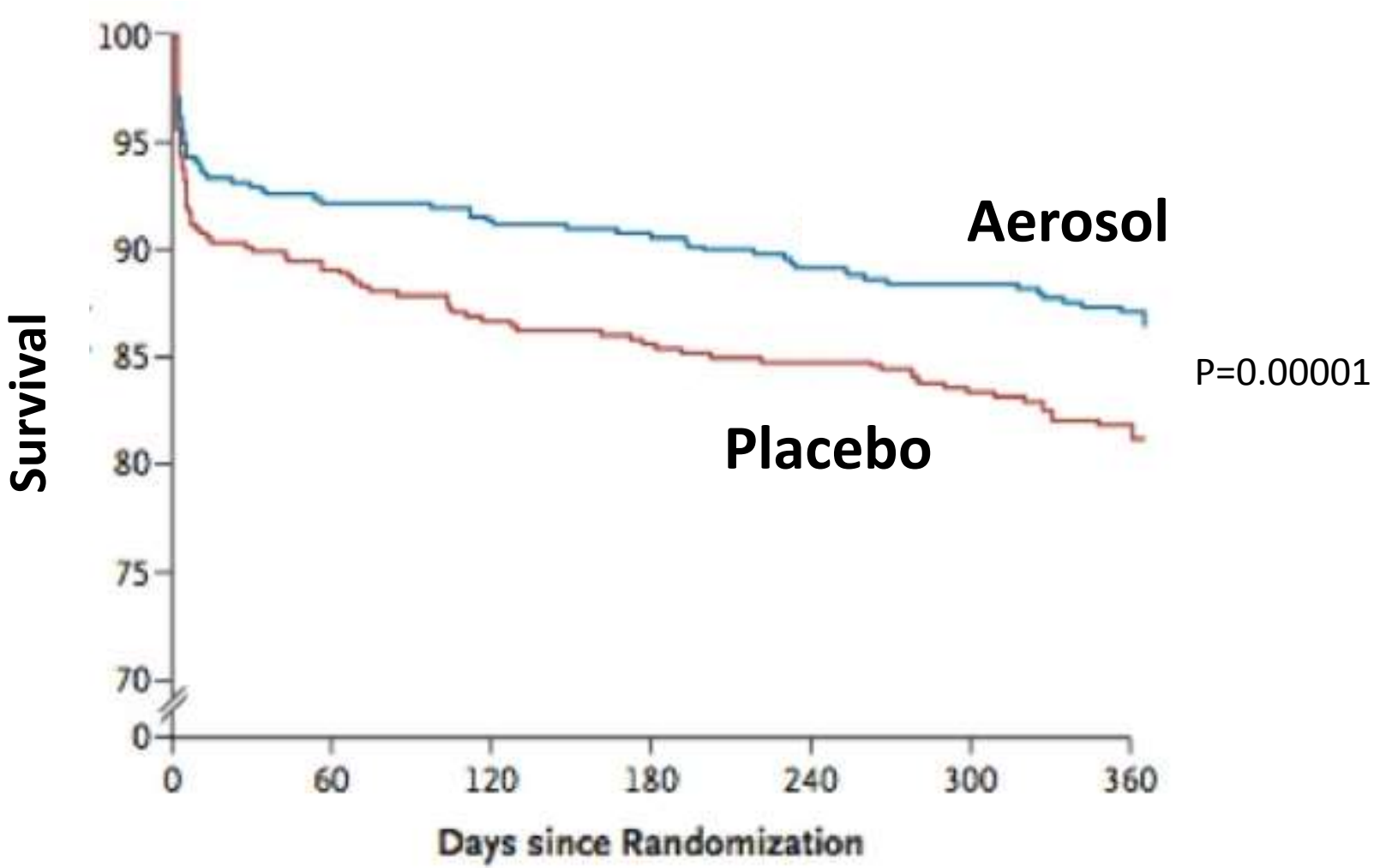
Quelles indications en réanimation?

Stephan EHRMANN

Liens d’intérêt

- Aerogen, Galway, Irlande
- Axess Vision Technology, Tours, France
- Bayer AG, Berlin, Allemagne
- Fisher & Paykel, Auckland, Nouvelle Zélande
- Hamilton médical, Bonaduz, Suisse
- Nihon Koheden, Higashinakano, Japon
- La diffusion technique française, Saint-Etienne, France
- Penn-Century Inc., Wyndmoor, Etats-Unis

The NEW ENGLAND JOURNAL of MEDICINE



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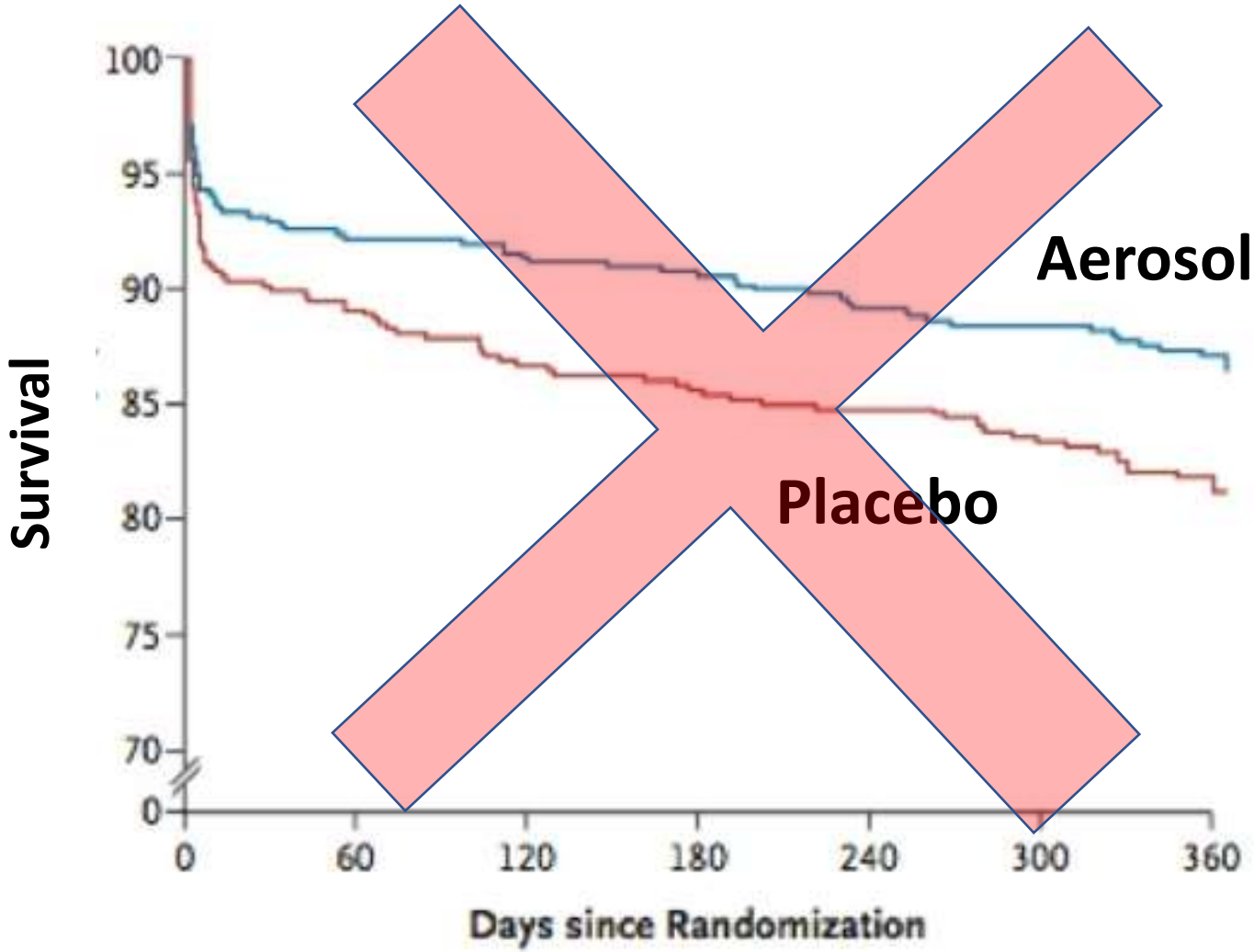
The NEW ENGLAND JOURNAL of MEDICINE



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Aérosols : une pratique très fréquente en réanimation

