2026 California Thoracic Society Annual Educational Conference

& Chronic Obstructive Pulmonary Disease Symposium

Thursday March 12, 2026-Sunday March 15, 2026

Earn up to 19 CME/CEU/MOC Credits

Jointly Provided by AKH Inc., Advancing Knowledge in Healthcare and the California Thoracic Society

PORTOLA HOTEL & SPA
AT MONTEREY BAY

Thursday March 12, 2026 (6 CME/CEU/MOC Credits)
COPD Symposium
Friday March 13, 2026 (6.5 CME/CEU/MOC Credits):
Advances in Interventional Pulmonary, Remote Monitoring in Pulmonary and Sleep Medicine, Approach to Symptom Management in Chronic Lung Disease and Critical Care
Saturday March 14, 2026 (6.5 CME/CEU/MOC Credits)
Sepsis and Shock, Extracorporeal Membrane Oxygenation, Inpatient Pulmonary Complications of Cancer Care
Sunday March 15, 2026
Fellow and Resident Track Symposium

California Thoracic Society
ATS Chapter Serving California and Arizona

AKH INC.
ADVANCING KNOWLEDGE IN HEALTHCARE

California Thoracic Society
Annual Conference
March 12-15, 2026
Portola Hotel and Spa, Monterey, CA

Thursday March 12, 2026

COPD Medical Management, Pathogenesis, and Epidemiology

11:00 am-11:45 am – The Immunology of Obstructive Lung Disease

- **Frank Sciurba, MD (University of Pittsburgh)** – This speaker will discuss the immunology of COPD and discuss novel approaches to anti-inflammatory medications and biologic therapy in COPD.

11:45 am -12:10 pm – Diagnosis and Case Finding in COPD

- **Lauren Eggert, MD (UC San Francisco)** – This speaker will discuss the diagnosis of COPD and new approaches for case finding using screening questionnaires, spirometry, and peak expiratory flow.

12:10 pm -12:35 pm – Epidemiology of COPD

- **Laura Myers, MD (Kaiser)** – This speaker will discuss the global, US, and California burden of COPD, the regional variability of COPD, and how COPD prevalence varies by social determinants of health.

12:35 pm – 1:00 pm – Update on the treatment algorithm of COPD from the 2025 GOLD Report

- **Anil Ghimire, MD (UCSF Fresno)** – This speaker will discuss the updated 2025 GOLD Report on COPD and how to approach therapy in this population with the current available modalities.

1:00 pm-1:10 – pm- Q&A

Lunch: 1:10-2:10 pm

Non-Medication Based Management in COPD

2:10 pm – 2:35 pm – Oxygen and Non-Invasive Ventilation in COPD

- **Solmaz Ehteshami-Afshar, MD (Stanford)** – This speaker will discuss the benefits of oxygen supplementation in COPD and the nuances of non-invasive ventilation in patients with COPD.

2:35 pm – 3:00 pm – Endobronchial valves in COPD

- **Madhav Chopra, MD (University of Arizona – Tucson)** – This speaker will discuss when to use endobronchial valves in COPD and the benefits and limitations of endobronchial valves.

3:00 pm – 3:25 pm – Pulmonary Rehabilitation for COPD

- **Richard Casaburi, MD PhD (Harbor-UCLA)** – This speaker will discuss how pulmonary rehabilitation can improve outcomes in patients with COPD, and how virtual pulmonary rehabilitation programs can benefit patients with COPD.

3:25 pm – 3:50 pm - Heterogeneity in COPD from diagnosis to ventilation

- **Igor Barjaktarevic, MD PhD (UC Los Angeles)** – This speaker will discuss the various phenotypes of COPD and how this impacts ventilation. They will also cover how to measure and treat ventilation heterogeneity in COPD.

