



# Treatment of eosinophilic and non-eosinophilic exacerbations of COPD

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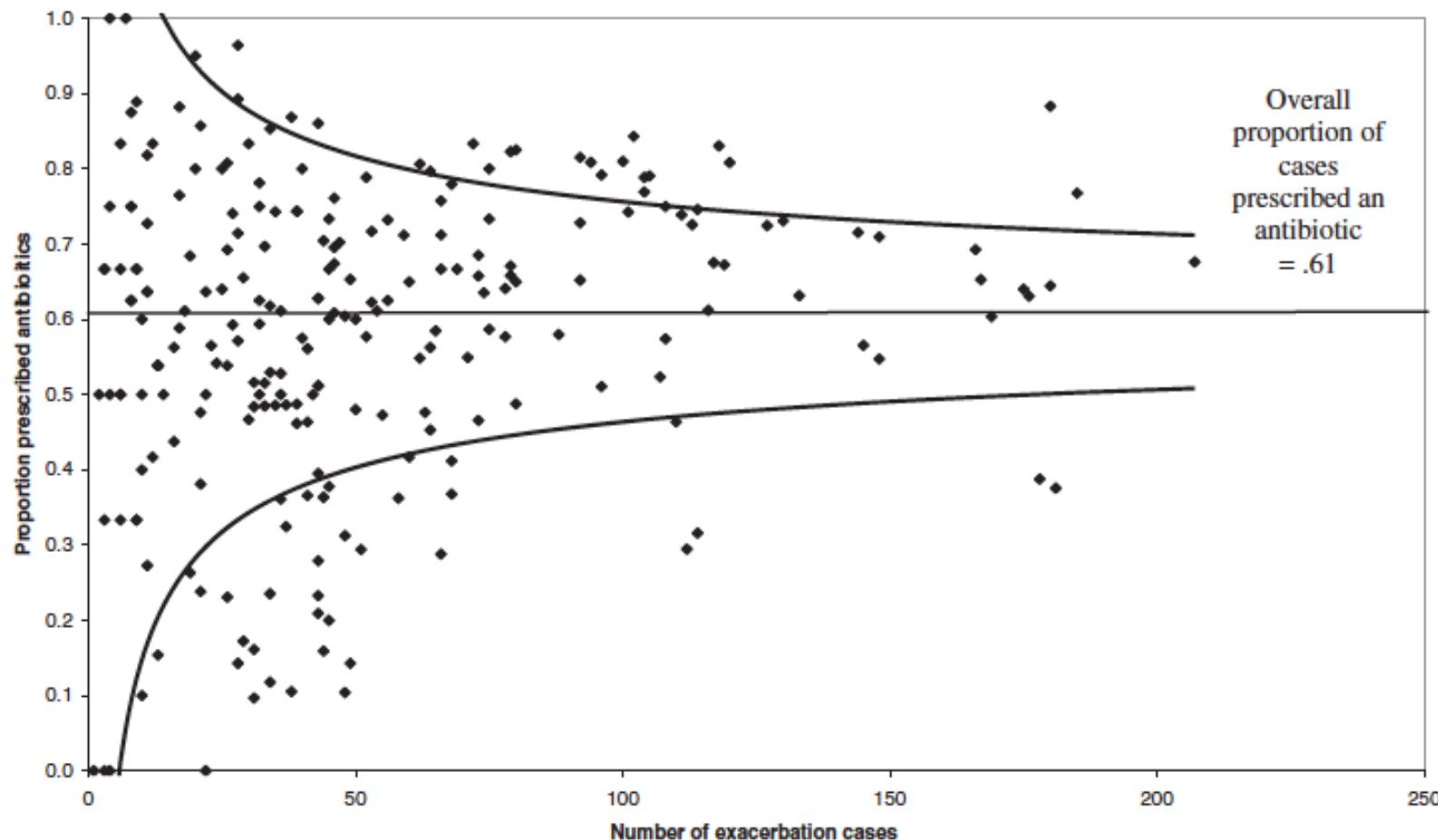


## **Conflicts of interest:**

- Marc Miravitles has received speaker fees from AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, Menarini, Rovi, Bial, Zambon, CSL Behring, Grifols and Novartis.
- Consulting fees from AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Bial, Gebro Pharma, CSL Behring, Laboratorios Esteve, Mereo Biopharma, Verona Pharma, TEVA, pH Pharma, Novartis and Grifols.
- Research grants from GlaxoSmithKline and Grifols.

# Variability of antibiotic prescribing in patients with chronic obstructive pulmonary disease exacerbations: a cohort study

Rachael Boggan<sup>1,2</sup>, Richard Hubbard<sup>3</sup>, Liam Smeeth<sup>4</sup>, Martin Gulliford<sup>5</sup>, Jackie Cassell<sup>6</sup>, Susan Eaton<sup>1</sup>, Munir Pirmohamed<sup>7</sup> and Tjeerd-Pieter van Staa<sup>1,2,4\*</sup>



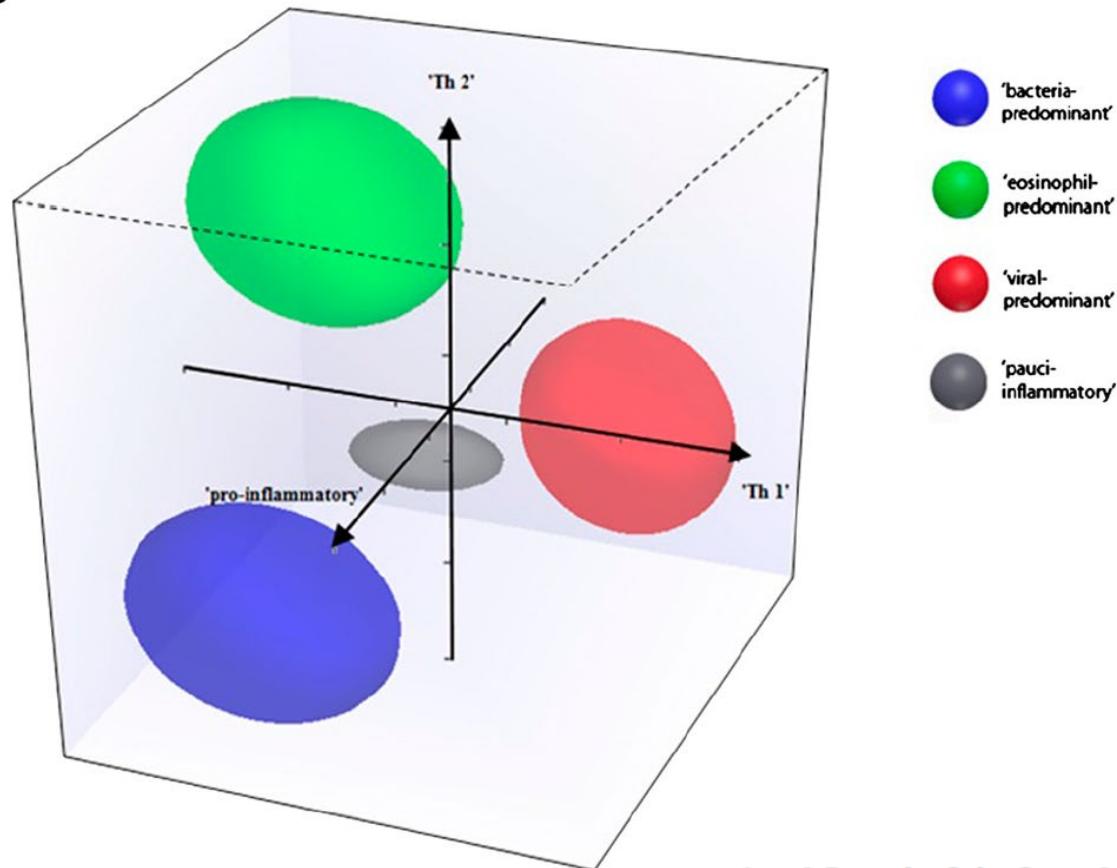


# Acute Exacerbations of Chronic Obstructive Pulmonary Disease

## Identification of Biologic Clusters and Their Biomarkers

Mona Bafadhel<sup>1,2</sup>, Susan McKenna<sup>1</sup>, Sarah Terry<sup>1</sup>, Vijay Mistry<sup>1,2</sup>, Carlene Reid<sup>1</sup>, Pranabashis Haldar<sup>2</sup>, Margaret McCormick<sup>3</sup>, Koirobi Haldar<sup>2</sup>, Tatiana Kebadze<sup>4</sup>, Annelyse Duvoix<sup>5</sup>, Kerstin Lindblad<sup>6</sup>, Hemu Patel<sup>7</sup>, Paul Rugman<sup>3</sup>, Paul Dodson<sup>3</sup>, Martin Jenkins<sup>3</sup>, Michael Saunders<sup>3</sup>, Paul Newbold<sup>3</sup>, Ruth H. Green<sup>1</sup>, Per Venge<sup>6</sup>, David A. Lomas<sup>5</sup>, Michael R. Barer<sup>2,7</sup>, Sebastian L. Johnston<sup>4</sup>, Ian D. Pavord<sup>1</sup>, and Christopher E. Brightling<sup>1,2</sup>

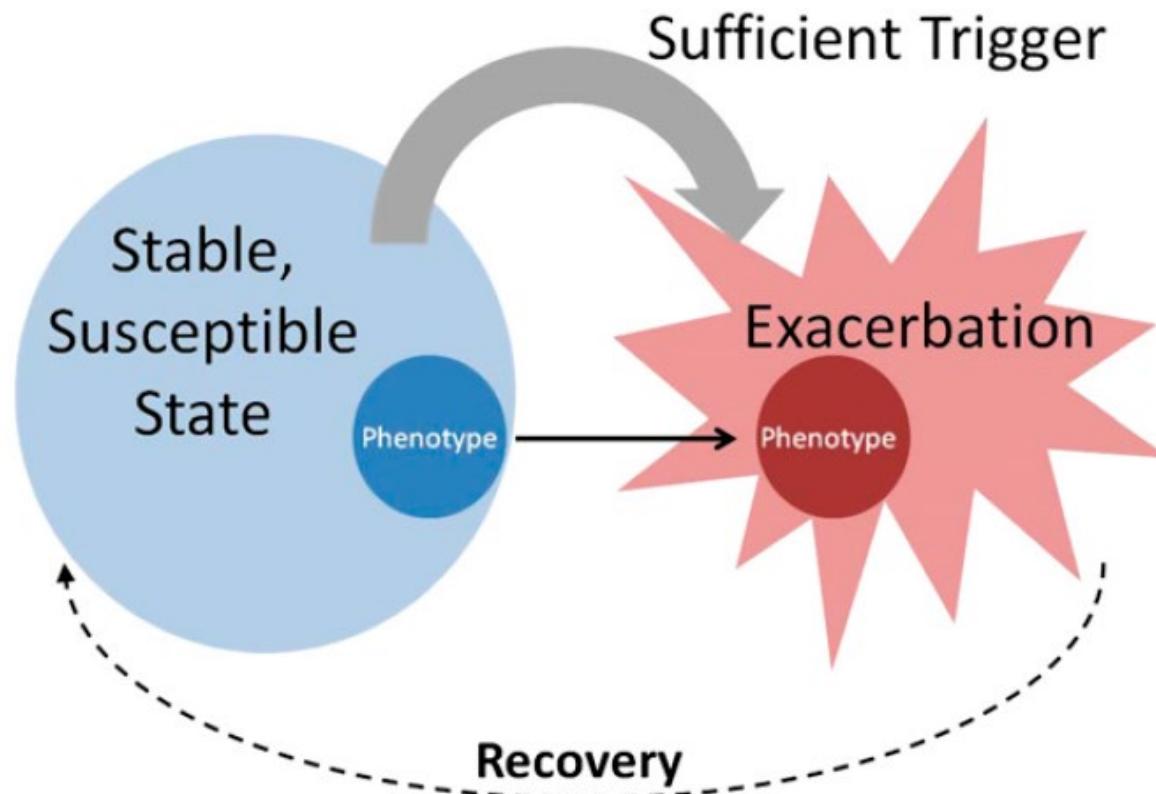
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# Exacerbation Phenotyping in Chronic Obstructive Pulmonary Disease

JOHN R. HURST, PH.D.