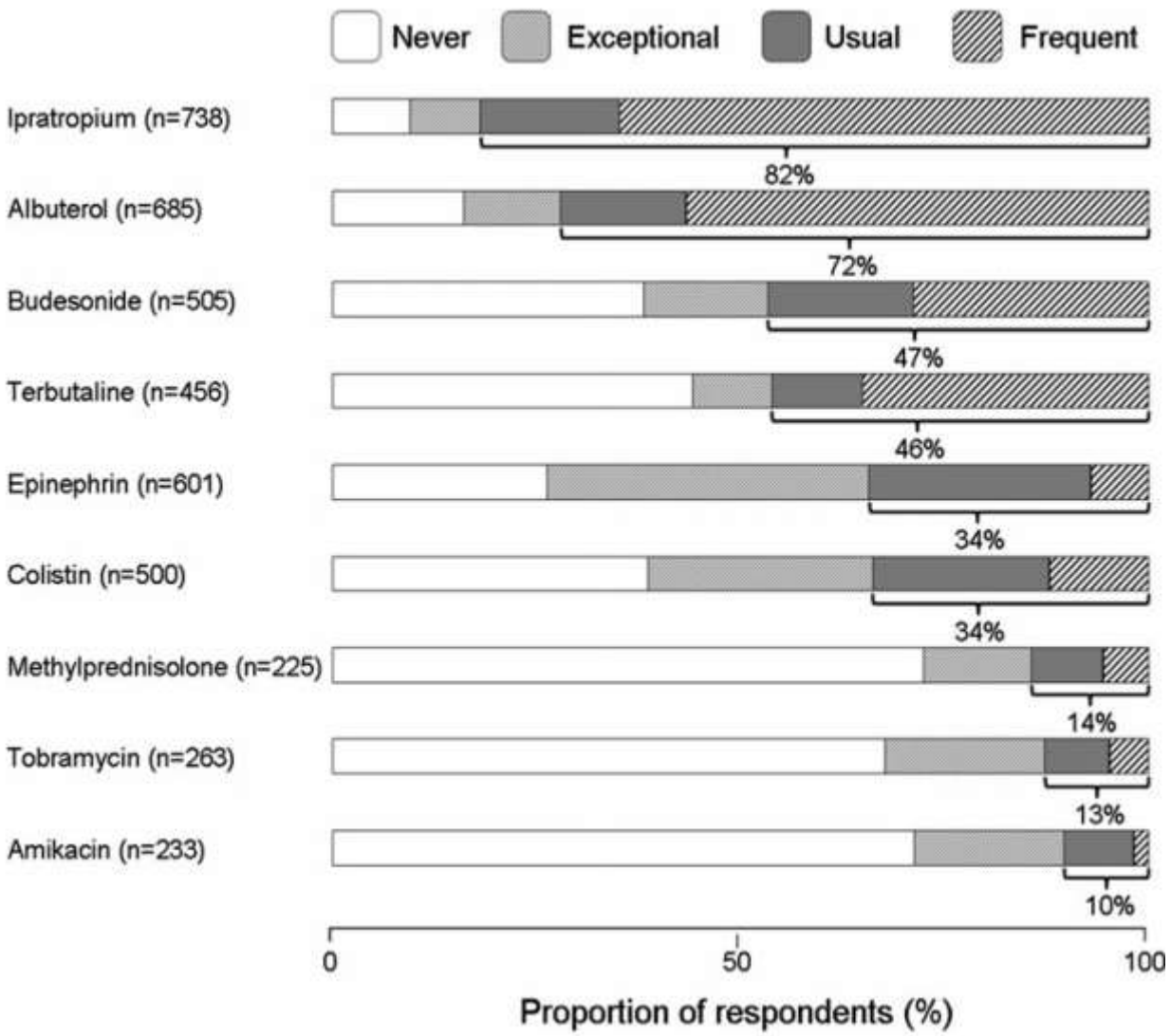
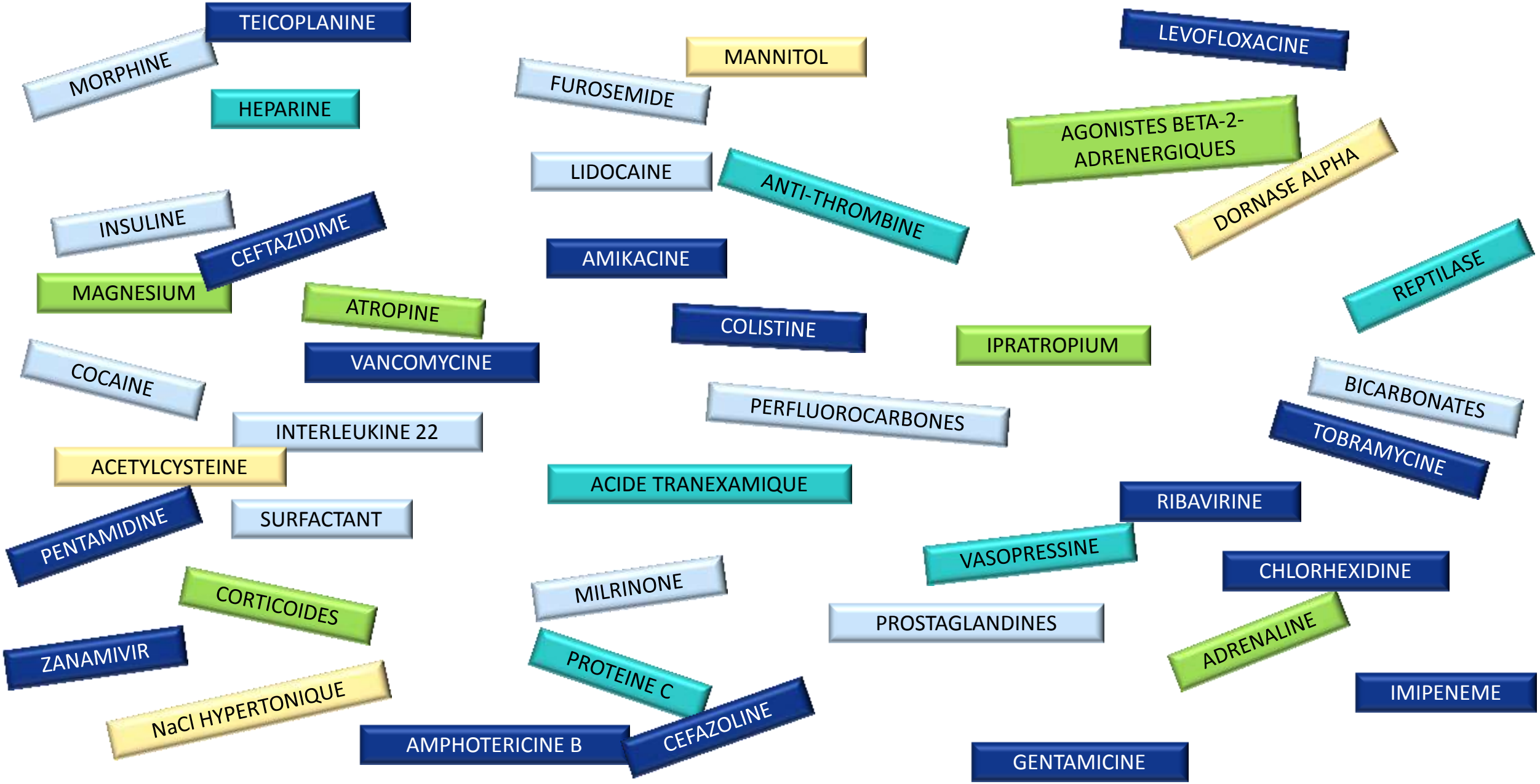


Table 1 Drugs reported to be aerosolized during MV

Drug class	Drug	No. (%) of respondents
Bronchodilators	Ipratropium[a]	738 (86)
	Albuterol[a]	685 (80)
	Epinephrine[a]	601 (70)
	Terbutaline[a]	456 (53)
	Magnesium	9 (1)
	Fenoterol	7 (1)
	Formoterol	1 (<0.5)
	Atropine	1 (<0.5)
Steroids	Budesonide[a]	505 (59)
	Methylprednisolone[a]	225 (26)
	Beclomethasone	11 (1)
	Dexamethasone	3 (<0.5)
	Betamethasone	3 (<0.5)
	Fluticasone	2 (<0.5)
	Hydrocortisone	2 (<0.5)
Anti-infective agents	Colistin[a]	500 (59)
	Tobramycin[a]	263 (31)
	Amikacin[a]	233 (27)
	Gentamicin	12 (1)
	Amphotericin B	11 (1)
	Vancomycin	5 (0.5)
	Pentamidine	2 (<0.5)
	Imipenem and cilastatin	1 (<0.5)
	Netilmicin	1 (<0.5)
	Ampicillin	1 (<0.5)
	Cefazolin	1 (<0.5)
	Ribavirin	1 (<0.5)
Analgesics	Lidocaine	7 (1)
	Morphine	3 (<0.5)
Mucolytic agents	Acetylcysteine	58 (7)
	Dornase alfa	8 (1)
	Mesna	7 (1)
	Ambroxol	5 (0.5)
	Bromhexine	4 (0.5)
	Gomenol	1 (<0.5)
	Tyloxapol	1 (<0.5)
Ionic solutions	Isotonic sodium chloride	21 (2)
	Hypertonic sodium chloride	10 (1)
	Sodium bicarbonate	1 (<0.5)
Other	Prostacyclin analogues	156 (18)
	Furosemide	4 (0.5)
	Heparin	2 (<0.5)
	Lung surfactant	1 (<0.5)
	Terlipressin	1 (<0.5)
	Tranexamic acid	1 (<0.5)
	Milrinone	1 (<0.5)
	Reptilase	1 (<0.5)

S Ehrmann, Intensive Care Med 2013

Molécules nébulisées chez l'homme :



Très fréquents en réanimation

Intensive Care Med
DOI 10.1007/s00134-015-4114-5

ORIGINAL

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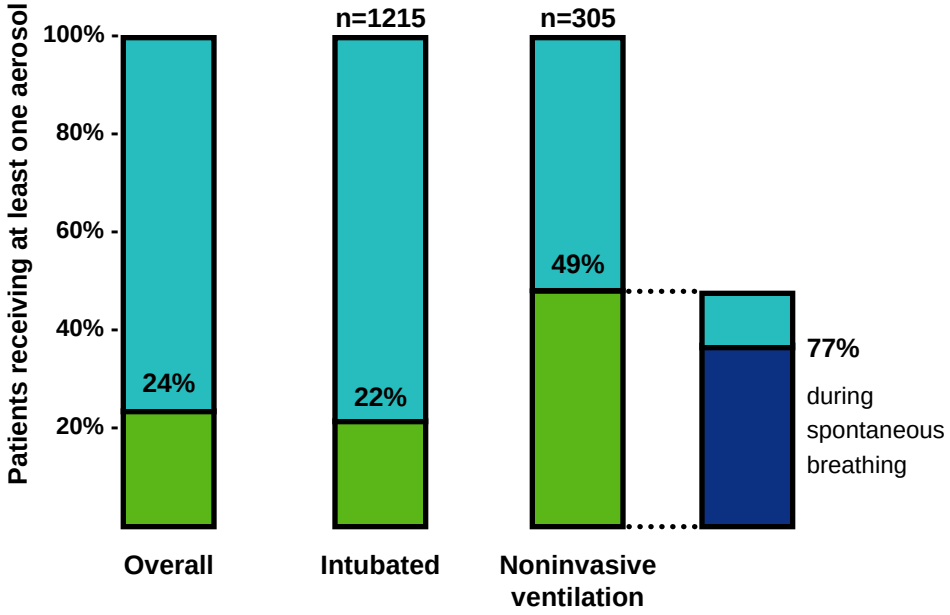
Carlos Lopes
Carlos Vicent
Arnaud Desachy
Gabriela Apiou-Sbirlea
Daniel Isabey
Laurent Brochard
Reva Research Network
AT@ICU Study Group

Aerosol therapy in intensive and intermediate care units: prospective observation of 2808 critically ill patients

n=2808 patients, 9714 aerosols



Quelles molécules?

