Corticothérapie systémique dans l'exacerbation aigue de BPCO

Fekri Abroug (MD)
CHU F.Bourguiba
Monastir. Tunisia

Quiz

Qui utilise la corticothérapie systémique au cours de l'Exacerbation Aigue de BPCO?

ctive pulmonary disease

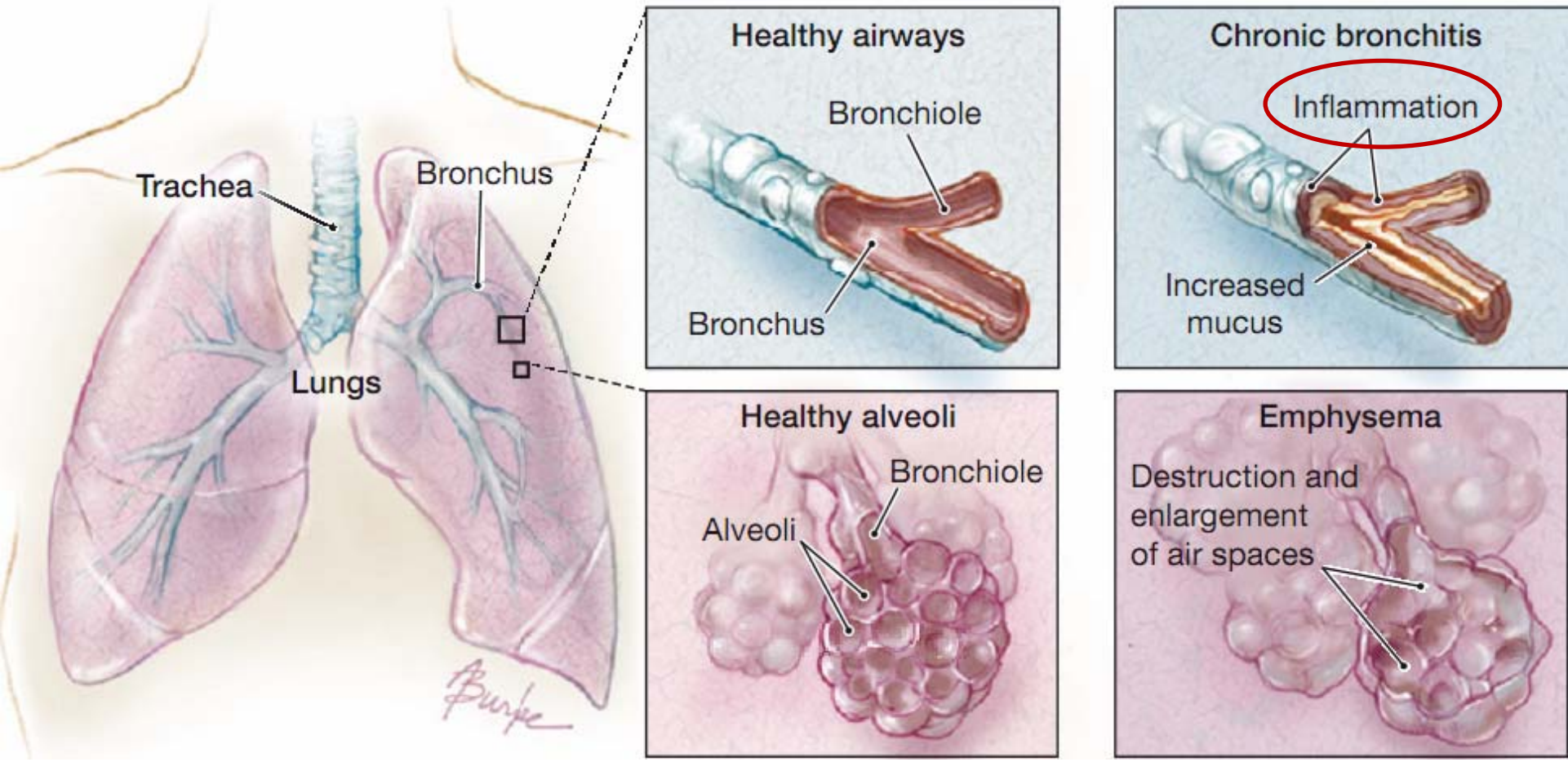
tion: a randomised

bes, Souheil Elatrous, Fekri Abroug

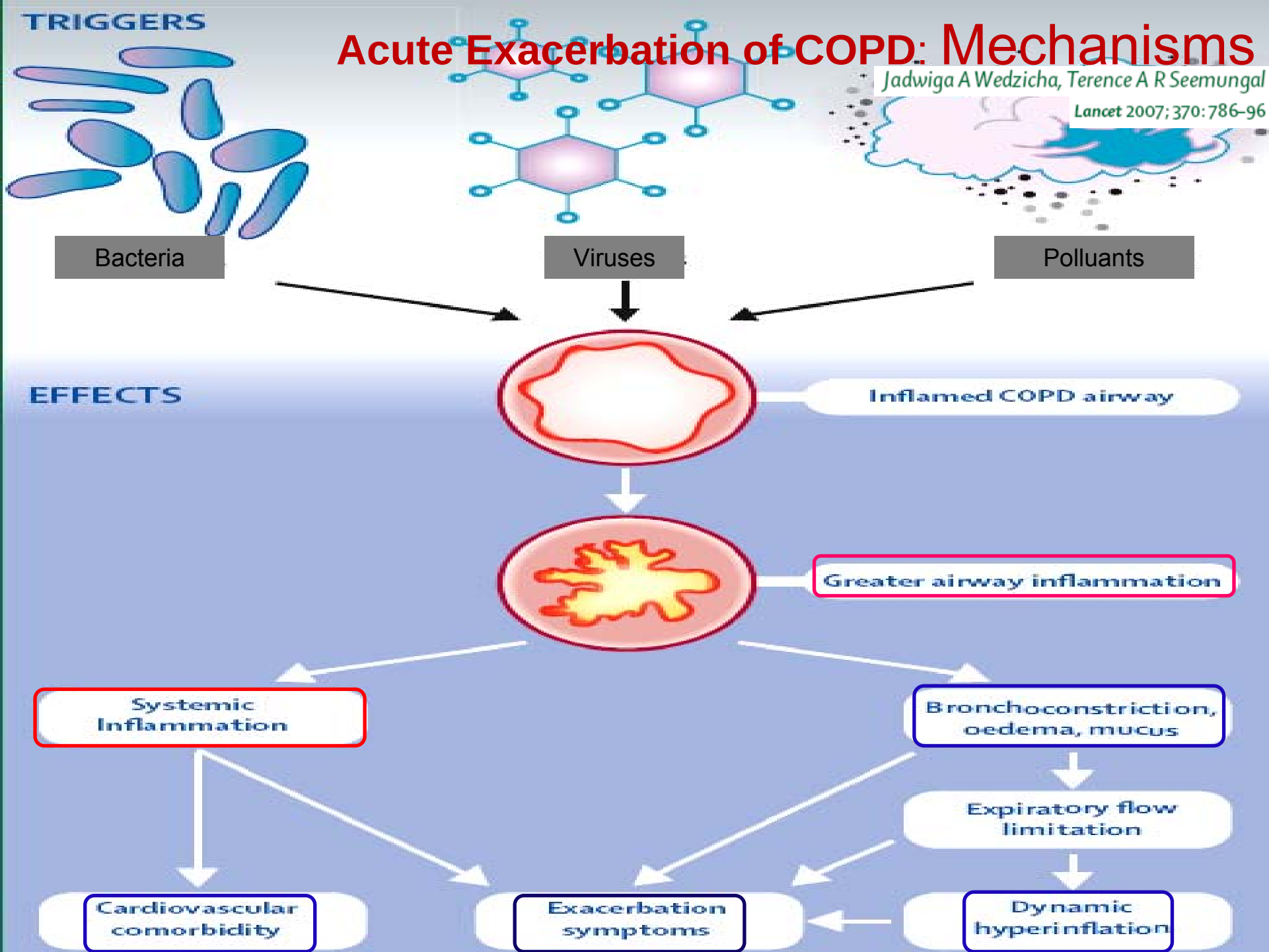
Lancet 2001; **358:** 2020–25

Characteristic	Ofloxacin (n=47)	Placebo (n=46)
Age (years)	66·2 (6·4)	66·5 (9·8)
Men	42 (89%)	42 (91%)
Smoking (pack-year)	55 (29)	54 (26)
Duration of chronic bronchitis (years)	11 (7)	11 (5)
Baseline FEV_1 (L/s)	0·79 (0·25)	0·74 (0·23
Exacerbations, number during past year	1·7 (1·6)	1·6 (1·2)
SAPSII	31 (9)	35 (10)
Temperature (°C)	37·5 (0·5)	37·7 (0·4)
⩾38·5°C	1 (2%)	2 (4%)
Blood leucocytes/μL	10 970 (3460)	11 560 (4250)
⩾12 000	14 (30%)	12 (26%)
Blood gases*		
PaO_2/FiO_2 (mm Hg)	210 (66)	224 (72)
$PaCO_2$ (mm Hg)	74 (22)	79 (21)
pH	7·22 (0·09)	7·21 (0·06
Initial ventilatory support		
Non-invasive	32 (68%)	32 (69%)
Conventional	15 (32%)	14 (31%)
Previous maintenance therapy		
Aminophylline	27 (57%)	29 (63%)
Inhaled β2-agonists	22 (47%)	19 (41%)
Home oxygen	5 (11%)	3 (6%)
Concomitant drugs		
Aminophylline	30 (64%)	32 (69%)
Nebulised β2-agonists	22 (47%)	22 (48%)

Corticoïdes systémiques?


Trachea
Bronchus
Lungs
Healthy airways
Bronchiole
Bronchus
Chronic bronchitis
Inflammation
Increased mucus
Healthy alveoli
Bronchiole
Alveoli
Emphysema
Destruction and enlargement of air spaces

Acute Exacerbation of COPD: Mechanisms



Jadwiga A Wedzicha, Terence A R Seemungal

Lancet 2007; 370: 786–96

Definition, evaluation and treatment (5)

- treatment for hospitalised patient

Bronchodilators

Short acting β_2-agonist (albuterol, salbutamol) and/or

Ipratropium MDI with spacer or hand-held nebuliser as needed

Supplemental oxygen (if saturation <90%)

Corticosteroids

If patient tolerates, prednisone 30–40 mg *per os q* day for 10 days

If patient can not tolerate oral intake, equivalent dose *i.v.* for up to 14 days

