Antibiothérapie dans l'exacerbation des BPCO En Réanimation

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EA BPCO

Une exacerbation de bronchopneumopathie chronique obstructive (BPCO) est définie par une modification des symptômes usuels de la BPCO :

- **dyspnée,**
- **toux**
- **expectorations**

au-delà des variations quotidiennes, et qui nécessite une modification du traitement usuel.

EA BPCO

- **Les exacerbations émaillent l'évolution de la BPCO avec une fréquence variable:**
  - 3-4 /an si BPCO sévère (GOLD III)
  - 2-3/an si BPCO modérée (GOLD II)
- **Exacerbations :**
  - 110000 décès
  - Plus de 500000 hospitalisations par an
  - Coût direct : $ 18 billions par an

Epidémiologie en réanimation

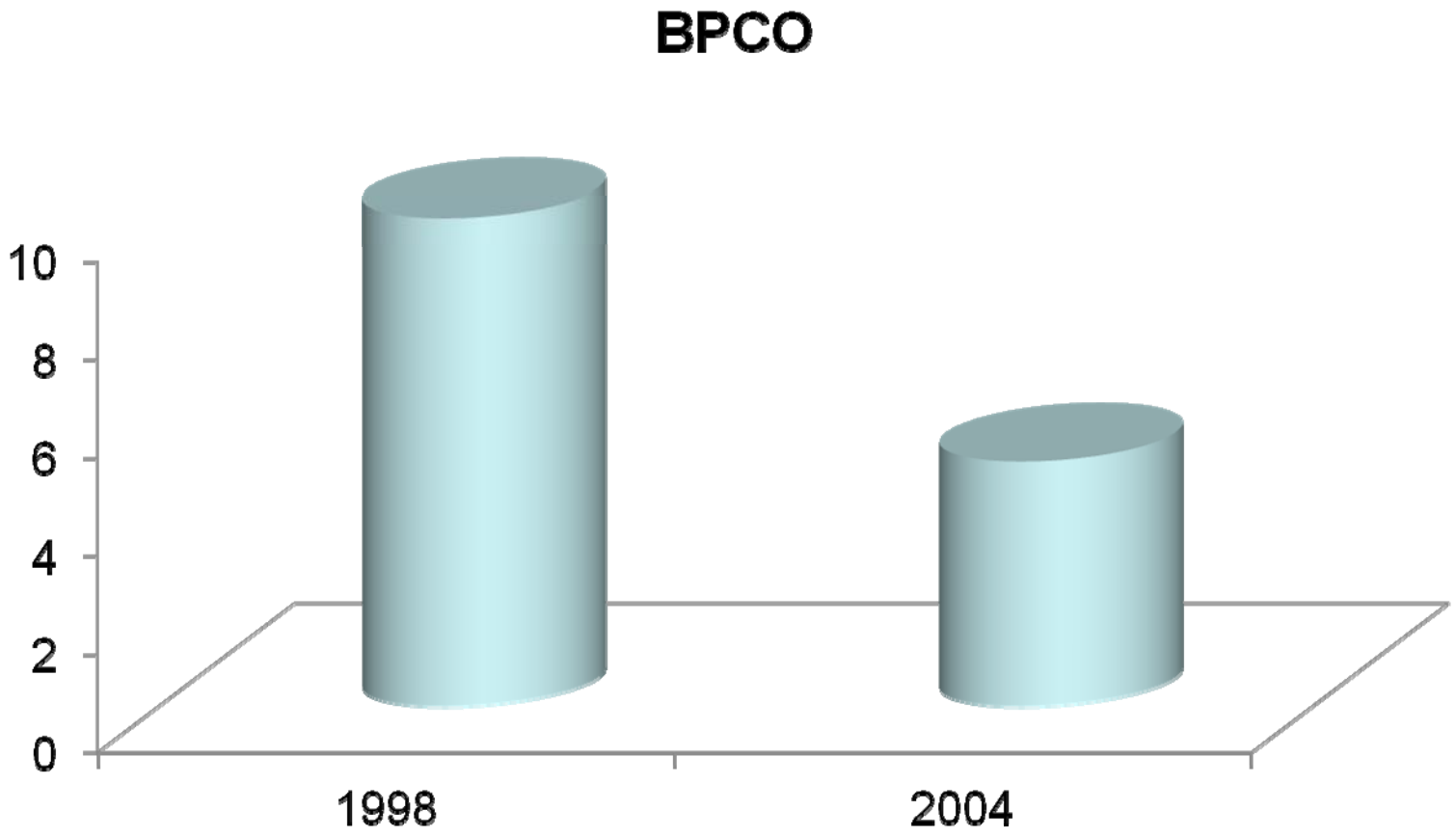
Table 1. Characteristics of the Studied Patients on Admission to the Intensive Care Unit (ICU)*

Characteristic	No. (%) of Patients Mechanically Ventilated (N = 5183)
Age, mean (SD) [median {IQR}], y	59.2 (17.3) [63 {48-73}]
Sex, females	1985 (38.7)
SAPS II score, mean (SD) [median {IQR}]	44.1 (17.0) [43 {32-54}]
Prior functional status, limited activity	2016 (38.9)
Medical/surgical	3428 (66.1)/1755 (33.9)
Reason for the initiation of mechanical ventilation	
Acute respiratory failure	3564 (68.8)
Coma	864 (16.7)
Acute respiratory failure on chronic pulmonary disease	
COPD	522 (10.1)
Asthma	79 (1.5)
Chronic respiratory disease (non-COPD)	60 (1.2)
Neuromuscular disease	94 (1.8)

