

EOSINOPHILIC (AND NON-EOSINOPHILIC) ASTHMA

JAMES FINGLETON

WHO AM I AND COI

- Respiratory SMO at Wellington Hospital
- Deputy Director of the Medical Research Institute of New Zealand
- Specialist interest in asthma and obstructive airways disease



WHO AM I AND COI

- I have received support to attend educational meetings from AstraZeneca, Boehringer-Ingelheim, GSK and Novartis and presented independent medical education at symposia funded by AstraZeneca, Boehringer-Ingelheim, and Novartis

Research funders:

Health Research Council

Wellington Medical Research
Foundation

Asthma Foundation New Zealand

AstraZeneca

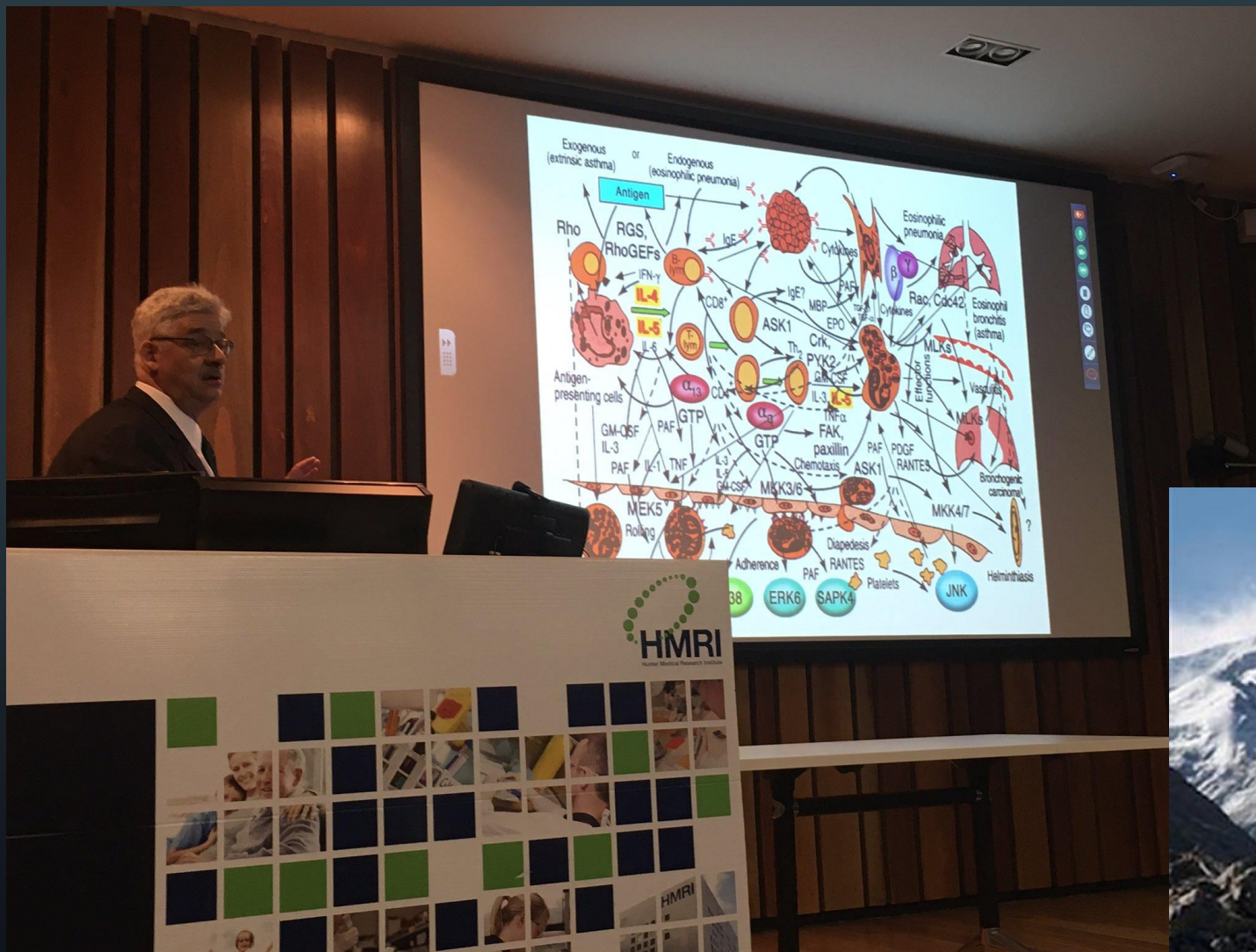
GSK

Fisher & Paykel

Genentech / Roche



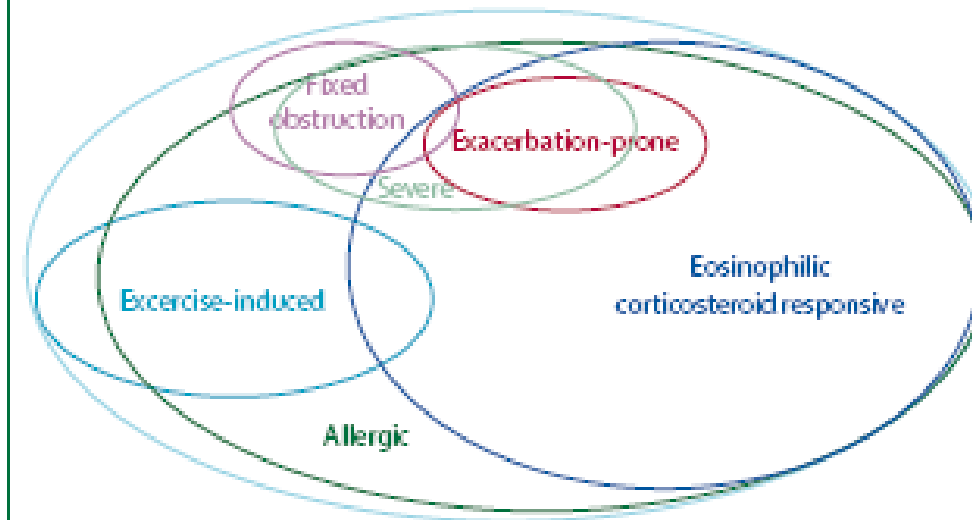
WHAT I'M NOT GOING TO ATTEMPT



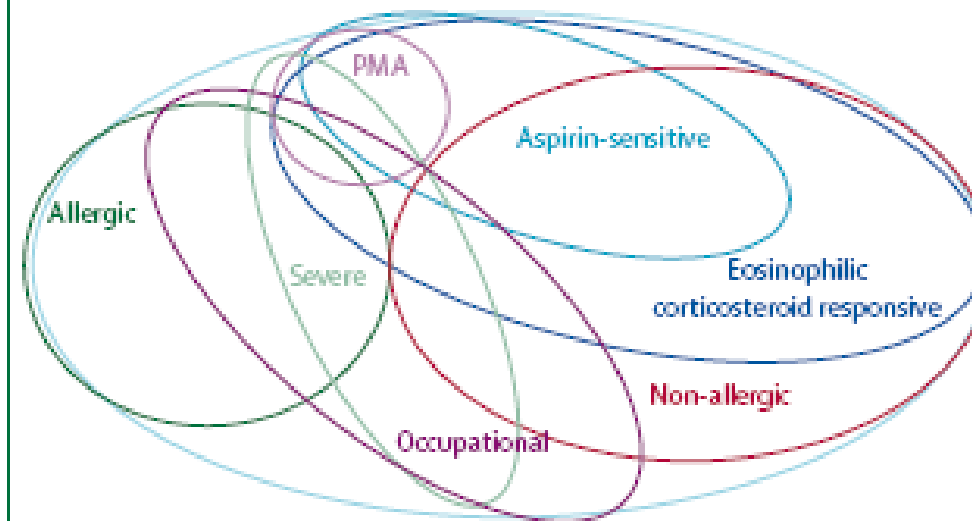
AIMS

- What is eosinophilic asthma?
- How is it diagnosed?
- Why should we care?
- What about non-eosinophilic / treatable traits?