	Aerosols (n = 9714)	Patients (n = 678)
Bronchodilators	7960 (82 %)	600 (89 %)
Short acting beta-2-adrenergic agonists	6780 (95 %)	463 (86 %)
Long acting beta-2-adrenergic agonists	88 (1 %)	24 (4 %)
Anticholinergic drugs	4958 (70 %)	198 (37 %)
Corticosteroids	1233 (13 %)	173 (26 %)
Beclomethasone dipropionate	269 (22 %)	31 (18 %)
Budesonide	897 (74 %)	130 (77 %)
Fluticasone	60 (5 %)	11 (6 %)
Other	5 (<1 %)	1 (<1 %)
Anti-infectious drugs	509 (5 %)	31 (5 %)
Amikacin	31 (6 %)	9 (30 %)
Amphotericin B	33 (6 %)	4 (13 %)
Colistin	400 (79 %)	19 (63 %)
Gentamicin	21 (4 %)	2 (7 %)
Ceftazidime	6 (1 %)	3 (10 %)
Tobramycin	14 (4%)	2 (<1 %)
Mucus modulating drugs	241 (3 %)	39 (6 %)
Acetylcysteine	136 (61 %)	22 (65 %)
Recombinant human deoxyribonuclease	12 (5 %)	7 (21 %)
2-Mercapto ethane sodium sulfonate (Mesna)	93 (42 %)	11 (32 %)
Electrolyte solutions	503 (5 %)	71 (9 %)
0.9 % sodium chloride[a]	440 (87 %)	65 (91 %)
Hypertonic sodium chloride	16 (3 %)	2 (3 %)
Sodium bicarbonate	47 (9 %)	4 (6 %)
Other	14 (<1 %)	5 (<1 %)

S Ehrmann, Intensive Care Med 2015

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S Ehrmann, Intensive Care Med 2015

GLOBAL INITIATIVE FOR ASTHMA

« Rapid acting inhaled beta2-agonists should be administered at regular intervals »

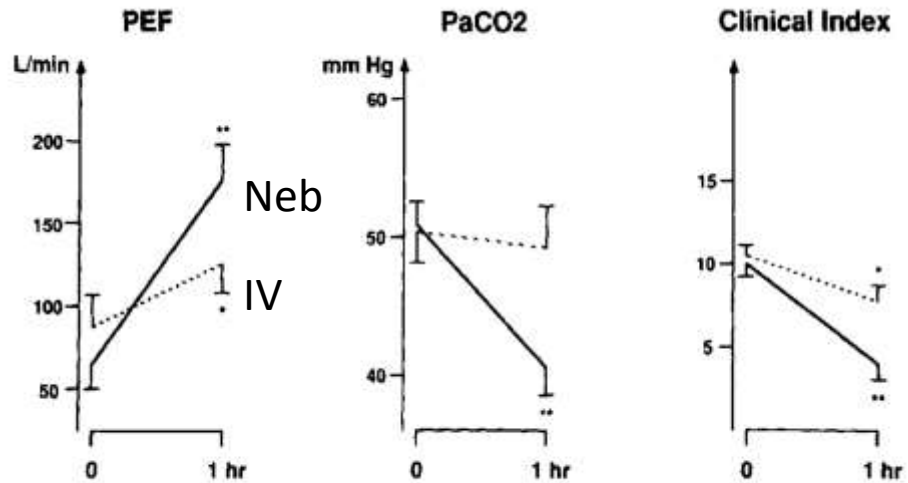
« There is no evidence to support the routine use of intravenous beta2-agonist in patients with severe asthma exacerbations »

Nebulized Versus Intravenous Albuterol in Hypercapnic Acute Asthma

A Multicenter, Double-blind, Randomized Study

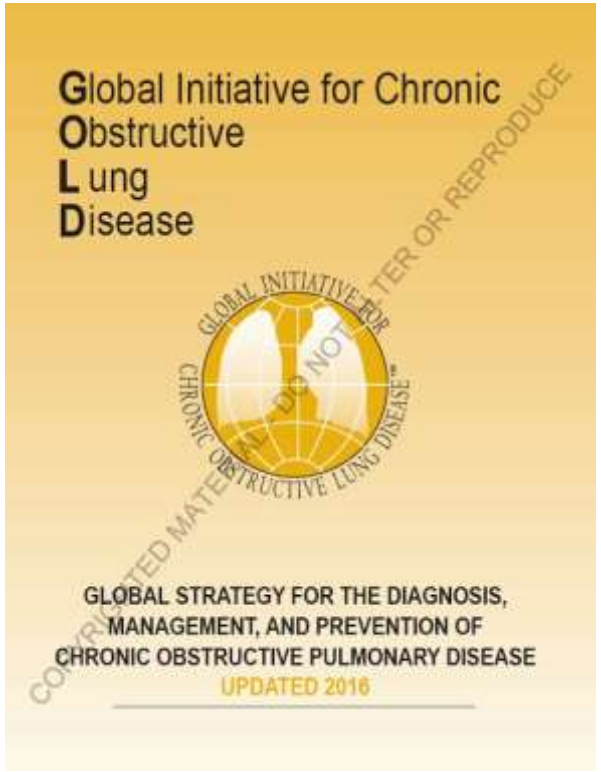
SERGIO SALMERON, LAURENT BROCHARD, HERVE MAL, ALAIN TENAILLON, MICHEL HENRY-AMAR, DOMINIQUE RENON, PIERRE DUROUX, and GERALD SIMONNEAU

Am J Respir Crit Care Med 1994



THERAPEUTIC RESPONSE AFTER 1 H*

	NEB Group (*n* = 21)	IV Group (*n* = 20)	p Value
ΔPEF, L/min	+107 ± 94	+42 ± 66	0.01
ΔPa_{CO_2}, mm Hg	−10 ± 5	−2 ± 12	< 0.01
Δ Clinical index	−5.9 ± 3.1	−2.0 ± 2.8	< 0.001
Successful treatment, n (%)	19 (86%)	12 (48%)	< 0.01



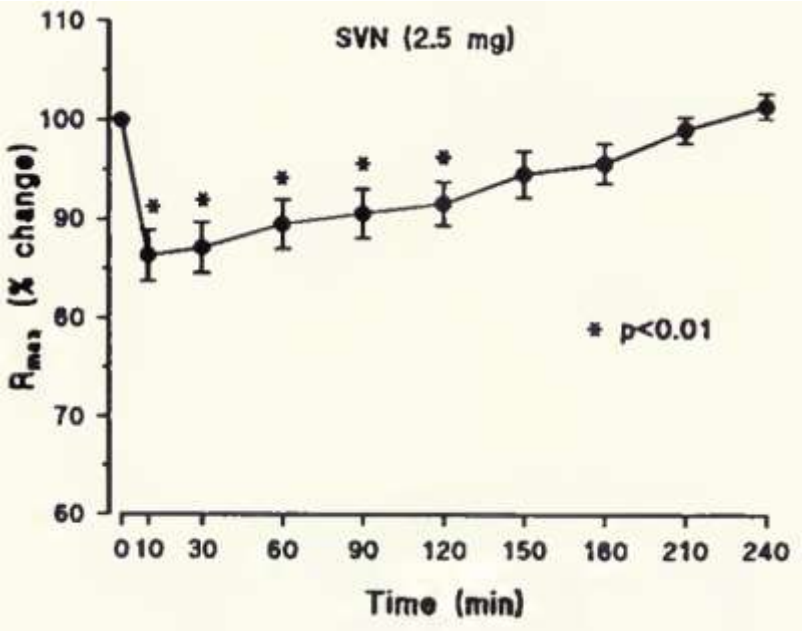
"Although there are no controlled trials,

short-acting inhaled beta2-agnosts with or without

short-acting anticholinergics are usually the preferred

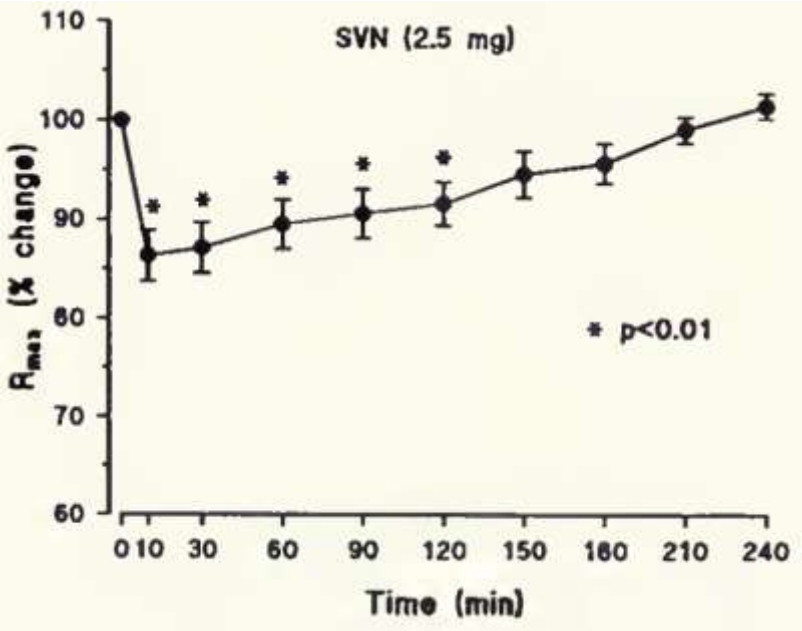
bronchodilators for treatment of exacerbation"

Nébulisation de Beta-2-mimétiques :



AG Duarte, Respir Care 2000

Nébulisation de Beta-2-mimétiques :



AG Duarte, Respir Care 2000

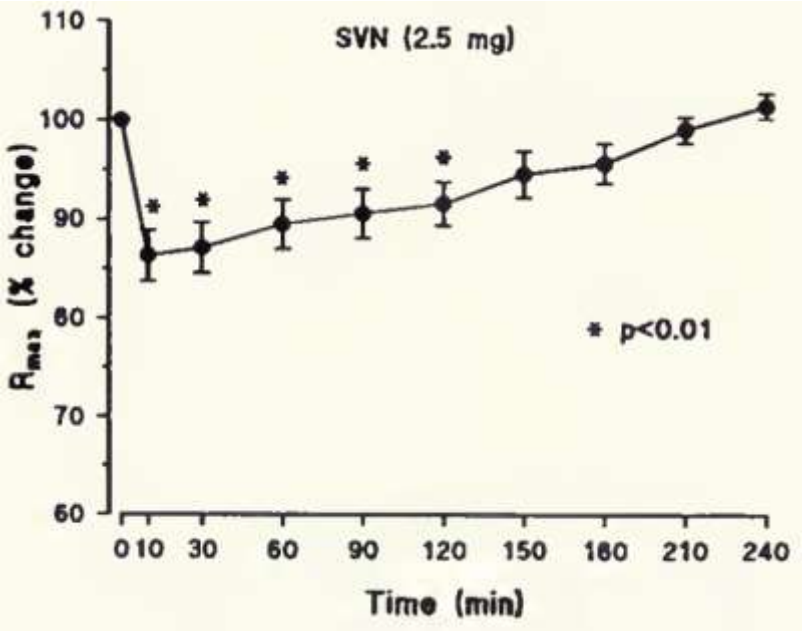
	Before Alb	After Alb	p Value
WOB, J/min	9.35 ± 1.05	8.33 ± 1.13	0.001
WOB, J/L	1.05 ± 0.10	0.96 ± 0.12	0.04
Wel, J/min	4.44 ± 0.68	4.13 ± 0.72	0.07
Wel, J/L	0.51 ± 0.07	0.47 ± 0.07	0.20
Wr, J/min	4.00 ± 0.60	3.40 ± 0.60	0.005
Wr, J/L	0.46 ± 0.07	0.39 ± 0.07	0.01
RL, cm H_2O/L/s	12.0 ± 1.7	9.8 ± 1.4	0.01

Definition of abbreviations: WOB (J/min) = power of breathing; WOB (J/L) = work of breathing per liter of ventilation; Wel = elastic component of the work performed against lung and airways; Wr = resistive component of the work; RL = lung and airway resistance.

* Values are mean ± SEM.

J Mancebo, Am Rev Respir Dis 1991

Nébulisation de Beta-2-mimétiques :



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* Values are mean ± SEM.