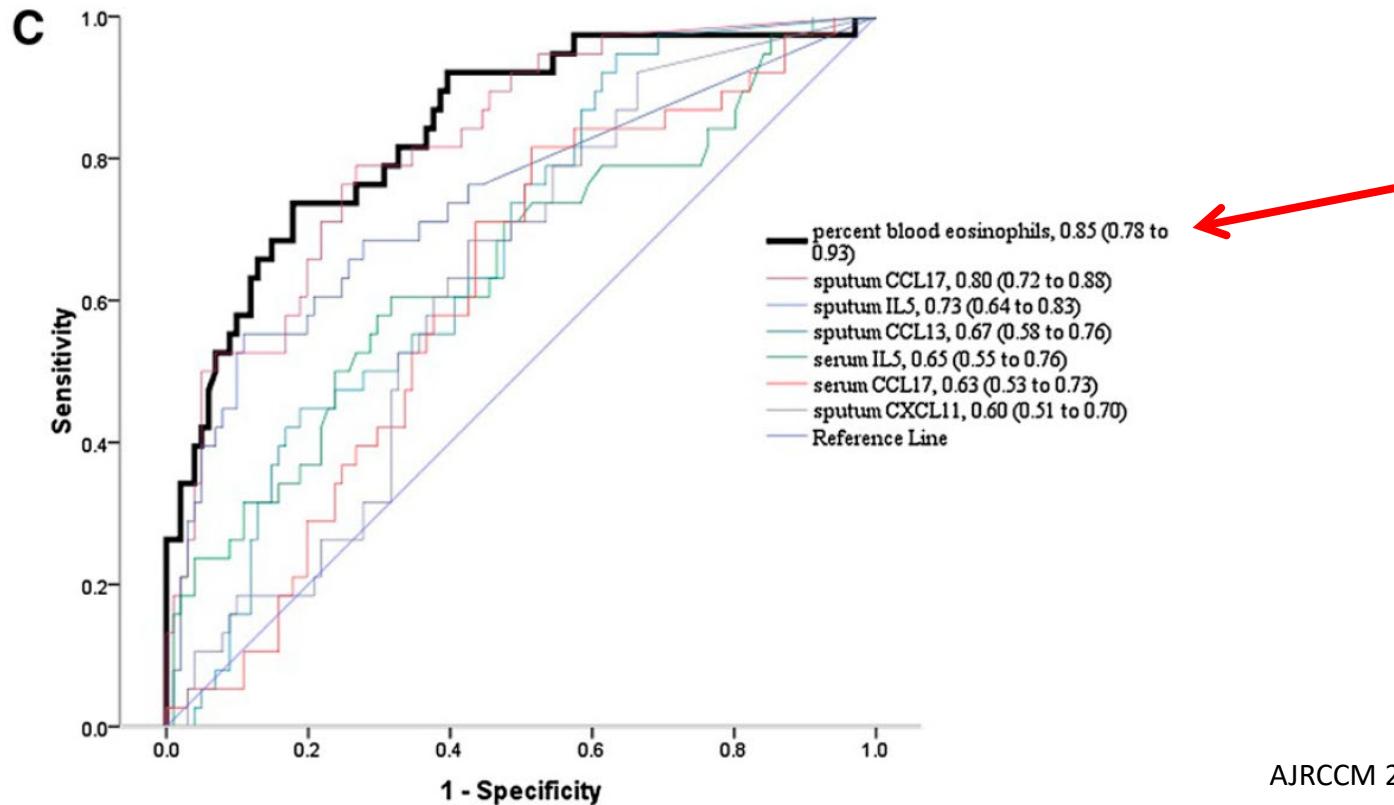




# Acute Exacerbations of Chronic Obstructive Pulmonary Disease

## Identification of Biologic Clusters and Their Biomarkers

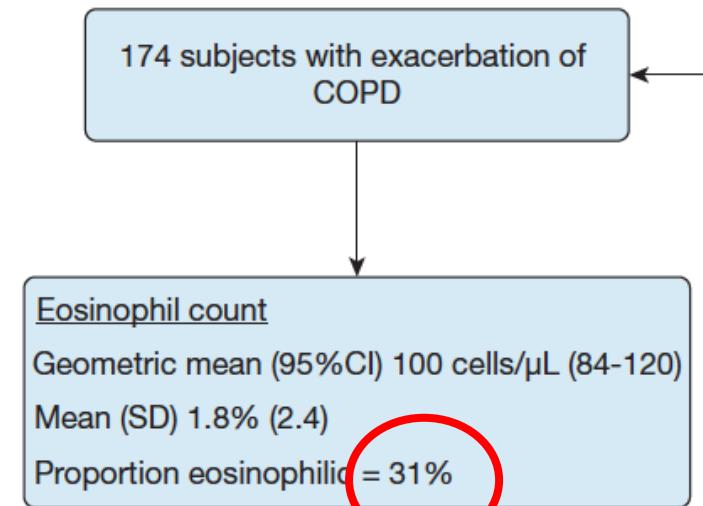
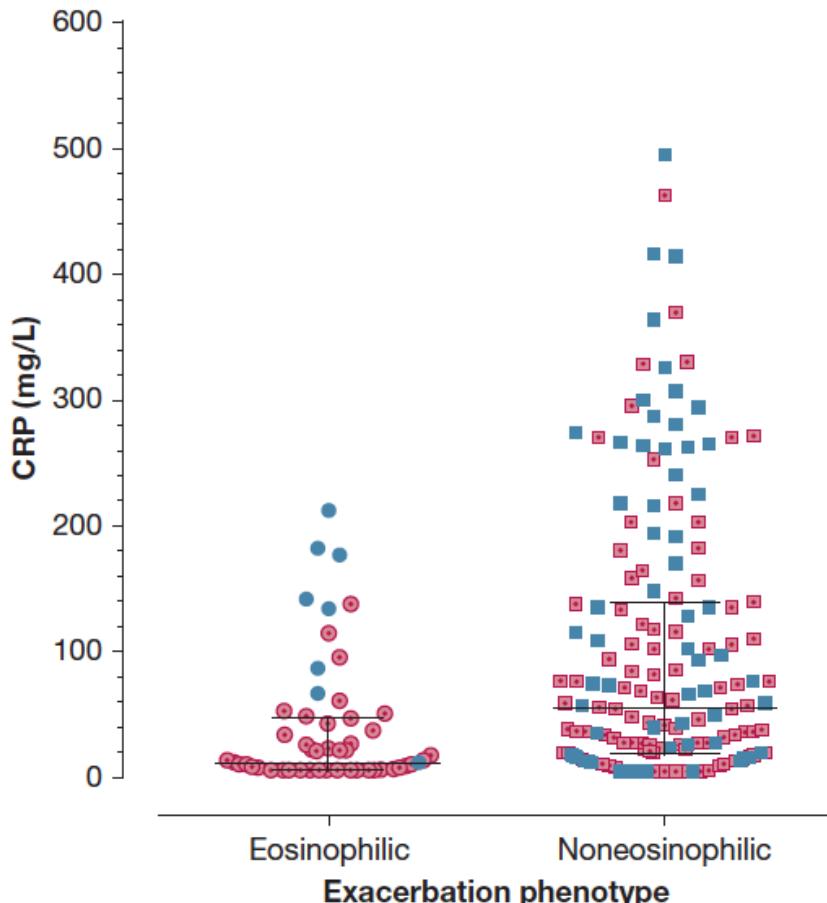
Mona Bafadhel<sup>1,2</sup>, Susan McKenna<sup>1</sup>, Sarah Terry<sup>1</sup>, Vijay Mistry<sup>1,2</sup>, Carlene Reid<sup>1</sup>, Pranabashis Haldar<sup>2</sup>, Margaret McCormick<sup>3</sup>, Koirobi Haldar<sup>2</sup>, Tatiana Kebadze<sup>4</sup>, Annelyse Duvoix<sup>5</sup>, Kerstin Lindblad<sup>6</sup>, Hemu Patel<sup>7</sup>, Paul Rugman<sup>3</sup>, Paul Dodson<sup>3</sup>, Martin Jenkins<sup>3</sup>, Michael Saunders<sup>3</sup>, Paul Newbold<sup>3</sup>, Ruth H. Green<sup>1</sup>, Per Venge<sup>6</sup>, David A. Lomas<sup>5</sup>, Michael R. Barer<sup>2,7</sup>, Sebastian L. Johnston<sup>4</sup>, Ian D. Pavord<sup>1</sup>, and Christopher E. Brightling<sup>1,2</sup>

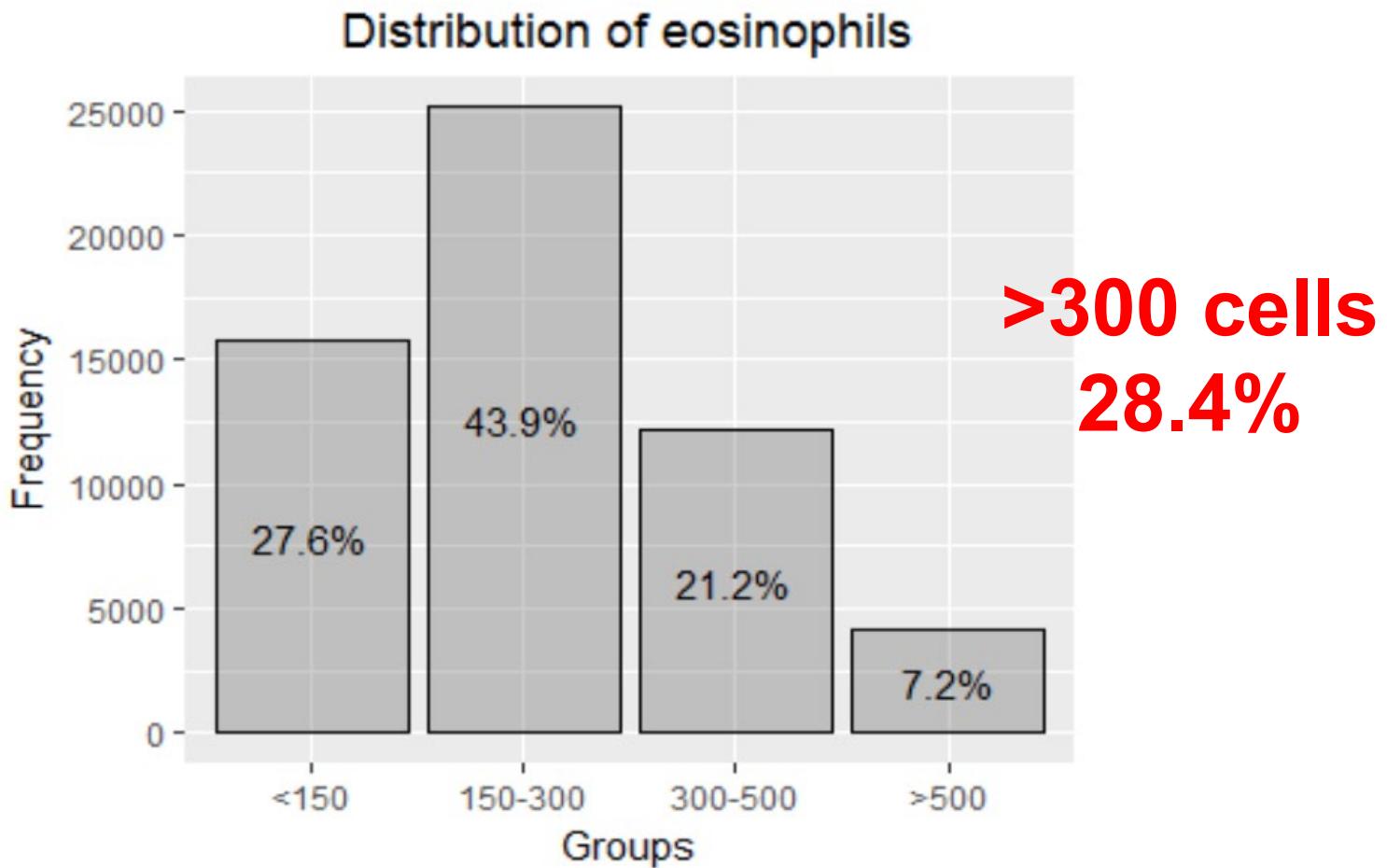




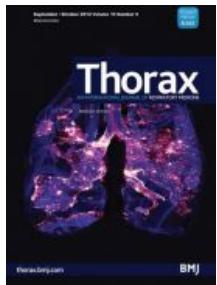
# Blood Eosinophils and Outcomes in Severe Hospitalized Exacerbations of COPD

Mona Bafadhel, PhD; Neil J. Greening, PhD; Theresa C. Harvey-Dunstan, PhD; Johanna E. A. Williams, PhD; Michael D. Morgan, PhD; Christopher E. Brightling, PhD; Syed F. Hussain, MD; Ian D. Pavord, MD; Sally J. Singh, PhD; and Michael C. Steiner, PhD



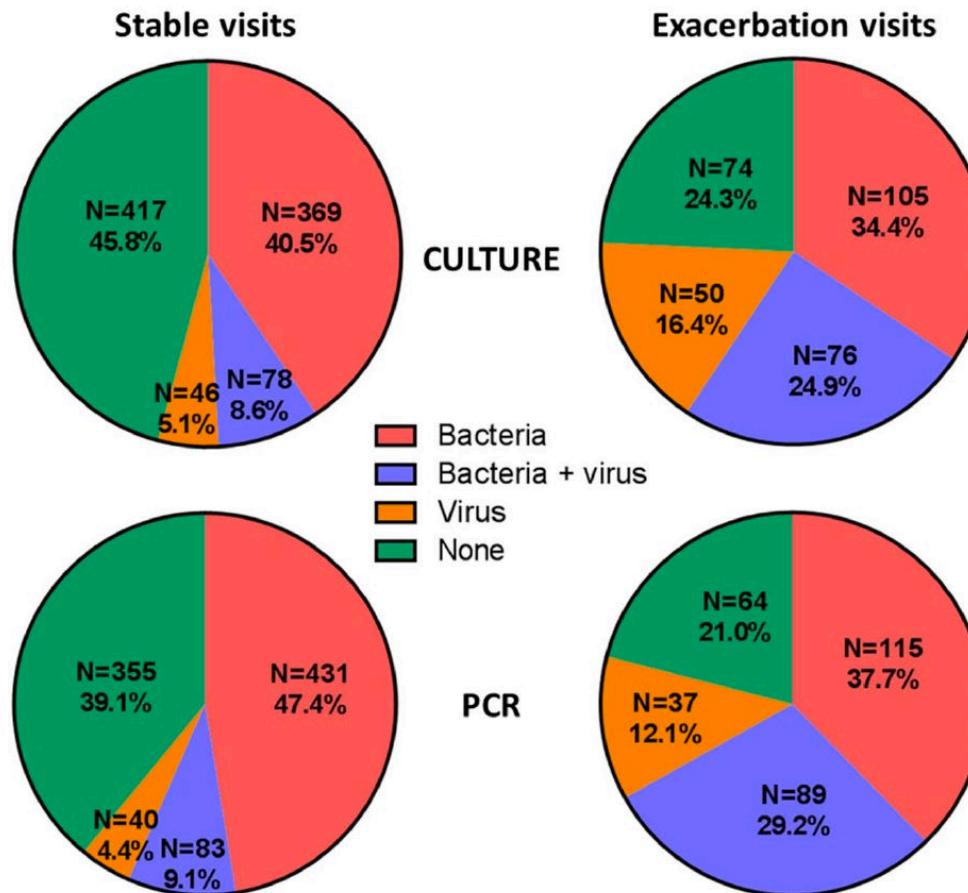


Data based on 57,209 COPD patients  
Submitted for publication



# A prospective, observational cohort study of the seasonal dynamics of airway pathogens in the aetiology of exacerbations in COPD

