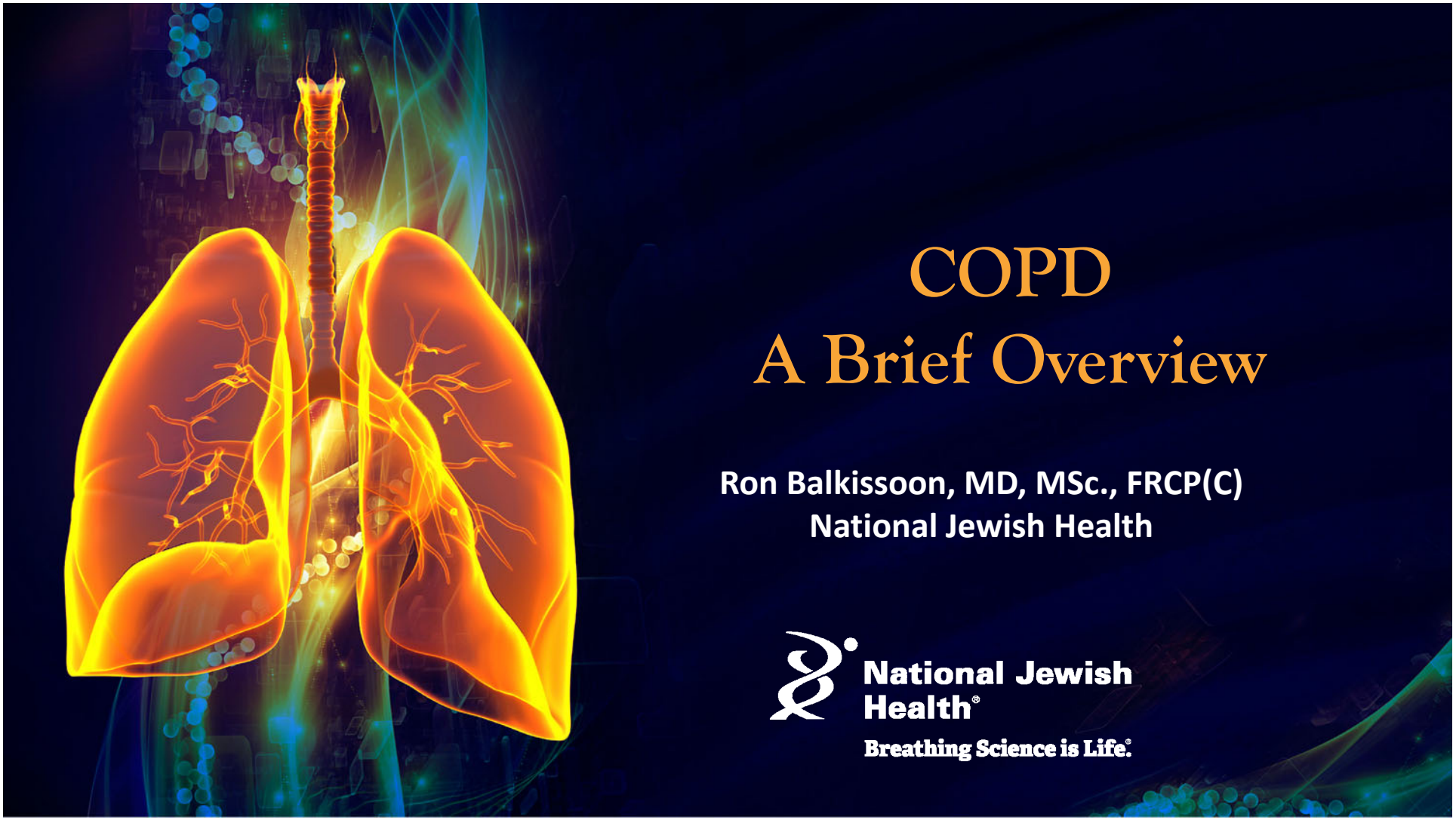

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Outline

1. Epidemiology and Burden of Illness
2. Pathobiology Of COPD
3. Treatment Paradigm
4. COPD vs Asthma: Overlap vs Co-exist
5. COPD, Steroids and Pneumonia/Dysbiosis
6. Possible decreased mortality benefit?
7. COPD and Cardiovascular Disease
8. Current Anti-inflammatory Alternatives
9. Phenotypes/Endotypes vs Treatable Traits
10. Unmet needs
11. Biologics in COPD

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The Majority of Healthcare Costs for Managing COPD Are Associated With Exacerbations

- **Total costs for COPD** were estimated to be $49 billion in 2020
- **Annual Cost of COPD** 3X higher in Severe COPD compared to Mild COPD
- **50%-75% of direct costs** for COPD are for services associated with **exacerbations**

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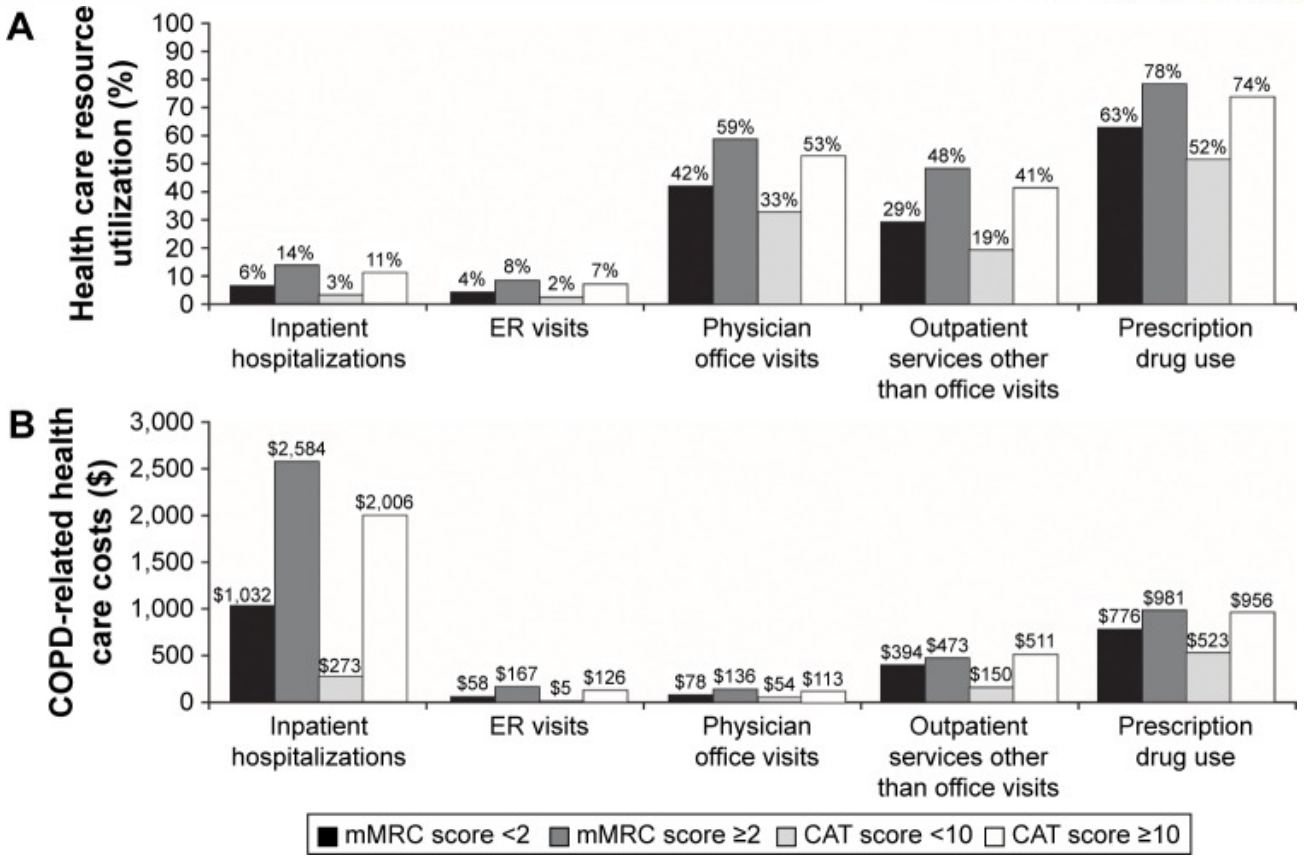
Health Care Utilization/Costs



Stephenson et al: *Int J Chron. Obstructive Lung Disease* 2017 12:1947-1959

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Major Causes of Death in COPD; Data from Major Clinical Trials

	(% of trial participants)							
Mean FEV_1(L)	**Cardio-vascular**	**Cancer**	**Respiratory (non-malignant)**	**Other**	**Trial Reference**	**Study size (n)**	**Deaths**	**Study follow-up**
2.75[a]	22%	54%	8%	16%	**LHS III**	5887	731	up to 14.5 years
2.54[b]	39%	39%	11%	11%	**EUROSCOP**	1277	18	3 years
1.41[a]	32%[c]	32%[c]	22%	13%[c]	**ISOLDE**	751	68	3 years
1.22[a]	26%	21%	35%	18%	**TORCH**	6184	911	3+ years
1.32[a]	16%	22%	39%	23%	**UPLIFT**	5993	941	4 years + 30 days

Berry et al *COPD*. 2010 October ; 7(5): 375–382

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Consequences of Exacerbations

- Accelerated frequency of future exacerbations
- Accelerated loss of lung function
- Reduced quality of life
- Increased risk of rehospitalization
- Increased risk of death (all cause mortality)
- Especially Severe (hospitalized) exacerbations

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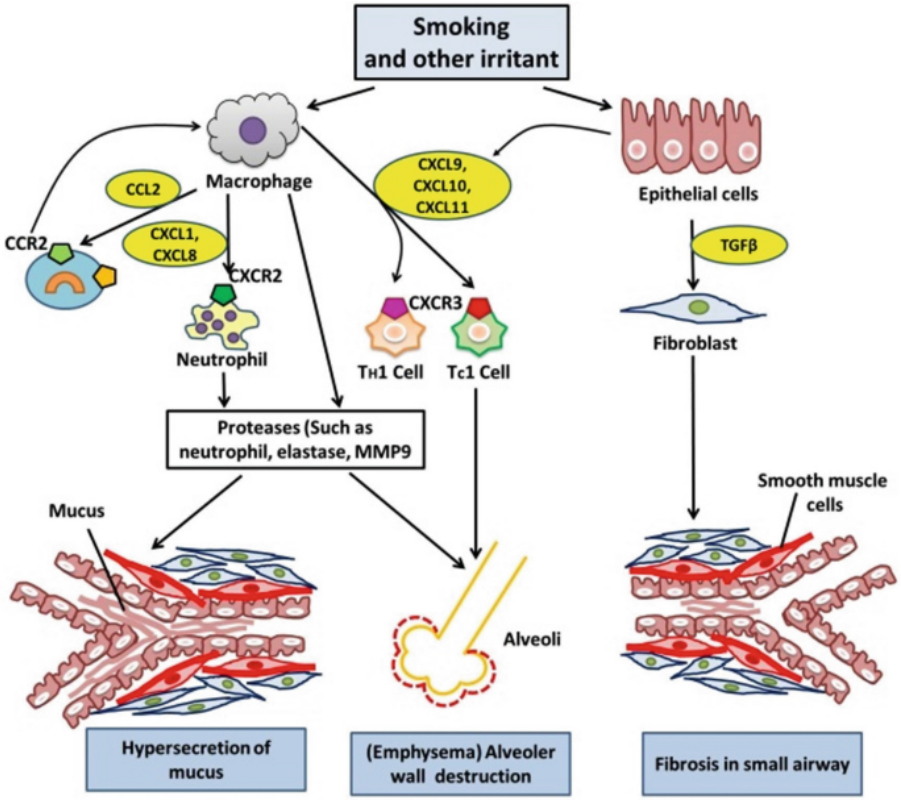
Pathobiology of COPD



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COPD vs Asthma Clinical Presentation

Asthma vs COPD Diagnosis

	Asthma	COPD
Who gets it?	Age usually < 45 History (personal or family) of atopy is frequent	Age usually > 45 Usually has smoked > 20 pack years
Symptoms?	Cough Dyspnea Wheeze Chest tightness *May be asymptomatic between exacerbations*	Cough Dyspnea Symptoms of right heart failure *Usually symptomatic between exacerbations*
Exam?	Usually normal, if between exacerbations	Decreased breath sounds Hyperresonance Hypoxemia/Cyanosis Barrel chest Pursed lip breathing Subxiphoid PMI
PFT findings?	Variably abnormal spirometry: ▪ $FEV_1/FVC < 70\%$ ▪ Scooped out expiratory flow-volume curve ▪ Low peak expiratory flow ▪ Improvement following bronchodilator ▪ Spirometry often normal or near normal between attacks	Persistently abnormal spirometry ▪ $FEV_1/FVC < 70\%$ ▪ Modest improvement following bronchodilator can be present

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Evaluation/Classification Of COPD Patients

Spirometrically confirmed diagnosis → Assessment of airflow obstruction → Assessment of symptoms/risk of exacerbations