J Mancebo, Am Rev Respir Dis 1991

	MDI		NEB	
	Before	After	Before	After
Rrs, cm $H_2O \cdot L^{-1} \cdot s$	16.49 ± 1.37	14.89 ± 1.08†	18.04 ± 1.85	15.15 ± 1.33†
Rint,rs, cm $H_2O \cdot L^{-1} \cdot s$	5.03 ± 0.81	4.10 ± 0.60†	5.23 ± 0.82	4.36 ± 0.62
ΔRrs, cm $H_2O \cdot L^{-1} \cdot s$	11.46 ± 1.04	10.79 ± 0.88	12.80 ± 1.59	10.79 ± 1.11†
PEEPt, cm H_2O	7.71 ± 0.90	6.43 ± 0.80†	7.69 ± 0.95	6.63 ± 0.80†
EELV, L	0.49 ± 0.07	0.41 ± 0.07†	0.50 ± 0.08	0.45 ± 0.08†
Est,rs, cm $H_2O \cdot L^{-1}$	17.68 ± 1.57	17.76 ± 1.56	17.51 ± 1.71	17.72 ± 1.62

C Guérin, Am J Respir Crit Care Med 1999

Bronchodilatateurs

Efficacité+++

Author, year (reference #)	Drug (dose, mg)	Aerosol device	Response
Guy, 1987[76]	Metaproterenol (1.8 mg)	Small-volume aerosol generator	Increase in expiratory flow at recoil pressure of 6 cm H_2O, and reduction in peak pressure and intrinsic PEEP
Wagener, 1987[77]	Ipratropium (0.2 mg)	pMDI and adapter	Decrease in inspiratory airway resistance and significant increase in paO_2
Fuller, 1990[72]	Fenoterol (0.65 mg) Ipratropium (1.75 mg)	pMDI-spacer Nebulizer	Decrease in peak airway pressure not significant with either device
Fernandez, 1990[78]	Albuterol (0.2 mg) or Ipratropium (0.04 mg)	pMDI and short catheter	Significant decrease in peak airway pressure and intrinsic PEEP
Bernasconi, 1990[73]	Fenoterol (0.4, 0.8, 1.2 mg)	Small-volume aerosol generator and jet nebulizer	Significant decrease in airway resistance, end-expiratory lung volume and intrinsic PEEP
Manzoho, 1987[81]	Albuterol (1.0 mg)	pMDI-spacer	Significant decrease in airway resistance
Guy, 1991[82]	Albuterol (0.3 mg) Albuterol (2.5 mg)	pMDI and adapter Nebulizer	Similar reductions in expiratory airflow resistance with each delivery device
Matthews , 1993[83]	Albuterol (up to 10 mg) Albuterol (2.5, 5, 7.5 mg)	pMDI and elbow adapter Nebulizer	No change in airway resistance with pMDI; significant reduction with nebulizer
Yang, 1994[85]	Ipratropium (0.5 mg)	Nebulizer	Significant reduction in peak airway pressure, mean airway pressure and mean airway resistance
Fernandez, 1994[86]	Fenoterol (0.1 mg) + Ipratropium (0.04 mg)	pMDI and short catheter	Significant decrease in airway resistance with combination
Dhand, 1995[28]	Albuterol (1.0 mg)	pMDI-spacer	Significant reduction of airway resistance for up to 60 min
Matthews, 1995[92]	Albuterol (0.5, 1.5, 3.0 mg cumulative dose)	pMDI-spacer	Significant reduction in airway resistance with 1.5 and 3.0 mg albuterol
Dhand, 1996[29]	Albuterol (0.4, 1.2, 2.8 mg cumulative dose)	pMDI-spacer	Significant reduction in airway resistance with 0.4, 1.2 and 2.8 mg of albuterol
Moukeudi, 1996[84]	Albuterol (0.6 mg) with or without end-inspiratory pause	pMDI-spacer	Significant reduction in airway resistance. No effect of end-inspiratory pause
Waugh, 1996[93]	Albuterol (0.4, 0.8 mg)	pMDI and chamber spacers	Reduction in airway resistance with 4 puffs and 8 puffs. No difference in response between 2 chamber spacers
Moukeudi, 1996[87]	Albuterol (0.6 mg)	pMDI-spacer	Significant reduction in airway resistance. No effect of tidal volume 8 mL/kg versus 12 mL/kg body weight
Guerin, 1996[94]	Fenoterol (0.2 mg) + Ipratropium (0.4 mg) Fenoterol (1.25 mg) + Ipratropium (0.5 mg)	pMDI-spacer Nebulizer	Significant reduction in airway resistance with both pMDI and nebulizer
Duarte, 2001[95]	Albuterol (0.4, 1.0 mg) Albuterol 2.5 mg	pMDI-spacer Nebulizer	Significant reduction in airway resistance with both pMDI and nebulizer for up to 2 h
Moukeudi, 2000[96]	Albuterol (0.2, 0.6 mg)	pMDI-spacer	Significant reduction in airway resistance. No effect of decelerating flow pattern (pressure control) versus square wave flow pattern (volume control)
Moukeudi, 2001[113]	Albuterol (0.6 mg)	pMDI-spacer	Significant reduction in airway resistance for up to 2 h, but the duration of effect was variable and unpredictable in individual patients
Moukeudi, 2001[90]	Albuterol (0.4 mg)	pMDI-spacer	Significant reduction in airway resistance. No effect of inspiratory flow rate (0.6 L/s versus 1.2 L/s constant flow, volume control ventilation)
Tzouli, 2001[97]	Albuterol (5 mg)	Nebulizer	Significant reduction in airway resistance. Application of external PEEP to counterbalance intrinsic PEEP provided additional benefits
Guerin, 2001[102]	Fenoterol (30 mg)	Nebulizer	Application of external PEEP did not provide additional benefits in reducing airway resistance or lung hyperinflation. External PEEP levels may need readjustment during treatment to prevent further hyperinflation
Mallatratis, 2002[98]	Albuterol (0.4 mg)	pMDI-spacer	Significant reduction in airway resistance for up to 2 hours, but there was no difference in the response during volume control versus pressure support ventilation with similar tidal volumes
Mallatratis, 2000[99]	Salmeterol (0.1 mg)	pMDI-spacer	Significant reduction in airway resistance for up to 8 h, but the duration of effect was variable and unpredictable in individual patients
Kondili, 2001[100]	Albuterol (0.4 mg)	pMDI-spacer	Expiratory resistance of the respiratory system (expiratory Rrs) was several-fold higher than inspiratory resistance. After albuterol, there was significant reduction in expiratory Rrs with increase in the rate of lung emptying beyond the end of

A Ari, J Aerosol Med Pulm Drug Deliv 2012

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Guerin, 2001[102]	Fenoterol (30 mg)	Nebulizer	Application of external PEEP did not provide additional benefits in reducing airway resistance or lung hyperinflation. External PEEP levels may need readjustment during treatment to prevent further hyperinflation
Mallatratis, 2002[95]	Albuterol (0.4 mg)	pMDI-spacer	Significant reduction in airway resistance for up to 2 hours, but there was no difference in the response during volume control versus pressure support ventilation with similar tidal volumes
Mallatratis, 2000[103]	Salmeterol (0.1 mg)	pMDI-spacer	Significant reduction in airway resistance for up to 8 h, but the duration of effect was variable and unpredictable in individual patients
Kondili, 2001[100]	Albuterol (0.4 mg)	pMDI-spacer	Expiratory resistance of the respiratory system (respiratory Rrs) was several-fold higher than inspiratory resistance. After albuterol, there was significant reduction in expiratory Rrs with increase in the rate of lung emptying toward the end of

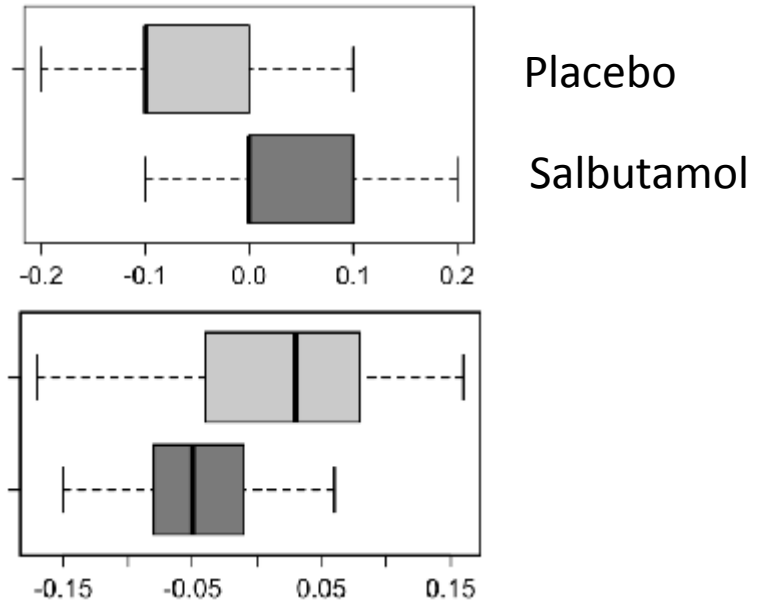
A Ari, J Aerosol Med Pulm Drug Deliv 2012

Efficacité+++

VNI

VEMS

Kaliémie



Placebo

Salbutamol

L Bodet Contentin, Réanimation 2017, O036

Intensive Care Med (1994) 20:199–202

Intensive Care Medicine

Comparison of one versus two bronchodilators in ventilated COPD patients

A. Fernandez, J. Muñoz, B. de la Calle, I. Alia, A. Ezpeleta, M.A. de la Cal, A. Reyes

	Ppeak (cmH_2O)	Pei (cmH_2O)	Pres (cmH_2O)	auto-PEEP (cmH_2O)	Inspiratory resistance ($cmH_2O/l/s$)	Compliance (ml/cmH_2O)
I. Bromide + fenoterol						
Baseline	35.4 (1.8)	22.7 (1.3)	12.6 (0.9)	9.6 (1)	23.4 (1.1)	62 (6.1)
Post – 60 min	31.6 (1.8)[a]	20.8 (1.2)[a]	10.8 (1.1)[a]	7.3 (0.8)[a]	19.6 (0.8)[a]	62.1 (7.9)[a]
I. Bromide						
Baseline	35.8 (1.5)	22.5 (1.2)	13.3 (1)	8.6 (1.1)	24.5 (12)	55.4 (4.7)
Post – 60 min	34 (1.8)	21.8 (1)	12.2 (1.6)	7.8 (0.9)	21.5 (23)	55.7 (5.4)

Intensive Care Med (1994) 20:199–202

Intensive Care Medicine

Comparison of one versus two bronchod in ventilated COPD patients

A. Fernandez, J. Muñoz, B. de la Calle, I. Alia, A. Ezpelet

	Ppeak (cmH_2O)	auto-PEEP (cmH_2O)		Compliance (ml/cmH_2O)
I. Bromide + fenoterol				
Baseline	35.4 (1.8)		9.6 (1)	62 (6.1)
Post – 60 min	31.6 (1.8)[a]	-2.3	7.3 (0.8)[a]	62.1 (7.9)[a]
I. Bromide				
Baseline	35.8 (1.5)		8.6 (1.1)	55.4 (4.7)
Post – 60 min	34 (1.8)	-0.8	7.8 (0.9)	55.7 (5.4)

