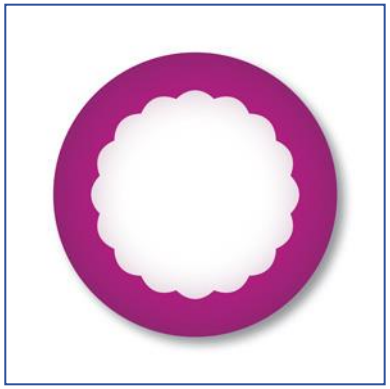
Pneumo Update Europe 2017

9-10 June, Vienna

COPD



David M. G. Halpin, UK

Outline

- GOLD
- screening/diagnosis
- pharmacotherapy
- oxygen
- exacerbations
- comorbidities
- *ACO*
- biomarkers
- α-1 antitrypsin deficiency
- palliative care

Not Included

- Non-invasive Ventilation
- Bronchoscopic Techniques
- Rehabilitation

GOLD 2017

Global Initiative for Chronic Obstructive Lung Disease

Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease

GOLD Report 2017

http://goldcopd.org/gold-2017-global-strategy-diagnosis-management-prevention-copd/

COPD Definition

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Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases.

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COPD definition – some aspects regarding symptoms

- Chronic respiratory symptoms may precede the development of airflow limitation and may be associated with the development of acute respiratory events
- Chronic respiratory symptoms also exist in individuals with normal spirometry
- A significant percentage have structural evidence of lung disease manifested by the varying presence of emphysema, airway wall thickening and gas trapping

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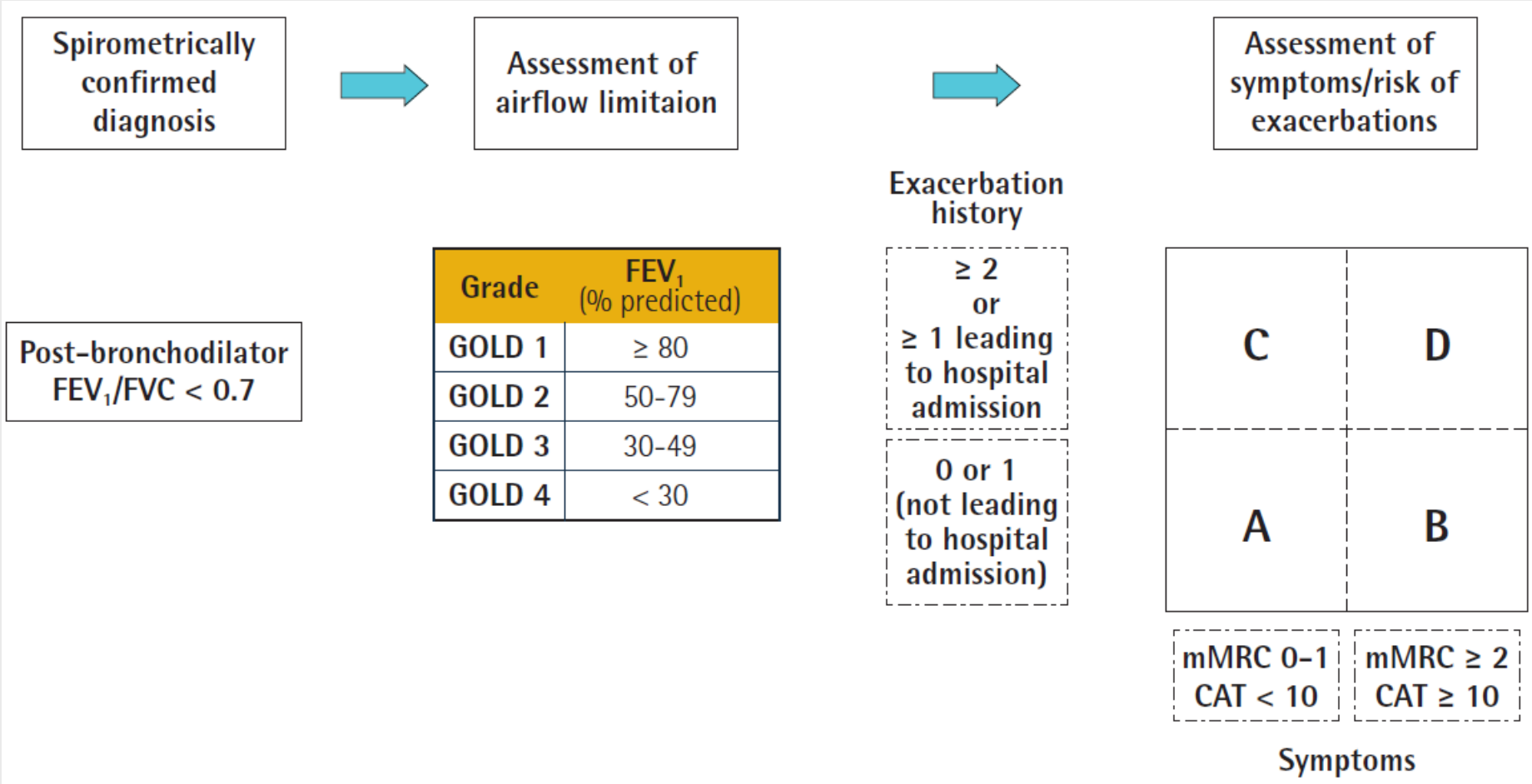
Diagnosis & Assessment



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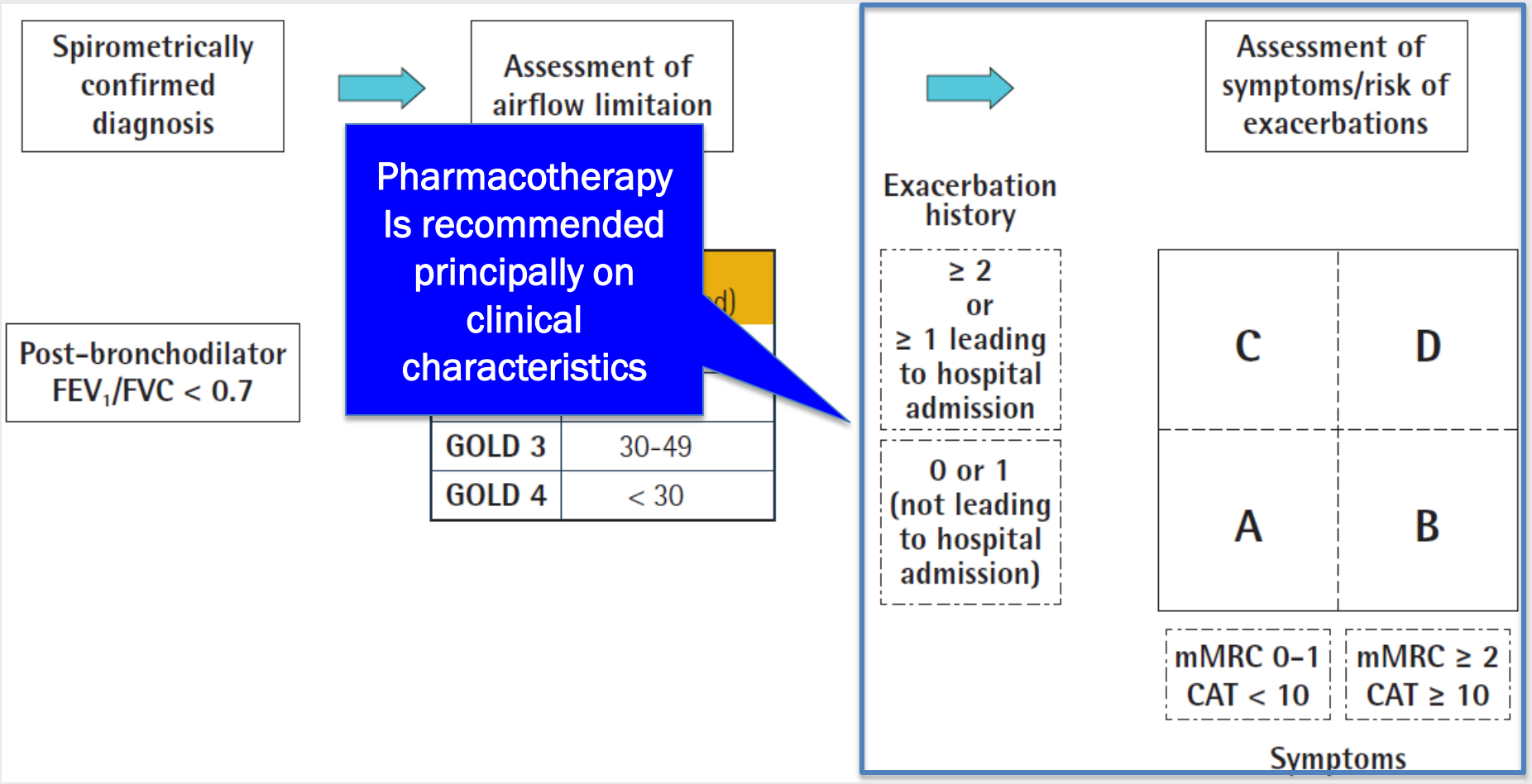
Diagnosis & Assessment



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Spirometry: Its role in COPD

- Diagnosis
- Assessment of severity of airflow obstruction (Prognosis)
- Follow-up assessment
  - Therapeutic decisions
    - Pharmacological changes
    - Consideration of alternative diagnoses
    - Non-pharmacological treatments (e.g., interventional)
  - Identification of rapid decline

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Overview of Treatments

Smoking cessation

Vaccination

Pharmacological treatments

Rehabilitation, education, integrated care

Palliative care, end of life, hospice care

Instrumental support

Surgery

Bronchoscopic techniques

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Goals for Treatment of Stable COPD

- Relieve symptoms
- Improve exercise tolerance
- Improve health status

Reduce symptoms

- Prevent disease progression
- Prevent and treat exacerbations
- Reduce mortality

Reduce risk

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Therapeutic recommendations

Table 4.8. Non-pharmacologic management of COPD			
Patient group	Essential	Recommended	Depending on local guidelines
A	Smoking cessation (can include pharmacologic treatment)	Physical activity	Flu vaccination Pneumococcal vaccination
B–D	Smoking cessation (can include pharmacologic treatment) Pulmonary rehabilitation	Physical activity	Flu vaccination Pneumococcal vaccination