Consider use inhaled corticosteroids by MDI or hand-held nebuliser

Antibiotics (based on local bacteria resistance patterns)

May be initiated in patients that have a change in their sputum characteristics (purulence and/or volume)

Choice should be based on local bacteria resistance patterns

Amoxicillin/clavulanate

Respiratory fluoroquinolones (gatifloxacin, levofloxacin, moxifloxacin)

If *Pseudomonas spp.* and/or other *Enterobactereaces spp.* are suspected, consider combination therapy

ERS-ATS COPD Guidelines

Definition, evaluation and treatment (6)

- treatment in patients requiring special or intensive care unit

Supplemental oxygen
Ventilatory support

Bronchodilators

Short-acting β_2-agonist (albuterol, salbutamol) and ipratropium MDI with spacer, two puffs every 2–4 h

If the patient is on the ventilator, consider MDI administration, consider long-acting β-agonist

Corticosteroids

If patient tolerates oral medications, prednisone 30–40 mg *per os q* day for 10 days

If patient can not tolerate, give the equivalent dose *i.v.* for up 14 days

Consider use inhaled corticosteroids by MDI or hand-held nebuliser

Antibiotics (based on local bacteria resistance patterns)

Choice should be based on local bacteria resistance patterns

Amoxicillin/clavulanate

Respiratory fluoroquinolones (gatifloxacin, levofloxacin, moxifloxacin)

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ERS-ATS COPD Guidelines


EVIDENCE

THE COCHRANE COLLABORATION®

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

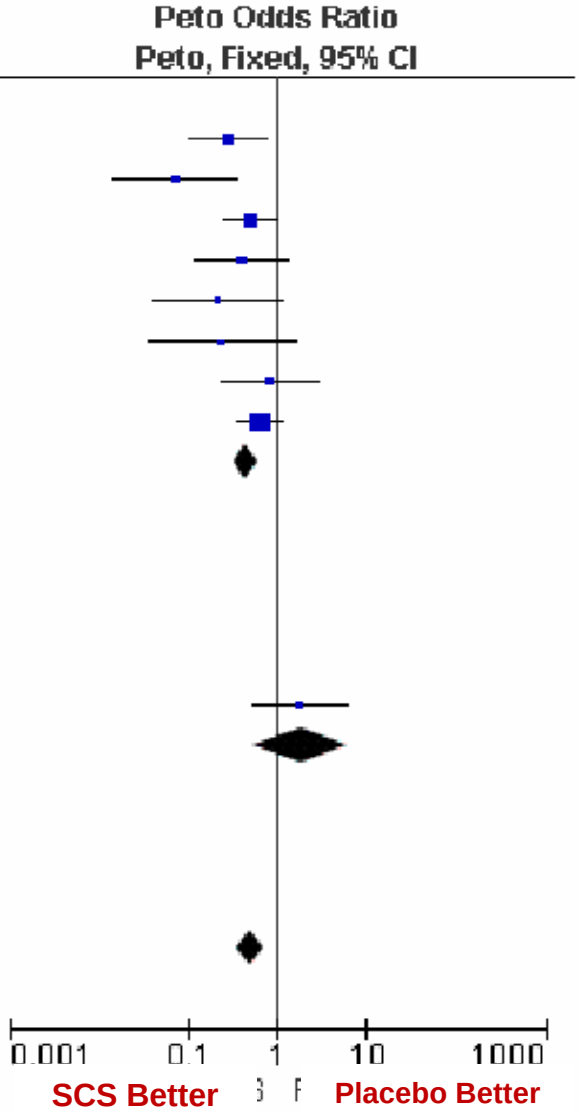
Walters JAE, Gibson PG, Wood-Baker R, Hannay M, Walters EH

- 10 studies contributed data for analyses (n=1051).
- There were significantly fewer treatment failures within thirty days in patients given corticosteroid treatment, OR:0.50; 95% CI: 0.36 to 0.69: NNT= 10.
- Duration of hospitalisation was significantly shorter with corticosteroid treatment, mean difference -1.22 days;
- For FEV1 there were significant treatment benefits with mean differences at end of treatment (up to 15 days) 80 ml.