Tom M A Wilkinson,<sup>1,2,3</sup> Emmanuel Aris,<sup>4</sup> Simon Bourne,<sup>1,5</sup> Stuart C Clarke,<sup>1,3</sup> Mathieu Peeters,<sup>4,6</sup> Thierry G Pascal,<sup>4</sup> Sonia Schoonbroodt,<sup>4</sup> Andrew C Tuck,<sup>7</sup> Viktoriya Kim,<sup>1,2</sup> Kristoffer Ostridge,<sup>1,2</sup> Karl J Staples,<sup>1,3</sup> Nicholas Williams,<sup>1,2</sup> Anthony Williams,<sup>3</sup> Stephen Wootton,<sup>8</sup> Jeanne-Marie Devaster,<sup>4</sup> on behalf of the AERIS Study Group





# Infections and Airway Inflammation in Chronic Obstructive Pulmonary Disease Severe Exacerbations

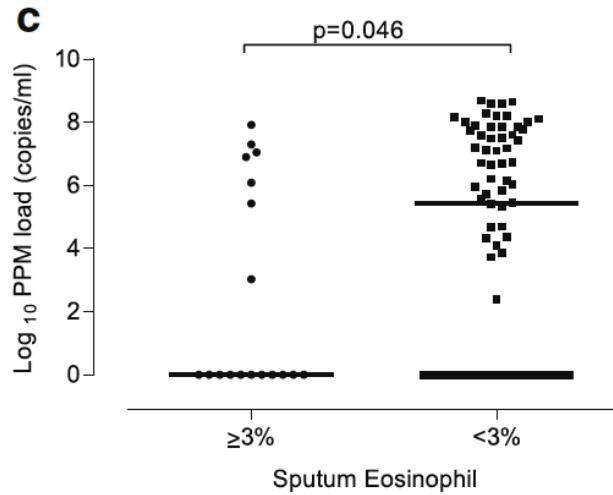
Alberto Papi, Cinzia Maria Bellettato, Fausto Braccioni, Micaela Romagnoli, Paolo Casolari, Gaetano Caramori, Leonardo M. Fabbri, and Sebastian L. Johnston

**Results:** Exacerbations were associated with impaired lung function ( $p < 0.01$ ) and increased sputum neutrophilia ( $p < 0.001$ ). Viral and/or bacterial infection was detected in 78% of exacerbations: viruses in 48.4% (6.2% when stable,  $p < 0.001$ ) and bacteria in 54.7% (37.5% when stable,  $p = 0.08$ ). Patients with infectious exacerbations (29.7% bacterial, 23.4% viral, 25% viral/bacterial coinfection) had longer hospitalizations ( $p < 0.02$ ) and greater impairment of several measures of lung function (all  $p < 0.05$ ) than those with noninfectious exacerbations.

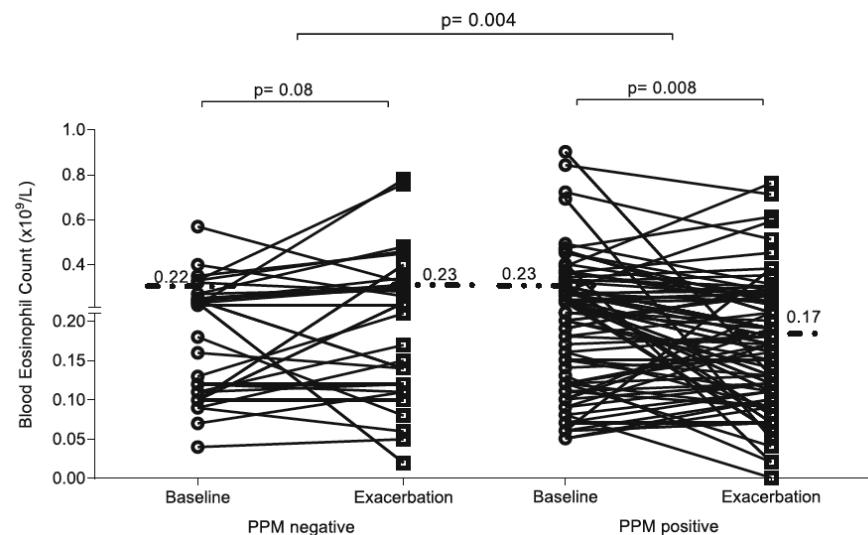
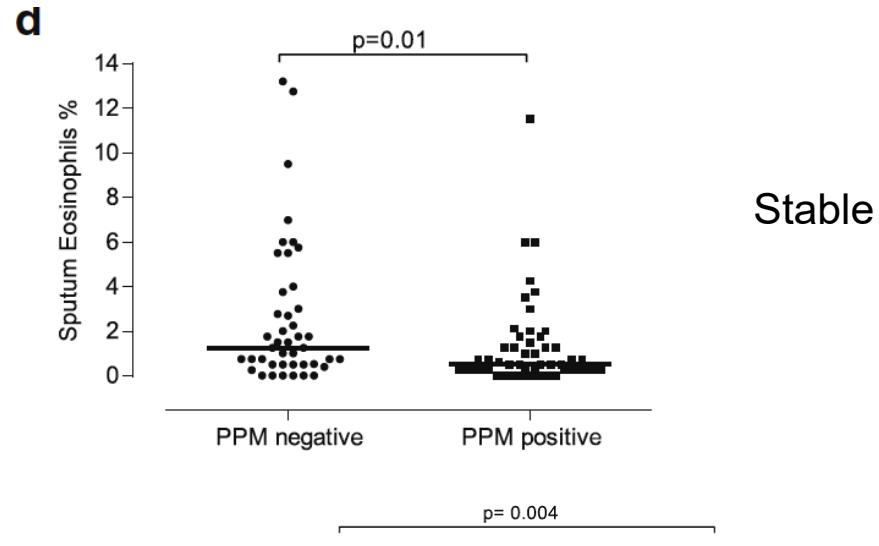


# Blood and sputum eosinophils in COPD; relationship with bacterial load

Umme Kolsum<sup>1\*</sup>, Gavin C. Donaldson<sup>2</sup>, Richa Singh<sup>2</sup>, Bethan L. Barker<sup>3</sup>, Vandana Gupta<sup>1</sup>, Leena George<sup>3</sup>, Adam J. Webb<sup>4</sup>, Sarah Thurston<sup>5</sup>, Anthony J Brookes<sup>4</sup>, Timothy D. McHugh<sup>5</sup>, Jadwiga A. Wedzicha<sup>2</sup>, Christopher E. Brightling<sup>3</sup> and Dave Singh<sup>1</sup>



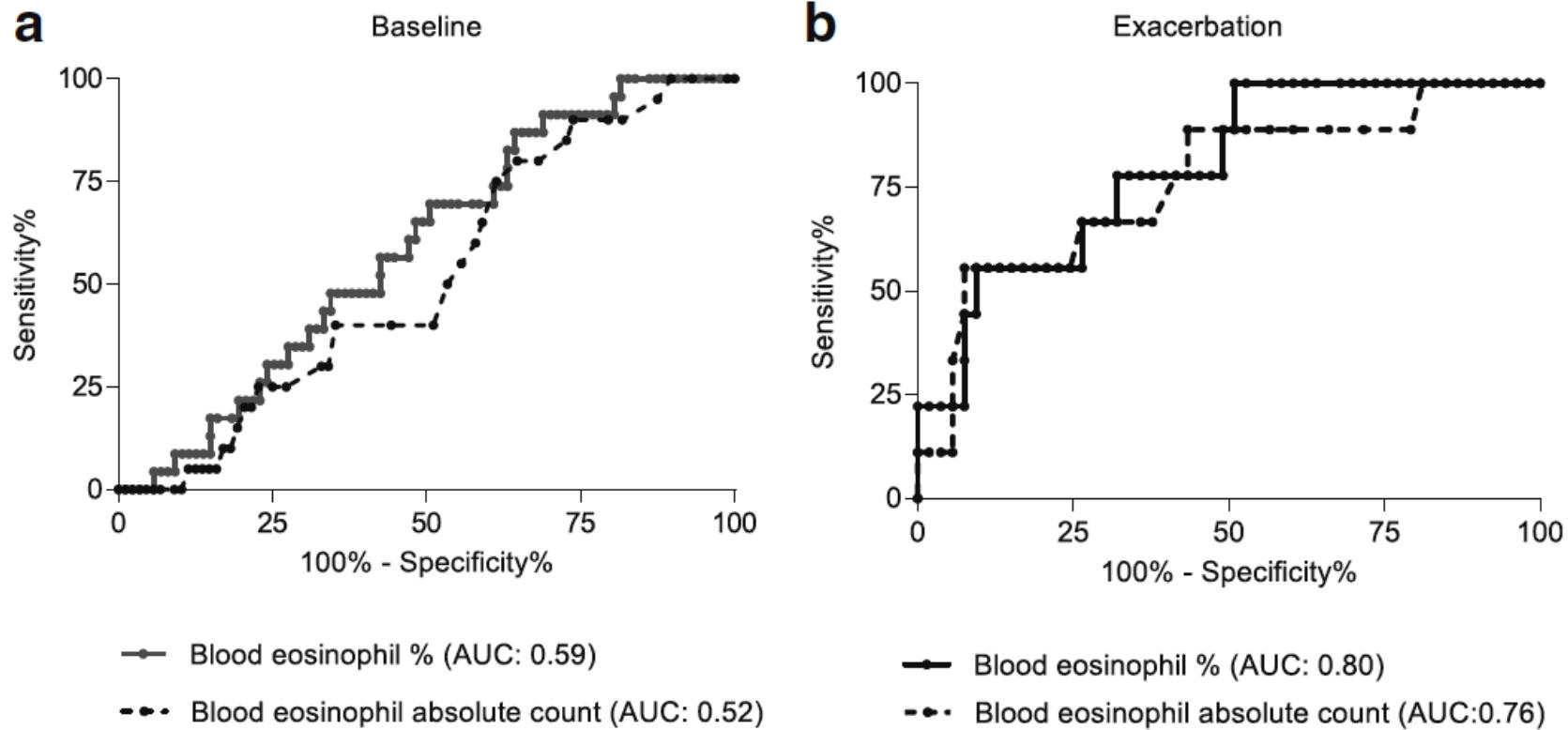
During exacerbation





# Blood and sputum eosinophils in COPD; relationship with bacterial load

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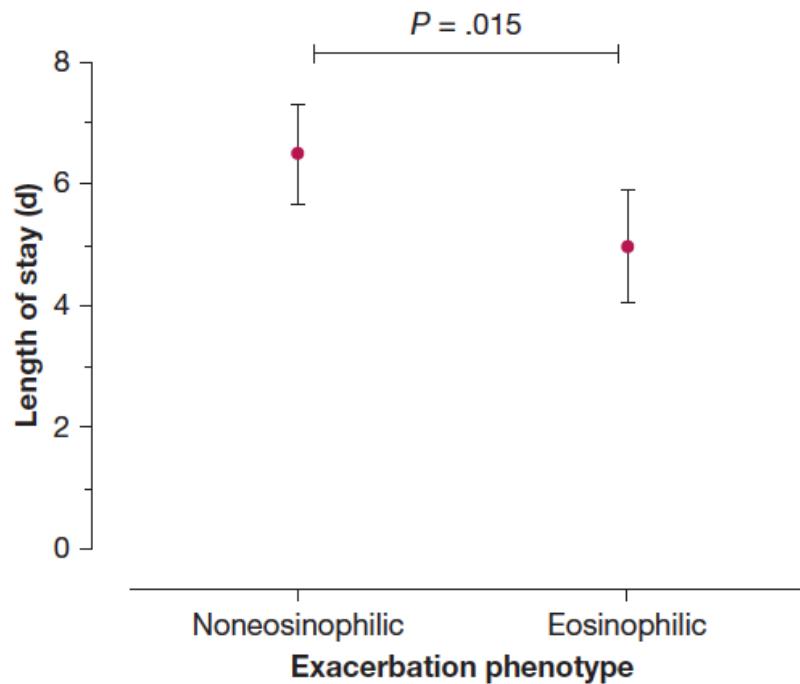




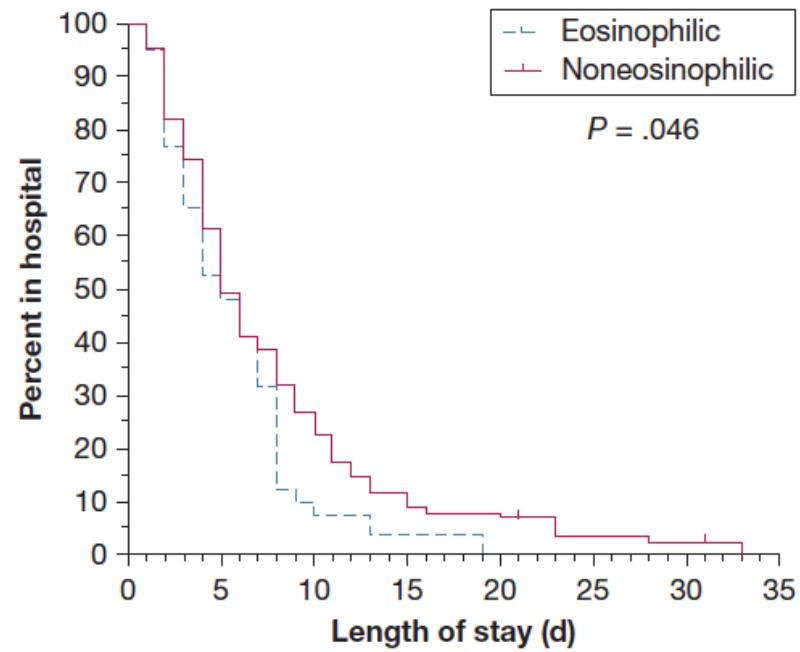
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A