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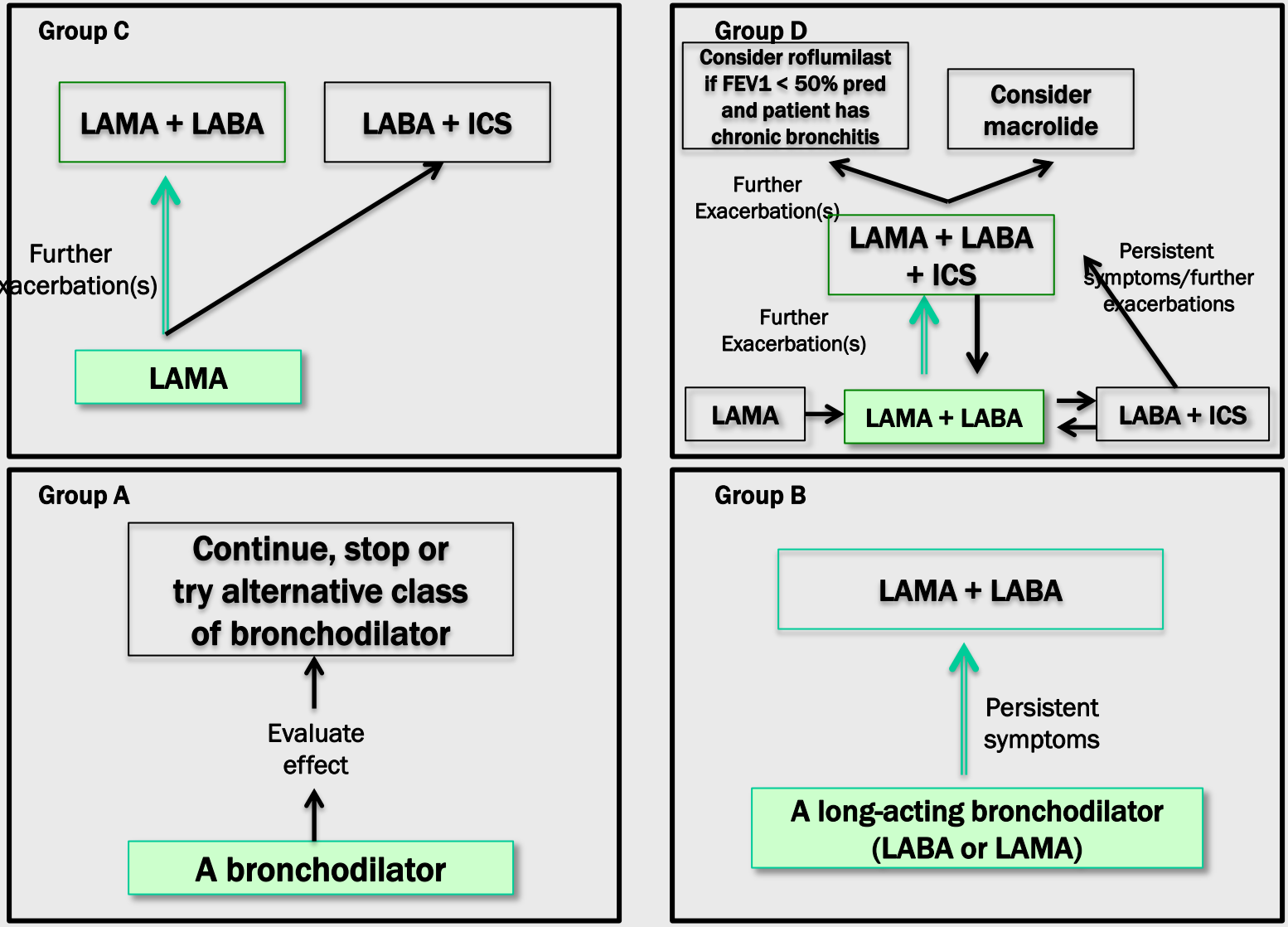
Therapeutic recommendations



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Inhaler devices – key points

- The importance of education and training in inhaler device technique cannot be over-emphasized
- Observational studies have identified a significant relationship between poor inhaler use and symptom control in patients with COPD
- The choice of inhaler device has to be individually tailored and will depend on access, cost, prescriber, and most importantly, patient's ability and preference.
- It is essential to provide instructions and to demonstrate the proper inhalation technique when prescribing a device, to ensure that inhaler technique is adequate and re-check at each visit that patients continue to use their inhaler correctly.
- Inhaler technique (and adherence to therapy) should be assessed before concluding that the current therapy requires modification.

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Non-pharmacological treatments

Pulmonary rehabilitation

- improves dyspnea, health status and exercise tolerance in stable patients (**Evidence A**).
- reduces hospitalizations among patients who have had a recent exacerbation (≤ 4 weeks from prior hospitalization) (**Evidence B**).

Education and self-management

- Education alone has not been shown to be effective (**Evidence C**).
- Self-management intervention with communication with a health care professional improves health status and decreases hospitalizations and emergency department visits (**Evidence B**).

Integrated care programs

- Integrated care and telehealth have no demonstrated benefit at this time (**Evidence B**).

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Palliative care, end of life & hospice care

- Opiates, neuromuscular electrical stimulation (NMES), oxygen and fans blowing air onto the face can relieve ***breathlessness*** (**Evidence** C).
- In ***malnourished*** patients, nutritional supplementation may improve respiratory muscle strength and overall health-related quality of life (**Evidence B**).
- ***Fatigue*** can be improved by self-management education, pulmonary rehabilitation, nutritional support and mind-body interventions (**Evidence B**).

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COPD Exacerbations

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COPD exacerbations are defined as an acute worsening of respiratory symptoms that result in additional therapy.

No significant changes in recommendations on management

- Suggested criteria for admission
- Pharmacotherapy
- Controlled oxygen
- NIV
- Discharge & follow-up

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Comorbidities & Management of COPD

- Whether or not COPD and comorbid diseases are related, management of the COPD patient must include identification and treatment of its comorbidities.

- Comorbidities with symptoms also associated with COPD may be overlooked e.g., heart failure and lung cancer (breathlessness) or depression (fatigue and reduced physical activity).

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Take-Home Messages

- The pharmacological management strategy for stable COPD should be predominantly based on the individualized assessment of symptoms and future risk of exacerbations.
- All individuals who smoke should be strongly encouraged and supported to quit.
- The main treatment goals remain reduction of symptoms and future risk of exacerbations.
- Bronchodilators are the mainstay of pharmacotherapy
- Management strategies are not limited to pharmacological treatments, and should be complemented by appropriate non-pharmacological interventions

Screening/Diagnosis

- Burden in un-diagnosed patients
- Improving diagnostic rates
- Evidence review for US Preventive Services Task Force
- Diagnostic instability
- Clinical features in people without airflow obstruction

Undiagnosed Chronic Obstructive Pulmonary Disease Contributes to the Burden of Health Care Use

Data from the CanCOLD Study

Laura E. Labonté[1], Wan C. Tan[2], Pei Z. Li[1], Palmina Mancino[1], Shawn D. Aaron[3], Andrea Benedetti[1,4], Kenneth R. Chapman[5], Robert Cowie[6], J. Mark FitzGerald[2], Paul Hernandez[7], François Maltais[8], Darcy D. Marciniuk[9], Dennis O'Donnell[10], Don Sin[2], and Jean Bourbeau[1]; for the Canadian Respiratory Research Network and the CanCOLD Collaborative Research Group*

- Most subjects with COPD in Canada remain undiagnosed
- These subjects are less symptomatic and impaired
- Patients with undiagnosed COPD experience fewer exacerbations than those with diagnosed COPD
- But they use a similar amount of health services for exacerbation events
- The overall health system burden of exacerbations in those with undiagnosed COPD is considerable

Labonte et al. Am J Respir Crit Care Med 2016;194(3):285-98

Targeted case finding for chronic obstructive pulmonary disease versus routine practice in primary care (TargetCOPD): a cluster-randomised controlled trial

Rachel E Jordan, Peymané Adab, Alice Sitch, Alexandra Enocson, Deirdre Blissett, Sue Jowett, Jen Marsh, Richard D Riley, Martin R Miller, Brendan G Cooper, Alice M Turner, Kate Jolly, Jon G Ayres, Shamil Haroon, Robert Stockley, Sheila Greenfield, Stanley Siebert, Amanda J Daley, K K Cheng, David Fitzmaurice

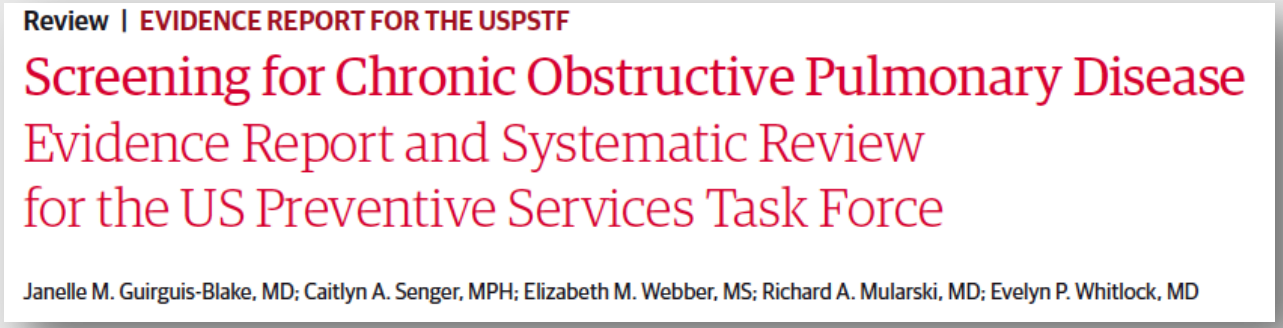
- COPD detected in 4% of targeted case finding patients v 1% in routine care

Case finding for chronic obstructive pulmonary disease in people attending long-term condition clinics in primary care

DMG Halpin, S Holmes, J Calvert and D McInerney

- 22% had symptoms and low FEV_1

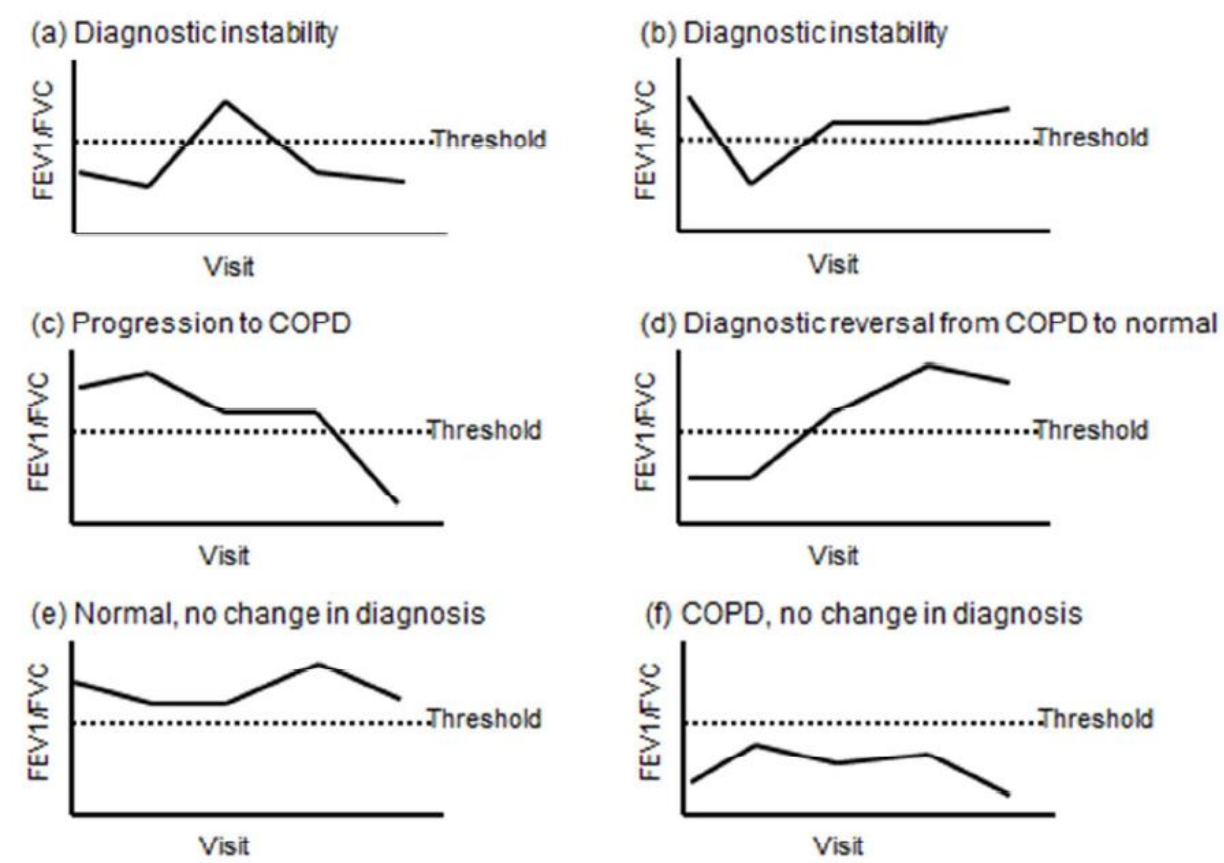
Jordan et al. Lancet Respir Med 2016;4(9):720-30
Halpin et al. Chron Respir Dis 2016;13(4):337–343



- There was no direct evidence available to determine the benefits and harms of screening asymptomatic adults for COPD using questionnaires or office-based screening pulmonary function testing or to determine the benefits of treatment in screen-detected populations.
- Indirect evidence suggests that the COPD Diagnostic Questionnaire has moderate overall performance for COPD detection.
- Among patients with mild to moderate COPD, the benefit of pharmacotherapy for reducing exacerbations was modest.