Post-bronchodilator FEV1/FVC < 0.7

GRADE	FEV1 (% predicted)
GOLD 1	≥ 80
GOLD 2	50-79
GOLD 3	30-49
GOLD 4	< 30

EXACERBATION HISTORY

- ≥ 2 moderate exacerbations or ≥ 1 leading to hospitalization → **E**
- 0 or 1 moderate exacerbations (not leading to hospitalization) → **A** / **B**

mMRC 0-1 CAT < 10	mMRC ≥ 2 CAT ≥ 10

SYMPTOMS

GOLD 2023Agusti et al: Archivos de Bronconeumología 59 (2023) 232–2

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Goals of COPD Maintenance Therapy

Reduce Symptoms:

- Dyspnea
- Cough
- Sputum production

Reduce Risk

- Exacerbations
- Hypoxia
- Hypercapnia

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Initial Pharmacological Treatment

≥ 2 moderate exacerbations or ≥ 1 leading to hospitalization	**GROUP E** **LABA + LAMA*** *consider LABA+LAMA+ICS* if blood eos ≥ 300*	
0 or 1 moderate exacerbations (not leading to hospital admission)	**GROUP A** **A bronchodilator** mMRC 0-1, CAT < 10	**GROUP B** **LABA + LAMA*** mMRC ≥ 2, CAT ≥ 10

*single inhaler therapy may be more convenient and effective than multiple inhalers
Exacerbations refers to the number of exacerbations per year

GOLD 2023: Agusti et al: Archivos de Bronconeumología 59 (2023) 232–248

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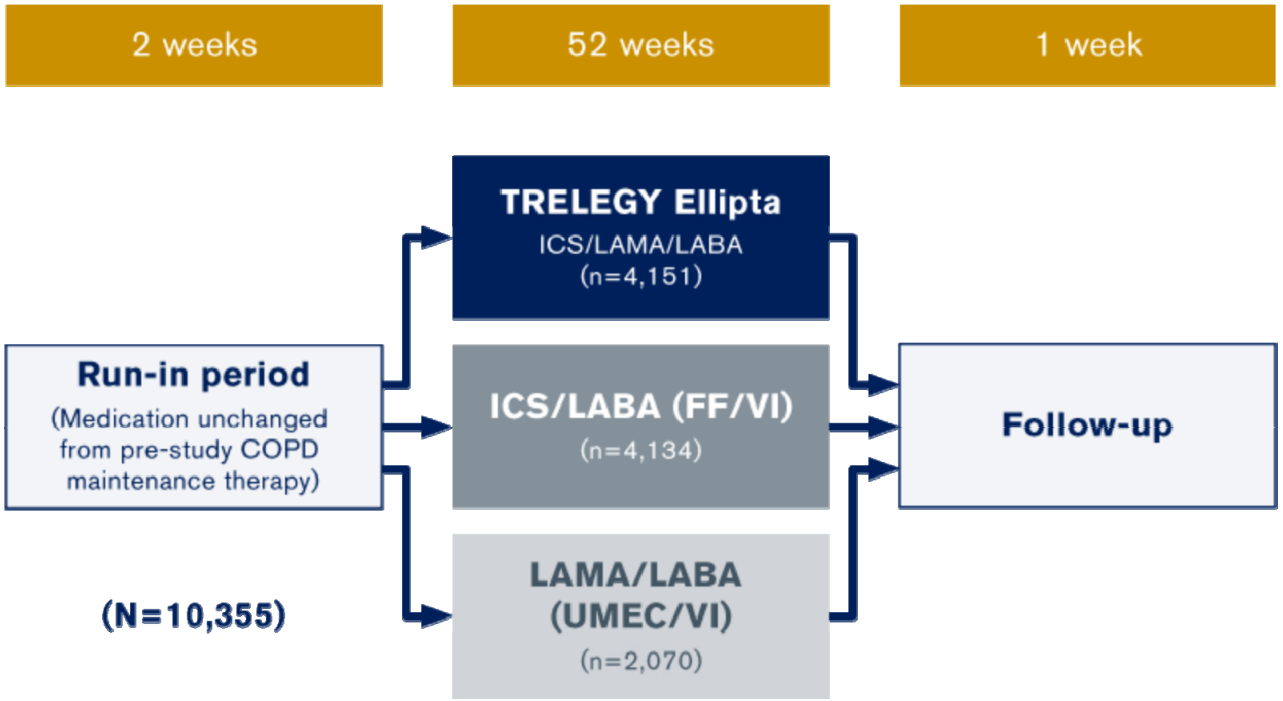
IMPACT TRIAL PROTOCOL

Study Design



Pasco et al: Eur. Respir. J. 2016;48(2):320-330.

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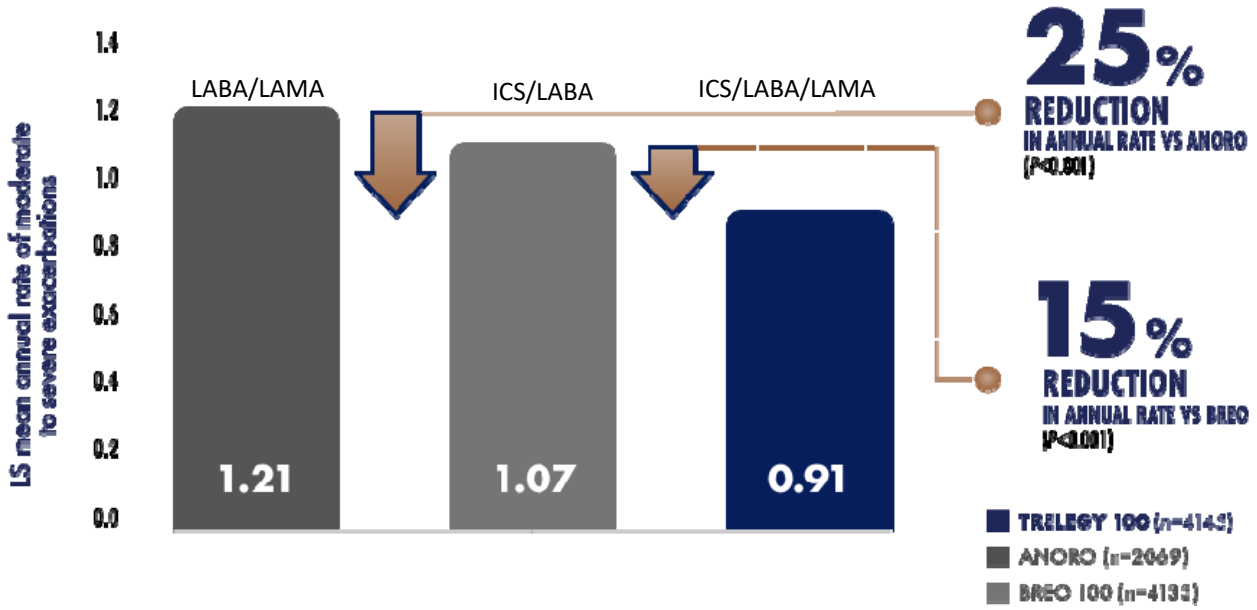
IMPACT TRIAL
Significant Reduction in Moderate to Severe Exacerbations



Lipson et al New Engl .J Med. 2018;378(18):1671-168

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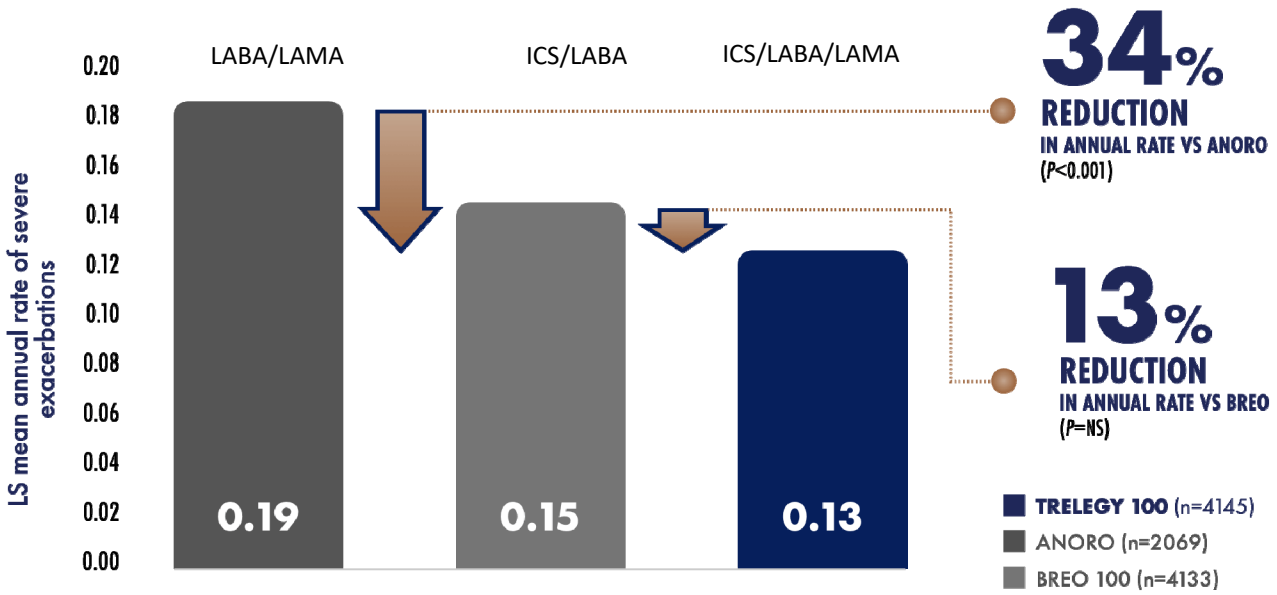
IMPACT TRIAL
Significant Reduction in Severe Exacerbations



Lipson et al: N Engl. J Med. 2018;378(18):1671-1680

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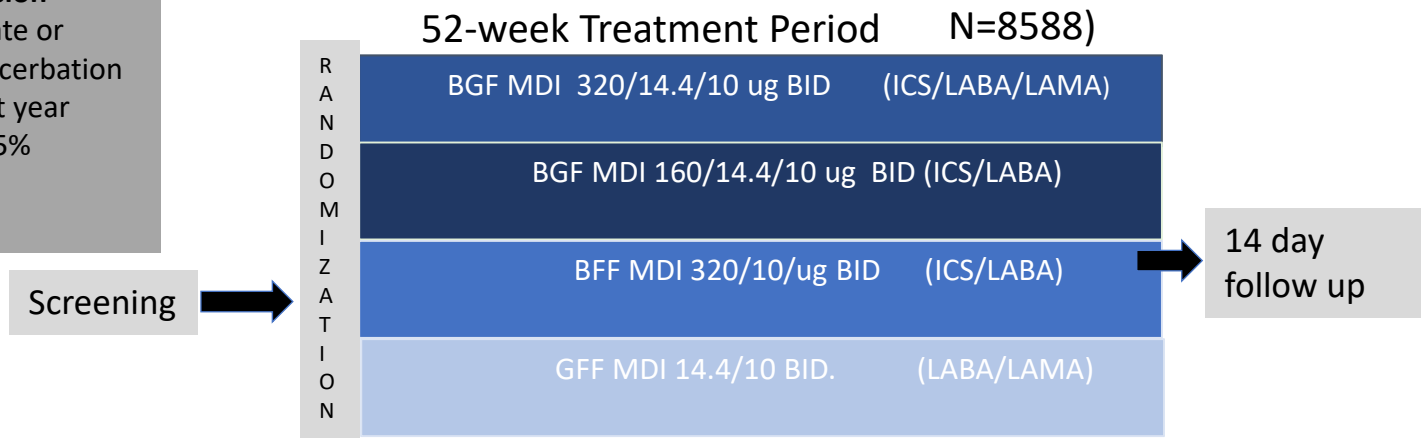
ETHOS Trial Study Design

Phase III, multicenter, randomized, double blind trial
Primary Outcome: Reduction in Moderate to Severe Exacerbations

Patient Inclusion
- ≥1 moderate or
- severe exacerbation
- within past year
- FEV1 25-65% predicted
- CAT ≥ 10