Treatment with systemic corticosteroids decreases the risk of treatment failure in AECOPD compared with placebo (2009)

THE COCHRANE COLLABORATION®

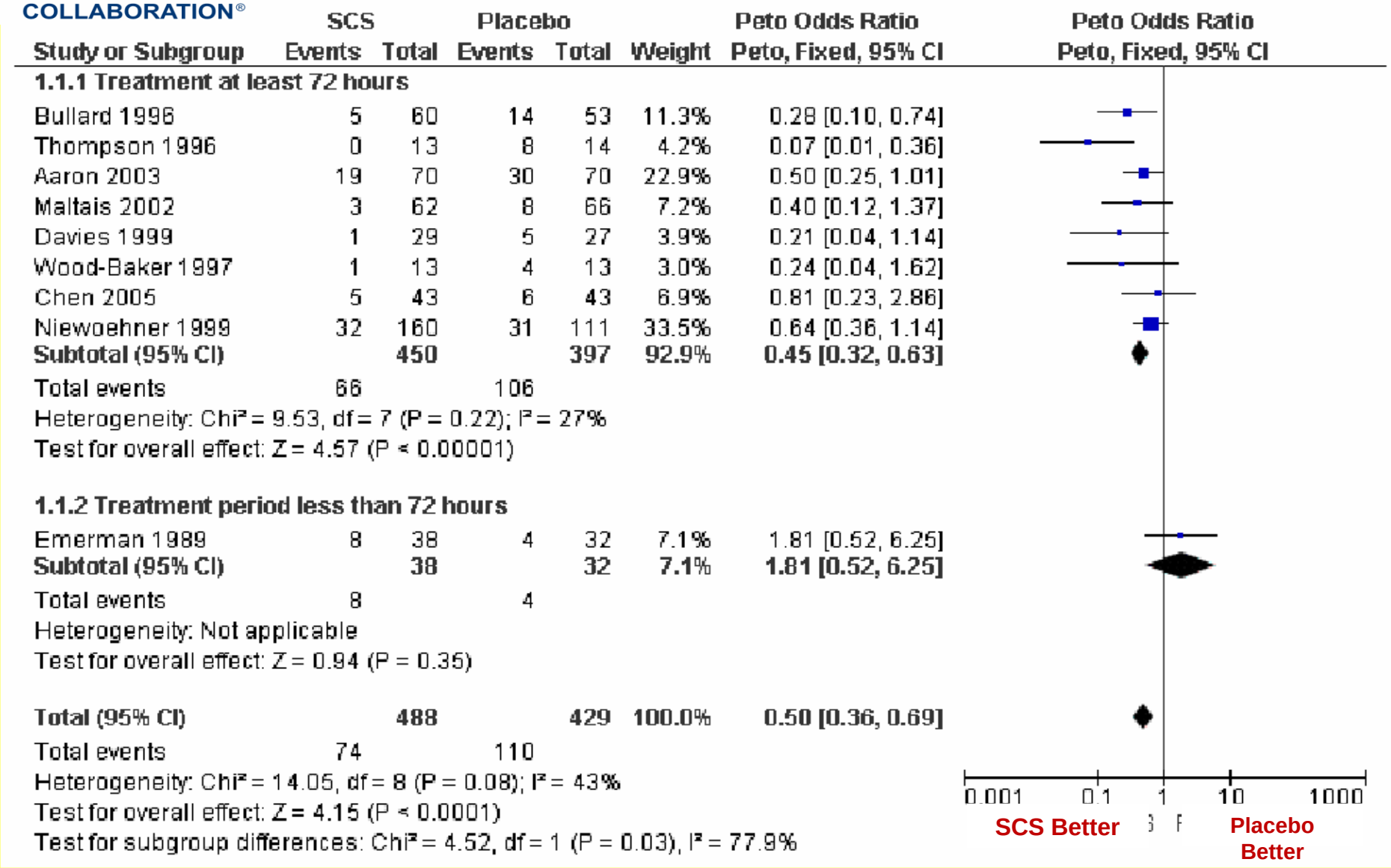
Study or Subgroup	SCS Events	SCS Total	Placebo Events	Placebo Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
1.1.1 Treatment at least 72 hours						
Bullard 1996	5	60	14	53	11.3%	0.28 [0.10, 0.74]
Thompson 1996	0	13	8	14	4.2%	0.07 [0.01, 0.36]
Aaron 2003	19	70	30	70	22.9%	0.50 [0.25, 1.01]
Maltais 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: $Z = 4.57$ ($P < 0.00001$)						
1.1.2 Treatment period less than 72 hours						
Emerman 1989	8	38	4	32	7.1%	1.81 [0.52, 6.25]
Subtotal (95% CI)		**38**		**32**	**7.1%**	**1.81 [0.52, 6.25]**
Total events	8		4			
Heterogeneity: Not applicable						
Test for overall effect: $Z = 0.94$ ($P = 0.35$)						
Total (95% CI)		**488**		**429**	**100.0%**	**0.50 [0.36, 0.69]**
Total events	74		110			
Heterogeneity: $Chi^2 = 14.05$, $df = 8$ ($P = 0.08$); $I^2 = 43\%$						
Test for overall effect: $Z = 4.15$ ($P < 0.0001$)						
Test for subgroup differences: $Chi^2 = 4.52$, $df = 1$ ($P = 0.03$), $I^2 = 77.9\%$						



- *Primary outcomes*
  - *1. Treatment Failure:*
    - *hospital readmission rates*
    - *return to emergency department*
    - *Deterioration leading to treatment intensification*
  - *2. Mortality*
- *Secondary outcomes*
  - *1. Lung function measurements*
  - *2. Arterial blood gas measurements (ABG), PaO2 and PaCO2*
  - *3. Symptom scores, Dyspnoea scores, sputum production*
  - *4. Health status (Quality of life) assessments (QOL)*
  - *6. Duration of hospitalisation*
  - *7. Adverse drug effects (ADE)*

Treatment with systemic corticosteroids decreases the risk of treatment failure in AECOPD compared with placebo (2009)

THE COCHRANE COLLABORATION®



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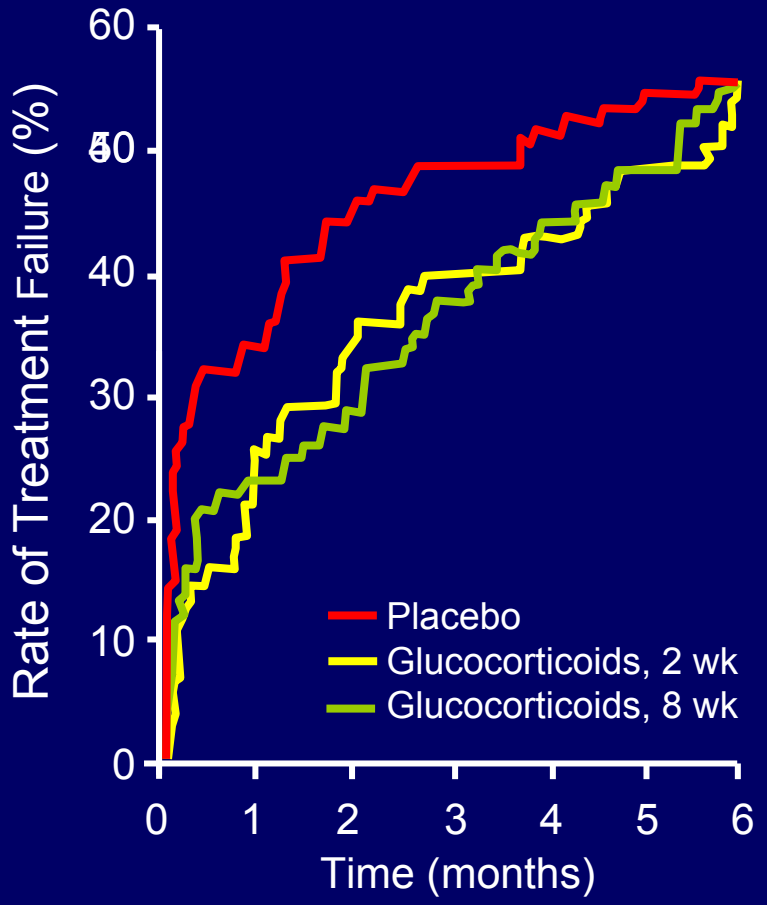
Peto Odds Ratio Peto, Fixed, 95% CI