Esteban et al. *JAMA* 2002

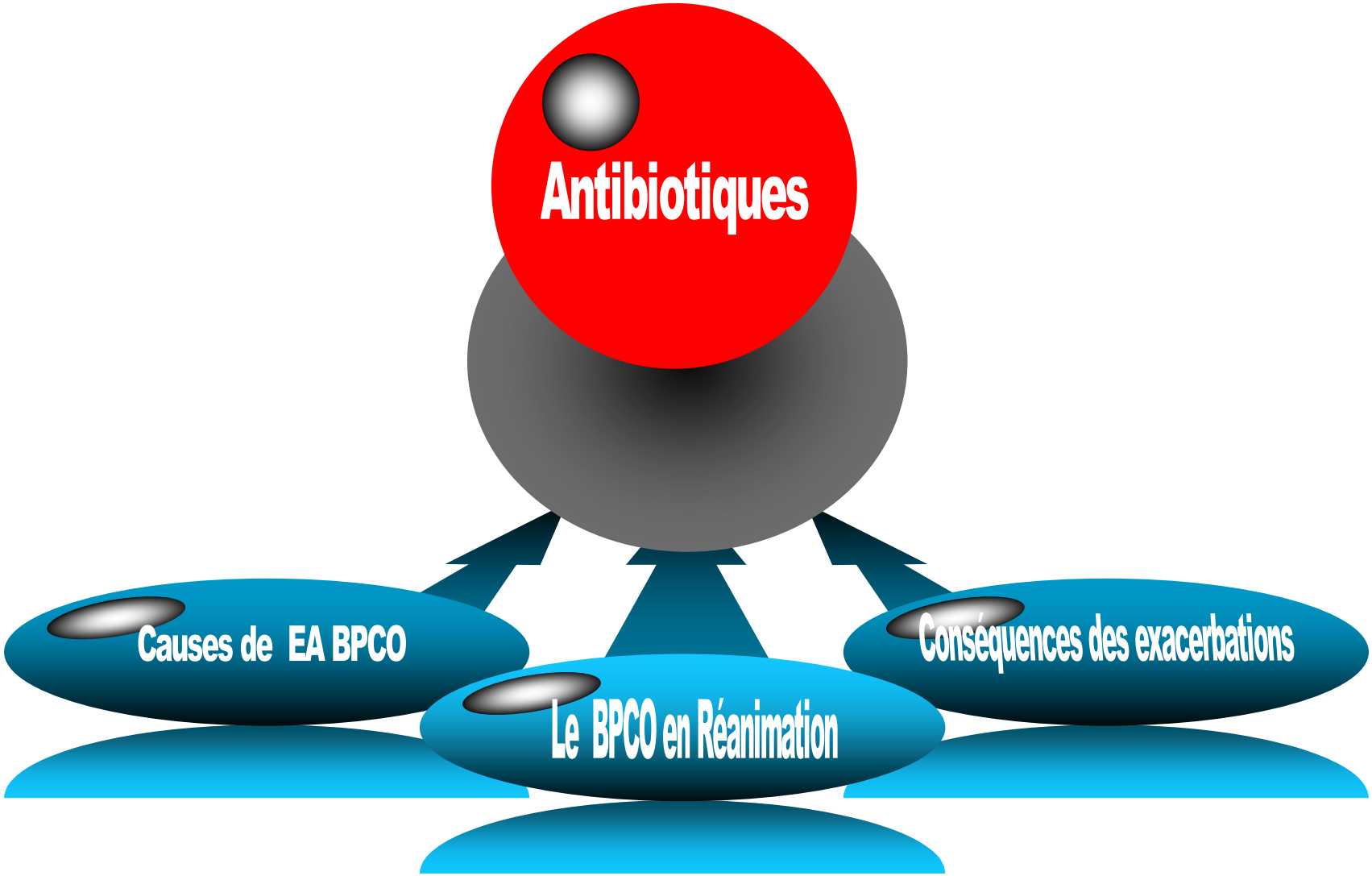
Epidémiologie en réanimation

Evolution of Mechanical Ventilation in Response to Clinical Research

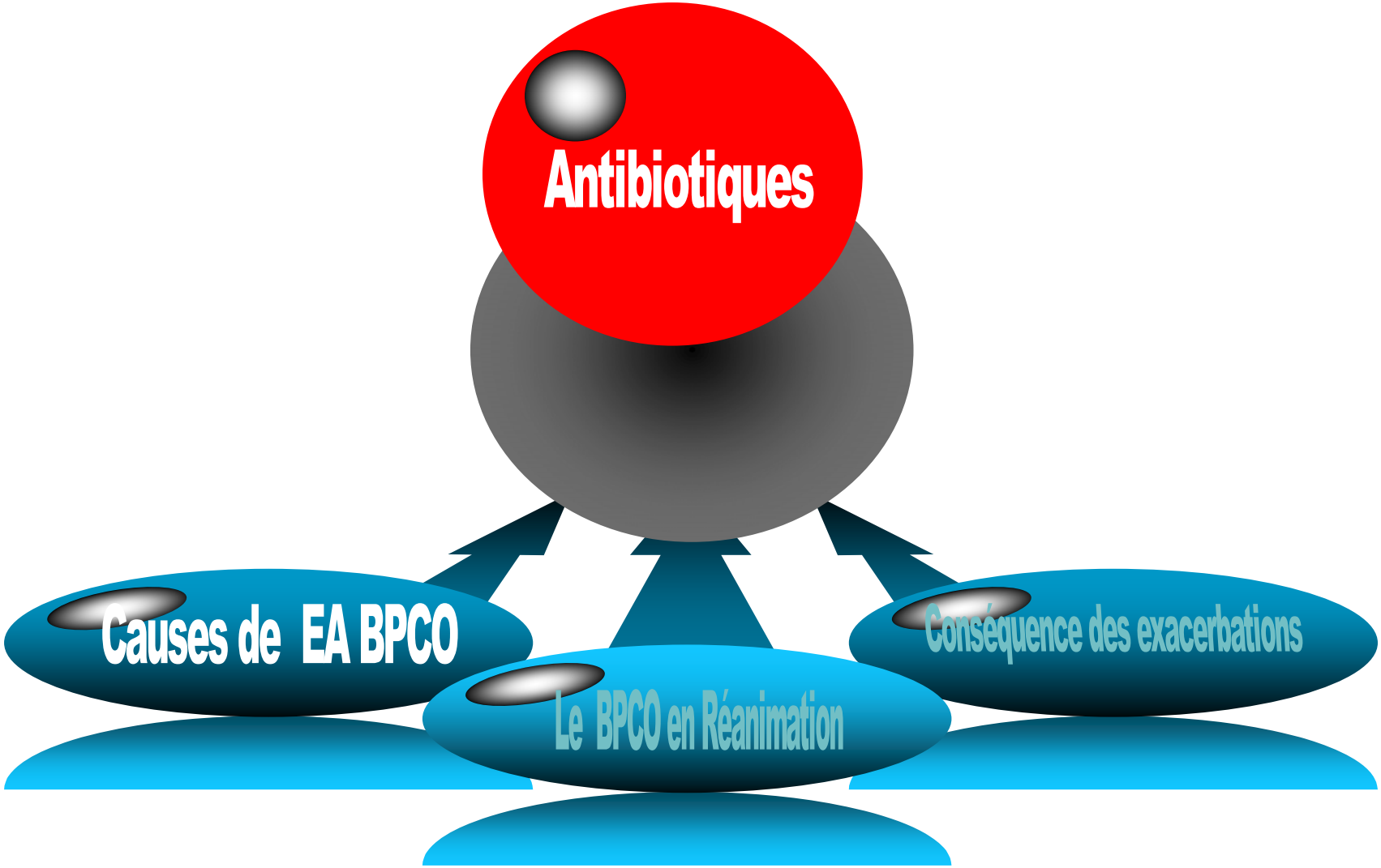


Esteban et al. *AJRCCM 2008*

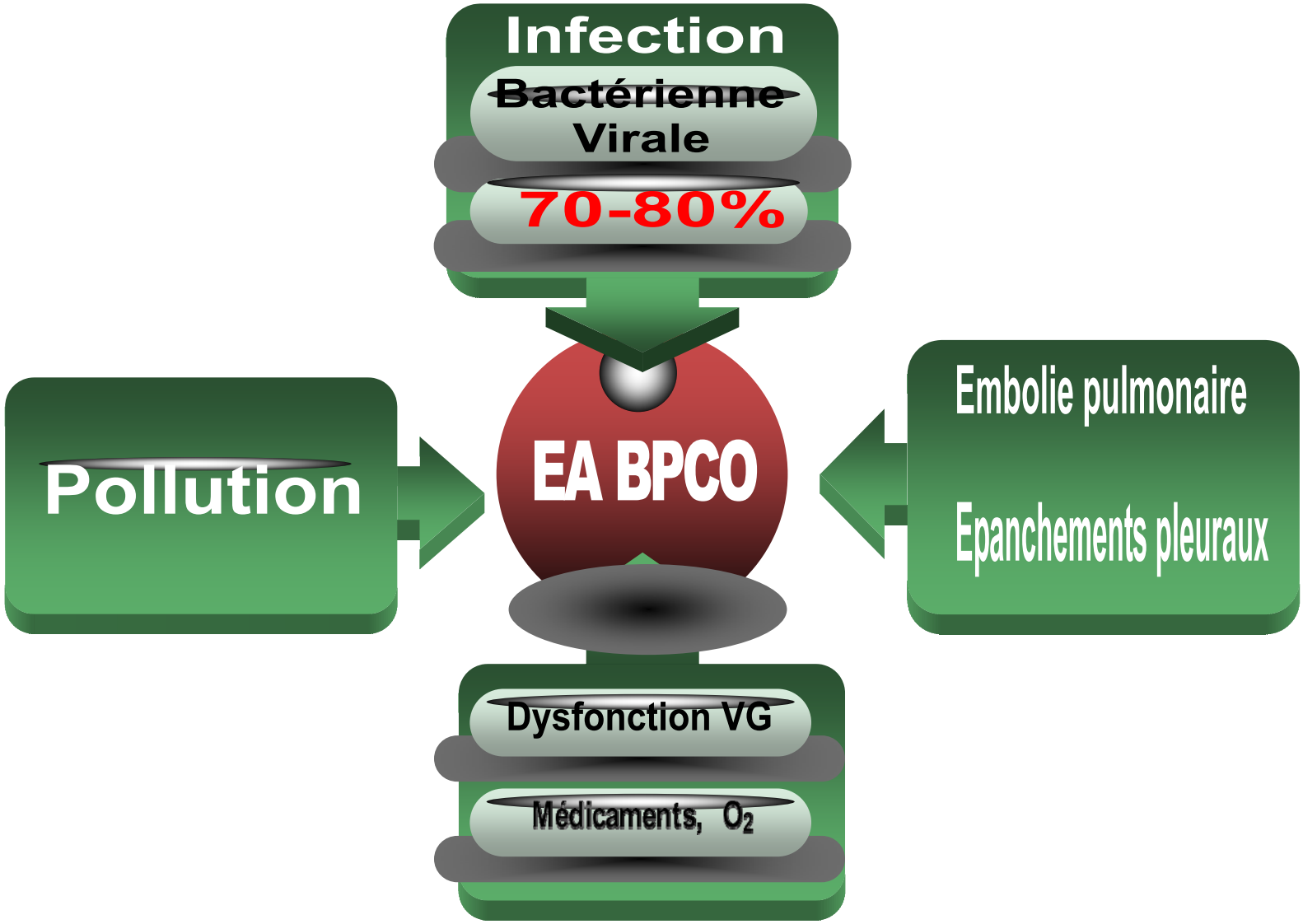
Pourquoi les antibiotiques dans EA BPCO



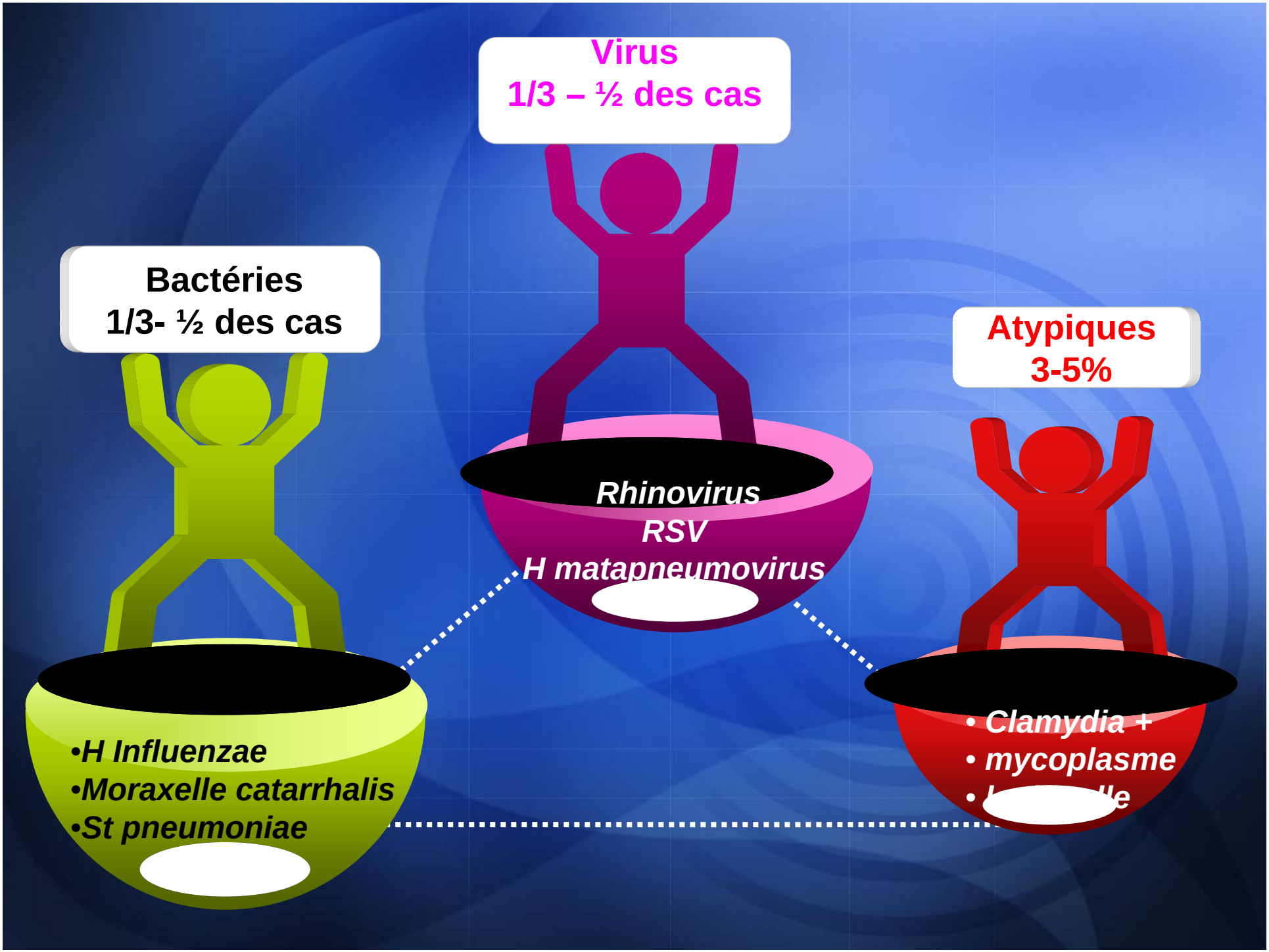
Pourquoi les antibiotiques dans EA BPCO



Causes des exacerbations de BPCO

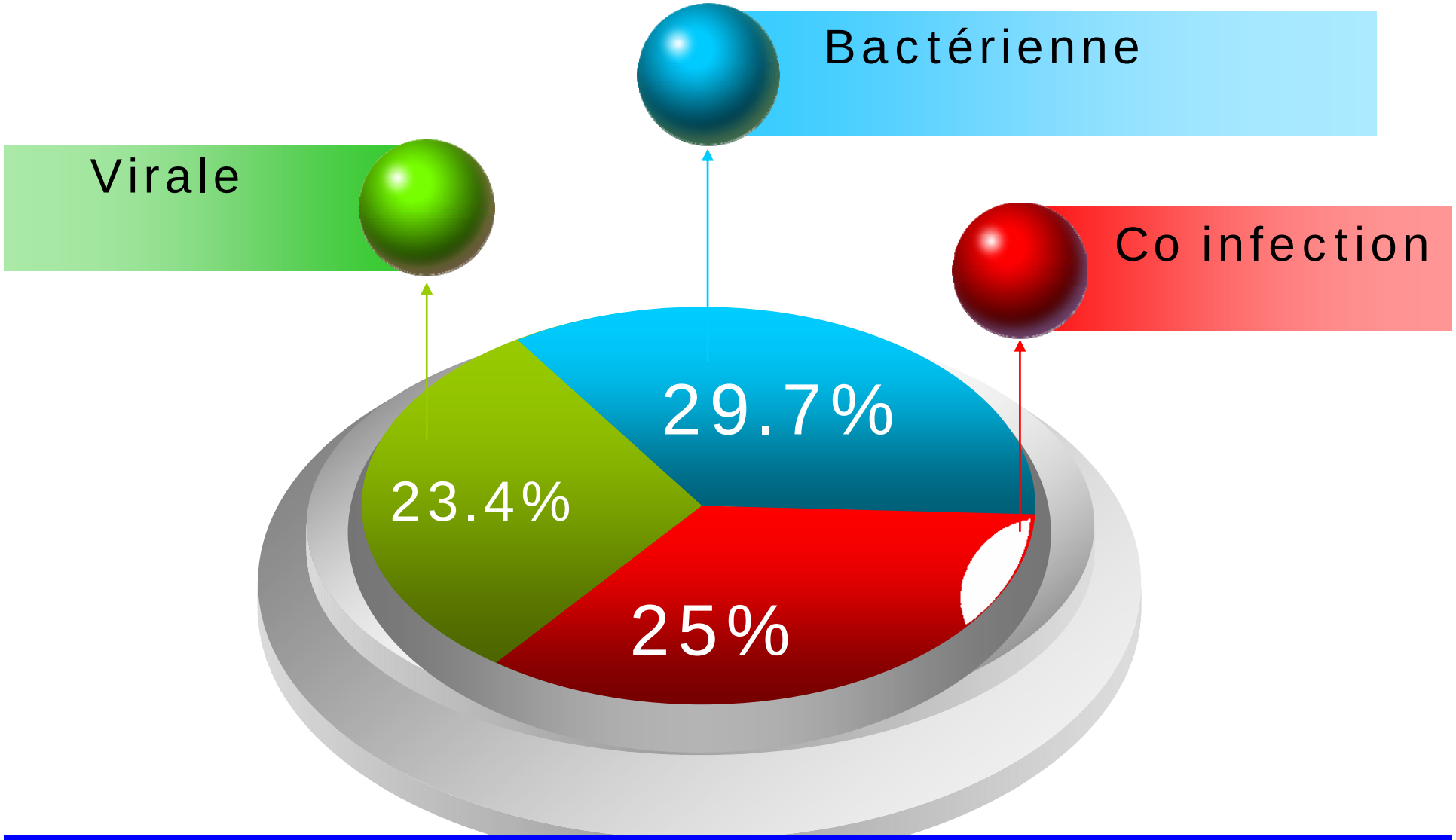


Ball P. *Chest.* 1995;108:43S-52S. Gump DW, et al. *Am Rev Respir Dis.* 1976;113:465-74.


Virus
1/3 – ½ des cas
Bactéries
1/3- ½ des cas
Atypiques
3-5%
Rhinovirus
RSV
H matapneumovirus
•H Influenzae
•Moraxelle catarrhalis
•St pneumoniae
• Clamydia +
• mycoplasme

Infections and Airway Inflammation in Chronic Obstructive Pulmonary Disease Severe Exacerbations

Alberto Papi, Cinzia Maria Bellettato, Fausto Braccioni, Micaela Romagnoli, Paolo Casolari, Gaetano Caramori, Leonardo M. Fabbri, and Sebastian L. Johnston



Am J Respir Crit Care Med 2006; 173: 1114–1121

CHEST Original Research
COPD

Effect of Interactions Between Lower Airway Bacterial and Rhinoviral Infection in Exacerbations of COPD*

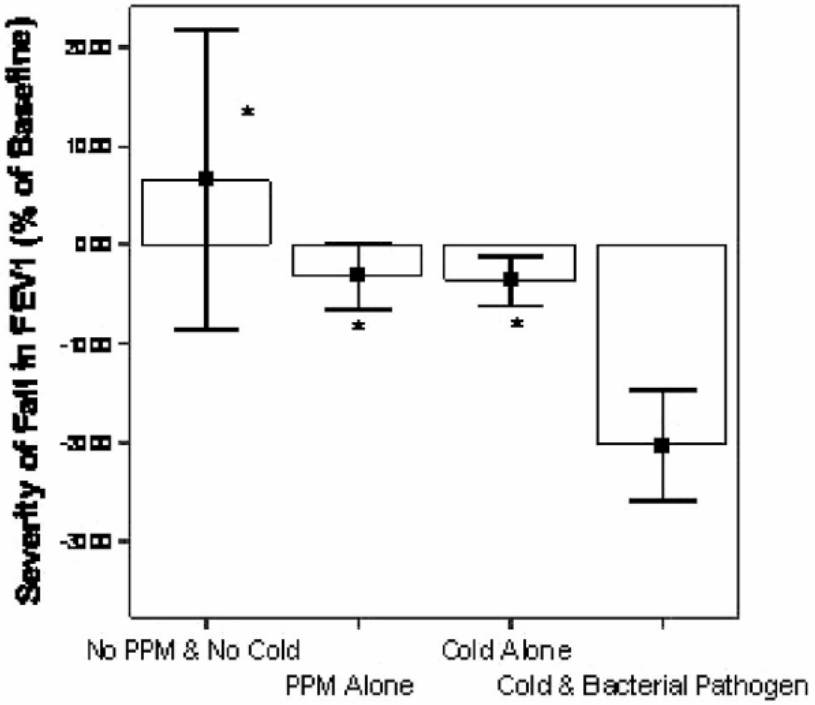


FIGURE 1. Effect of airway pathogens and pathogen combinations on percentage fall in FEV_1 at exacerbation. Columns represent mean values with error bars as SEM *Significant ($p < 0.05$) difference between this category and cold and bacterial pathogen category ($n = 56$).

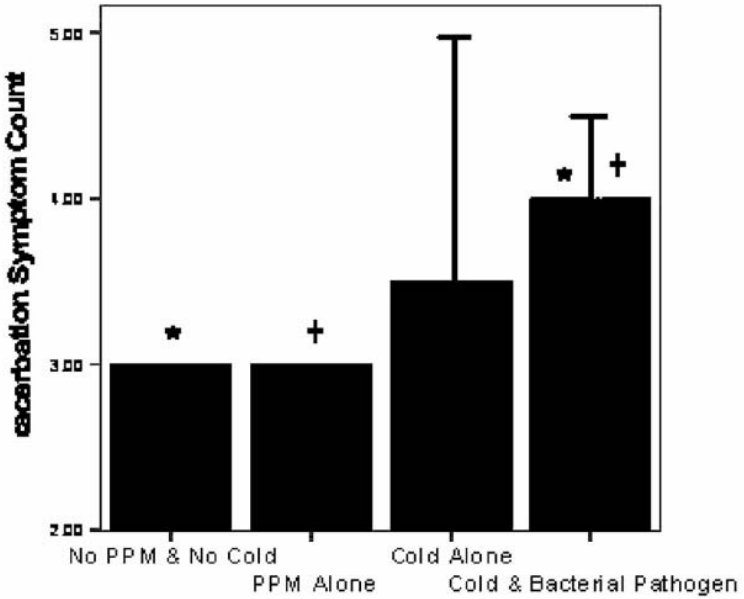


FIGURE 2. Effect of airway pathogens and pathogen combinations on symptom severity (median symptom count at exacerbation onset). Columns represent median values, bars indicate IQR, and * and + denote statistically significant ($p < 0.05$) differences between corresponding labeled categories ($n = 56$; *$p = 0.029$; + $p = 0.019$).

CHEST Original Research
COPD

Upper-Respiratory Viral Infection, Biomarkers, and COPD Exacerbations

Omar Kherad, MD; Laurent Kaiser, MD; Pierre-Olivier Bridevaux, MD; François Sarasin, MD; Yves Thomas, PhD; Jean-Paul Janssens, MD; and Olivier T. Rutschmann, MD

CHEST 2010; 138(4):896–904

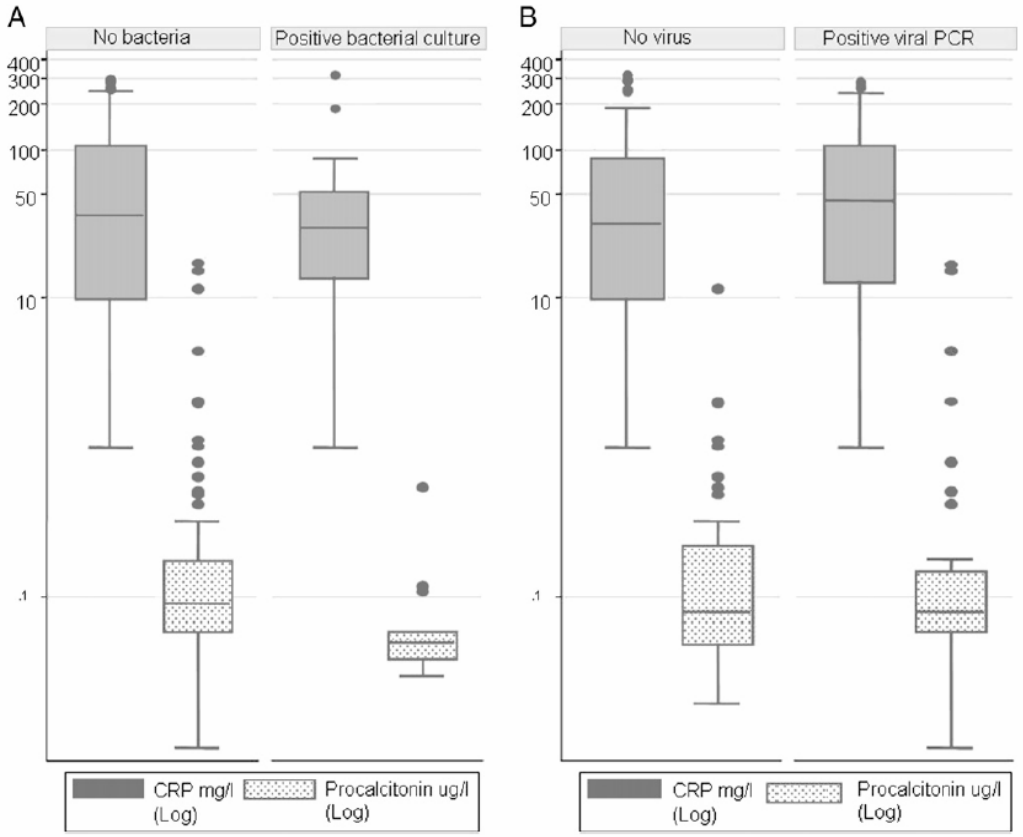


FIGURE 5. Serum CRP (n = 86) and procalcitonin (PCT) (n = 81) in patients with AECOPD. Five values are missing for PCT (two in the virus-positive group; three in the virus-negative group). Patients with (n = 20) and without bacterial infection (n = 68) identified by semiquantitative bacterial analysis of sputum at admission for AECOPD (*A*). Patients with (n = 44) and without (n = 42) viral nucleic acids identified by RT-PCR of nasopharyngeal swabs at admission for AECOPD (*B*). Data are expressed as medians (interquartile range). CRP = C-reactive protein. See Figure 2 and 3 legends for expansion of other abbreviations.

Rôle des bactéries dans EA BPCO

1. BPCO Stable

- Bactéries à pouvoir pathogène
  - 25%

2. Exacerbations BPCO

- Bactéries à pouvoir pathogène
  - 50%
  - [ ] plus élevée
  - nouveaux pathogènes

ORIGINAL INVESTIGATION

Microbiologic Determinants of Exacerbation in Chronic Obstructive Pulmonary Disease

Antoni Rosell, MD; Eduard Monsó, MD; Néstor Soler, MD; Ferràn Torres, MD; Joaquim Angrill, MD; Gerdt Riise, MD; Rafael Zalacaín, MD; Josep Morera, MD; Antoni Torres, MD

Arch Intern Med. 2005;165:891-897

Table 3. Potentially Pathogenic Microorganisms

Variable	Healthy Individuals (n = 70)	Patients With Stable COPD (n = 181)	*P* Value*	Patients With Exacerbated COPD (n = 86)	*P* Value†
PPM culture ≥10^2 CFU/mL, No. (%)	3 (4)	53 (29)	<.001	46 (54)	<.001
PPM load, No. (%)					
10^2 CFU/mL	1 (1)	5 (3)		4 (5)	
10^3 CFU/mL	1 (1)	34 (19)	<.001	24 (28)	.001
≥10^4 CFU/mL	1 (1)	14 (8)		18 (21)	
Microorganisms, No. (%)					
Haemophilus influenzae	3 (4)	31 (17)	.008	26 (30)	.01
Streptococcus pneumoniae	0	16 (9)	.004	6 (7)	.60
Moraxella catarrhalis	0	7 (4)	.10	6 (7)	.21
Enterobacteria	0	5 (3)	.19	6 (7)	.10
Pseudomonas aeruginosa	0	2 (1)	>.99	8 (9)	.002
Staphylococcus aureus	0	2 (1)	>.99	0	>.99
Polymicrobial culture	0	9 (6)	.05	6 (7)	.57

Abbreviations: CFU, colony-forming units; COPD, chronic obstructive pulmonary disease; PPM, potentially pathogenic microorganism.
*Comparison of healthy individuals and patients with stable COPD; χ^2 test or Fisher exact test as required.
†Comparison of patients with stable vs exacerbated COPD; χ^2 test or Fisher exact test as required.

ORIGINAL INVESTIGATION

Microbiologic Determinants of Exacerbation in Chronic Obstructive Pulmonary Disease

Antoni Rosell, MD; Eduard Monsó, MD; Néstor Soler, MD; Ferràn Torres, MD; Joaquim Angrill, MD; Gerdt Riise, MD; Rafael Zalacaín, MD; Josep Morera, MD; Antoni Torres, MD

Arch Intern Med. 2005;165:891-897

Table 4. Microbiologic Risk Factors for Exacerbation in 267 Patients With COPD

Variable	Stable COPD (n = 181)	Exacerbated COPD (n = 86)	Crude OR (95% CI)	*P* Value	Adjusted OR (95%CI)	*P* Value
Clinical variables						
Age, mean (SD), y	64.5 (8.6)	66.8 (8.2)	1.03 (1.00-1.07)	.04	NA	NA
Sex (male), No. (%)	173 (96)	84 (98)	1.94 (0.40-9.35)	.41	NA	NA
Current smoking, No. (%)	96 (53)	31 (36)	0.50 (0.29-0.85)	.01	NA	NA
FEV_1%, mean (SD)	56.1 (16.7)	36.6 (13.8)	0.92 (0.90-0.94)	<.001	0.92 (0.90-0.94)	<.001
Microbial load, No. (%)*						
Sterile/low	128 (71)	40 (47)	NA	NA	NA	NA
Medium	39 (22)	27 (31)	2.21 (1.21-4.06)	.01	1.55 (0.77-3.09)	.22
High	14 (8)	19 (22)	4.34 (2.00-9.44)	<.001	3.62 (1.47-8.90)	.005
PPM, No. (%)†						
Haemophilus influenzae	31 (17)	26 (30)	2.10 (1.15-3.82)	.02	1.12 (0.49-2.55)	.79
Streptococcus pneumoniae	16 (9)	6 (7)	0.77 (0.29-2.05)	.61	NA	NA
Moraxella catarrhalis	7 (4)	6 (7)	1.86 (0.61-5.73)	.28	NA	NA
Enterobacteria	5 (3)	8 (9)	2.64 (0.78-8.90)	.12	0.74 (0.13-4.07)	.73
Pseudomonas aeruginosa	2 (1)	8 (9)	9.18 (1.91-44.21)	.006	11.12 (1.17-105.82)	.04

Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease; FEV_1%, forced expiratory volume in 1 second as a percentage of predicted; NA, not applicable; OR, odds ratio; PPM, potentially pathogenic microorganism.

