Impact of Exacerbations: *new perspectives*

John Hurst

Professor of Respiratory Medicine
j.hurst@ucl.ac.uk

UCL Respiratory | Faculty of Medical Sciences

Where I work and what I do...

Overview

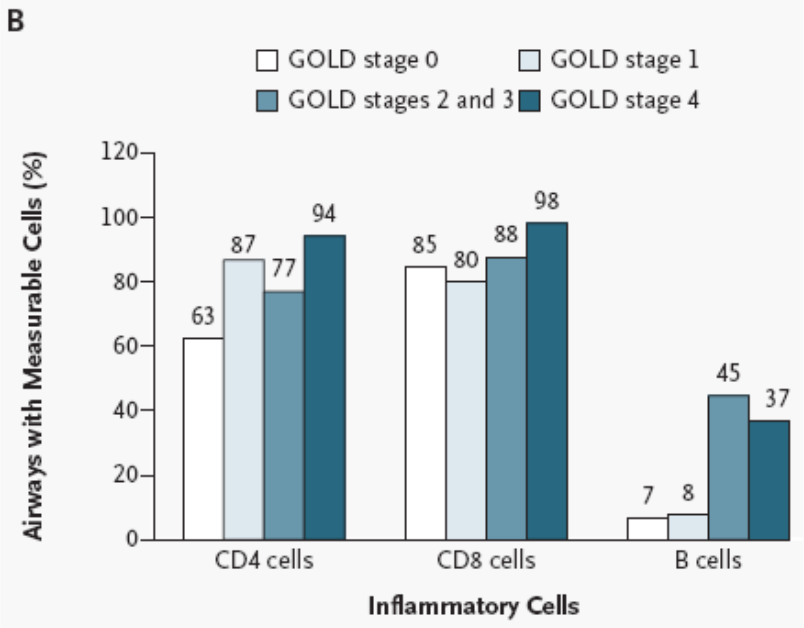
- What is COPD?
- What is a COPD exacerbation and how to assess severity?
- Management of Exacerbations
- Prevention of Exacerbations
- Beyond exacerbations: mortality reduction in COPD

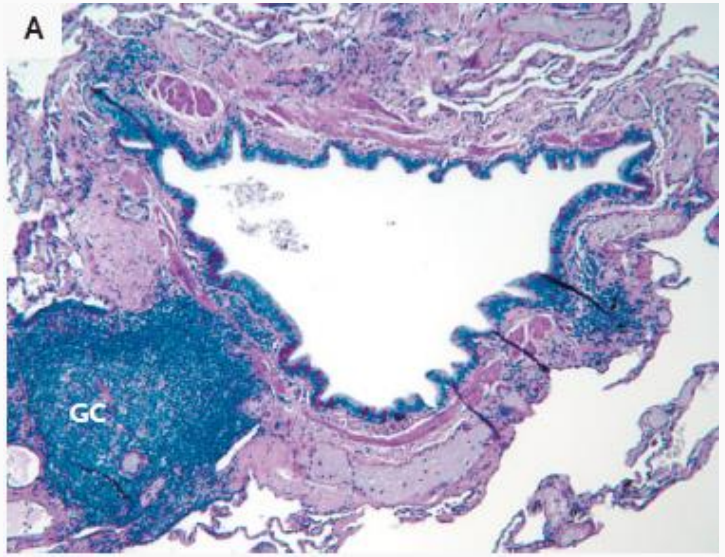
What is COPD?

"COPD is a heterogeneous lung condition characterized by chronic respiratory symptoms (dyspnea, cough, sputum production and/or exacerbations) due to abnormalities of the airways and/or alveoli that cause persistent, often progressive airflow obstruction"

www.goldcopd.org

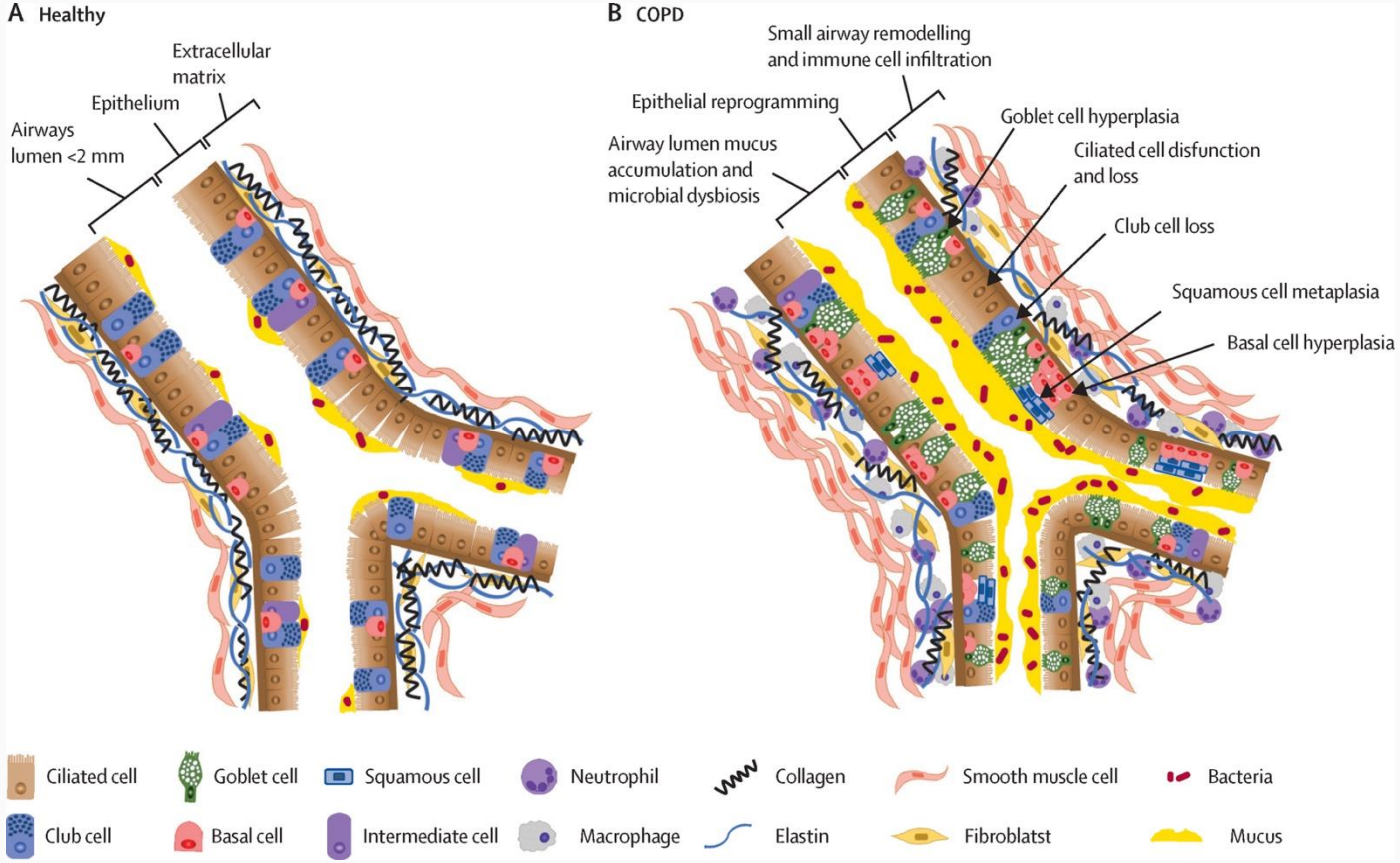
What is COPD?





Hogg JC, Chu F, Utokaparch S, Woods R, Elliott WM, Buzatu L, Cherniack RM, Rogers RM, Sciurba FC, Coxson HO, Paré PD. The nature of small-airway obstruction in chronic obstructive pulmonary disease. N Engl J Med. 2004 Jun 24;350(26):2645-53. doi: 10.1056/NEJMoa032158. PMID: 15215480.

What is COPD?



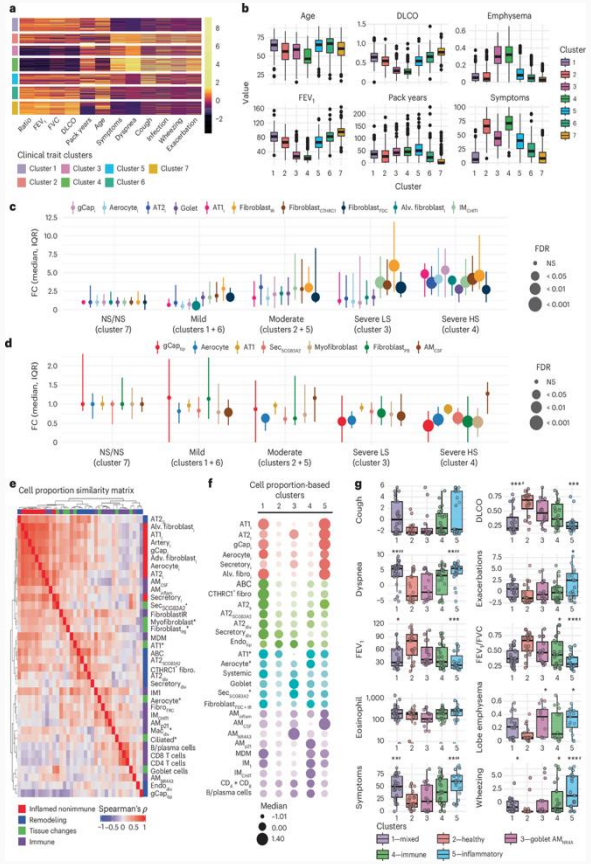
***Epithelial Reprogramming**, driven by exposure-induced oxidant injury → squamous differentiation and goblet cells.*

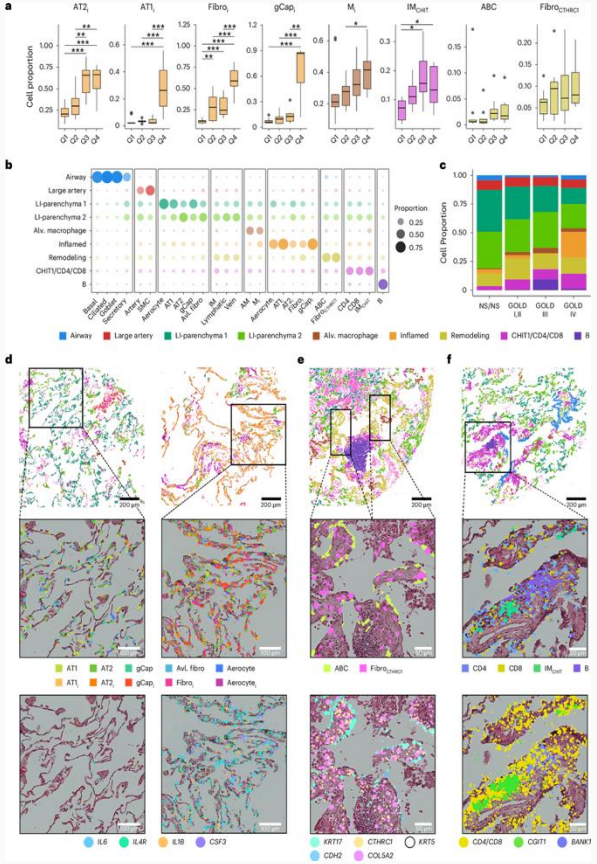
*Dysfunctional cilia and altered microenvironment with CMH → **mucosal obstruction and dysbiosis**.*

*Later **airway remodelling and inflammation**, initially neutrophils and macrophages (but defective phagocytosis). Later adaptive response with follicles.*

Christenson SA, Smith BM, Bafadhel M, Putcha N. Chronic obstructive pulmonary disease. Lancet. 2022 May 6:S0140-6736(22)00470-6. doi: 10.1016/S0140-6736(22)00470-6. Epub ahead of print. PMID: 35533707.

What is COPD?





Few stratification tools in COPD.

Single cell RNA-seq, integrated with spatial transcriptomics, lung and plasma proteomics.

FINDINGS:
Multicellular inflammatory network involving structural cells with pro-inf phenotype, generally more pronounced with symptoms and exacerbation risk.
Evidence of aberrant repair mechanisms

→ → → ***Potential for biology-guided intervention, in target enriched populations.***

Zhang Y et al. Aberrant cellular communities underlying disease heterogeneity in chronic obstructive pulmonary disease. Nat Genet. 2026 Jan 23. doi: 10.1038/s41588-025-02480-z. Epub ahead of print. PMID: 41578022.

The goals of COPD care

REDUCE SYMPTOMS

Relieve symptoms

Improve exercise tolerance

Improve health status

+

REDUCE RISK

Prevent disease progression

Prevent and treat exacerbations

Reduce mortality

Overview

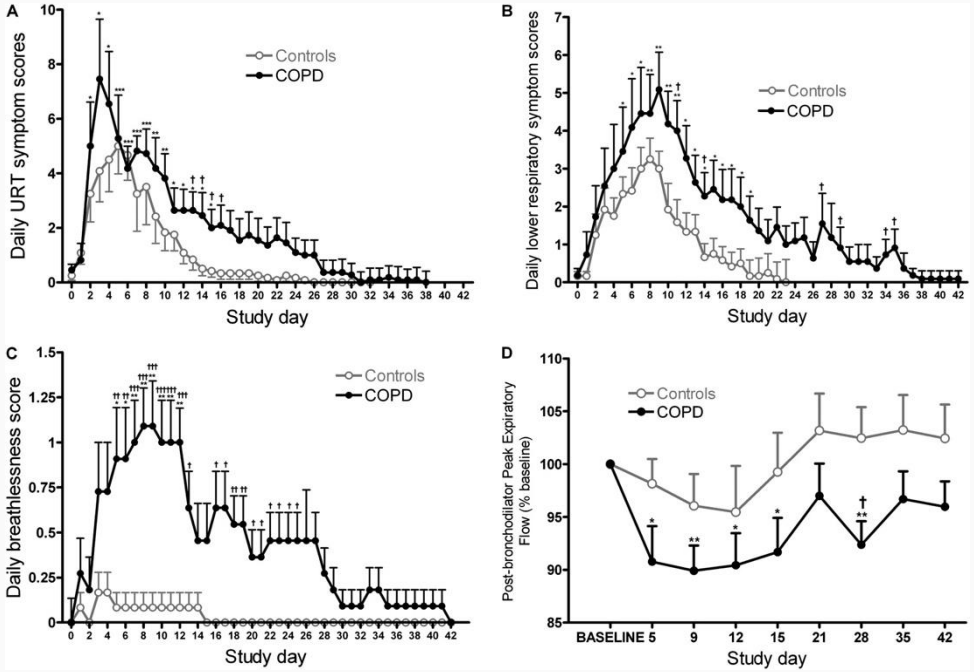
- What is COPD?
- What is a COPD exacerbation and how to assess severity?
- Management of Exacerbations
- Prevention of Exacerbations
- Beyond exacerbations: mortality reduction in COPD

GOLD: Exacerbation Definition

“An exacerbation of COPD is an acute event with symptoms worsening over a few days and characterized by increased dyspnea and/or cough and sputum that many be accompanied by tachypnea and/or tachycardia. Exacerbations are often associated with increased local and systemic inflammation caused by airway infection, pollution or other insults to the lung”.

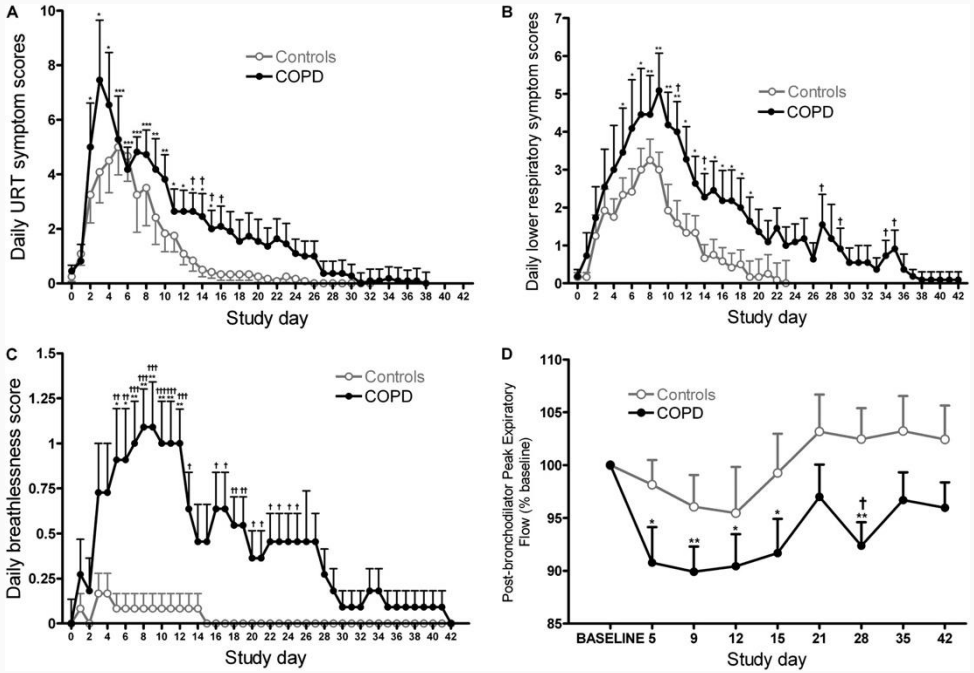
https://goldcopd.org/2026-gold-report-and-pocket-guide/

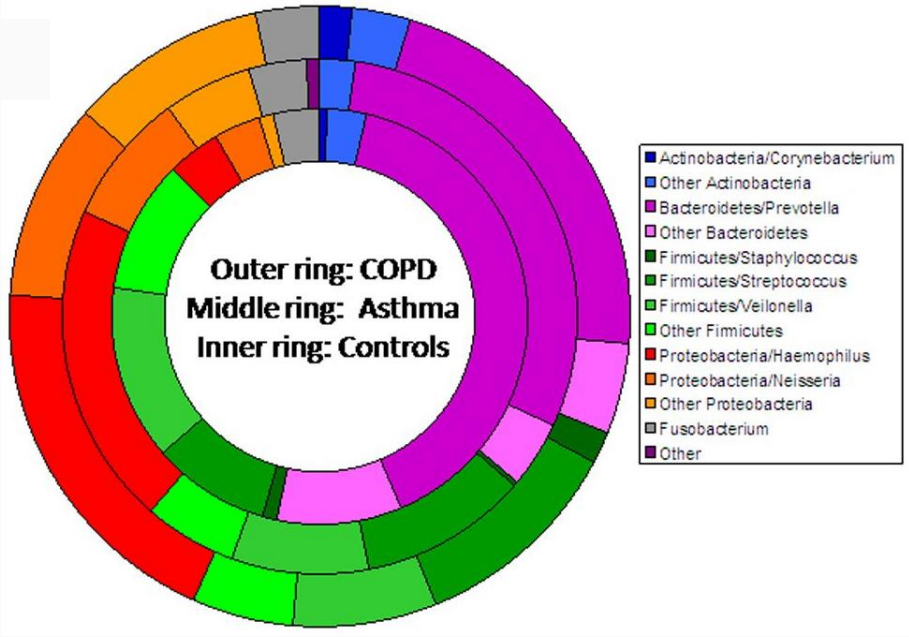
Exacerbation aetiology



Mallia P et al. Experimental rhinovirus infection as a human model of chronic obstructive pulmonary disease exacerbation. Am J Respir Crit Care Med. 2011 Mar 15;183(6):734-42. doi: 10.1164/rccm.201006-0833OC. Epub 2010 Oct 1. PMID: 20889904; PMCID: PMC3081284.