Week	-4			0	4	8	12	16	20	24	28	36	44	52	54
Visit	1	2	3	4		6	7	8	9	10	11	12	13	14	

B: Budesonide. G: Glycopyrolate. F: Formoterol Fumarate

Rabe et al New. Engl J Med 202;35-48

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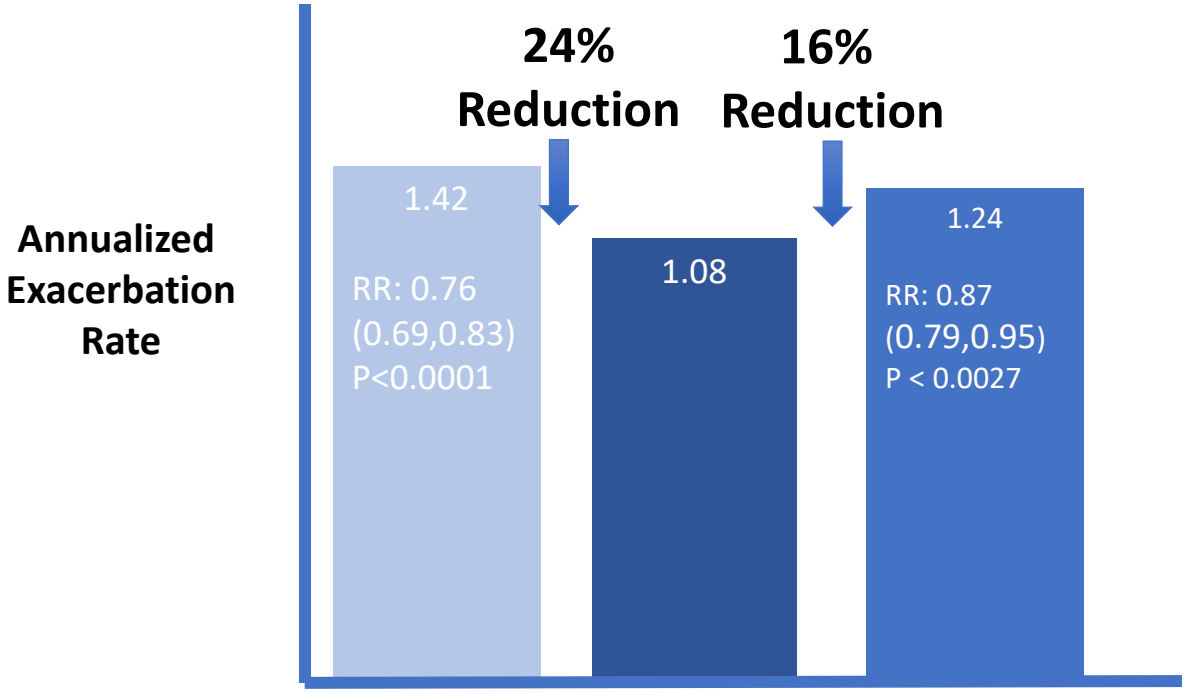
Significant Reduction in Moderate to Severe Exacerbations



Rabe et al New Engl. J Med 2018 202;35-48

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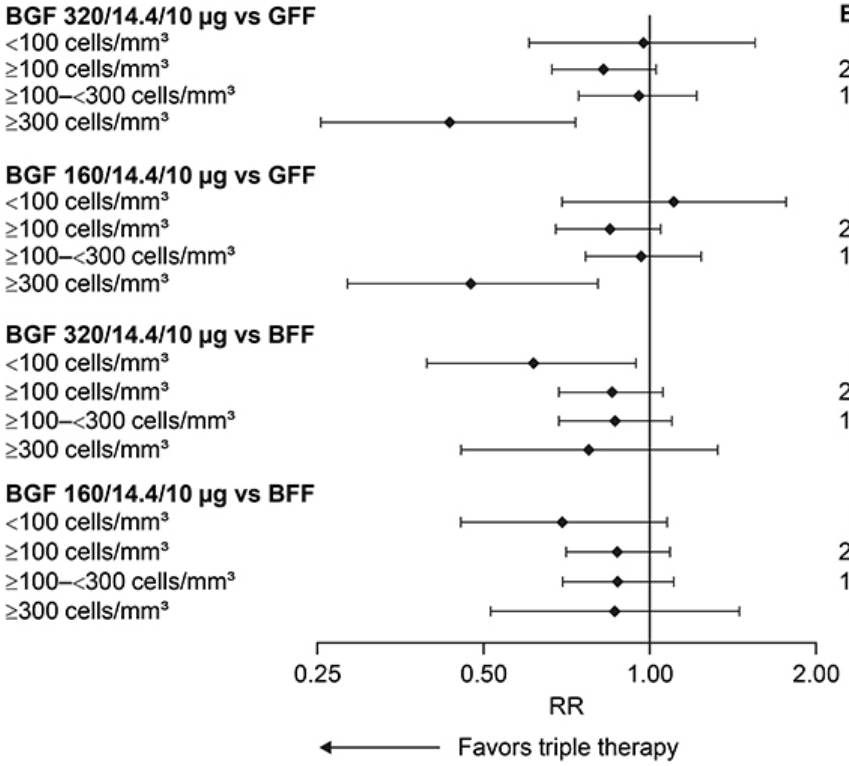
ETHOS Trial: Higher Eosinophil Counts Favor Triple Therapy

Annual rate. Of severe exacerbations



	Events (n)	RR (95% CI)	P-value
BGF 320/14.4/10 µg vs GFF			
<100 cells/mm³	53 vs 49	0.97 (0.60, 1.55)	0.8864
≥100 cells/mm³	219 vs 238	0.82 (0.66, 1.02)	0.0741
≥100–<300 cells/mm³	183 vs 184	0.95 (0.74, 1.21)	0.6640
≥300 cells/mm³	36 vs 54	0.43 (0.25, 0.73)	0.0019
BGF 160/14.4/10 µg vs GFF			
<100 cells/mm³	57 vs 49	1.10 (0.69, 1.76)	0.6902
≥100 cells/mm³	228 vs 238	0.84 (0.67, 1.04)	0.1129
≥100–<300 cells/mm³	188 vs 184	0.96 (0.76, 1.23)	0.7564
≥300 cells/mm³	40 vs 54	0.47 (0.28, 0.80)	0.0053
BGF 320/14.4/10 µg vs BFF			
<100 cells/mm³	53 vs 72	0.61 (0.39, 0.94)	0.0264
≥100 cells/mm³	219 vs 251	0.85 (0.68, 1.05)	0.1364
≥100–<300 cells/mm³	183 vs 205	0.86 (0.68, 1.09)	0.2047
≥300 cells/mm³	36 vs 46	0.77 (0.45, 1.32)	0.3492
BGF 160/14.4/10 µg vs BFF			
<100 cells/mm³	57 vs 72	0.69 (0.45, 1.07)	0.0976
≥100 cells/mm³	228 vs 251	0.87 (0.70, 1.08)	0.1991
≥100–<300 cells/mm³	188 vs 205	0.87 (0.69, 1.10)	0.2522
≥300 cells/mm³	40 vs 46	0.86 (0.51, 1.45)	0.5656

Rabe et al New. Engl J Med 202;35-48

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ICS Use and Blood Eosinophil Count

PULMONARY PERSPECTIVE

Blood Eosinophils and Chronic Obstructive Pulmonary Disease
A Global Initiative for Chronic Obstructive Lung Disease Science Committee 2022 Review

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ORCID IDs: 0000-0001-8918-7075 (D.S.); 0000-0002-6924-4500 (A.P.); 0000-0002-9798-2527 (C.F.V.); 0000-0003-2009-4406 (D.M.G.H.).

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) published its first report for the diagnosis and management of chronic obstructive pulmonary disease (COPD) in 2001 (1). Since then, GOLD has updated it yearly (2), the last time in 2022 (www.goldcopd.org). To do so, GOLD critically evaluates the new evidence since the previous publication and decides whether it merits (or not) inclusion in the most recent update. GOLD publishes specific recommendations and, sometimes, the main arguments behind them, but it often lacks space for a detailed discussion regarding the pros and cons behind each recommendation. To address this limitation, the Scientific Committee of GOLD decided to publish, separately from the main annual update, a series of papers that review and discuss topics of particular current interest for clinical practice.

The GOLD 2019 report recommended using blood eosinophil counts (BEC) as part of a precision medicine strategy to identify the most suitable patients for inhaled corticosteroids (ICS) treatment (3). Recent publications have provided further evidence and insights concerning BEC in COPD. Here, we discuss the role of BEC as a COPD biomarker, focusing on new advances and summarizing the associated changes in the GOLD 2022 report (shown in Table 1).

A Brief Overview of Eosinophil Biology

Eosinophils originate from bone marrow stem cells in response to stimulation by granulocyte–monocyte colony-stimulating factor, IL-3, and IL-5 (4). The subsequent proliferation, activation, tissue infiltration, and survival of eosinophils are controlled by type-2 (T2) inflammation mediators, such as IL-4, IL-5, IL-13, and eotaxins. Eosinophil degranulation releases major basic proteins, eosinophil cationic protein, eosinophil peroxidase, and eosinophil-derived neurotoxin, which provide host defense against parasitic infection (5). These proteins also promote bacterial and viral clearance, although the extent of these roles in humans, as opposed to animal models, is unclear (4, 5). Eosinophil-derived granule proteins can cause tissue injury and remodeling, whereas eosinophil peroxidase drives changes in the physicochemical properties of mucus that underlie airway mucus plugging (4, 6). There is also evidence that eosinophil subsets exist, with tissue-resident cells having a predominantly homeostatic role, whereas inflammatory eosinophils are recruited into the lungs (7). Asthma and systemic hypereosinophilic diseases are examples in which increased systemic and lung eosinophil numbers, coupled with activation, contribute to disease pathophysiology (4).

BEC as a Predictor of ICS Benefit

COPD is a heterogeneous condition, exemplified by the between-individual variation in the nature and severity of airway inflammation (3, 8–10). The use of antiinflammatory treatments, therefore, requires a selective approach based on clinical characteristics (phenotyping) and biological information (endotyping) to target therapies to subgroups of individuals who

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Author Contributions: D.S. and D.M.G.H. prepared the first version of the manuscript. All authors discussed and agreed to the manuscript content, reviewed and edited the paper, and approved the final version.

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Copyright © 2022 by the American Thoracic Society
Originally Published in Press as DOI: 10.1164/rccm.202201-0209PP on June 23, 2022
Internet address: www.atsjournals.org

Singh et al . *Am. J. Respir Crit Care Med* 2022 Jul 1;206(1)17-24

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GOLD 2022 Report: Key Evidence and Recommendations for Blood Eosinophil Counts (BEC) in Chronic Obstructive Pulmonary Disease

Prediction of ICS benefits

- BEC should be used with exacerbation risk history
- Relationship is continuous as BEC increase the greater likelihood of benefit
- < 100 eos/mcL Lowest benefit/ > 300 eosinophils/mcL greatest likelihood of benefit
- These are Estimates not precise cutoff values

T2 Inflammation

- High BEC correlate with higher lung eosinophils and higher T2 markers in the airways
- The difference in T-2 inflammation c/w the differential ICS response according to BEC.
- **Microbiome**
- Lower BEC associated with a greater presence of protobacteria, Hemophilus, increased bacterial infections and pneumonia

Future Risk of Exacerbations/disease progression:

- **In younger individuals without COPD** - the higher the BEC the > increased risk of FEV1 decline and development of COPD

Singh et al. *Am J Respir Crit Care Med* 2022 Jul 1;206(1)17-24

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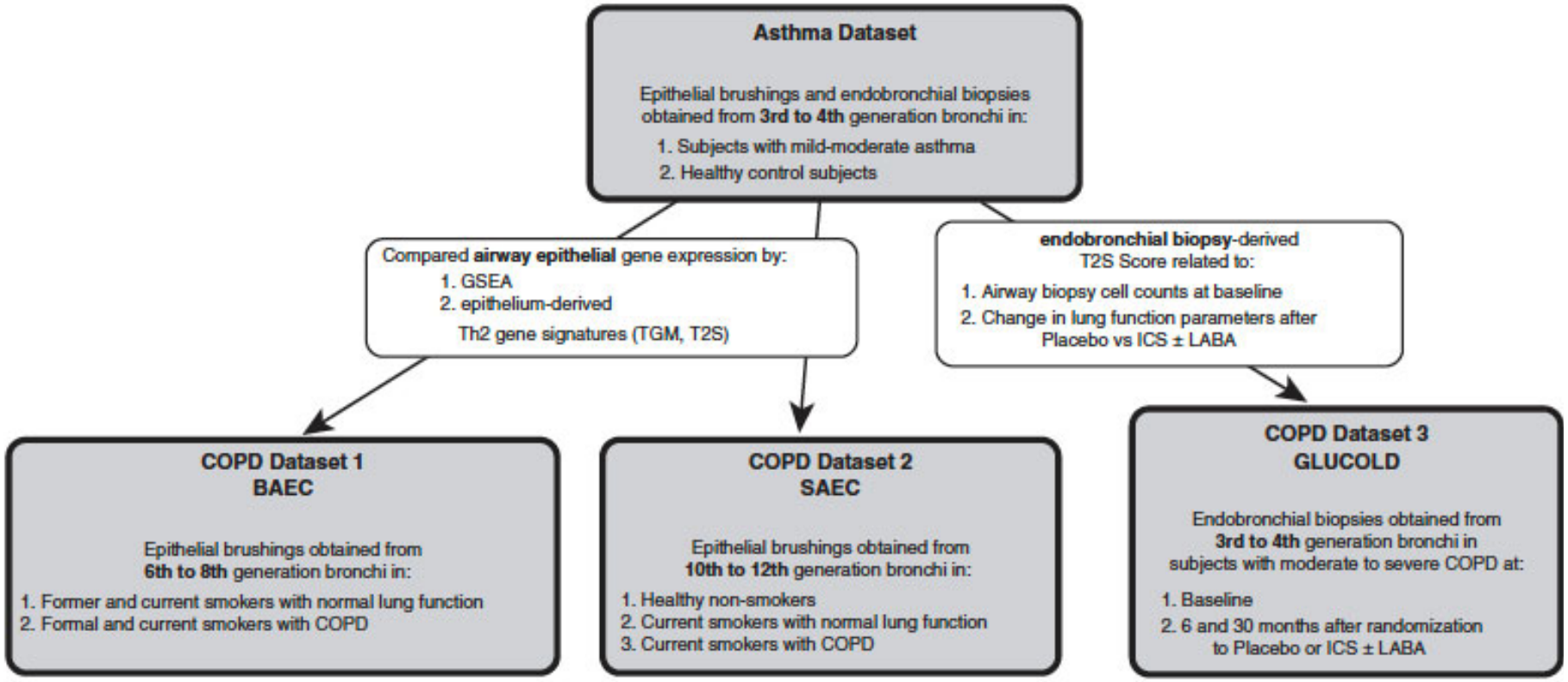
T-2 Genetic Signature Predicts Steroid Response in COPD patients

Christensen, S. et al AJRCCM 2015



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T-2 Genetic Signature Predicts Steroid Response in COPD patients

- Higher T2 score (T2S) Associated with:
- Greater Airflow obstruction ($p<0.001$)
- Decreased Lung function ($p<0.001$)
- Increased airway wall eosinophil counts
- Increased blood eosinophil percentage ($p=0.03$)
- Bronchodilator reversibility ($p=0.01$)
- Improvements with hyperinflation after corticosteroid treatment ($p=0.019$)
- *Not with asthma history (N.S.)