0.001 0.1 1 10 1000

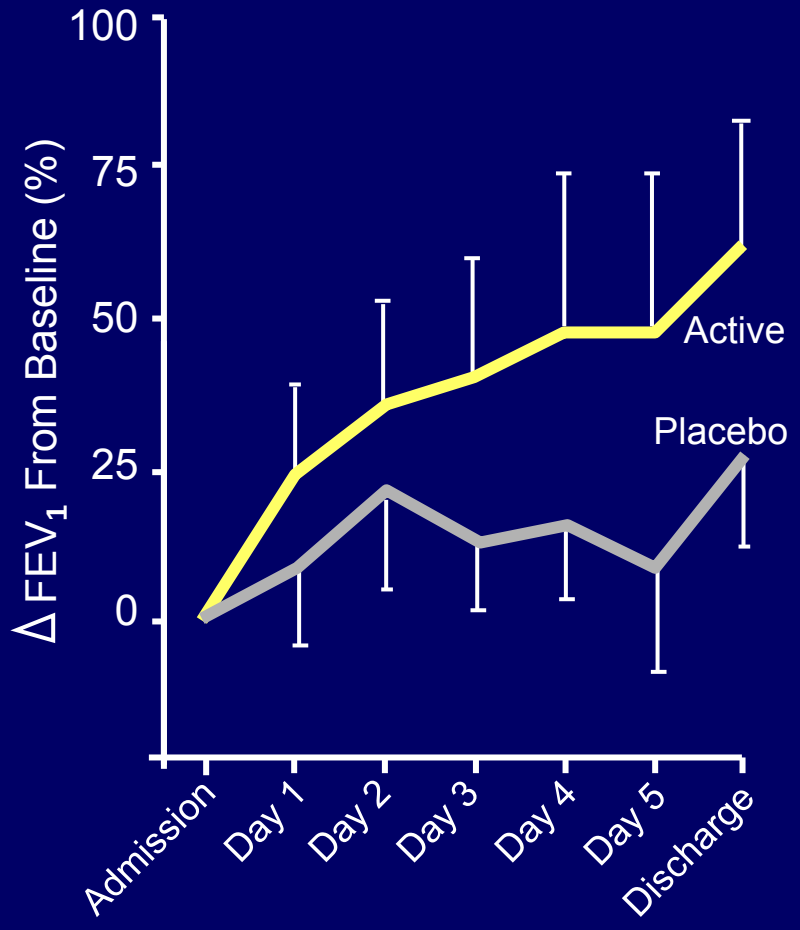
SCS Better

Placebo Better

Oral Corticosteroids in Acute Exacerbations

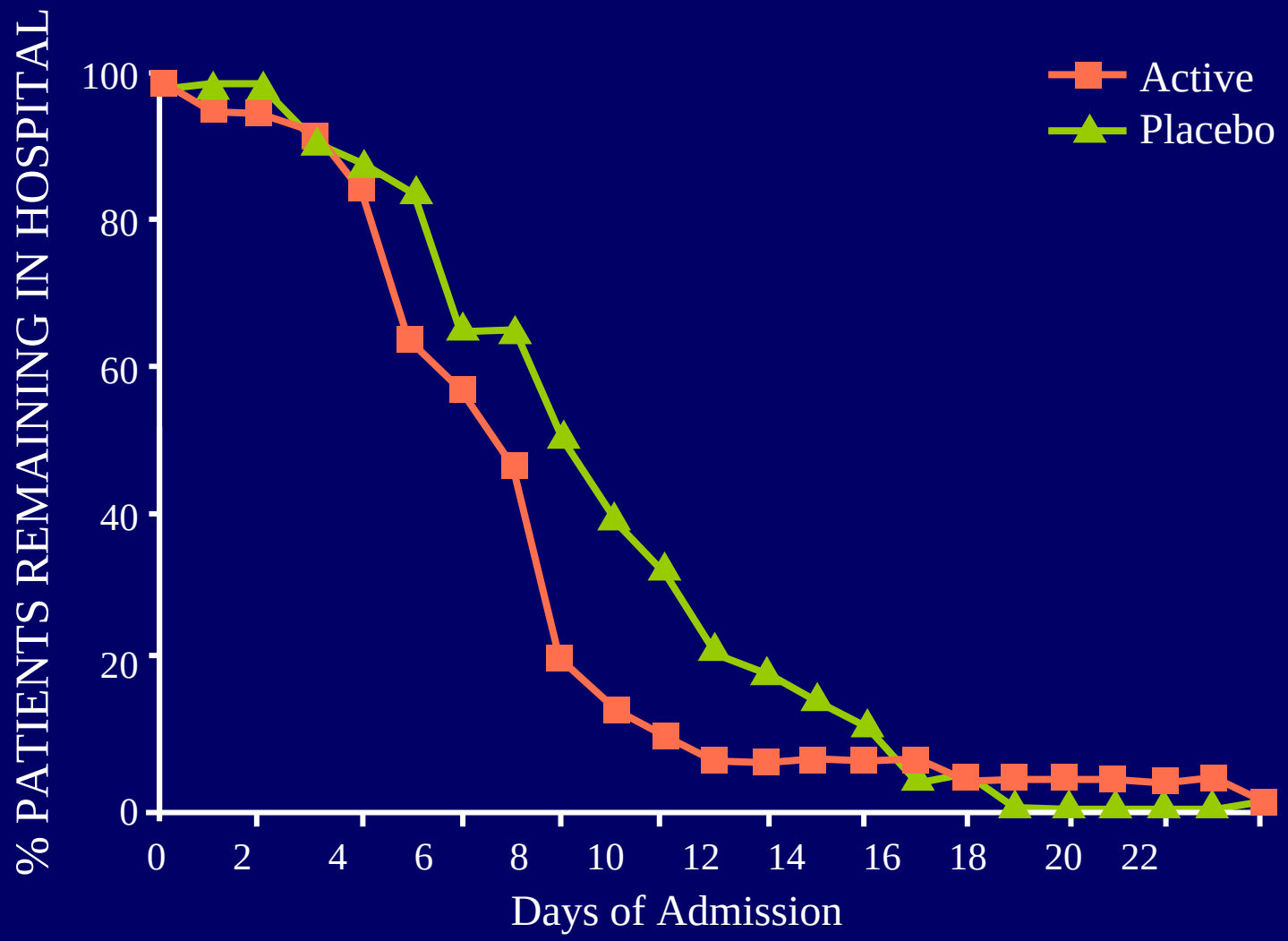


Niewoehner et al. *N Eng J Med.* 1999;340:1941.