Bronchodilatateurs

Corticoïdes

Antibiotiques

Autres

Bronchodilatateurs

Corticoïdes

Antibiotiques

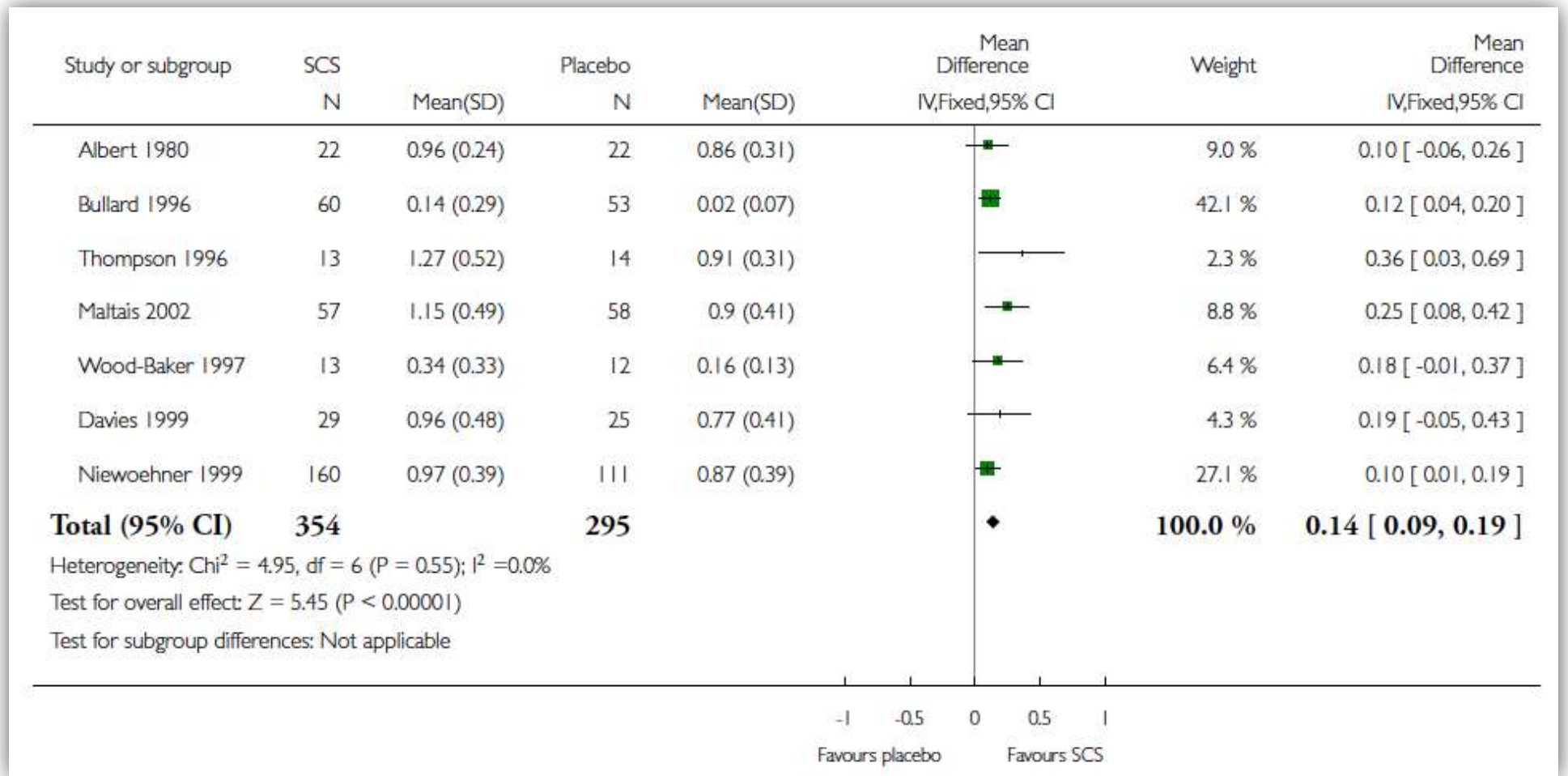
Autres

Systemic corticosteroids for acute exacerbations of chronic obstructive pulmonary disease (Review)

JAWalters , Cochrane 2009

Voie IV hors réanimation

Amélioration du VEMS



Systemic corticosteroids for acute exacerbations of chronic obstructive pulmonary disease (Review)

JAWalters , Cochrane 2009

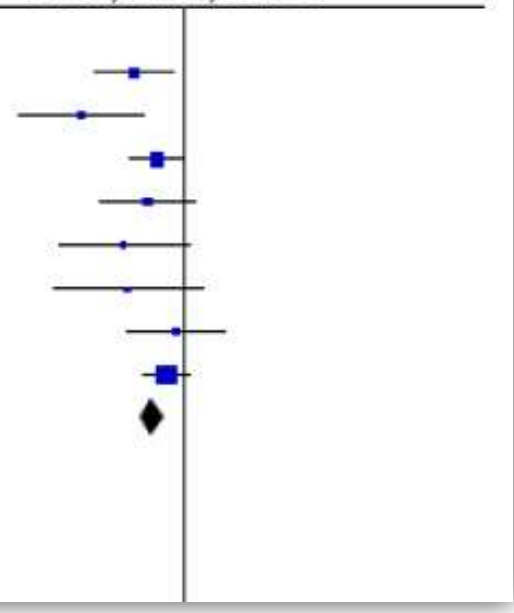
Voie IV hors réanimation

Échec de traitement

Study or Subgroup	SCS Events	SCS Total	Placebo Events	Placebo Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
1.1.1 Treatment at least 72 hours						
Bullard 1996	5	60	14	53	11.3%	0.28 [0.10, 0.74]
Thompson 1996	0	13	8	14	4.2%	0.07 [0.01, 0.36]
Aaron 2003	19	70	30	70	22.9%	0.50 [0.25, 1.01]
Maltais 2002	3	62	8	66	7.2%	0.40 [0.12, 1.37]
Davies 1999	1	29	5	27	3.9%	0.21 [0.04, 1.14]
Wood-Baker 1997	1	13	4	13	3.0%	0.24 [0.04, 1.62]
Chen 2005	5	43	6	43	6.9%	0.81 [0.23, 2.86]
Niewoehner 1999	32	160	31	111	33.5%	0.64 [0.36, 1.14]
Subtotal (95% CI)		**450**		**397**	**92.9%**	**0.45 [0.32, 0.63]**
Total events	66		106			

Heterogeneity: $Chi^2 = 9.53$, $df = 7$ ($P = 0.22$); $I^2 = 27\%$

Test for overall effect: $Z = 4.57$ ($P < 0.00001$)

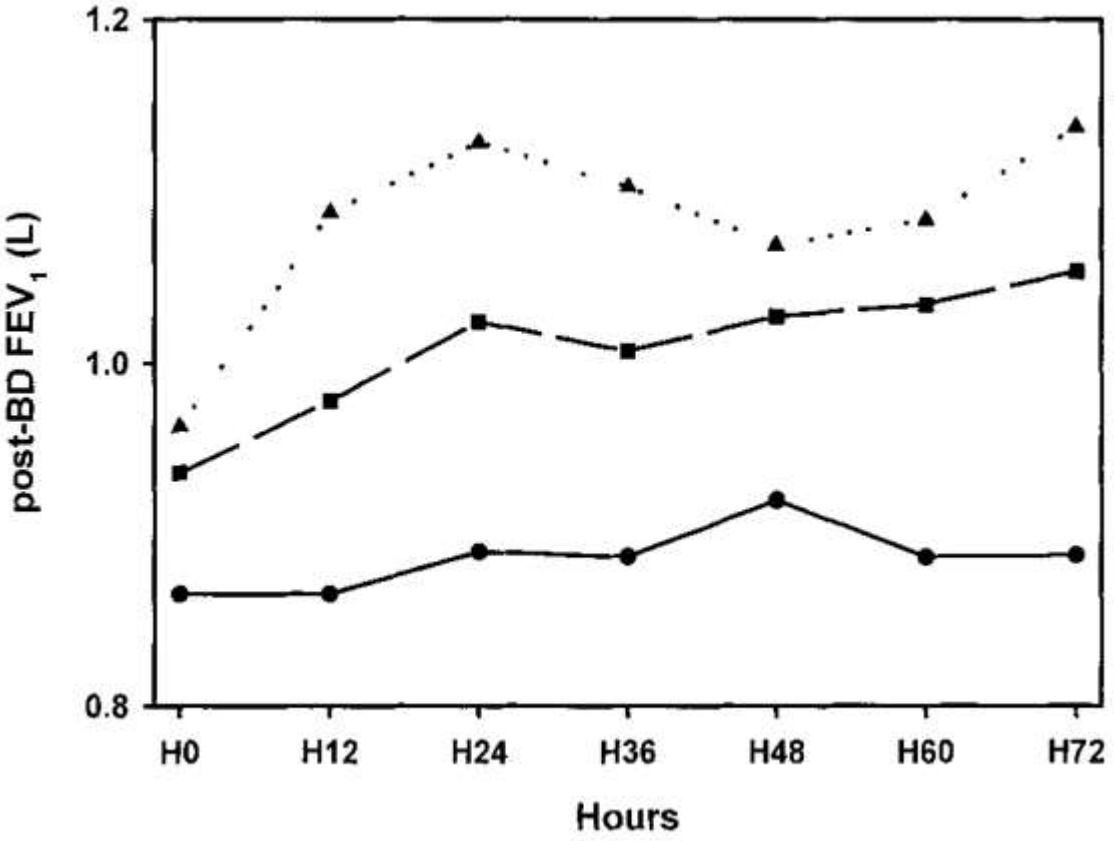


Comparison of Nebulized Budesonide and Oral Prednisolone with Placebo in the Treatment of Acute Exacerbations of Chronic Obstructive Pulmonary Disease

A Randomized Controlled Trial

FRANÇOIS MALTAIS, JULIETTE OSTINELLI, JEAN BOURBEAU, ANDRÉ BERNARD TONNEL, NADINE JACQUEMET, JENNIFER HADDON, MICHEL ROULEAU, MOHAMED BOUKHANA, JEAN BENOÎT MARTINOT, and PIERRE DUROUX

Hors réanimation



Oral

Nébulisé

Placebo

Efficacy of Corticosteroid Therapy in Patients With an Acute Exacerbation of Chronic Obstructive Pulmonary Disease Receiving Ventilatory Support

Inmaculada Alia, MD; Miguel A. de la Cal, MD; Andrés Esteban, MD, PhD; Ana Abella, MD; Ricard Ferrer, MD; Francisco J. Molina, MD; Antoni Torres, MD, PhD; Federico Gordo, MD; José J. Elizalde, MD; Raúl de Pablo, MD; Alejandro Huete, MD; Antonio Anzueto, MD, PhD