3:50 pm – 4:00 pm – Q&A

Coffee Break with exhibitors: 4:00 pm – 4:30 pm

In the Weeds of COPD

4:30 pm – 4:55 pm – Genetics in COPD

- **Russell Buhr, MD PhD (UC Los Angeles)** – This speaker will discuss various genetic factors associated with COPD, including Alpha-1 Antitrypsin Deficiency, and how clinical management differs in those with genetic-associated COPD.

4:55 pm – 5:20 pm – Pulmonary Hypertension from COPD

- **Yuri Matusov, MD (Cedars-Sinai)** – This speaker will discuss how patients with COPD can develop Pulmonary Hypertension the management of PH-COPD, and upcoming trials focused on PH-COPD.

5:20 pm – 5:45 pm – Lung Transplant for COPD

- **Julia Maheshwari, MD (UC San Francisco)** – This speaker will discuss the referral criteria for lung transplantation in patients with COPD, and how transplantation can improve quality of life for patients with COPD.

5:45 pm – 6:10 pm – Population Health Approach to COPD

- **Brooks Kuhn, MD (UC Davis)** - This speaker will discuss how health system approaches can improve care for patients with COPD.

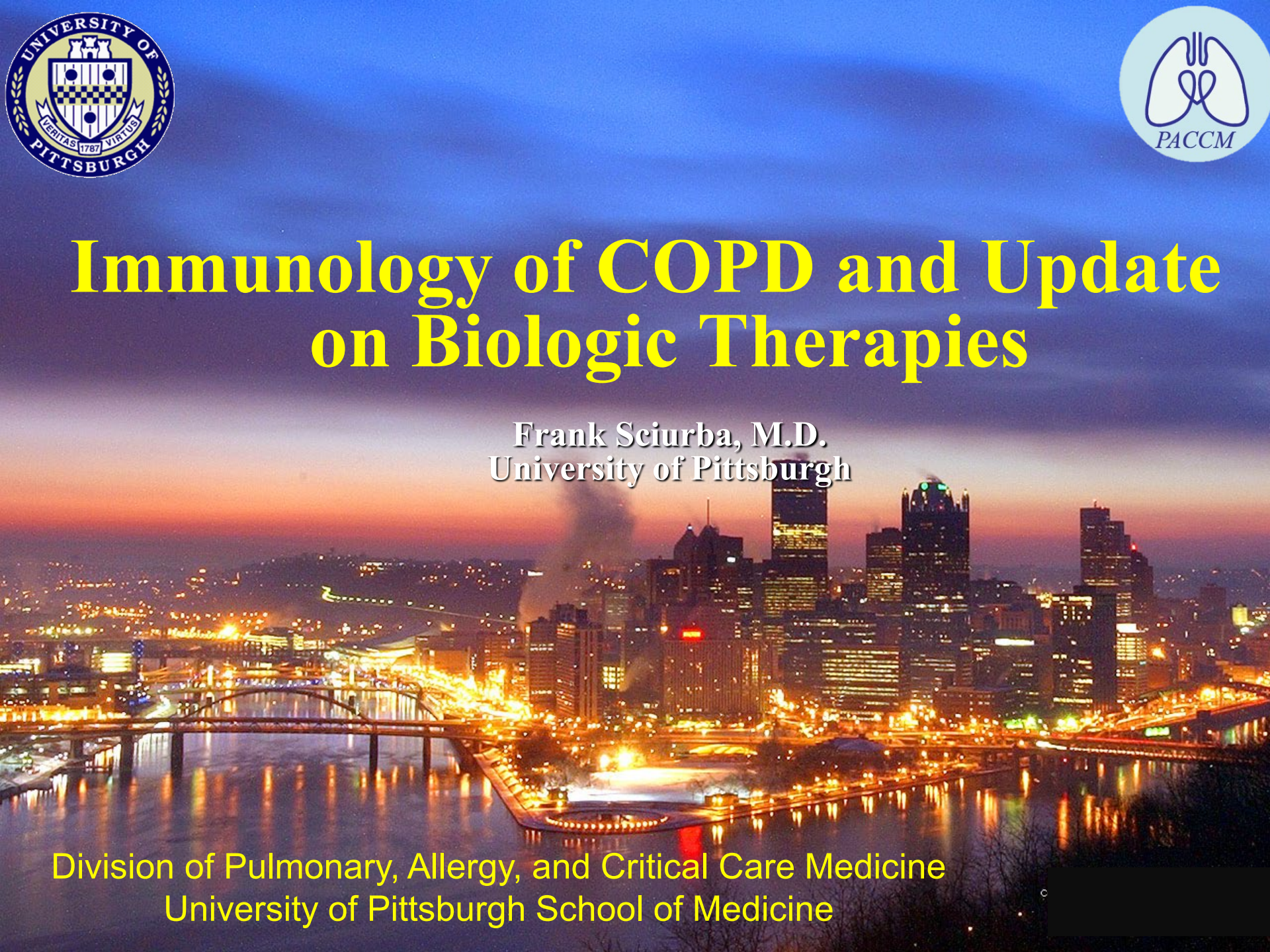
6:00 pm – 6:10 pm – Q&A

Frank C. Sciurba, M.D., FCCP is a Tenured Professor at the University of Pittsburgh School of Medicine. He is the director of the Emphysema COPD Research Center and the Director of the Clinical Pulmonary physiology laboratories and pulmonary rehabilitation program. He earned his B.S. degree in Biochemistry from the University of Illinois and attended medical school at the University of Chicago Pritzker School of Medicine. Dr. Sciurba completed his residency and fellowship in Pulmonary and Critical Care Medicine at the University of Pittsburgh Medical Center.

Dr. Sciurba's research has been inspired by real clinical problems facing his patients. He has authored over 400 peer reviewed publications with a particular emphasis on lung physiology and COPD. Dr. Sciurba is fully supported on grants from the National Institutes of Health, foundations, and industry. He is also a member of the Western PA Regional American Lung Association Board.

Immunology of COPD and Update on Biologic Therapies

Frank Sciurba, M.D.
University of Pittsburgh



Division of Pulmonary, Allergy, and Critical Care Medicine
University of Pittsburgh School of Medicine