Christensens.A et al AJRCCM 2015 vol. 191.7.758-766

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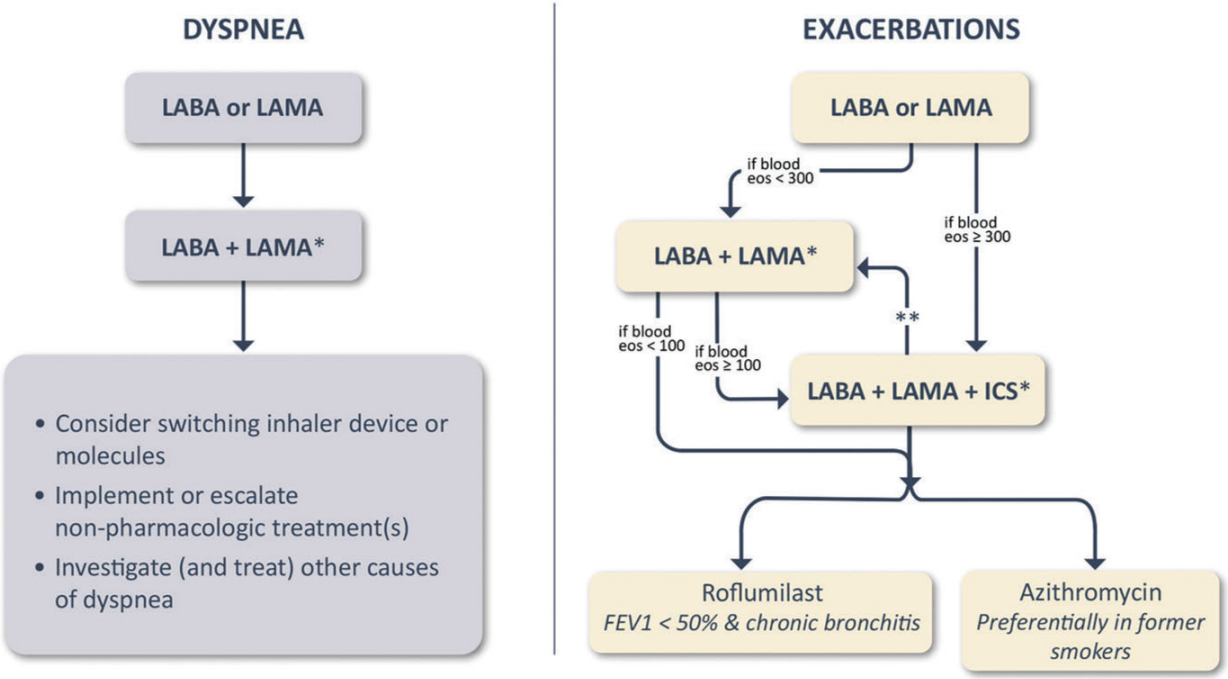
1. **IF RESPONSE TO INITIAL TREATMENT IS APPROPRIATE, MAINTAIN IT.**
2. **IF NOT:**
   - Check adherence, inhaler technique and possible interfering comorbidities
   - Consider the predominant treatable trait to target (dyspnea or exacerbations)
     - Use exacerbation pathway if both exacerbations and dyspnea need to be targeted
   - Place patient in box corresponding to current treatment & follow indications
   - Assess response, adjust and review
   - These recommendations do not depend on the ABE assessment at diagnosis



GOLD 2023Agusti et al: Archivos de Bronconeumología 59 (2023) 232–24

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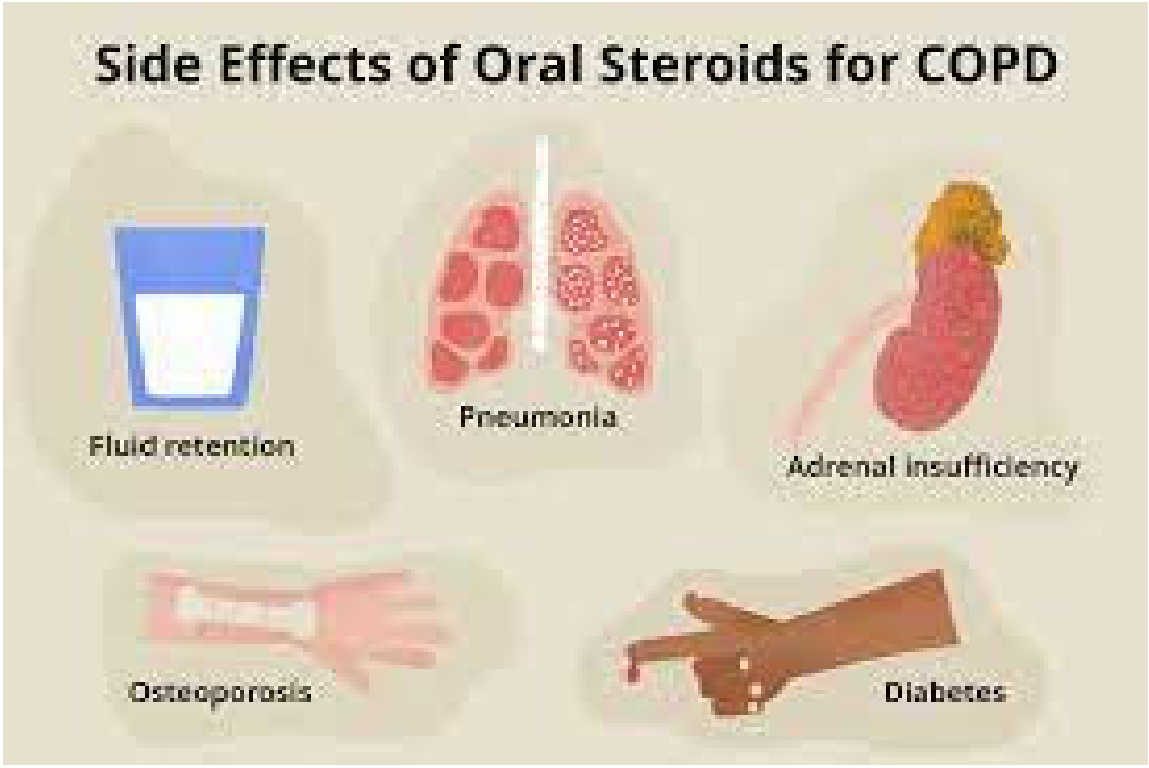
Effects of oral corticosteroids



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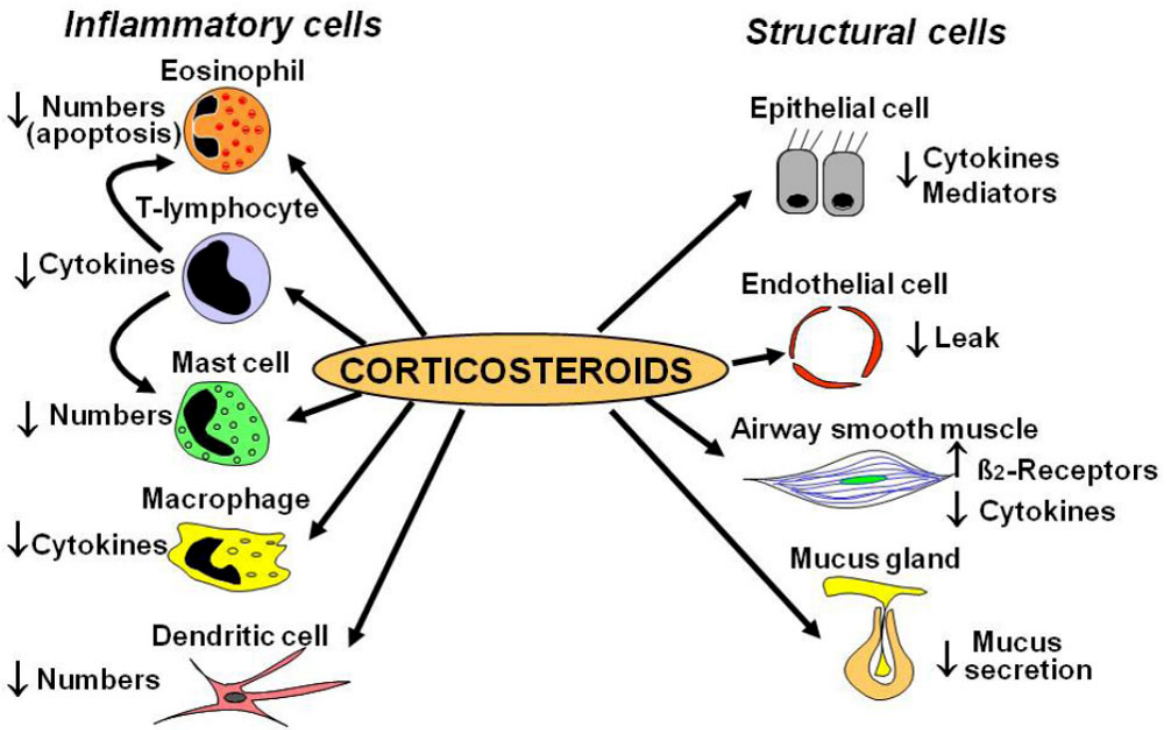
Inhaled Corticosteroids and Pneumonia



Barnes PJ. Inhaled Corticosteroids. *Pharmaceuticals*. 2010; 3(3):514-540. https://doi.org/10.3390/ph3030514

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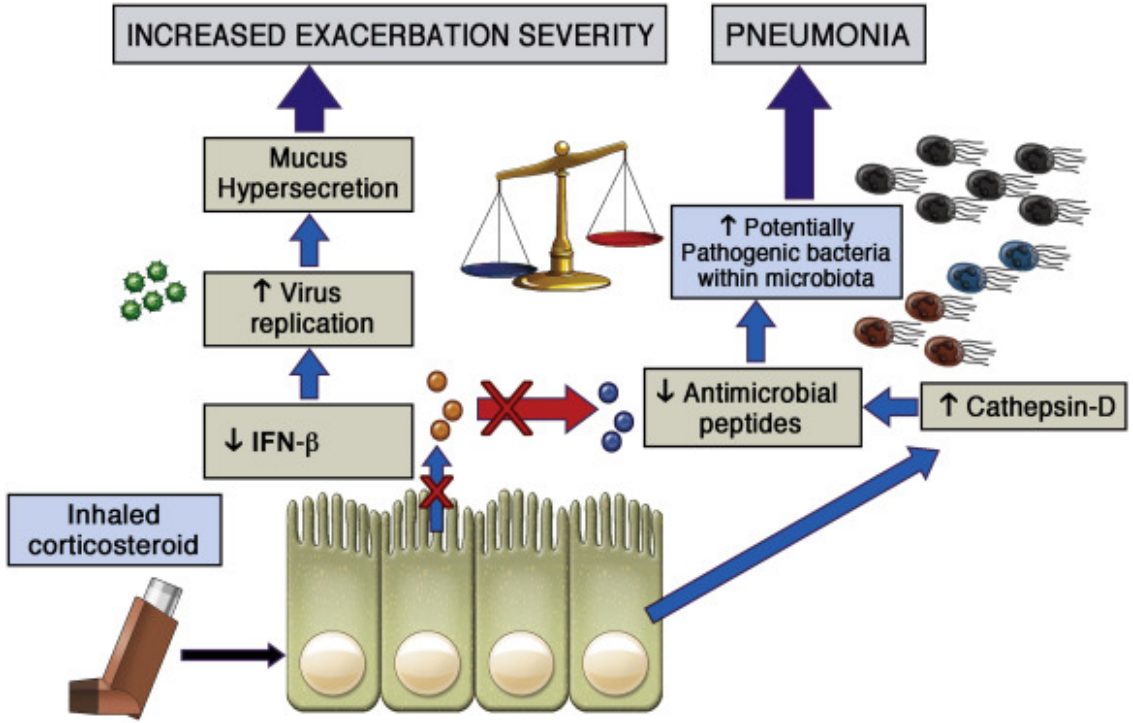
Risks of ICS Use in COPD patients