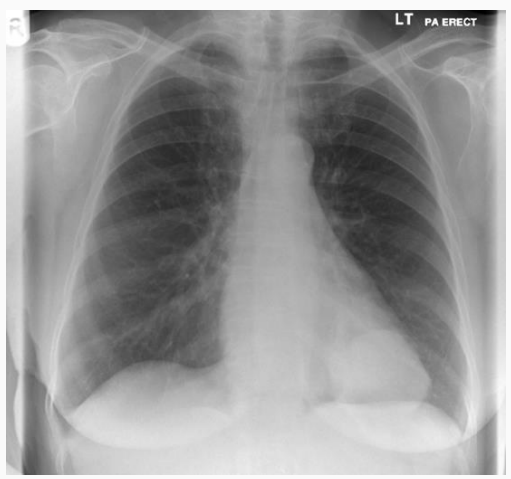
Exacerbation aetiology

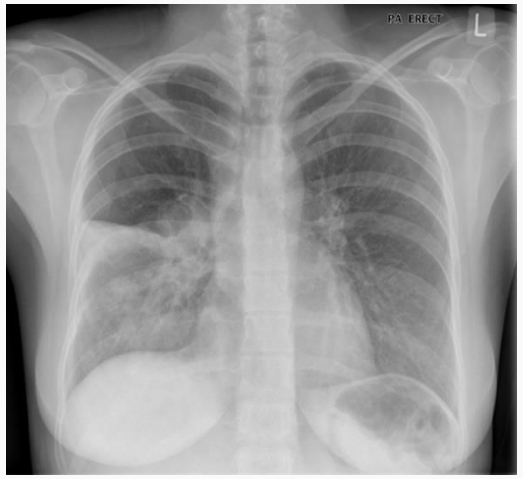




Hilty M, Burke C, Pedro H, Cardenas P, Bush A, Bossley C, Davies J, Ervine A, Poulter L, Pachter L, Moffatt MF, Cookson WO. Disordered microbial communities in asthmatic airways. PLoS One. 2010 Jan 5;5(1):e8578. doi: 10.1371/journal.pone.0008578. PMID: 20052417; PMCID: PMC2798952.

What is (and is not) an exacerbation of COPD?

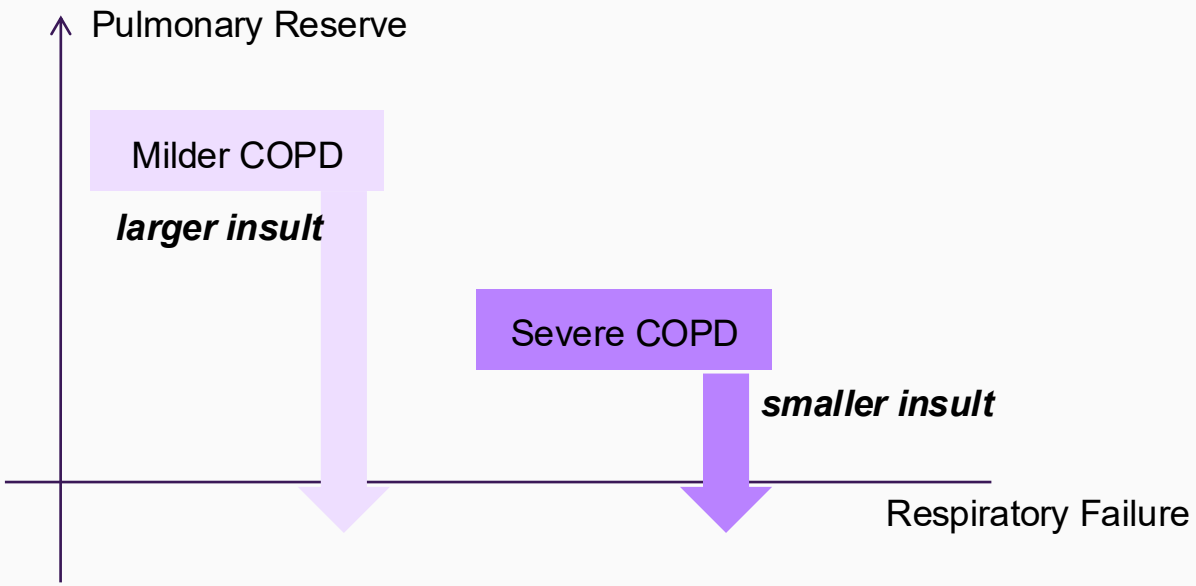




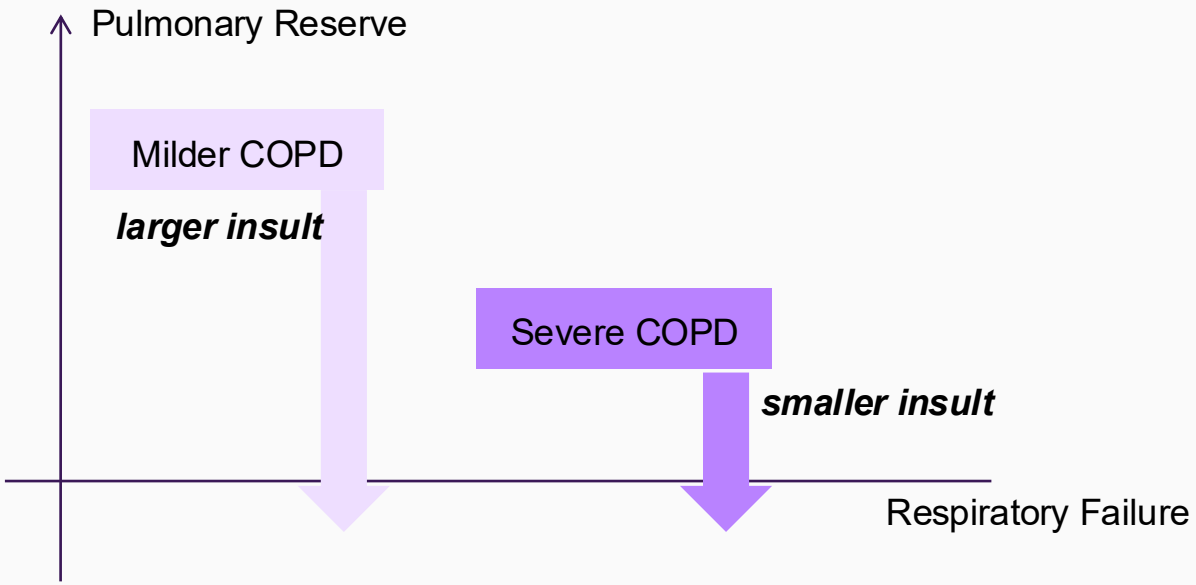
Exacerbation severity

Previous classification	
Mild	Increase in SABA
Moderate	Oral antibiotics/ steroids
Severe	Hospitalised

Exacerbation acuity

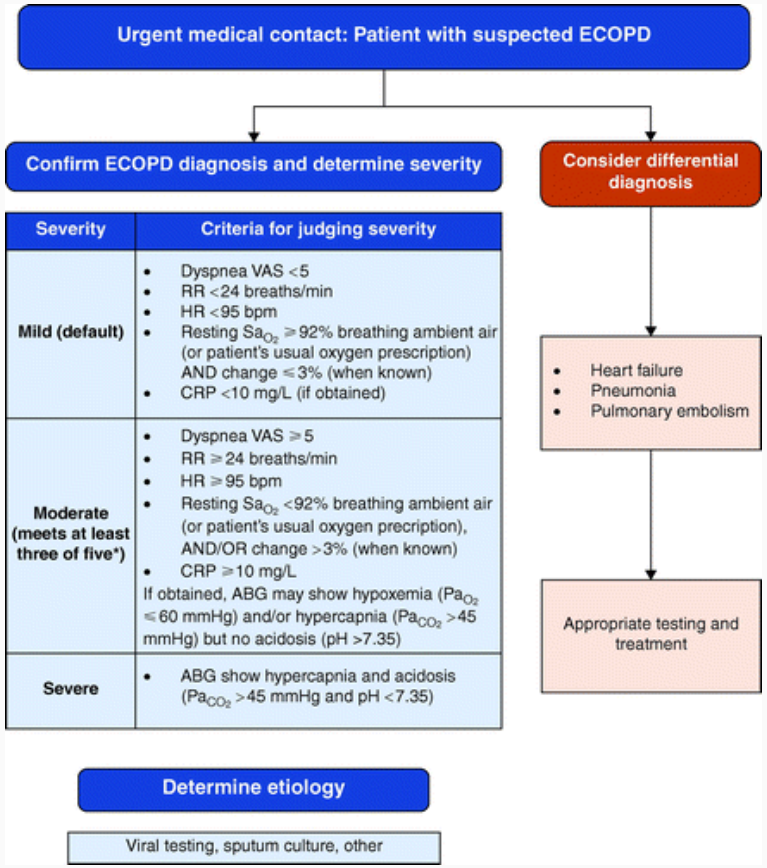


Exacerbation acuity



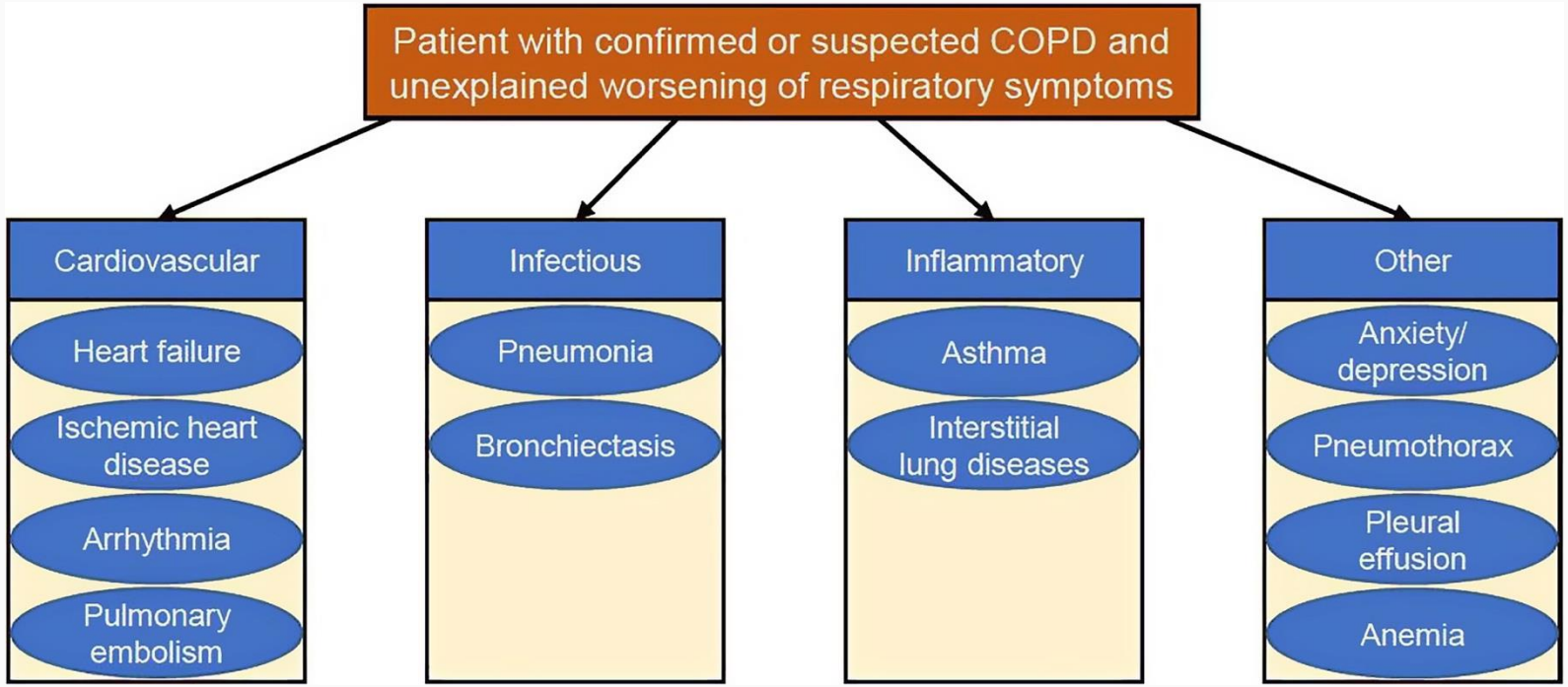
Exacerbation$^{\text{Severity}}$ = COPD$^{\text{Severity}}$ + Insult$^{\text{Severity}}$ + Co-Morbidity

‘Rome’ Exacerbation Assessment



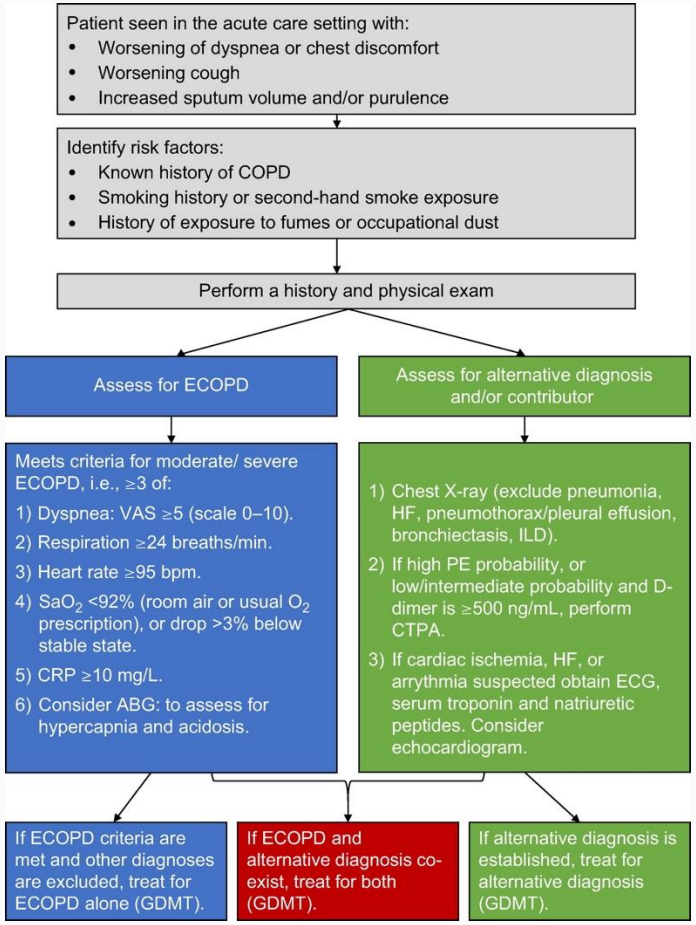
Celli BR et al. An Updated Definition and Severity Classification of Chronic Obstructive Pulmonary Disease Exacerbations: The Rome Proposal. Am J Respir Crit Care Med. 2021 Dec 1;204(11):1251-1258. doi: 10.1164/rccm.202108-1819PP. PMID: 34570991.

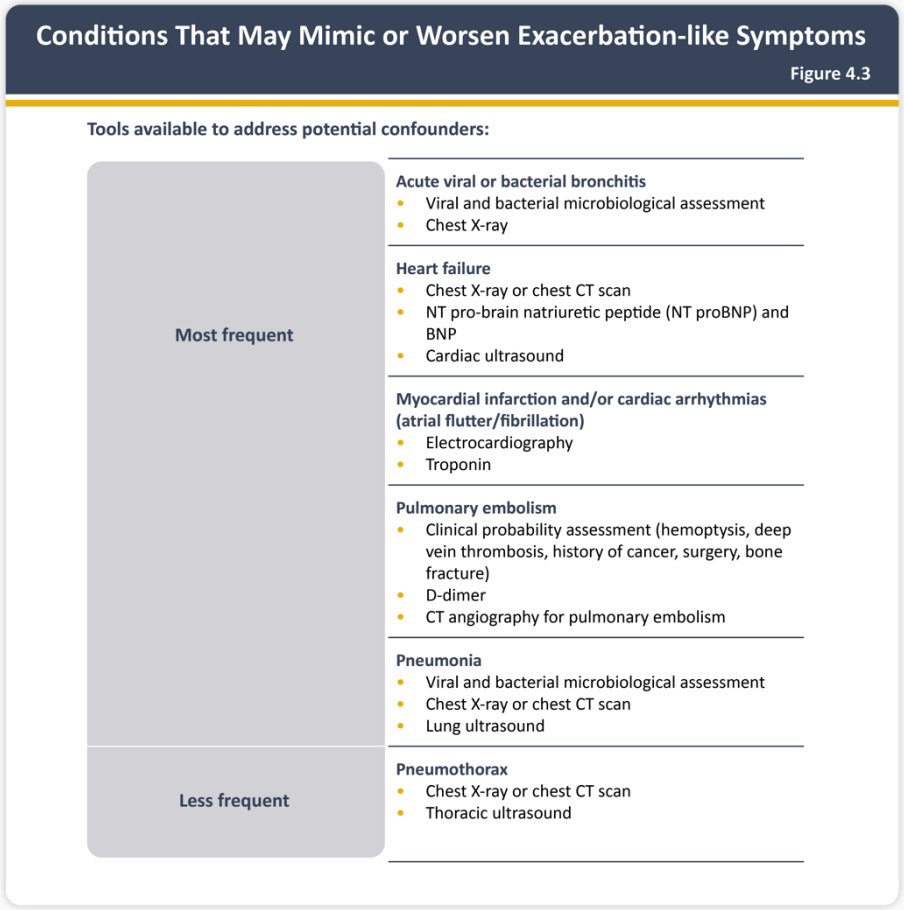
Differential diagnosis of exacerbation



Celli BR et al. Differential Diagnosis of Suspected Chronic Obstructive Pulmonary Disease Exacerbations in the Acute Care Setting: Best Practice. Am J Respir Crit Care Med. 2023 May 1;207(9):1134-1144. doi: 10.1164/rccm.202209-1795CI. PMID: 36701677; PMCID: PMC10161746.