*Adjusted for the statistically significant variables in the adjusted clinical model. Sterile/low: $\leq 10^1$ colony-forming units (CFU) per milliliter; medium: 10^2-10^3 CFU/mL; and high: $\geq 10^4$ CFU/mL. Sterile/low was used as the reference.

†Patients with polymicrobial cultures were excluded. Adjusted for the statistically significant variables in the adjusted clinical and microbial load models. *Staphylococcus aureus* (n<10) was not included in the analysis.

The New England Journal of Medicine

VOLUME 347 AUGUST 15, 2002 NUMBER 7

NEW STRAINS OF BACTERIA AND EXACERBATIONS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

SANJAY SETHI, M.D., NANCY EVANS, R.N., BRYDON J.B. GRANT, M.D., AND TIMOTHY F. MURPHY, M.D.

TABLE 4. RELATIVE RISK OF AN EXACERBATION ACCORDING TO WHETHER A NEW STRAIN OF BACTERIAL PATHOGEN WAS ISOLATED.

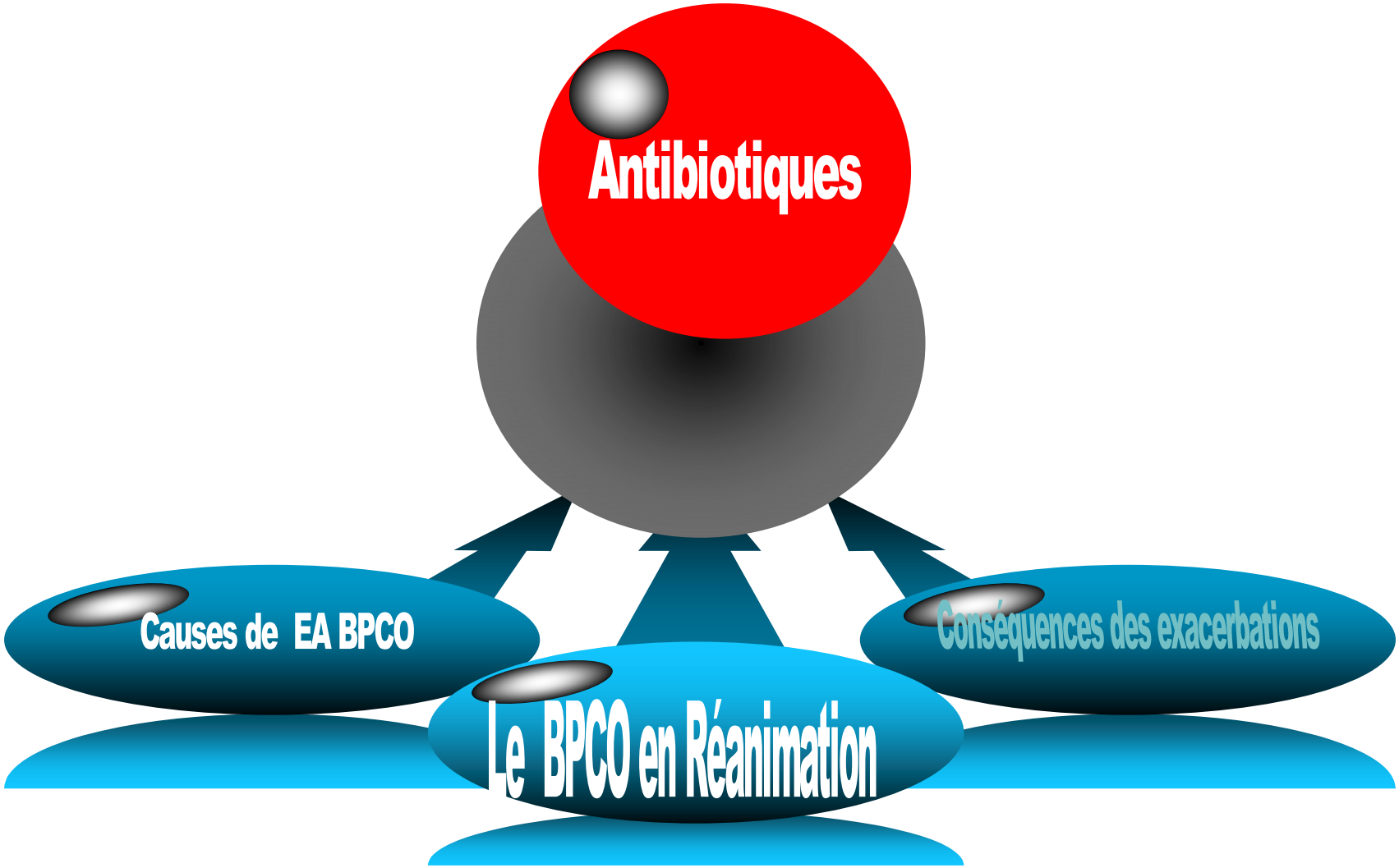
NEW STRAIN	FREQUENCY OF EXACERBATION		P VALUE	RELATIVE RISK (95% CI)*
	NEW STRAIN	NO NEW STRAIN		
	no. of exacerbations/ total no. of visits (%)			
Any strain	89/270 (33.0)	213/1385 (15.4)	<0.001	2.15 (1.83–2.53)
Haemophilus influenzae	38/145 (26.2)†	257/1503 (17.1)	<0.001	1.69 (1.37–2.09)
Moraxella catarrhalis	41/84 (48.8)	261/1571 (16.6)	<0.001	2.96 (2.39–3.67)
Streptococcus pneumoniae	8/25 (32.0)	294/1630 (18.0)	0.01	1.77 (1.14–2.75)
Pseudomonas aeruginosa	3/22 (13.6)‡	297/1631 (18.2)	0.38	0.61 (0.21–1.82)

*The relative risk of an exacerbation was for the presence of a new strain in sputum, as compared with its absence. Relative risks were calculated with the use of generalized estimating equations. CI denotes confidence interval.

†Seven visits were excluded because of simultaneous isolation of new strains of *M. catarrhalis* (six visits) and *P. aeruginosa* (one visit).

‡Two visits were excluded because of simultaneous isolation of new strains of *M. catarrhalis*.

Pourquoi les antibiotiques dans EA BPCO

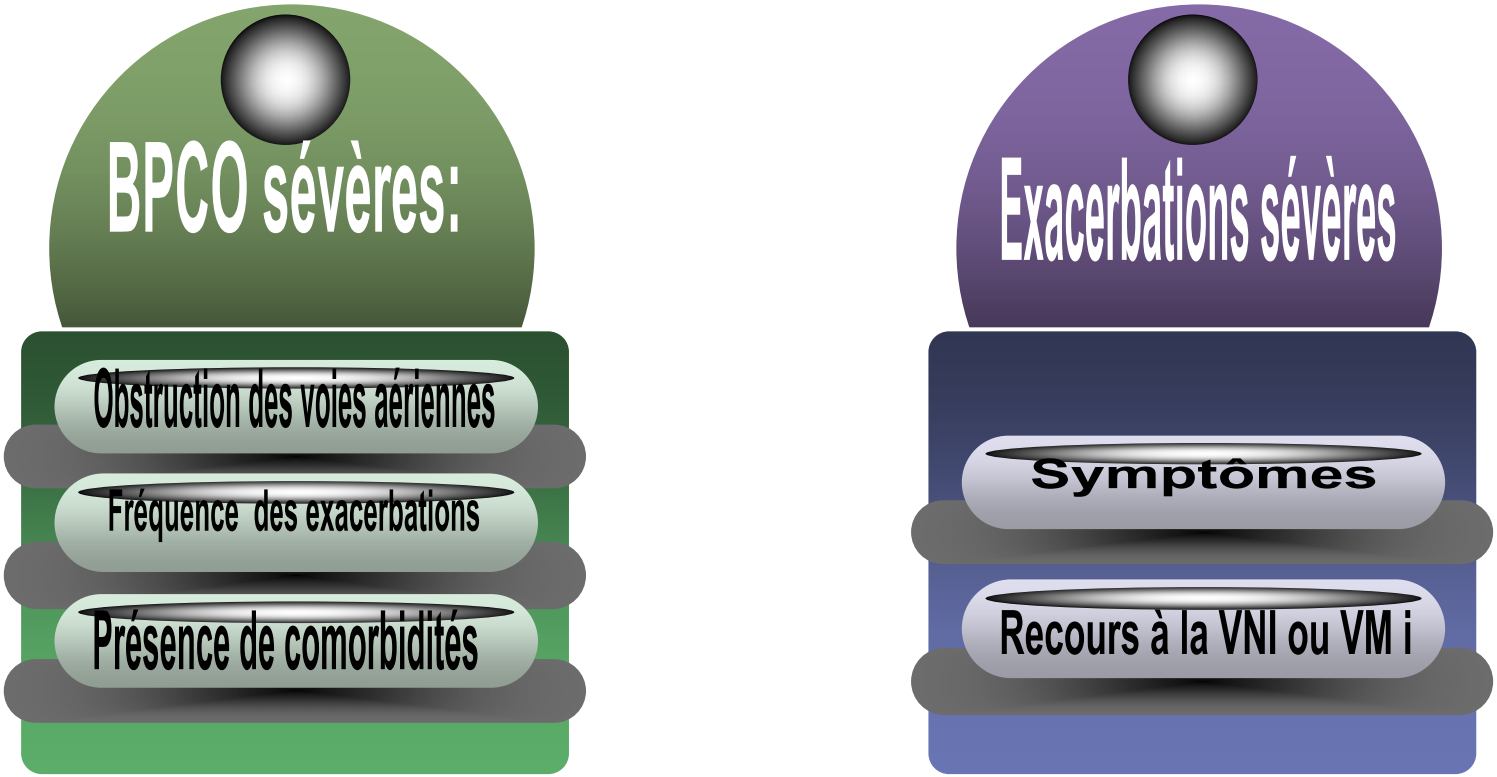


BPCO hospitalisés en Réanimation

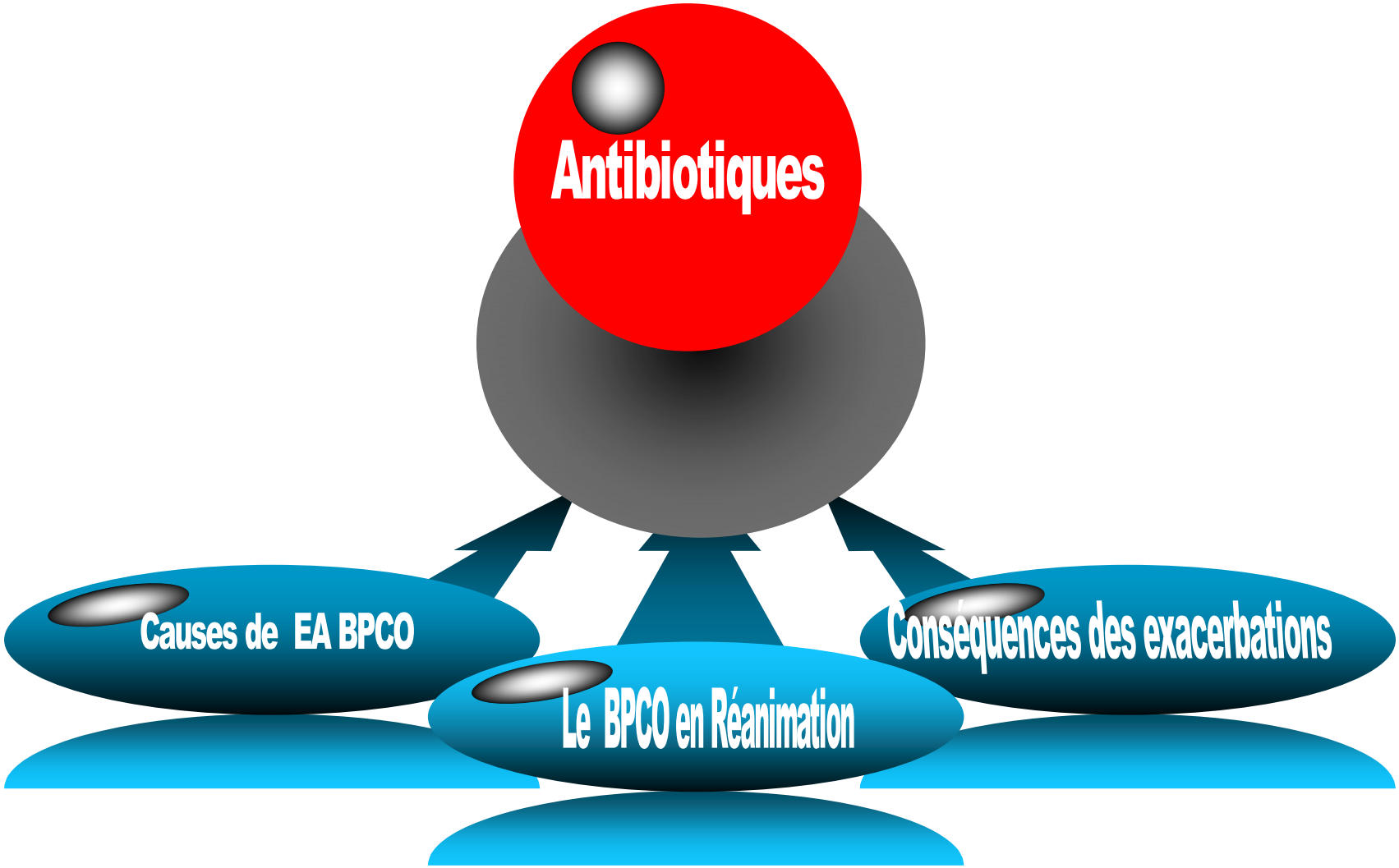
Characteristic	Ofloxacin (n=47)	Placebo (n=46)
Age (years)	66·2 (6·4)	66·5 (9·8)
Men	42 (89%)	42 (91%)
Smoking (pack-year)	55 (29)	54 (26)
Duration of chronic bronchitis (years)	11 (7)	11 (5)
Baseline FEV_1 (L/s)	0·79 (0·25)	0·74 (0·23)
Exacerbations, number during past year	1·7 (1·6)	1·6 (1·2)
SAPSII	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%)

Nouira et al. ,the Lancet 2001; 358:2020-25

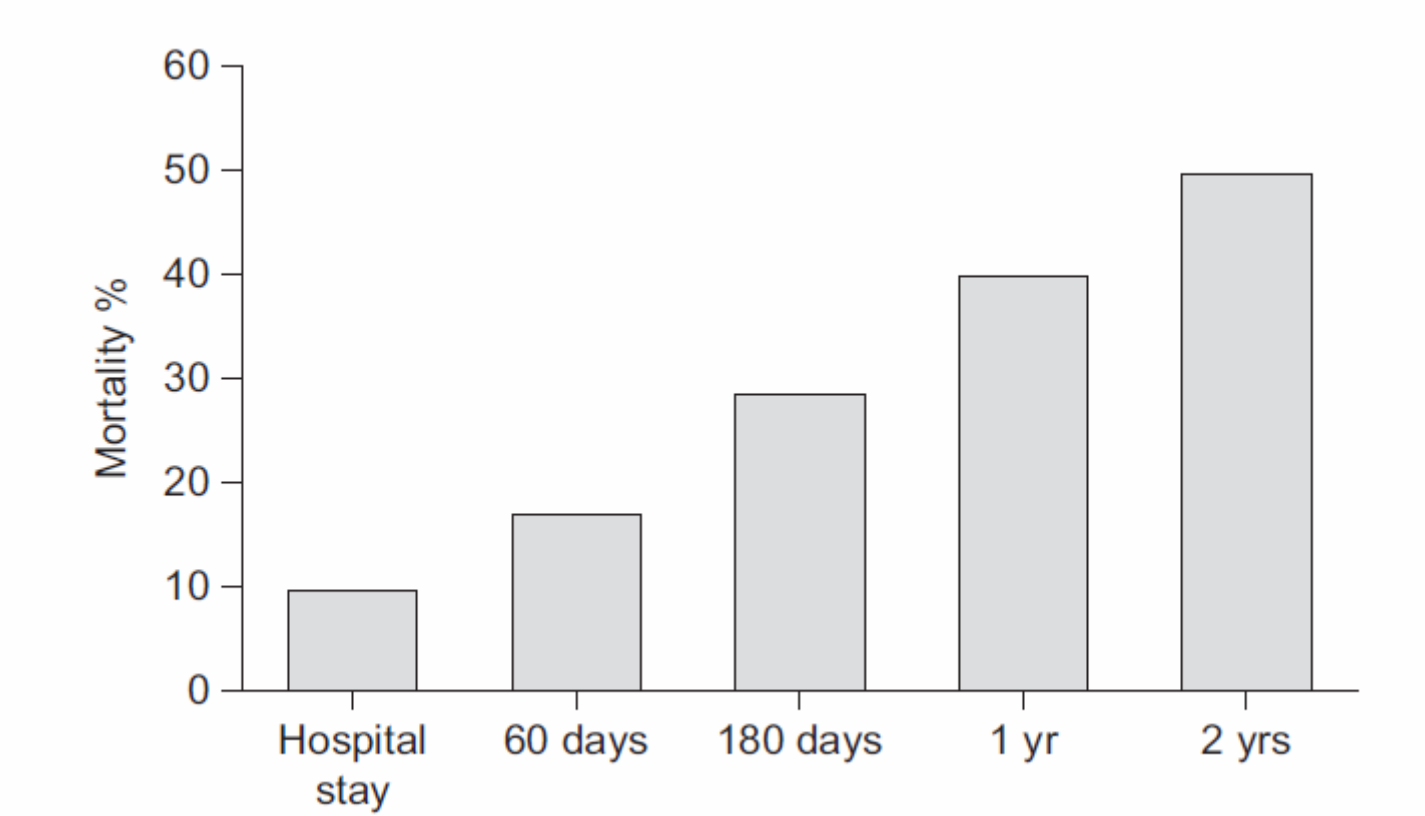
BPCO hospitalisés en Réanimation



Pourquoi les antibiotiques dans EA BPCO



Exacerbations et mortalité



Anzueto A Eur Respir Rev 2010 19:116,113-118

Exacerbations et mortalité

Severe acute exacerbations and mortality in patients with chronic obstructive pulmonary disease

J J Soler-Cataluña, M Á Martínez-García, P Román Sánchez, E Salcedo, M Navarro, R Ochando

Thorax 2005;**60**:925–931. doi: 10.1136/thx.2005.040527

305 patients , suivi 5 ans

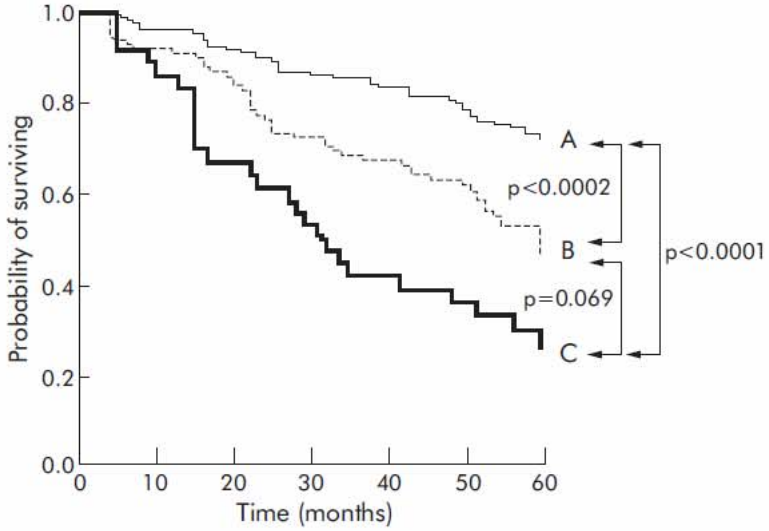


Figure 1 Kaplan-Meier survival curves by frequency of exacerbations in patients with COPD: group A, patients with no acute exacerbations of COPD; group B, patients with 1–2 acute exacerbations of COPD requiring hospital management; group C, patients with ⩾3 acute exacerbations of COPD.