Table 2. Outcome Measures

Outcome[a]	Placebo Group (n=40)	Corticosteroid Group (n=43)	*P* Value
Duration of mechanical ventilation, d	4 (3-7)	3 (2-6)	.04
NIMV	4 (2-5)	2 (2-3)	.008
CMV	7 (4-11)	5 (3-7)	.09
Length of ICU stay, d	7 (5-12)	6 (4-10)	.09
NIMV	5 (4-9)	4 (3-5)	.04
CMV	10 (7-18)	9 (6-12)	.18
Length of hospital stay, d	15 (11-21)	13 (8-21)	.30
NIMV	15 (9-20)	14 (8-19)	.99
CMV	17 (12-31)	13 (8-22)	.07
In-ICU mortality, No. (%)	4 (10)	5 (12)	.81
NIMV	1/19 (5)	0/18 (0)	>.99
CMV	3/21 (14)	5/25 (20)	.71
Failure of NIMV, No. (%)	7/19 (37)	0/18 (0)	.004
Reintubation within 48 h,[b] No. (%)	5/26 (19)	3/22 (14)	.71

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Prednisone in COPD exacerbation requiring ventilatory support: an open-label randomised evaluation

Fekri Abroug[1,2], Lamia Ouanes-Besbes[1,2], Mohamed Fkih-Hassen[2,3], Islem Ouanes[1,2], Samia Ayed[2,3], Fahmi Dachraoui[1,2], Laurent Brochard[4] and Souheil ElAtrous[2,3]

Prednisone 1 mg/kg per os vs placebo
N=217 patients

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	Prednisone	Control	Relative risk (95% CI)	p-value
Primary efficacy end-point				
ICU mortality	17/111 (15.3)	15/106 (14.2)	1.08 (0.6–2.05)	0.81
ICU mortality in patients ventilated with NIV	8/76 (10.5)	8/71 (11.3)	0.93 (0.37–2.35)	0.88
ICU mortality in patients ventilated conventionally	9/35 (25.7)	7/35 (20.0)	1.28 (0.54–3)	0.57
Secondary end-points				
NIV failure	12/76 (15.7)	9/71 (12.7)	1.25 (0.56–2.8)	0.59
Mechanical ventilation duration days	6 (4–12)	6 (3.8–12)		0.87
ICU length of stay days	9 (6–14)	8 (6–14)		0.88
Safety end-point				
Hyperglycaemic episodes requiring initiation or alteration of insulin therapy	55/111 (49.5)	35/106 (33.0)	1.5 (1.08–2.08)	0.015

Controlled Short-term Trial of Fluticasone Propionate in Ventilator-Dependent Patients With COPD*

Chest 2000;118;990-999

Stefano Nava and Maria Laura Compagnoni

Aérosol-Doseur : 4 x 250 µg / 12h

	Trachéotomisés / ventilés au long cours		
	J0	J6	
PEEPi	4,3±2,4	3,1±1,7	P<0,01
Rmax	19,0±6,5	14,6±6,0	P<0,001
Rmin	14,8±4,2	10,5±3,4	P<0,001

Bronchodilatateurs

Corticoïdes

Antibiotiques

Autres

Efficacité microbiologique

PAVM à BGN

Q Lu, Am J Respir Crit Care Med 2011

Gram negative VAP

PAVM à BGN

TABLE 2. ANTIBIOTIC TREATMENT EFFICIENCY

	Aerosol ($n = 20$)	Intravenous ($n = 20$)	*P* Value
Cure of *P. aeruginosa* VAP on Day 9, n (%)	14 (70)	11 (55)	0.33
Day 9: Positive BAL $\geq 10^4$ cfu·ml^{-1} or mini-BAL $\geq 10^3$ cfu·ml^{-1}, n	3	6	
Persisting *P. aeruginosa* VAP on Day 9, n (%)	3 (15)	6 (30)	0.26
VAP caused by superinfection on Day 9, n (%)	3 (15)	3 (15)	NS
Recurrence of *P. aeruginosa* VAP, n	3	1	NS
Recurrence of VAP caused by superinfection, n	2	0	NS
Duration of MV, median (IQR)	29 (22–38)	18 (13–31)	0.13
Duration of MV after inclusion, median (IQR)	14 (7–22)	8 (6–12)	0.18
Length of stay in ICU, median (IQR)	38 (29–55)	29 (18–44)	0.08
Length of stay in ICU after inclusion, median (IQR)	24 (18–48)	16 (11–23)	0.08
Mortality on Day 28, n (%)	2 (10)	1 (5)	0.55

Q Lu, Am J Respir Crit Care Med 2011

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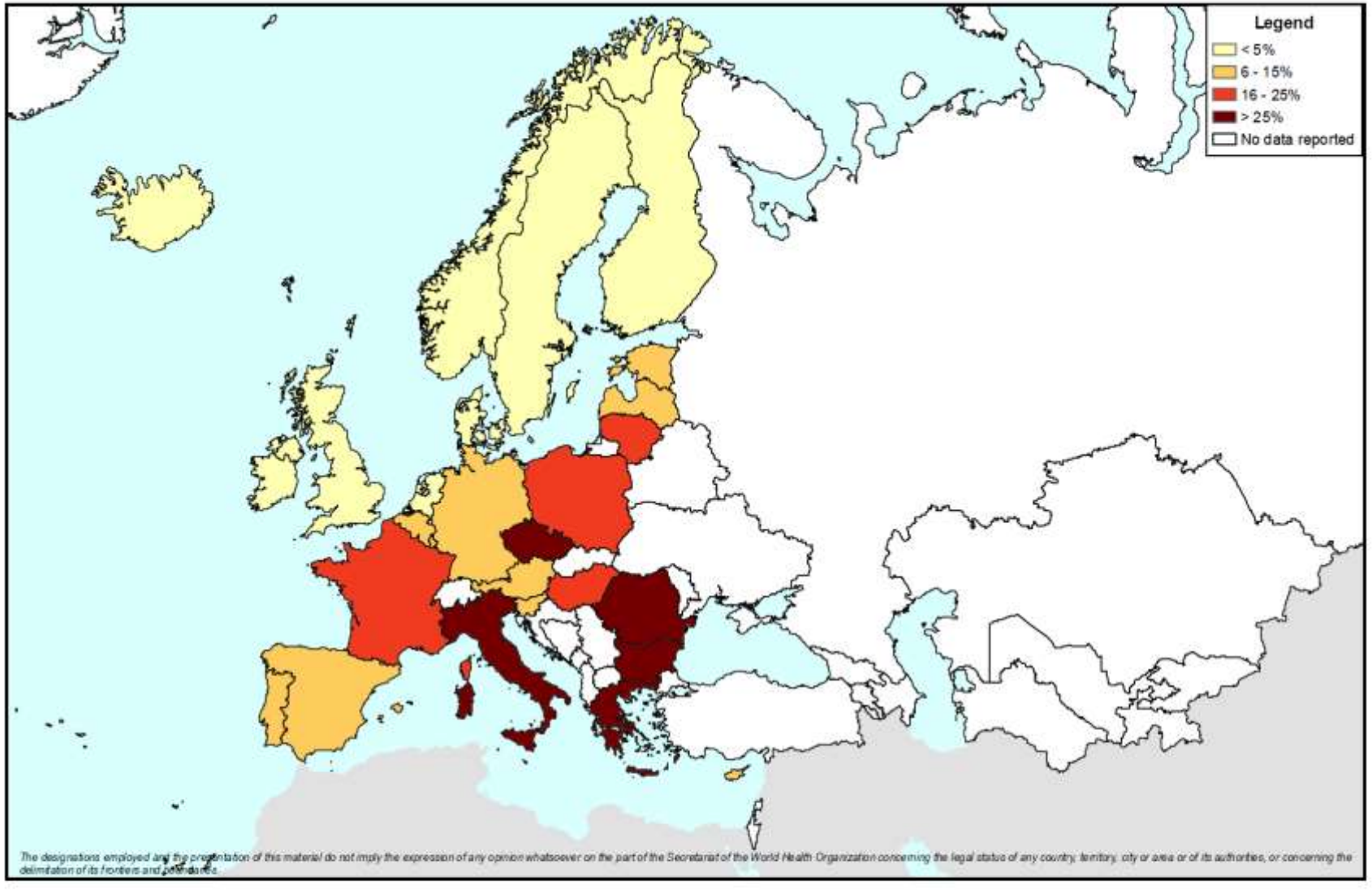
Q Lu, Am J Respir Crit Care Med 2011

Bactéries hautement résistantes



***Pseudomonas aeruginosa*:proportion of invasive isolates resistant to three or more antibiotic classes (piperacillin±tazobactam, fluoroquinolones, ceftazidime, aminoglycosides, carbapenems)**

Source: data from Antibicrobial resistance surveillance in Europe 2009. Stockholm, European Centre for Disease Prevention and Control, 2010.

Colistine

Cohortes :

DP Kofteridis, Clin Infect Dis 2010
IP Korbila, Clin Microbiol Infect 2010
R Naesns BMC Infect Dis 2011
MJ Pérez-Pedrero, Med Intensive 2011
G Kalin J Infect Chemother 2012
NM Doshi, BMC Anesthesiol 2013
M Tumbarello, Chest 2013
M Amin, Egypt J Chest Dis Tuberculosis 2013
TZ Bogovic, Signa Vitae 2014

} Rétrospectif, Colistine IV vs. IV + Nébulisée

Q Lu, Anesthesiology 2012

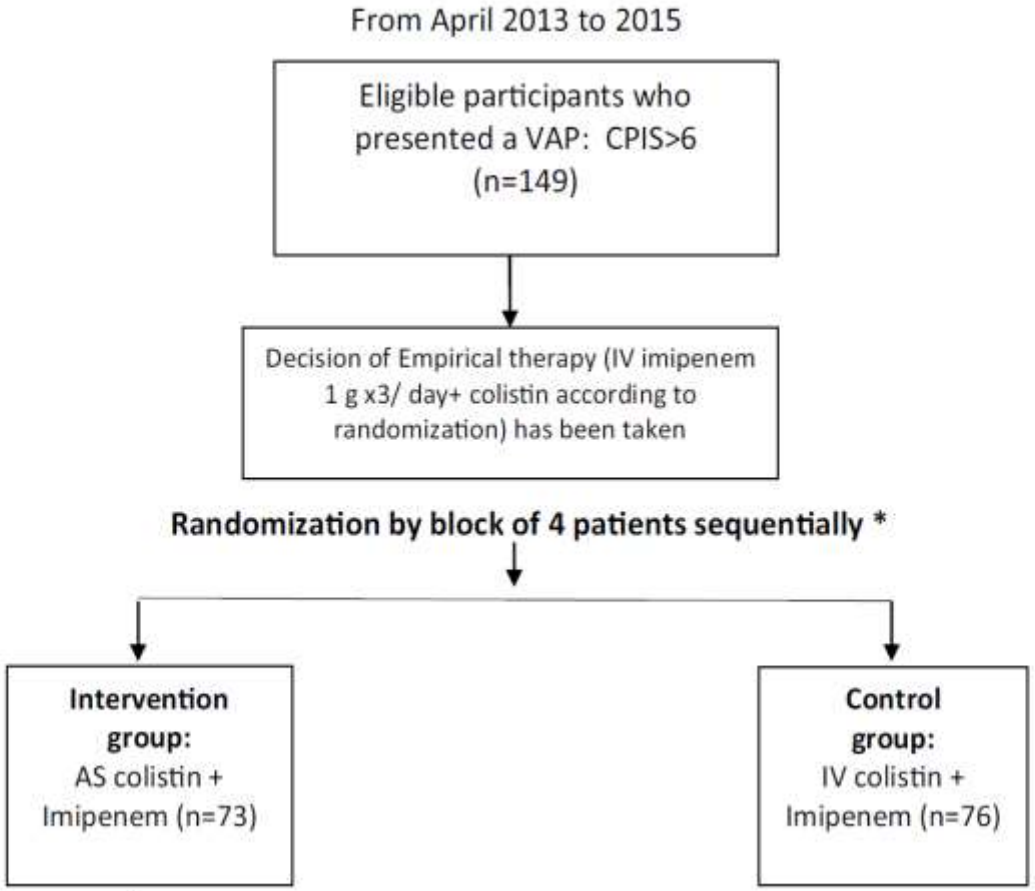
Prospectif,
Groupe BMR Colistine Nébulisée (5 MU x 3/J)
vs.
Germes sensibles traitement habituel