Davies et al. *Lancet.* 1999;354:456.

Corticosteroids and Duration of Hospitalisation



Davies et al, Lancet 1999: 354:456

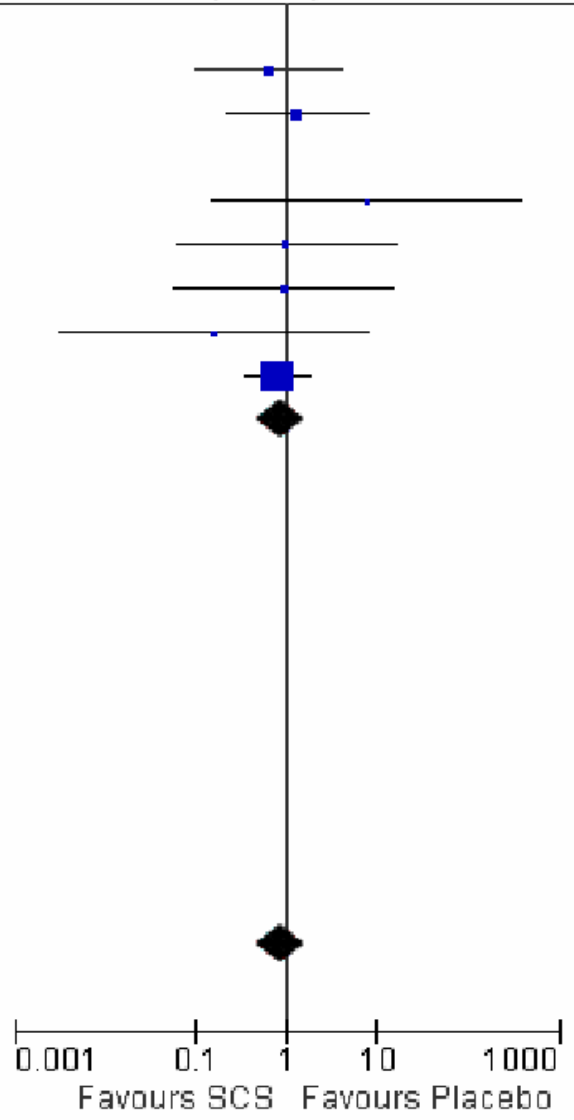
Systemic corticosteroids for acute exacerbations of chronic obstructive pulmonary disease (Review)

Walters JAE, Gibson PG, Wood-Baker R, Hannay M, Walters EH

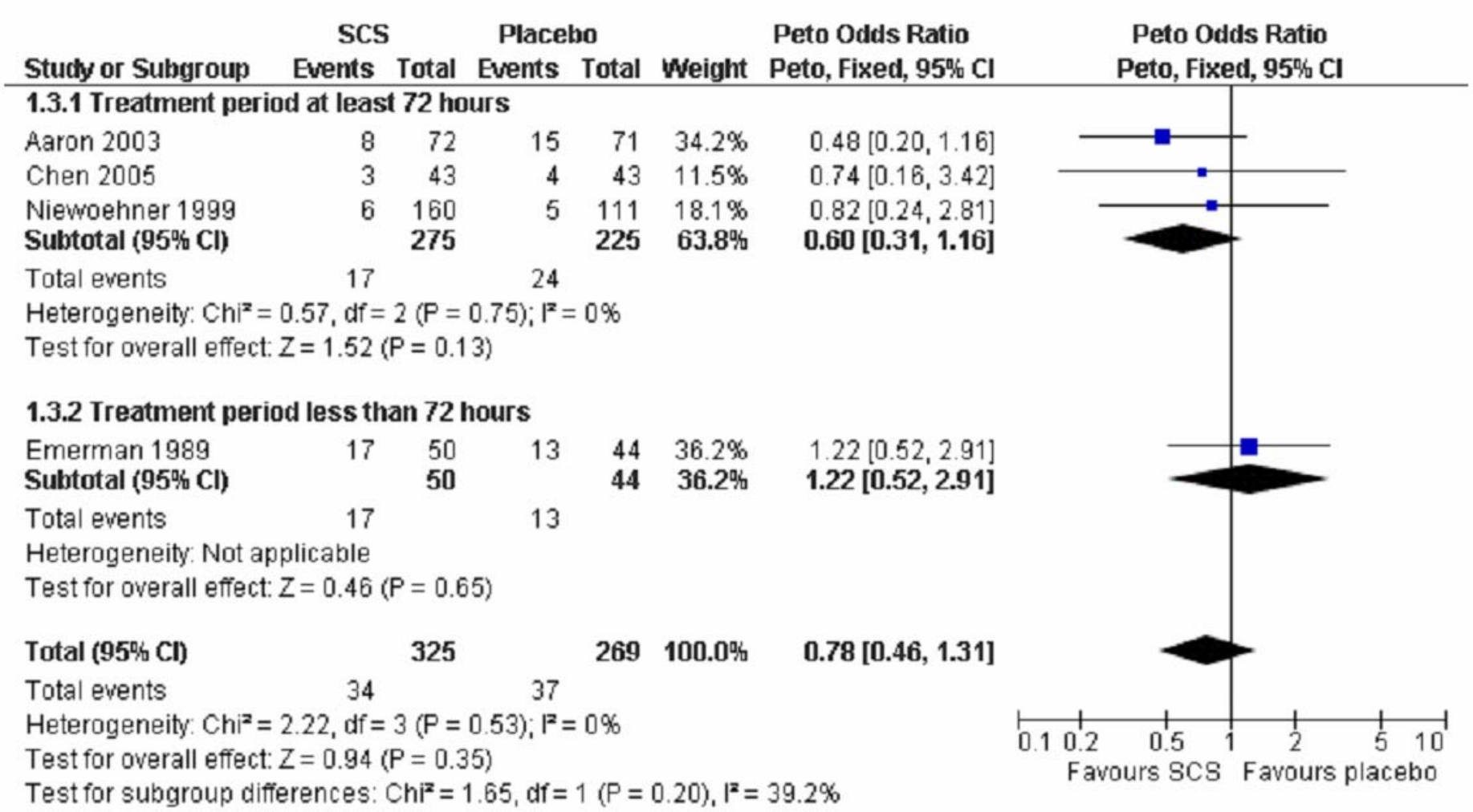
- There was no significant effect on mortality
- There was no significant effect on relapse rate

Mortality

Study or Subgroup	SCS Events	SCS Total	Placebo Events	Placebo Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
1.4.1 Treatment at least 72 hours						
Albert 1980	2	22	3	22	12.4%	0.64 [0.10, 4.05]
Bullard 1996	3	60	2	53	13.2%	1.33 [0.22, 7.97]
Thompson 1996	0	13	0	14		Not estimable
Maltais 2002	1	62	0	66	2.7%	7.88 [0.16, 397.96]
Aaron 2003	1	74	1	73	5.4%	0.99 [0.06, 15.92]
Davies 1999	1	29	1	27	5.4%	0.93 [0.06, 15.28]
Wood-Baker 1997	0	14	1	17	2.7%	0.16 [0.00, 8.29]
Niewoehner 1999	13	160	11	111	58.2%	0.80 [0.34, 1.88]
Subtotal (95% CI)		**434**		**383**	**100.0%**	**0.87 [0.45, 1.66]**
Total events	21		19			
Heterogeneity: Chi² = 2.28, df = 6 (P = 0.89); I² = 0%						
Test for overall effect: Z = 0.43 (P = 0.67)						
1.4.2 Treatment less than 72 hours						
Emerman 1989	0	52	0	44		Not estimable
Subtotal (95% CI)		**52**		**44**		**Not estimable**
Total events	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
Total (95% CI)		**486**		**427**	**100.0%**	**0.87 [0.45, 1.66]**
Total events	21		19			
Heterogeneity: Chi² = 2.28, df = 6 (P = 0.89); I² = 0%						
Test for overall effect: Z = 0.43 (P = 0.67)						
Test for subgroup differences: Not applicable						