ISN'T ALL ASTHMA THE SAME?



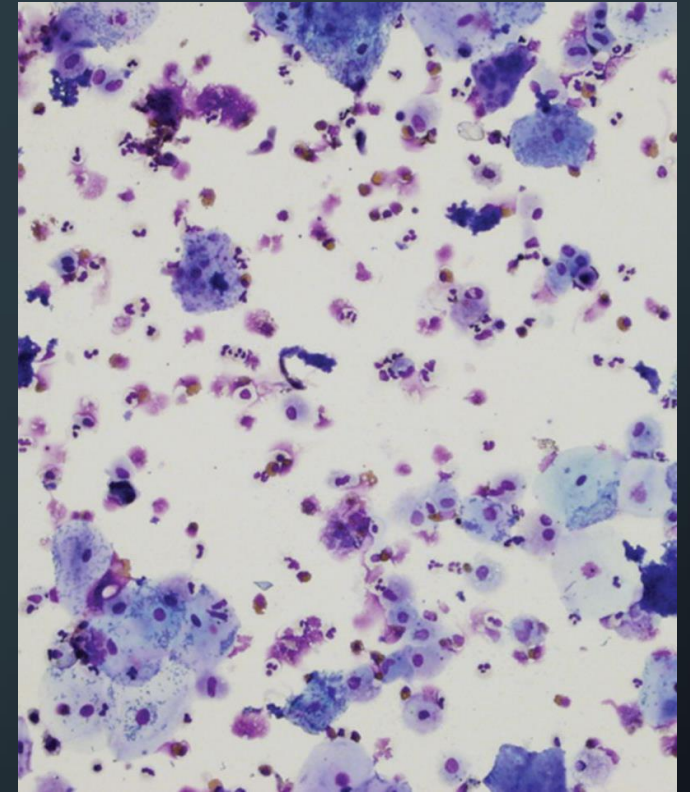
Early/childhood onset phenotypes



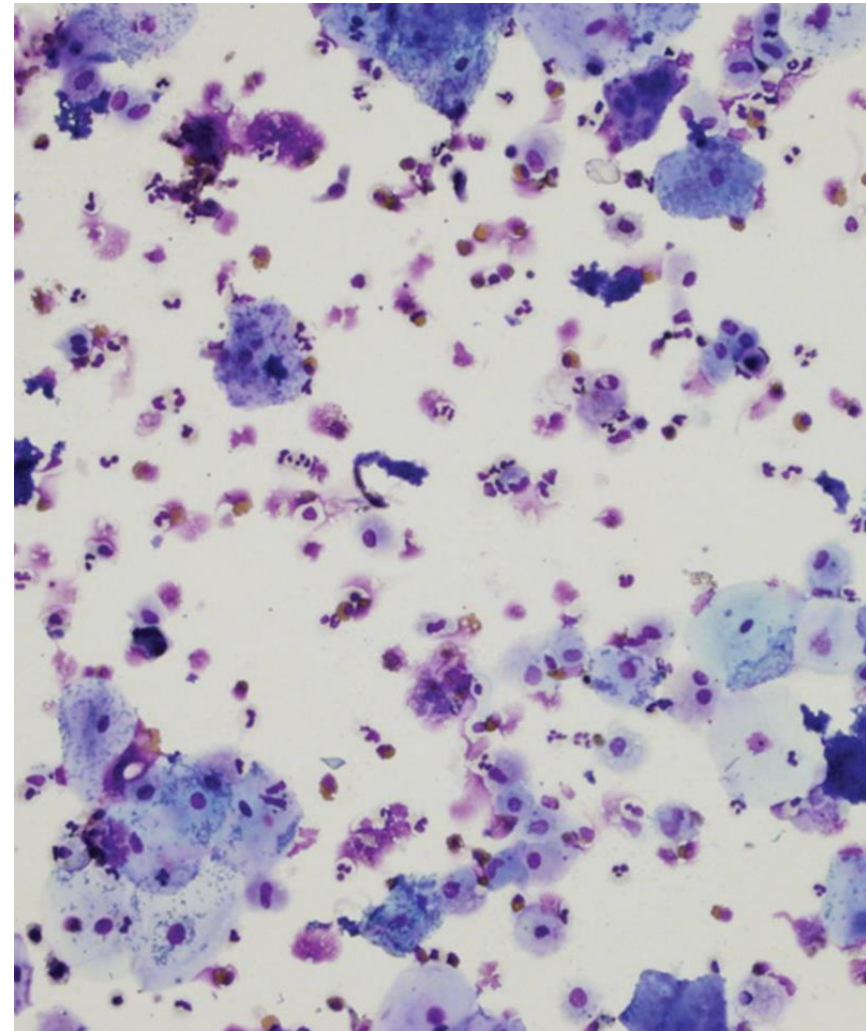
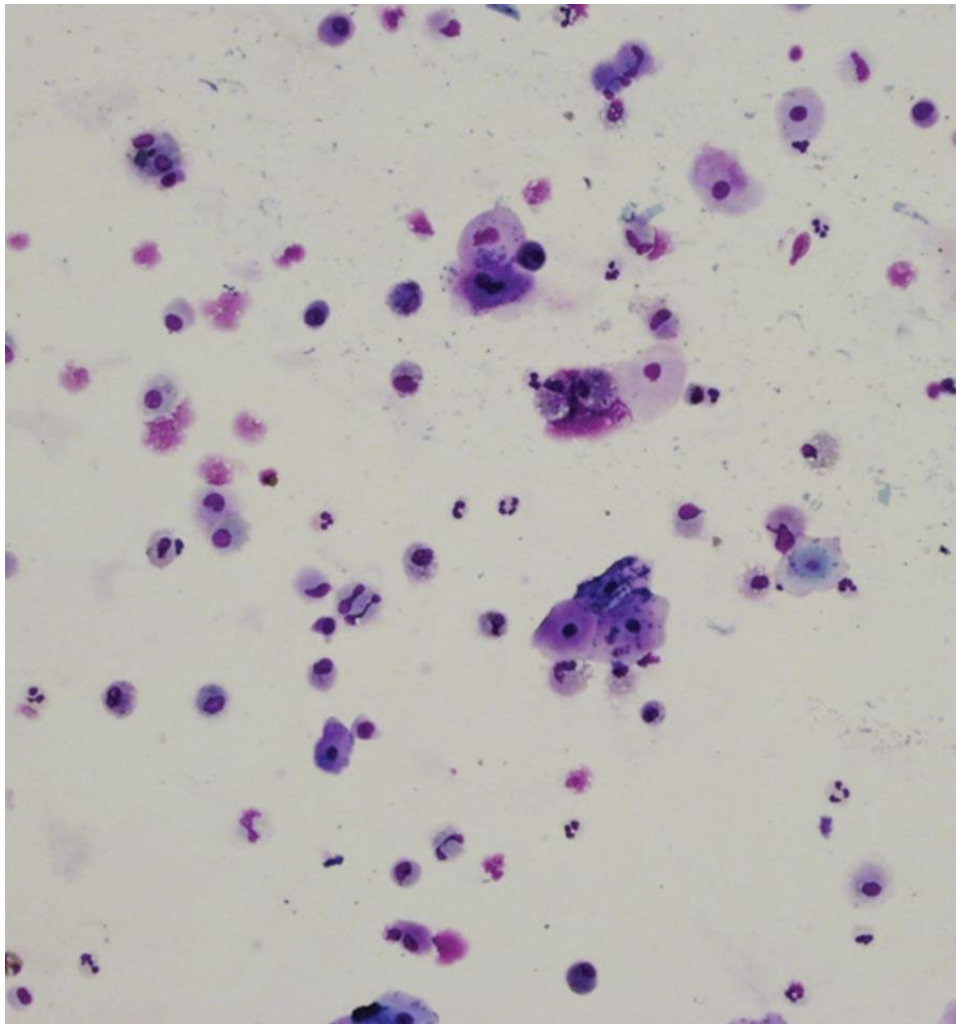
Late/adult onset

HOW IS EOSINOPHILIC ASTHMA DIAGNOSED?