Guirguis-Blake et al. JAMA 2016;315(13):1378-93

Diagnostic Instability and Reversals of COPD Diagnosis in Subjects with Mild to Moderate Airflow Obstruction



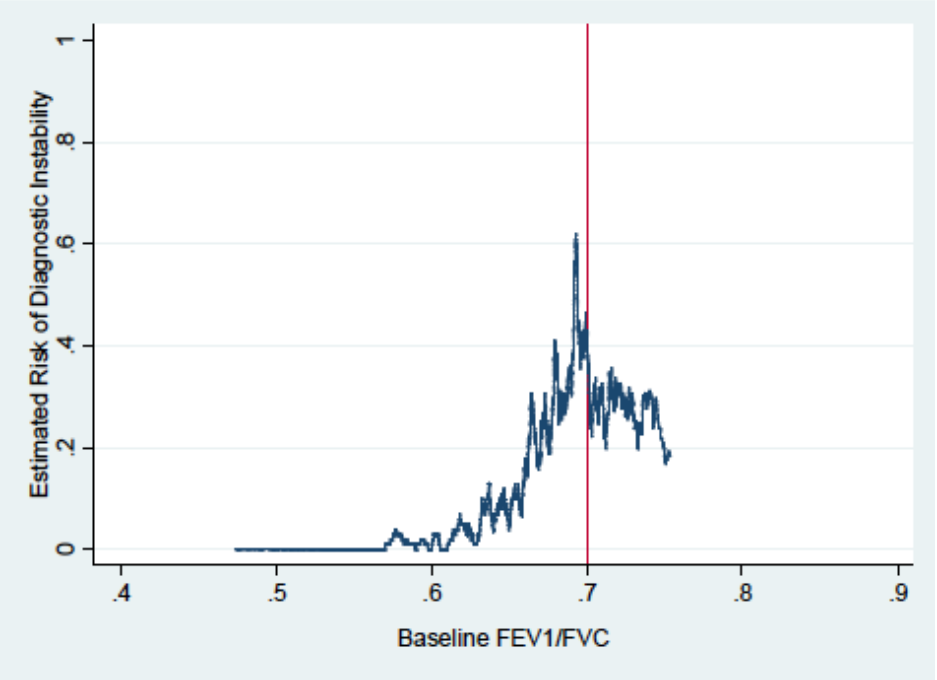
Aaron et al. Am J Respir Crit Care Med 2017 10.1164/rccm.201612-2531OC

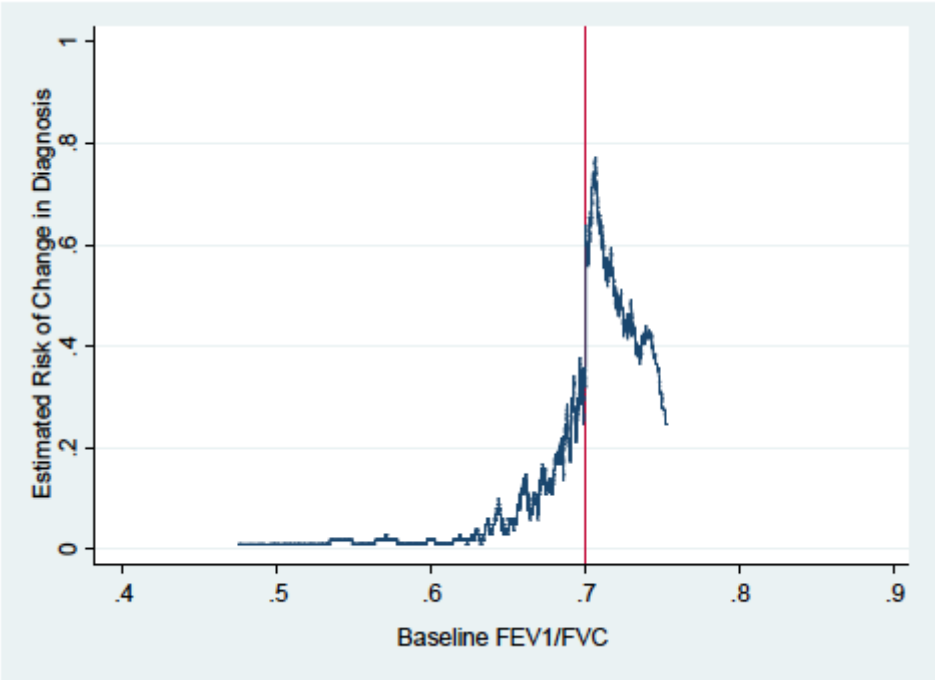
Diagnostic Instability and Reversals of COPD Diagnosis in Subjects with Mild to Moderate Airflow Obstruction

- 12-27% of subjects with mild to moderate COPD at baseline reversed their diagnosis of COPD over a 4 to 5 year period.
- There is considerable variability of spirometry results around the FEV_1/FVC threshold
- A single spirometric assessment may not be reliable to diagnose COPD in patients with mild to moderate airflow obstruction.

Aaron et al. Am J Respir Crit Care Med 2017 10.1164/rccm.201612-2531OC

Diagnostic Instability and Reversals of COPD Diagnosis in Subjects with Mild to Moderate Airflow Obstruction





Aaron et al. Am J Respir Crit Care Med 2017 10.1164/rccm.201612-2531OC

Clinical Significance of Symptoms in Smokers with Preserved Pulmonary Function

Prescott G. Woodruff, M.D., R. Graham Barr, M.D., Dr.P.H., Eugene Bleecker, M.D., Stephanie A. Christenson, M.D., David Couper, Ph.D., Jeffrey L. Curtis, M.D., Natalia A. Gouskova, Ph.D., Nadia N. Hansel, M.D., Eric A. Hoffman, Ph.D., Richard E. Kanner, M.D., Eric Kleerup, M.D., Stephen C. Lazarus, M.D., Fernando J. Martinez, M.D., Robert Paine, III, M.D., Stephen Rennard, M.D., Donald P. Tashkin, M.D., and MeiLan K. Han, M.D., for the SPIROMICS Research Group*

- Exacerbations, activity limitation, and evidence of airway disease (lower FEV_1 & wall thickening)
- Use respiratory medications without any evidence base.

Clinical Features of Smokers With Radiological Emphysema But Without Airway Limitation

Ana B. Alcaide, MD; Pablo Sanchez-Salcedo, MD; Gorka Bastarrika, MD; Arantza Campo, MD; Juan Berto, MD; Maria del Mar Ocon, RN; Alejandro Fernandez-Montero, MD, PhD; Bartolome R. Celli, MD; Javier J. Zulueta, MD; and Juan P. de-Torres, MD

- Alterations in quality of life, number of exacerbations, DLCO & oxygen saturation during the 6MWT test

Woodruff et al. N Engl J Med 2016;374(19):1811-21
Alcaide et al. CHEST 2017;151(2):358-65

Take-Home Message

- People with undiagnosed COPD have morbidity
- Case finding is effective, population screening is not
- There is some diagnostic instability
- People have symptoms and/or pathology of COPD without meeting spriometric criteria

Pharmacotherapy

- LABA/LAMA
  - v LABA or LAMA
  - v LABA/ICS
- “Triple therapy”
- PDE4 Inhibitors

- *Adherence*

LABA/LAMA

Beeh et al. Int J Chron Obstruct Pulmon Dis 2016;11:193-205
Derom et al. Int J Chron Obstruct Pulmon Dis 2016;11:3163-77
Donohue et al. Respir Med 2016;112:65-74
Donohue et al. Respir Med 2016;116:41-8
Ferguson et al. Int J Chron Obstruct Pulmon Dis 2016;11:2701-10
Ferguson et al. NPJ Prim Care Respir Med 2017;27(1):7
Martinez et al. CHEST 2017;151(2):340-57
Singh et al. Int J Chron Obstruct Pulmon Dis 2016;11:1413-24
Vogelmeier et al. Int J Chron Obstruct Pulmon Dis 2016;11:3189-97
Watz et al. BMC Pulm Med 2016;16(1):95
Wedzicha et al. N Engl J Med 2016;374(23):2222-34

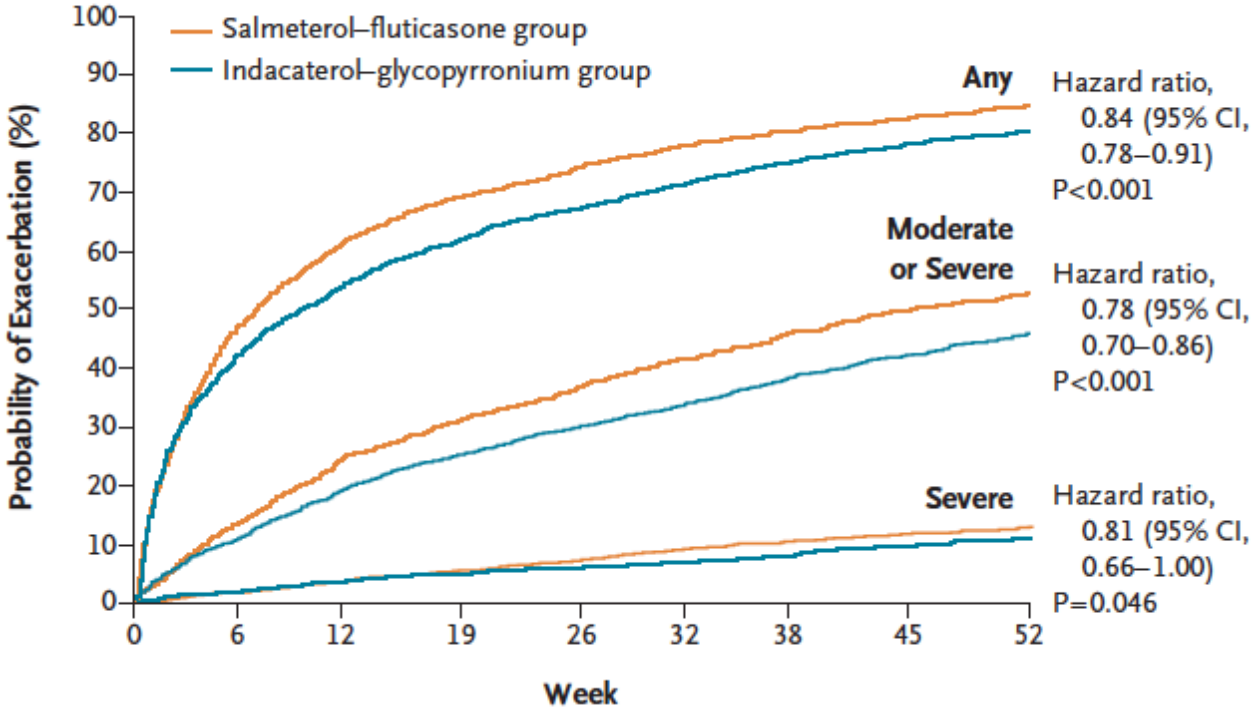
Rodrigo et al. Int J Chron Obstruct Pulmon Dis 2017;12:907-22
Horita et al. Cochrane Database Syst Rev 2017;2:CD012066