A. Singanayagam, et al *J Allergy Clin Immunol* 2020;146:1292-4.

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CT Scan of COPD Patient with Recurrent Pneumonia

- 62-year-old male with COPD X 8 years of Recurrent Pneumonias
- 30 pack-year-history
- D/C about 5 years ago
- 4 exacerbations in past 12 months treated with antibiotics and OCS
- Maintenance Medication
  - ICS/LABA/LAMA
  - Albuterol rescue
  - Adherence, compliance, good technique confirmed

PMH:

- GERD
- Asthma
- Hypertension

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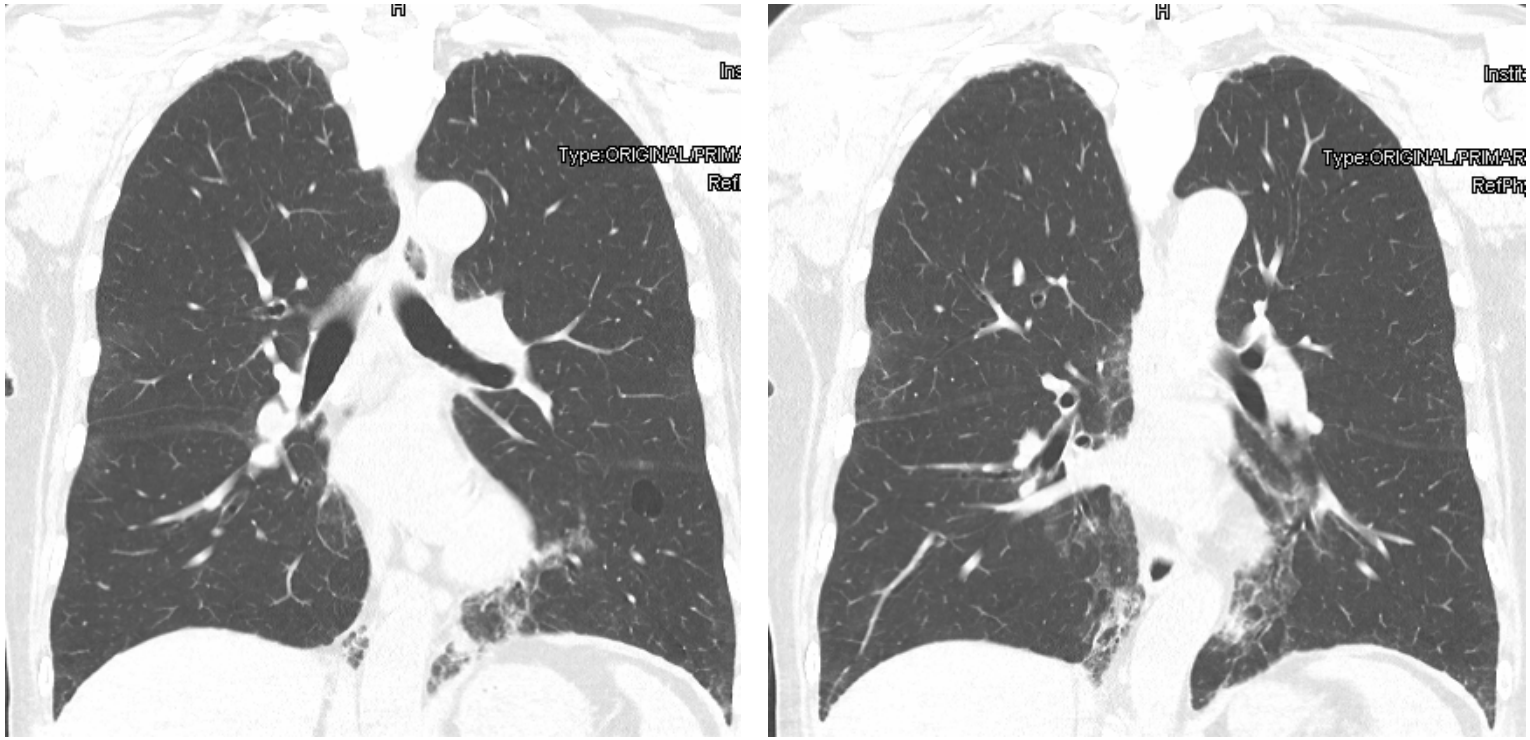
CT Scan of COPD Patient with Recurrent Pneumonia



Consistent With Recurrent Aspiration

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ICS and Reduced Mortality "Signal"

Evidence Supporting a Reduction in Mortality with Pharmacotherapy and Non-pharmacotherapy in COPD Patients

Figure 6

Therapy	RCT*	Treatment effect on mortality	Patient characteristics
Pharmacotherapy			
LABA+LAMA+ICS[1]	Yes	Single inhaler triple therapy compared to dual LABD therapy relative risk reduction: IMPACT: HR 0.72 (95% CI: 0.53, 0.99)[1a] ETHOS: HR 0.51 (95% CI: 0.33, 0.80)[1b]	Symptomatic people with a history of frequent and/or severe exacerbations
Non-pharmacological Therapy			
Smoking cessation[2]	Yes	HR for usual care group compared to intervention group (smoking cessation) HR 1.18 (95% CI: 1.02, 1.37)[2]	Asymptomatic or mildly symptomatic
Pulmonary rehabilitation[3 #]	Yes	Old trials: RR 0.28 (95% CI 0.10, 0.84)[3a] New trials: RR 0.68 (95% CI 0.28, 1.67)[3b]	Hospitalized for exacerbations of COPD (during or ≤ 4 weeks after discharge)
Long-term oxygen therapy[4]	Yes	NOTT: ≥ 19 hours of continuous oxygen vs ≤ 13 hours: 50% reduction[4a] MRC: ≥ 15 hours vs no oxygen: 50% reduction[4b]	PaO_2 ≤ 55 mmHg or < 60 mmHg with *cor pulmonale* or secondary polycythemia
Noninvasive positive pressure ventilation[5]	Yes	12% in NPPV (high IPAP level) and 33% in control HR 0.24 (95% CI 0.11, 0.49)[5]	Stable COPD with marked hypercapnia
Lung volume reduction surgery[6]	Yes	0.07 deaths/person-year (LVRS) vs 0.15 deaths/ person-year (UC) RR for death 0.47 (p = 0.005)[6]	Upper lobe emphysema and low exercise capacity

*RCT with pre-specified analysis of the mortality outcome (primary or secondary outcome); #Inconclusive results likely due to differences in pulmonary rehabilitation across a wide range of participants and settings.

1. a) IMPACT trial (Lipson et al. 2020) and b) ETHOS trials (Martinez et al. 2021); 2.Lung Health Study (Anthonisen et al. 2005); 3. a) Puhan et al. (2011) and b) Puhan et al. 2016; 4. a) NOTT (NOTT, 1980) and b) MRC (MRC, 1981); 5. Kohlein trial (Kohlein et al. 2014); 6. NETT trial (Fishman et al. 2003)

ICS: inhaled corticosteroid; IPAP: inspiratory positive airway pressure; LABA: long-acting beta$_2$-agonist; LABD: long-acting bronchodilator; LAMA: long-acting anti-muscarinic; LTOT: long-term oxygen therapy; NPPV: noninvasive positive pressure ventilation; LVRS: lung volume reduction surgery; UC: usual treatment control group.

GOLD 2023

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Triple Therapy and "MortalitySignal"

Balkissoon Journal of COD Foundation COPD Journal 2021

Chronic Obstructive Pulmonary Diseases:
Journal of the COPD Foundation

Journal Club

Journal Club: Do Inhaled Corticosteroids Reduce All-Cause Mortality in Chronic Obstructive Pulmonary Disease? What is the Latest Evidence?

Ron Balkissoon, MD, MSc, DIH, FRCPC[1]

Abbreviations: chronic obstructive pulmonary disease, **COPD**; Towards a Revolution in COPD Health study, **TORCH**; fluticasone propionate, **FP**; salmeterol, **SAL**; Study to Understand Mortality and Morbidity in COPD, **SUMMIT**; fluticasone furoate, **FF**; vilanterol, **VI**; Investigating New Standards for Prophylaxis in Reducing Exacerbations study, **INSPIRE**; inhaled corticosteroid, **ICS**; long-acting beta2-agonist, **LABA**; long-acting muscarinic antagonist, **LAMA**; bipropionate, **BDP**; formaterol fumorate, **FORF**; glycopyrronium bromide, **G**; InforMing the Pathway of COPD Treatment, **IMPACT**; Efficacy and Safety of Triple Therapy in Obstructive Lung Disease, **ETHOS**; forced expiratory volume in 1 second, **FEV_1**; umeclidinium, **UMEC**; budesonide, **BUD**

Citation: Balkissoon R. Journal club— Do inhaled corticosteroids reduce all-cause mortality in chronic obstructive pulmonary disease? What is the latest evidence? *Chronic Obstr Pulm Dis.* 2021;8(1):177-184. doi: https://doi.org/10.15326/jcopdf.2020.0196

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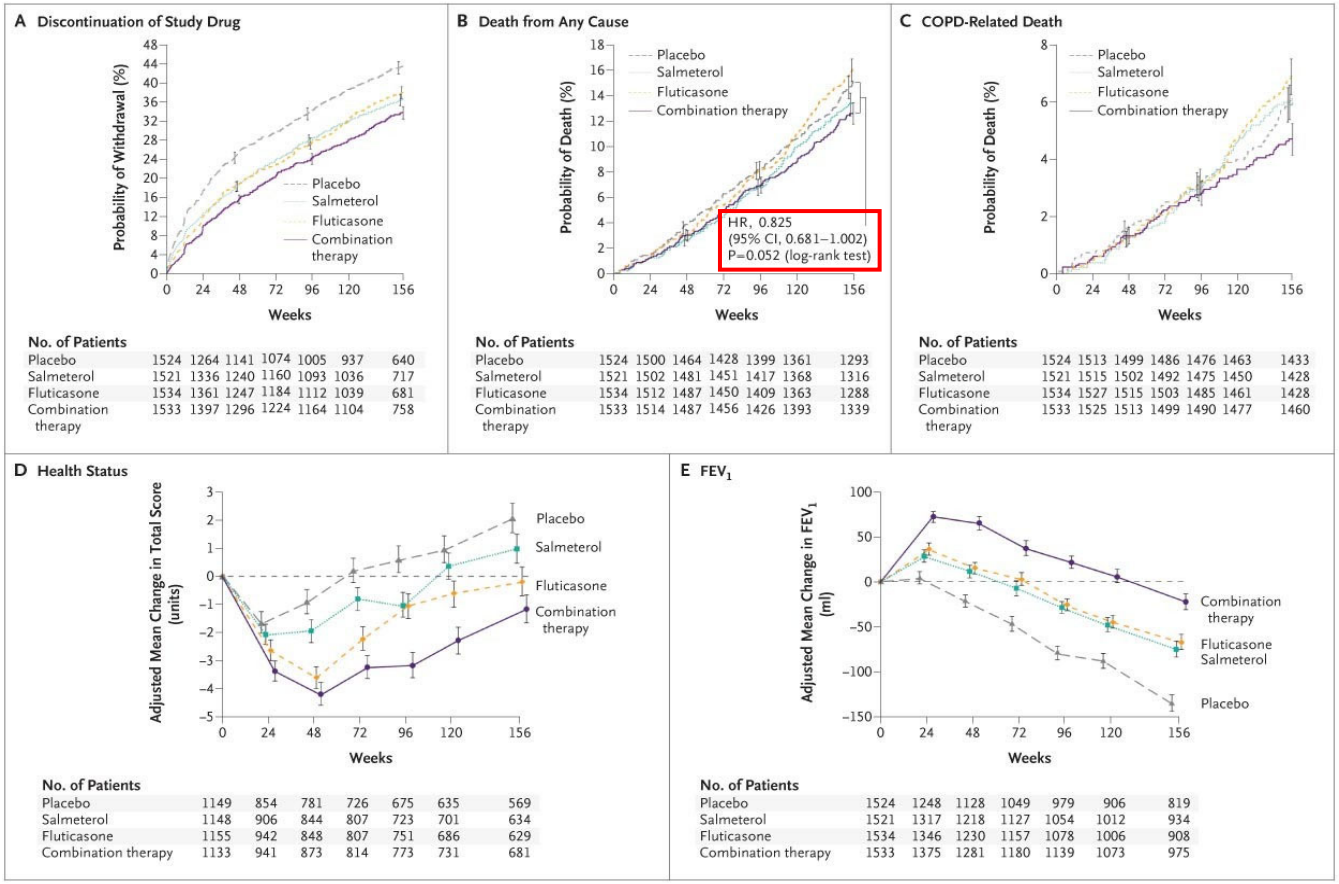
Torch Trial