- Induced sputum
- Blood eosinophils
- Exhaled nitric oxide



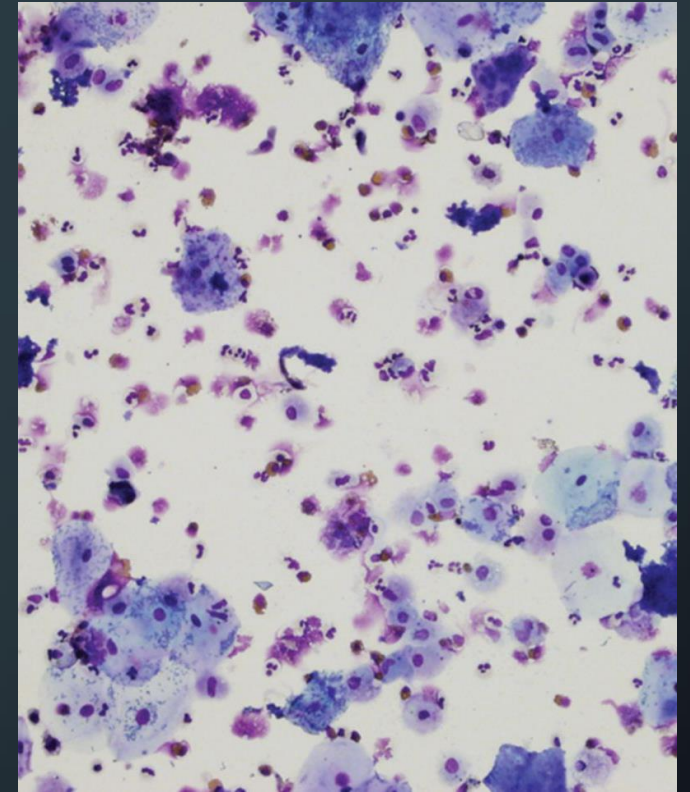
Induced sputum samples



Zsoka Weiszhar, and Ildiko Horvath Breathe 2013;9:300-306

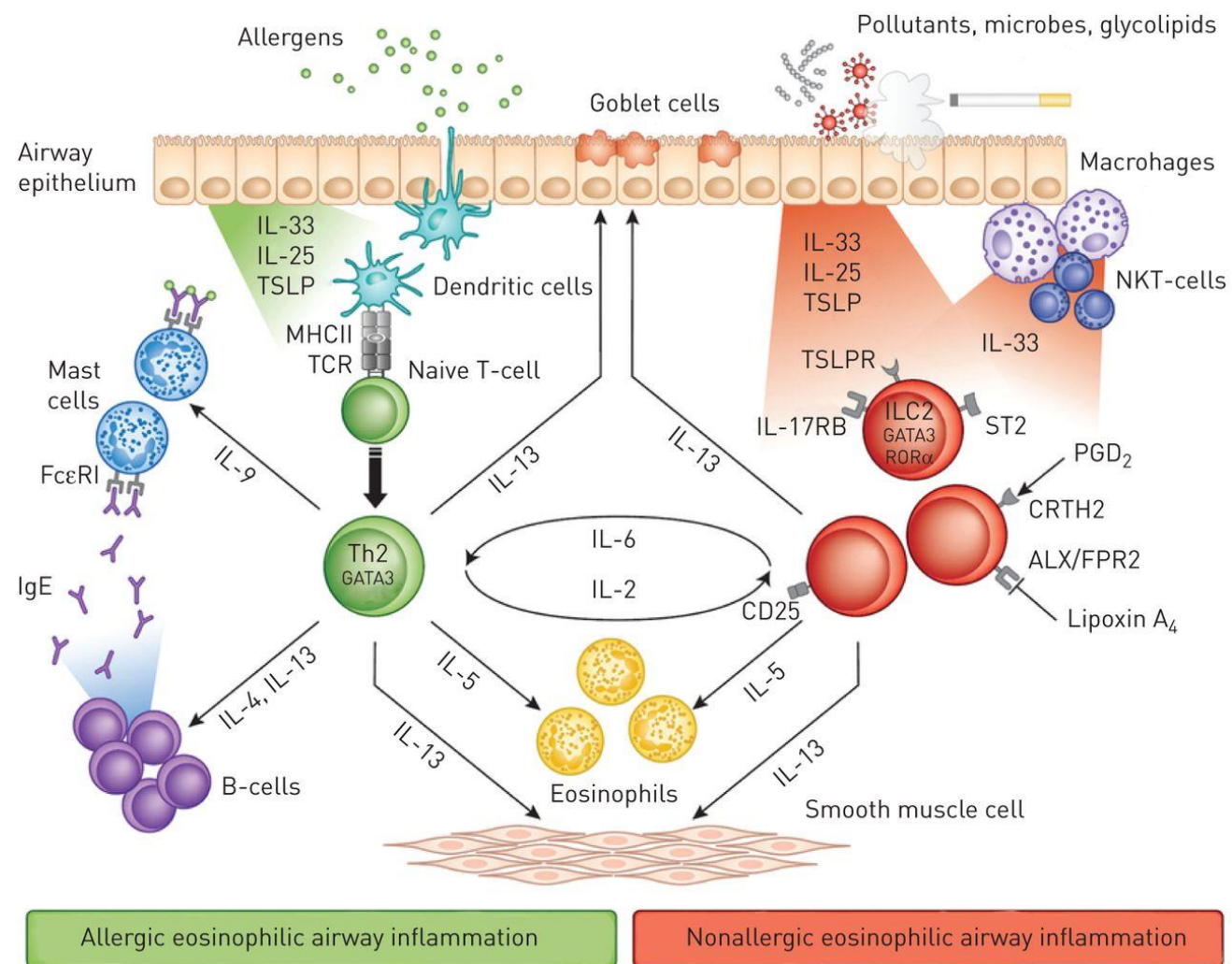
HOW IS IT DIAGNOSED?

- Induced sputum
- Blood eosinophils
- Exhaled nitric oxide



WHAT CAUSES IT?

Two different pathways lead to eosinophilic airway inflammation in asthma.