Etudes randomisée

P Rattanaumpawan, J Antimicrob Chemother 2010 — 1 MU x 2/J

S Abdellatif, Ann Intensive Care 2016 — 4 MU x 3/J

Colistine : RCT



- Nébuliseur à tamis vibrant
- 4 MU x 3 / J
- 8 mL/Kg ; FR 12 ; I/E 1/1 ; Plat 20%

S Abdellatif, Ann Intensive Care 2016

Colistine : RCT

- Nébuliseur à tamis vibrant
- 4 MU x 3 / J
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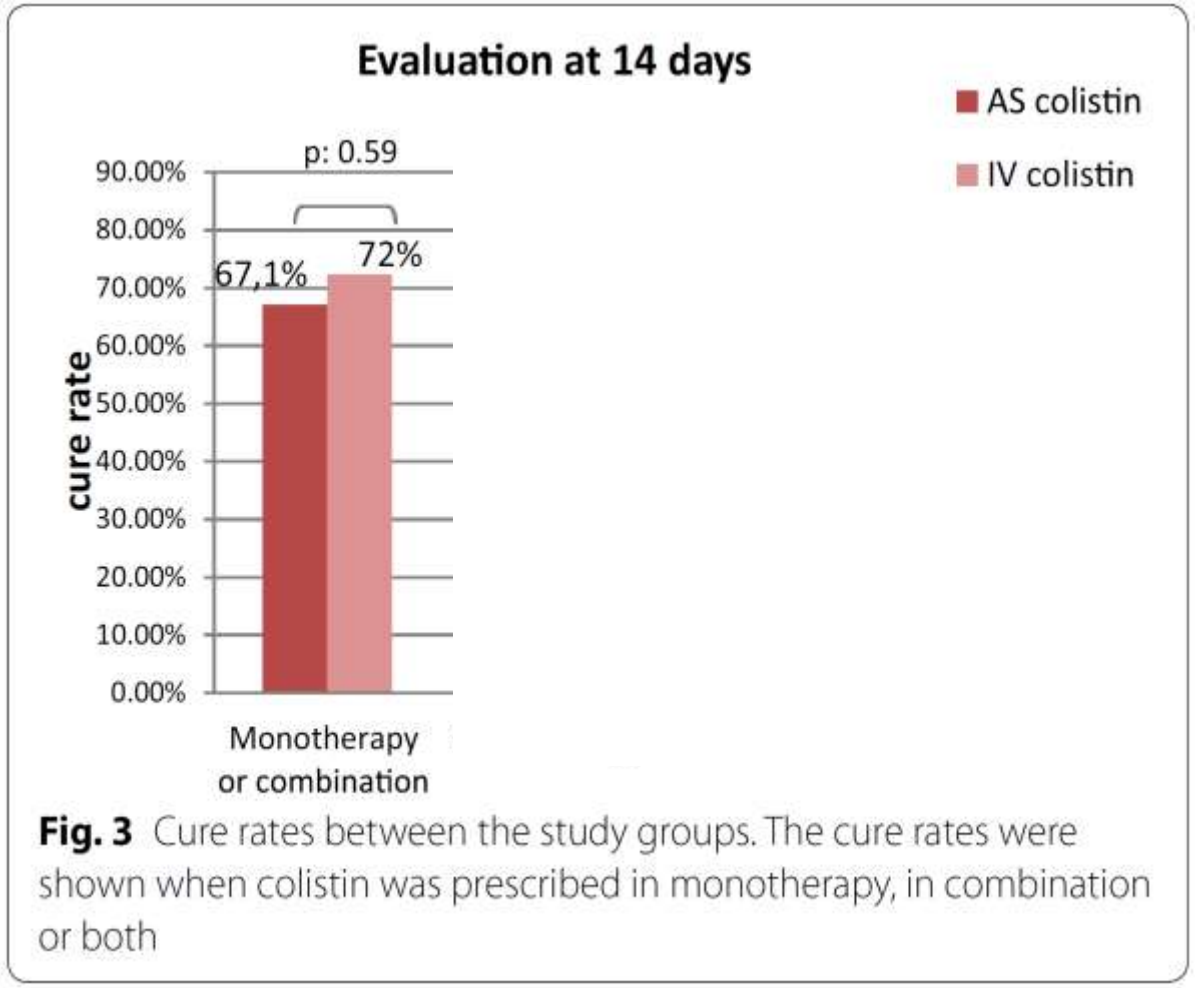

Fig. 3 Cure rates between the study groups. The cure rates were shown when colistin was prescribed in monotherapy, in combination or both

S Abdellatif, Ann Intensive Care 2016

Colistine : RCT

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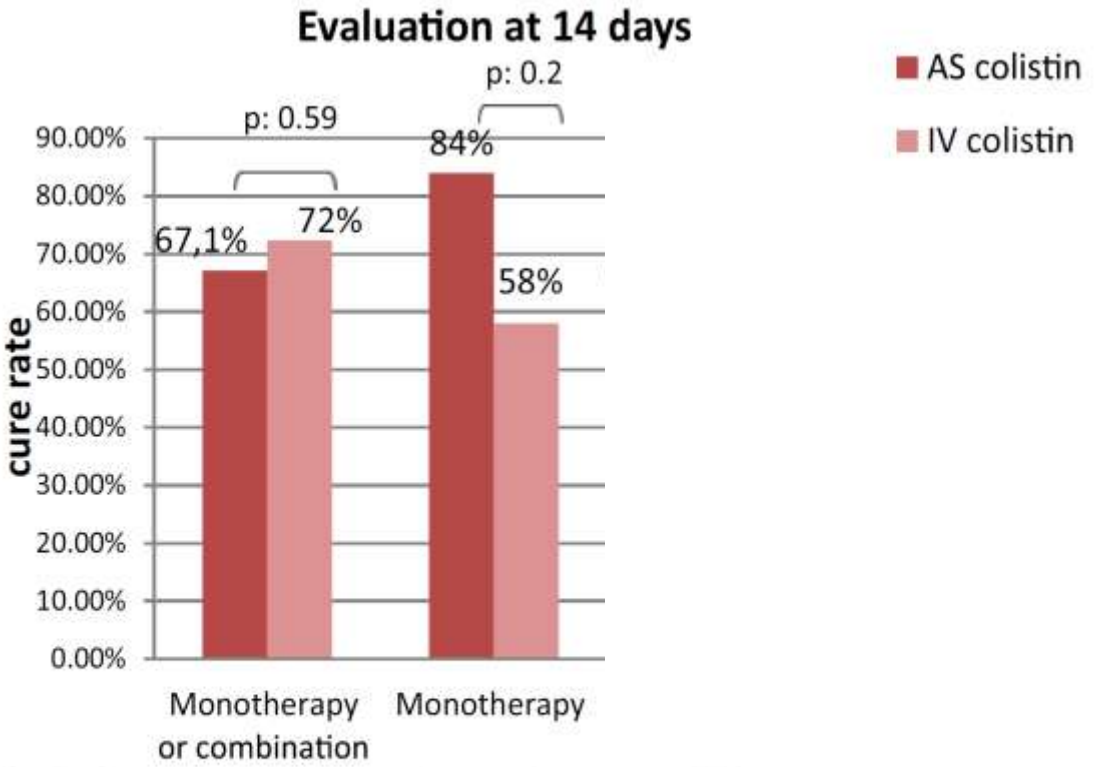

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S Abdellatif, Ann Intensive Care 2016

Décontamination bronchique

Colistine 500 MIU / 8h durant 10 jours
N=168

TABLE 2 Outcomes of participants in the two arms of the study[#]

	Overall n=168	Col group n=84	NS group n=84	p-value
Primary outcome				
VAP	39 (23.2)	14 (16.7)	25 (29.8)	0.07
Secondary outcomes				
VAP IDR	18	11.4	25.6	<0.01
GNB-VAP	30 (17.9)	9 (10.7)	21 (25)	0.03
MDR-VAP	22 (13.1)	6 (7.1)	16 (19)	0.04
VAP due to *Acinetobacter baumannii*	13 (7.7)	2 (2.8)	11 (13.1)	0.02
VAP due to *Staphylococcus* species	9 (5.4)	5 (6)	4 (4.8)	1.0
VAP during the 10-day prophylaxis	28 (16.7)	9 (10.7)	19 (22.6)	0.06
VAP post 10-day prophylaxis	11 (6.5)	5 (6)	6 (7.1)	1.0
VAP following VAT	6 (3.6)	4 (4.8)	2 (2.4)	0.68
VAT IDR	5.3	4.1	6.6	<0.01
VAT	11 (6.5)	5 (6)	6 (7.1)	1.0
GNB-VAT	11 (6.5)	5 (6)	6 (7.1)	1.0
MDR-VAT	9 (5.4)	4 (4.8)	5 (6)	1.0
VAT due to *Acinetobacter baumannii*	5 (3)	2 (2.4)	3 (3.6)	1.0
VAT during the 10-day prophylaxis	7 (4.2)	2 (2.4)	5 (6)	0.44