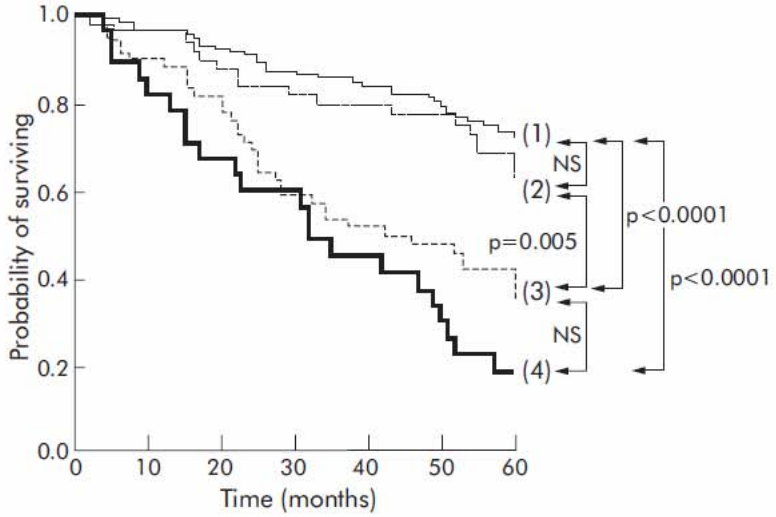


Figure 2 Kaplan-Meier survival curves by severity of exacerbations in patients with COPD: (1) no acute exacerbations of COPD; (2) patients with acute exacerbations of COPD requiring emergency service visits without admission; (3) patients with acute exacerbations of COPD requiring one hospital admission; (4) patients with readmissions.

Exacerbations et qualité de vie

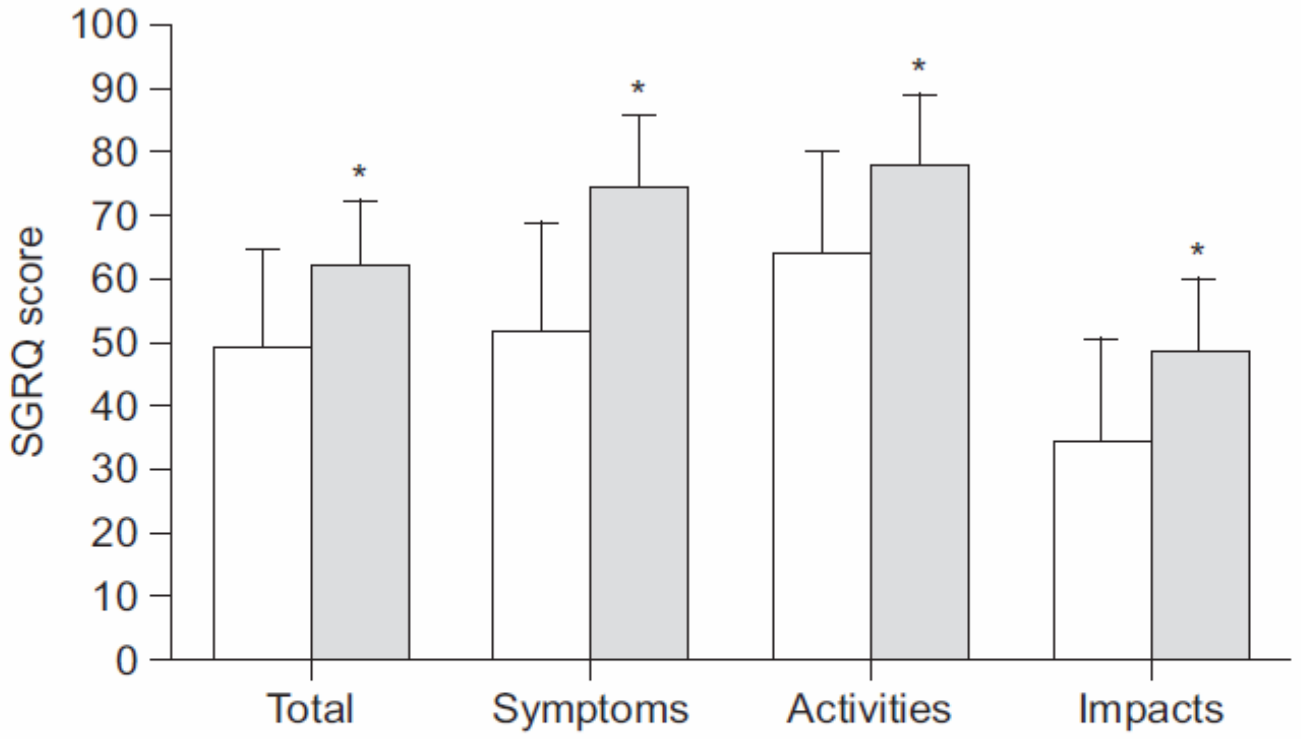


FIGURE 1. Relationship between exacerbation frequency and quality of life parameters. □: 0–2 exacerbations per year; ■: 3–8 exacerbations per year. SGRQ: St George's Respiratory Questionnaire. *: $p<0.05$. Reproduced from [37] with permission from the publisher.

Anzueto A Eur Respir Rev 2010 19:116,113-118

Exacerbations et qualité de vie

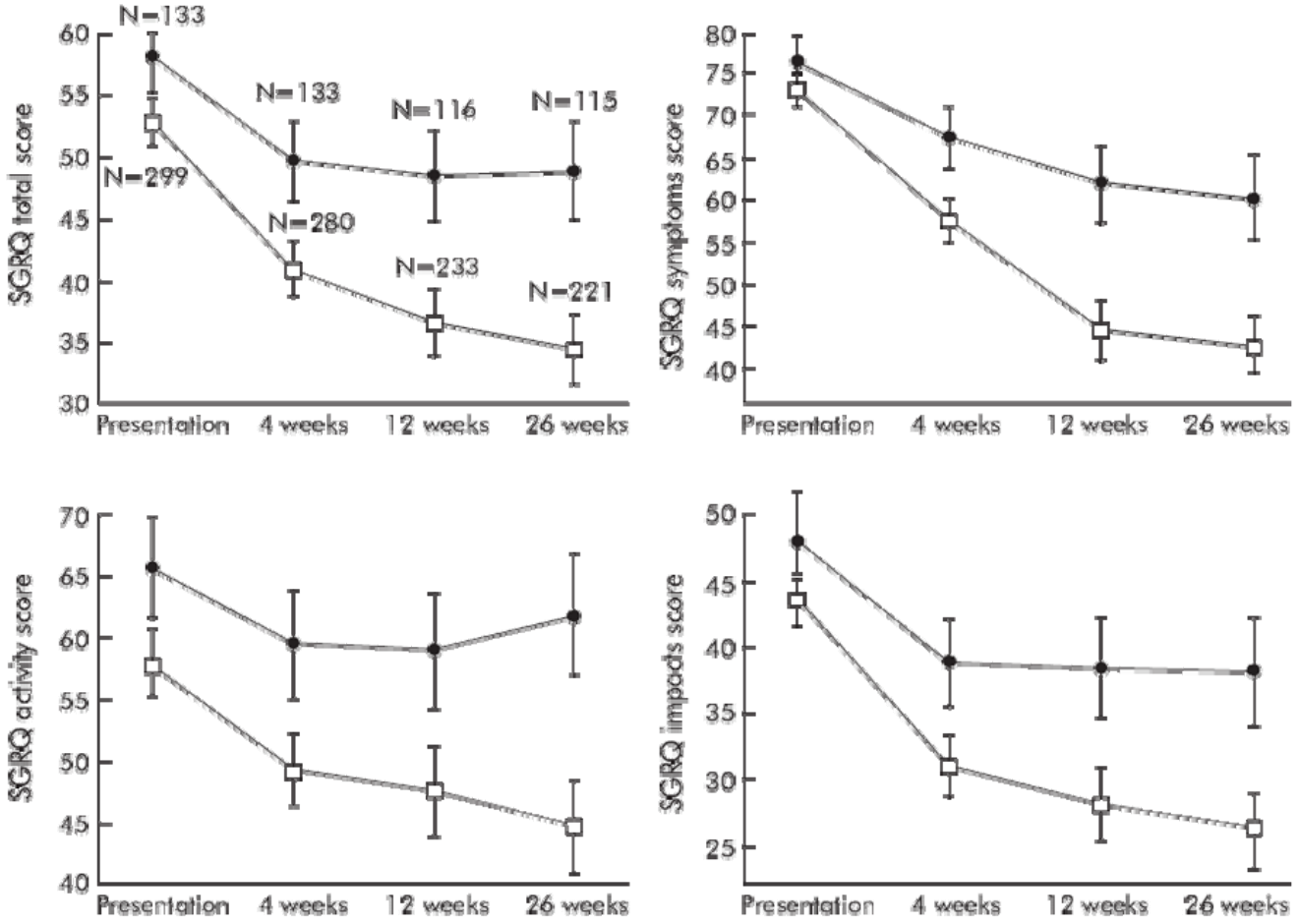


Figure 1 SGRQ study scores by exacerbation status (bars indicate 95% confidence intervals) in patients with no exacerbation (□) and patients with a further exacerbation during the follow up period (•). The numbers represent patients remaining in the study at that time point.

S Spencer Thorax 2003;58:589–593

Exacerbation et fonction respiratoire

ORIGINAL ARTICLE

Relationship between exacerbation frequency and lung function decline in chronic obstructive pulmonary disease

Table 3 Initial and annual change in lung function in patients with infrequent and frequent exacerbations

	Starting value		Annual change	
	Infrequent	Frequent	Infrequent	Frequent
Exacerbations (reported and unreported)			<50% percentile, <2.92 per year (n=63)	> 50% percentile >2.92 per year (n=46)
PEF (l/min)	214	232	–0.72 (n=16)	–2.94*** (n=16)
FEV_1 (ml)	893	950	–32.1	–40.1*

PEF=peak expiratory flow; FEV_1=forced expiratory volume in 1 second.
*p<0.05, ***p<0.001 annual rates of change between infrequent and frequent exacerbators.

G C Donaldson and al. Thorax 2002; 57: 847-852

ORIGINAL ARTICLE

Relationship between bacterial colonisation and the frequency, character, and severity of COPD exacerbations

I S Patel, T A R Seemungal, M Wilks, S J Lloyd-Owen, G C Donaldson, J A Wedzicha

Thorax 2002;57:759–764

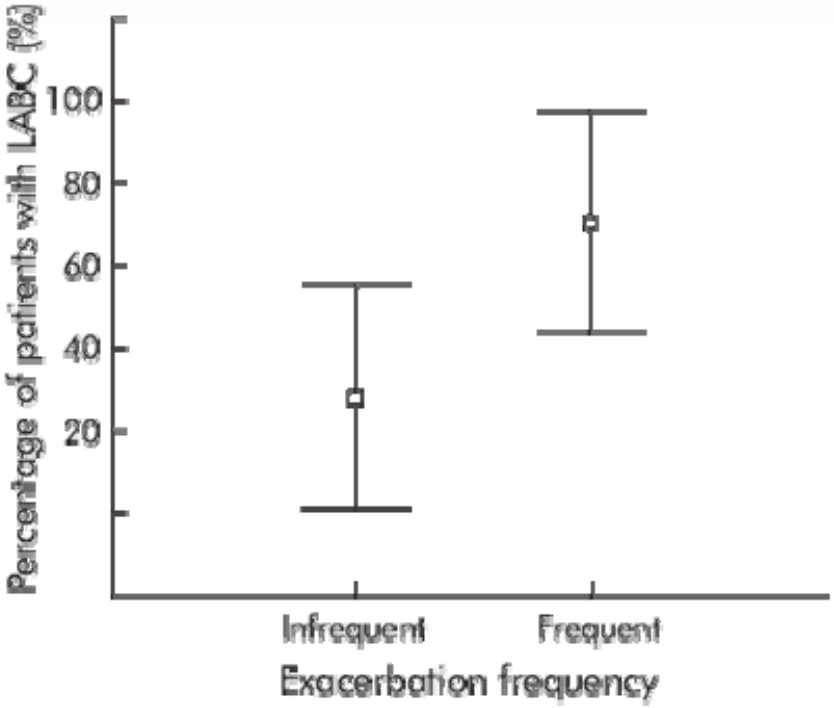
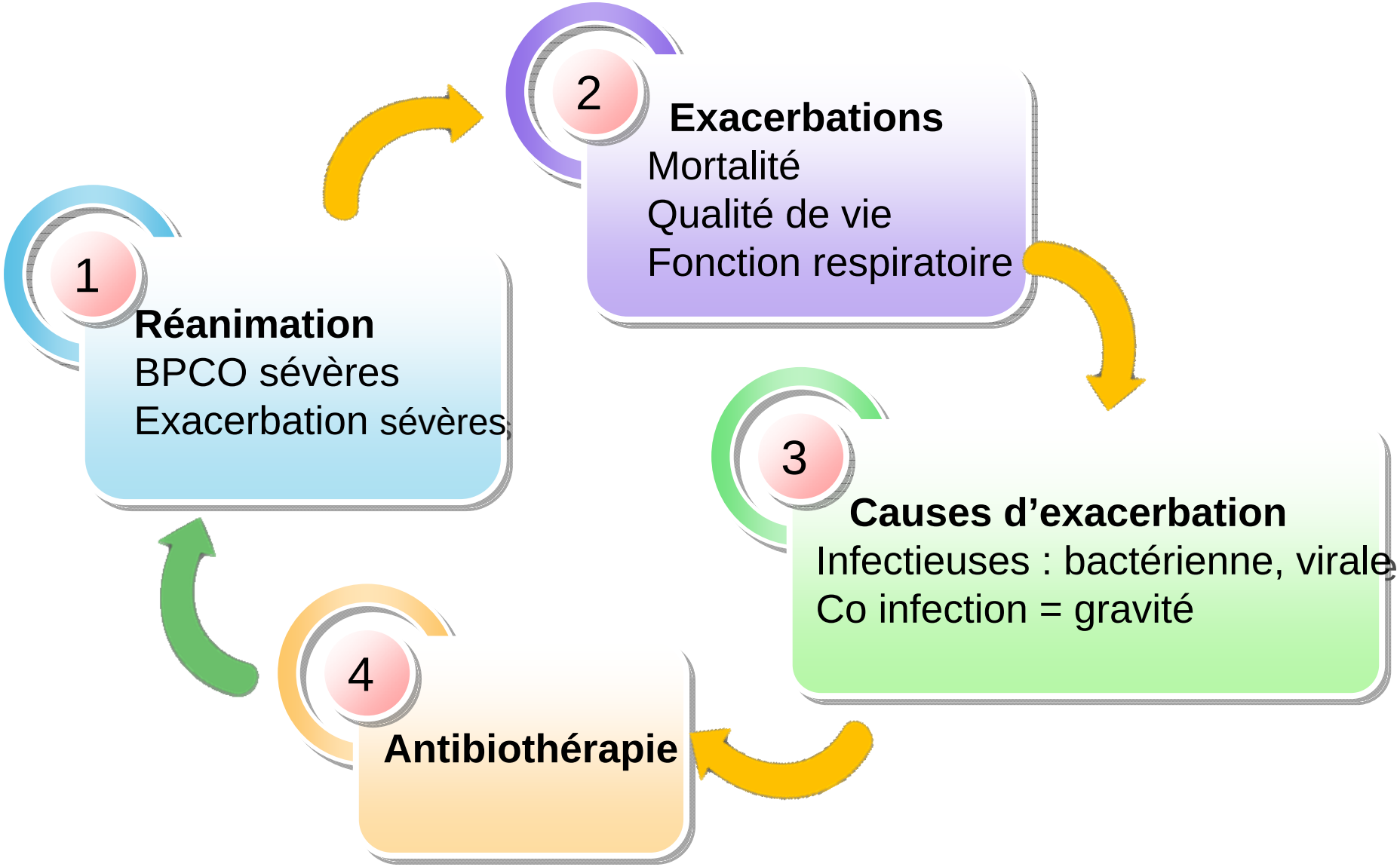


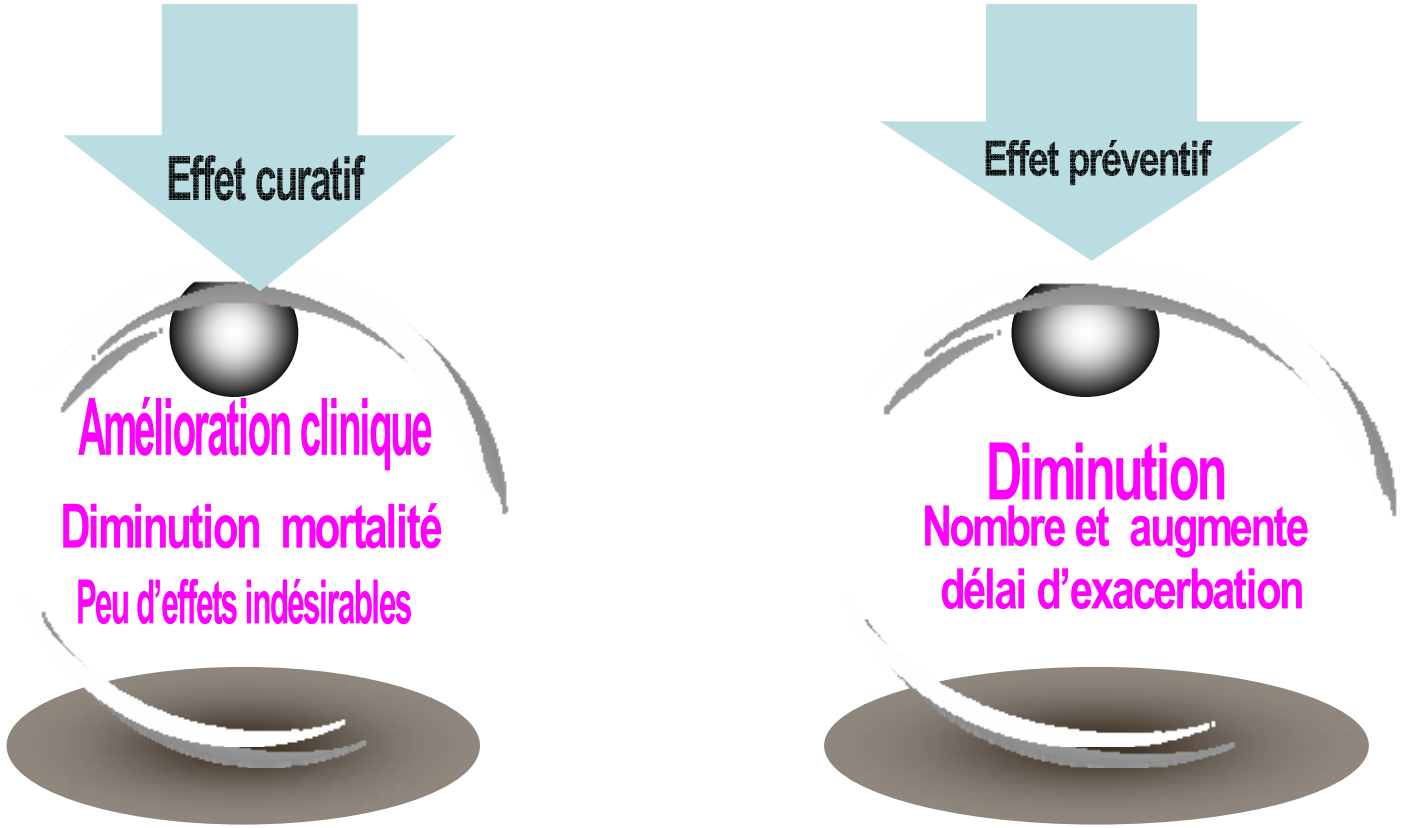
Figure 2 Relationship between lower airway bacterial colonisation (LABC) by a possible pathogen in induced sputum and frequent (>2.58 exacerbations per year; n=14) and infrequent exacerbations (≤2.58 exacerbations per year; n=14) with 95% confidence intervals.