LABA/LAMA

- LABA/LAMA
  - Increase FEV_1 v mono-components
  - Improve PROs v mono-components
  - increase FEV_1 v LABA/ICS
  - reduce exacerbation rates v LABA/ICS
  - increase exercise capacity v mono-components

Indacaterol–Glycopyrronium versus Salmeterol–Fluticasone for COPD

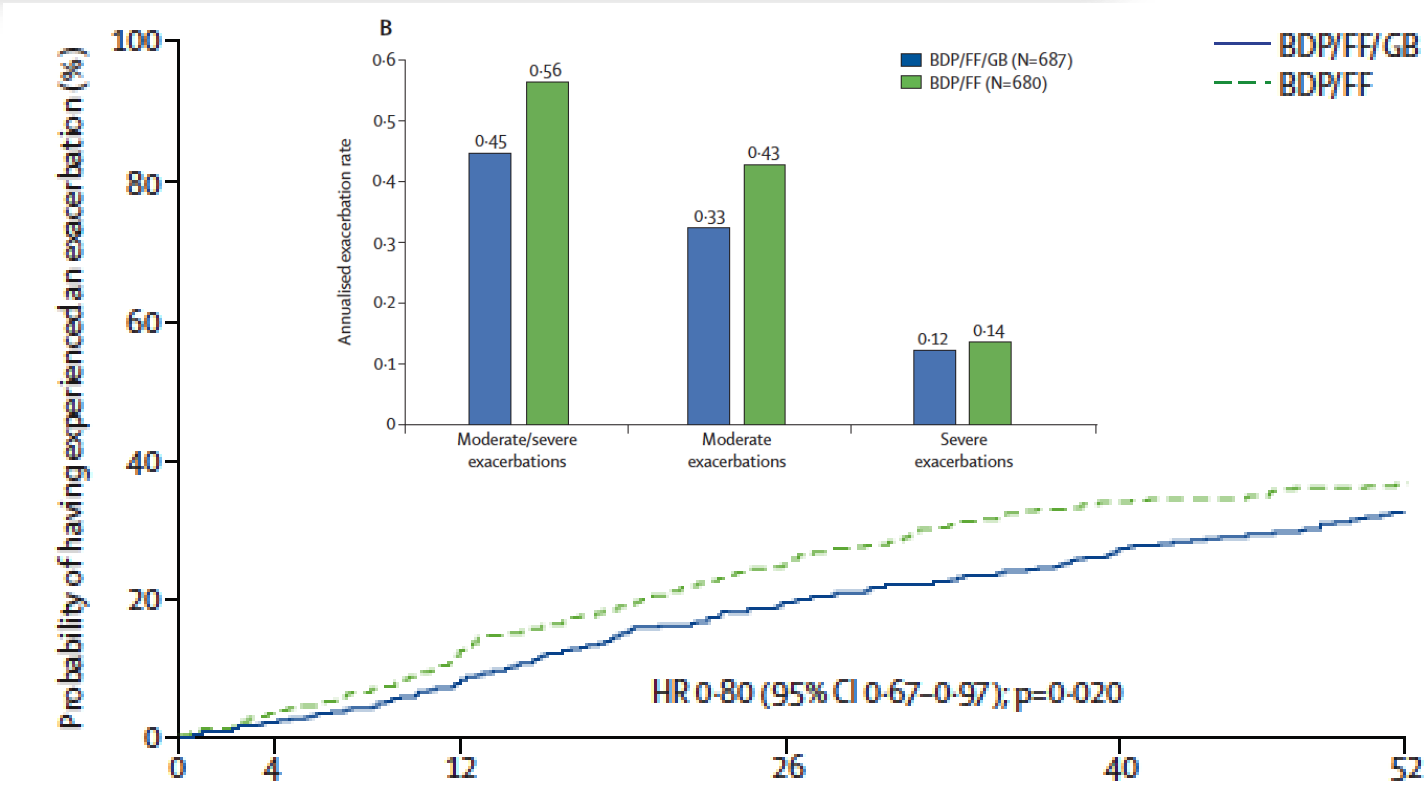
Jadwiga A. Wedzicha, M.D., Donald Banerji, M.D., Kenneth R. Chapman, M.D., Jørgen Vestbo, M.D., D.M.Sc., Nicolas Roche, M.D., R. Timothy Ayers, M.Sc., Chau Thach, Ph.D., Robert Fogel, M.D., Francesco Patalano, M.D., and Claus F. Vogelmeier, M.D., for the FLAME Investigators*



Wedzicha et al.. N Engl J Med 2016;374(23):2222-34

Single inhaler triple therapy versus inhaled corticosteroid plus long-acting β_2-agonist therapy for chronic obstructive pulmonary disease (TRILOGY): a double-blind, parallel group, randomised controlled trial

Dave Singh, Alberto Papi, Massimo Corradi, Ilona Pavlišová, Isabella Montagna, Catherine Francisco, Géraldine Cohuet, Stefano Vezzoli, Mario Scuri, Jørgen Vestbo



Singh et al. Lancet 2016; 388: 963-73

FULFIL Trial: Once-Daily Triple Therapy in Patients with Chronic Obstructive Pulmonary Disease

David A. Lipson[1,2], Helen Barnacle[3], Ruby Birk[3], Noushin Brealey[3], Nicholas Locantore[1], David A. Lomas[4], Andrea Ludwig-Sengpiel[5], Rajat Mohindra[3*], Maggie Tabberer[3], Chang-Qing Zhu[3], and Steven J. Pascoe[1]

Annual rate of COPD exacerbations	Up to 24 weeks		Up to 52 weeks	
	FF/UMEC/VI 100/62.5/25 (n=911)	BUD/FOR 400/12 (n=899)	FF/UMEC/VI 100/62.5/25 (n=210)	BUD/FOR 400/12 (n=220)
Population, n	907	892	210	219
Moderate and severe exacerbations				
Mean rate	0.22	0.34	0.20	0.36
Ratio (95% CI); p-value	0.65 (0.49 to 0.86); 0.002		0.56 (0.37 to 0.85); 0.006	
Reduction in rate, % (95% CI)	35 (14 to 51)		44 (15 to 63)	
Mild, moderate and severe exacerbations				
Mean rate	0.25	0.39	0.22	0.40
Ratio (95% CI); p-value	0.65 (0.50 to 0.84); <0.001		0.55 (0.37 to 0.81); 0.003	
Reduction in rate, % (95% CI)	35 (16 to 50)		45 (19 to 63)	

Ratios and p-values are calculated for FF/UMEC/VI vs BUD/FOR

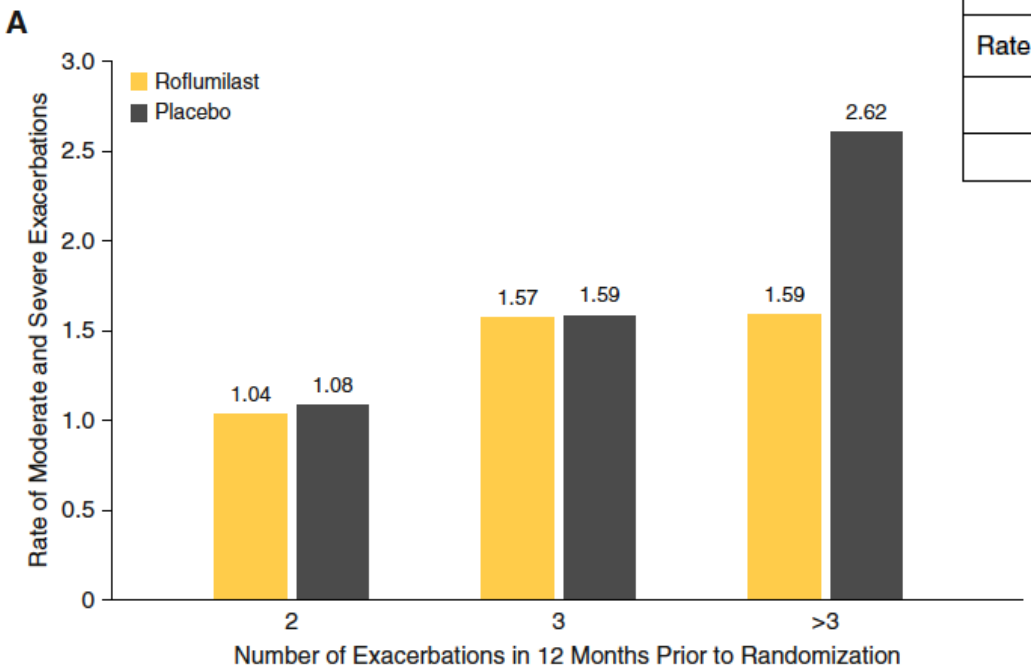
Lipson et al. Am J Respir Crit Care Med 2017 10.1164/rccm.201703-0449OC

Effect of Roflumilast and Inhaled Corticosteroid/Long-Acting β_2-Agonist on Chronic Obstructive Pulmonary Disease Exacerbations (RE^{2}SPOND)

A Randomized Clinical Trial

Fernando J. Martinez[1], Klaus F. Rabe[2,3,4], Sanjay Sethi[5], Emilio Pizzichini[6], Andrew McIvor[7], Antonio Anzueto[8,9], Vijay K. T. Alagappan[10], Shahid Siddiqui[10], Ludmyla Rekeda[11], Christopher J. Miller[10], Sofia Zetterstrand[12], Colin Reisner[13], and Stephen I. Rennard[14,15]

- Severe COPD with bronchitis and history of exacerbations treated with LABA/ICS



	Roflumilast (n=1,178)	Placebo (n=1,174)
Rate Per Patient Per Year (95%, CI)	1.17 (1.06, 1.28)	1.27 (1.17, 1.39)
RR (95%, CI)	0.92 (0.81, 1.04)	
P-Value	*P*=0.163	

- Withdrawls: 11.7% v 5.4%
- Weight loss: 8% v 2%

Martinez et al. Am J Respir Crit Care Med 2017;195(7):881-8

Oxygen

A Randomized Trial of Long-Term Oxygen for COPD with Moderate Desaturation

The Long-Term Oxygen Treatment Trial Research Group*

- 738 patients with stable COPD and resting or exercise-induced moderate desaturation
- long-term supplemental oxygen did not result in a longer time to death or first hospitalization than no long-term supplemental oxygen
- no consistent benefit on quality of life, lung function, and 6MWD