Relapse within 30 days readmission



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

Walters JAE, Gibson PG, Wood-Baker R, Hannay M, Walters EH

- Increased likelihood of an adverse event associated with corticosteroid treatment, OR 2.33; 95% CI 1.60 to 3.40. NNH=5
- The risk of hyperglycaemia was significantly increased, OR 4.95

Intensive Care Med (2004) 30:1685–1688
DOI 10.1007/s00134-004-2325-2

BRIEF REPORT

Christian Christiansen
Palle Toft
Hans Skriver Jørgensen
Søren Kæseler Andersen
Else Tønnesen

Hyperglycaemia and mortality in critically ill patients

A prospective study

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 2, 2006 VOL. 354 NO. 5

Intensive Insulin Therapy in the Medical ICU

Greet Van den Berghe, M.D., Ph.D., Alexander Wilmer, M.D., Ph.D., Greet Hermans, M.D., Wouter Meersseman, M.D., Pieter J. Wouters, M.Sc., Ilse Milants, R.N., Eric Van Wijngaerden, M.D., Ph.D., Herman Bobbaers, M.D., Ph.D., and Roger Bouillon, M.D., Ph.D.

Hyperglycaemia as a predictor of outcome during non-invasive ventilation in decompensated COPD

B Chakrabarti,[1] R M Angus,[2] S Agarwal,[2] S Lane,[3] P M A Calverley[1]

Thorax 2009;**64**:857–862

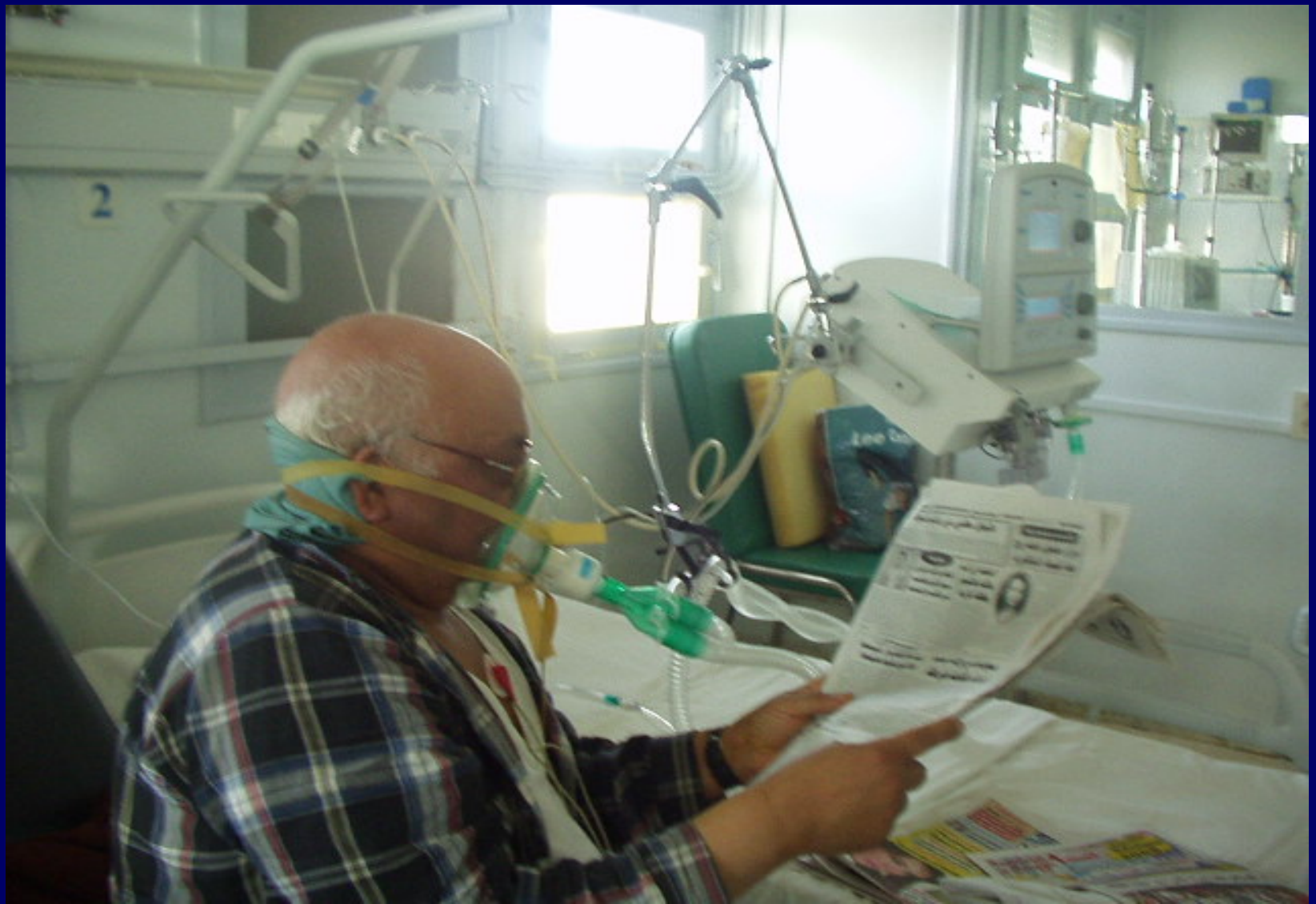
Table 2 Relationship between glycaemia and outcome from NIV

Random blood glucose quartile (mmol/l)	NIV success (no. of cases)	NIV failure (no. of cases)
0–6 (n = 28)	27 (96%)	1 (4%)
6–6.9 (n = 16)	16 (100%)	0 (0%)
7–8.9 (n = 26)	17 (65%)	9 (35%)
>9 (n = 18)	12 (67%)	6 (33%)

Conclusions: In acute decompensated ventilatory failure complicating COPD, hyperglycaemia upon presentation was associated with a poor outcome. Baseline RR and