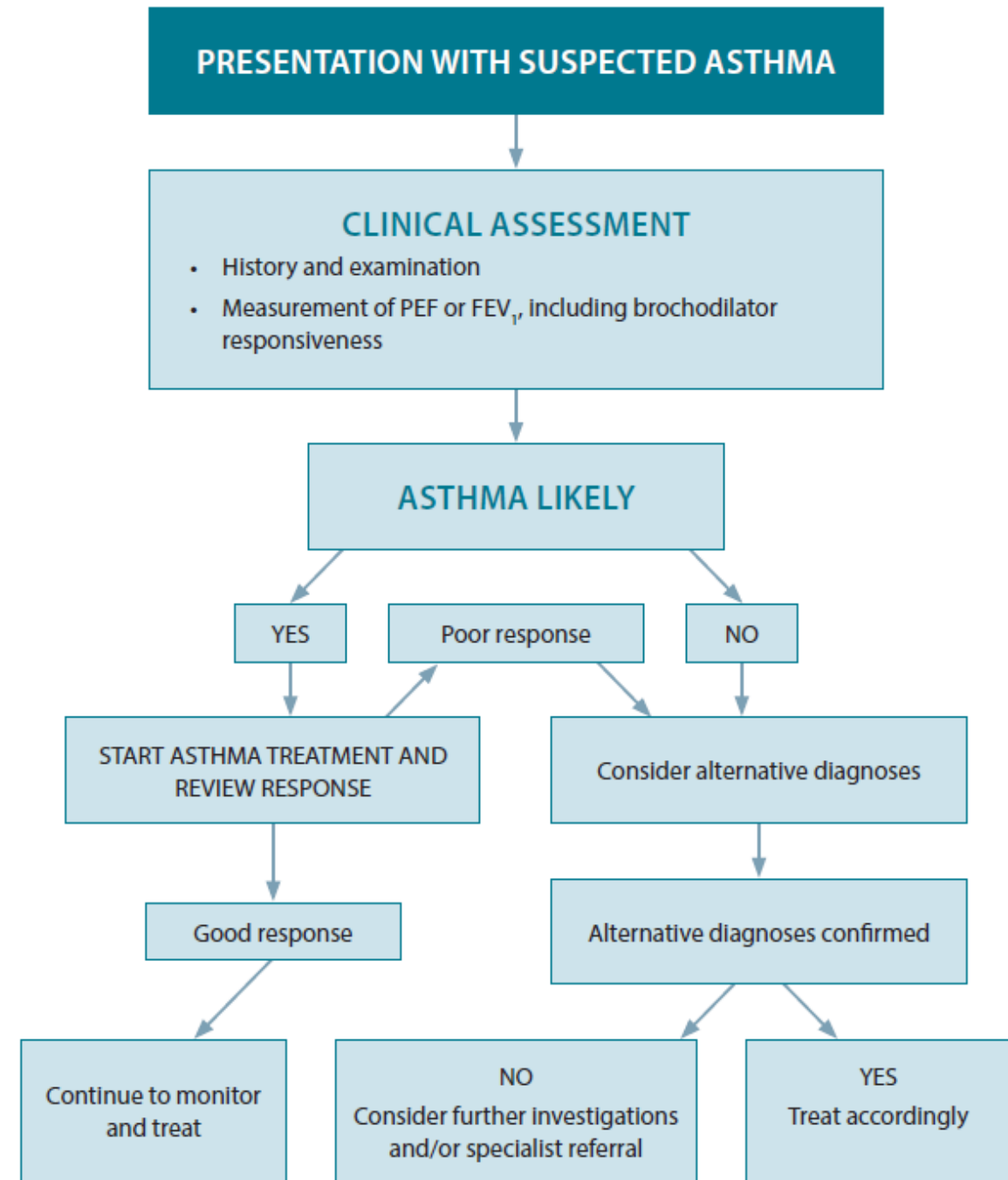


Jantina C. de Groot et al. ERJ Open Res 2015;1:00024-2015

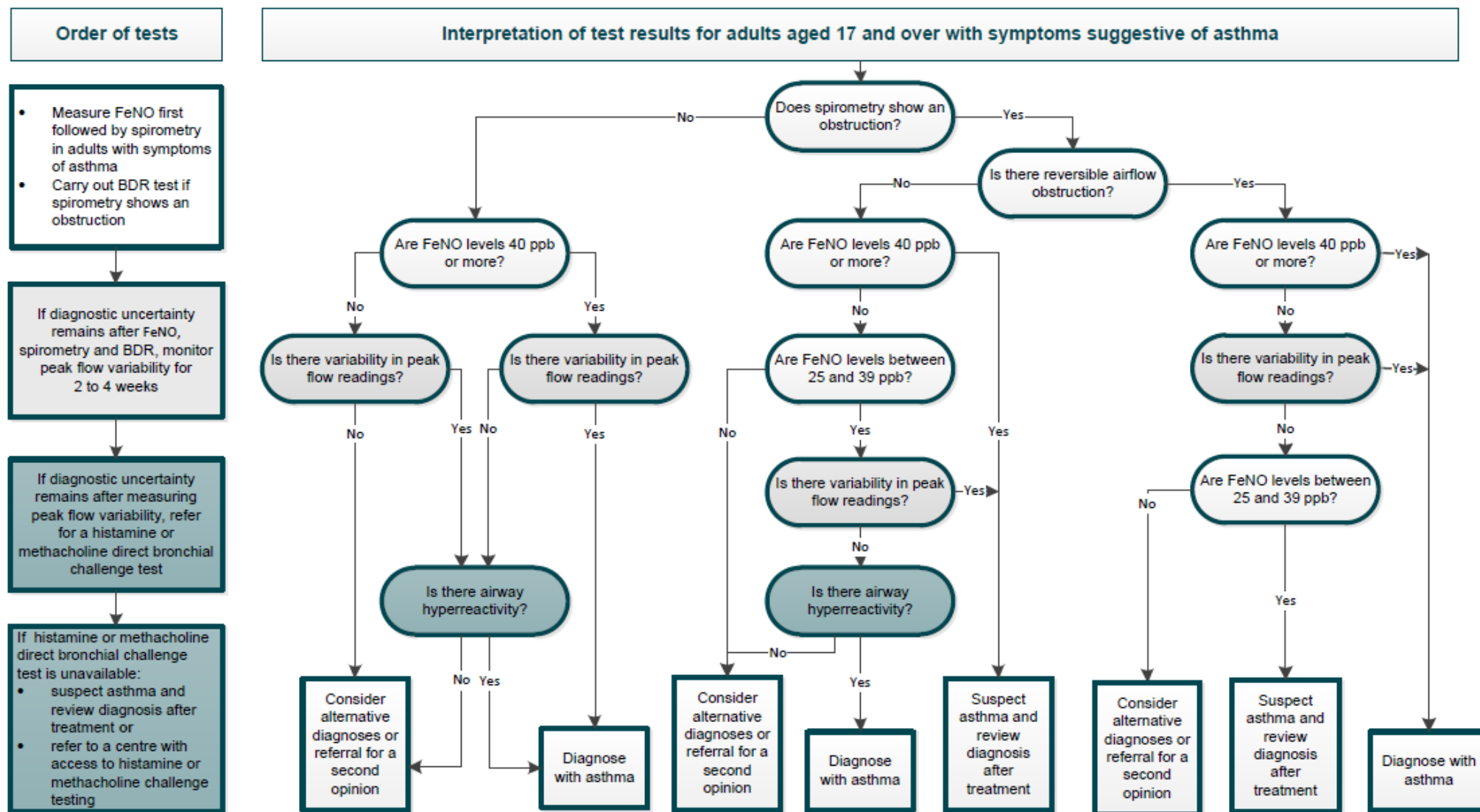
WHY SHOULD I CARE?

- Diagnosis of asthma
- Management of asthma

DIAGNOSIS OF ASTHMA



Algorithm C Objective tests for asthma in adults aged 17 and over



Abbreviations:

FeNO, fractional exhaled nitric oxide
BDR, bronchodilator reversibility

This algorithm is based on recommendations from NICE's guideline on [asthma: diagnosis, monitoring and chronic asthma management](#) (2017)

Positive test thresholds

Obstructive spirometry: FEV1/FVC ratio less than 70% (or below the lower limit of normal if available)

FeNO: 40 ppb or more

BDR: improvement in FEV1 of 12% or more and increase in volume of 200 ml or more

Peak flow variability: variability over 20%

Direct bronchial challenge test with histamine or methacholine: PC20 of 8 mg/ml or less