Pourquoi les antibiotiques dans EA BPCO



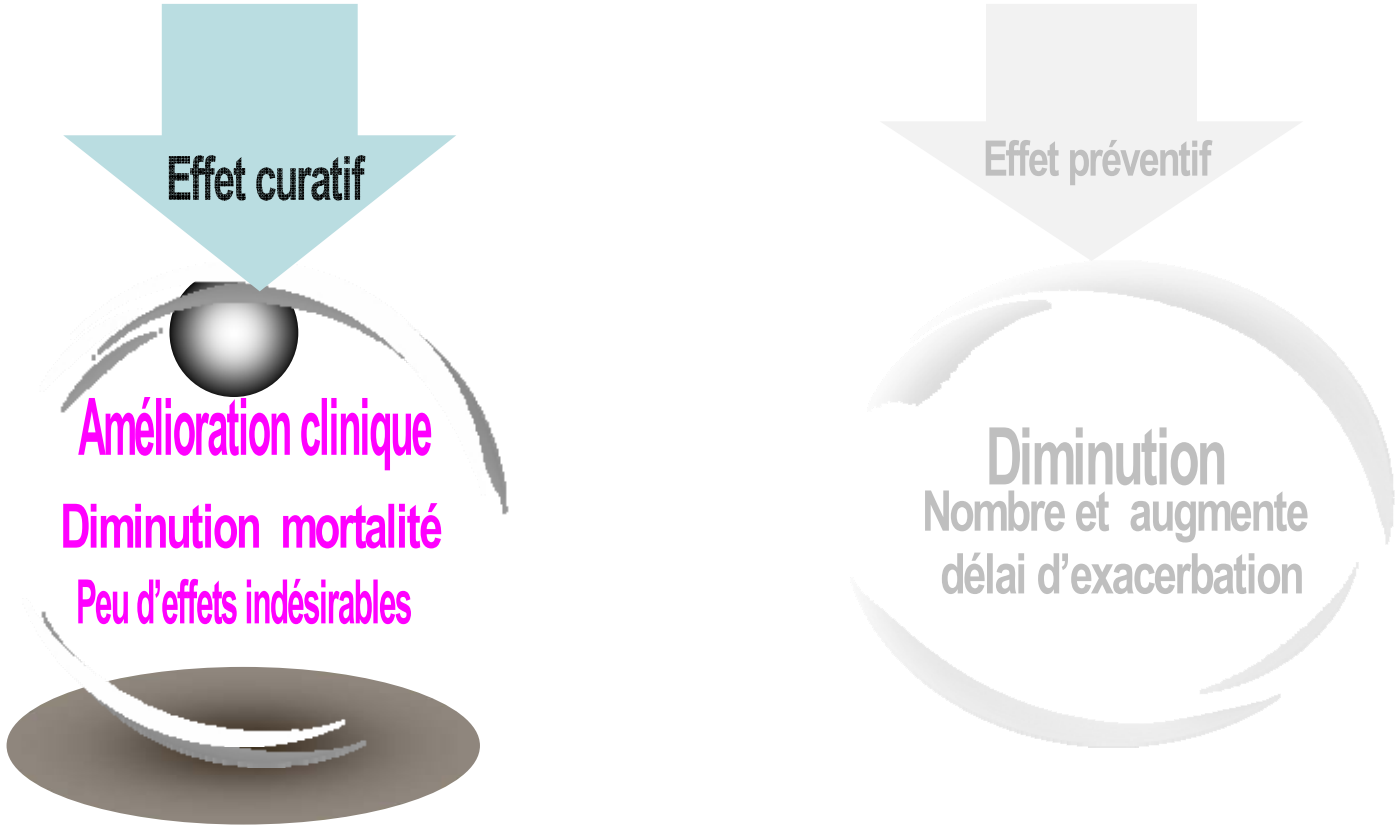
Etudes cliniques

Antibiothérapie

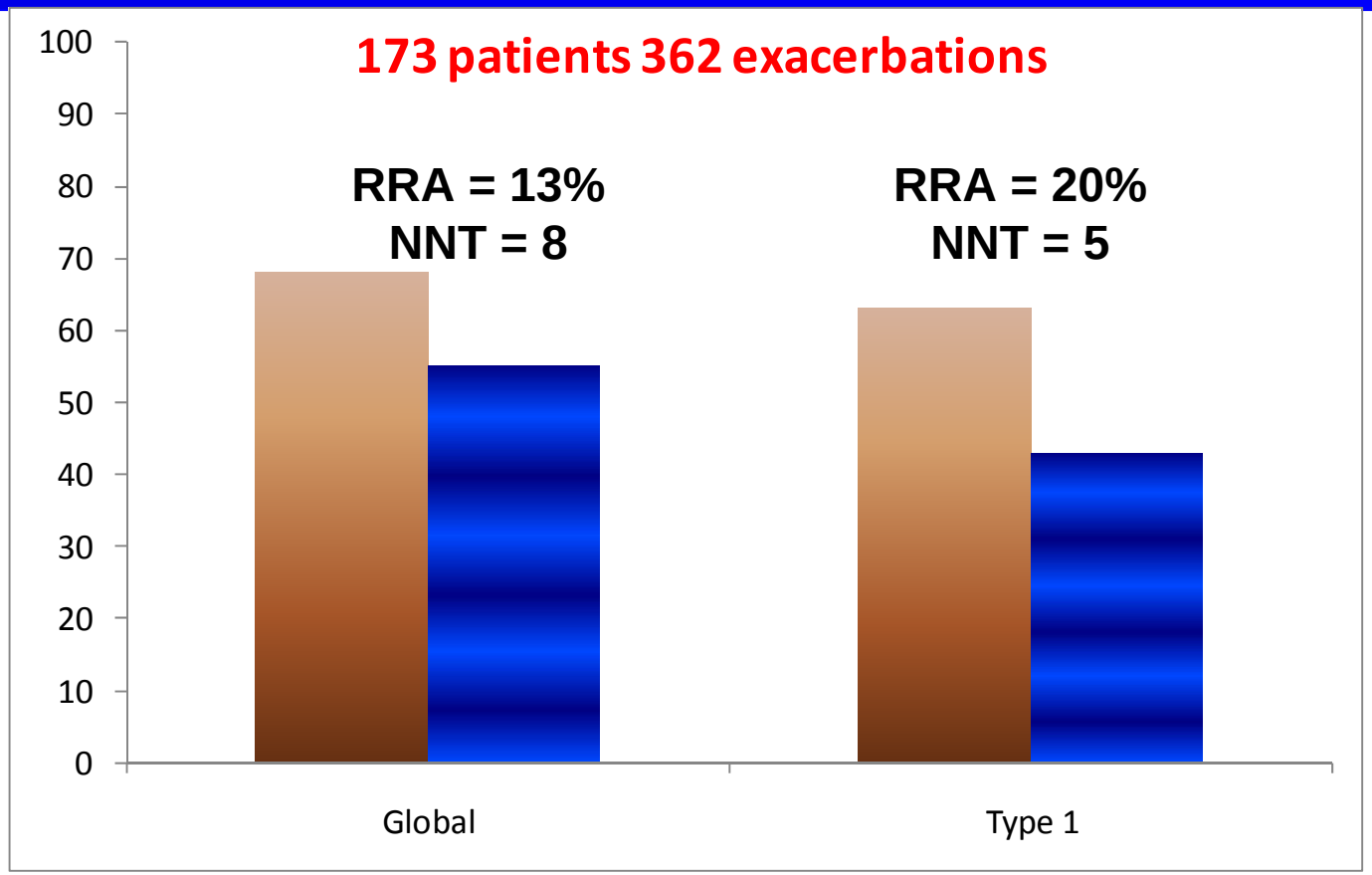


Etudes cliniques

Antibiothérapie



Clinical improvement

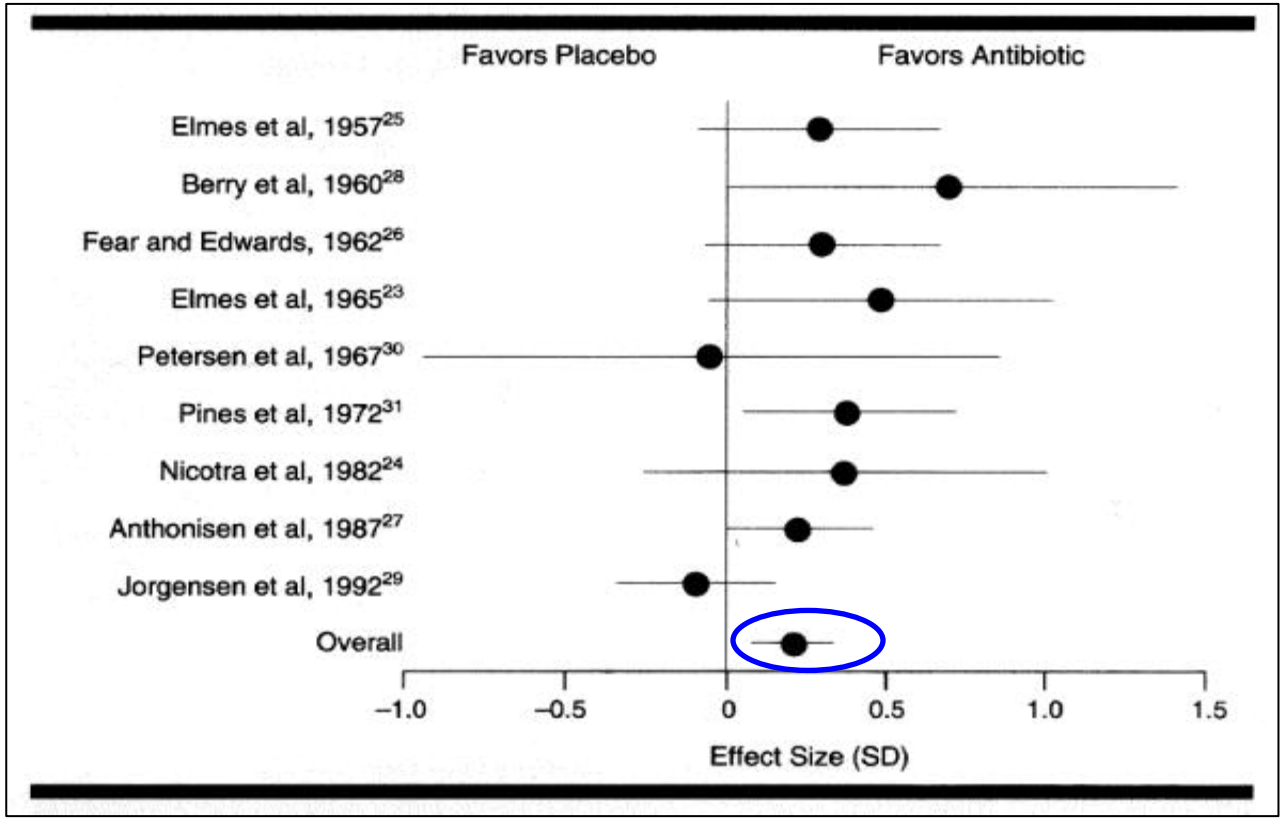


❖ Le risque d'aggravation de l'exacerbation était **2 fois supérieur** chez les patients traités par placebo

❖ Le **bénéfice des antibiotiques** était net pour les patients ayant une exacerbation de type 1

Anthonisen NR. Ann Intern Med 1987; 106:196

Antibiotics in Chronic Obstructive Pulmonary Disease Exacerbations: A Meta-analysis. Saint, Sanjay; JAMA. 273(12):957-960, Mar 22, 1995.



Effect sizes of randomized trials and summary overall estimate: **0.22 (95% confidence interval (CI), 0.10 to 0.34)**

Antibiotic Treatment and Baseline Severity of Disease in Acute Exacerbations of Chronic Bronchitis: A Re-evaluation of Previously Published Data of a Placebo-controlled Randomized Study

Table 5 Observed outcome of chronic obstructive pulmonary disease exacerbations according to treatment in our 335 study patients.

	Antibiotic group (n = 176)		Placebo group (n = 159)	
	No.	%	No.	%
Success	97	55.1	41	25.8
Improvement	98	31.3	42	24.8
Failure	24	13.6	79	49.7

P value <0.001 (χ^2 test for heterogeneity or independence).

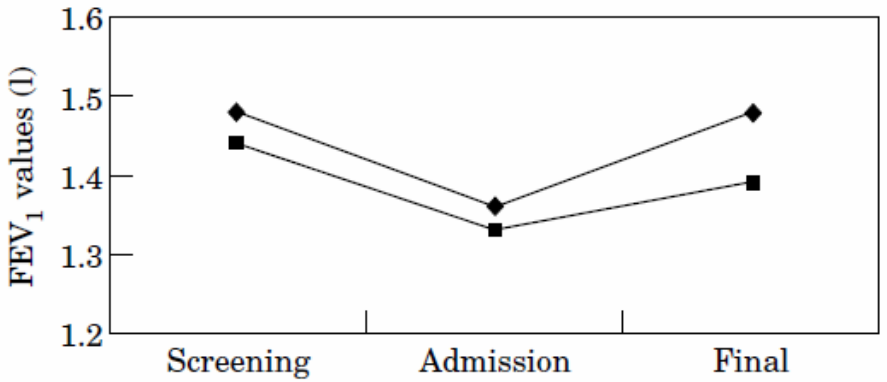
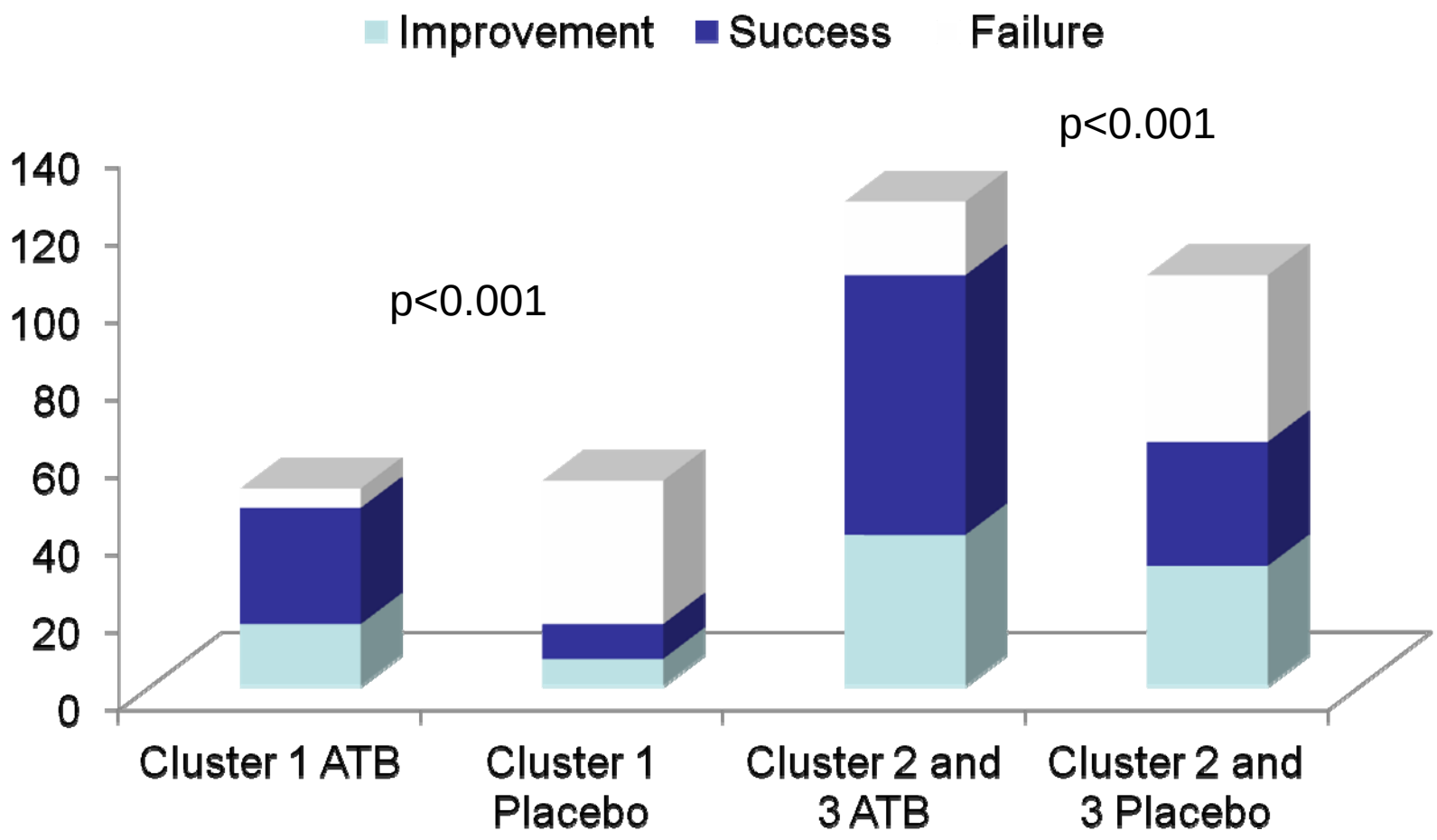


Fig. 4 FEV_1 values at screening, admission and final evaluation in patients with exacerbations of chronic bronchitis. [Significant difference between antibiotic and placebo at final evaluation (P<0.01)]. Antibiotic (n = 176, —◆—; placebo (n = 159, —■—).