Differential diagnosis of exacerbation





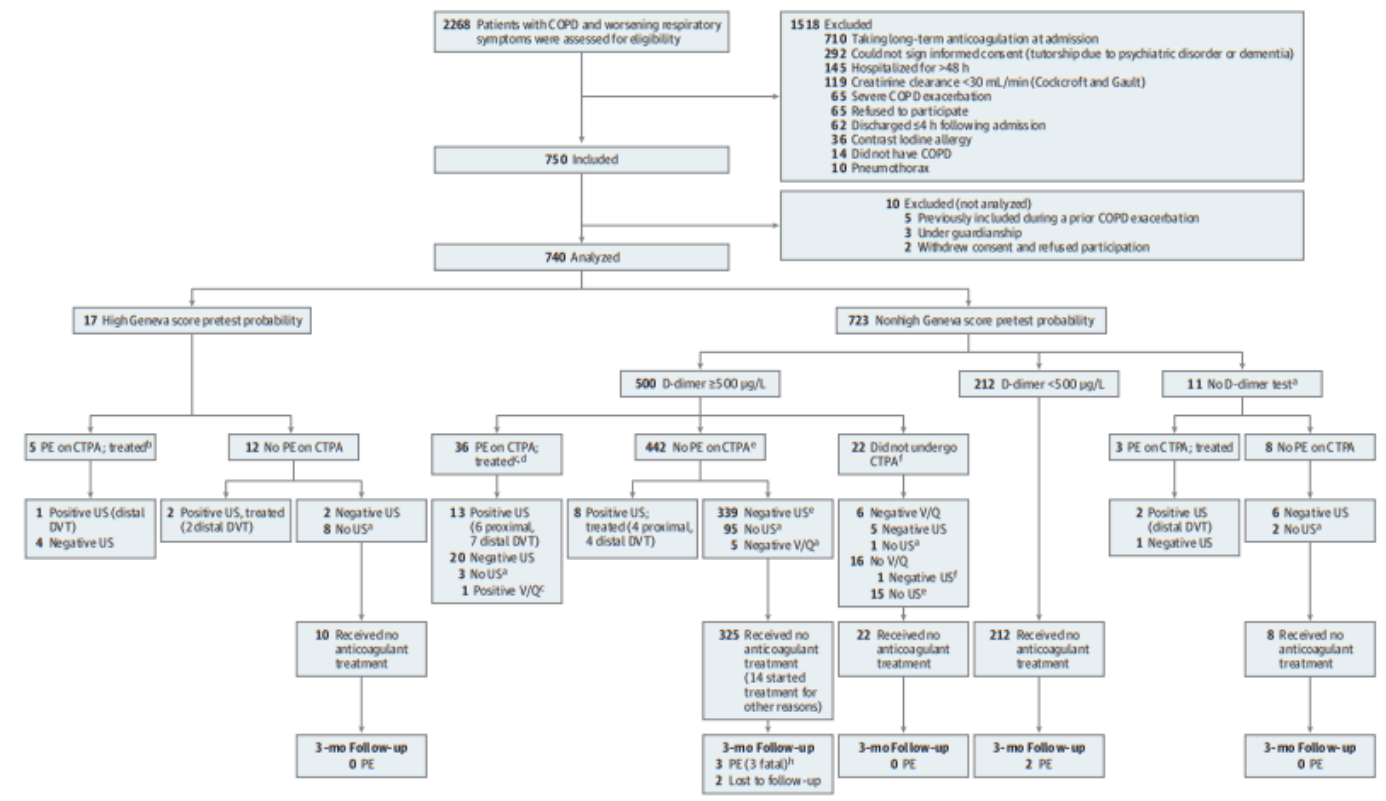
Celli BR et al. Differential Diagnosis of Suspected Chronic Obstructive Pulmonary Disease Exacerbations in the Acute Care Setting: Best Practice. Am J Respir Crit Care Med. 2023 May 1;207(9):1134-1144. doi: 10.1164/rccm.202209-1795CI. PMID: 36701677; PMCID: PMC10161746.

PE and symptom changes in COPD

- Consecutive patients with COPD admitted for worsening symptoms
- Previous PFT or diagnosis of COPD by a pulmonologist.
- Exclusion criteria: anticoagulant, pneumothorax, severe exacerbation making imaging unfeasible.
- Clinical probability of PE assessed using revised Geneva score.
- Patients with high clinical probability (score ≥11) proceeded to CTPA and doppler.
- D-dimer test for patients with a low or intermediate probability (score <11). In patients with a negative D-dimer (<500 ng/mL), PE excluded.
- Follow-up to three months.
- Primary outcome was PE within 48 hours.

Couturaud F et al. Prevalence of Pulmonary Embolism Among Patients With COPD Hospitalized With Acutely Worsening Respiratory Symptoms. JAMA. 2021 Jan 5;325(1):59-68. doi: 10.1001/jama.2020.23567. PMID: 33399840; PMCID: PMC7786241.

PE and symptom changes in COPD



33% included
<u>31% on anti-coagulation</u>

2% need CT as high-risk
68% need CT as D-dimer elevated

8% of scans positive

Overall 5.9% PE (and additional 1.4% DVT)

3/12 Mortality 26% with VTE vs. 5% without (mostly cancer)

Couturaud F et al. Prevalence of Pulmonary Embolism Among Patients With COPD Hospitalized With Acutely Worsening Respiratory Symptoms. JAMA. 2021 Jan 5;325(1):59-68. doi: 10.1001/jama.2020.23567. PMID: 33399840; PMCID: PMC7786241.

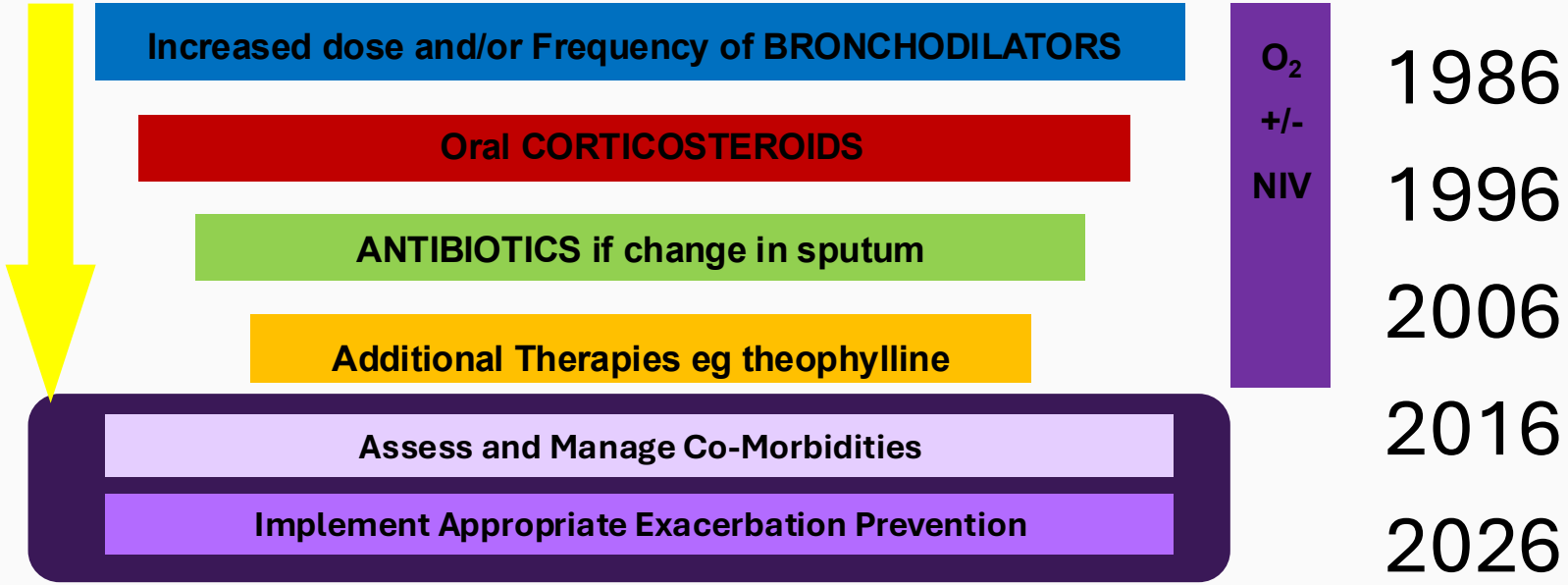
A different perspective...

Act on COPD campaign.

Overview

- What is COPD?
- What is a COPD exacerbation and how to assess severity?
- Management of Exacerbations
- Prevention of Exacerbations
- Beyond exacerbations: mortality reduction in COPD

Exacerbation management



Exacerbation management

Management of Severe but not Life-threatening Exacerbations*

Figure 4.5

Assess severity of symptoms, blood gases, chest radiograph

Bronchodilators:

- Increase doses and/or frequency of short-acting bronchodilators
- Combine short-acting $beta_2$-agonists and anticholinergics
- Consider use of long-acting bronchodilators when patient becomes stable
- Use spacers or air-driven nebulizers when appropriate

Consider oral corticosteroids

Consider antibiotics (oral) in patients with purulent oral secretions, prior positive sputum bacteria culture or requiring mechanical ventilation (invasive or noninvasive)

Consider high flow oxygen (HFNT) or noninvasive ventilation (NIV), obtain serial blood gas, venous blood gas and pulse oximetry measurements

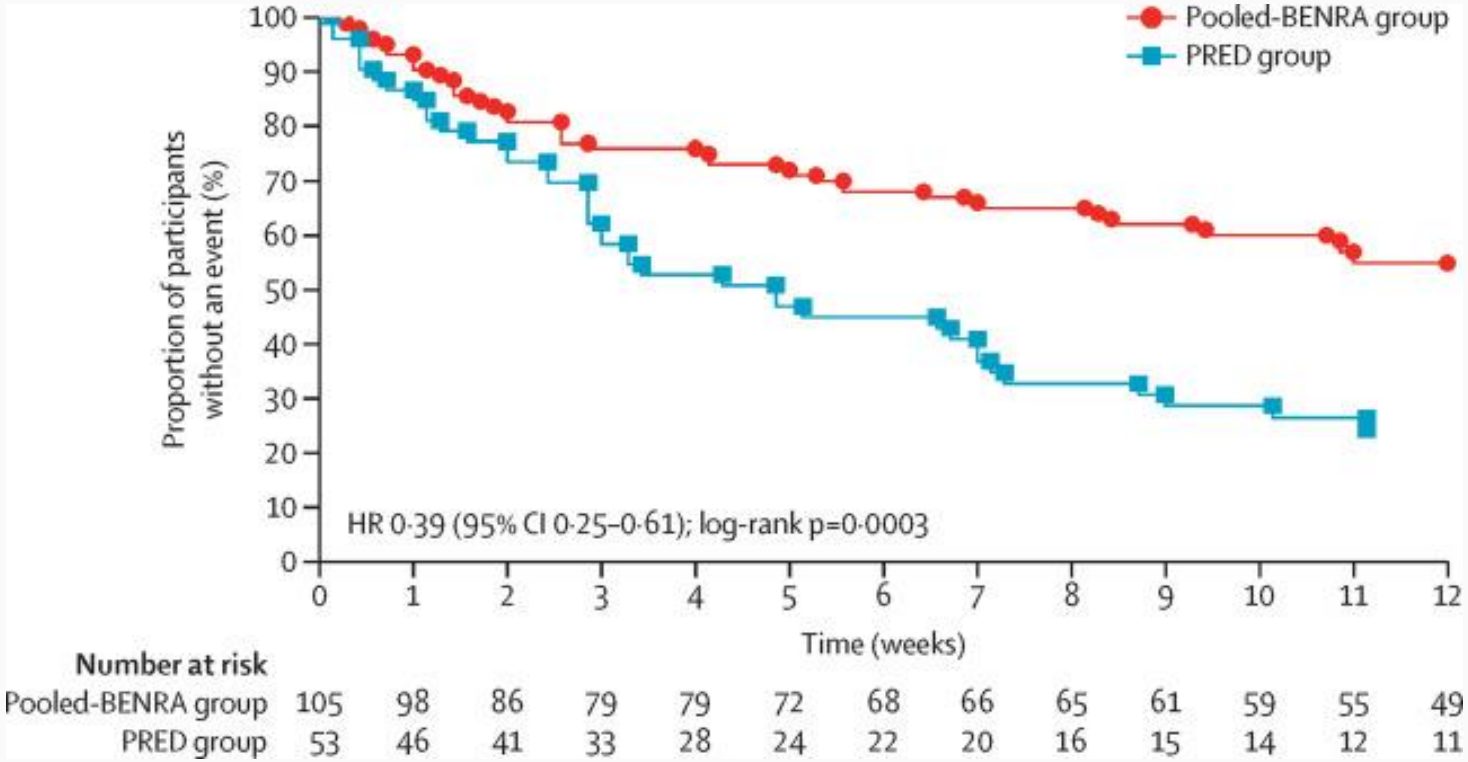
At all times:

- Monitor fluid balance
- Consider subcutaneous heparin or low molecular weight heparin for thromboembolism prophylaxis
- Identify and treat associated conditions (e.g., heart failure, arrhythmias, pulmonary embolism etc.)

*Local resources need to be considered

https://goldcopd.org/2026-gold-report-and-pocket-guide/

Exacerbation management: ABRA

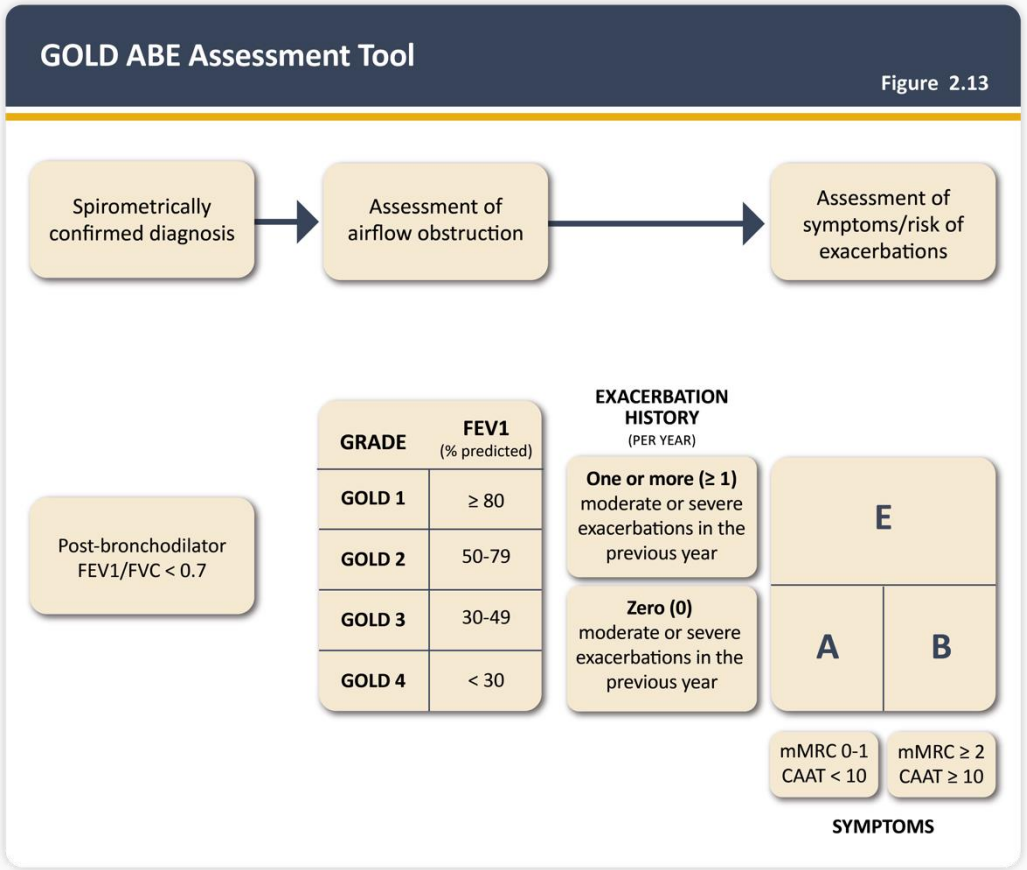


Ramakrishnan S et al. Treating eosinophilic exacerbations of asthma and COPD with benralizumab (ABRA): a double-blind, double-dummy, active placebo-controlled randomised trial. Lancet Respir Med. 2025 Jan;13(1):59-68. doi: 10.1016/S2213-2600(24)00299-6. Epub 2024 Nov 29. PMID: 39615502.