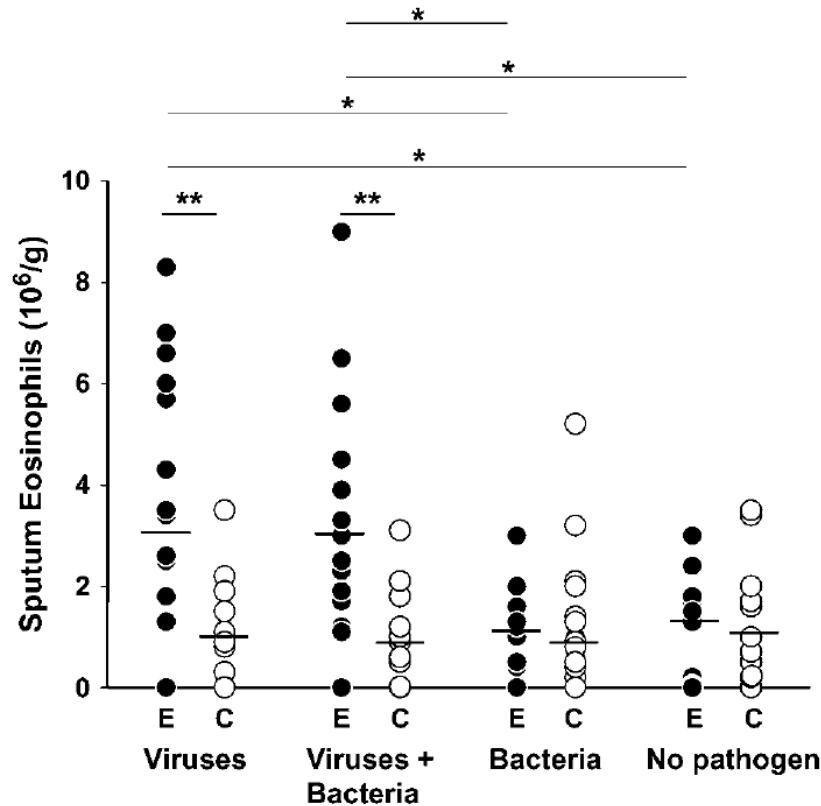
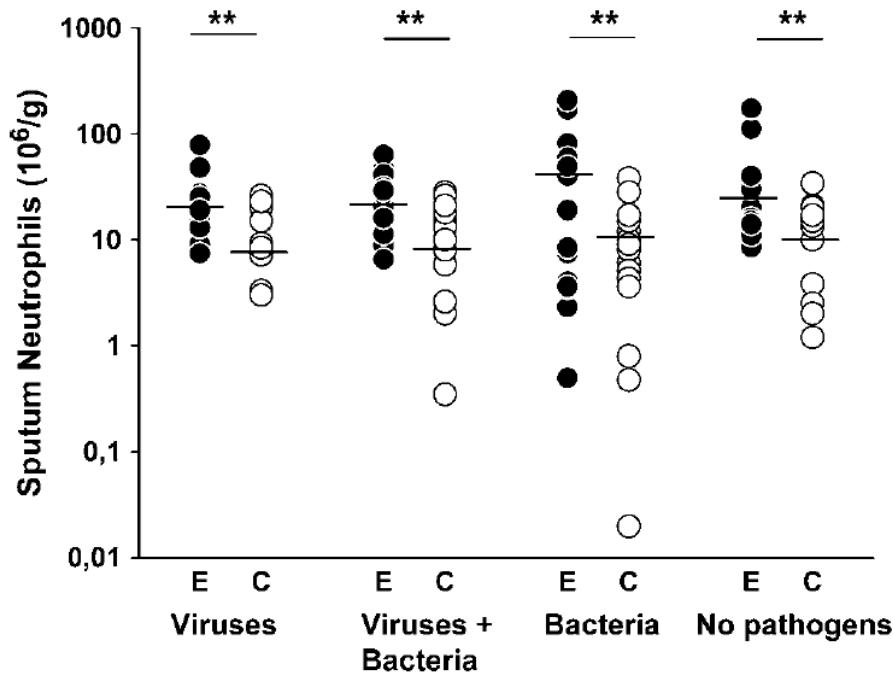
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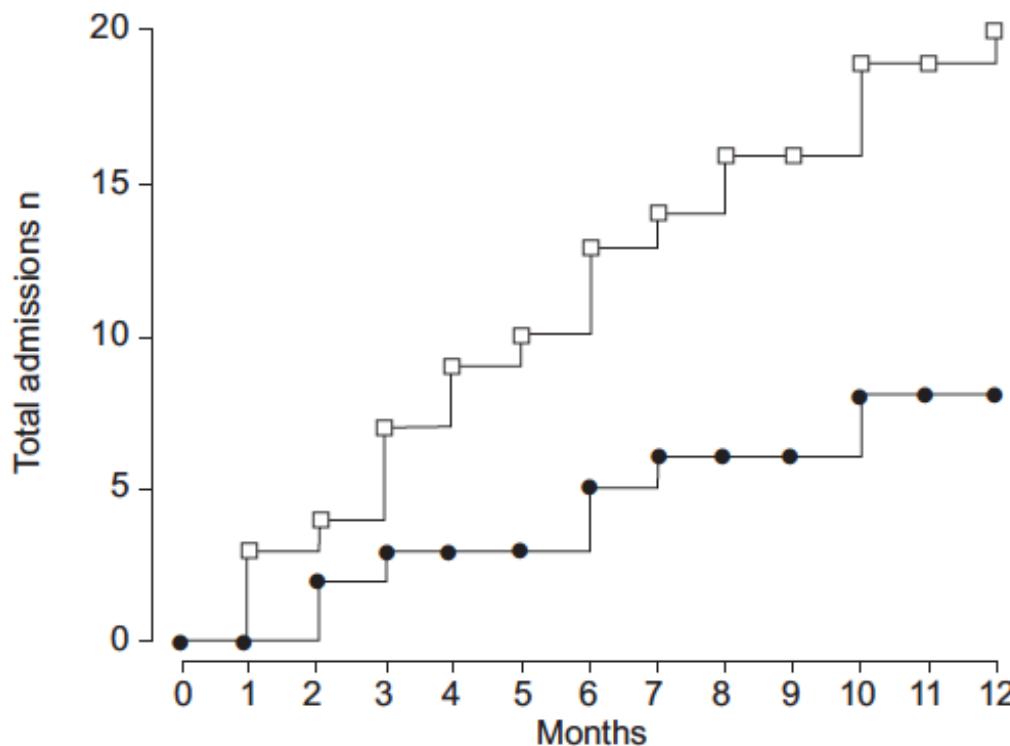
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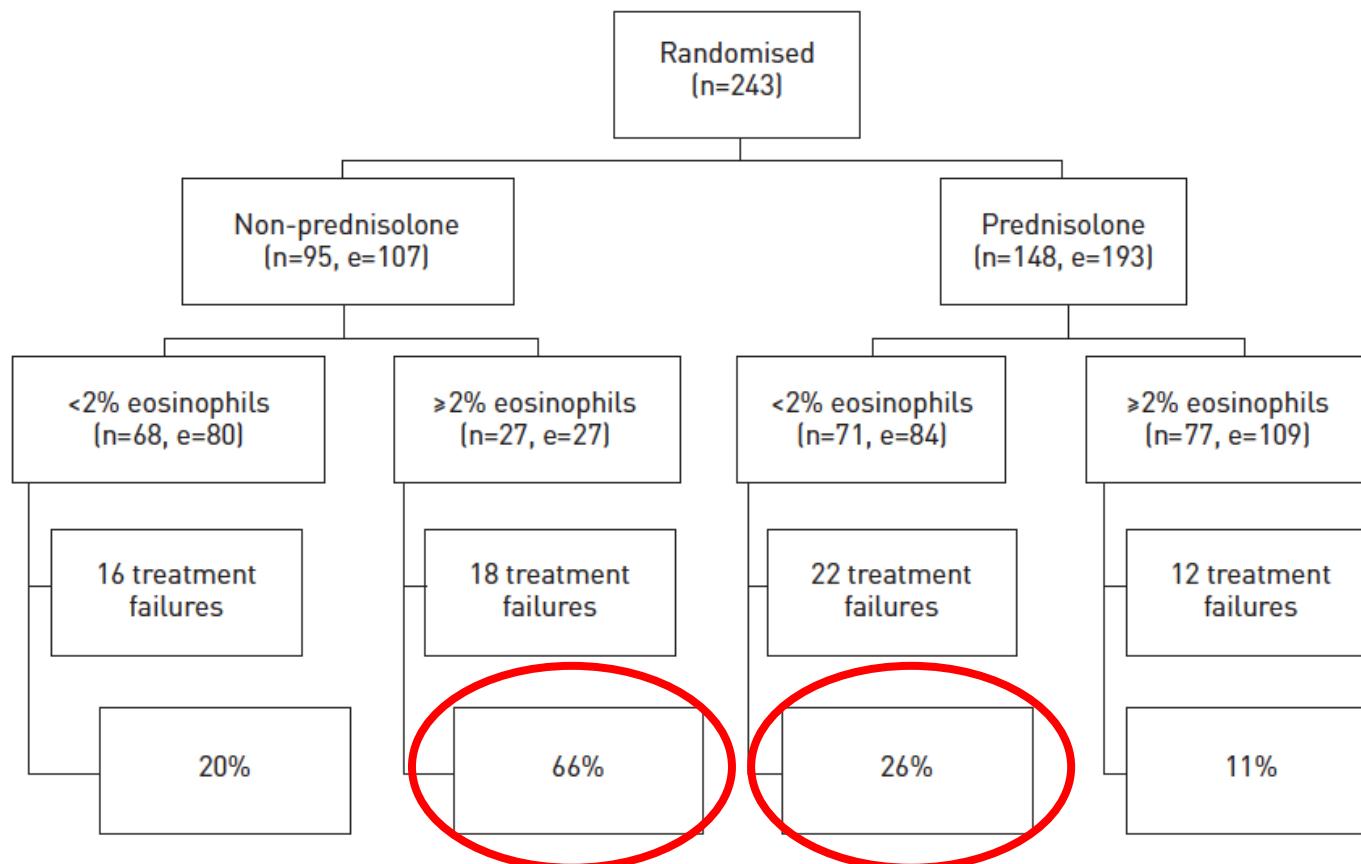
# Eosinophilic airway inflammation and exacerbations of COPD: a randomised controlled trial

R. Siva, R.H. Green, C.E. Brightling, M. Shelley, B. Hargadon, S. McKenna, W. Monteiro, M. Berry, D. Parker, A.J. Wardlaw and I.D. Pavord



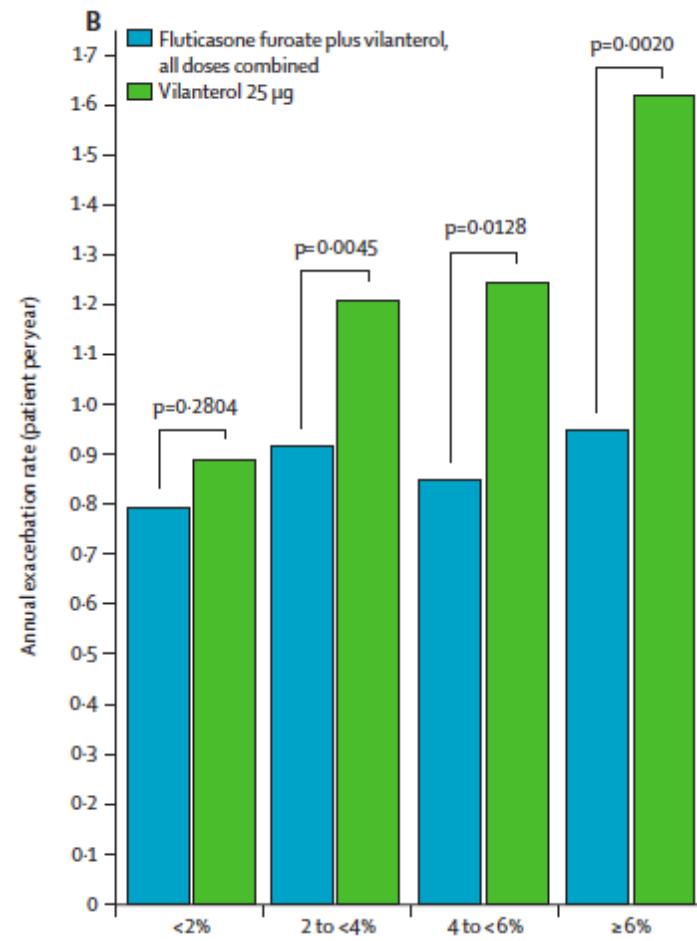
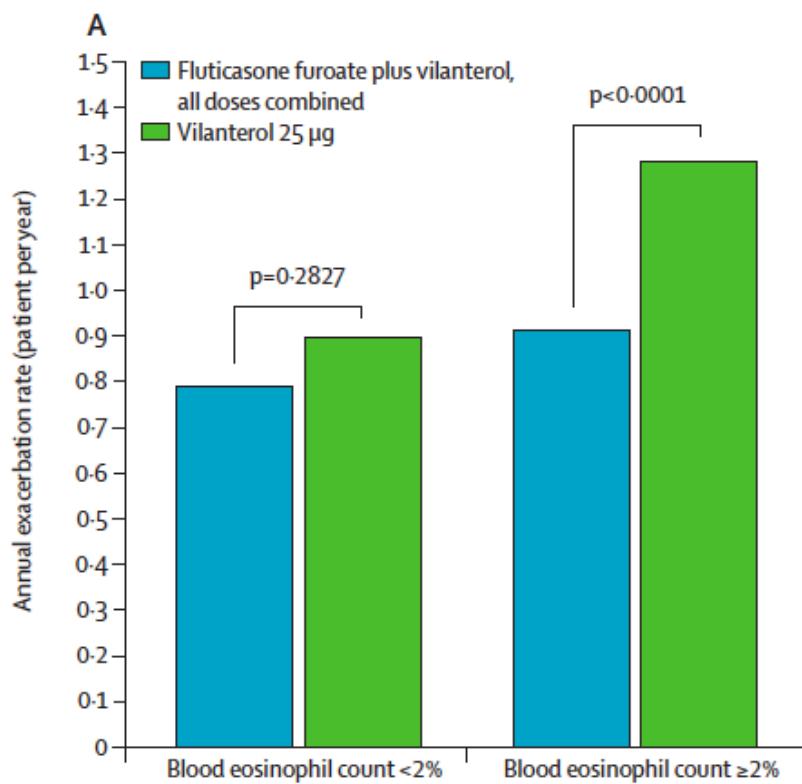
# Blood eosinophil guided prednisolone therapy for exacerbations of COPD: a further analysis