Allegra Pulmonary pharmacology and therapeutics 2001; 14:149-155

Antibiotic Treatment and Baseline Severity of Disease in Acute Exacerbations of Chronic Bronchitis: A Re-evaluation of Previously Published Data of a Placebo-controlled Randomized Study



Allegra Pulmonary pharmacology and therapeutics 2001; 14:149-155

Once daily oral ofloxacin in chronic obstructive pulmonary disease exacerbation requiring mechanical ventilation: a randomised placebo-controlled trial

	Ofloxacin (n=47)	Placebo (n=46)	Absolute risk reduction (95% CI)	p
Primary outcome				
Death				
ICU	2 (4%)	8 (17%)	13·2 (0·8 to 25·6)	0·05
Hospital	2 (4%)	10 (22%)	17·5 (4·3 to 30·7)	0·01
Need for additional antibiotics	3 (6%)	16 (35%)	28·4 (12·9 to 43·9)	0·0006
Combined events	5 (11%)	26 (57%)	45·9 (29·1 to 62·7)	<0·0001
Secondary outcome				
Duration of mechanical ventilation (days)	6·4 (3·1)	10·6 (5·1)	4·2 (2·5 to 5·9)	0·04
Duration of stay (days)				
ICU	9·4 (5·2)	14·5 (6·0)	5·1 (3·9 to 6·3)	0·02
Hospital	14·9 (7·4)	24·5 (8·5)	9·6 (3·4 to 12·8)	0·01
Adverse events				
Rash	1	0		
Facial oedema	1	0		
Diarrhoea	1	1		
Abnormal serum AST and ALT	2	3		
Total	5 (11%)	4 (9%)	1·9 (–10·0 to 13·8)	0·75

Data are number of patients (%) or mean (SD). ICU=intensive-care unit; AST=aspartate aminotransferase; ALT=alanine aminotransferase.

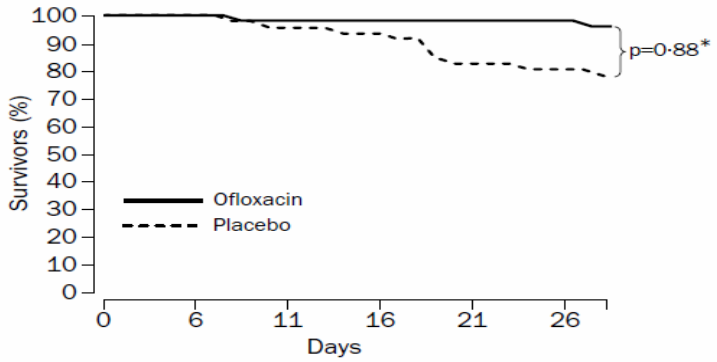


Figure 2: **Kaplan-Meier survival analysis of deaths in patients given ofloxacin or placebo**

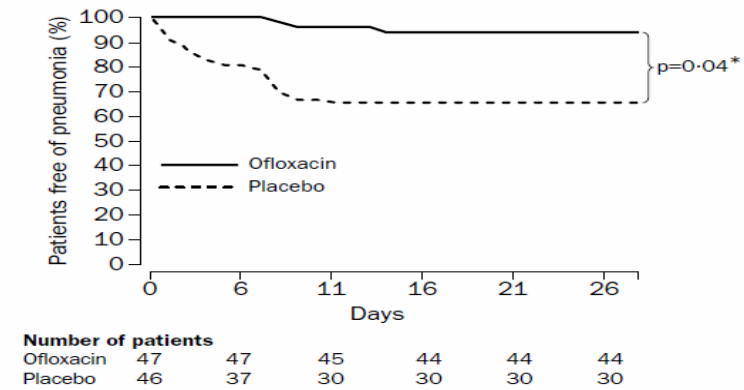


Figure 3: **Kaplan-Meier survival analysis showing pneumonia-free intervals in patients on ofloxacin or placebo**
*By log-rank test.

Semir Nouira, Soudani Marghli, Makhlouf Belghith, Lamia Besbes, Souheil Elatrous, Fekri Abroug *Lancet* 2001; **358:** 2020–25

Antibiotics for exacerbations of chronic obstructive pulmonary disease (Review)

THE COCHRANE COLLABORATION®

Analysis 01.01. Comparison 01 Antibiotics versus placebo, Outcome 01 Mortality (short-term) during study intervention

Review: Antibiotics for exacerbations of chronic obstructive pulmonary disease

Comparison: 01 Antibiotics versus placebo

Outcome: 01 Mortality (short-term) during study intervention

Study	Antibiotic Group n/N	Placebo Group n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Elmes 1965a	1/29	5/29		18.0	0.20 [0.02, 1.61]
Nouira 2001	4/47	18/46		65.6	0.22 [0.08, 0.59]
Pines 1968	1/15	3/15		10.8	0.33 [0.04, 2.85]
Pines 1972	0/89	1/86		5.5	0.32 [0.01, 7.80]
Total (95% CI)	180	176		100.0	0.23 [0.10, 0.52]

Total events: 6 (Antibiotic Group), 27 (Placebo Group)

Test for heterogeneity chi-square=0.19 df=3 p=0.98 I^2 =0.0%

Test for overall effect z=3.55 p=0.0004

Analysis 01.02. Comparison 01 Antibiotics versus placebo, Outcome 02 Treatment failure (no resolution or deterioration of symptoms after trial medication of any duration or death)

Review: Antibiotics for exacerbations of chronic obstructive pulmonary disease

Comparison: 01 Antibiotics versus placebo

Outcome: 02 Treatment failure (no resolution or deterioration of symptoms after trial medication of any duration or death)

Study	Antibiotic Group n/N	Placebo Group n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Alonso 1992	2/29	6/29		3.5	0.33 [0.07, 1.52]
Anthonisen 1987	19/57	28/59		16.2	0.70 [0.45, 1.11]
Elmes 1965a	6/29	19/29		11.2	0.32 [0.15, 0.68]
Jørgensen 1992	49/132	49/136		28.4	1.03 [0.75, 1.41]
Pines 1968	6/15	15/15		8.8	0.40 [0.22, 0.74]
Pines 1972	31/89	53/86		31.8	0.57 [0.41, 0.79]
Total (95% CI)	351	354		100.0	0.67 [0.56, 0.80]

Total events: 113 (Antibiotic Group), 170 (Placebo Group)

Test for heterogeneity chi-square=15.46 df=5 p=0.009 I^2 =67.7%

Test for overall effect z=4.27 p=0.00002

Research

Open Access

Exacerbations of chronic obstructive pulmonary disease: when are antibiotics indicated? A systematic review

Milo A Puhan*, Daniela Vollenweider, Tsogyal Latshang, Johann Steurer and Claudia Steurer-Stey

Respiratory Research 2007, **8**:30

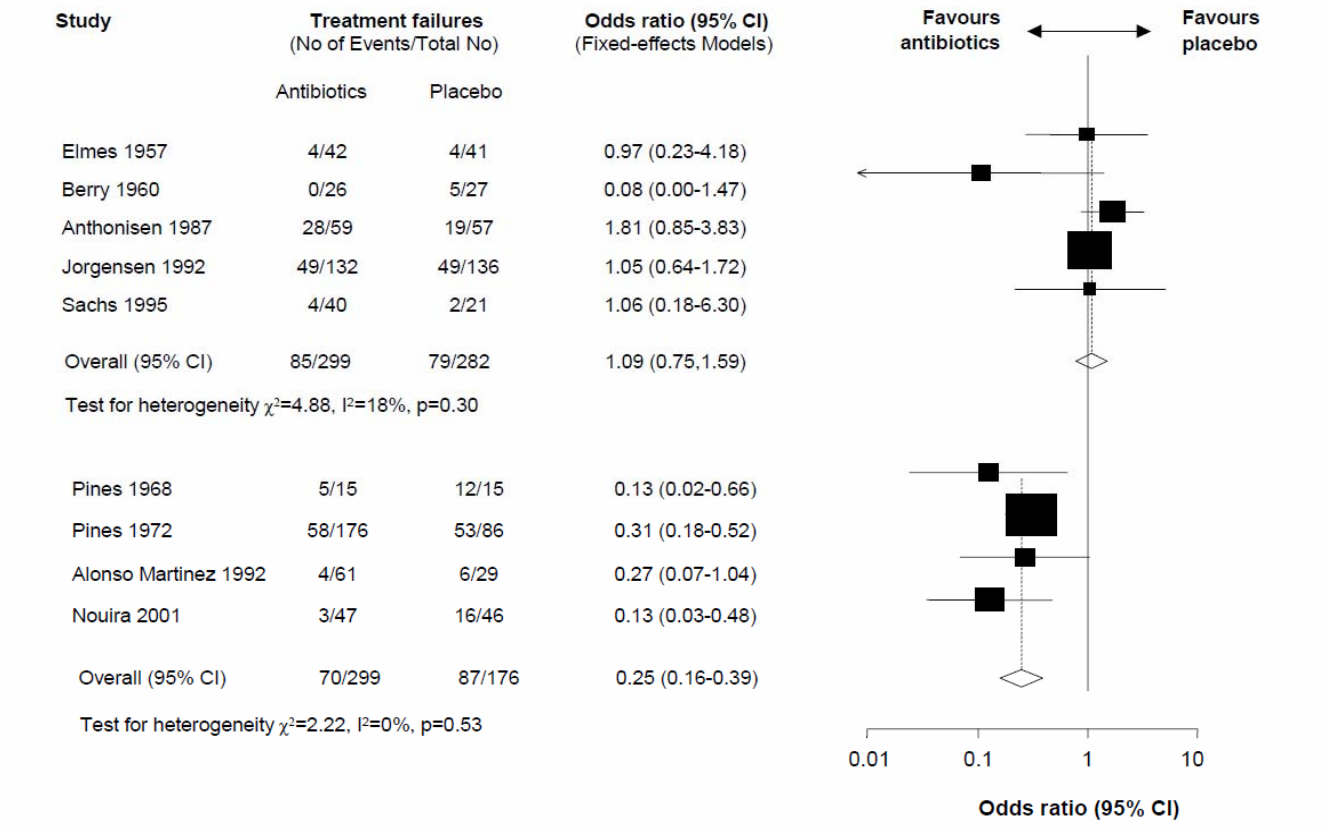


Figure 3
Forest plot showing nine studies grouped according to severity of exacerbation. One study with a substantially higher treatment failure rate and a short follow-up of five days was not considered in the analysis. The upper five studies included patients with mild to moderate exacerbations and the four studies below included patients with severe exacerbations. The x-axis represents the odds ratio for treatment failure. An odds ratio below 1 represents a lower chance of treatment failure with antibiotics. Studies not reporting treatment failures could not be included in the meta-analysis.

Research

Open Access

Exacerbations of chronic obstructive pulmonary disease: when are antibiotics indicated? A systematic review

Milo A Puhan*, Daniela Vollenweider, Tsogyal Latshang, Johann Steurer and Claudia Steurer-Stey

Respiratory Research 2007, **8**:30

Study	Deaths (No of Deaths/Total No)		Odds ratio (95% CI) (Fixed-Effects Model)
	Antibiotics	Placebo	
Petersen 1967	0/9	1/9	0.33 (0.01-9.26)
Pines 1968	1/15	3/15	0.29 (0.03-3.12)
Pines 1972	0/173	1/86	0.16 (0.01-4.07)
Nouira 2001	2/47	10/46	0.16 (0.03-0.78)
Overall (95% CI)	3/244	15/156	0.20 (0.06-0.62)

Test for heterogeneity χ^2=0.27, I^2=0%, p=0.97

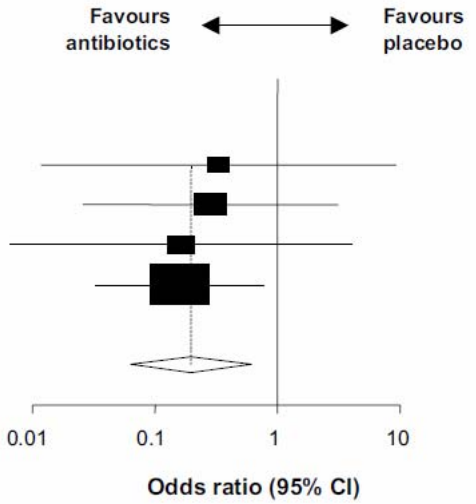


Figure 4
Forest plot showing the four studies that included patients with severe exacerbations. The x-axis represents the odds ratio for mortality. An odds ratio below 1 represents a lower chance of mortality with antibiotics. Studies not reporting mortality could not be included in the meta-analysis.

Research

Open Access

Exacerbations of chronic obstructive pulmonary disease: when are antibiotics indicated? A systematic review

Milo A Puhan*, Daniela Vollenweider, Tsogyal Latshang, Johann Steurer and Claudia Steurer-Stey

Respiratory Research 2007, **8**:30

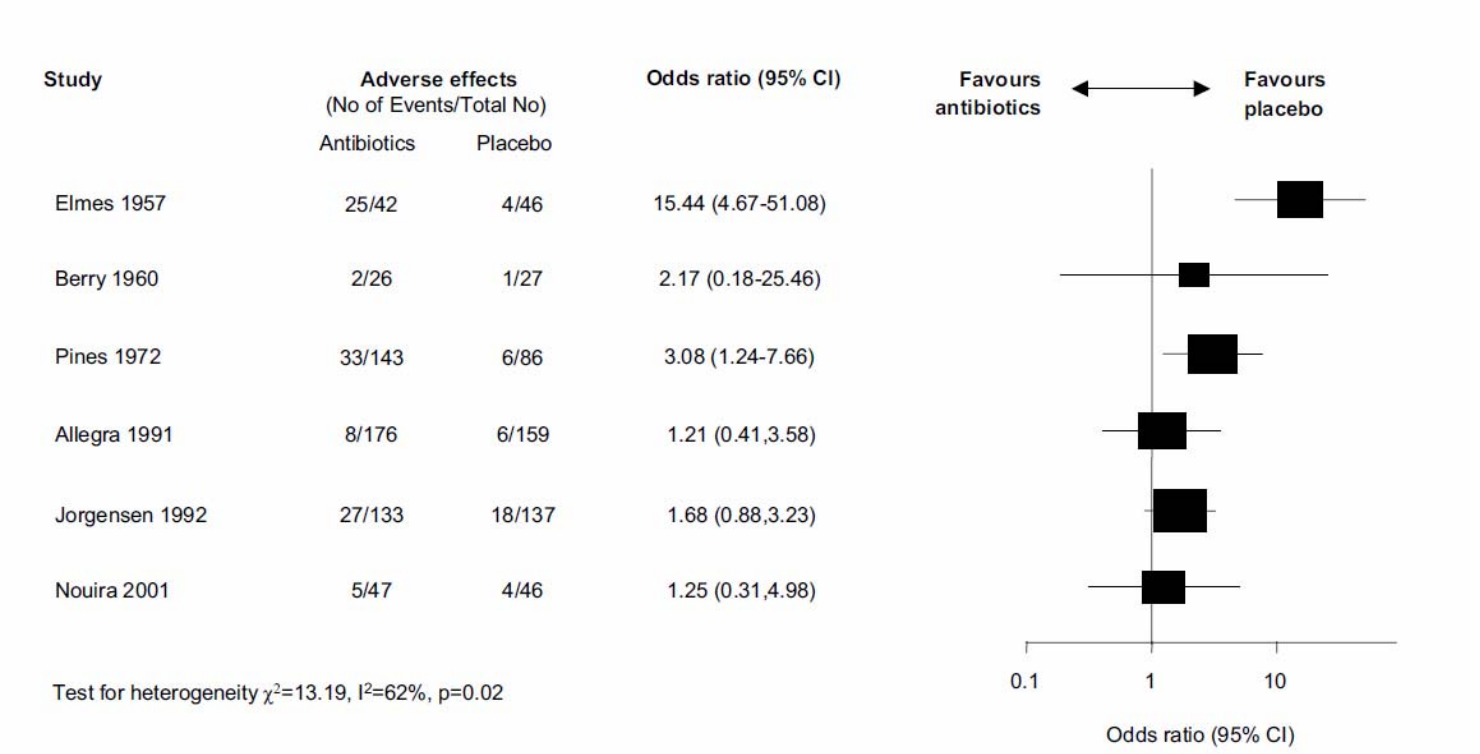


Figure 5
Forest plot showing six studies reporting on adverse effects. The x-axis represents the odds ratio for adverse effects. An odds ratio above 1 represents a lower chance of adverse effects with placebo. Studies not reporting adverse effects could not be included in the meta-analysis.