Calverley et al. *N Engl J Med* 2007; 356:775-789

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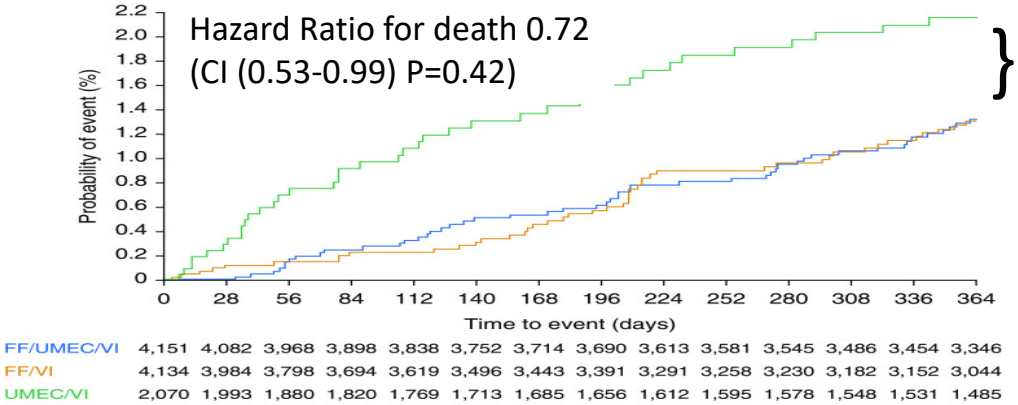
IMPACT
FF/UMEC/VI Reduces Risk of All Cause Mortality compared to UMEC/VI

On Treatment Deaths

FF/UMEC/VI: 1.20%
FF/VI: 1.19%
UMEC/VI 1.88%

A

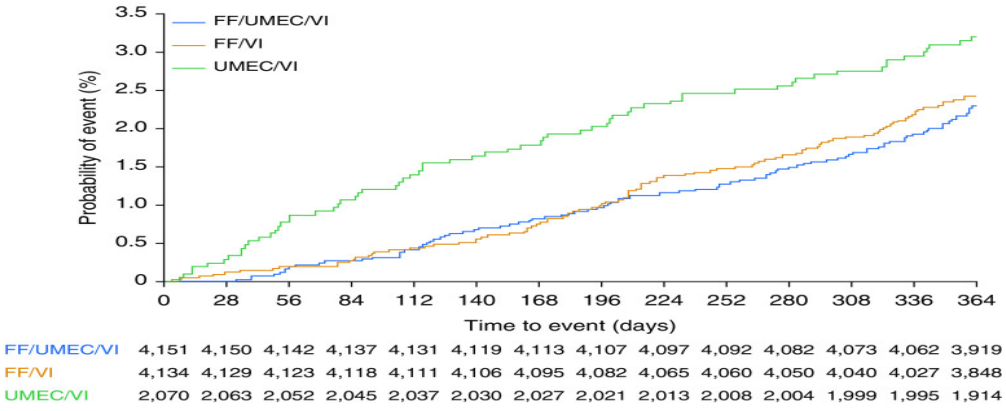


28% observed relative Difference FF/UMEC/VI vs UMEC/VI

Lower Rates of Cardiovascular and Respiratory Deaths

Off Treatment. Deaths

B



Lipson et al *Am J Respir Crit Care Med.* 2020 Jun 15; 201(12): 1508–1516

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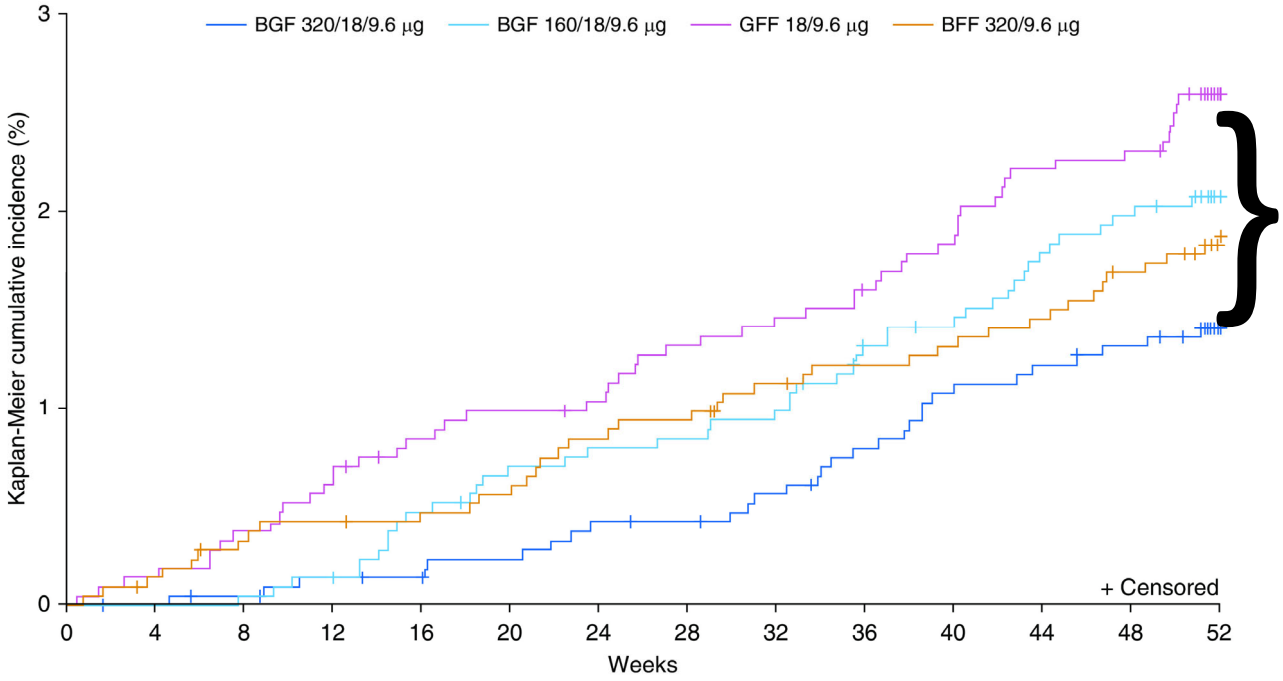
Ethos Trial: Reduction in All Cause Mortality for Triple Therapy Versus ICS LABA an LABA/LAMA



49% relative difference in Mortality with ICS/LABA/LAMA vs LAMA/LABA

Patients at risk														
BGF 320/18/9.6 µg	2,137	2,136	2,134	2,131	2,130	2,127	2,123	2,122	2,118	2,112	2,106	2,103	2,100	2,075
BGF 160/18/9.6 µg	2,121	2,121	2,120	2,118	2,110	2,104	2,102	2,101	2,098	2,087	2,084	2,076	2,072	2,062
GFF 18/9.6 µg	2,120	2,117	2,112	2,106	2,100	2,097	2,095	2,089	2,086	2,082	2,077	2,069	2,067	2,045
BFF 320/9.6 µg	2,131	2,127	2,122	2,120	2,118	2,116	2,110	2,108	2,102	2,099	2,097	2,094	2,088	2,075

Rabe et al New Engl. J Med 2018 202;35-48

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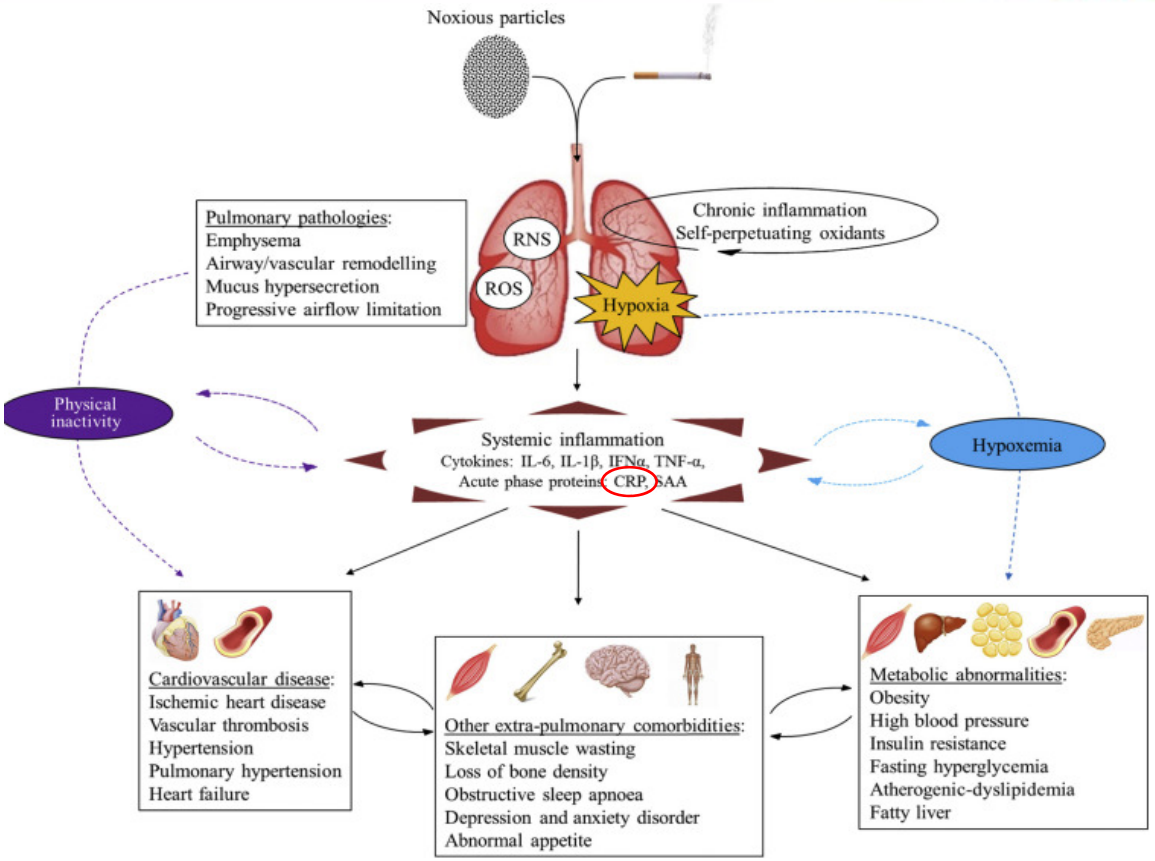
CRP. And Pathogenesis of Cardiovascular Disease And Other Comorbidities in COPD



Chan et al Pharmacol Ther. 2019 Jun; 198: 160–188

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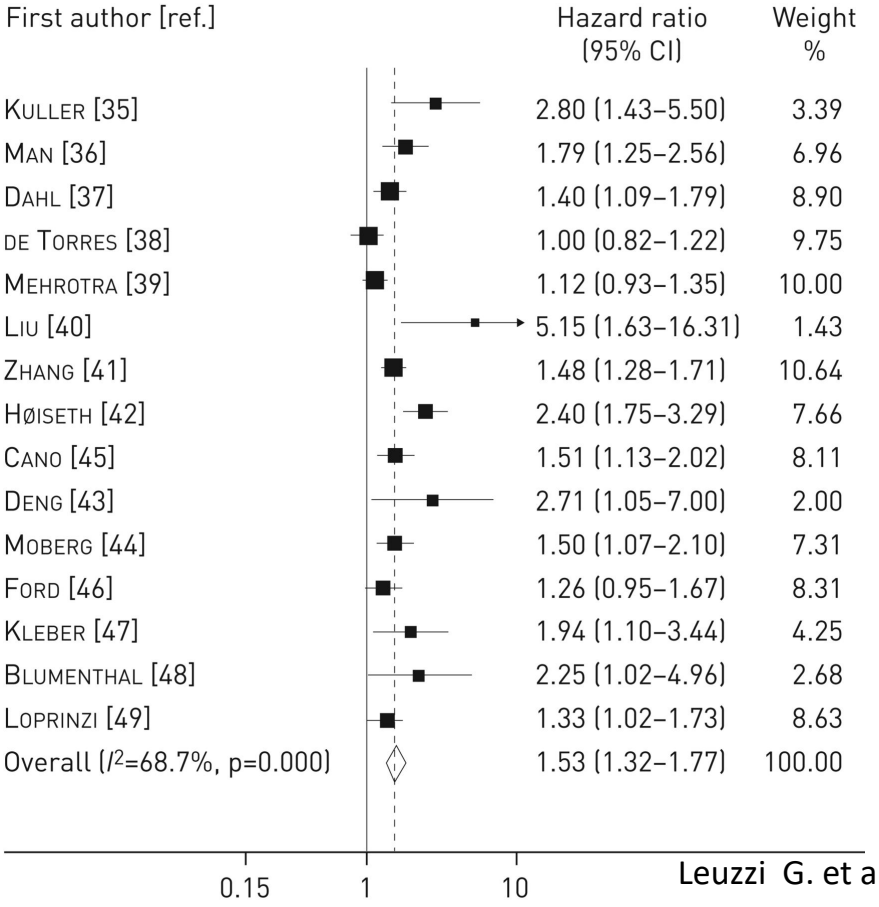
CRP Levels Demonstrate Correlation with Mortality in COPD