Financial Disclosure

Institutional support: NIH, COPD foundation,

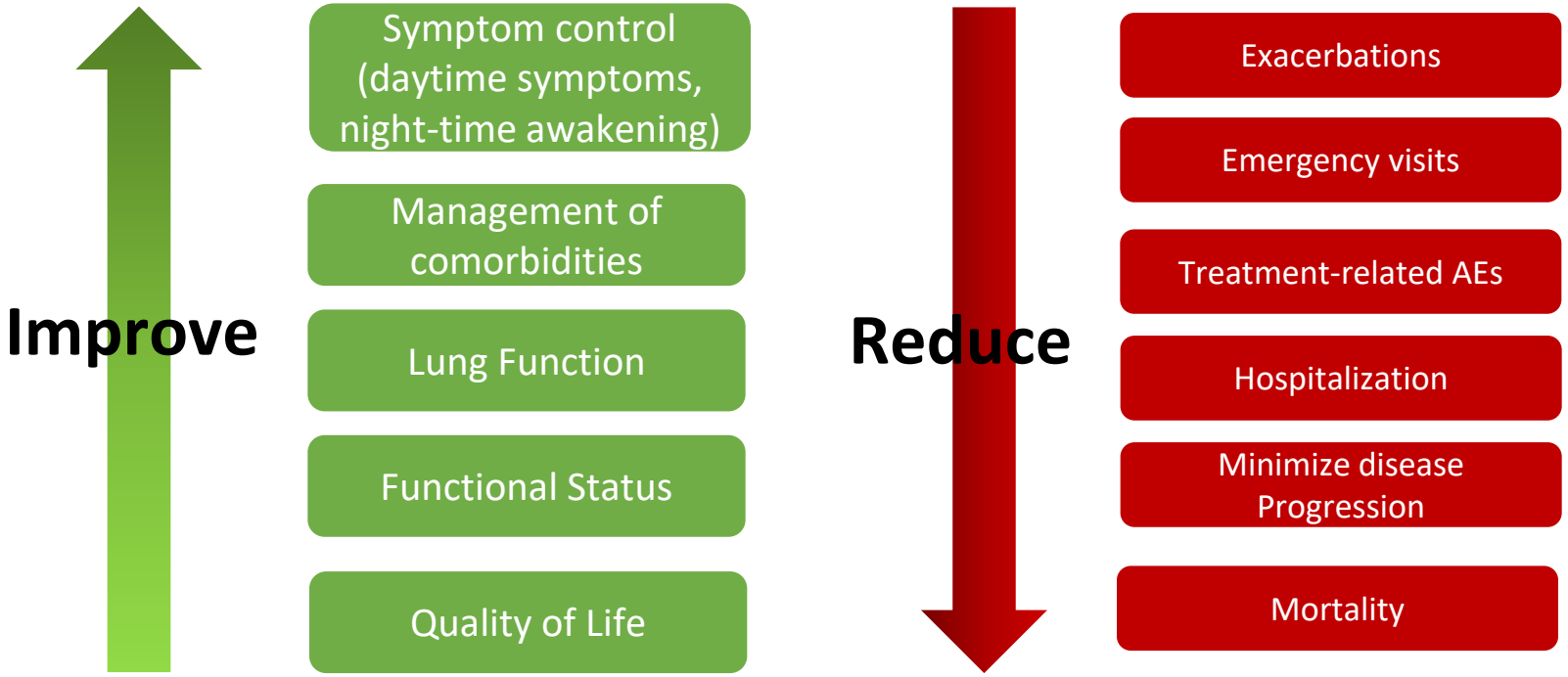
AstraZeneca, GSK, Uniquity, Pulmonx, Galvanize Therapeutics, Apreo, Nuvaira.

Consulting: AstraZeneca, GSK, Sanofi, Regeneron,Amgen, Uniquity, United therapeutics, Rhyme Medical, Pulmonx, Apreo.