NICE National Institute for Health and Care Excellence

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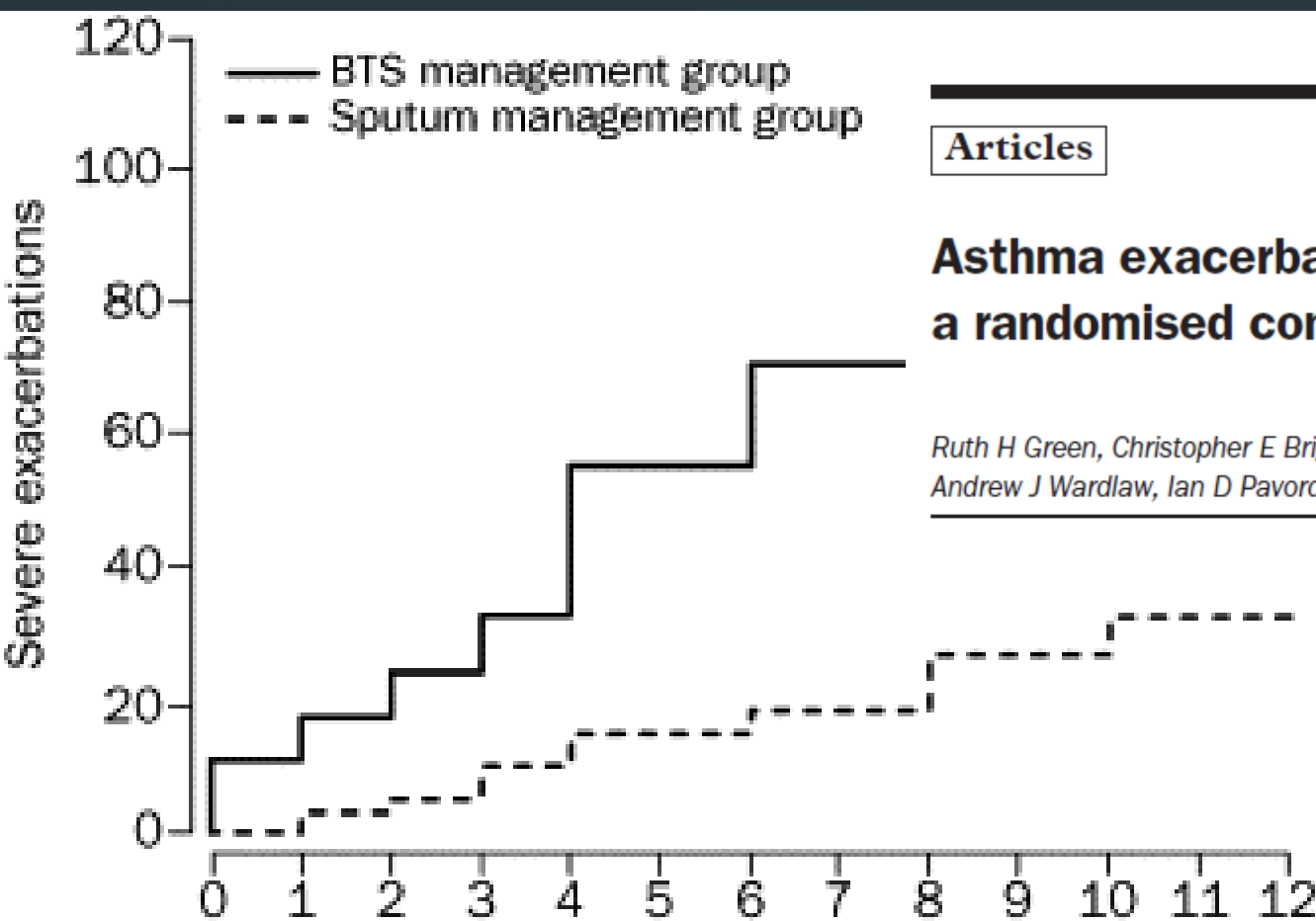
ASTHMA MANAGEMENT

ASTHMA

Pathological features and inhaled corticosteroid response of eosinophilic and non-eosinophilic asthma

Mike Berry, Angela Morgan, Dominick E Shaw, Deborah Parker, Ruth Green, Christopher Brightling, Peter Bradding, Andrew J Wardlaw, Ian D Pavord

Thorax 2007;62:1043–1049. doi: 10.1136/thx.2006.073429



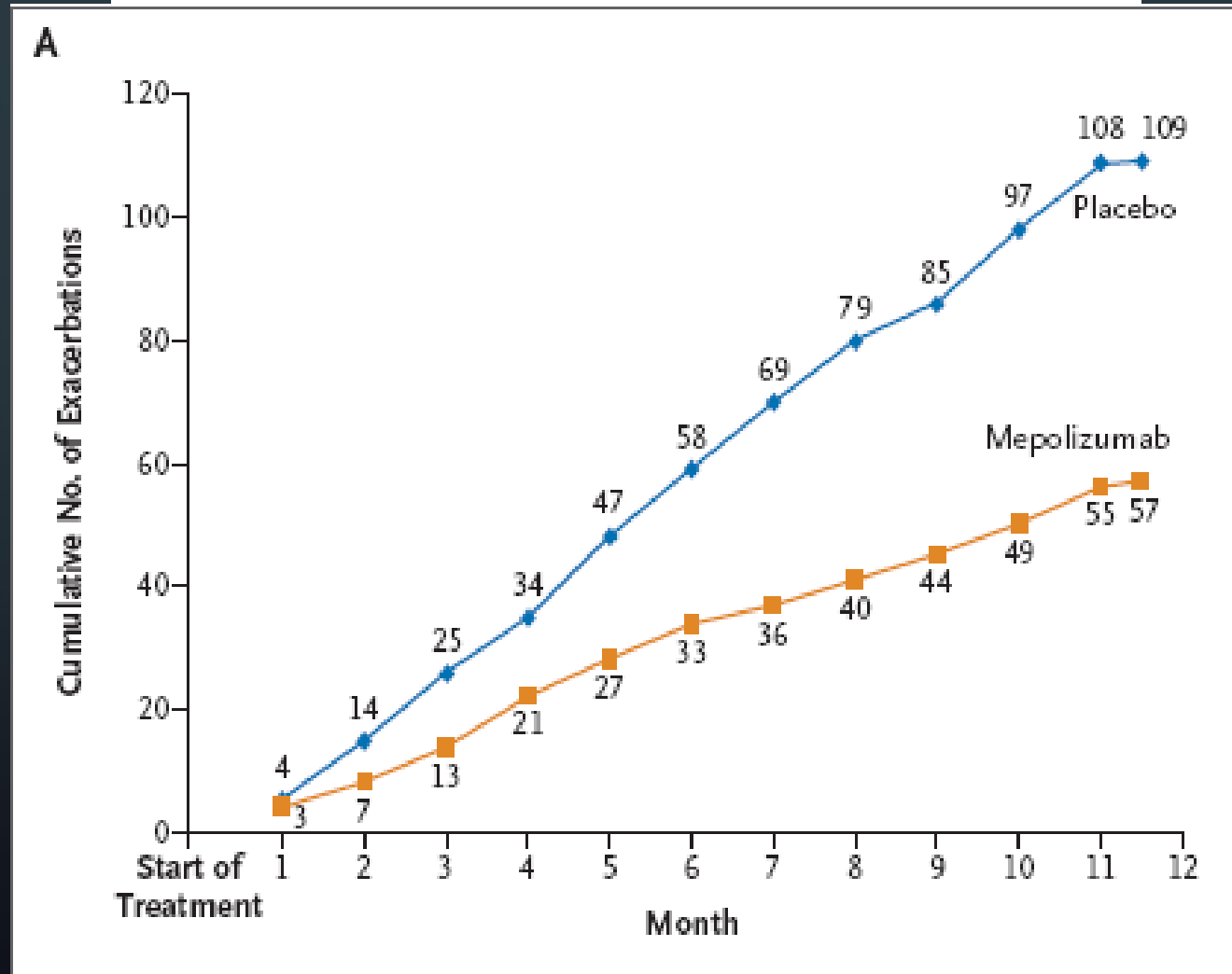
Articles

Asthma exacerbations and sputum eosinophil counts: a randomised controlled trial

Ruth H Green, Christopher E Brightling, Susan McKenna, Beverley Hargadon, Debbie Parker, Peter Bradding, Andrew J Wardlaw, Ian D Pavord

Mepolizumab and Exacerbations of Refractory Eosinophilic Asthma

Pranabashis Haldar, M.R.C.P., Christopher E. Brightling, Ph.D., F.R.C.P.,
Beverley Hargadon, R.G.N., Sumit Gupta, M.R.C.P., William Monteiro, M.Sc.,
Ana Sousa, Ph.D., Richard P. Marshall, Ph.D., M.R.C.P.,
Peter Bradding, D.M., F.R.C.P., Ruth H. Green, M.D., F.R.C.P.,
Andrew J. Wardlaw, Ph.D., F.R.C.P., and Ian D. Pavord, D.M., F.R.C.P.