Albert et al. N Engl J Med 2016;375(17):1617-27

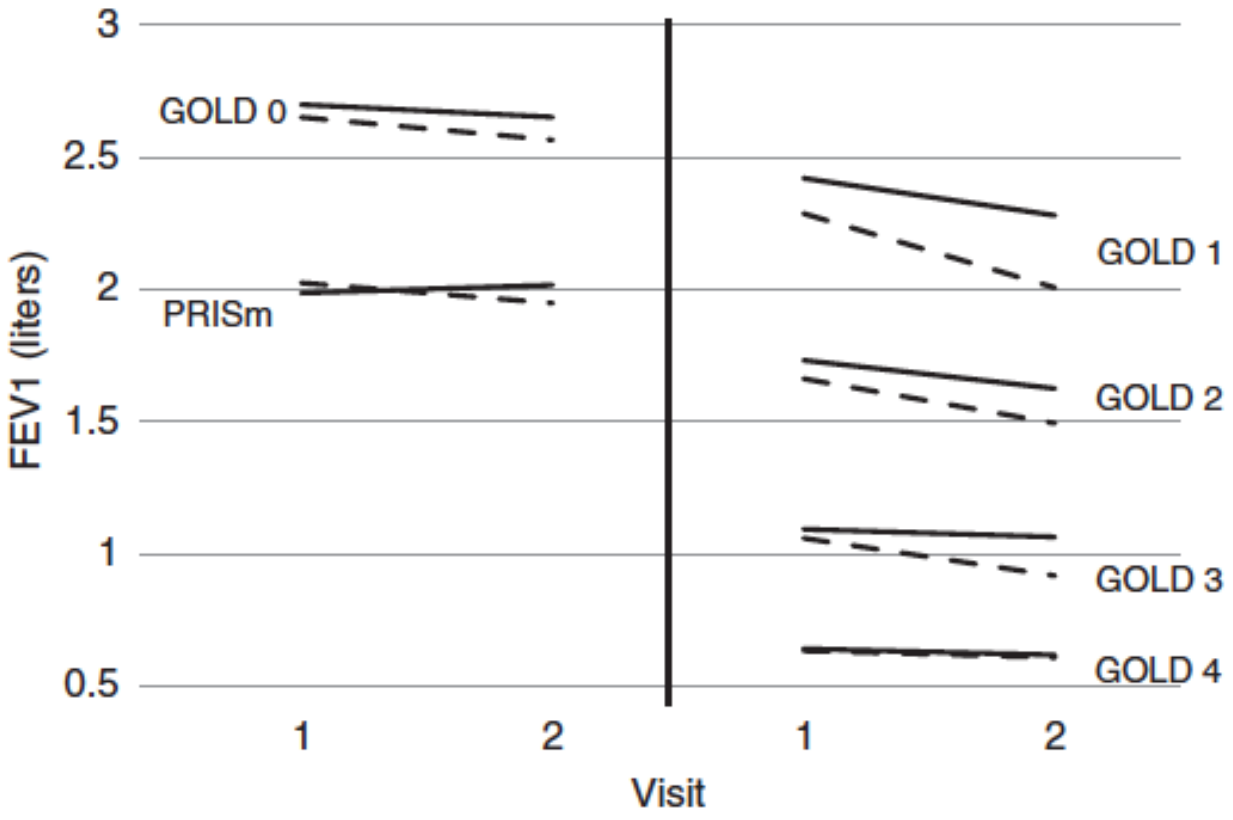
Take-Home Message

- Evidence for benefits of dual bronchodilator therapy is growing
- Evidence for benefit of adding LAMA to LABA/ICS is emerging
- PDE4 inhibitors added to LABA/ICS ± LAMA have benefits in frequent exacerbators
- LTOT remains indicated only in people with severe resting hypoxaemia

Exacerbations

Acute Exacerbations and Lung Function Loss in Smokers with and without Chronic Obstructive Pulmonary Disease

Mark T. Dransfield[1,2*], Ken M. Kunisaki[3,4*], Matthew J. Strand[5], Antonio Anzueto[6,7], Surya P. Bhatt[1], Russell P. Bowler[5], Gerard J. Criner[8], Jeffrey L. Curtis[9,10], Nicola A. Hanania[11], Hrudaya Nath[1], Nirupama Putcha[12], Sarah E. Roark[9], Emily S. Wan[13], George R. Washko[13], J. Michael Wells[1,2], Christine H. Wendt[3,4], and Barry J. Make[5]; for the COPDGene Investigators

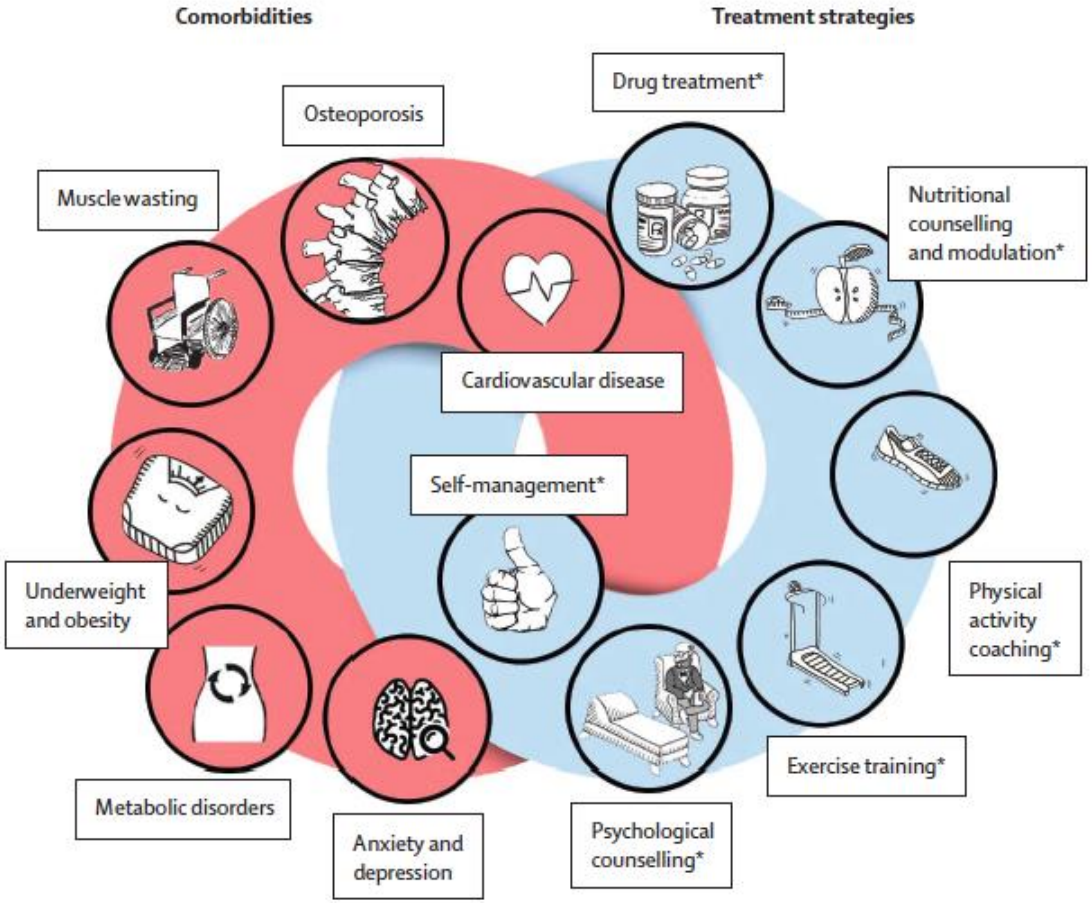


Dransfield et al. Am J Respir Crit Care Med 2017;195(3):324-30

Comorbidities

Management of chronic obstructive pulmonary disease beyond the lungs

Lowie E G W Vanfleteren, Martijn A Spruit, Emiel F M Wouters, Frits M E Franssen



Vanfleteren et al. Lancet Respir Med 2016;4(11):911-24

Impact of chronic obstructive pulmonary disease on prognosis in atrial fibrillation: A report from the EURObservational Research Programme Pilot Survey on Atrial Fibrillation (EORP-AF) General Registry

Marco Proietti, MD, [a] Cécile Laroche, MSc, [b] Marcin Drozd, MD, [c,d] Johan Vijgen, MD, [e] Dragos C. Cozma, MD, [f] Jaroslaw Drozdz, MD, PhD, [g] Aldo P. Maggioni, MD, PhD, [b,h] Giuseppe Boriani, MD, PhD, [i,j] and Gregory Y. H. Lip, MD [a,k], on behalf of EORP-AF Investigators *Birmingham, United Kingdom; Sophia Antipolis, France; Wroclaw, Poland; Hasselt, Belgium; Timisoara, Romania; Lodz, Poland; Firenze, Bologna, Modena, Italy; and Aalborg, Denmark*

- In people with AF, COPD was associated with higher rates of:
  - CV death,
  - all-cause death,
  - composite outcome of any thromboembolic event/bleeding/CV death.

Proietti et al. Am Heart J 2016;181:83-91

Alpha-1 Antitrypsin Deficiency

Diagnosis of alpha-1 antitrypsin deficiency: a population-based study

- 12,409 AAT determinations
  - 663 (5.3%) had intermediate AATD (50–100 mg/dL),
  - 24 (0.2%) individuals had a severe deficiency (<50 mg/dL)
- 9 (41%) of the adults with severe deficiency had a previous diagnosis of COPD/emphysema,
- 4 (16.7%) were diagnosed with COPD within 6 months.

Barrecheguren et al. Int J Chron Obstruct Pulmon Dis 2016;11:999-1004

Intravenous alpha-1 antitrypsin augmentation therapy for treating patients with alpha-1 antitrypsin deficiency and lung disease (Review)

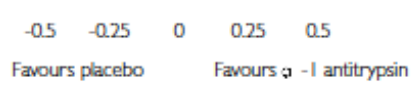
Gøtzsche PC, Johansen HK

Study or subgroup	Alpha-1 antitrypsin N	Mean(SD)	Placebo N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
Chapman 2015	83	-3.1 (10.7)	67	-2.3 (13.1)		53.0 %	-0.07 [-0.39, 0.25]
Dirksen 1999	28	-78.9 (63.5)	28	-59.1 (63)		19.8 %	-0.31 [-0.84, 0.22]
Dirksen 2009	38	-43 (60.1)	39	-23 (60.9)		27.2 %	-0.33 [-0.78, 0.12]
Total (95% CI)	**149**		**134**			**100.0 %**	**-0.19 [-0.42, 0.05]**

Heterogeneity: $Chi^2 = 1.11$, $df = 2$ ($P = 0.57$); $I^2 = 0.0\%$

Test for overall effect: $Z = 1.55$ ($P = 0.12$)

Test for subgroup differences: Not applicable

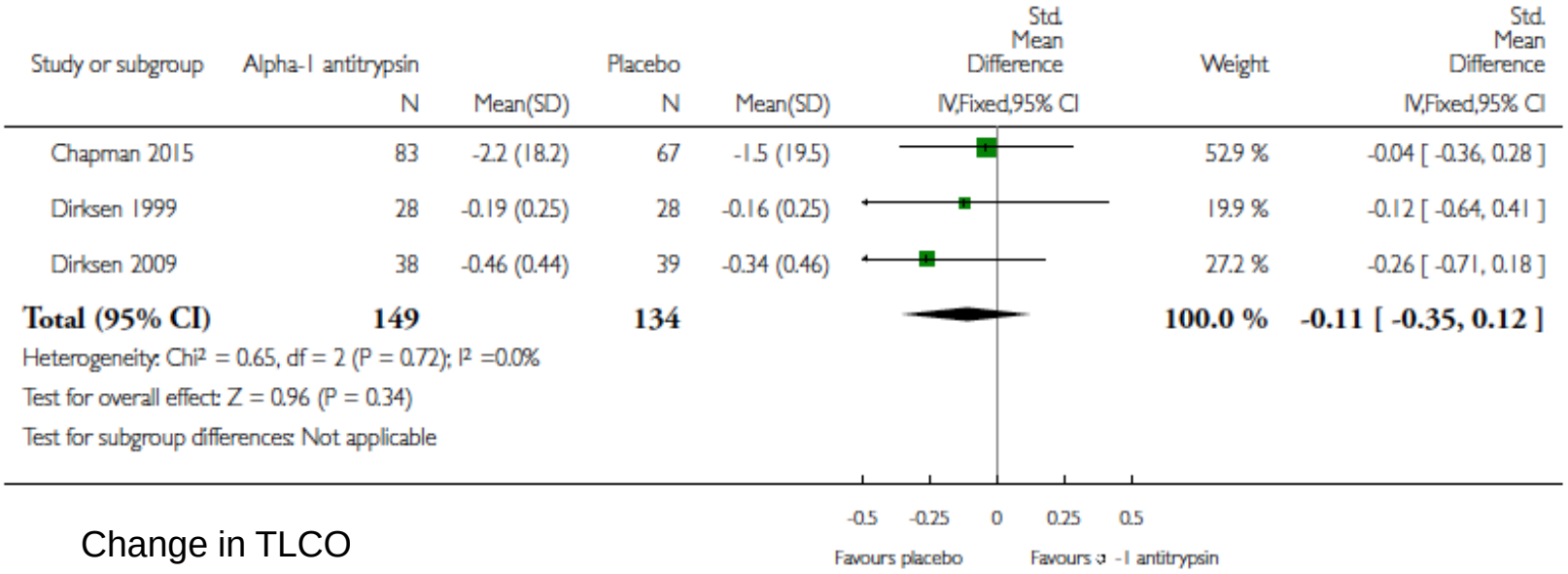


Change in FEV_1

Gotzsche et al. Cochrane Database Syst Rev 2016;9:CD007851

Intravenous alpha-1 antitrypsin augmentation therapy for treating patients with alpha-1 antitrypsin deficiency and lung disease (Review)

Gøtzsche PC, Johansen HK



Change in TLCO

Gotzsche et al. Cochrane Database Syst Rev 2016;9:CD007851

Does Protease–Antiprotease Imbalance Explain Chronic Obstructive Pulmonary Disease?