M Karvouniaris, Eur Respir J 2015

Décontamination bronchique

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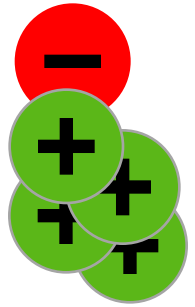
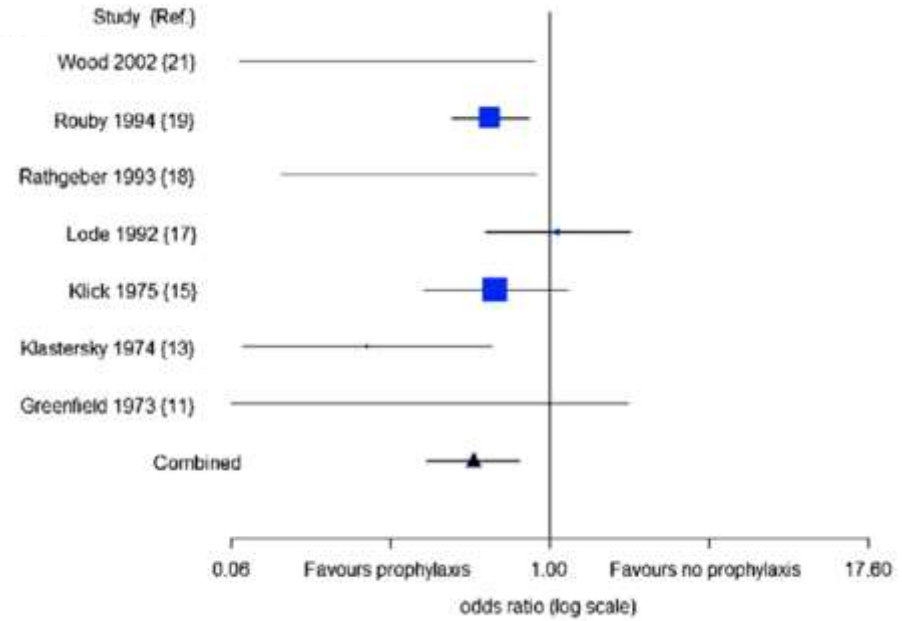


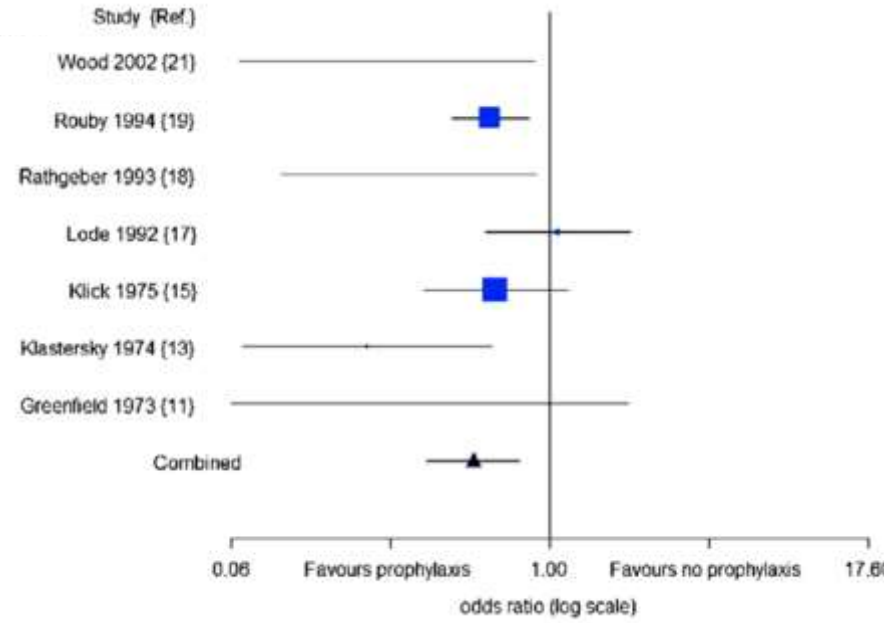
M Karvouniaris, Eur Respir J 2015

Décontamination bronchique

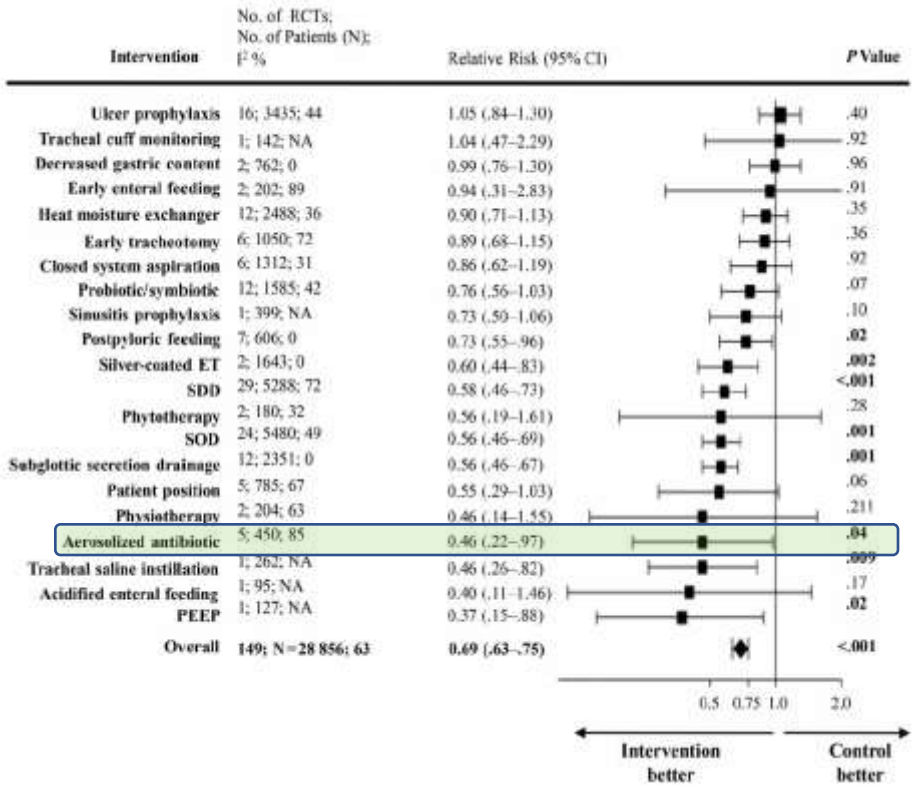


ME Falagas, Crit Care 2006

Décontamination bronchique

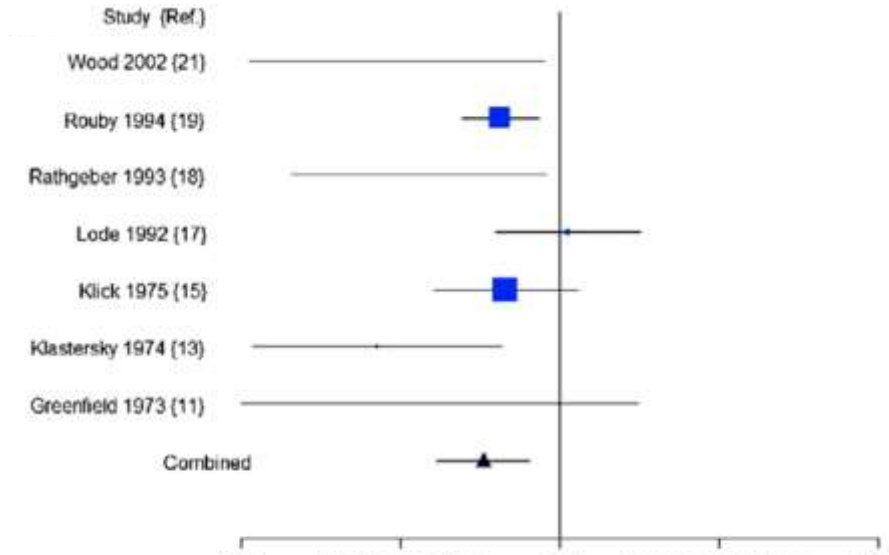


ME Falagas, Crit C



A Roquilly, Clin Infect Dis 2015

Décontamination bronchique



Intervention	No. of RCTs; No. of Patients (N); I^2 %	Relative Risk (95% CI)	*P* Value
Ulcer prophylaxis	16; 3435; 44	1.05 (.84–1.30)	.40
Tracheal cuff monitoring	1; 142; NA	1.04 (.47–2.29)	.92
Decreased gastric content	2; 762; 0	0.99 (.76–1.30)	.96
Early enteral feeding	2; 202; 89	0.94 (.31–2.83)	.91
Heat moisture exchanger	12; 2488; 36	0.90 (.71–1.13)	.35
Early tracheotomy	6; 1050; 72	0.89 (.68–1.15)	.36
Closed system aspiration	6; 1312; 31	0.86 (.62–1.19)	.92
Probiotic/symbiotic	12; 1585; 42	0.76 (.56–1.03)	.07
Sinusitis prophylaxis	1; 399; NA	0.73 (.50–1.06)	.10
Postpyloric feeding	7; 606; 0	0.73 (.55–.96)	**.02**
Patient position	5; 785; 67	0.55 (.29–1.03)	
Physiotherapy	2; 204; 63	0.46 (.14–1.55)	.21!
Aerosolized antibiotic	5; 450; 85	0.46 (.22–.97)	**.04**
Tracheal saline instillation	1; 262; NA	0.46 (.26–.82)	**.009**
Acidified enteral feeding	1; 95; NA	0.40 (.11–1.46)	.17
PEEP	1; 127; NA	0.37 (.15–.88)	**.02**
Overall	**149; N=28 856; 63**	**0.69 (.63–.75)**	**<.001**

A Roquilly, Clin Infect Dis 2015

Bronchodilatateurs

Corticoïdes

Antibiotiques

Autres

Quelles molécules?

	Aerosols (n = 9714)	Patients (n = 678)
Bronchodilators	7960 (82 %)	600 (89 %)
Short acting beta-2-adrenergic agonists	6780 (95 %)	463 (86 %)
Long acting beta-2-adrenergic agonists	88 (1 %)	24 (4 %)
Anticholinergic drugs	4958 (70 %)	198 (37 %)
Corticosteroids	1233 (13 %)	173 (26 %)
Beclomethasone dipropionate	269 (22 %)	31 (18 %)
Budesonide	897 (74 %)	130 (77 %)
Fluticasone	60 (5 %)	11 (6 %)
Other	5 (<1 %)	1 (<1 %)
Anti-infectious drugs	509 (5 %)	31 (5 %)
Amikacin	31 (6 %)	9 (30 %)
Amphotericin B	33 (6 %)	4 (13 %)
Colistin	400 (79 %)	19 (63 %)
Gentamicin	21 (4 %)	2 (7 %)
Ceftazidime	6 (1 %)	3 (10 %)
[illegible]	[illegible]	[illegible]
Mucus modulating drugs	241 (3 %)	39 (6 %)
Acetylcysteine	136 (61 %)	22 (65 %)
Recombinant human deoxyribonuclease	12 (5 %)	7 (21 %)
2-Mercapto ethane sodium sulfonate (Mesna)	93 (42 %)	11 (32 %)
Electrolyte solutions	503 (5 %)	71 (9 %)
0.9 % sodium chloride[a]	440 (87 %)	65 (91 %)
Hypertonic sodium chloride	16 (3 %)	2 (3 %)
Sodium bicarbonate	47 (9 %)	4 (6 %)
Other	14 (<1 %)	5 (<1 %)

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Conclusion

Pas de données de “haut niveau de prevue”

Bronchodilatateurs : OUI

Corticoïdes : des études à construire

Antibiotiques : au cas par cas

Autres ?

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Merci pour votre attention,