Meta Analysis 26 articles on COPD late and early mortality

- 15 late mortality
- 16 early mortality



Leuzzi G. et al Eur. Resp. Review 2017; 26:

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CRP Levels and Mortality in COPD

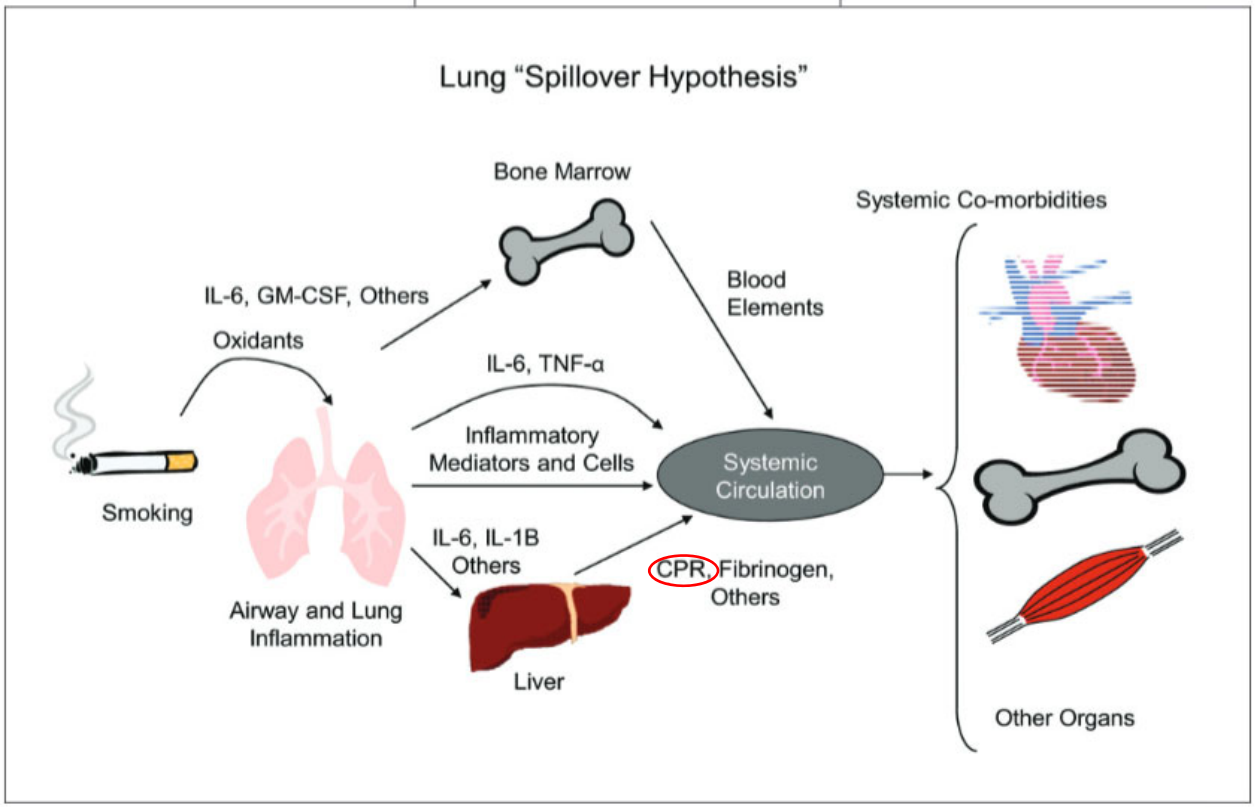

Figure – The "spillover hypothesis" for comorbid conditions in patients with COPD.[20]

CRP, C-reactive protein; GM-CSF, granulocyte macrophage colony-stimulating factor; IL, interleukin; TNF-α, tumor necrosis factor alpha.

Reprinted with permission from: Kao CC, Hanania NA. Co-morbidities of COPD: systemic inflammation. In: Crapo J, ed. *Atlas of Chronic Obstructive Pulmonary Disease*. Philadelphia, PA: Current Medicine Group; 2009:169-177.

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Macrolide Properties

- Antimicrobial
- Anti-inflammatory
- Augment Macrophage function
- Enhance Steroid efficacy

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Azithromycin: Mechanisms of Action and Their Relevance for Clinical Applications.

Inhibit:

- IL-8
- IL-6
- TNF alpha
- LTB_4
- PG-E2
- NF Kappa B

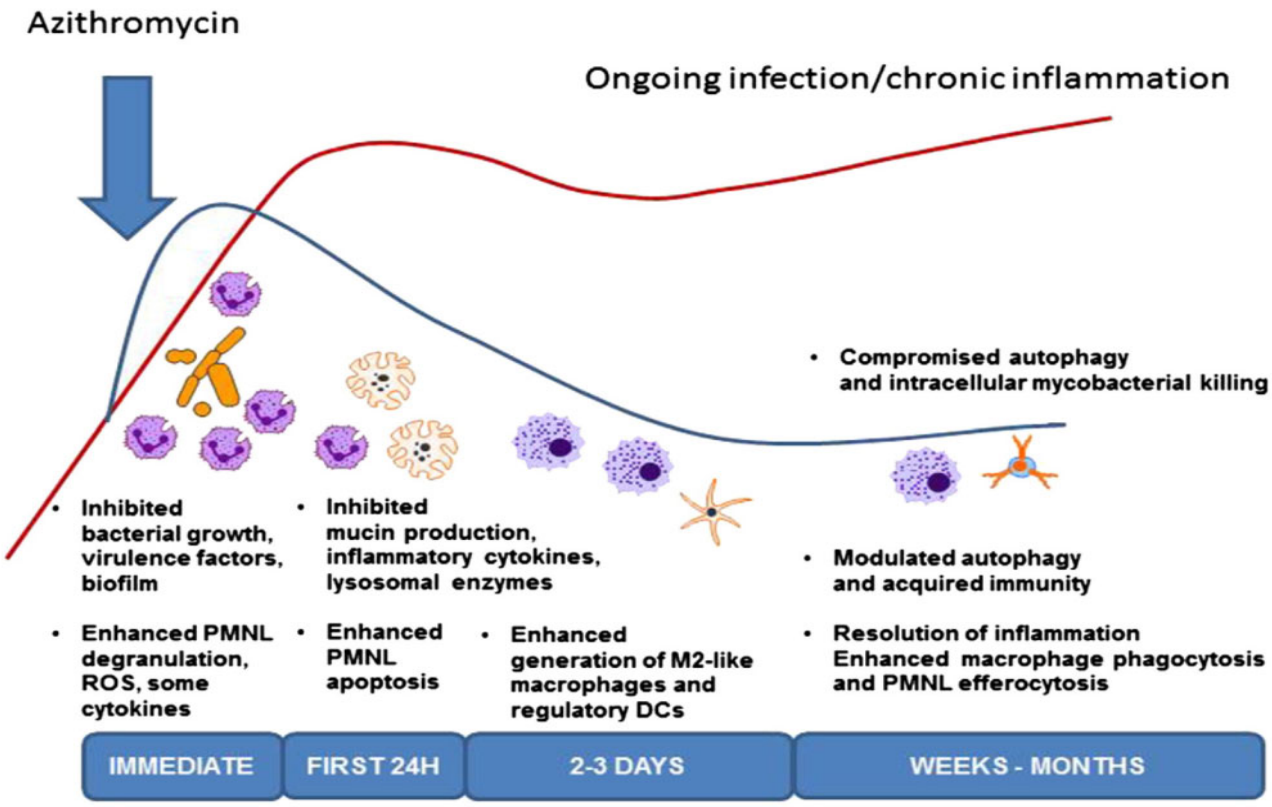

Fig. 2. Proposed time course of azithromycin actions on infection and chronic inflammation.

Parnham et al. *Pharmacology&Therapeutics* 143(2014)

Increase:

Histone deacetylase - Restores anti-inflammatory effect of steroids

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Azithromycin for Prevention of Exacerbations of COPD

DESIGN:

- azithromycin, 250 mg daily (570 participants) vs placebo (572 participants)
- 1 year in addition to their usual care.
- follow-up: 89% in the azithromycin group; 90% in the placebo group.

RESULTS:

- The **median time to the first exacerbation** was
  - Azithromycin: 266 days (95% confidence interval [CI], 227 to 313) azithromycin
  - Placebo: 174 days (95% CI, 143 to 215) (P<0.001).
- The **frequency of exacerbations:** exacerbations per patient-year
  - Azithromycin: 1.48 vs Placebo: 1.83 (P=0.01)

Hazard ratio for having an acute exacerbation of COPD per patient-year for azithromycin group was **0.73 (95% CI, 0.63 to 0.84; P<0.001)**

Albert et al. *NEJM* 2011 Aug 25;365(8)**:689-98**

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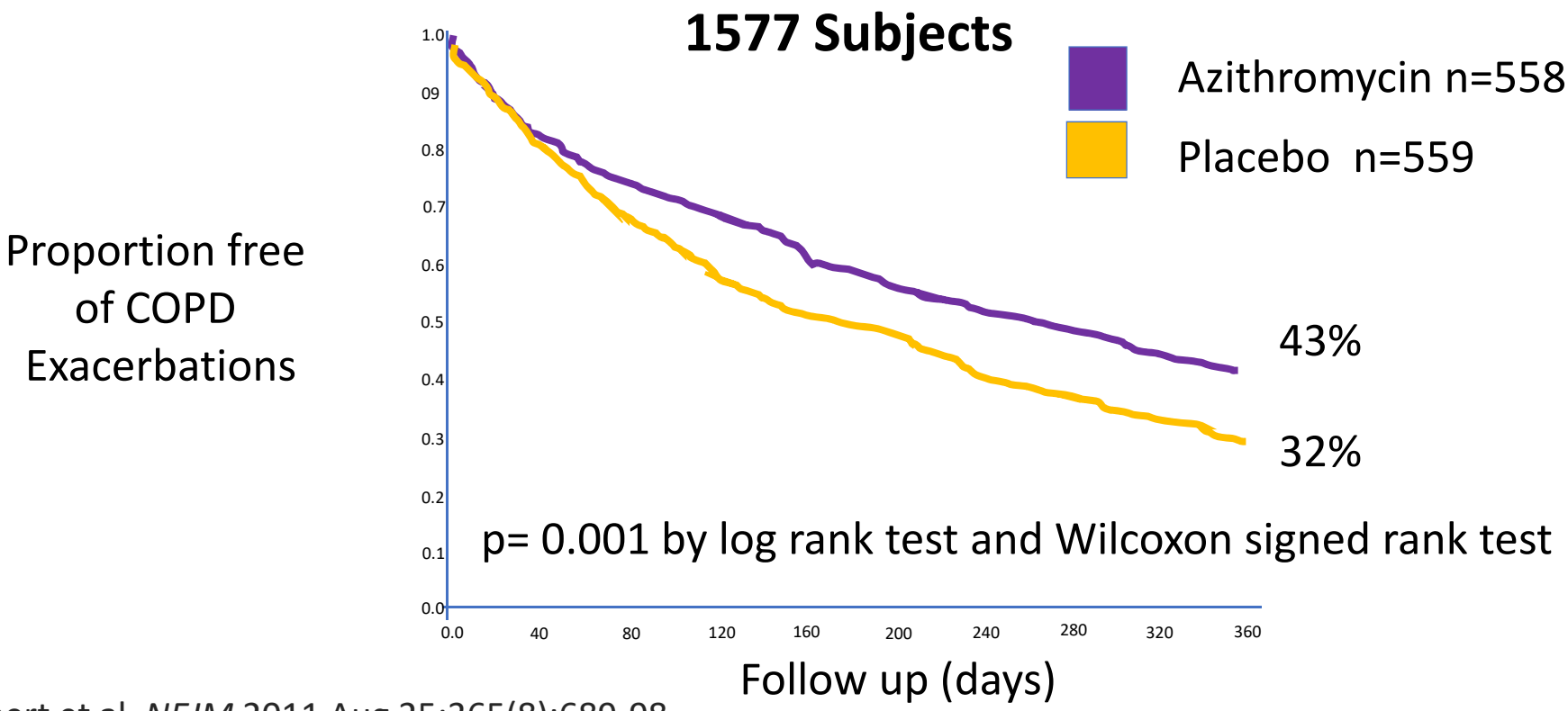
Azithromycin for Prevention of Exacerbations of COPD