David A. Lomas

Wolfson Institute for Biomedical Research, Division of Medicine, University College London, London, United Kingdom

- Articulates why suppression of protease activity in alpha-1 antitrypsin deficiency may be insufficient to prevent the progression of COPD

- Alpha-1 antitrypsin deficiency may be better treated by:
  - small-molecules that that block the intracellular polymerization of Z alpha-1 antitrypsin
  - RNA-silencing to reduce inclusion body formation
  - other strategies that target protein misfolding

Lomas. Ann Am Thorac Soc 2016;13 Suppl 2:S130-7

Take-Home Message

- alpha-1 antitrypsin deficiency is rare
- impact of augmentation therapy on mortality, exacerbations, hospitalization & quality of life remains uncertain
- new approaches may be more effective

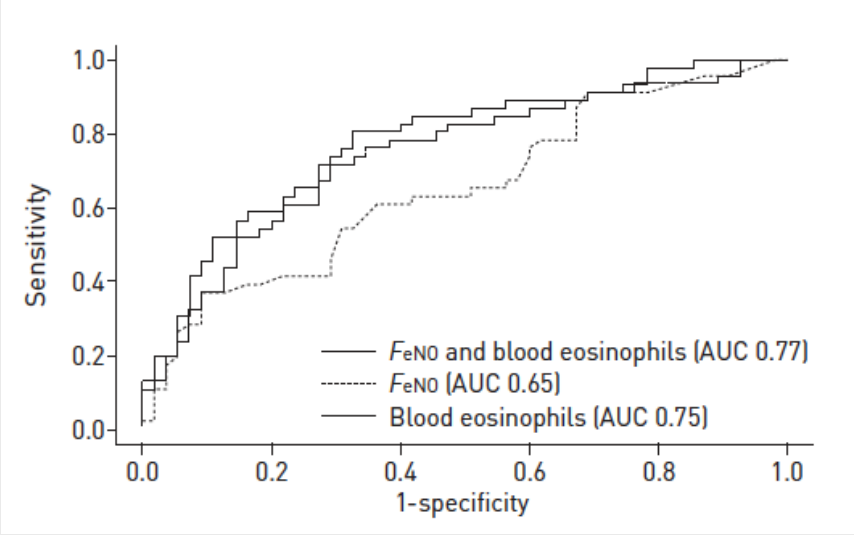
Biomarkers

Eosinophils

- Blood or sputum
- Markers of exacerbation risk
  - cut point or continuous ?
- Markers of ICS response
  - Exacerbations
  - Decline in FEV1
- Response to withdrawing ICS

Blood eosinophil count to predict bronchial eosinophilic inflammation in COPD

Schleich et al. Eur Respir J 2016;47(5):1562-4



Peripheral blood eosinophils: a surrogate marker for airway eosinophilia in stable COPD

Negewo et al. Int J Chron Obstruct Pulmon Dis 2016;11:1495-504

Stability of blood eosinophils in COPD and controls and the impact of gender, age, smoking and baseline counts

Olorunfemi A. Oshagbemi, MPH[1-4], Andrea M. Burden PhD [1,2,3], Dionne C.W. Braeken, MSc[3,4,6], Yvonne Henskens PhD[7], Emiel F.M. Wouters MD PhD[4,6], Johanna H.M. Driessen[1,2,3], Anke H Maitland-van der Zee[3], Frank de Vries, PharmD PhD[1,2,,5] Frits M.E. Franssen, MD PhD[4,6]

Table 1: Baseline characteristics of COPD patients and non-COPD controls				
Characteristics	**COPD patients (n=39,824)**		**Non-COPD controls (n=90,772)**	
Index Blood eosinophil count				
Absolute eosinophil count (x10^9 cells/L)*	0.23	0.26	0.21	0.35
Eosinophil counts (%) *	3.0	3·2	2.9	3·0
Low (<2.0%)	14,492	36·4	33,486	36·9
Moderate (2.0%- 3.9%)	15,231	38·3	35,755	39·4
High(4.0%-5.9%)	6,496	16·3	14,644	16·1
Very High(≥6.0%)	3,605	9·2	6,887	7·6

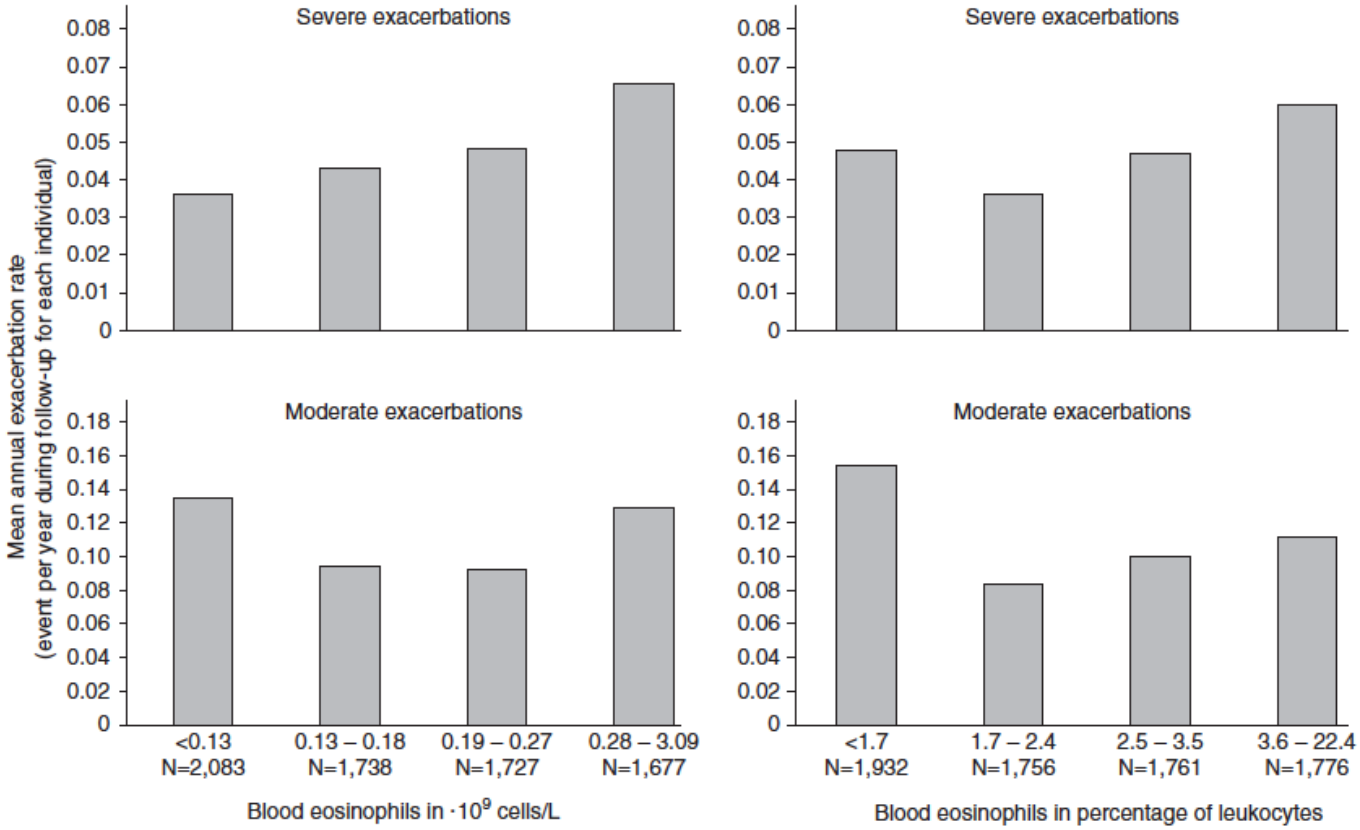
	6 months	9 months	1 year	2 years	4 years	6 years	8 years
COPD patients	85%	82%	75%	62%	49%	42%	35%
Absolute blood eosinophil count(cells/L)							
<0.34 x 10^9 cells/L	95%	93%	90%	86%	80%	77%	75%
≥0.34 x 10^9 cells/L	80%	70%	63%	45%	30%	23%	18%

Oshagbemi et al. Am J Respir Crit Care Med 2017 10.1164/rccm.201701-0009LE

Blood Eosinophils and Exacerbations in Chronic Obstructive Pulmonary Disease

The Copenhagen General Population Study

Signe Vedel-Krogh[1,2,3], Sune F. Nielsen[1,2,3], Peter Lange[3,4,5], Jørgen Vestbo[6], and Børge G. Nordestgaard[1,2,3]



Vedel-Krogh et al. Am J Respir Crit Care Med 2016;193(9):965-74

Blood Eosinophils and Exacerbations in Chronic Obstructive Pulmonary Disease

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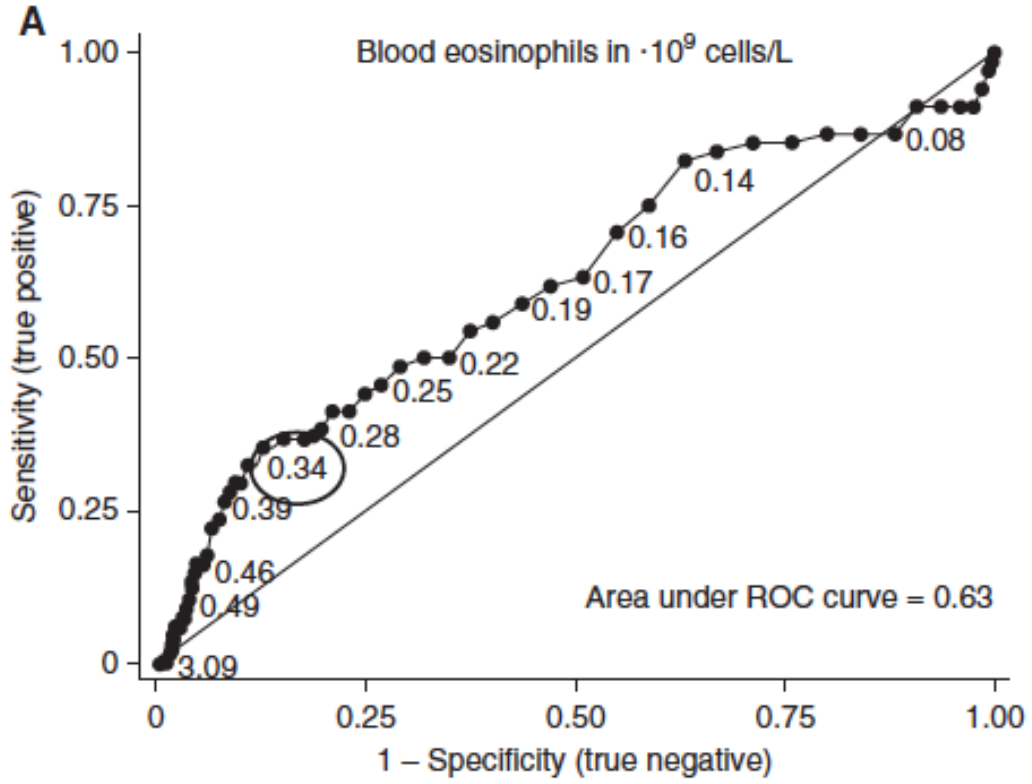
Signe Vedel-Krogh[1,2,3], Sune F. Nielsen[1,2,3], Peter Lange[3,4,5], Jørgen Vestbo[6], and Børge G. Nordestgaard[1,2,3]