Mona Bafadhel<sup>1</sup>, Lisa Davies<sup>2</sup>, Peter M.A. Calverley<sup>2,3</sup>, Shawn D. Aaron<sup>4</sup>, Christopher E. Brightling<sup>5</sup> and Ian D. Pavord<sup>1</sup>



# Blood eosinophil counts, exacerbations, and response to the addition of inhaled fluticasone furoate to vilanterol in patients with chronic obstructive pulmonary disease: a secondary analysis of data from two parallel randomised controlled trials

Steven Pascoe, Nicholas Locantore, Mark T Dransfield, Neil C Barnes, Ian D Pavord

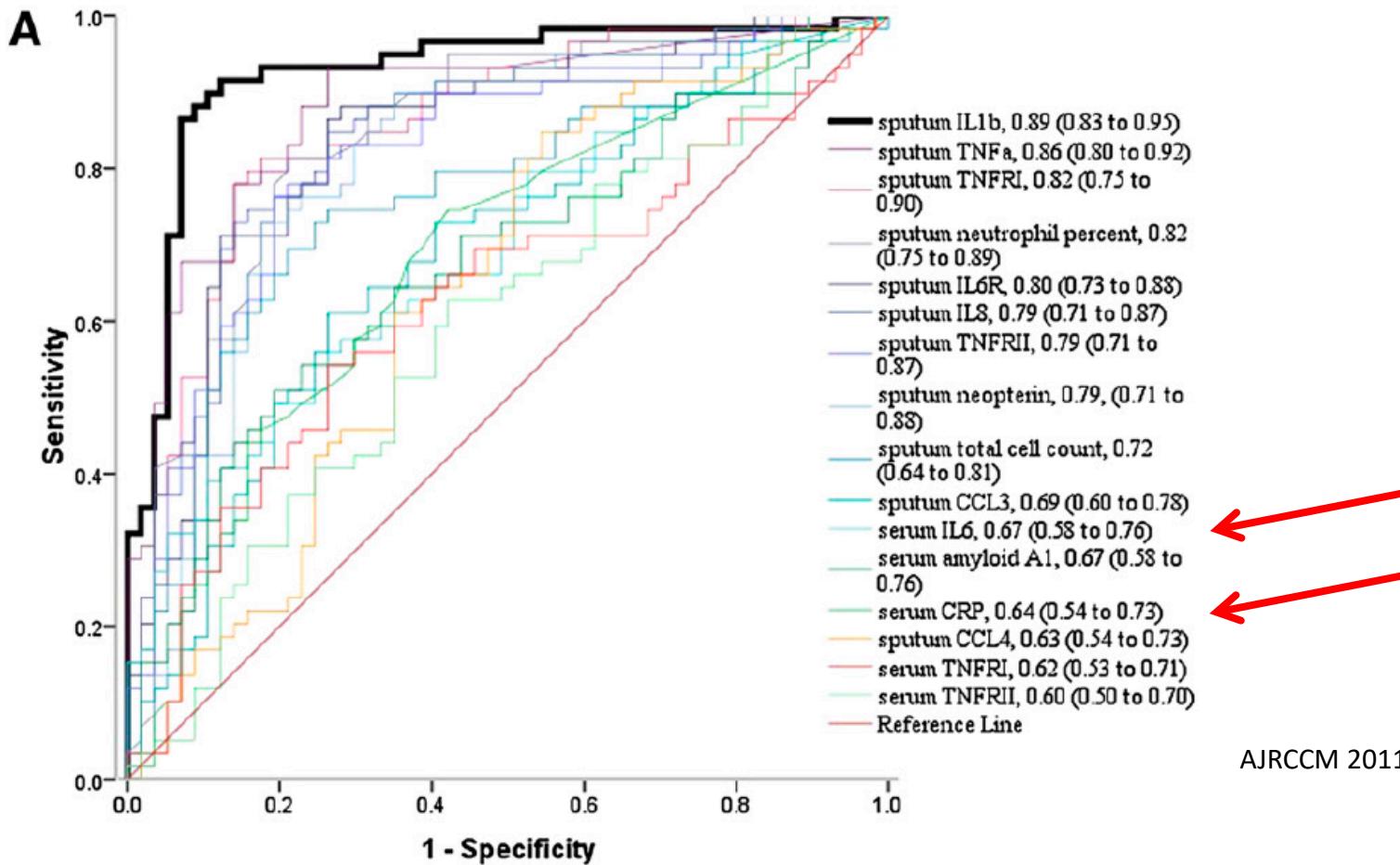




# Acute Exacerbations of Chronic Obstructive Pulmonary Disease

## Identification of Biologic Clusters and Their Biomarkers

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## **Non-purulent**



Clear

## **Purulent**



Yellow



Green

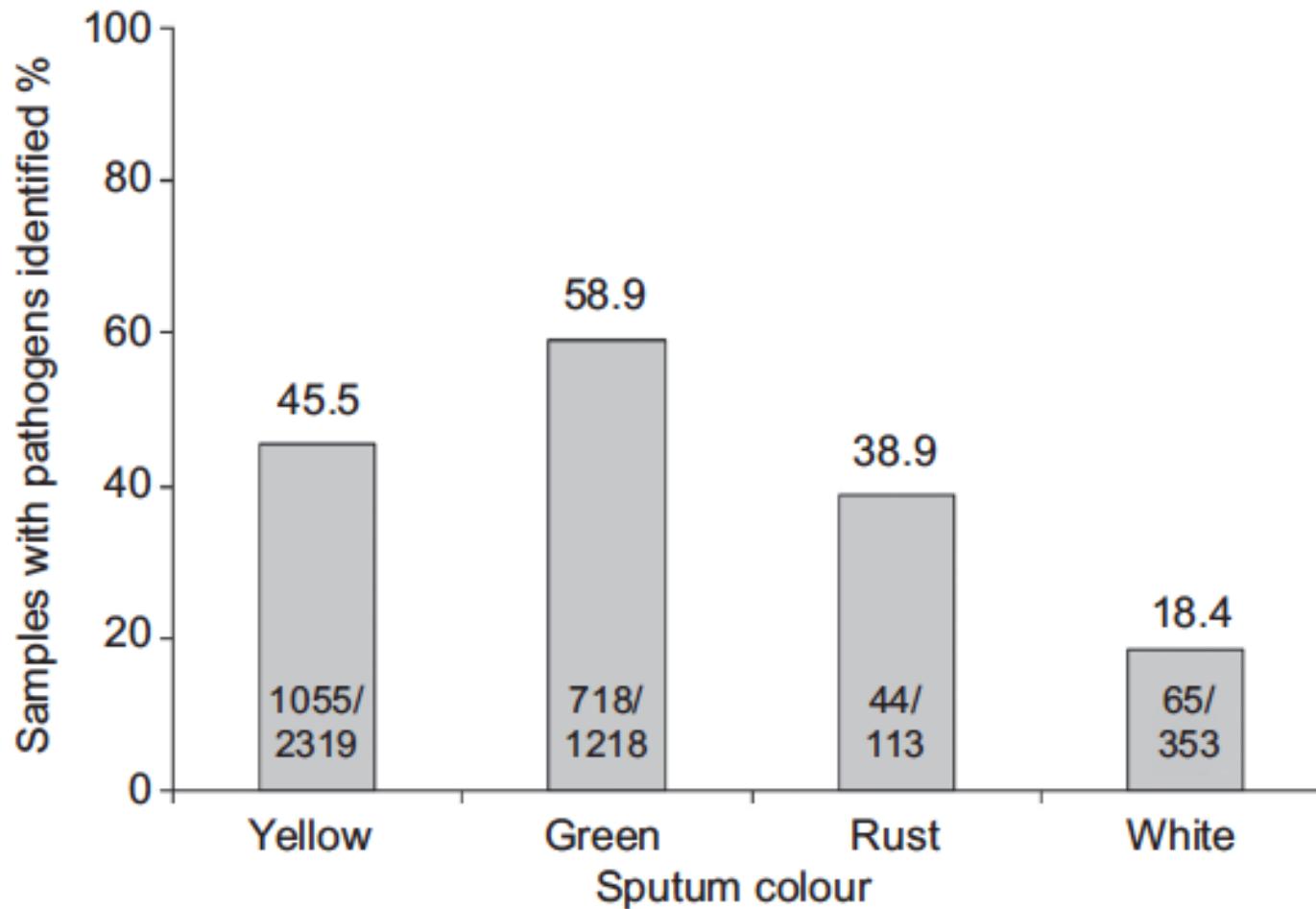


Rust

Courtesy of R. Wilson. Host Defence Unit.  
Royal Brompton Hospital London, UK

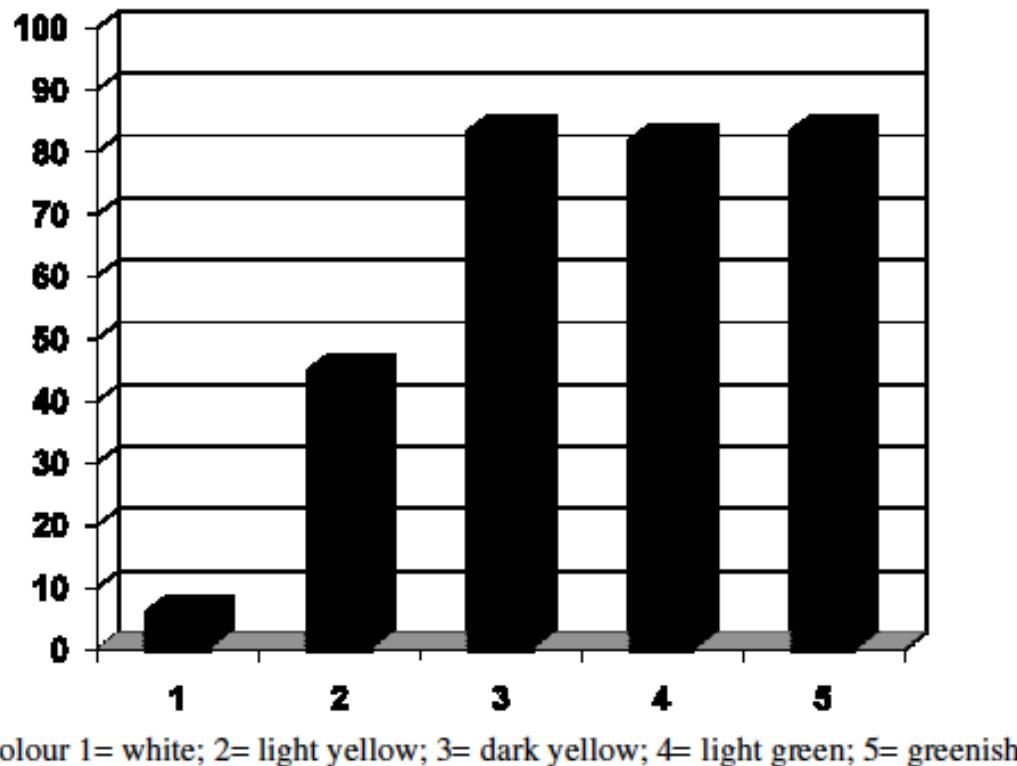
# Sputum colour and bacteria in chronic bronchitis exacerbations: a pooled analysis

Marc Miravitles\*, Frank Kruesmann#, Daniel Haverstock†, Renee Perroncel†,  
Shurjeel H. Choudhri+ and Pierre Arvis§

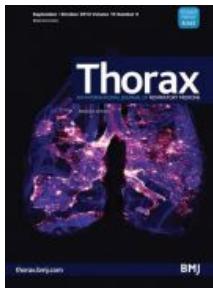


# Colour of sputum is a marker for bacterial colonisation in chronic obstructive pulmonary disease

Marc Miravitlles<sup>\*1</sup>, Alicia Marín<sup>2</sup>, Eduard Monsó<sup>3</sup>, Sara Vilà<sup>1</sup>, Cristian de la Roza<sup>4</sup>, Ramona Hervás<sup>3</sup>, Cristina Esquinas<sup>1</sup>, Marian García<sup>3</sup>, Laura Millares<sup>3</sup>, Josep Morera<sup>3</sup> and Antoni Torres<sup>5</sup>