Study ID	Setting	SSC (Rx Duration)	Age Mean (SD)	FEV1 Mean (SD)	Previous ICS use
Aaron 2003	*Outpatient/*	**Oral Prednisone 40mg (10 days)**	69.4 (10.5)	**1.0 (0.5)**	52%
Albert 1980	*Inpatient/*	**IV Methylpred. 0.5 mg/kg 4hrly x 72 hours (3 days)**	61.5 (9)	**0.8 (0.3)**	Not known
Bullard 1996	*ED-Inpatient 76%/*	**IV hydrocortisone x 96 hours+ 4 days oral prednisone 40mg (5-8 days)**	66 (10.8)	**0.53 (0.53)**	not known
Davies 1999	*Inpatient/*	**Oral prednisone 30mg (14 days)**	67 (8.5)	**1.7**	80%
Emerman 1989	*ED-Inpatient 63%/*	**IV 100mg methylpred. x single dose (1 day)**	64 (7.8)	**64% (35)**	not known
Maltais 2002	*Inpatient/*	**Oral prednisone 40mg x 3 days then 30 mg x 7 days** (10 days)	70 (8)	**0.91 (0.4)**	59%
Niewoehner 1999	*Inpatient/*	**IV methylpred 72hrs + oral prednisolone. 60mg tapering over 57 days (group I) or 12 days (group 2) or IV placebo + oral placebo 57 days (group 3) (15 or 60 days)**	67.4 (10)	**0.76 (0.27)**	45%
Rostom 1994	*Inpatient/*	**IV methyl prednisolone. 72 hrs + oral prednisolone 15 days (19 days)**	not known	**not known**	not known
Thompson 1996	*Outpatient/*	**Oral prednisone 60 mg tapering 9 days (9 days)**	67.5 (8)	**1.35 (0.5)**	30%
Wood-Baker 1997	*Inpatient/*	**Oral prednisone high dose 2.5 mg/kgm x 3 days OR medium dose 0.6 - 0.3 mg/kg x 14 days (14 days or 3 day high dose)**	72 (6.3)	**0.6**	not known
Chen 2005	*Inpatient/*	**1.Prednisolone 30mg/day 7 days + placebo 7 days 2.Prednisolone 30mg/day 10 days + 15 mg/day 5 days 3.Placebo 14 days (14 days)** (data from group 2 used)	72 (6.7)	**0.73 (0.25)**	not known

Patients centered outcomes (PiCO)



Amélioration des « patients' centered outcomes »

Objectifs pneumologiques

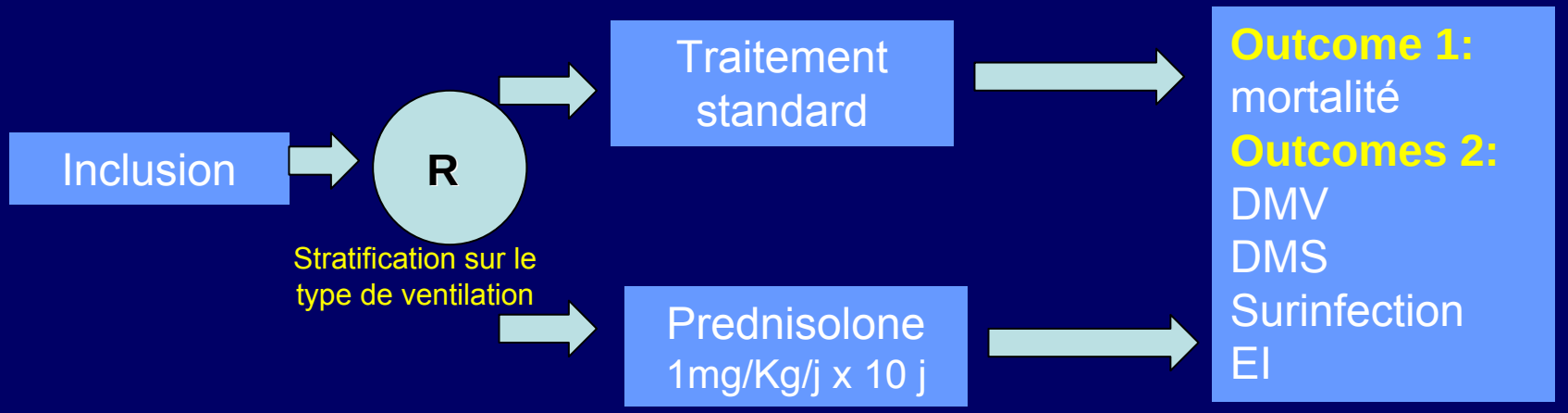
- Qualité de vie
- Fréquence des exacerbations
- Prolongation de la survie

Objectifs Réanimatoires

- Mortalité en Réanimation
- Durée de séjour en réanimation
- Durée de ventilation
- Echec de la VNI
- Impact sur la vie post réanimation

Matériel & Méthodes

- Patients en EABPCO sévère nécessitant l'assistance ventilatoire
  - Exacerbation: critères d'Anthonisen
  - Sévérité: $PaCO_2 \geq 45mmHg$ & $pH \leq 7.35$ & signes de fatigue respiratoire
  - Exclusion: foyer infectieux évident, corticothérapie systémique dans les 30 jours précédents



Hypothèse: 150 patients par groupe pour détecter 10% de réduction de mortalité (base 25%)

Study patients characteristics

	Steroids (n=111)	Control (n=106)
Age (years)	68±9	69±9
M/F	99/12	92/14
FEV1 (ml/s)	903±476	892±355
Home oxygen (%)	72	67
History of Diabetes (%)	15	12
History of Hypertension (%)	8	7

Characteristics of the index exacerbation

	Steroids (n=111)	Control (n=106)
pH	7.28±0.06	7.28±0.07
PaCO2 (kPa)	8.9±1.8	9.1±2
SaO2	88±5	86±6
SAPS II	31±9	29±8
Respiratory rate	30±5	29±7
NIV n (%)	84 (76)	80 (76)

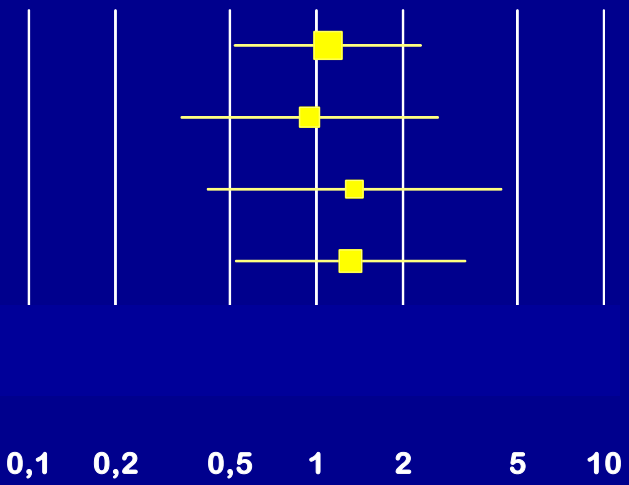
Outcomes: Efficacy

	Steroids (n=111)	Control (n=106)	p
ICU mortality n (%)	17 (15.3)	15 (14.3)	NS
NIV mortality	8 (9.5)	8 (10)	NS
IV mortality	9 (50)	7 (37)	NS
NIV failure	12 (14.2)	9 (11.2)	NS
MV duration	8.5±7	8.2±6	NS
ICU LOS	11±8	11±8	NS