Overview

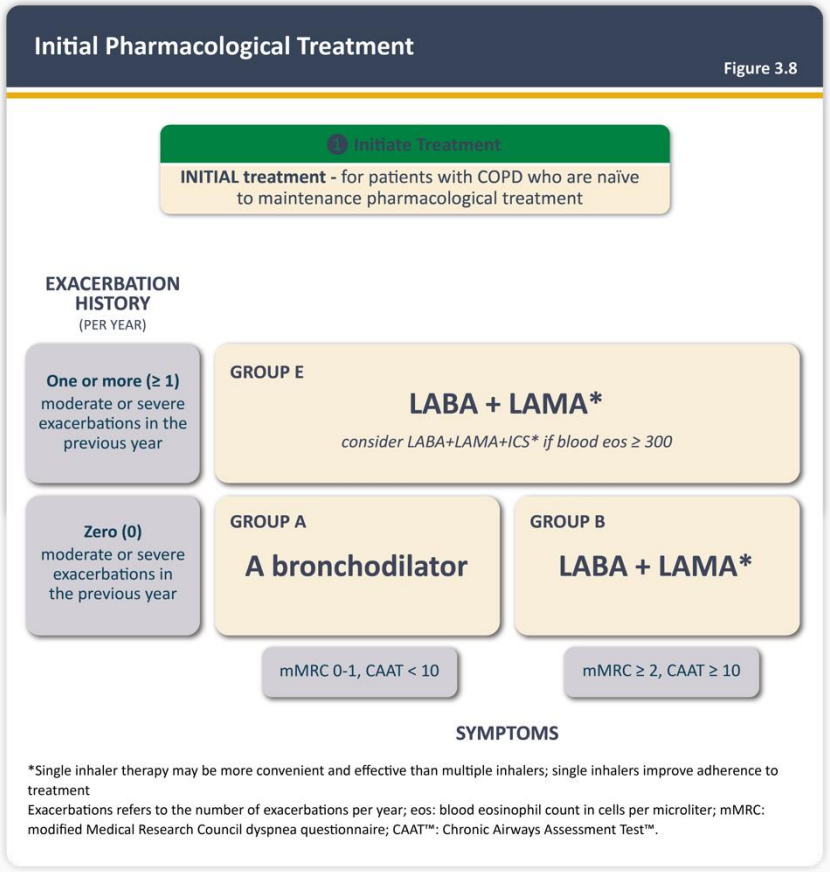
- What is COPD?
- What is a COPD exacerbation and how to assess severity?
- Management of Exacerbations
- Prevention of Exacerbations
- Beyond exacerbations: mortality reduction in COPD

GOLD 2026



https://goldcopd.org/2026-gold-report-and-pocket-guide/

GOLD 2026



https://goldcopd.org/2026-gold-report-and-pocket-guide/

GOLD 2026

Non-Pharmacological Management of COPD*

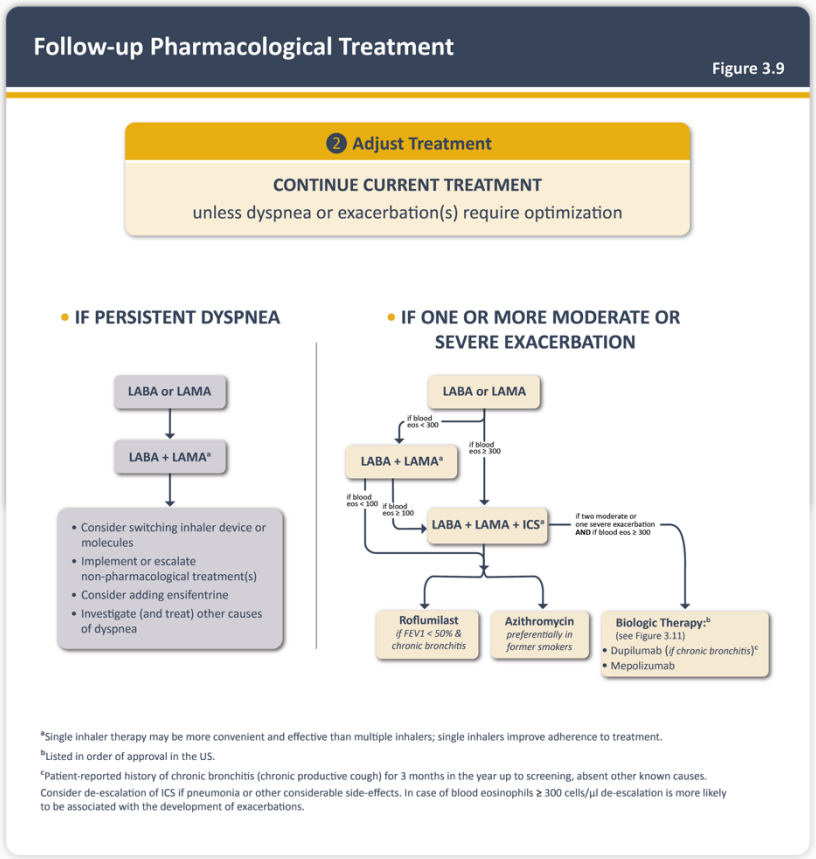
Figure 3.15

Patient Group	Essential	Recommended	Depending on Local Guidelines
A	Smoking cessation (can include pharmacological treatment)	Physical activity	Influenza vaccination COVID-19 vaccinations Pneumococcal vaccination Pertussis vaccination Shingles vaccination RSV vaccination
B and E	Smoking cessation (can include pharmacological treatment) Pulmonary rehabilitation	Physical activity	Influenza vaccination COVID-19 vaccinations Pneumococcal vaccination Pertussis vaccination Shingles vaccination RSV vaccination

*Can include pharmacological treatment

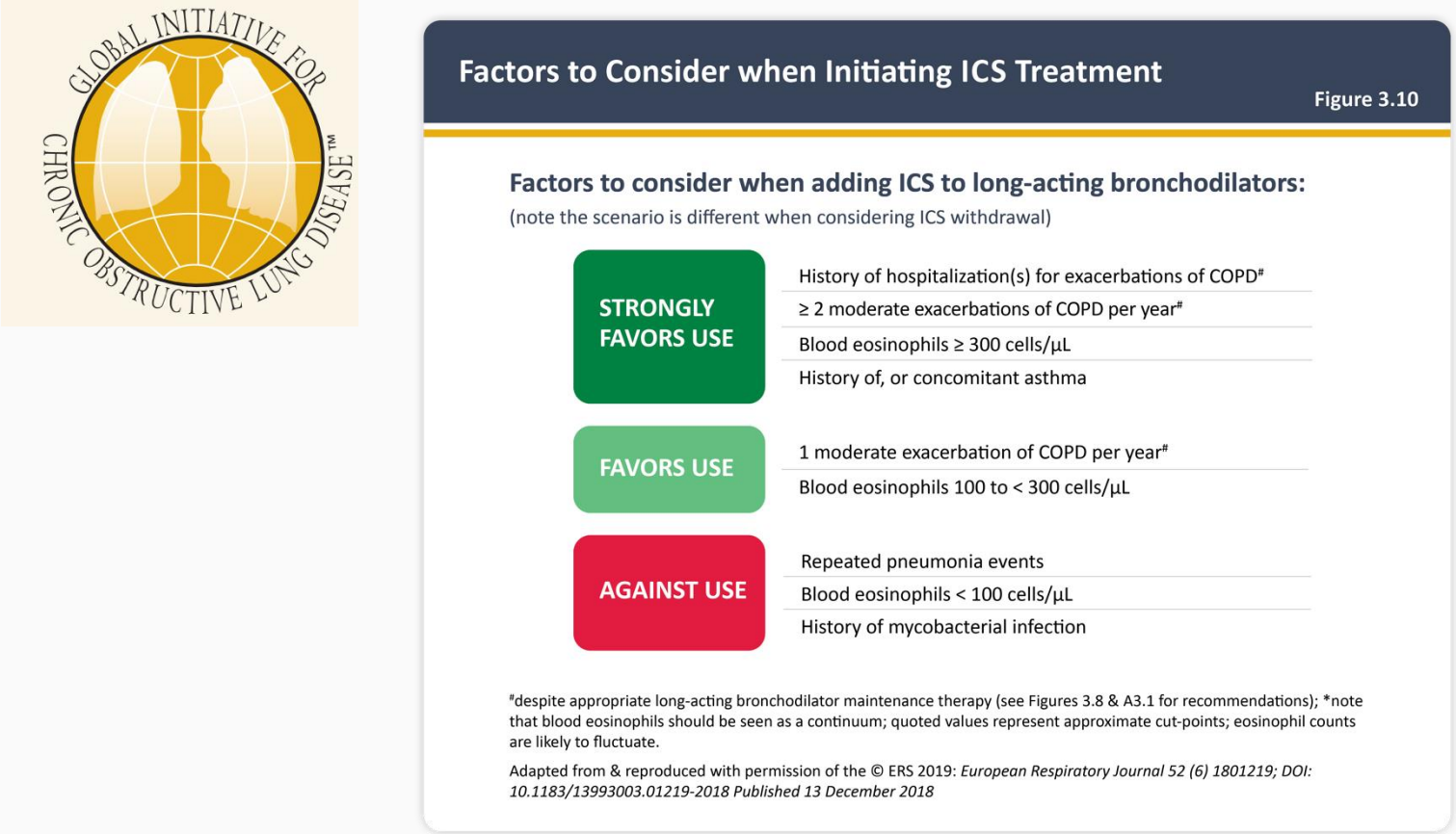
https://goldcopd.org/2026-gold-report-and-pocket-guide/

GOLD 2026



https://goldcopd.org/2026-gold-report-and-pocket-guide/

GOLD 2026: ICS or not?



Factors to Consider when Initiating ICS Treatment

Figure 3.10

Factors to consider when adding ICS to long-acting bronchodilators:

(note the scenario is different when considering ICS withdrawal)

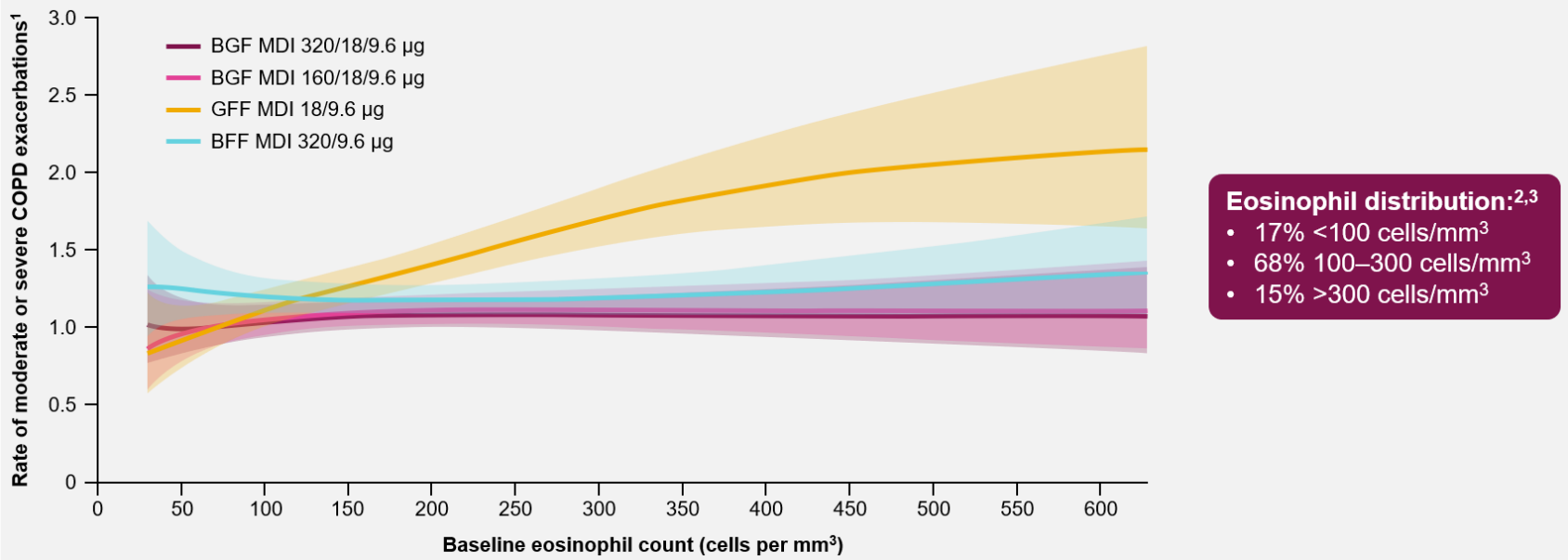
STRONGLY FAVORS USE	History of hospitalization(s) for exacerbations of COPD[#]
	≥ 2 moderate exacerbations of COPD per year[#]
	Blood eosinophils ≥ 300 cells/µL
	History of, or concomitant asthma
FAVORS USE	1 moderate exacerbation of COPD per year[#]
	Blood eosinophils 100 to < 300 cells/µL
AGAINST USE	Repeated pneumonia events
	Blood eosinophils < 100 cells/µL
	History of mycobacterial infection

[#]despite appropriate long-acting bronchodilator maintenance therapy (see Figures 3.8 & A3.1 for recommendations); *note that blood eosinophils should be seen as a continuum; quoted values represent approximate cut-points; eosinophil counts are likely to fluctuate.

Adapted from & reproduced with permission of the © ERS 2019: *European Respiratory Journal 52 (6) 1801219; DOI: 10.1183/13993003.01219-2018 Published 13 December 2018*

https://goldcopd.org/2026-gold-report-and-pocket-guide/

Blood Eosinophils: stratified medicine in COPD



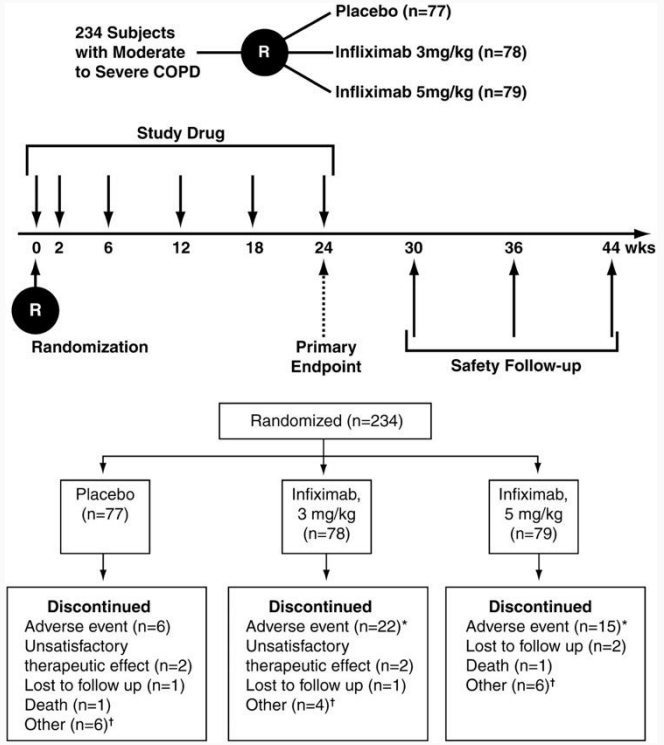
Eosinophil distribution:[2,3]

- 17% <100 cells/mm^3
- 68% 100–300 cells/mm^3
- 15% >300 cells/mm^3

Rabe KF, Martinez FJ, Ferguson GT, Wang C, Singh D, Wedzicha JA, Trivedi R, St Rose E, Ballal S, McLaren J, Darken P, Aurivillius M, Reisner C, Dorinsky P; ETHOS Investigators. Triple Inhaled Therapy at Two Glucocorticoid Doses in Moderate-to-Very-Severe COPD. N Engl J Med. 2020 Jul 2;383(1):35-48. doi: 10.1056/NEJMoa1916046. Epub 2020 Jun 24. PMID: 32579807.

Biologics in COPD?

Biologics in COPD?

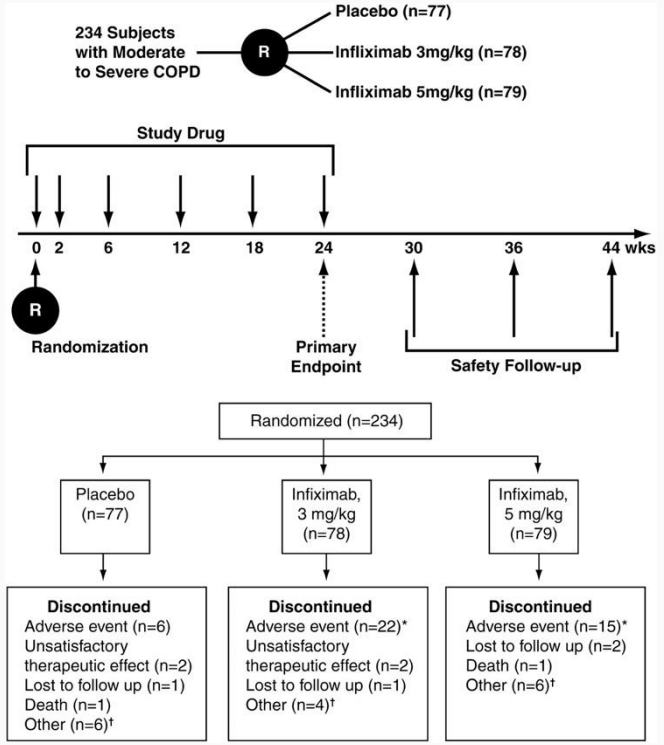


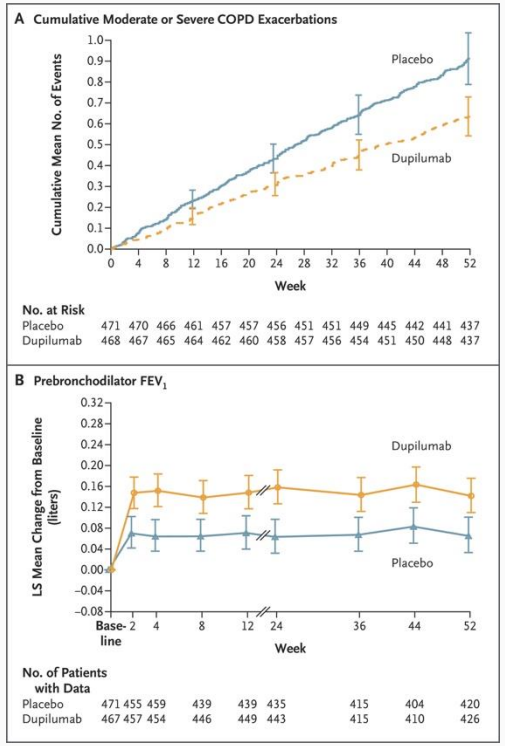
Rennard SI et al. The safety and efficacy of infliximab in moderate to severe chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2007 May 1;175(9):926-34. doi: 10.1164/rccm.200607-995OC. Epub 2007 Feb 8. PMID: 17290043.