Vedel-Krogh et al. Am J Respir Crit Care Med 2016;193(9):965-74

Blood Eosinophils and Exacerbations in Chronic Obstructive Pulmonary Disease

The Copenhagen General Population Study

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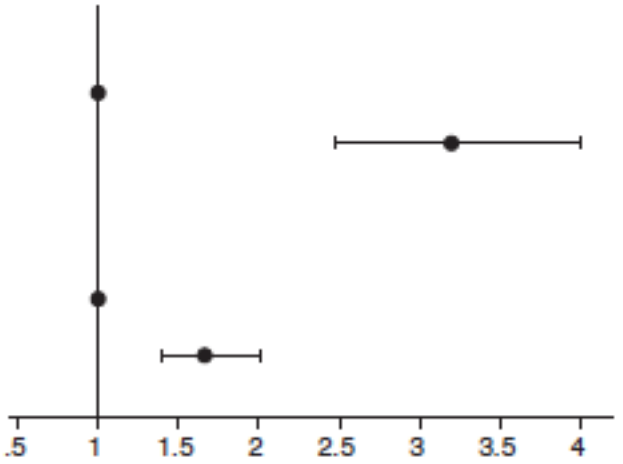
Clinical COPD

Blood eosinophils	N/Events	Person years of follow-up	IRR (95% CI)
Severe exacerbations			
< 0.34 ·10^9 cells/L (ref.)	165/194	593	1.00
≥ 0.34 ·10^9 cells/L	38/110	140	3.21 (2.49–4.14)
Moderate exacerbations			
< 0.34 ·10^9 cells/L (ref.)	165/492	593	1.00
≥ 0.34 ·10^9 cells/L	38/166	140	1.69 (1.40–2.04)



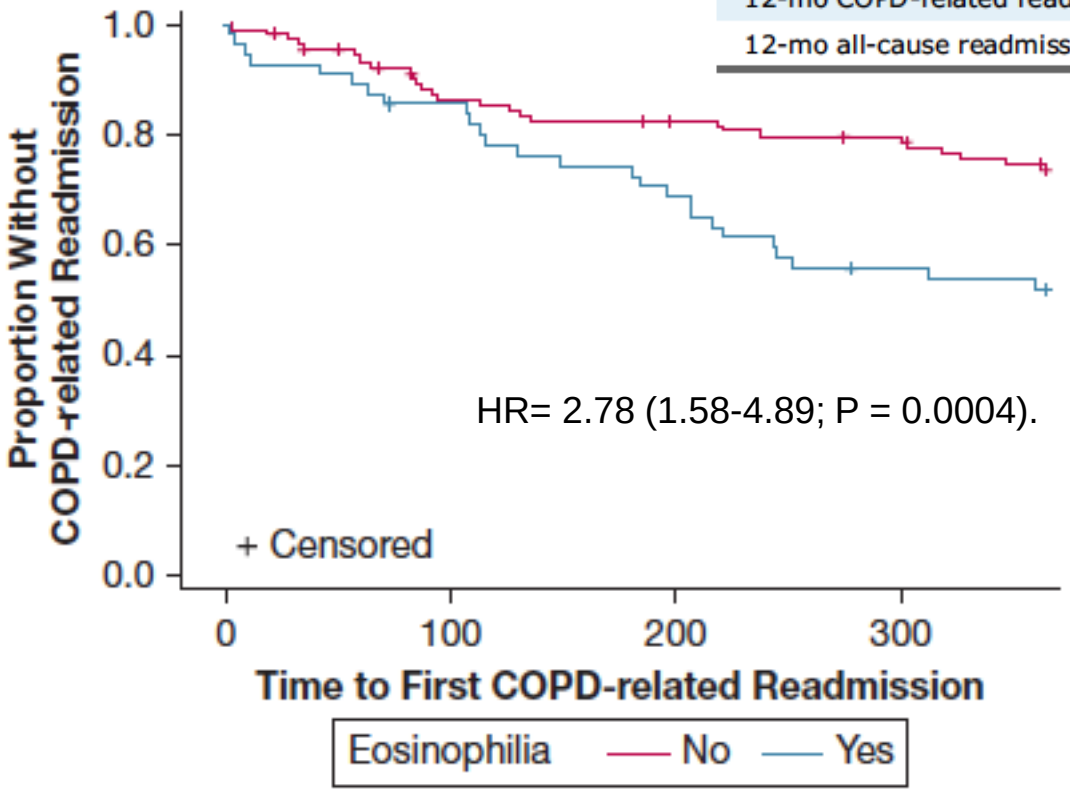
Vedel-Krogh et al. Am J Respir Crit Care Med 2016;193(9):965-74

Eosinophils in COPD Exacerbations Are Associated With Increased Readmissions

Simon Couillard, MD; Pierre Larivée, MD; Josiane Courteau, PhD; and Alain Vanasse, MD, PhD

Outcome	Eosinophilic COPD (n = 55) No. (%)	Noneosinophilic COPD (n = 112) No. (%)
12-mo COPD-related readmission *	26 (47.3)	28 (25.0)
12-mo all-cause readmission	37 (67.3)	60 (53.6)

*Adjusted OR: 3.59 [1.65-7.82]

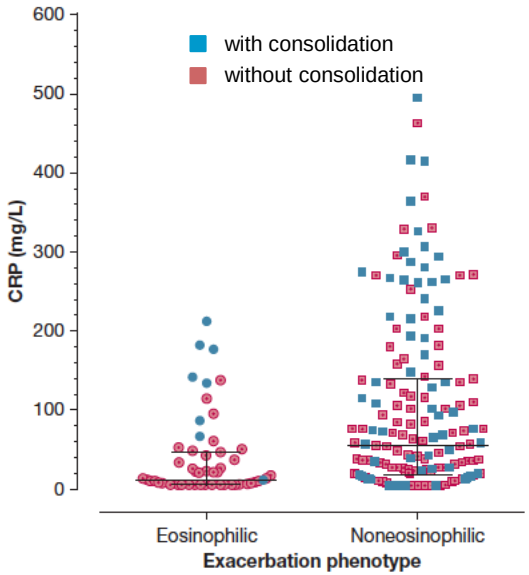


HR= 2.78 (1.58-4.89; P = 0.0004).

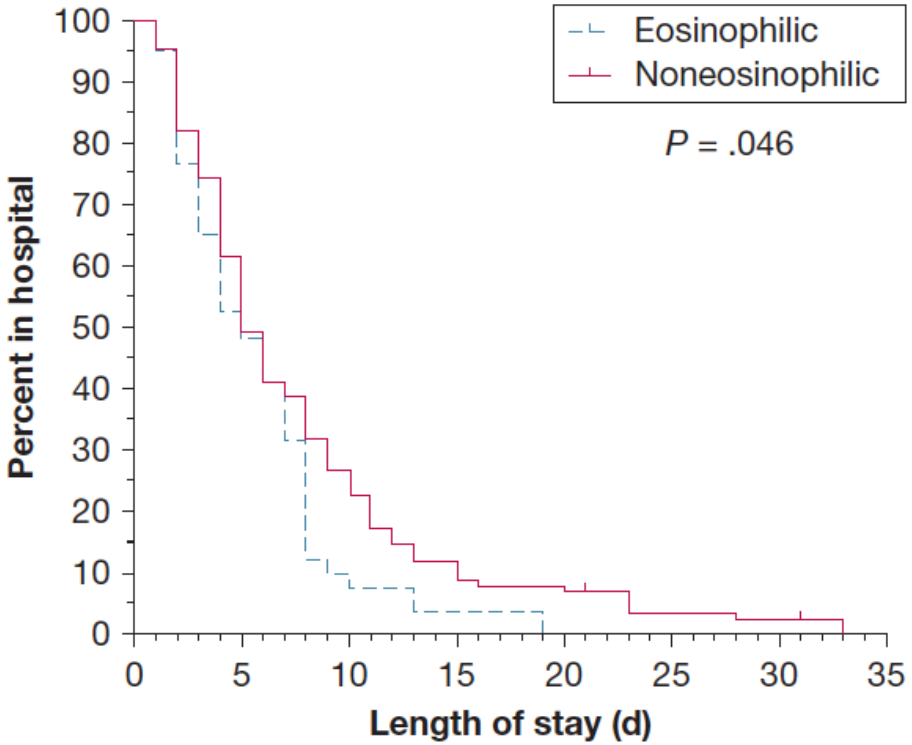
Couillard et al. CHEST 2017;151:366-73

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



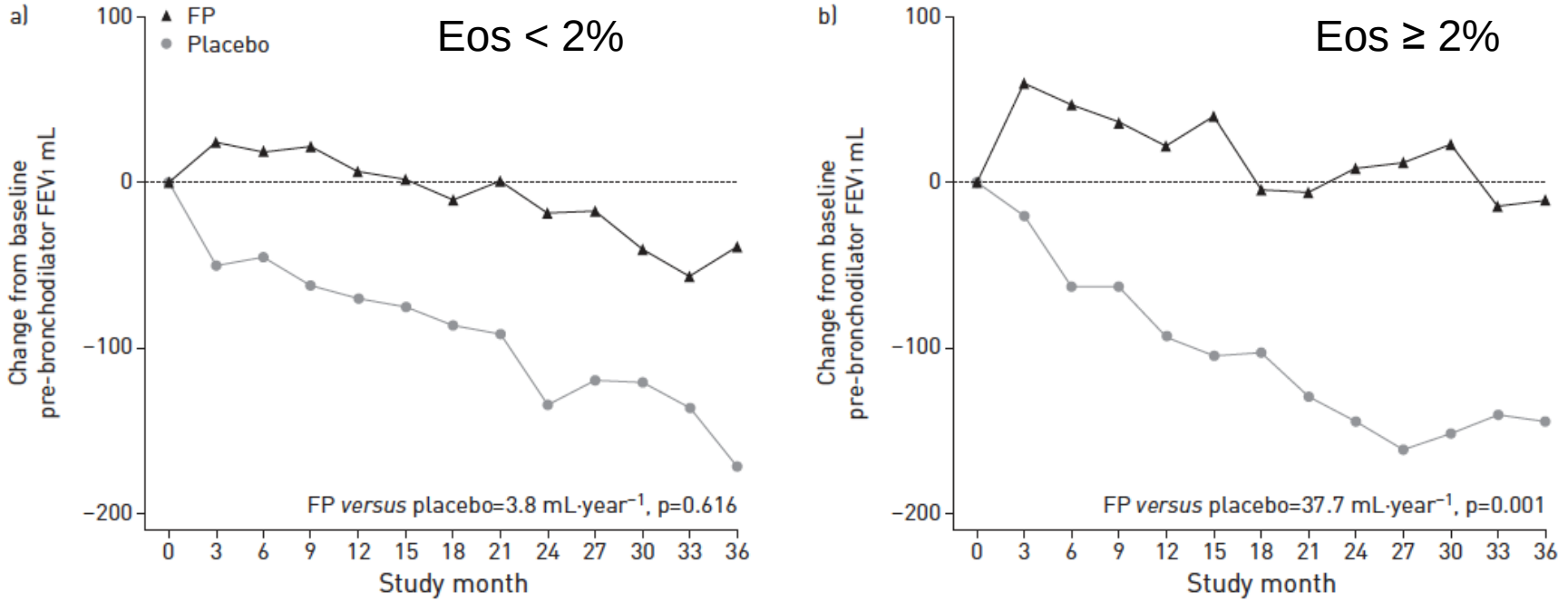
243 patients with COPD
- 174 with no consolidation
  (31% eosinophilic)
- 69 with consolidation
  (12% eosinophilic)