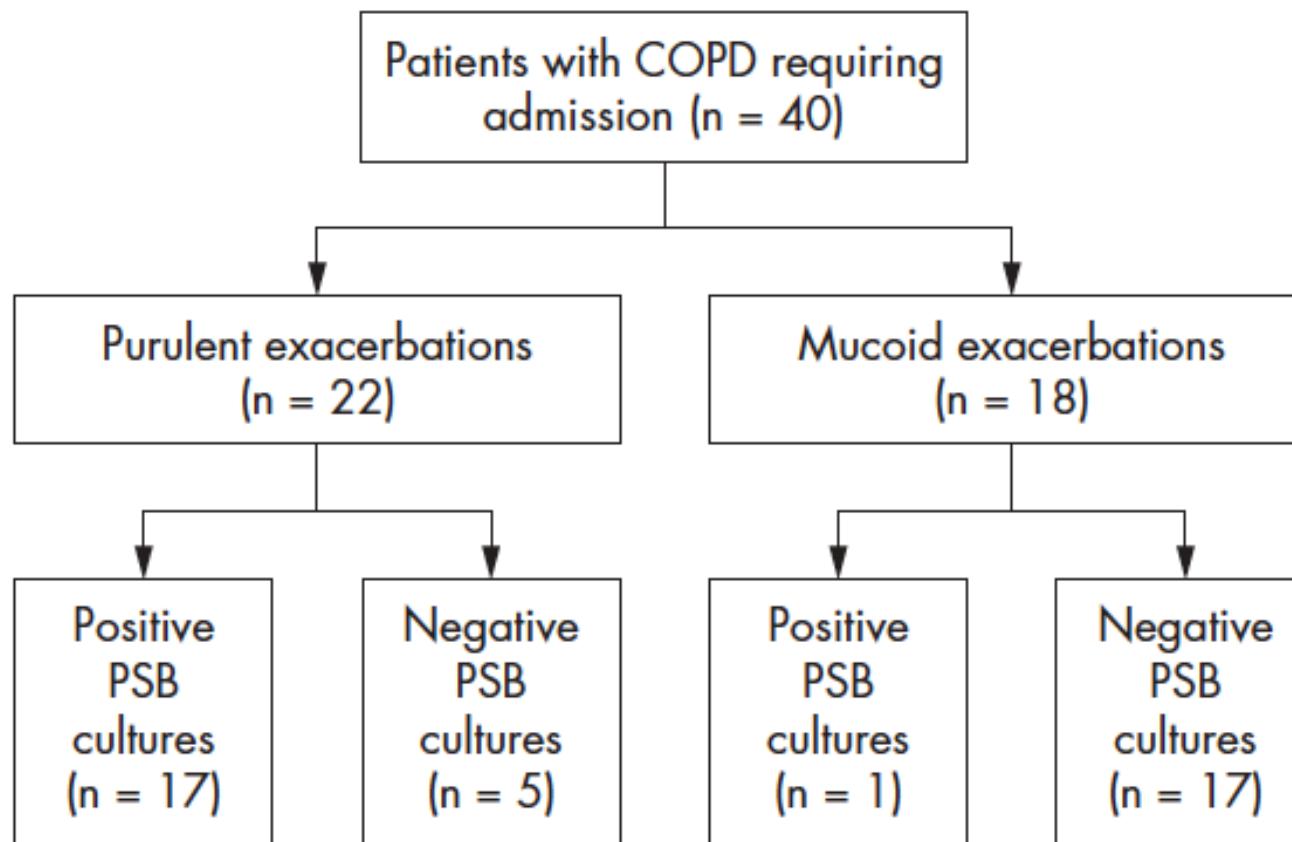


**Figure 1** Percentage of bacterial colonisation according to sputum colour (differences statistically significant at  $P < 0.001$ ).

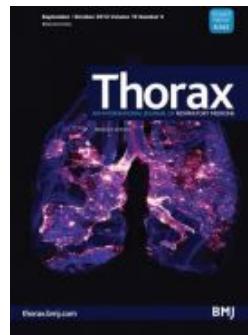


# Bronchoscopic validation of the significance of sputum purulence in severe exacerbations of chronic obstructive pulmonary disease

Néstor Soler, Carlos Agustí, Joaquim Angrill, Jorge Puig De la Bellacasa, Antoni Torres

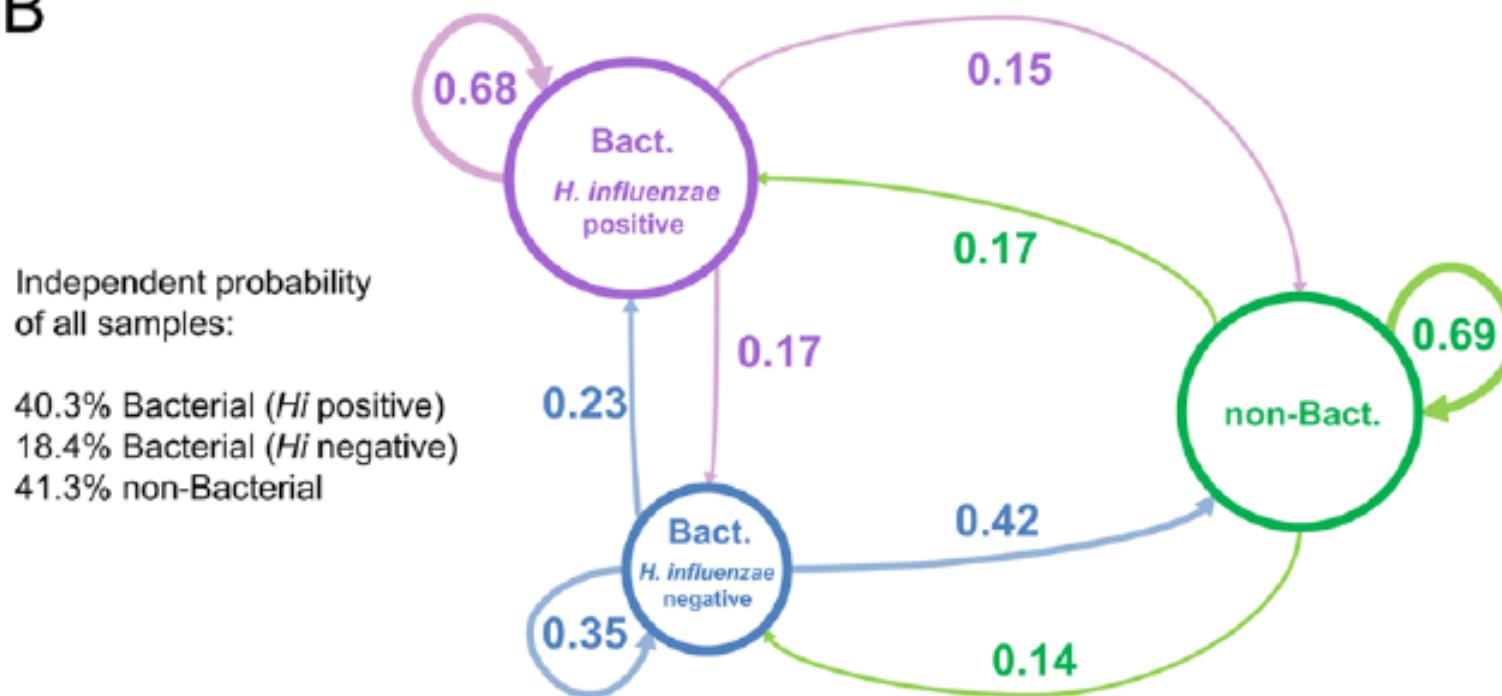


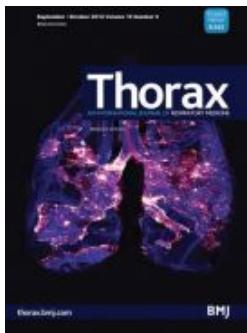
# Longitudinal profiling of the lung microbiome in the AERIS study demonstrates repeatability of bacterial and eosinophilic COPD exacerbations



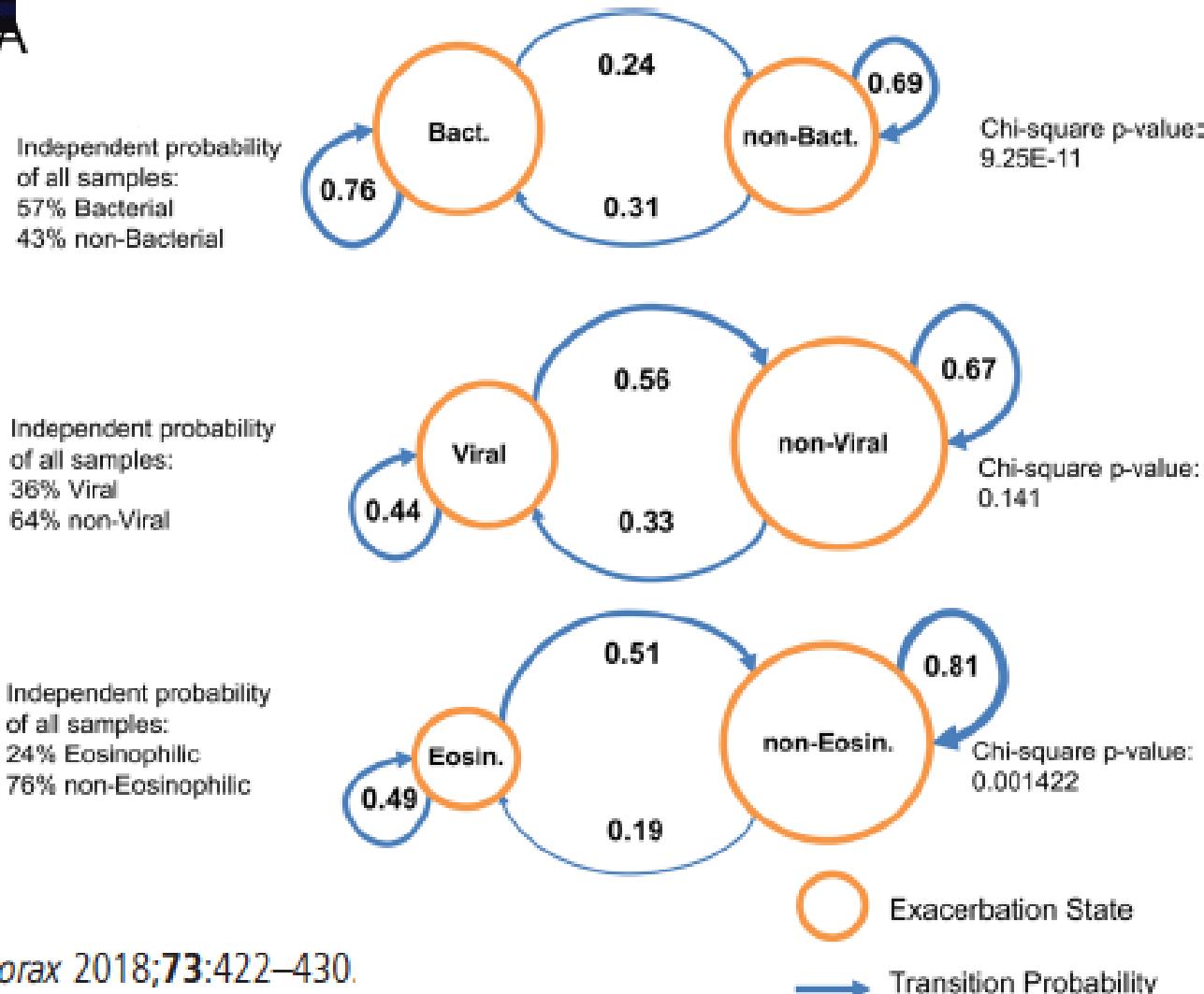
David Mayhew,<sup>1</sup> Nathalie Devos,<sup>2</sup> Christophe Lambert,<sup>2</sup> James R Brown,<sup>1</sup> Stuart C Clarke,<sup>3,4</sup> Viktoriya L Kim,<sup>4</sup> Michal Magid-Slav,<sup>1</sup> Bruce E Miller,<sup>5</sup> Kristoffer K Ostridge,<sup>4</sup> Ruchi Patel,<sup>6</sup> Ganesh Sathe,<sup>6</sup> Daniel F Simola,<sup>1</sup> Karl J Staples,<sup>3,4,7</sup> Ruby Sung,<sup>5</sup> Ruth Tal-Singer,<sup>5</sup> Andrew C Tuck,<sup>3</sup> Stephanie Van Horn,<sup>6</sup> Vincent Weynants,<sup>2</sup> Nicholas P Williams,<sup>4</sup> Jeanne-Marie Devaster,<sup>2</sup> Tom M A Wilkinson,<sup>3,4,7</sup> on behalf of the AERIS Study Group

B





# Longitudinal profiling of the lung microbiome in the AERIS study demonstrates repeatability of bacterial and eosinophilic COPD exacerbations





# Efficacy of Antibiotic Therapy for Acute Exacerbations of Mild to Moderate Chronic Obstructive Pulmonary Disease

Carl Llor<sup>1</sup>, Ana Moragas<sup>2</sup>, Silvia Hernández<sup>2</sup>, Carolina Bayona<sup>3</sup>, and Marc Miravitles<sup>4</sup>