Why don’t biologics work better in COPD?

Heterogeneity
Established organ dysfunction
Airway microbiome
Increased risk of cancer

Biologics in COPD?





Bhatt SP et al. Dupilumab for COPD with Type 2 Inflammation Indicated by Eosinophil Counts. N Engl J Med. 2023 Jul 20;389(3):205-214. doi: 10.1056/NEJMoa2303951. Epub 2023 May 21. PMID: 37272521.

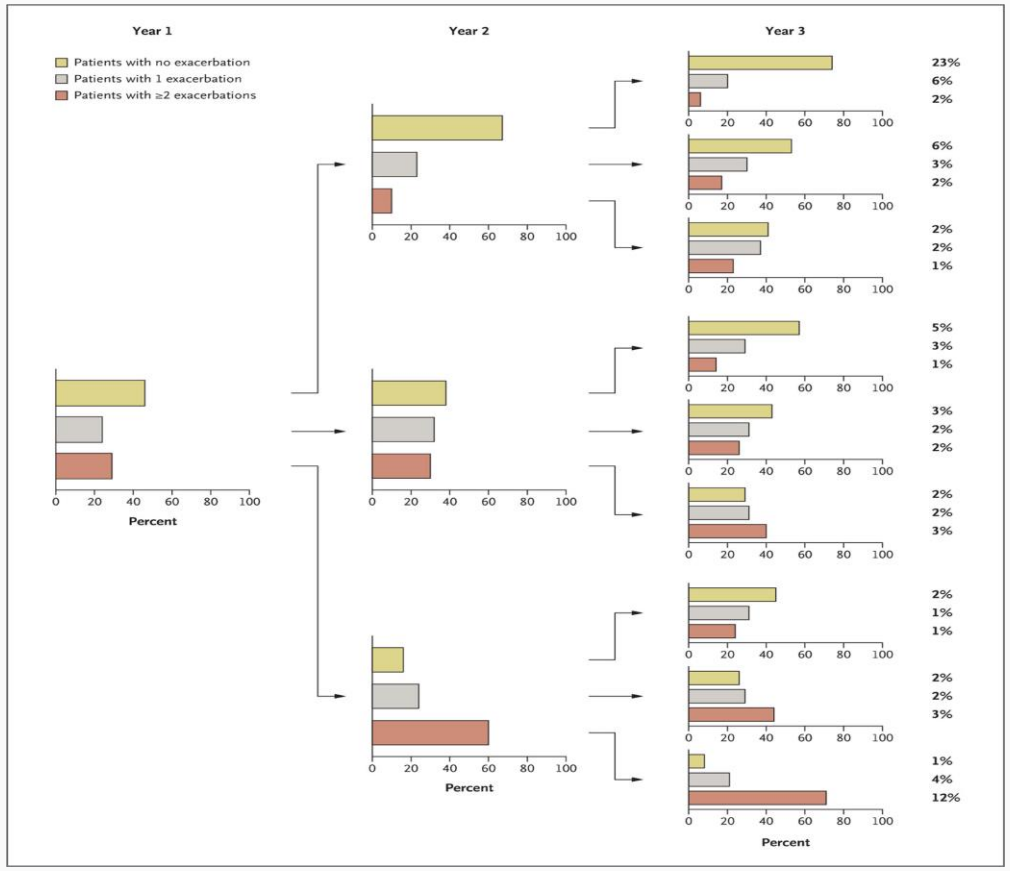
An exacerbation susceptibility phenotype

Table 3. Factors Associated with Increased Exacerbation Frequency in the Stepwise Multivariate Model.*

Factor	Number of Exacerbations						P Value for Overall Model
	≥2 vs. 0		1 vs. 0		≥2 vs. 1		
	odds ratio (95% CI)	*P value*	*odds ratio (95% CI)*	*P value*	*odds ratio (95% CI)*	*P value*	
Exacerbation during previous yr — any vs. none	5.72 (4.47–7.31)	<0.001	2.24 (1.77–2.84)	<0.001	2.55 (1.96–3.31)	<0.001	<0.001
FEV_1 — per 100-ml decrease	1.11 (1.08–1.14)	<0.001	1.06 (1.03–1.08)	<0.001	1.05 (1.02–1.09)	<0.001	<0.001
SGRQ score for COPD — per increase of 4 points	1.07 (1.04–1.10)	<0.001	1.01 (0.99–1.04)	0.38	1.06 (1.03–1.09)	<0.001	<0.001
History of reflux or heartburn — yes vs. no	2.07 (1.58–2.72)	<0.001	1.61 (1.23–2.10)	<0.001	1.29 (0.97–1.70)	<0.005	<0.001
White-cell count — per increase of $1\times10^3/mm^3$	1.08 (1.03–1.14)	0.002	1.02 (0.97–1.08)	0.45	1.06 (1.01–1.12)	<0.001	0.007

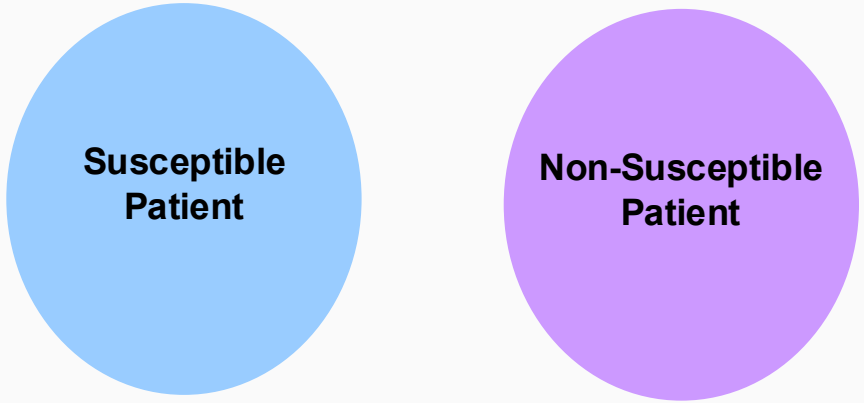
Hurst JR et al. Susceptibility to exacerbation in chronic obstructive pulmonary disease. N Engl J Med. 2010 Sep 16;363(12):1128-38. doi: 10.1056/NEJMoa0909883. PMID: 20843247.

An exacerbation susceptibility phenotype

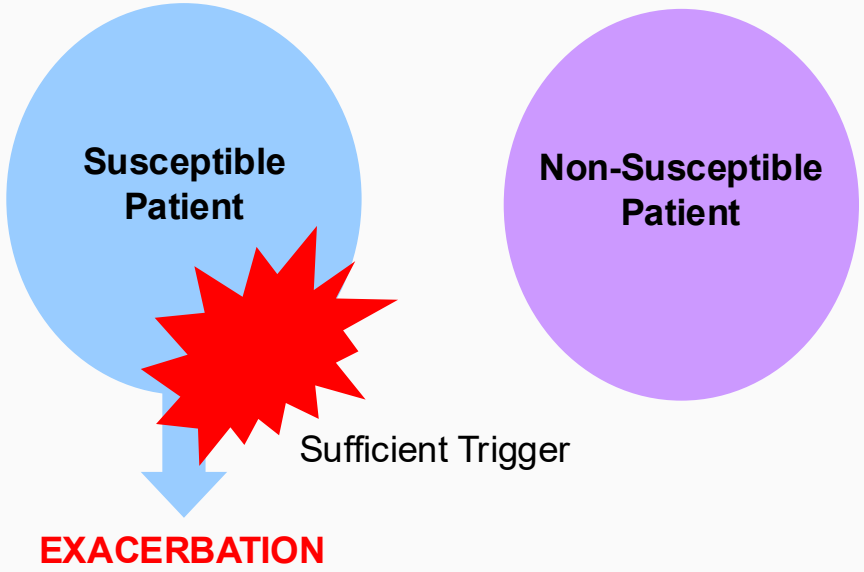


Hurst JR et al. Susceptibility to exacerbation in chronic obstructive pulmonary disease. N Engl J Med. 2010 Sep 16;363(12):1128-38. doi: 10.1056/NEJMoa0909883. PMID: 20843247.

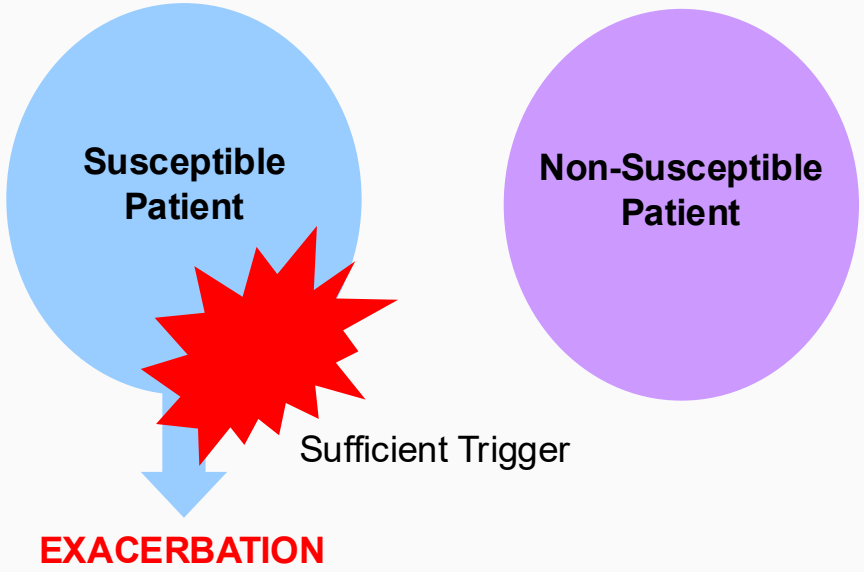
Phenotype discrepancy



Phenotype discrepancy



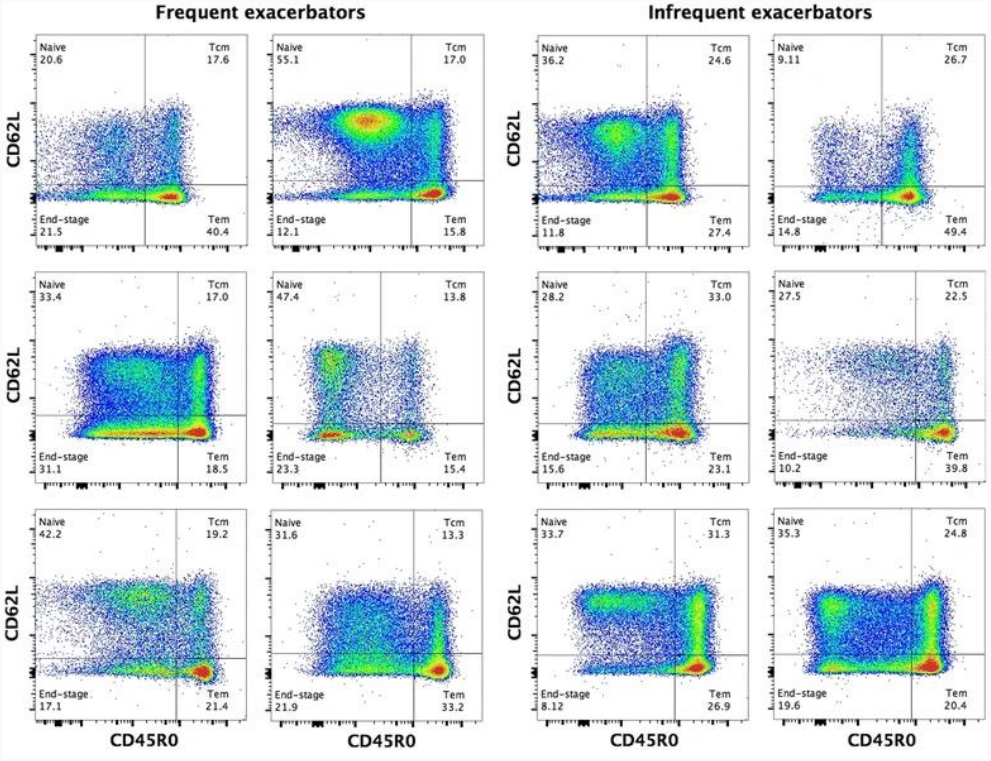
Phenotype discrepancy



EXACERBATION = SUSCEPTIBLE PATIENT + SUFFICIENT TRIGGER

$E = P_{susc} + T_{suff}$

An exacerbation susceptibility phenotype



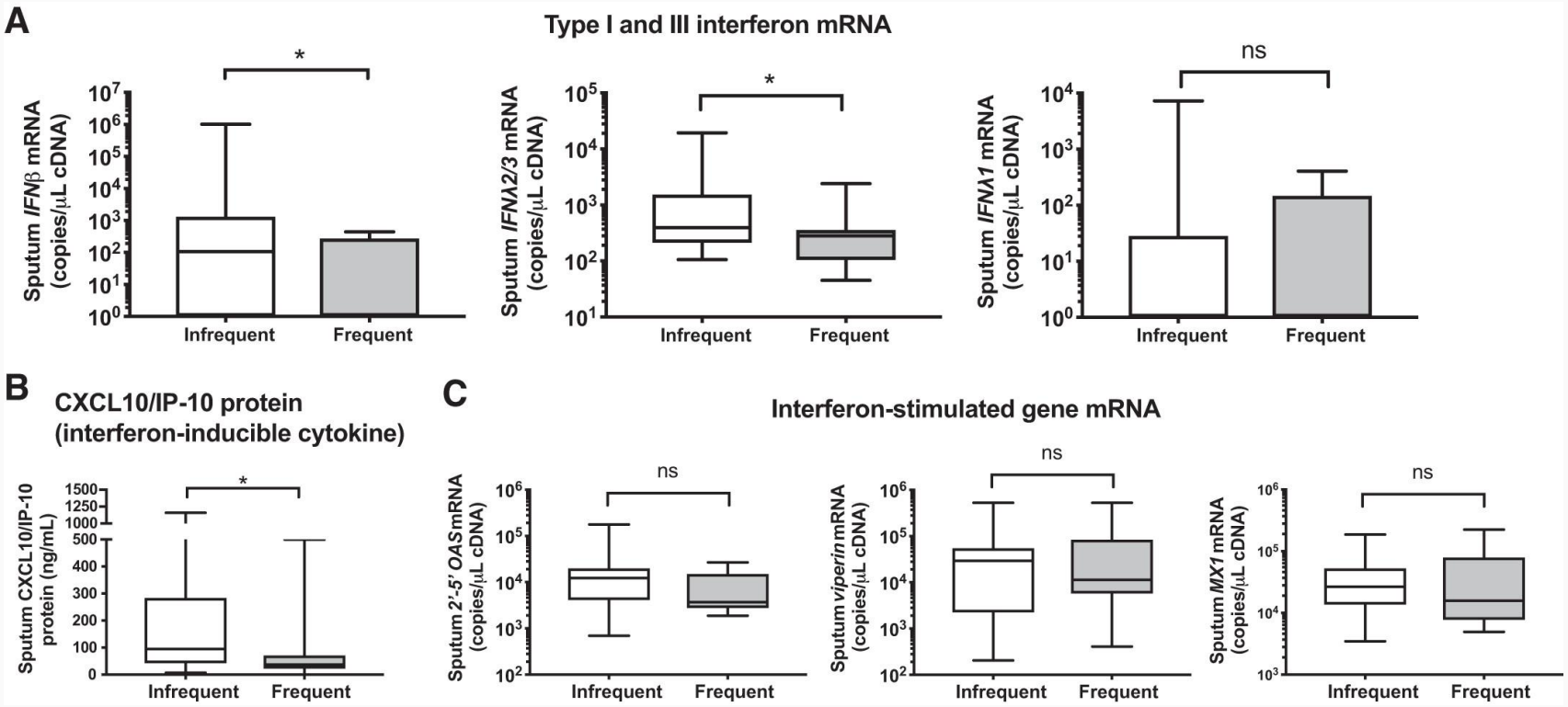
"Differences in the adaptive systemic immune system associate with exacerbation susceptibility in the 'frequent exacerbator' phenotype. These differences include fewer CD4+ T central memory cells and CD8+ T effector memory cells".

Representative plots of CD4+ T central memory cells in patients with frequent and infrequent exacerbations.

CD4+ Tcm cells identified as CD45R0+ and CD62L+ (top-right gate).

Geerdink JX, Simons SO, Pike R, Stauss HJ, Heijdra YF, Hurst JR. Differences in systemic adaptive immunity contribute to the 'frequent exacerbator' COPD phenotype. Respir Res. 2016 Oct 28;17(1):140. doi: 10.1186/s12931-016-0456-y. PMID: 27793198; PMCID: PMC5084432.