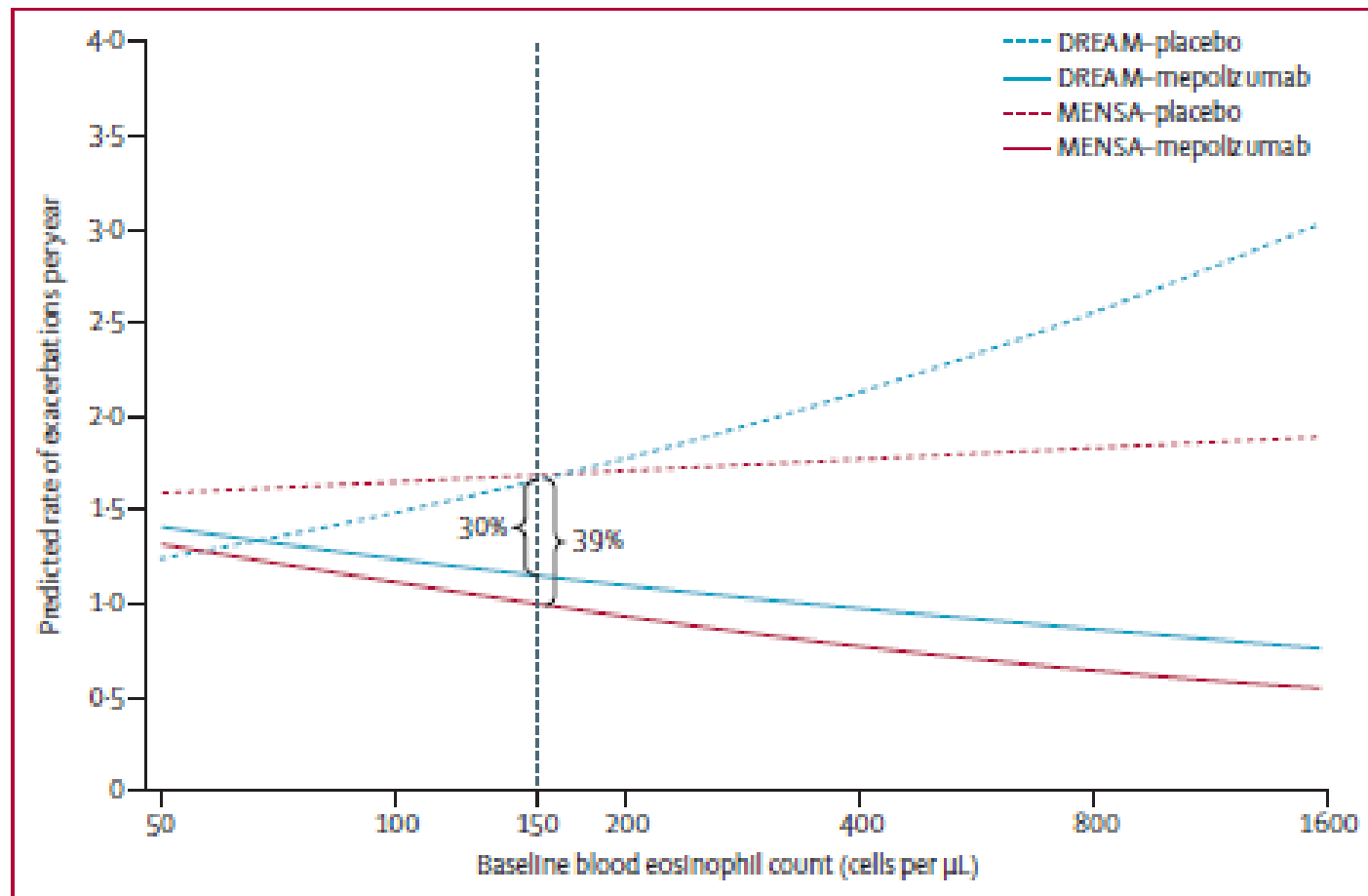


[2009]

Severe eosinophilic asthma treated with mepolizumab stratified by baseline eosinophil thresholds: a secondary analysis of the DREAM and MENSA studies



Hector G Ortega, Steven W Yancey, Bhabita Mayer, Necdet B Gunsoy, Oliver N Keene, Eugene R Bleecker, Christopher E Brightling, Ian D Pavord



spir 2016]

ASTHMA MANAGEMENT

- Blood eosinophils >0.4 is a marker of increased risk of exacerbations
- Presence of eosinophilia predicts response to inhaled steroids
- Adjusting steroid dosing based on sputum eosinophils can improve outcomes
- Persistent eosinophilia despite treatment may indicate steroid insensitive disease OR poor adherence / technique
- Eosinophilia predicts response to anti- IL5 therapies

WHAT ABOUT NON-EOSINOPHILIC ASTHMA?

- Look for other treatable traits
- Try to avoid excessive steroids
- If frequent infective exacerbations and nothing else to optimise consider azithromycin

PERSPECTIVE
PRECISION MEDICINE FOR AIRWAY DISEASES



Treatable traits: toward precision medicine of chronic airway diseases



CrossMark

Alvar Agusti¹, Elisabeth Bel², Mike Thomas³, Claus Vogelmeier⁴,
Guy Brusselle^{5,6}, Stephen Holgate⁷, Marc Humbert⁸, Paul Jones⁹,
Peter G. Gibson¹⁰, Jørgen Vestbo¹¹, Richard Beasley¹² and Ian D. Pavord¹³

TREATABLE TRAITS

TREATABLE TRAITS

Specific characteristics of patients including phenotypes of airways disease, overlapping disorders, comorbidities, environmental and lifestyle factors, that potentially contribute to respiratory health, that are potentially amenable to specific treatments.

Table 5: Treatable traits in asthma.

Overlapping disorders:

- COPD
- Bronchiectasis
- Allergic bronchopulmonary aspergillosis
- Dysfunctional breathing including vocal cord dysfunction.

Comorbidities:

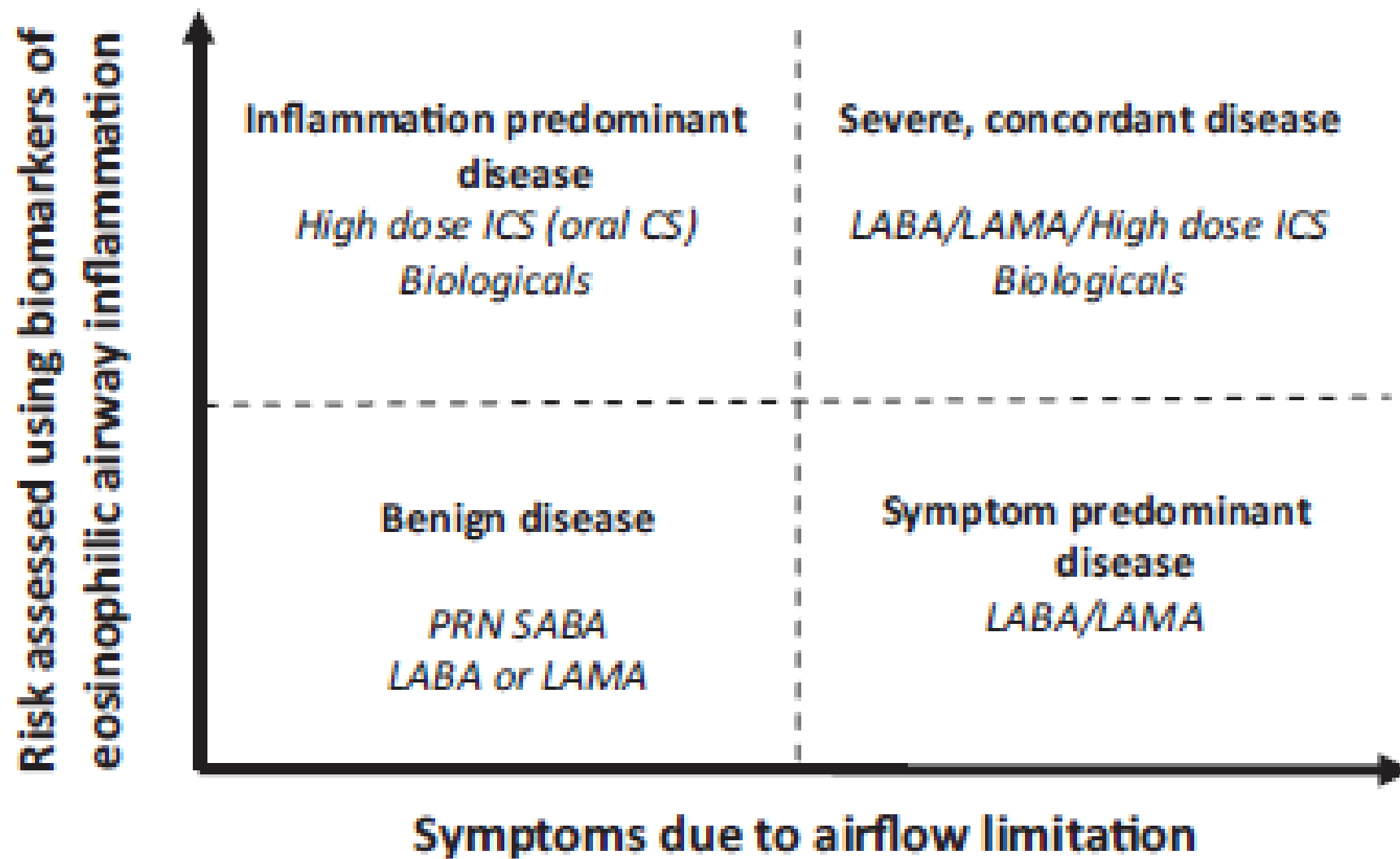
- Obesity
- Gastro-oesophageal reflux disease
- Rhinitis
- Sinusitis
- Depression/anxiety.

Environmental:

- Smoking
- Occupational exposures
- Provoking factors including aspirin, other NSAIDs and beta blockers.

Behavioural:

- Adherence
- Inhaler technique.



SUMMARY

- Not all asthma is the same
- Around 50% of patients with asthma have evidence of eosinophilic inflammation
- Assessment of eosinophils in asthma:
 - Can help confirm the diagnosis of asthma
 - Can hint at poor adherence
 - Can help guide the use of steroids in asthma
 - In the (near) future will be essential to determine eligibility for biological therapies
- Considering treatable traits may help you personalise treatment for your patient

ANY QUESTIONS?

Effect of azithromycin on asthma exacerbations and quality of life in adults with persistent uncontrolled asthma (AMAZES): a randomised, double-blind, placebo-controlled trial

Prof Peter G Gibson, MBBS, Prof Ian A Yang, MBBS, Prof John W Upham, MBBS, Prof Paul N Reynolds, MD, Prof Sandra Hodge, PhD, Prof Alan L James, FRACP, Prof Christine Jenkins, MD, Prof Matthew J Peters, MBBS, Prof Guy B Marks, PhD, Melissa Baraket, PhD, Heather Powell, MMedSc, Steven L Taylor, BSC, Lex E X Leong, PhD, Prof Geraint B Rogers, PhD, Prof Jodie L Simpson, PhD

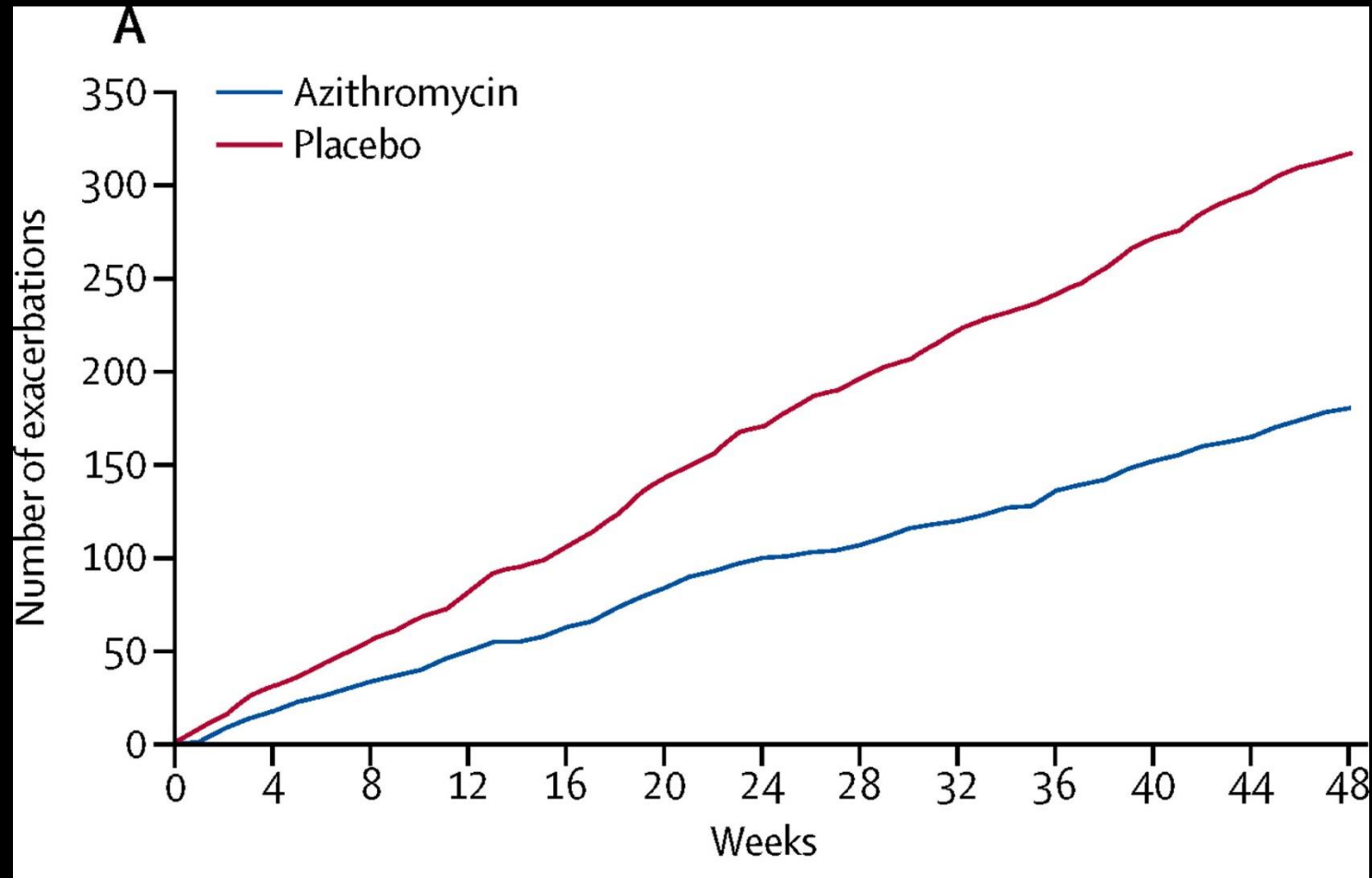
The Lancet

Volume 390, Issue 10095, Pages 659-668 (August 2017)