Albert et al. *NEJM* 2011 Aug 25;365(8):689-98

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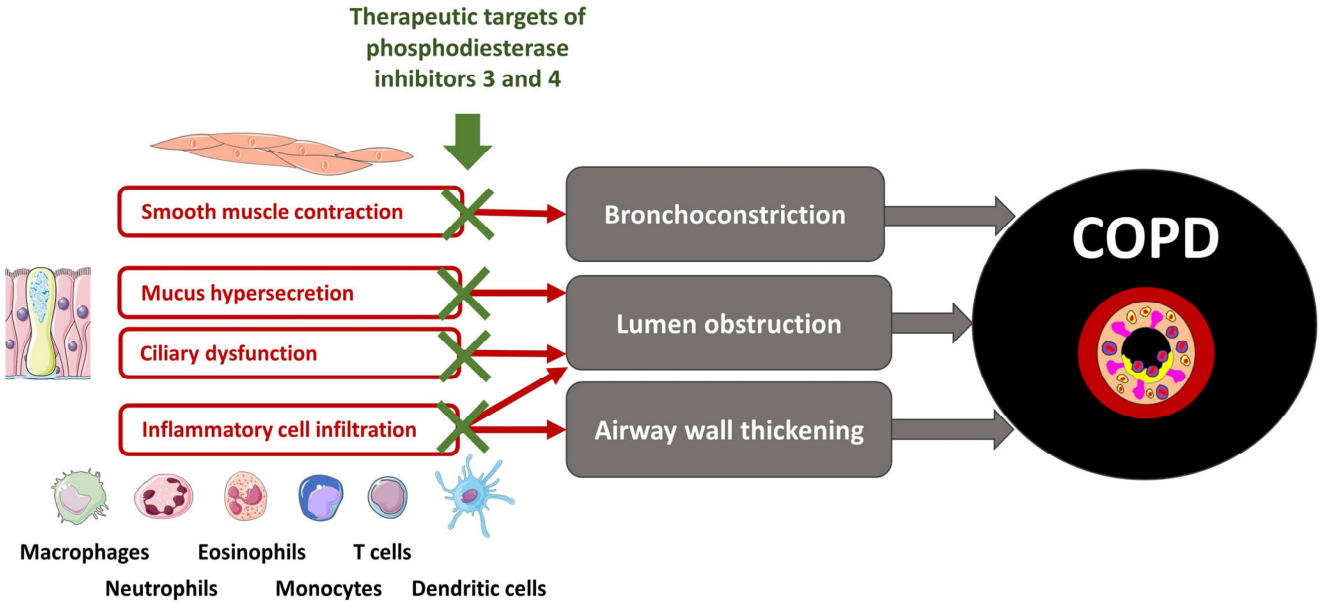
PDE3/PDE4 Inhibitor

- Inhaled agent
- PDE3 smooth muscle relaxant
- PDE4 anti-inflammatory with effects on neutrophils



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Safety Adverse Effects of PDE3/PDE4

Roflumilast(PDE4) : oral

Gastrointestinal: diarrhea, nausea, weight loss

RPL554/Ensifentrine (PDE3/PDE 4) 0.4 mg to 24 mg inhaled

Fewer side effects: Christensen, S. et al AJRCCM 2015

- Increased heart rate
- Fall in blood pressure

*Recent ATS Abstract showed Phase 3 study improved lung function and reduced exacerbations Poster session B22 K Rickard et al

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Challenges/Questions

- Smoking cessation
- Alternative Treatments to Steroids
- Optimum Identification/treatment of Comorbidities
- Understanding T-2 vs Non-T2 COPD
- Understanding role of Microbiome in COPD
- Defining Other Phenotypes\Endotypes
- Rapid Decliners
- Preserved Ratio Impaired spirometry (PRISm)
- **Role for biologics?**

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Precision Medicine: Treatable Traits

Precision medicine is defined as “treatments targeted to the needs of individual patients on the basis of genetic, biomarker, phenotypic, or psychosocial characteristics that distinguish a given patient from other patients with similar clinical patients.”

Agusti, et al. *ERJ* 2016;47:359-361.

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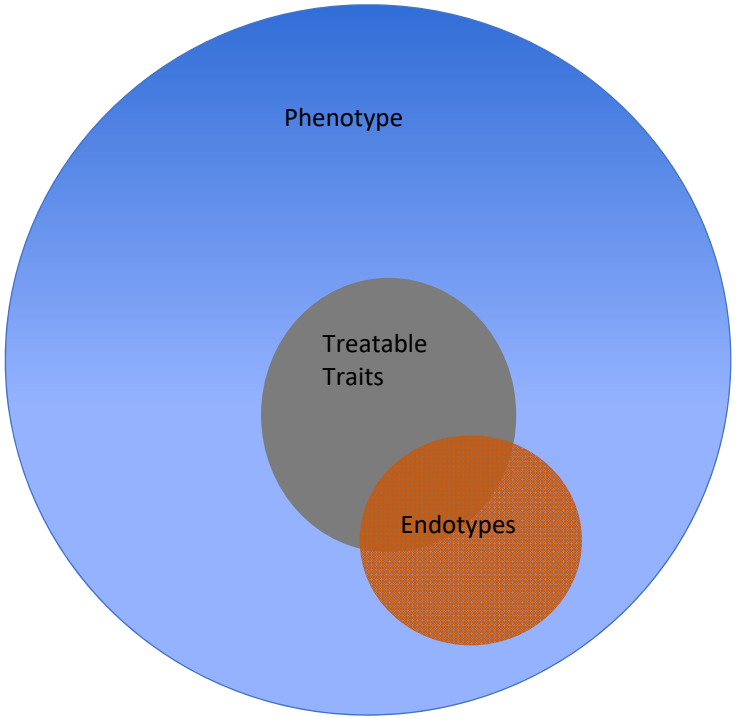
Phenotype to Endotype



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Current and Proposed COPD Phenotypes

Accepted Phenotypes

1. Alpha-1 AT Deficiency
2. Emphysema/hyperinflation
3. Frequent Exacerbator

Proposed Phenotypes

1. Non-smokers
2. Rapid decliners
3. Asthma/COPD overlap
4. Eosinophilic
5. Mild airflow obstruction/severe dyspnea
6. Chronic bronchitis
7. GERD comorbidity
8. Cardiovascular co-morbidity
9. OSA comorbidity
10. CT Phenotypes

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Phenotype and Networks
Many overlaps and connections are endless

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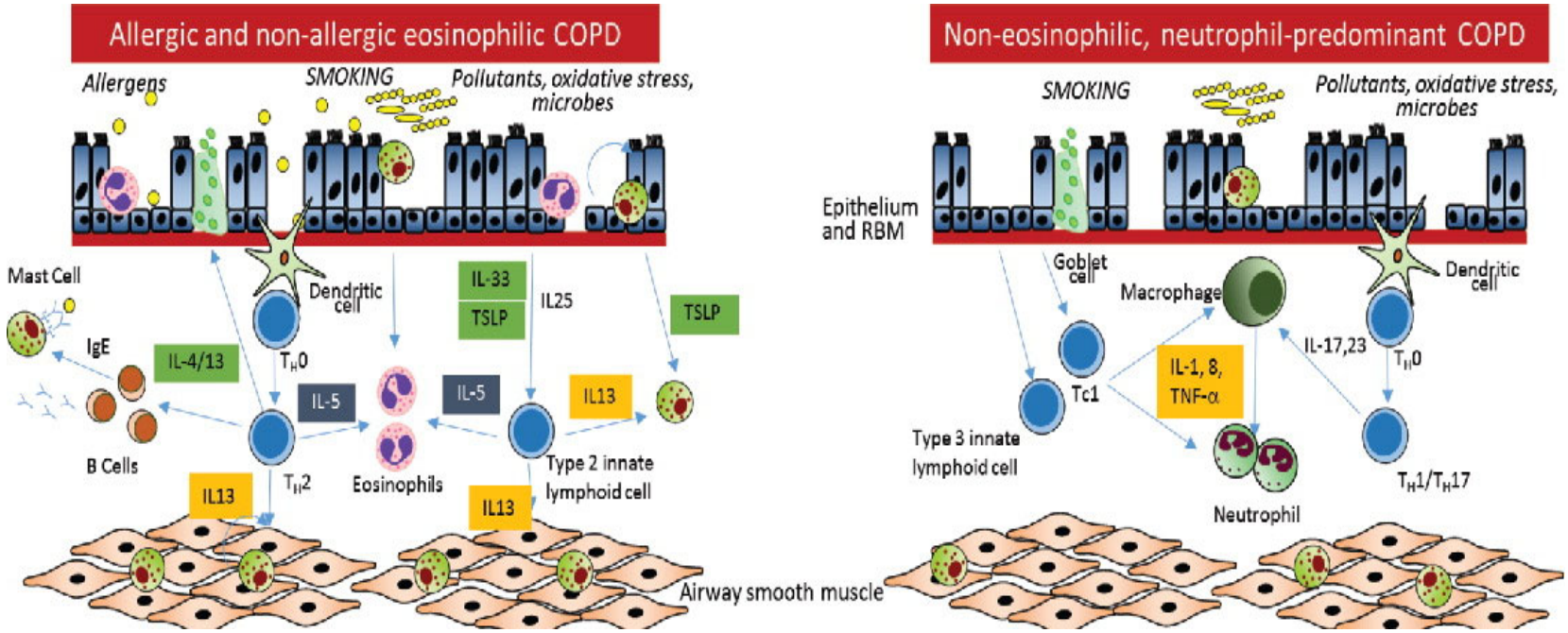
T2 High COPD vs Non T2 COPD

Biologic Drugs: A new Target Therapy in COPD



Yousef A et al *JCOPD*:2018;15(2)99-107

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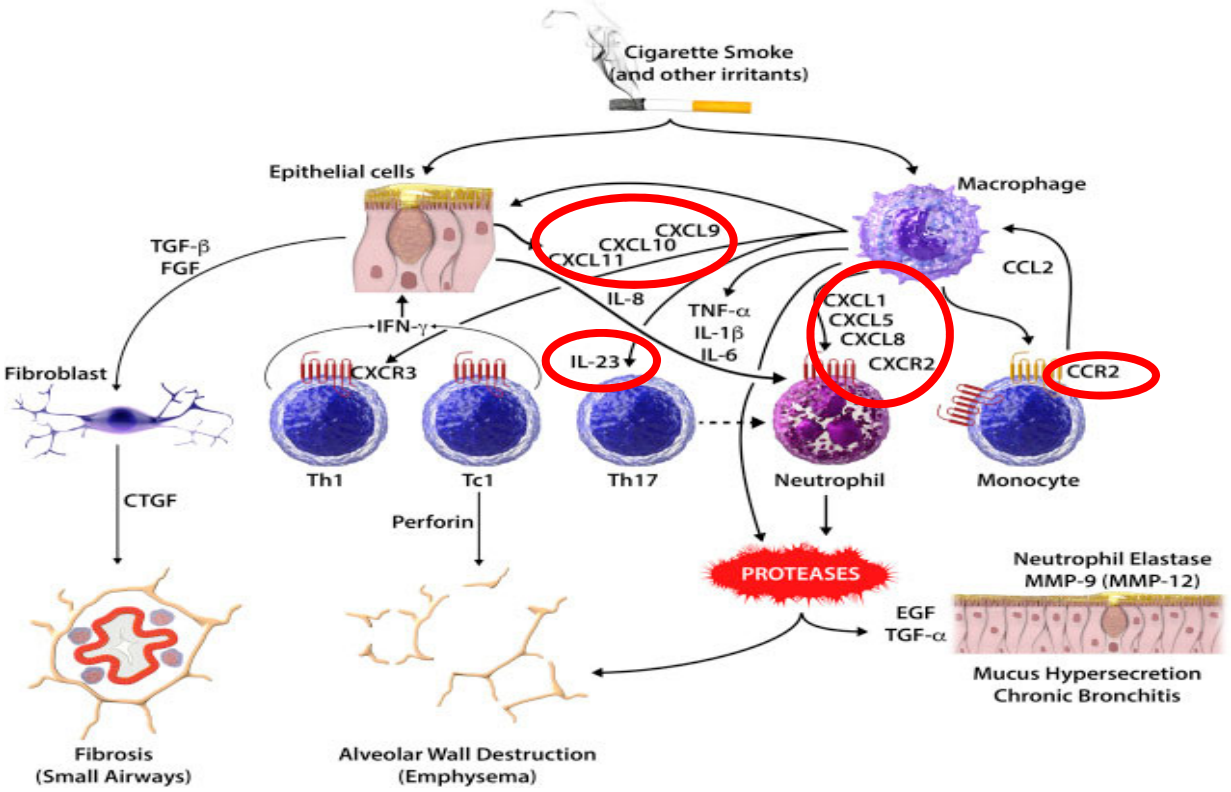
BIOLOGIC TARGETS FOR NON T2 COPD



Pavord et al. *JACI* 2018: 141; 1983-1991

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TREATMENT OPTIONS FOR: COPD SUMMARY

- COPD patients are a **heterogeneous population** with a wide array of **variable characteristics** that can impact response to treatment
- **Phenotypes lack precision** to find one intervention that will address all components of their COPD
- **Identifying treatable traits** is the most practical approach
- **Identifying endotypes** will allow for greater precision in treatment
- **Managing co-morbidities** is often as important as managing their COPD

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