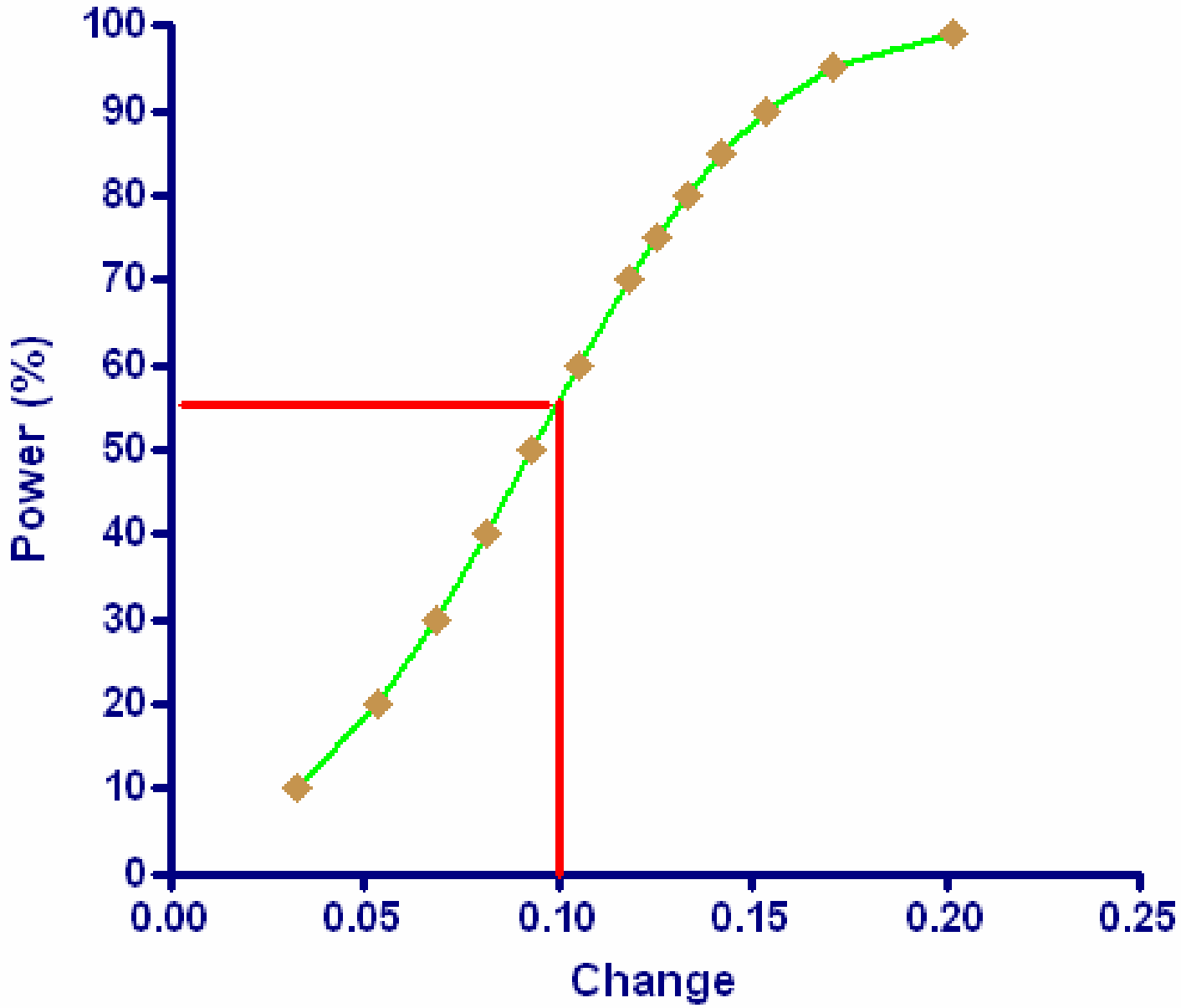
Study name	Odds ratio	Lower limit	Upper limit	p-Value
ICU Mortality	1,097	0,517	2,327	0,809
NIV mortality	0,947	0,338	2,658	0,918
IV mortality	1,357	0,417	4,414	0,612
NIV failure	1,315	0,522	3,314	0,562

Statistics for each study

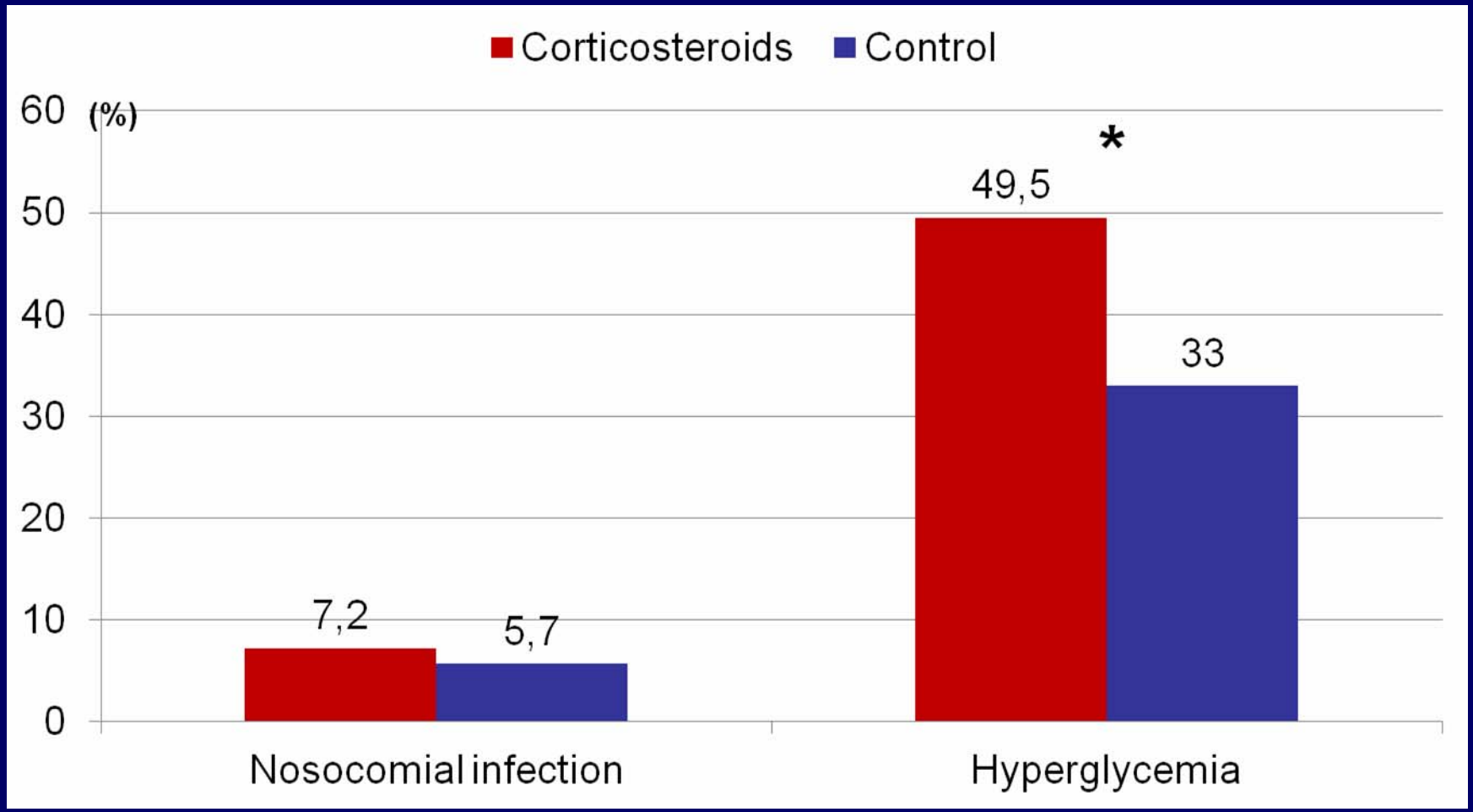
Odds ratio and 95% CI



Puissance de l'étude sur le critère mortalité



Outcomes: Side effects



Conclusion

- Malgré la ferme recommandation de la corticothérapie systémique par les sociétés savantes, il y a peu de données publiées pertinentes aux malades de réanimation.
- Notre expérience n'est pas favorable à ce type de prescription si on évalue des critères centrés sur le patient.