DOI: 10.1016/S0140-6736(17)31281-3



Figure 2



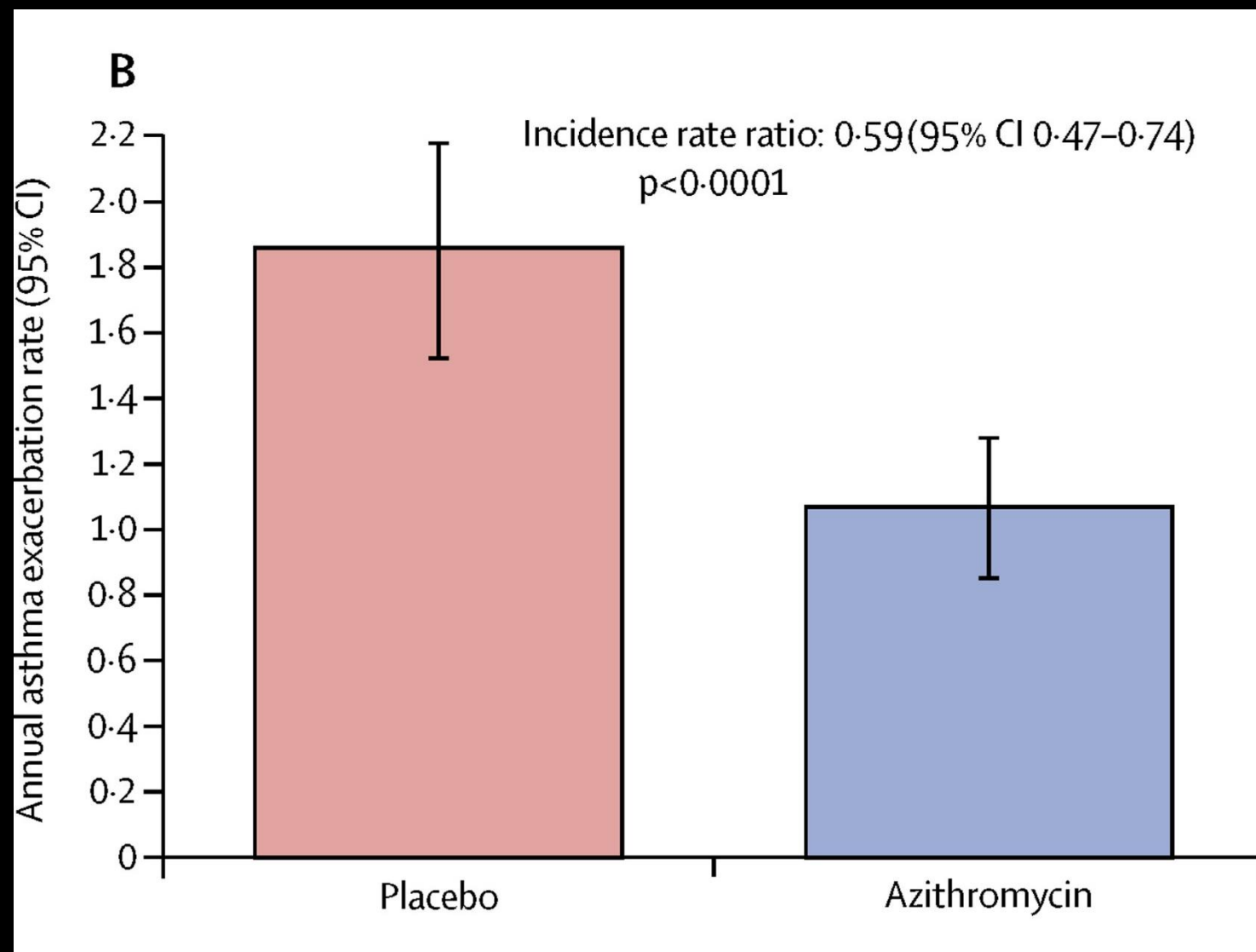
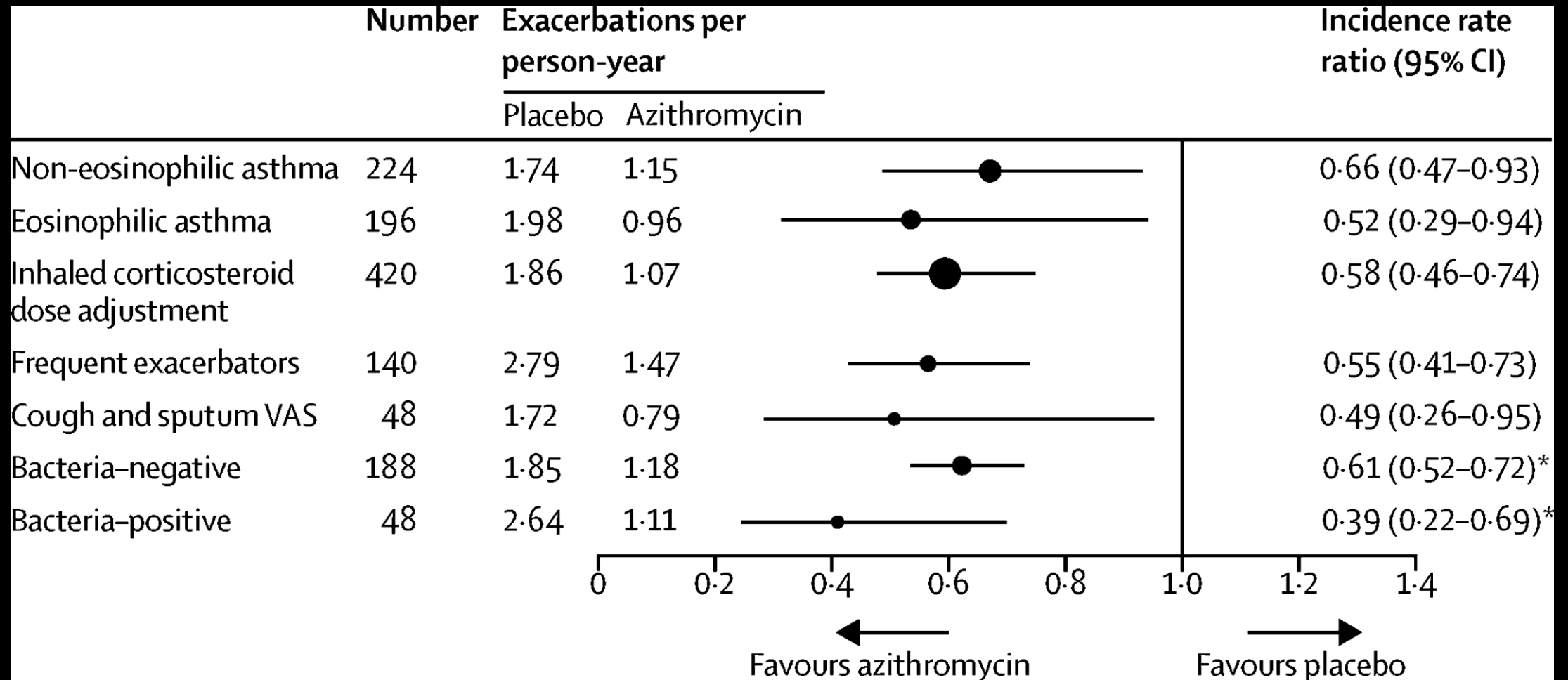


Figure 3



CASE

45 year old female factory worker with atopic asthma

On 'Step 3' ICS/LABA treatment, Fluticasone/salmeterol 50/25 ii BD

Repeat courses of oral steroids for exacerbations

Background of anxiety/depression.

DEFAULT OPTION

The standard stepwise approach would be to either:

- Increase the ICS dose by stepping up to a higher dose FP/SM 100/25 2 bd.
On the basis that this is likely to be ICS responsive eosinophilic asthma.
- Change to budesonide/formoterol 200/6 2 bd and one as required on the basis that a change to the SMART regimen reduces the risk of severe exacerbations.

POTENTIAL TREATABLE TRAITS IN THIS CASE

- Eosinophilic asthma
- Psychogenic vocal cord dysfunction
- Allergic bronchopulmonary aspergillosis
- Chronic rhinosinusitis
- Occupational asthma
- Adherence, inhaler technique