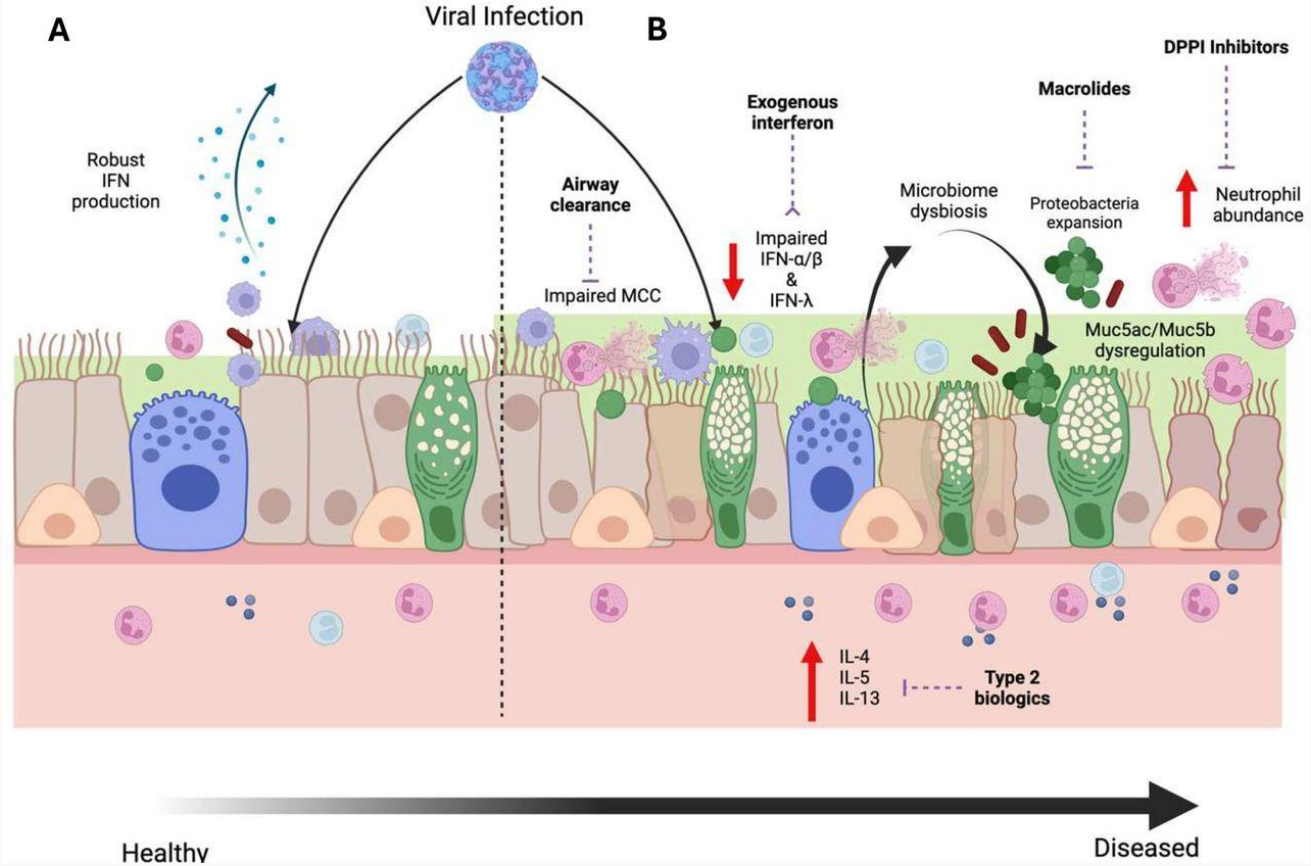
An exacerbation susceptibility phenotype



"Frequent exacerbators had reduced sputum mRNA expression of antiviral immune mediator interferons and reduced interferon-stimulated gene expression when stable and during virus-associated exacerbation".

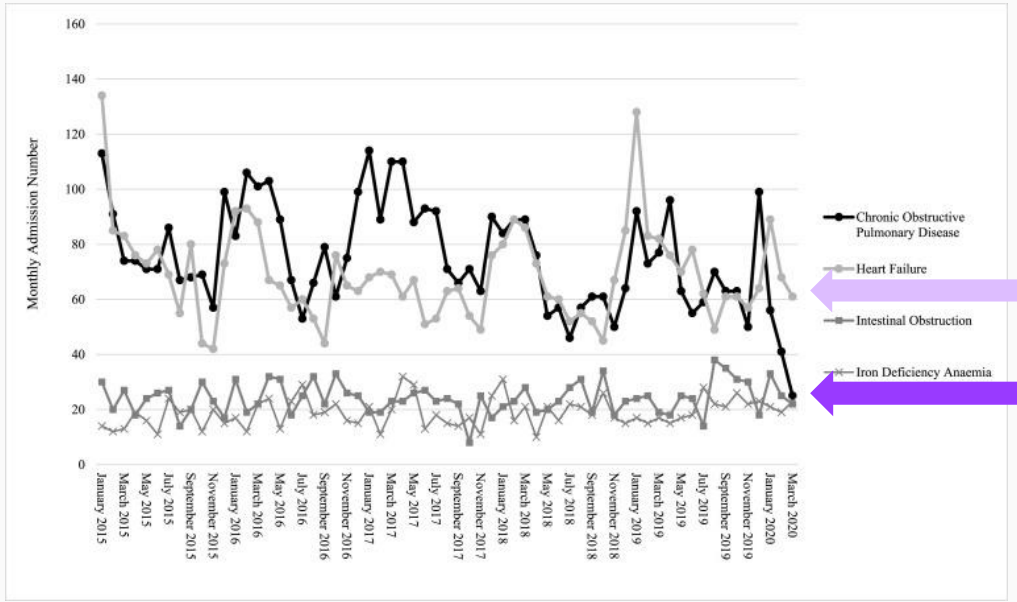
Singanayagam A et al. Antiviral immunity is impaired in COPD patients with frequent exacerbations. Am J Physiol Lung Cell Mol Physiol. 2019 Dec 1;317(6):L893-L903. doi: 10.1152/ajplung.00253.2019. Epub 2019 Sep 12. PMID: 31513433; PMCID: PMC6962603.

Immune dysfunction and viral exacerbations



McKenzie J, Carter C, Jackson MM, Singanayagam A, Shah A. Mechanisms driving immunopathogenesis of viral exacerbations in chronic respiratory disease. Thorax. 2026 Jan 2:thorax-2024-222169. doi: 10.1136/thorax-2024-222169. Epub ahead of print. PMID: 41482480.

50% exacerbation reduction

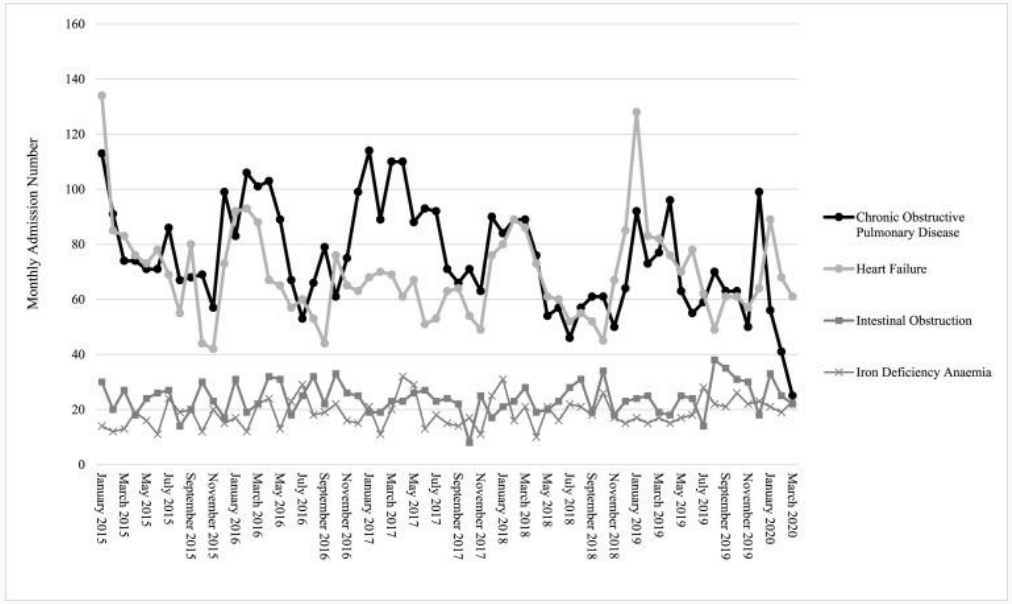


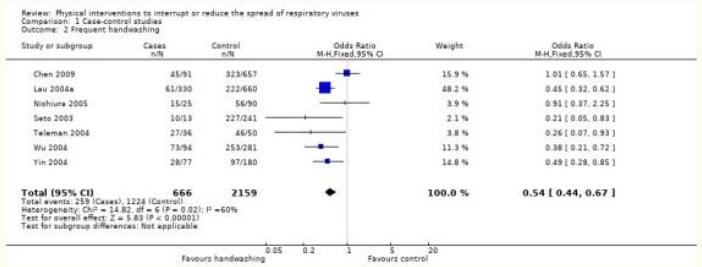
HEART FAILURE

AECOPD

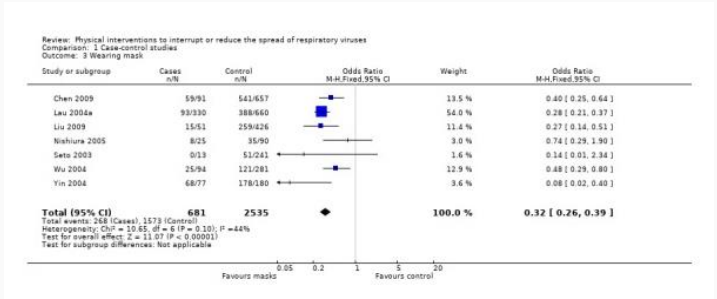
Chan KPF et al. Significant reduction in hospital admissions for acute exacerbation of chronic obstructive pulmonary disease in Hong Kong during coronavirus disease 2019 pandemic. Respir Med. 2020 Sep;171:106085. doi: 10.1016/j.rmed.2020.106085. Epub 2020 Jul 12. PMID: 32917356; PMCID: PMC7354382.

50% exacerbation reduction





Hand Washing

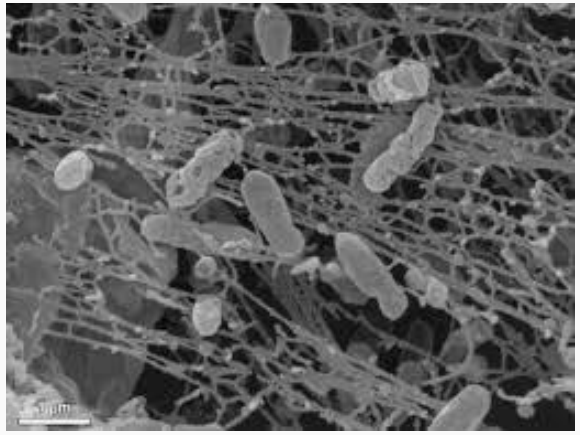


Face Mask

"Simple low-cost interventions would be useful for reducing transmission of epidemic respiratory viruses. Routine long-term implementation of some measures might be difficult without the threat of an epidemic".

Jefferson T et al. Physical interventions to interrupt or reduce the spread of respiratory viruses. Cochrane Database Syst Rev. 2011 Jul 6;2011(7):CD006207. doi: 10.1002/14651858.CD006207.pub4. Update in: Cochrane Database Syst Rev. 2020 Nov 20;11:CD006207. PMID: 21735402; PMCID: PMC6993921.

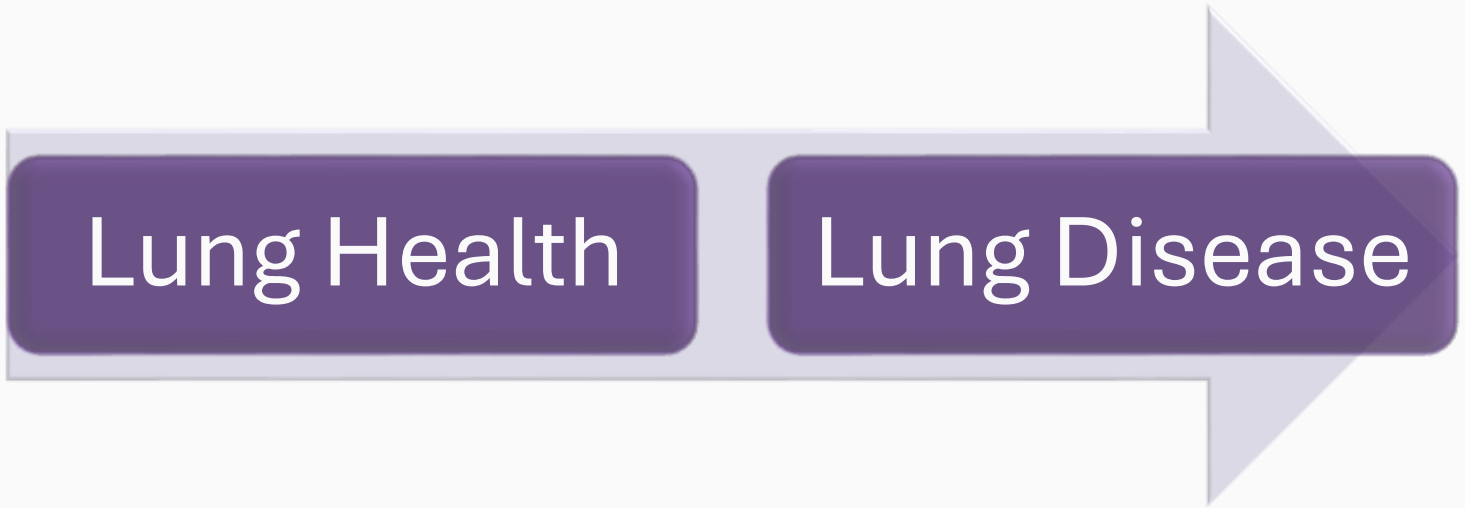
Novel interventions for neutrophilic COPD



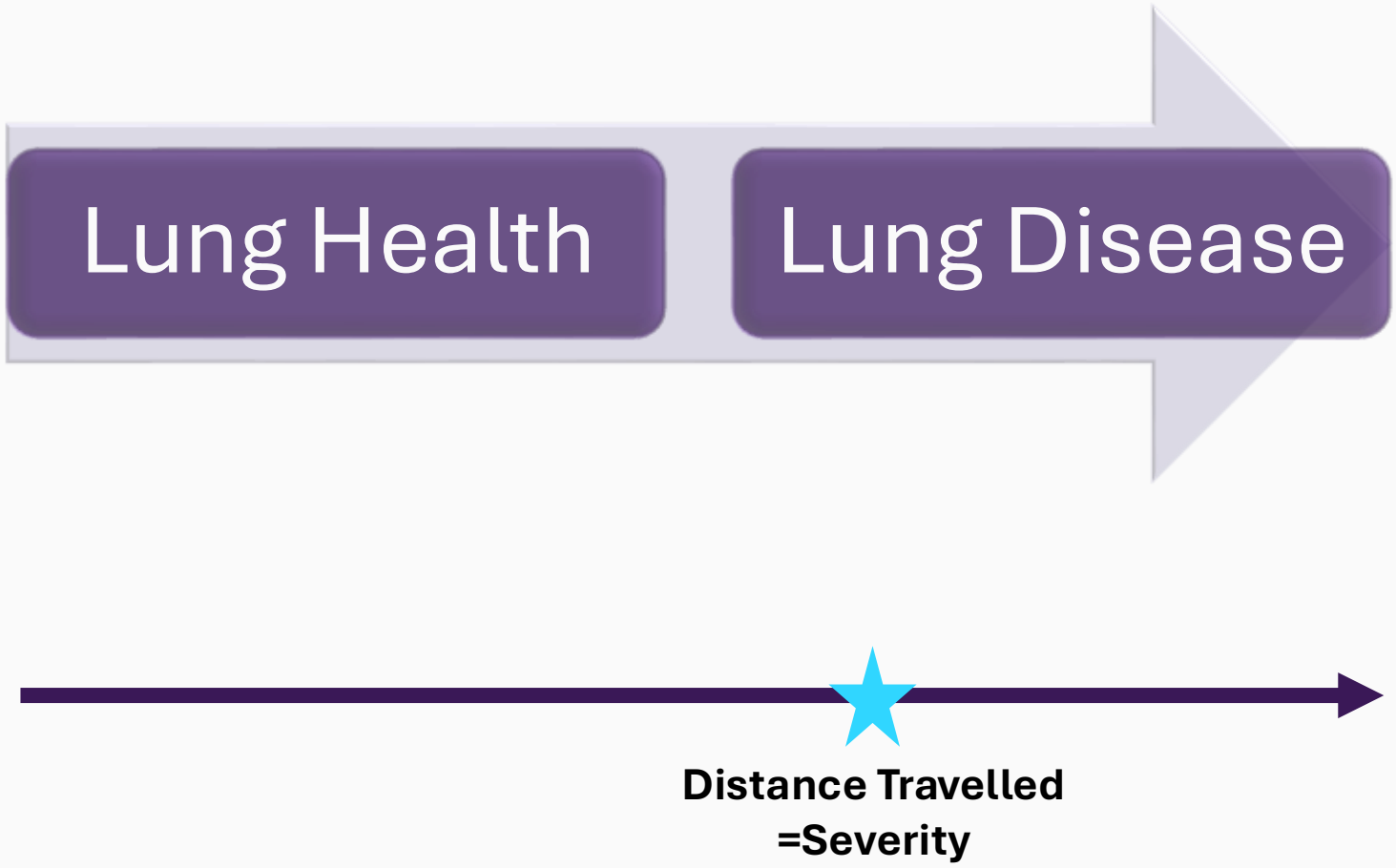
- Phase IIa
- Randomised, Double Blind, Placebo Controlled, Parallel Arm, Multi-Centre Study
- Efficacy and Safety of Mitiperstat (AZD4831), for 12-24 weeks, in people living with COPD
- Irreversible MPO inhibitor (for HFpEF)
- Benefit vs. Harm
- Results in revision