TABLE 2. SUMMARY OF CLINICAL EFFICACY RESULTS AT END-OF-TREATMENT VISIT IN THE INTENTION-TO-TREAT POPULATION

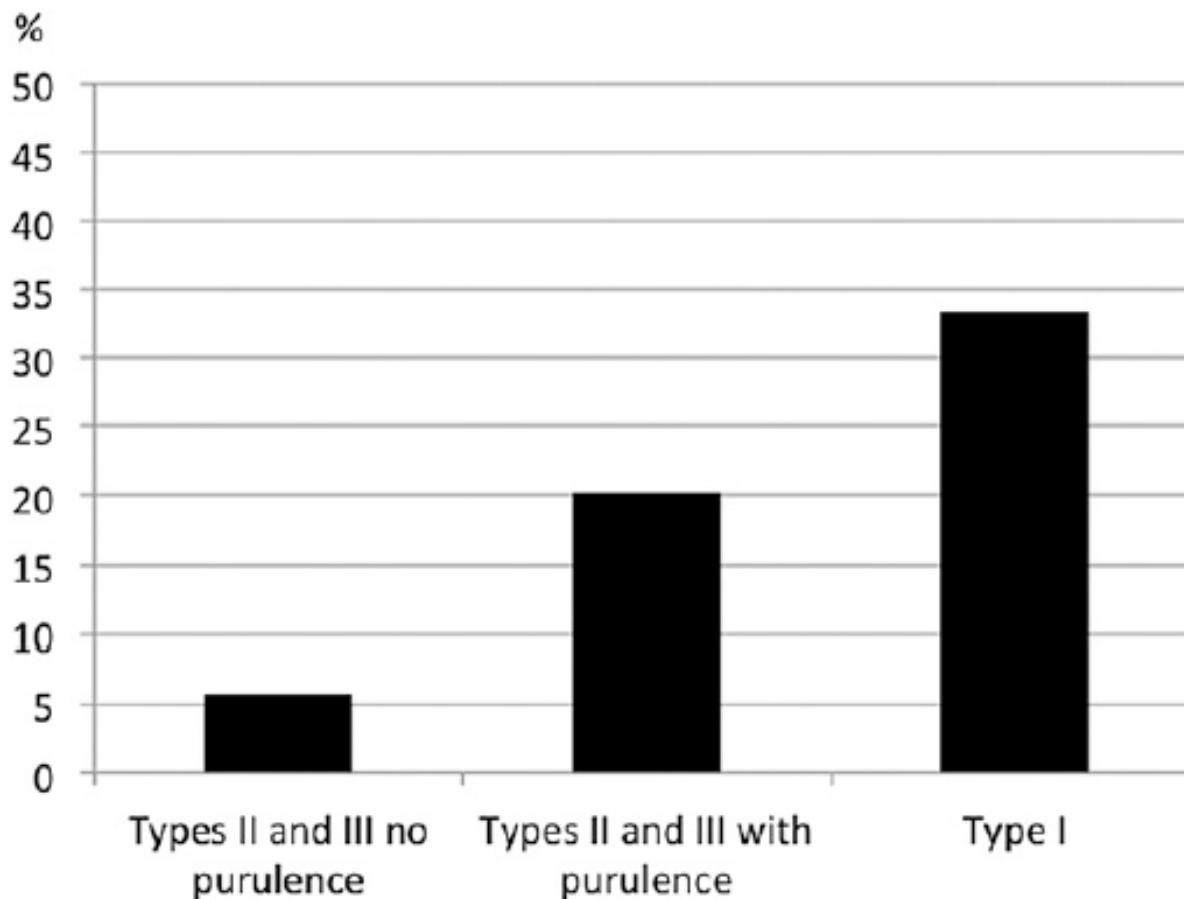
	AMX n/Total (%)	PBO n/Total (%)	P Value
Primary outcomes			
Clinical cure at Days 9–11	117/158 (74.1)	91/152 (59.9)	0.016
Clinical success at Days 9–11	143/158 (90.5)	123/152 (80.9)	0.022
Secondary outcomes			
Clinical cure at Day 20	129/158 (81.6)	103/152 (67.8)	0.006
Clinical success at Day 20	143/158 (90.5)	122/152 (80.3)	0.015
Days until next exacerbation, median (IQR)	233 (110–365)	160 (66–365)	0.015
Change of peak expiratory flow from basal and EOT visits, L/min, mean (SD)	52.8 (61.8)	38.5 (56.0)	0.039

Definition of abbreviations: AMX = amoxicillin/clavulanate; EOT = end of treatment; IQR = interquartile range; PBO = placebo.



# Is It Possible to Identify Exacerbations of Mild to Moderate COPD That Do Not Require Antibiotic Treatment?

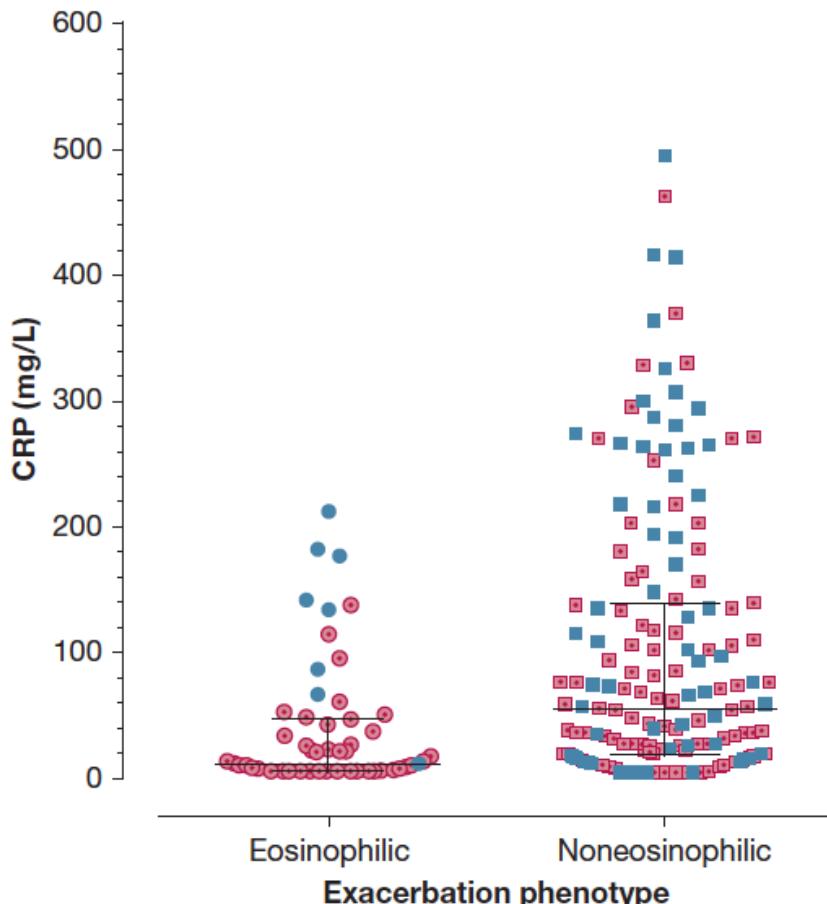
Marc Miravitles, MD; Ana Moragas, MD; Silvia Hernández, MD; Carolina Bayona, MD; and Carl Llor, MD





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174 subjects with exacerbation of COPD

## Eosinophil count

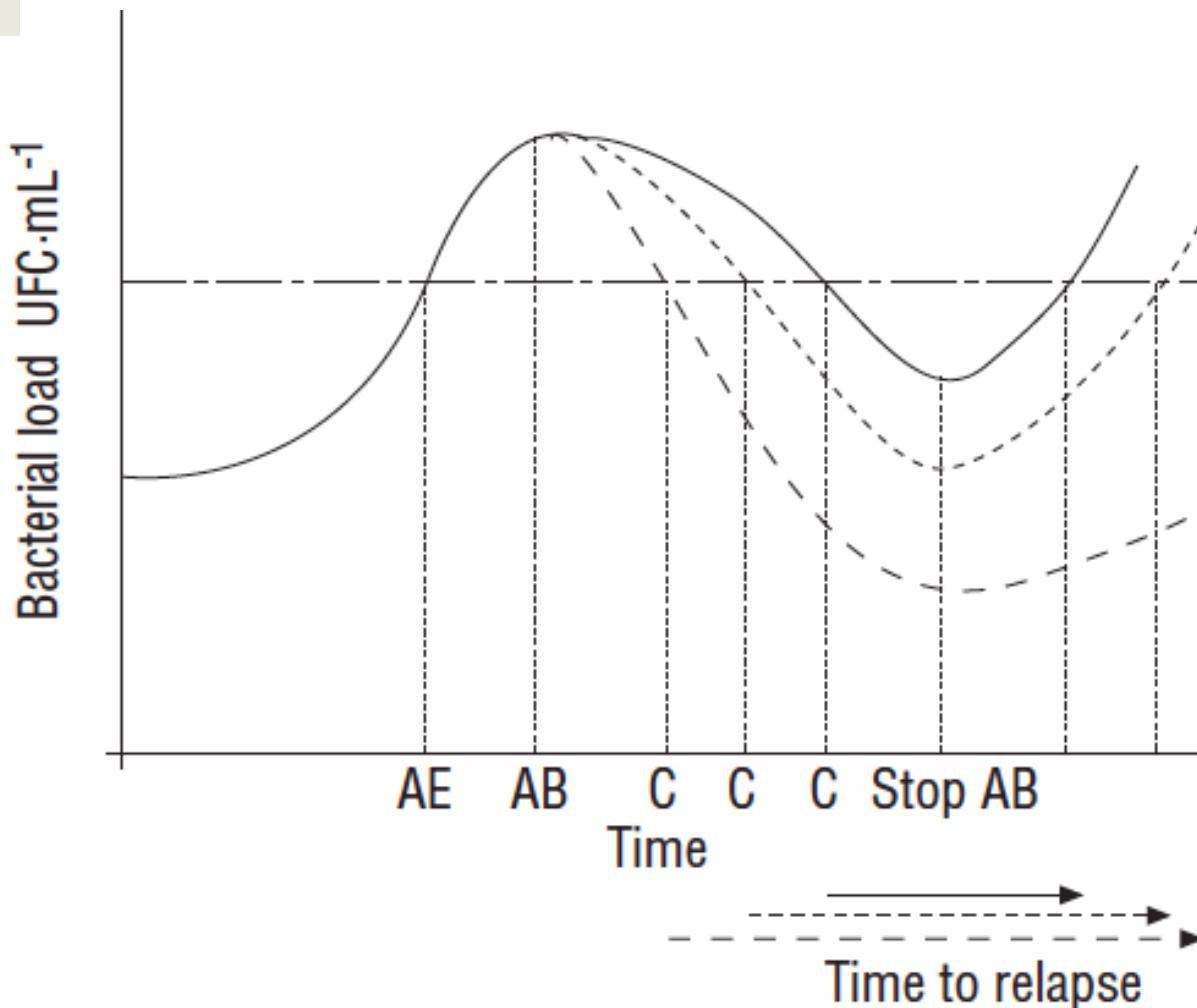
Geometric mean (95%CI) 100 cells/ $\mu$ L (84-120)

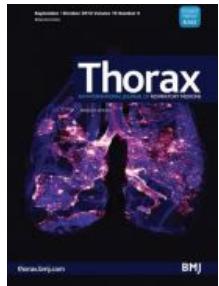
Mean (SD) 1.8% (2.4)

Proportion eosinophilic = 31%

# Exacerbations of chronic obstructive pulmonary disease: when are bacteria important?

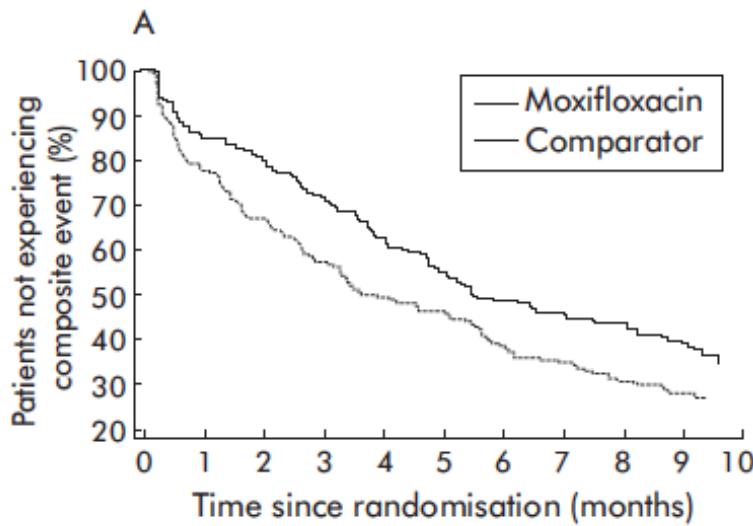
M. Miravitles



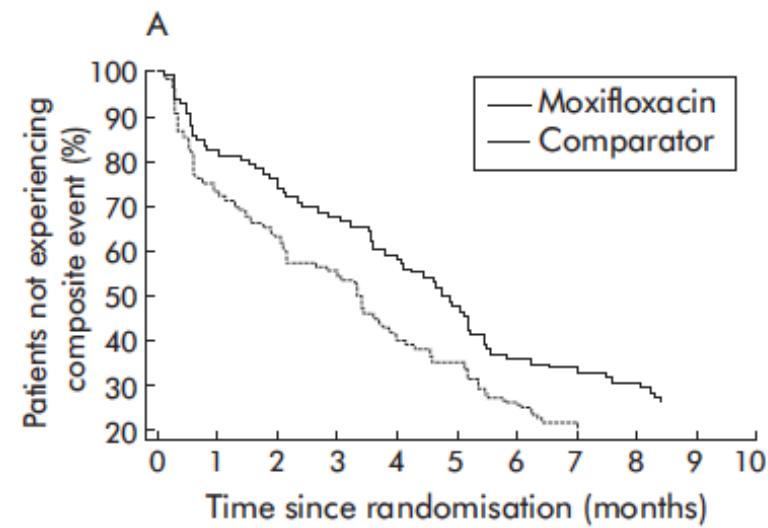


# Antibiotic treatment and factors influencing short and long term outcomes of acute exacerbations of chronic bronchitis

R Wilson, P Jones, T Schaberg, P Arvis, I Duprat-Lomon, P P Sagnier, for the MOSAIC Study Group