Bafadhel et al. CHEST 2017;150:320-328

Blood eosinophils as a marker of response to inhaled corticosteroids in COPD

Neil C. Barnes[1,2], Raj Sharma[1], Sally Lettis[3] and Peter M.A. Calverley[4]



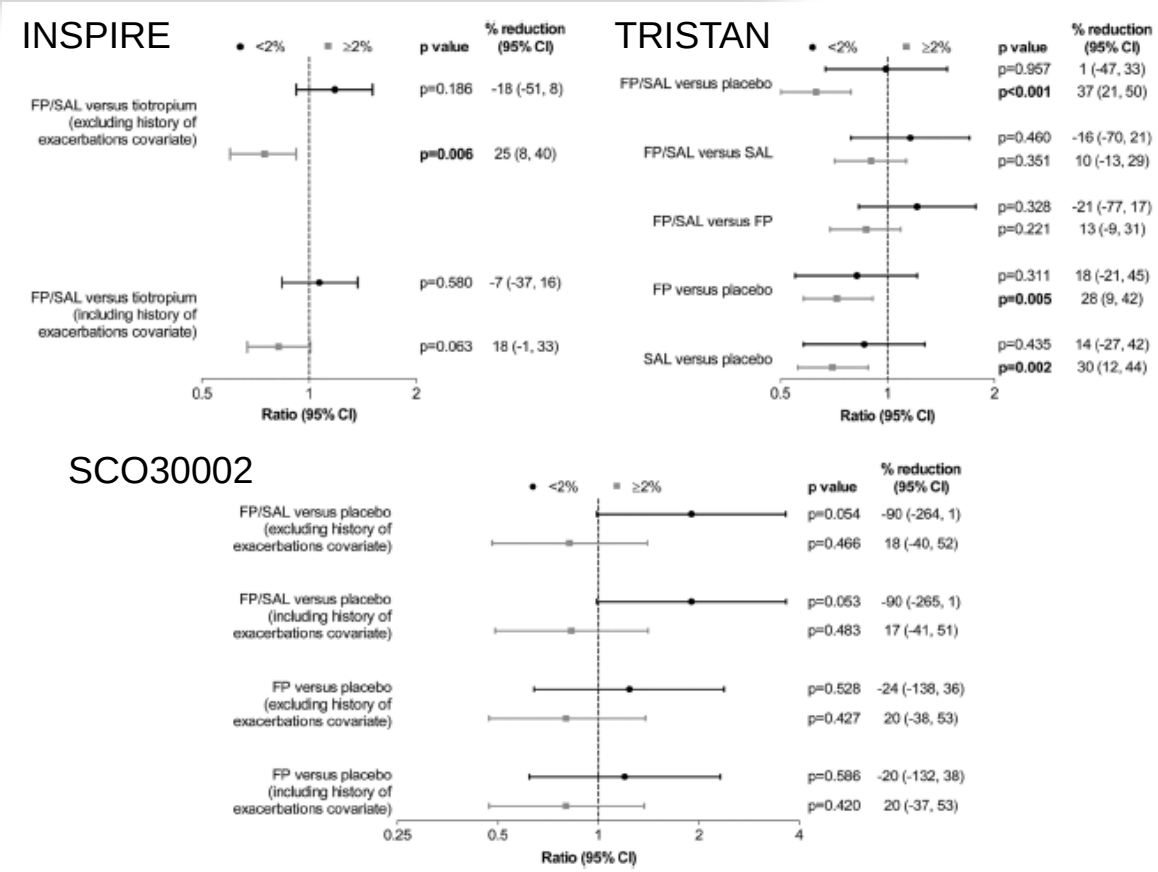
Data from ISOLDE study

Barnes et al. Eur Respir J 2016;47(5):1374-82

ORIGINAL ARTICLE

Blood eosinophils and inhaled corticosteroid/long-acting β-2 agonist efficacy in COPD

Ian D Pavord,[1] Sally Lettis,[2] Nicholas Locantore,[3] Steve Pascoe,[3] Paul W Jones,[4] Jadwiga A Wedzicha,[5] Neil C Barnes[6,7]

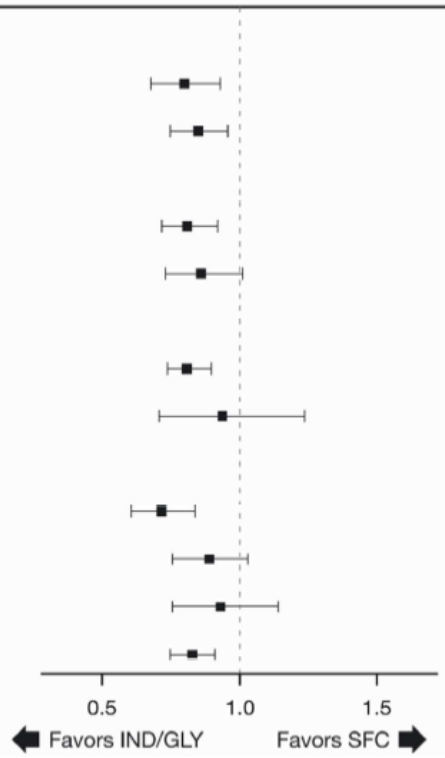


Pavord et al. Thorax 2016;71(2):118-25

Blood Eosinophils and Response to Maintenance COPD Treatment: Data from the FLAME Trial

Nicolas Roche[1],Kenneth R. Chapman[2], Claus F. Vogelmeier[3], Felix J.F. Herth[4], Chau Thach[5], Robert Fogel[5], Petter Olsson[6], Francesco Patalano[7], Donald Banerji[5], and Jadwiga A. Wedzicha[8]

Subgroup	No. of patients IND/GLY	No. of patients SFC	Annualized rate IND/GLY	Annualized rate SFC	Rate ratio (95% CI)
Blood eosinophils count					
< 2 %	620	659	0.99	1.24	0.80 (0.68, 0.93)
≥ 2%	1,026	993	0.98	1.15	0.85 (0.75, 0.96)
Blood eosinophils count					
< 3 %	1,041	1,037	0.99	1.22	0.81 (0.72, 0.92)
≥ 3 %	605	615	0.98	1.14	0.86 (0.73, 1.01)
Blood eosinophils count					
< 5 %	1,442	1,444	0.98	1.20	0.81 (0.74, 0.90)
≥ 5 %	204	208	1.01	1.08	0.94 (0.71, 1.24)
Blood eosinophils count					
< 150 cells/µl	623	654	0.90	1.26	0.72 (0.61, 0.84)
150 to < 300 cells/µl	655	631	1.04	1.17	0.89 (0.76, 1.03)
≥ 300 cells/µl	368	367	1.03	1.11	0.93 (0.76, 1.14)
Overall	1,651	1,656	0.98	1.19	0.83 (0.75, 0.91)



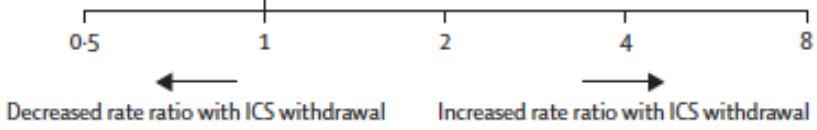
Roche et al. Am J Respir Crit Care Med 2017 10.1164/rccm.201701-0193OC

Blood eosinophil count and exacerbations in severe chronic obstructive pulmonary disease after withdrawal of inhaled corticosteroids: a post-hoc analysis of the WISDOM trial

Henrik Watz, Kay Tetzlaff, Emiel F M Wouters, Anne Kirsten, Helgo Magnussen, Roberto Rodriguez-Roisin, Claus Vogelmeier, Leonardo M Fabbri, Pascal Chanez, Ronald Dahl, Bernd Disse, Helen Finnigan, Peter M A Calverley

B

	n	Rate ratio (95% CI)	p value
Total	2296	**1·10 (0·96–1·26)**	**0·17**
Baseline eosinophils (<150 cells per µL vs ≥150 cells per µL)			
<150 cells per µL	1067	1·08 (0·88–1·32)	0·44
≥150 cells per µL	1172	1·17 (0·97–1·41)	0·094
Baseline eosinophils (<300 cells per µL vs ≥300 cells per µL)			
<300 cells per µL	1791	1·04 (0·89–1·21)	0·59
≥300 cells per µL	448	1·56 (1·14–2·13)	0·0055
Baseline eosinophils (<400 cells per µL vs ≥400 cells per µL)			
<400 cells per µL	1992	1·07 (0·92–1·23)	0·39
≥400 cells per µL	247	1·73 (1·15–2·62)	0·0090
Baseline eosinophils (mutually exclusive subgroups)			
<150 cells per µL	1067	1·08 (0·88–1·32)	0·44
150 to <300 cells per µL	724	1·00 (0·80–1·27)	0·97
300 to <400 cells per µL	201	1·30 (0·80–2·11)	0·28
≥400 cells per µL	247	1·73 (1·15–2·62)	0·0089



Watz et al. Lancet Respir Med 2016;4(5):390-8

Take-Home Message

- Blood eosinophils look promising as a biomarker
- Uncertainty about cut point
- ? Differences between “eosinophilic” and “non-eosinophilic” exacerbations
- Conflicting evidence on prediction of response to ICS

Palliative Care

A retrospective population based cohort study of access to specialist palliative care in the last year of life: who is still missing out a decade on?

Lorna Rosenwax[1*], Katrina Spilsbury[2], Beverley A. McNamara[1] and James B. Semmens[2]

- 12,817 deaths in Western Australia
- The majority (69 %; n = 4928) of decedents with cancer accessed palliative care during the last year of life.
- Only 14 % (n = 729) of decedents with non-cancer conditions accessed specialist palliative care
- 17.9 % of decedents with COPD accessed specialist palliative care
- There had been a 10.7% increase in the number of decedents with COPD who accessed specialist palliative care over 10 years

Rosenwax et al. BMC Palliat Care 2016;15:46

And finally ...

COPD, 13:262–273, 2016
ISSN: 1541-2555 print / 1541-2563 online

DOI: 10.3109/15412555.2015.1043521

REVIEW

Early History of Chronic Obstructive Pulmonary Disease 1808–1980

R. Ann Watson and Neil B. Pride

Watson & Pride COPD 2016;13(2):262-73

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