https://esla.www.astrazenecaclinicaltrials.com/study/D6582C00001/

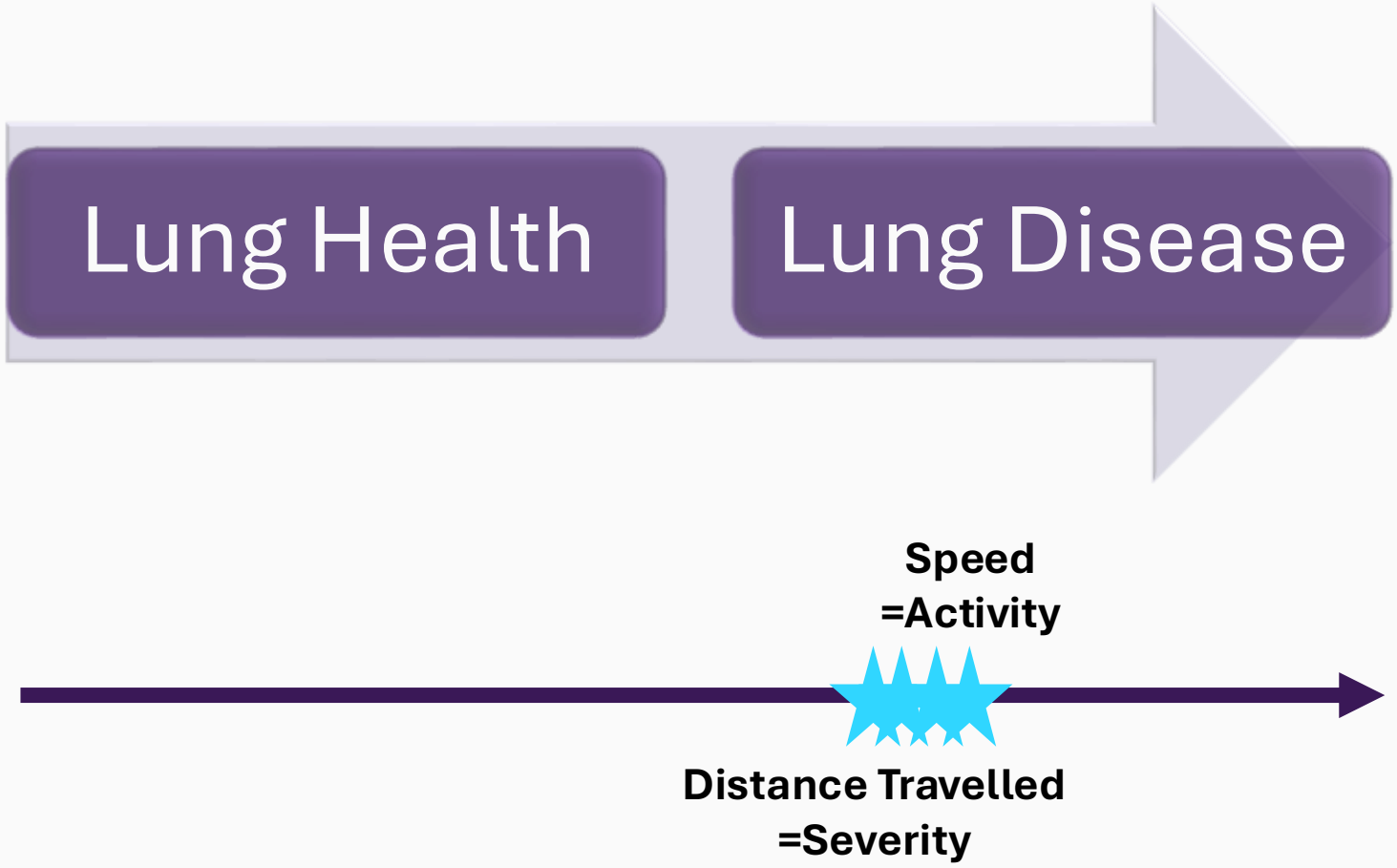
Disease Activity and Severity in COPD



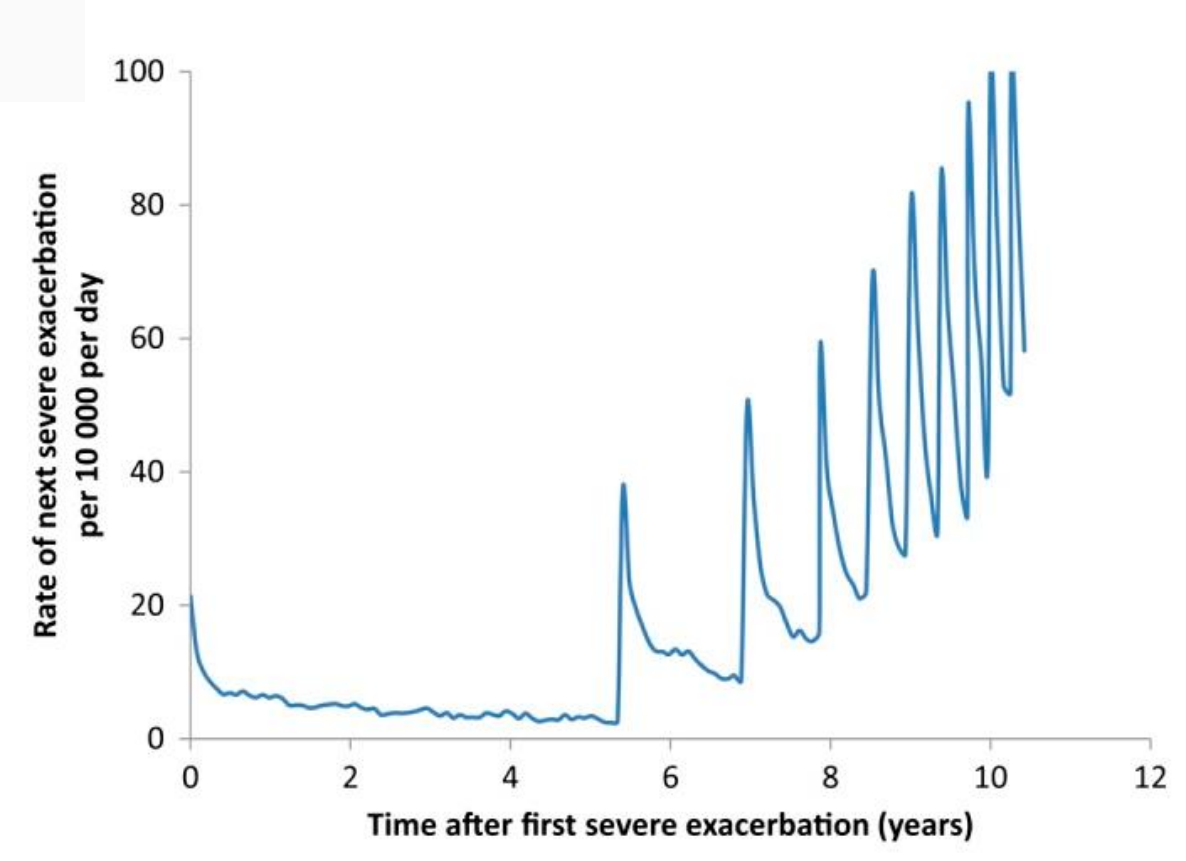
Disease Activity and Severity in COPD



Disease Activity and Severity in COPD

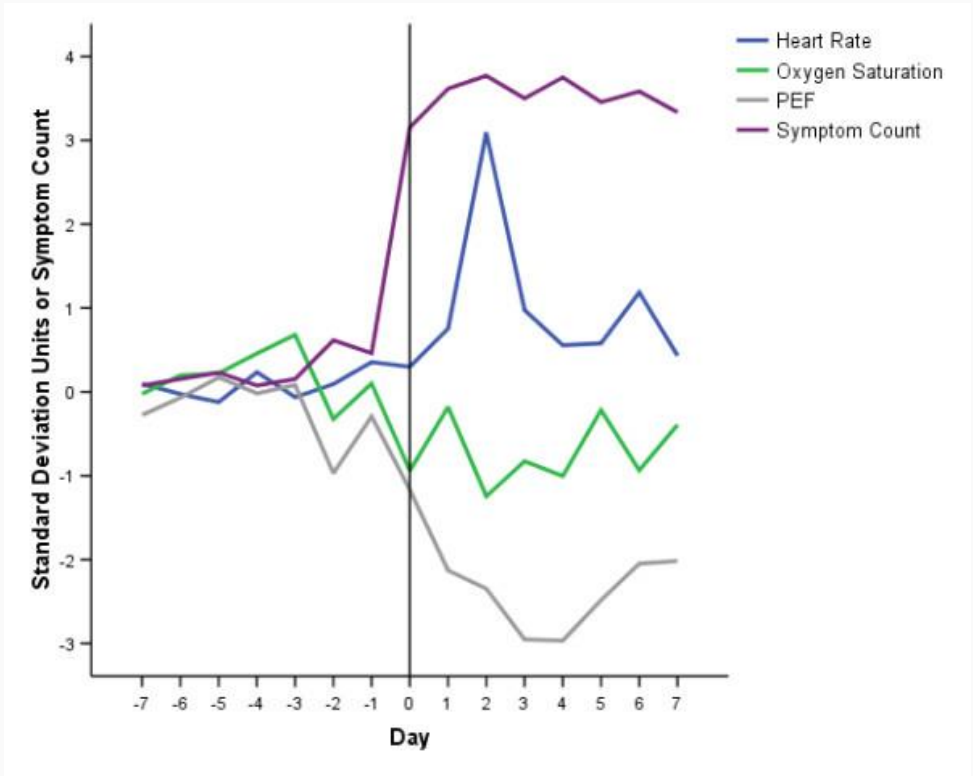


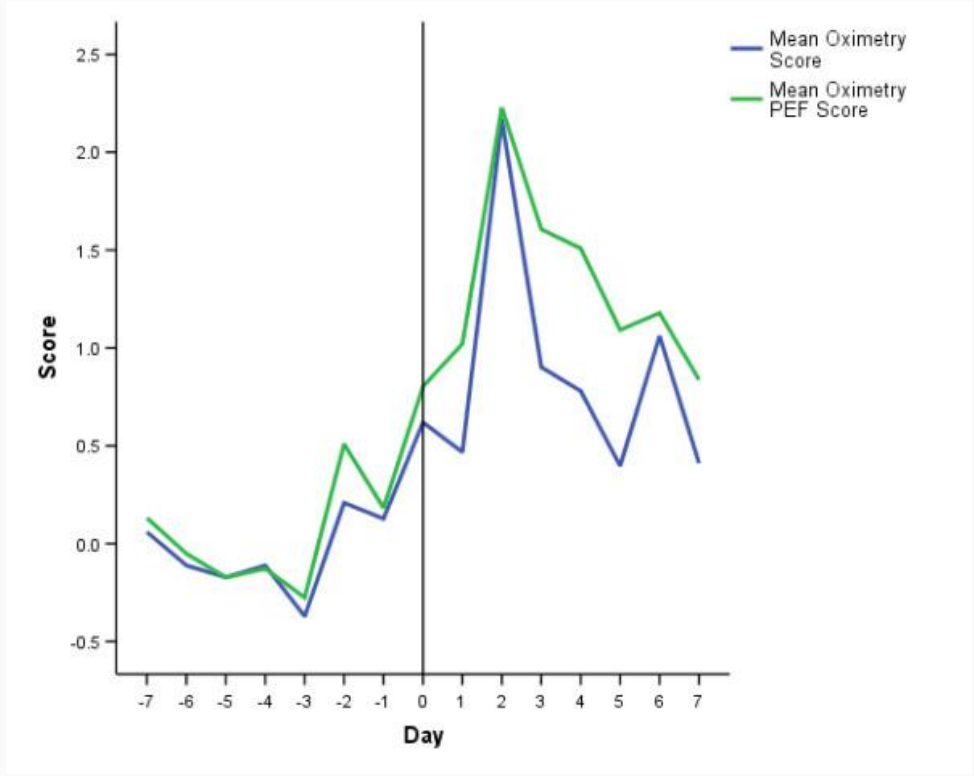
The rhythm of COPD exacerbations



Suissa S, Dell'Aniello S, Ernst P. Long-term natural history of chronic obstructive pulmonary disease: severe exacerbations and mortality. Thorax. 2012 Nov;67(11):957-63. doi: 10.1136/thoraxjnl-2011-201518. Epub 2012 Jun 8. PMID: 22684094; PMCID: PMC3505864.

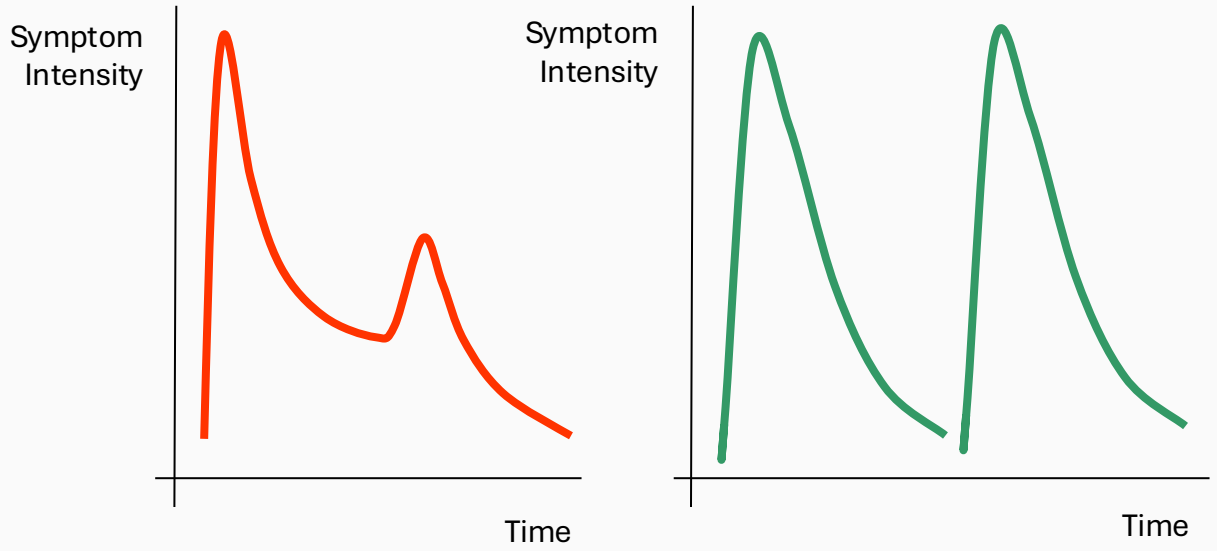
Early detection of COPD exacerbations





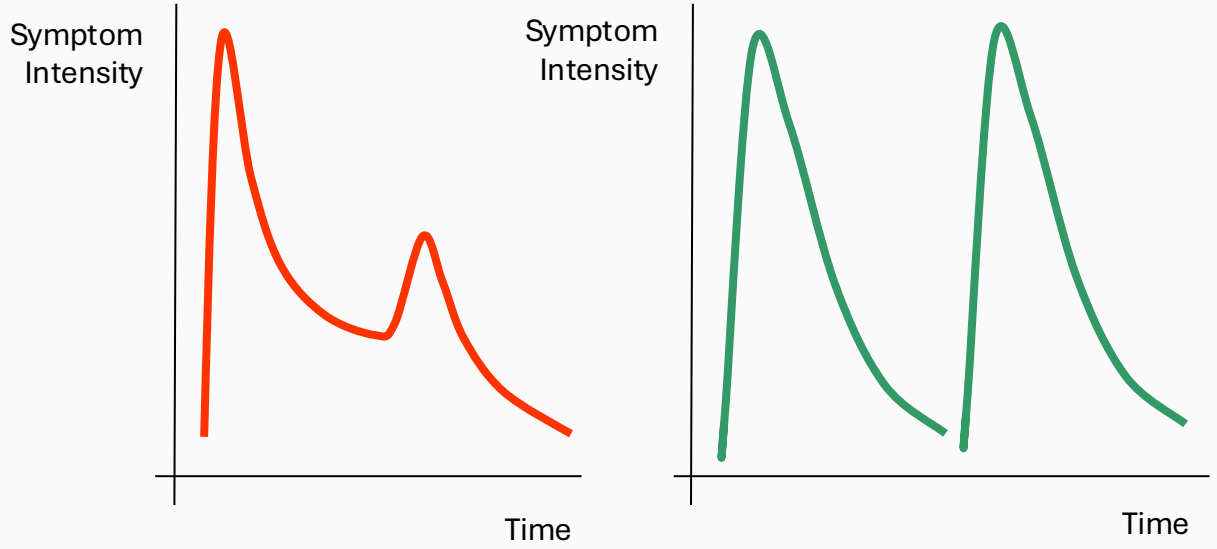
Hurst JR, Donaldson GC, Quint JK, Goldring JJ, Patel AR, Wedzicha JA. Domiciliary pulse-oximetry at exacerbation of chronic obstructive pulmonary disease: prospective pilot study. BMC Pulm Med. 2010 Oct 20;10:52. doi: 10.1186/1471-2466-10-52. PMID: 20961450; PMCID: PMC2978135.

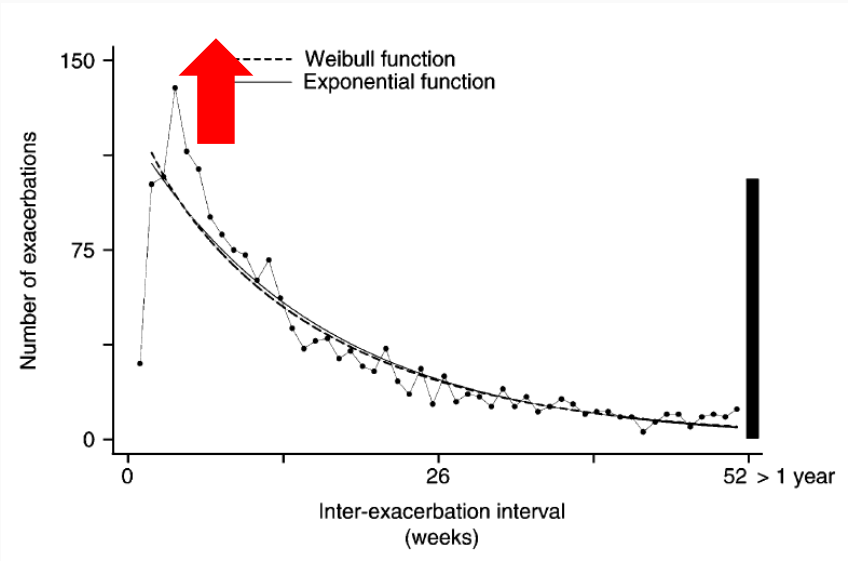
High Risk Times (and high risk patients)



High Risk Times (and high risk patients)

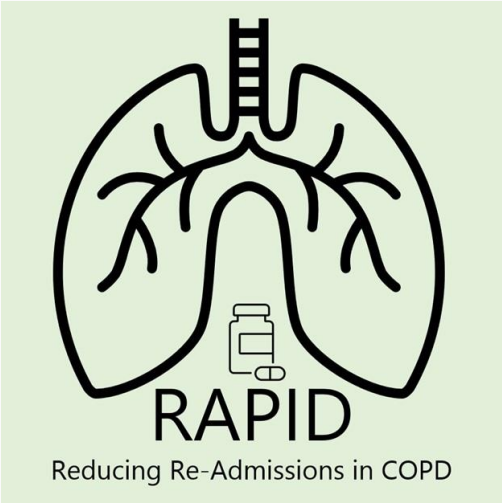
27% of exacerbations associated with a 2nd within 8 weeks





Hurst JR, Donaldson GC, Quint JK, Goldring JJ, Baghai-Ravary R, Wedzicha JA. Temporal clustering of exacerbations in chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2009 Mar 1;179(5):369-74. doi: 10.1164/rccm.200807-1067OC. Epub 2008 Dec 12. PMID: 19074596.