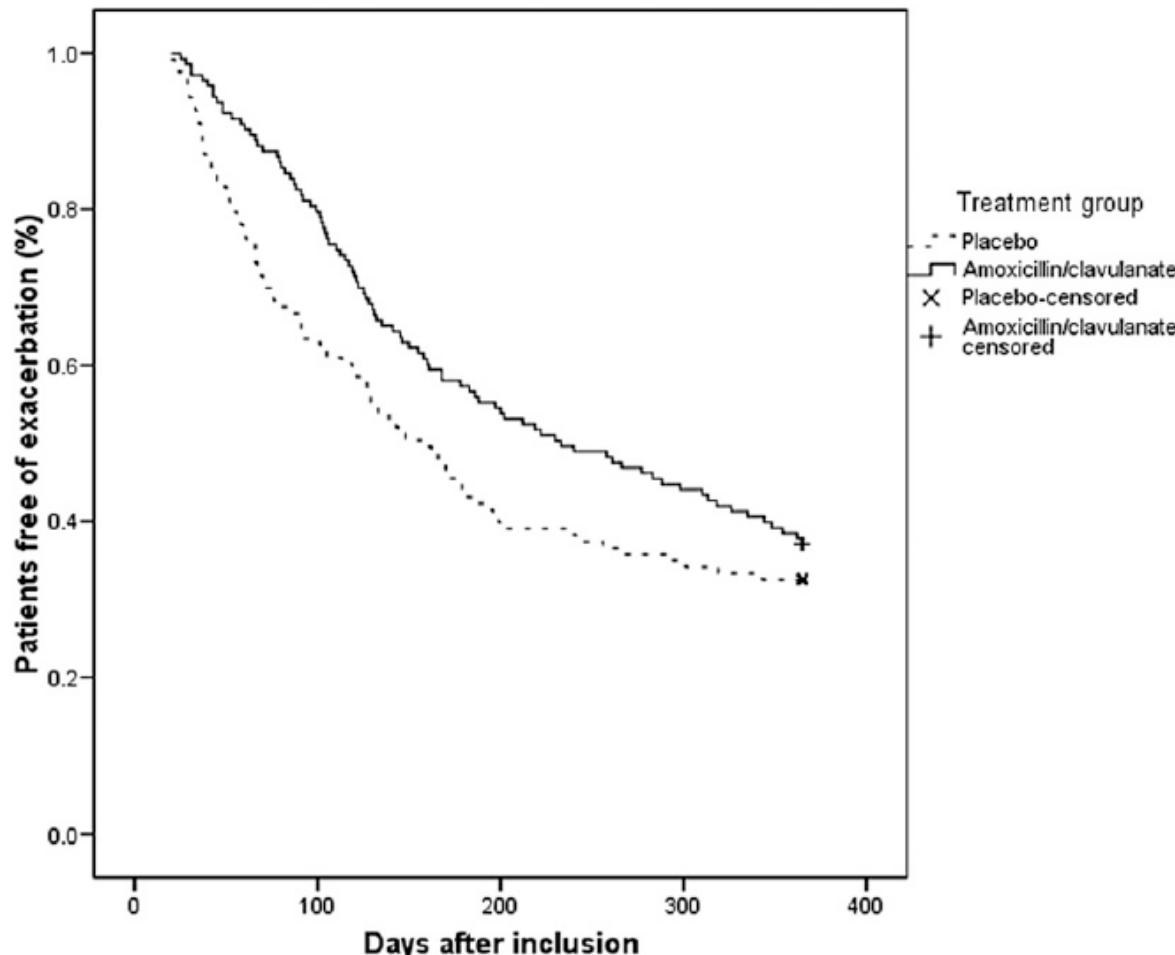
>65 years



4 or more ECOPD

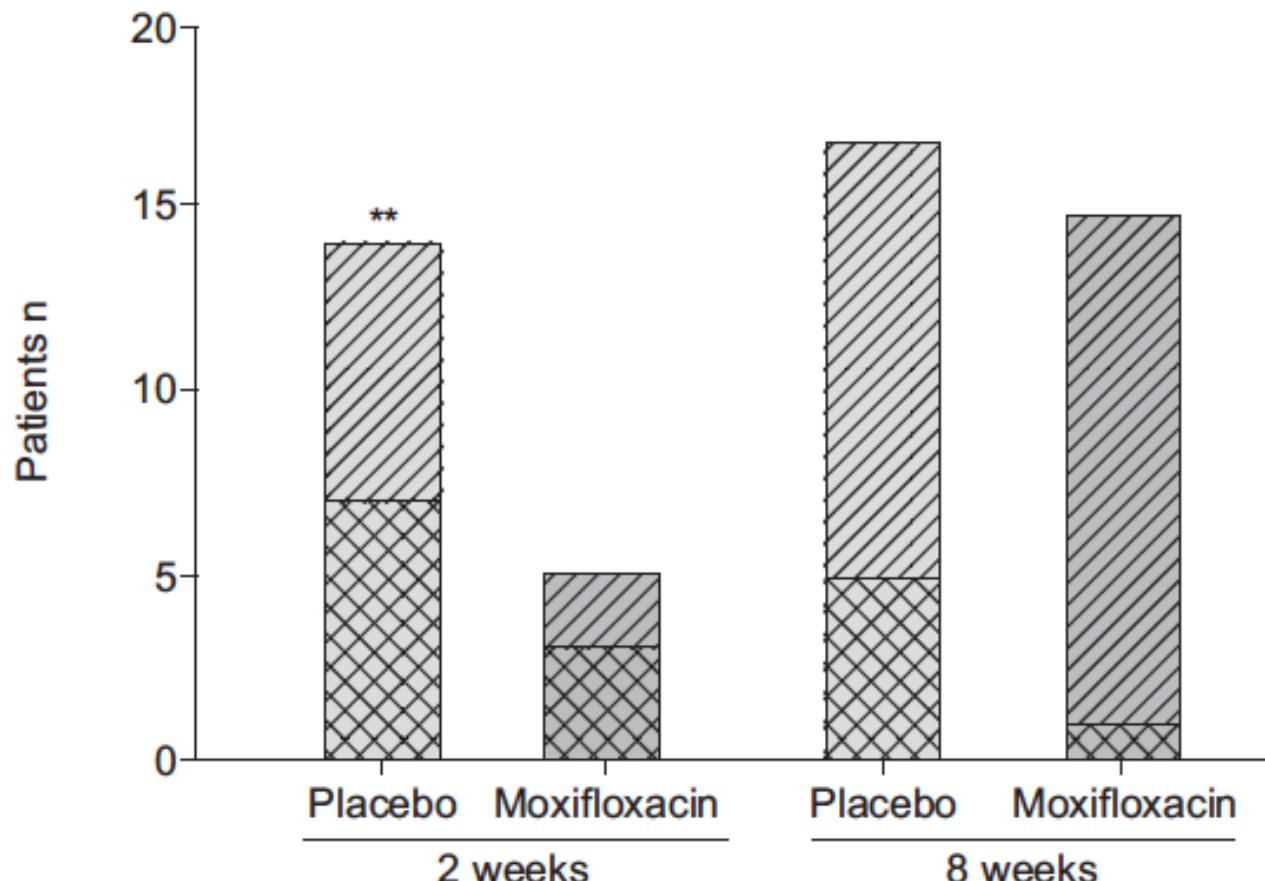
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Carl Llor<sup>1</sup>, Ana Moragas<sup>2</sup>, Silvia Hernández<sup>2</sup>, Carolina Bayona<sup>3</sup>, and Marc Miravitles<sup>4</sup>



# Efficacy of moxifloxacin in the treatment of bronchial colonisation in COPD

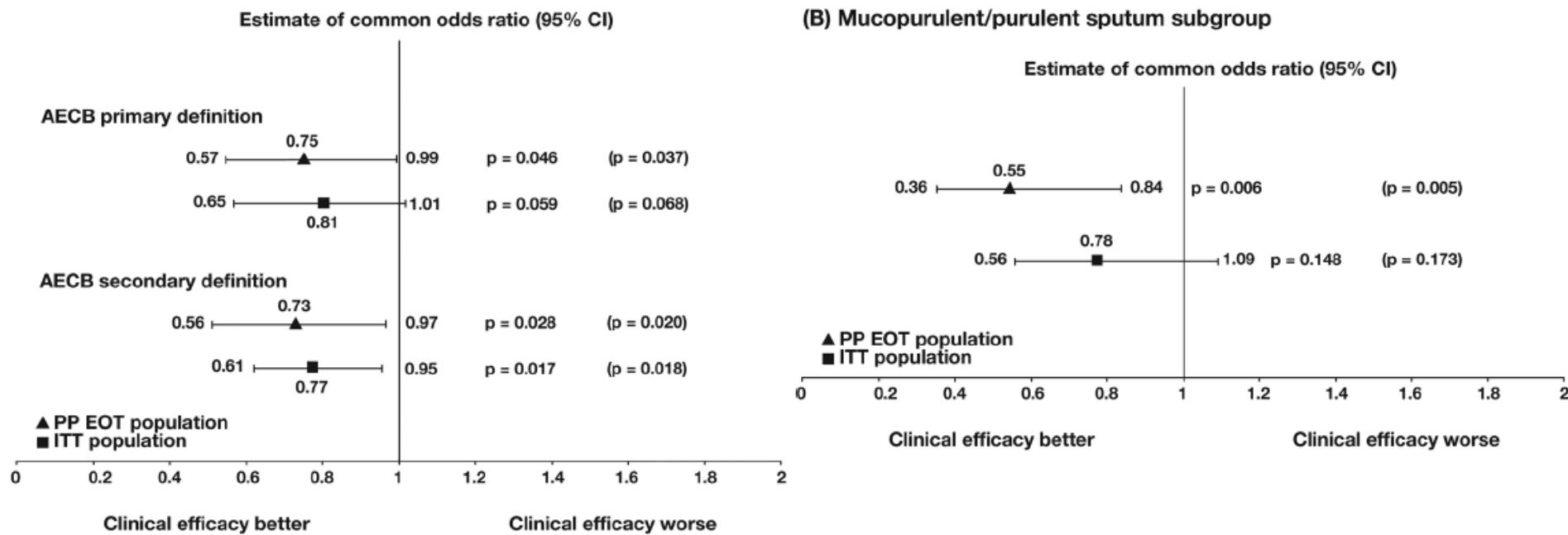
M. Miravitles\*, A. Marín#, E. Monsó†, S. Vilà\*, C. de la Roza+, R. Hervás†,  
C. Esquinas\*, M. García†, L. Millares†, J. Morera† and A. Torres§





# Pulsed moxifloxacin for the prevention of exacerbations of chronic obstructive pulmonary disease: a randomized controlled trial

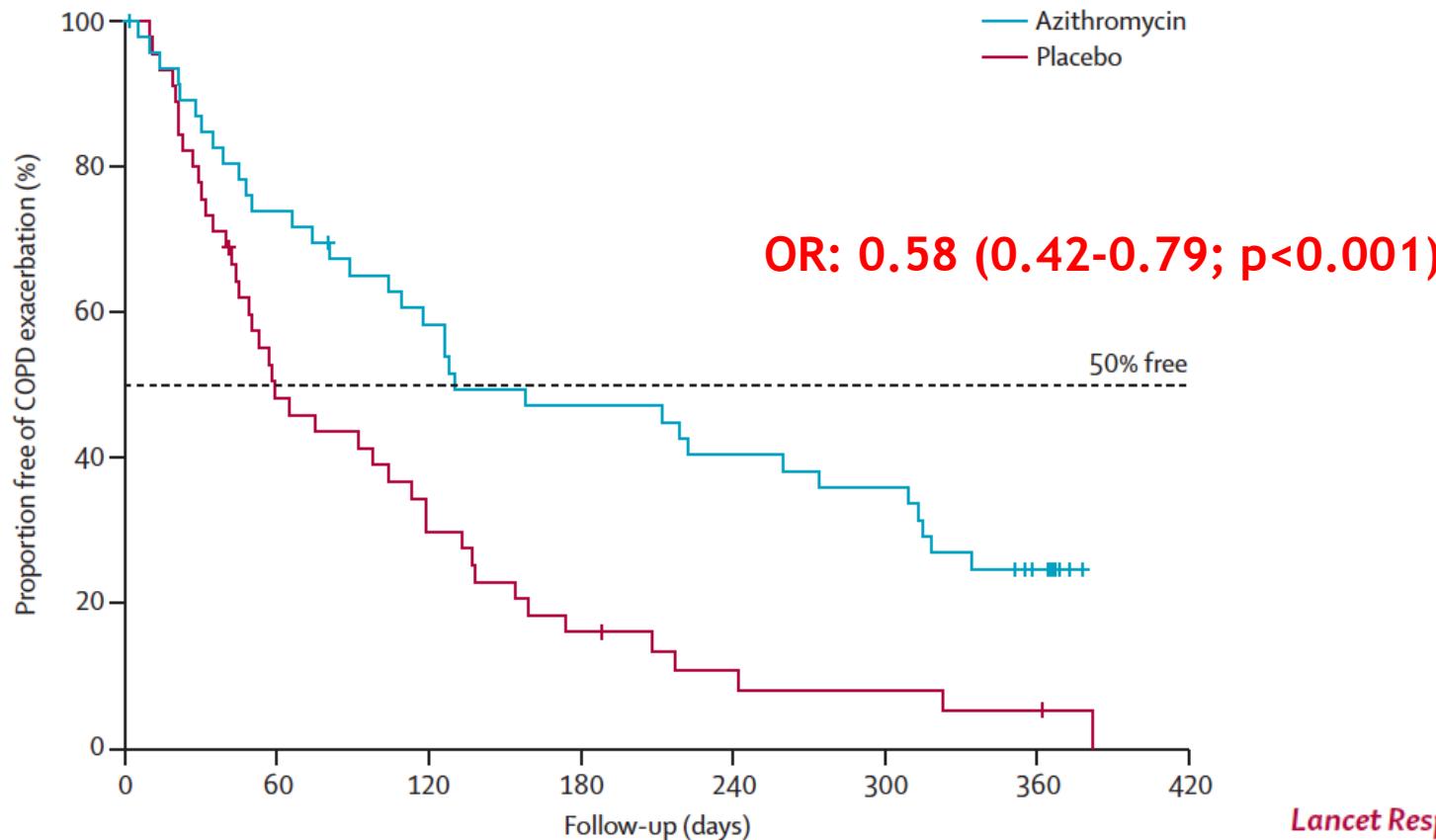
Sanjay Sethi<sup>1\*</sup>, Paul W Jones<sup>2</sup>, Marlize Schmitt Theron<sup>3</sup>, Marc Miravitles<sup>4</sup>, Ethan Rubinstein<sup>5</sup>, Jadwiga A Wedzicha<sup>6</sup>, Robert Wilson<sup>7</sup>, the PULSE Study group





# Azithromycin maintenance treatment in patients with frequent exacerbations of chronic obstructive pulmonary disease (COLUMBUS): a randomised, double-blind, placebo-controlled trial

Sevim Uzun, Remco S Djamin, Jan A J W Kluytmans, Paul G H Mulder, Nils E van't Veer, Anton A M Ermens, Aline J Pelle, Henk C Hoogsteden, Joachim G J V Aerts\*, Menno M van der Eerden\*



Number at risk

Azithromycin	47	34	26	21	18	16	8
Placebo	45	20	12	6	3	2	1

Lancet Respir Med 2014;  
2: 361-68



# Pharmacological strategies to reduce exacerbation risk in COPD: a narrative review

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## PRESENTATION