Contemporary Management of Acute Exacerbations of COPD*: A Systematic Review and Metaanalysis

Bradley S. Quon, Wen Qi Gan and Don D. Sin

Chest 2008;133:756-766

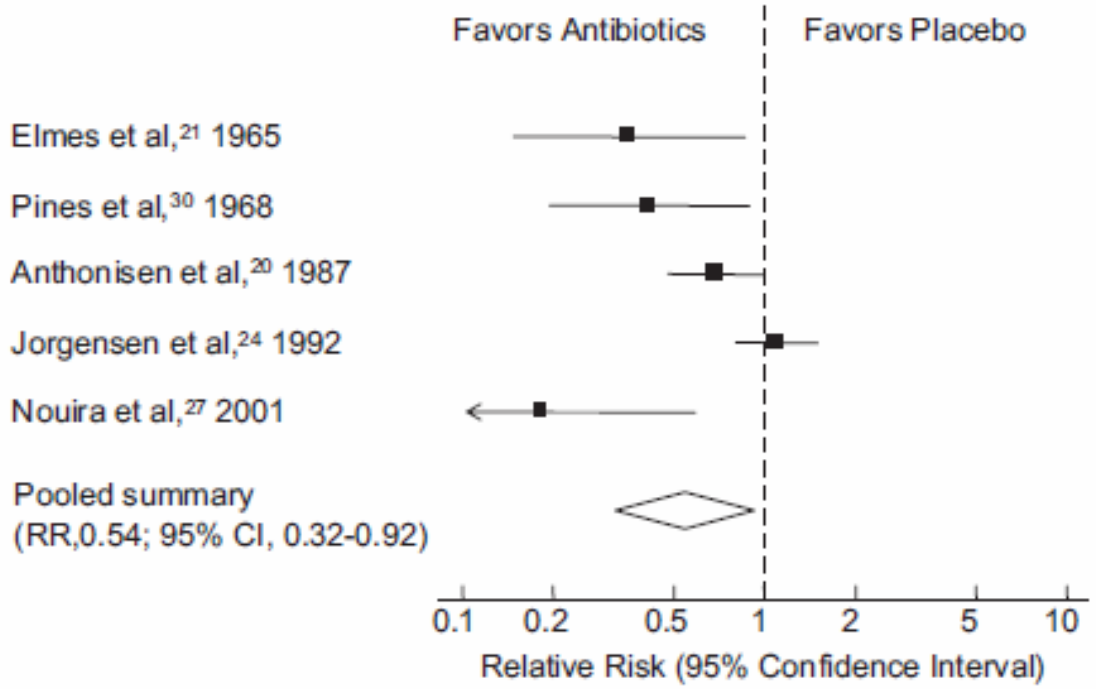


FIGURE 3. Effects of antibiotic therapy on the risk of treatment failure.

Antibiotic Therapy and Treatment Failure in Patients Hospitalized for Acute Exacerbations of Chronic Obstructive Pulmonary Disease

JAMA, May 26, 2010—Vol 303, No. 20 **2035**

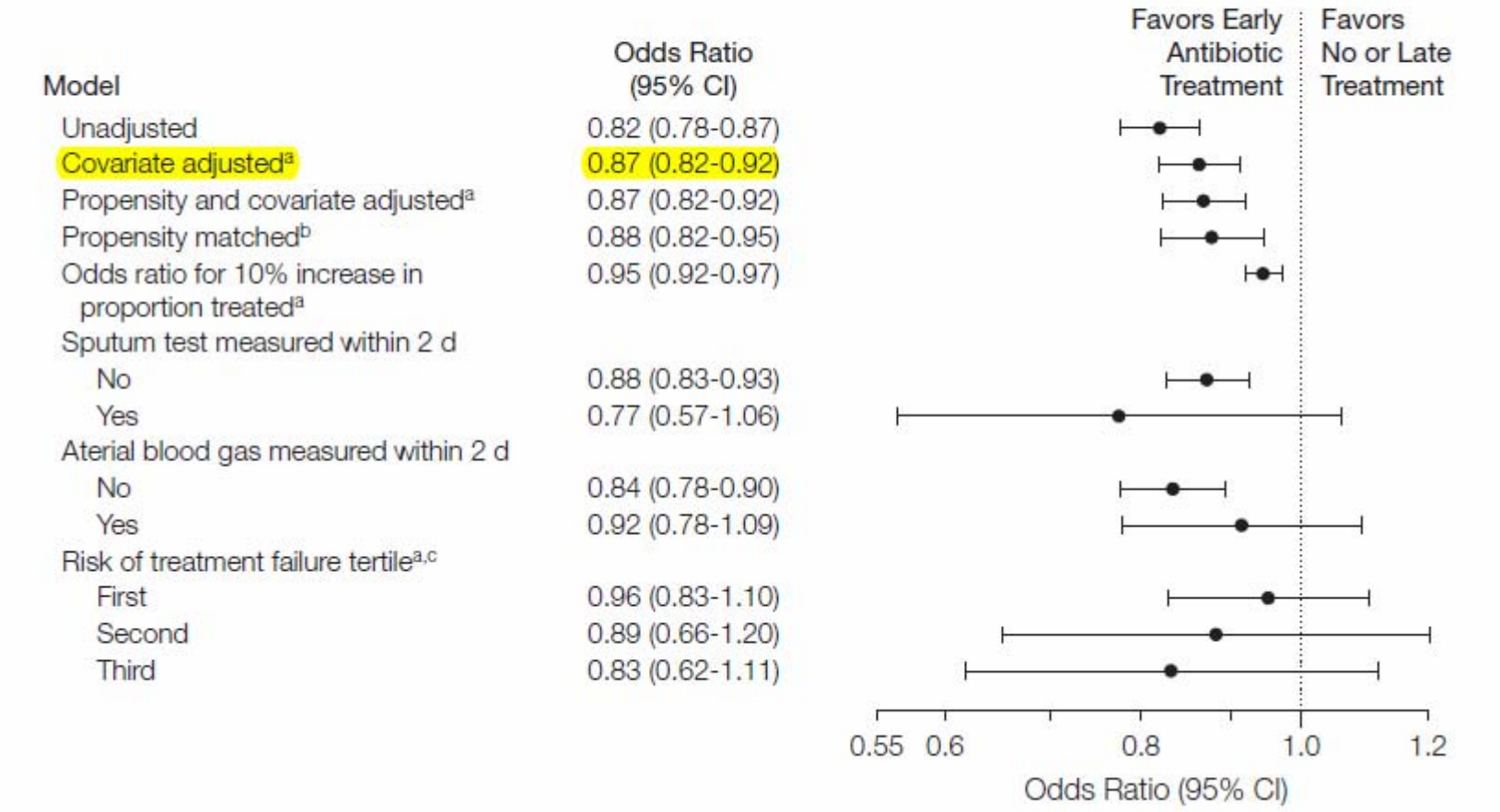
- Cohorte Rétrospective
- **84621** patients âgés de plus de 40 ans hospitalisés du 1 Janvier 2006 au 31 Décembre 2007 pour exacerbation aigue de BPCO
- 413 unités au USA
- **Antibiothérapie précoce vs tardive ou pas d'antibiothérapie**
- Critère de jugement composite :
  - VM après 48 H ,
  - mortalité,
  - réadmission pour exacerbation dans les 30 jours après la sortie

Antibiotic Therapy and Treatment Failure in Patients Hospitalized for Acute Exacerbations of Chronic Obstructive Pulmonary Disease

Table 3. Unadjusted Outcomes by Antibiotic Exposure

Patient Outcomes	No. (%) [95% Confidence Interval] Early Antibiotics (n = 67 229)	No/Late Antibiotics (n = 17 392)	*P* Value
Late ventilation, after day 2	721 (1.07) [1.06-1.08]	313 (1.80) [1.78-1.82]	<.001
In-hospital mortality	700 (1.04) [1.03-1.05]	277 (1.59) [1.57-1.61]	<.001
Treatment failure[b]	6571 (9.77) [9.75-9.80]	2043 (11.75) [11.70-11.79]	<.001
Allergic reaction	88 (0.13) [0.13-0.13]	35 (0.20) [0.19-0.19]	.03
Clostridium difficile testing after hospital day 2	1172 (1.74) [1.73-1.75]	280 (1.61) [1.59-1.63]	.23
Antibiotics for presumed *C difficile* diarrhea	603 (0.90) [0.89-0.90]	147 (0.85) [0.83-0.86]	.52
Diarrhea diagnosis	1124 (1.67) [1.66-1.68]	293 (1.68) [1.67-1.70]	.91
Readmission within 30 d			
COPD[a]	5321 (7.91) [7.89-7.94]	1528 (8.79) [8.74-8.83]	<.001
Diarrhea[a]	152 (0.23) [0.22-0.23]	22 (0.13) [0.12-0.13]	.01
C difficile diarrhea[a]	129 (0.190) [0.187-0.193]	15 (0.090) [0.086-0.094]	.003
	Median (Interquartile Range)		
Length of stay, d			
All patients	4 (3-6)	4 (3-6)	.16[c]
Excluding patients with values >3 SDs from overall patient mean	4 (3-6)	4 (3-6)	.013
Total cost, US $[d]			
All patients	4925 (3496-7261)	5084 (3547-7652)	<.001[c]
Excluding patients with values >3 SDs from overall patient mean	4881 (3479-7135)	5012 (3522-7451)	<.001

Figure 1. Treatment Failure for Early Antibiotic Treatment vs Late or No Treatment



Antibiotics in Addition to Systemic Corticosteroids for Acute Exacerbations of Chronic Obstructive Pulmonary Disease

Johannes M. A. Daniels[1], Dominic Snijders[1], Casper S. de Graaff[1], Fer Vlaspolder[2], Henk M. Jansen[3], and Wim G. Boersma[1]

Am J Respir Crit Care Med Vol 181. pp 150–157, 2010

223 P 265 Exacerbations

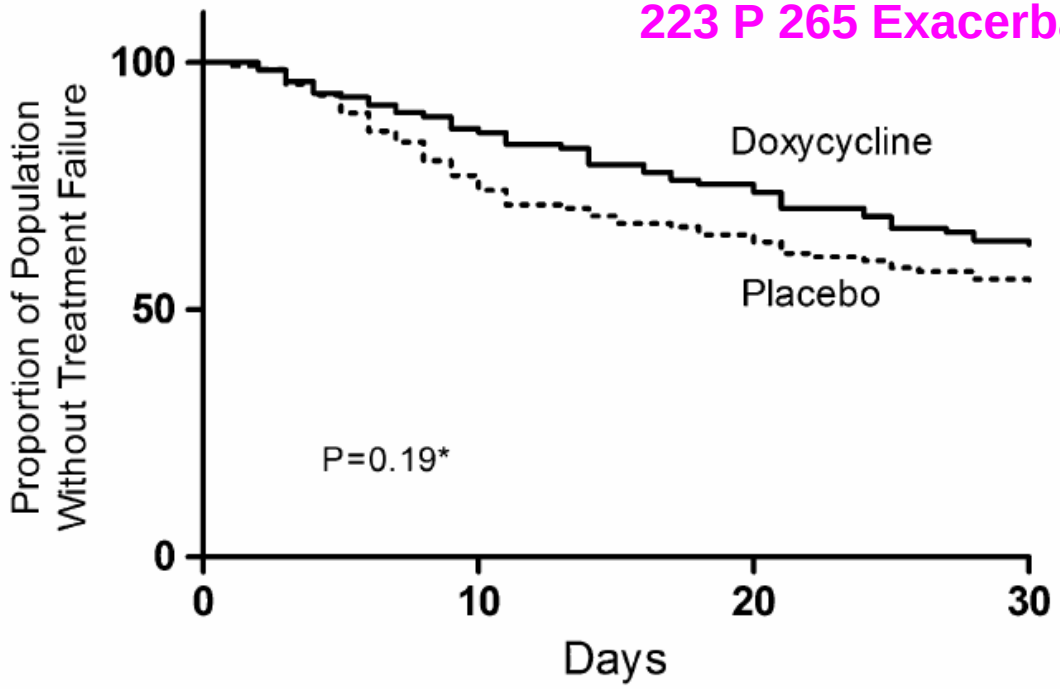
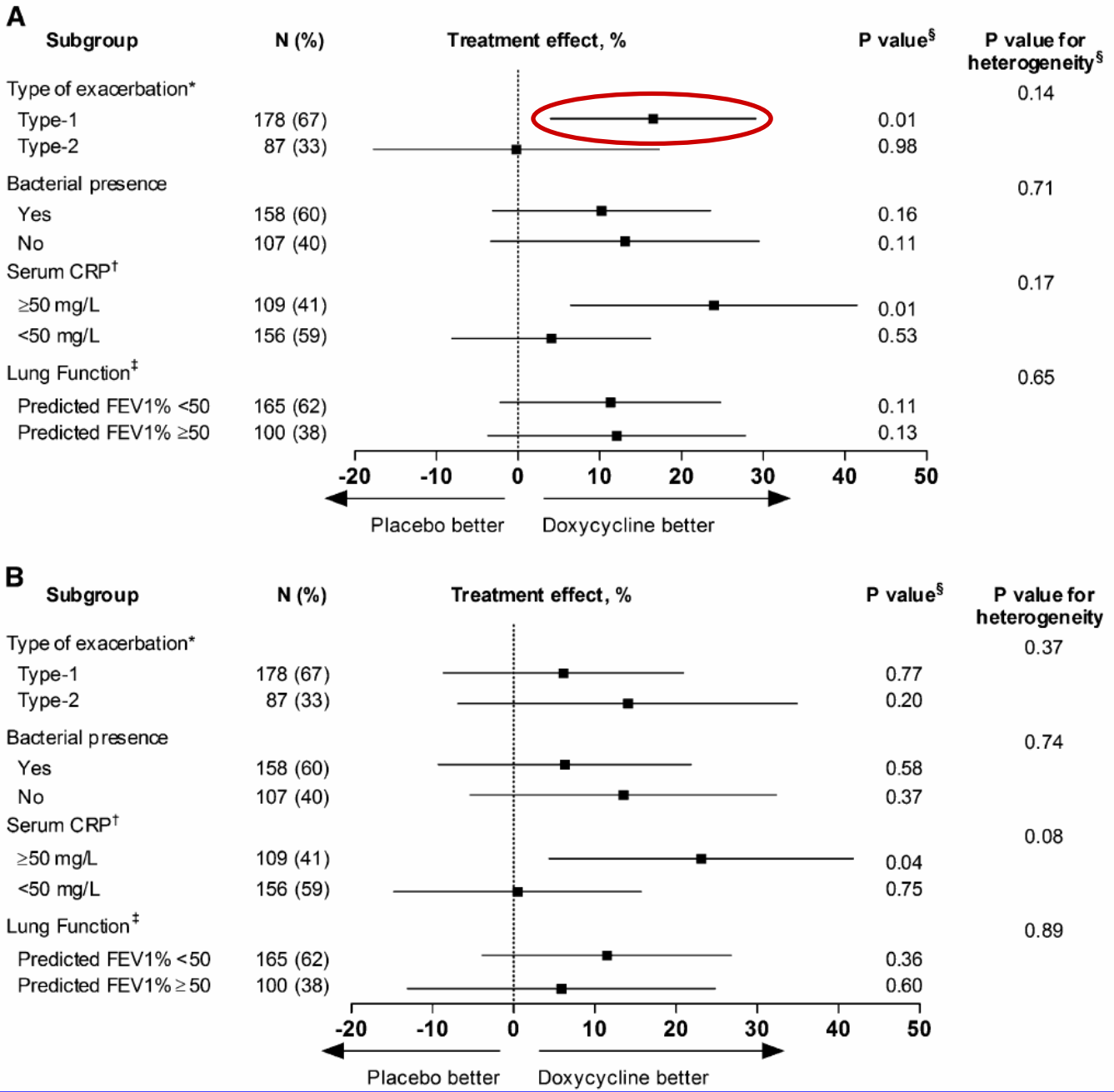


Figure 2. Kaplan-Meier curves showing the effect of the intervention on time to treatment failure in the intention-to-treat population. *Corrected for within-patient clustering.

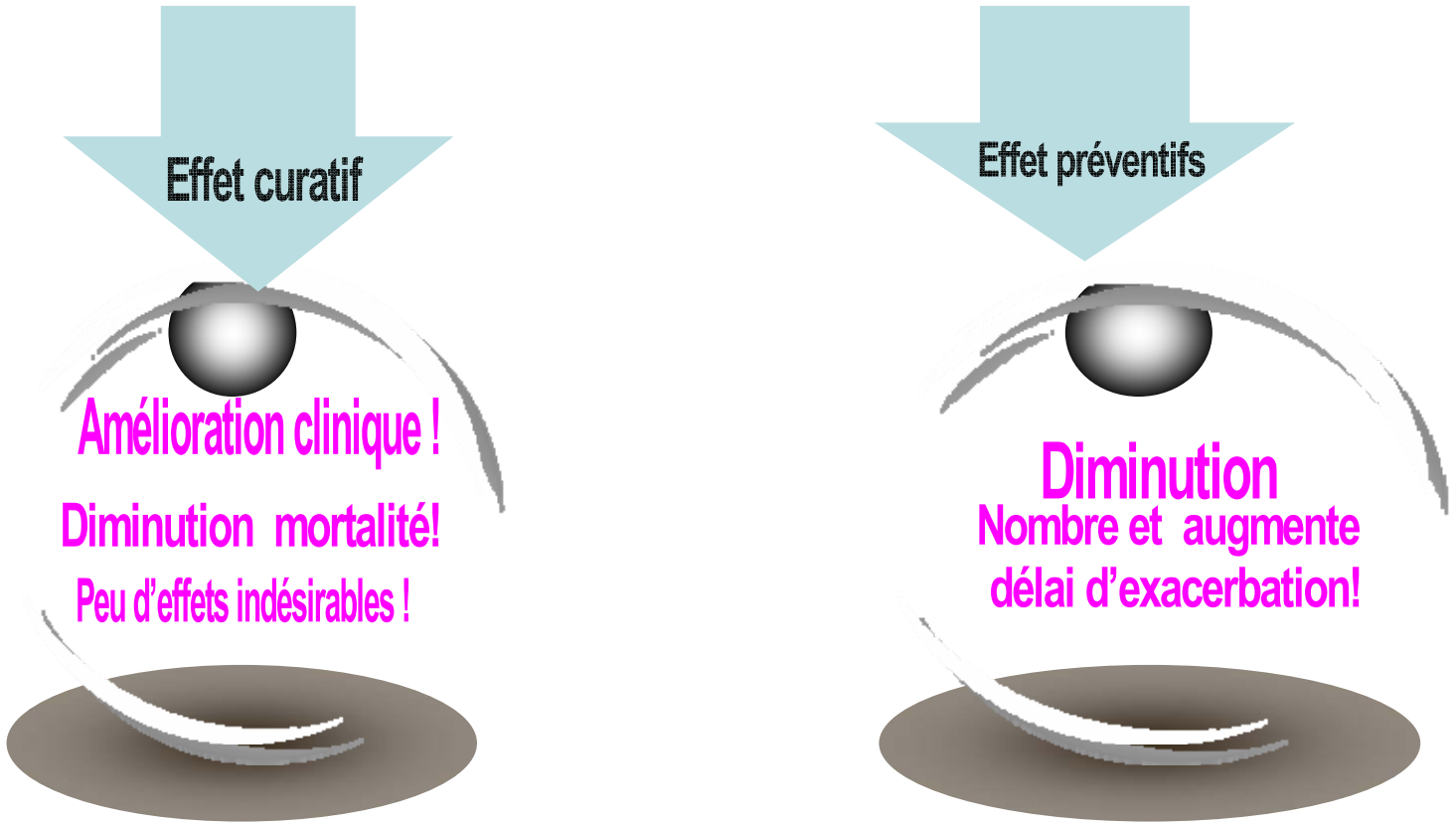
TABLE 3. BACTERIOLOGICAL RESPONSE ON DAY 10 IN SUBJECTS FROM THE INTENTION-TO-TREAT POPULATION WITH BACTERIAL INFECTION