RAPID Rescue



- P: 1400 people being discharged from hospital after a COPD exacerbation
- I: provision of a rescue pack, and how to use it, with twice-weekly reminder calls or texts
- C: usual care
- O: Re-admission to hospital in 90 days

https://ctu.co.uk/rapid/

Overview

- What is COPD?
- What is a COPD exacerbation and how to assess severity?
- Management of Exacerbations
- Prevention of Exacerbations
- Beyond exacerbations: mortality reduction in COPD

Causes of death in COPD

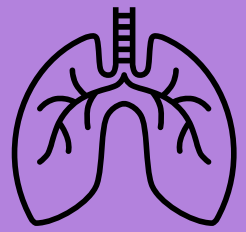
Milder COPD

CVD

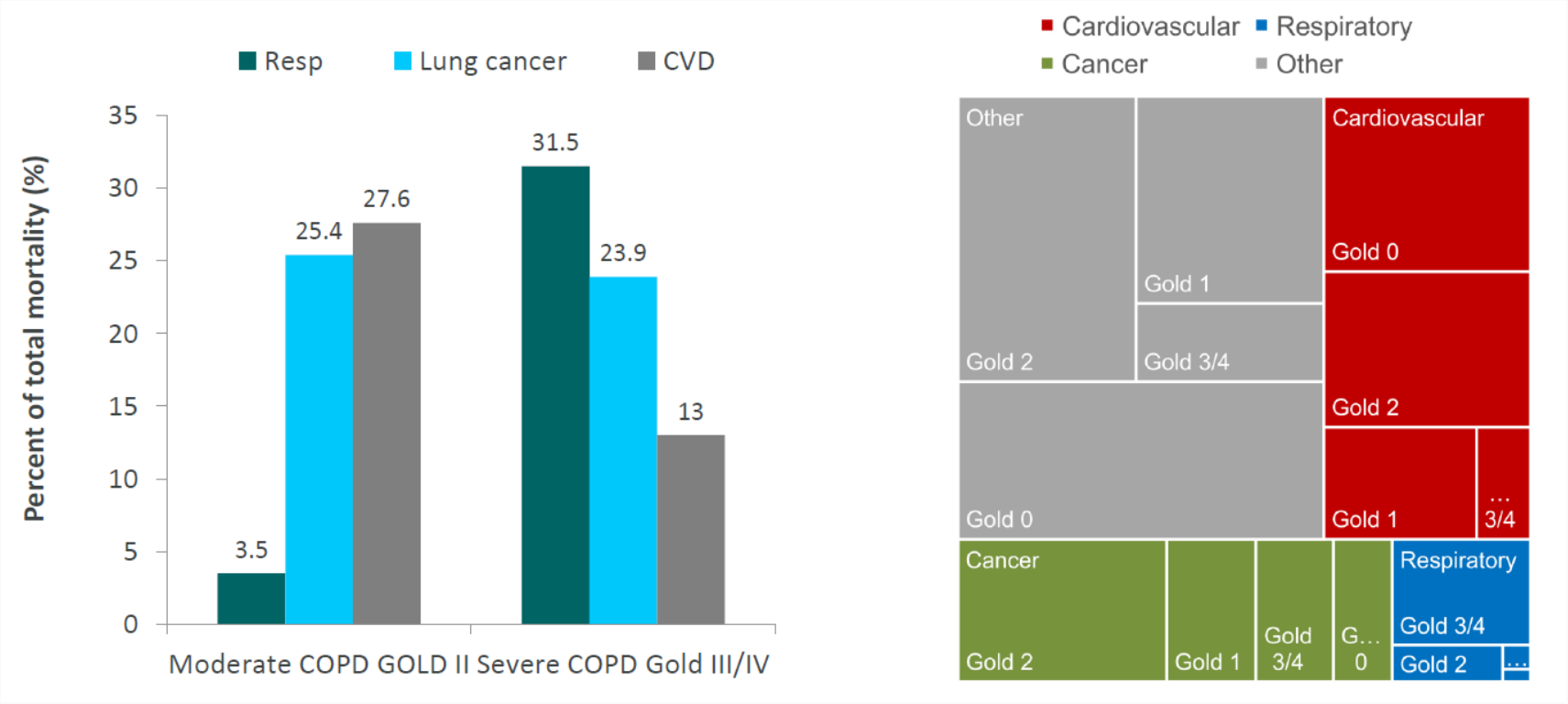
Lung Cancer

More severe COPD

COPD-related

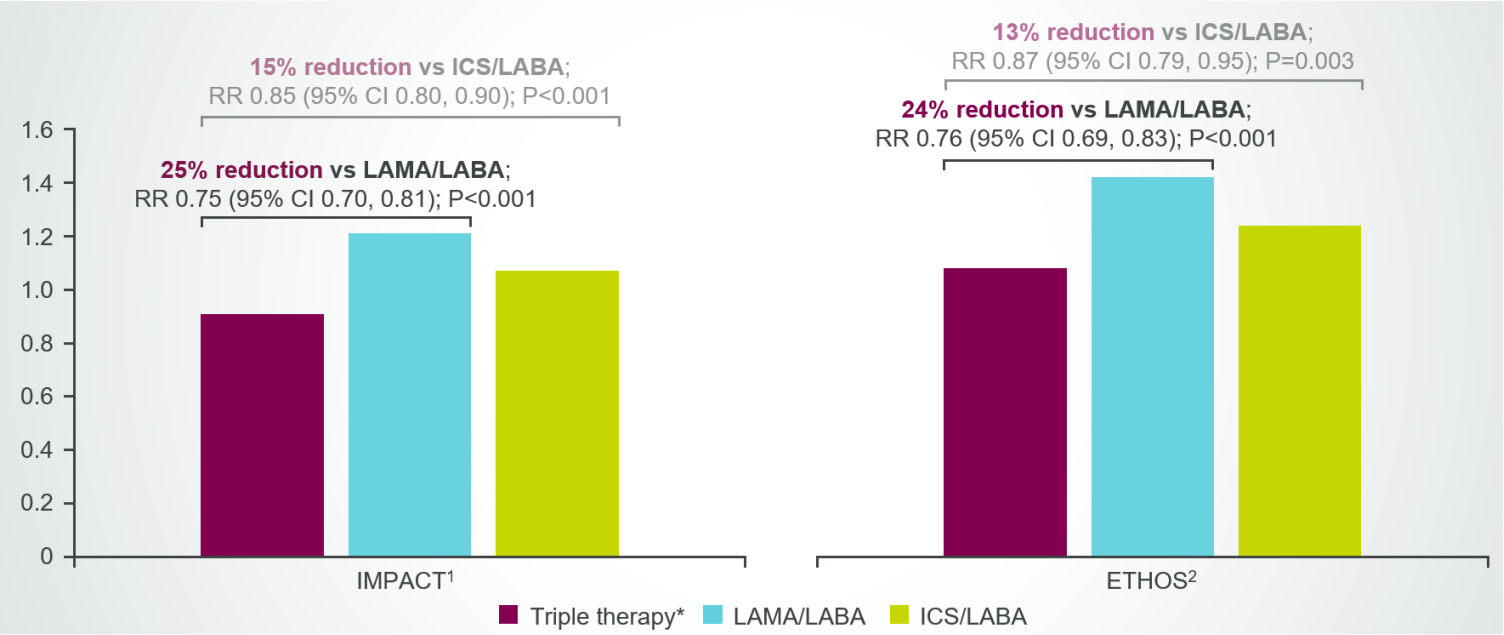


Causes of death in COPD



Mannino DM, Doherty DE, Sonia Buist A. Global Initiative on Obstructive Lung Disease (GOLD) classification of lung disease and mortality: findings from the Atherosclerosis Risk in Communities (ARIC) study. Respir Med. 2006 Jan;100(1):115-22. doi: 10.1016/j.rmed.2005.03.035. PMID: 15893923.

ETHOS and IMPACT



And, in secondary analysis of both studies, a reduction in **ALL CAUSE MORTALITY** with ICS-LABA-LAMA over the LABA-LAMA...

1. Lipson DA, et al. N Engl J Med 2018;378:1671–1680
2. Rabe KF, et al. N Engl J Med 2020;383:35–48

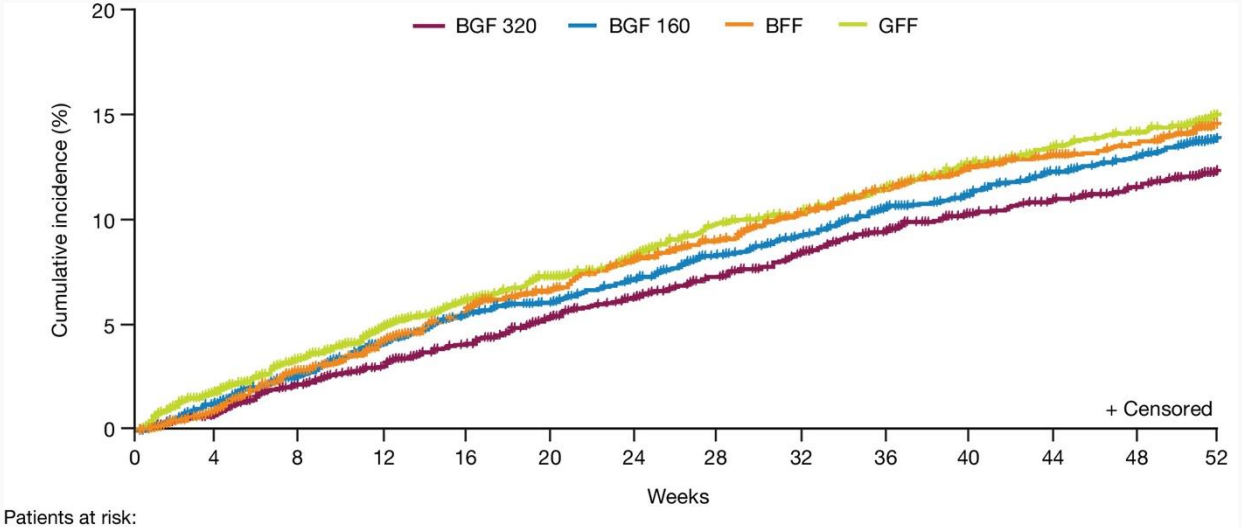
ETHOS: causes of death

	BGF 320/18/9.6 µg (*N* = 2,137)	BGF 160/18/9.6 µg (*N* = 2,121)	GFF 18/9.6 µg (*N* = 2,120)	BFF 320/9.6 µg (*N* = 2,131)	All Patients (*N* = 8,509)
Total deaths*					
Original dataset	30 (1.4)	44 (2.1)	52 (2.5)	38 (1.8)	164 (1.9)
Final retrieved dataset	37 (1.7)	55 (2.6)	64 (3.0)	46 (2.2)	202 (2.4)
Deaths included in the time-to-death analyses†					
Original dataset	28 (1.3)	39 (1.8)	49 (2.3)	34 (1.6)	150 (1.8)
Final retrieved dataset	30 (1.4)	44 (2.1)	56 (2.6)	40 (1.9)	170 (2.0)
Adjudicated deaths‡					
Original dataset	27 (1.3)	42 (2.0)	47 (2.2)	35 (1.6)	151 (1.8)
Final retrieved dataset	28 (1.3)	43 (2.0)	50 (2.4)	35 (1.6)	156 (1.8)§
Cardiovascular	11 (0.5)	16 (0.8)	29 (1.4)	11 (0.5)	67 (0.8)
Respiratory	7 (0.3)	13 (0.6)	8 (0.4)	6 (0.3)	34 (0.4)
COPD	5 (0.2)	7 (0.3)	5 (0.2)	5 (0.2)	22 (0.3)
Pneumonia	2 (<0.1)	3 (0.1)	3 (0.1)	1 (<0.1)	9 (0.1)
Other respiratory	0	3 (0.1)	0	0	3 (<0.1)
Cancer	2 (<0.1)	6 (0.3)	3 (0.1)	7 (0.3)	18 (0.2)
Other	8 (0.4)	8 (0.4)	10 (0.5)	11 (0.5)	37 (0.4)
Nonadjudicated deaths (all-cause)					
Original dataset	3 (0.1)	2 (<0.1)	5 (0.2)	3 (0.1)	13 (0.2)
Final retrieved dataset	9 (0.4)	12 (0.6)	14 (0.7)	11 (0.5)	46 (0.5)

... that seems to be driven by a reduction in **CARDIOVASCULAR DEATHS** with ICS-LABA-LAMA over LABA-LAMA

Martinez FJ et al. Reduced All-Cause Mortality in the ETHOS Trial of Budesonide/Glycopyrrolate/Formoterol for Chronic Obstructive Pulmonary Disease. A Randomized, Double-Blind, Multicenter, Parallel-Group Study. Am J Respir Crit Care Med. 2021 Mar 1;203(5):553-564. PMID: 33252985.

Exacerbations and cardio-pulmonary risk



Patients at risk:

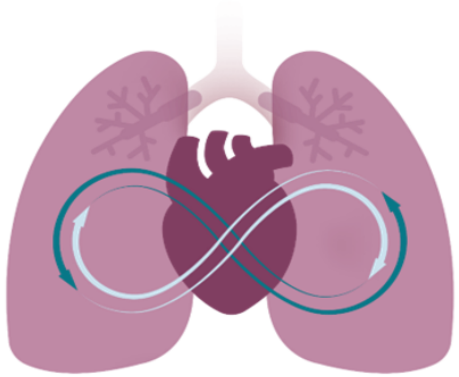
BGF 320	2137	2084	2006	1958	1905	1849	1808	1762	1724	1685	1636	1608	1576	1296
BGF 160	2121	2056	1990	1932	1872	1834	1798	1750	1712	1673	1638	1601	1576	1271
BFF	2131	2051	1957	1886	1817	1770	1730	1686	1641	1597	1561	1533	1508	1217
GFF	2120	2015	1903	1827	1753	1704	1658	1602	1579	1549	1511	1484	1458	1182

Singh D et al. Effect of Triple Therapy on Cardiovascular and Severe Cardiopulmonary Events in Chronic Obstructive Pulmonary Disease: A Post Hoc Analysis of a Randomized, Double-Blind, Phase 3 Clinical Trial (ETHOS). Am J Respir Crit Care Med. 2025 Feb;211(2):205-214. doi: 10.1164/rccm.202312-2311OC. PMID: 39213002.

Exacerbations and cardio-pulmonary risk

Exacerbations

Precursor of **further pulmonary**[1] and **cardiac events.**[2,3,4]
Catalyst for **inflammation,**[2] **hyperinflation,**[3,5] and **hypoxemia**[6]



Inflammation

Lung inflammation can trigger **systemic inflammation,** resulting in **atherothrombosis** in the heart and vasculature[2]

Hyperinflation

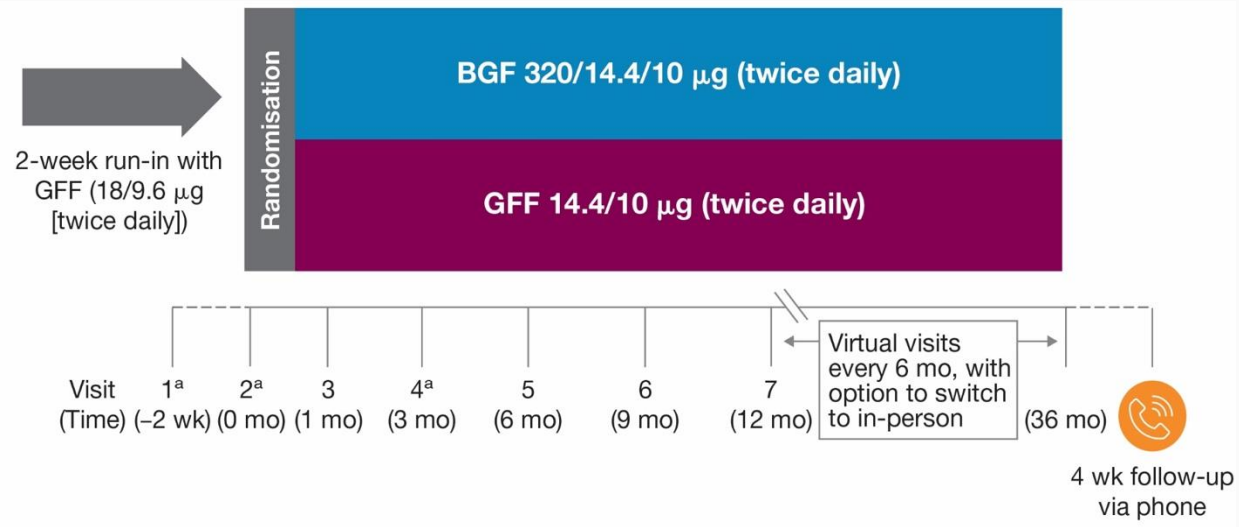
Hyperinflation **compresses the heart, hinders blood pumping** and oxygenation[7]

Hypoxemia

Hypoxic vasoconstriction in the lungs can cause **pulmonary hypertension,**[6] which can result in right heart failure and reduced cardiac output[5]

1. Müllerová H et al. BMJ Open. 2014;4:e006171; 2. Van Eeden S et al. Am J Respir Crit Care Med. 2012;186:11-16; 3. Crisan L et al. Front Cardiovasc Med. 2019;6:79; 4. Calderón Montero A. Semergen. 2023;49(4):101928; 5. Rabe KF et al. Eur Respir Rev. 2018;27:180057; 6. Kent BD et al. Int J Chron Obstruct Pulmon Dis. 2011;6:199-208; 7. Aisanov Z et al. J Thorac Dis. 2020;12:2791-2802.

Exacerbations and cardio-pulmonary risk



Martinez FJ et al. Effect of budesonide/glycopyrronium/formoterol fumarate dihydrate on cardiopulmonary outcomes in COPD: rationale and design of the THARROS trial. ERJ Open Research 2025: in press

Summary

- What is COPD?
- What is a COPD exacerbation and how to assess severity?
- Management of Exacerbations
- Prevention of Exacerbations
- Beyond exacerbations: mortality reduction in COPD

Acknowledgement
My team, our funders, collaborators and research participants

Thank You

John Hurst

Professor of Respiratory Medicine
j.hurst@ucl.ac.uk

UCL Respiratory | Faculty of Medical Sciences