End Point	n	Doxycycline (*n* = *78*) n/total (%)	Placebo (*n* = *73*) n/total (%)	Odds Ratio (95% CI)*	*P* Value*
Overall success, no. (%)	151	52/78 (67)	25/73 (34)	3.8 (1.9 to 7.5)	<0.001
Success per pathogen					
Haemophilus influenzae	86	28/44 (64)	14/42 (33)	3.5 (1.4 to 8.5)	0.006
Streptococcus pneumoniae	50	18/23 (78)	9/27 (33)	6.9 (1.9 to 24.8)	0.003
Moraxella catarrhalis	46	18/22 (82)	10/24 (42)	5.1 (1.4 to 18.9)	0.015
Pseudomonas spp.	7	1/4 (25)	2/3 (67)		
Staphylococcus aureus	6	4/4 (100)	2/2 (100)		
Haemophilus parainfluenzae	6	5/5 (100)	1/1 (100)		
Serratia marcescens	2		2/2 (100)		
Escherichia coli	2	1/1 (100)	1/1 (100)		
Enterobacterium spp.	1		1/1 (100)		
Xanthomonas maltophilia	1	1/1 (100)			
Mycoplasma pneumoniae†	3	0/1 (0)	1/2 (50)		
Chlamydia pneumoniae†	2		1/2 (50)		


A
Subgroup
N (%)
Treatment effect, %
P value§
P value for heterogeneity§
Type of exacerbation*
0.14
Type-1
178 (67)
0.01
Type-2
87 (33)
0.98
Bacterial presence
0.71
Yes
158 (60)
0.16
No
107 (40)
0.11
Serum CRP†
0.17
≥50 mg/L
109 (41)
0.01
<50 mg/L
156 (59)
0.53
Lung Function‡
0.65
Predicted FEV1% <50
165 (62)
0.11
Predicted FEV1% ≥50
100 (38)
0.13
-20 -10 0 10 20 30 40 50
Placebo better
Doxycycline better
B
Subgroup
N (%)
Treatment effect, %
P value§
P value for heterogeneity
Type of exacerbation*
0.37
Type-1
178 (67)
0.77
Type-2
87 (33)
0.20
Bacterial presence
0.74
Yes
158 (60)
0.58
No
107 (40)
0.37
Serum CRP†
0.08
≥50 mg/L
109 (41)
0.04
<50 mg/L
156 (59)
0.75
Lung Function‡
0.89
Predicted FEV1% <50
165 (62)
0.36
Predicted FEV1% ≥50
100 (38)
0.60
-20 -10 0 10 20 30 40 50
Placebo better
Doxycycline better

Etudes cliniques

Antibiothérapie



Etudes cliniques

Antibiotic treatment is associated with reduced risk of a subsequent exacerbation in obstructive lung disease: an historical population based cohort study

B M Roede,[1,2] P Bresser,[3] P J E Bindels,[2] A Kok,[4] M Prins,[1,4] G ter Riet,[2,5] R B Geskus,[6] R M C Herings,[7] J M Prins[1]

- 19 000 exacerbations
- Ttt corticoïdes ± antibiotiques
  - Gr Corticoïdes vs Gr Corticoïdes + ATB
- **Délai médian pour une 2ème exacerbation :** 418 vs 321 pour les groupes Corticoïdes + ATB vs Corticoïdes seul.
- **Délai médian entre 2ème et 3ème exacerbation :** 240 vs 127 jours

Thorax 2008;63:968–973

Etudes cliniques

Antibiotic treatment is associated with reduced risk of a subsequent exacerbation in obstructive lung disease: an historical population based cohort study

B M Roede,[1,2] P Bresser,[3] P J E Bindels,[2] A Kok,[4] M Prins,[1,4] G ter Riet,[2,5] R B Geskus,[6] R M C Herings,[7] J M Prins[1]

Table 2 Hazard ratios of determinants of developing a next exacerbation after oral corticosteroids with antibiotics—compared with oral corticosteroids only—treatment in a multivariable Cox model

	HR of new exacerbation	99% CI for hazard ratio	
		Lower	Upper
Antibiotics added to treatment with oral corticosteroids			
0–3 months following treatment	0.62	0.60	0.65
3–6 months following treatment	0.68	0.65	0.73
6–12 months following treatment	1.03	0.96	1.12
>12 months following treatment	1.31	1.18	1.45
Exposure to antibiotics after previous exacerbation	0.82	0.78	0.87
Female sex	0.95	0.91	1.00
Inhaled corticosteroids as maintenance medication	0.91	0.84	0.98
Co-medication cardiovascular	1.16	1.10	1.23
Co-medication for diabetes	1.05	0.98	1.12
Hospitalisation* for COPD†	1.45	1.35	1.57
Hospitalisation for pneumonia	1.19	1.05	1.34

The variables "age" and "number of respiratory drugs dispensings in 2003" were included in the Cox model, but were not fitted linearly, and therefore HR are not presented.
*Once or more in previous 2 years. †Diagnosis: chronic bronchitis, emphysema or COPD.
COPD, chronic obstructive pulmonary disease; HR, hazard ratio.

Thorax 2008;63:968–973

Reduced risk of next exacerbation and mortality associated with antibiotic use in COPD

B.M. Roede*,#, P. Bresser¶, J.M. Prins*, F. Schellevis+,§, T.J.M. Verheij^ and P.J.E. Bindels#

842 patients plus d'une exacerbation

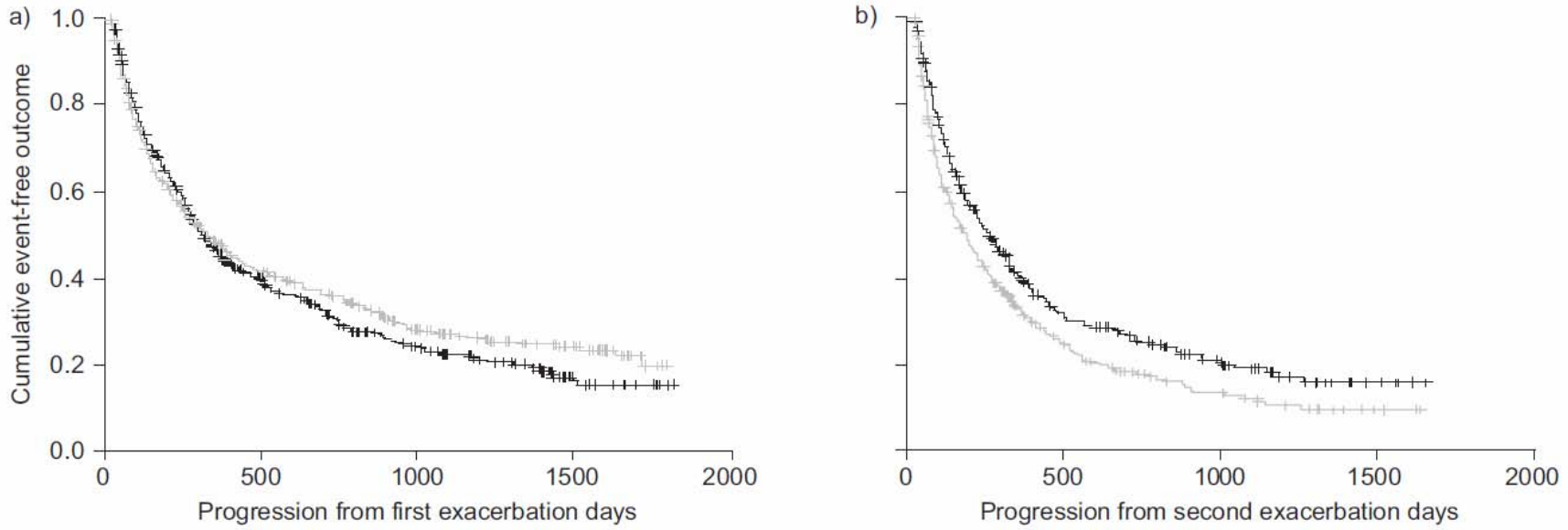


FIGURE 2. Kaplan–Meier estimates of the fraction of patients free of a) a second or b) a third exacerbation, stratified according to treatment type (grey line: oral corticosteroids only; black line: oral corticosteroids and antibiotics). Calculated median difference between both treatment groups is 19 days, p=0.31, by log-rank (a). Calculated median difference between both treatment groups is 69 days, p<0.01, by log-rank (b). a) n=842; b) n=595.

Eur Respir J 2009; 33: 282–288

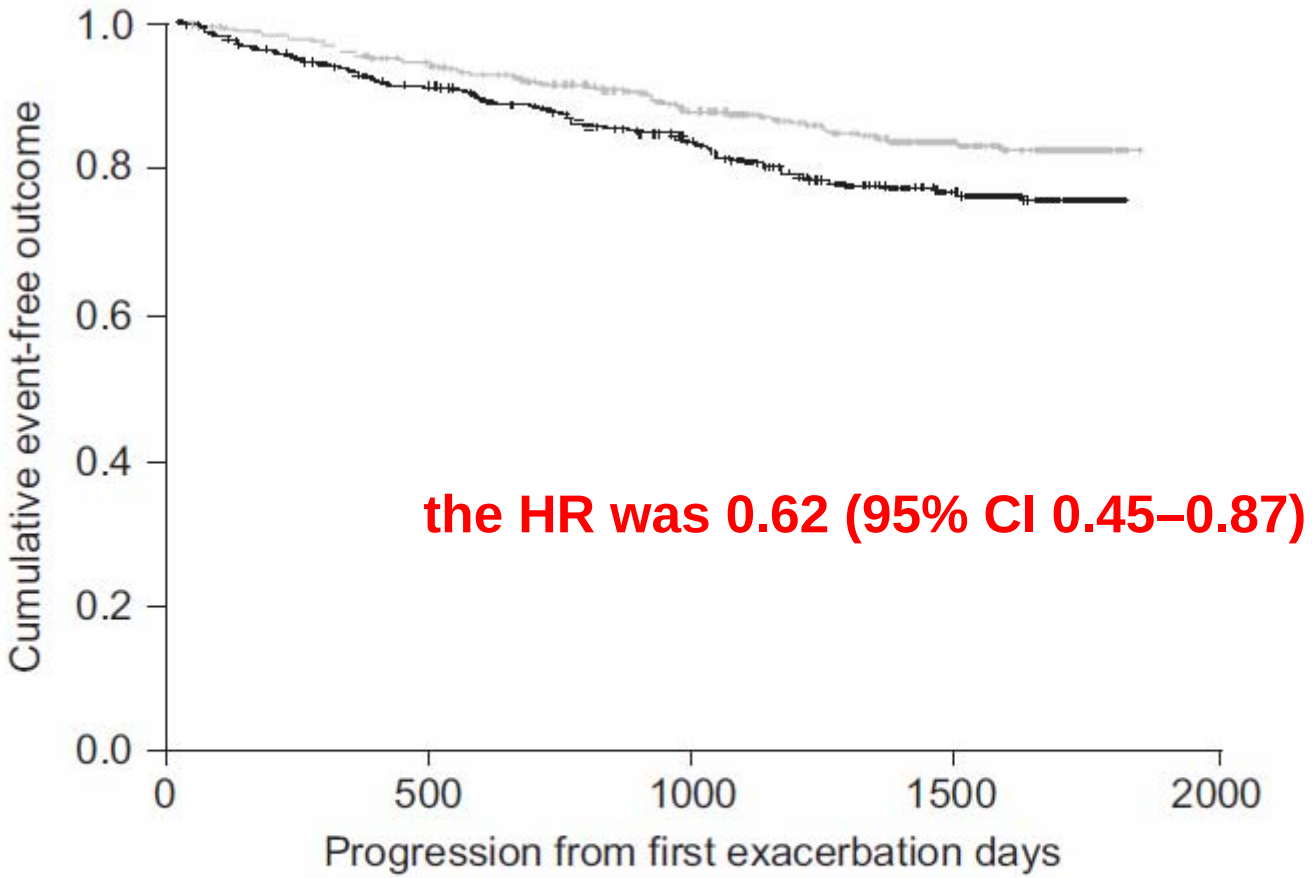


FIGURE 3. Kaplan–Meier estimates of the cumulative survival stratified according to treatment type (black line: oral corticosteroids only; grey line: oral corticosteroids and antibiotics). Difference between both treatment groups p=0.02, by log-rank. n=842.

Antibiotic Treatment of Exacerbations of COPD*: A Randomized, Controlled Trial Comparing Procalcitonin-Guidance With Standard Therapy

Daiana Stolz, Mirjam Christ-Crain, Roland Bingisser, Jörg Leuppi, David Miedinger, Christian Müller, Peter Huber, Beat Müller and Michael Tamm

Chest 2007;131;9-19

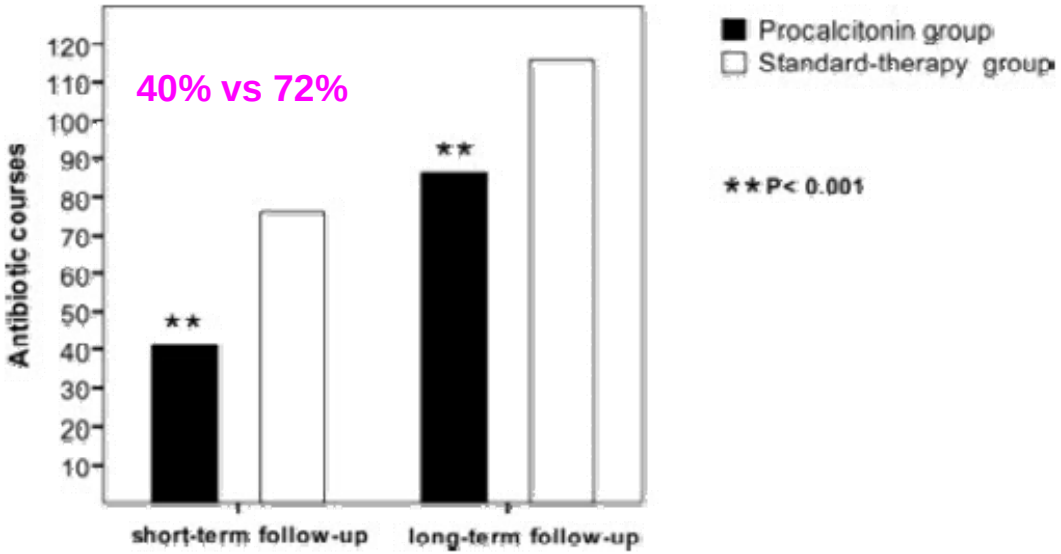


FIGURE 3. Total number of antibiotic courses at short-term and long-term follow-up in 102 patients in the procalcitonin-guided group and 106 patients in the standard-therapy group.

Stolz D Chest 2007;131:9-189

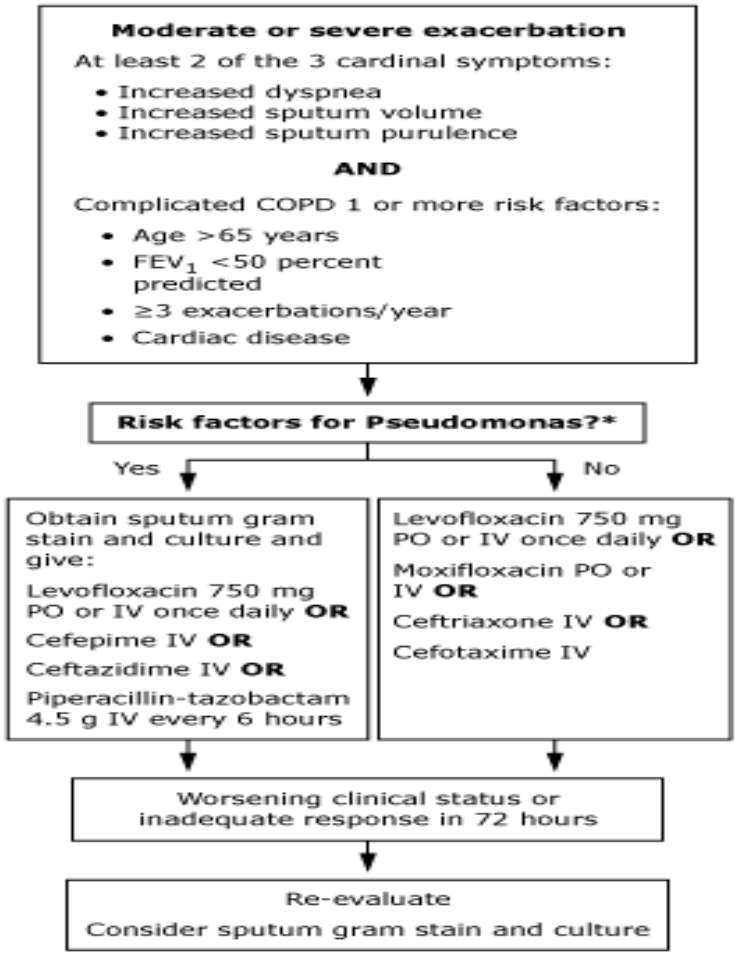
Table 2—*Clinical Outcome Parameters at Short-term Follow-up in Both Randomized Groups**

Outcomes	Procalcitonin Group (n = 102)	Standard Group (n = 106)	p Value
Clinical success	84 (82.4)	89 (83.9)	0.853
Hospital stay < 24 h	22 (21.6)	24 (22.6)	0.852
Length of hospital stay, d	9 (1–15)	10 (1–15)	0.960
Need for ICU stay	8 (7.8)	11 (10.4)	0.526
Duration of ICU stay, d	3.3 ± 2.7	3.7 ± 2.1	0.351
Steroid use (%)	89 (87.3)	93 (87.7)	0.916
Steroid dose, mg	250 (119–400)	280 (183–421)	0.303
ECOPD rate within 6 mo	44 (43.1)	43 (40.1)	0.607
Hospitalization rate for ECOPD within 6 mo	18 (17.7)	22 (20.8)	0.507
Death of any cause within 6 mo	5 (4.9)	9 (8.5)	0.409

*Values are given as No. (%), median (IQR), or mean ± SD, unless otherwise indicated.

Conclusions: ***Procalcitonin guidance for exacerbations of COPD offers a sustained advantage*** **over standard therapy in reducing antibiotic use for up to 6 months with a number-needed-to-treat of 3.**

Antibiotic treatment of acute exacerbations of COPD in hospitalized patients



* Pseudomonas risk factors:
- Frequent administration of antibiotics (4 or more courses over the past year)
- Recent hospitalization (2 or more days' duration in the past 90 days)
- Isolation of Pseudomonas during a previous hospitalization
- Severe underlying COPD (FEV1 <50 percent predicted)

Antibiotique ou pas antibiotique lors des exacerbations de BPCO?

Antibiotique

Autres questions

- Choix de l'antibiotique?
- Durée ?
- Antiviraux?
- Prévention
  - Vaccin
  - antibiotiques