Biologics in COPD

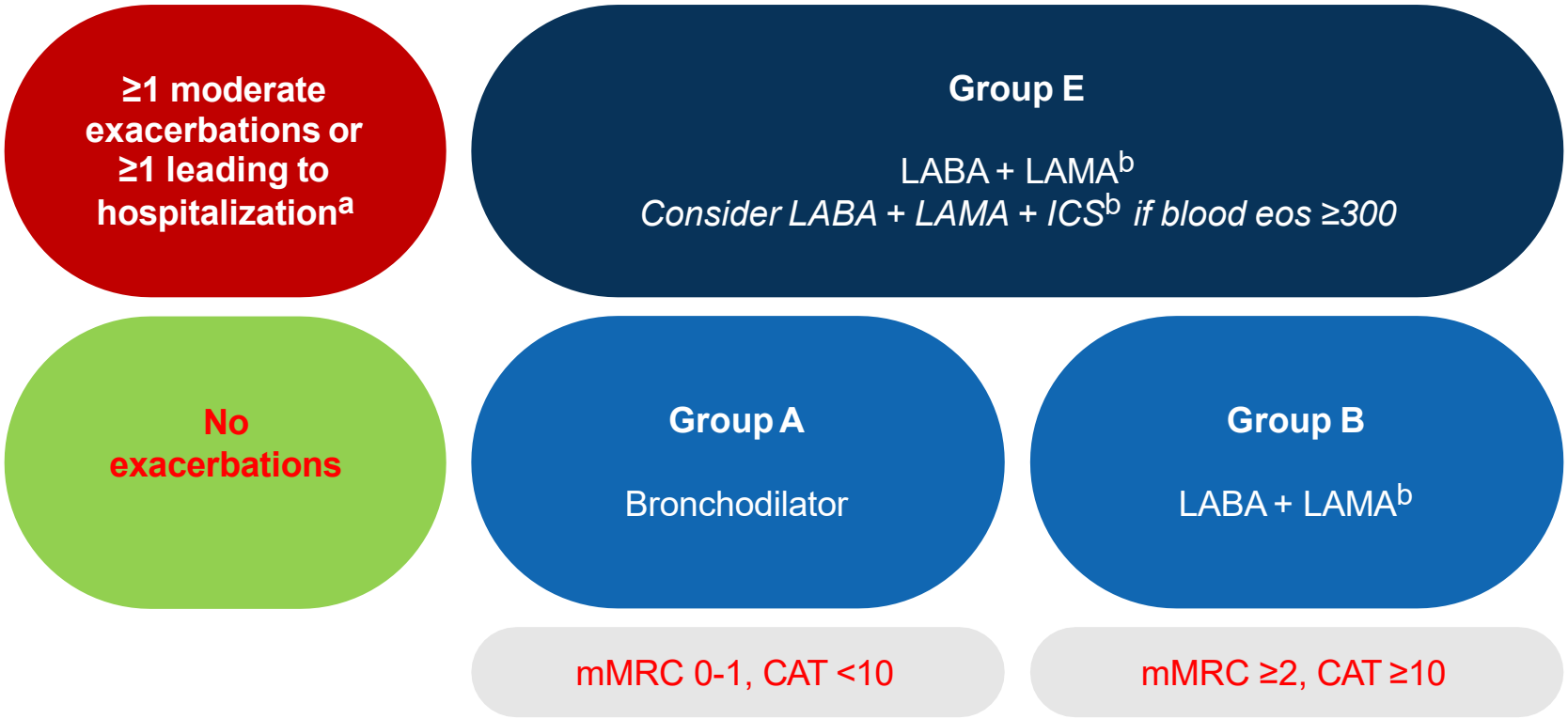
- Why do we need them & What are they?
- TH2 cytokine targeting biologics
- Alarmins and non-TH2 targets
- Practical aspects of biologics use

Goals of Management in COPD (Can be Independent of Each Other)



Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Updated 2025. Accessed Feb 23, 2025. https://goldcopd.org/2025-gold-repor

Initial Treatment Recommendations: GOLD[1]



[a] Exacerbations refers to the number of exacerbations per year.
[b] Single-inhaler therapy may be more convenient and effective than multiple inhalers; single inhalers improve adherence to treatment.

1. Global Initiative for Chronic Obstructive Lung Disease. 2026 Report. https://goldcopd.org/2026-gold-report.

Unmet Need Persists Post Guideline Based Tx

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 3, 2018 VOL. 378 NO. 18

Once-Daily Single-Inhaler Triple versus Dual Therapy in Patients with COPD

David A. Lipson, M.D., Frank Barnhart, D.V.M., Noushin Brealey, M.D., Jean Brooks, M.Sc., Gerard J. Criner, M.D., Nicola C. Day, Ph.D., Mark T. Dransfield, M.D., David M.G. Halpin, M.D., MeiLan K. Han, M.D., C. Elaine Jones, Ph.D., Sally Kilbride, M.Sc., Peter Lange, M.D., David A. Lomas, M.D., Ph.D., Fernando J. Martinez, M.D., Dave Singh, M.D., Maggie Tabberer, M.Sc., Robert A. Wise, M.D., and Steven J. Pascoe, M.B., B.S., for the IMPACT Investigators

- 77% Group "E", FEV_1 45.5±14.8
- **15 -25% reductions in EVENTS PER PATIENT**
  but….
- **6% relative reduction in PROPORTION OF PATIENTS w/ EVENTS**
- **~50% of patients had at least one moderate-to-severe event**

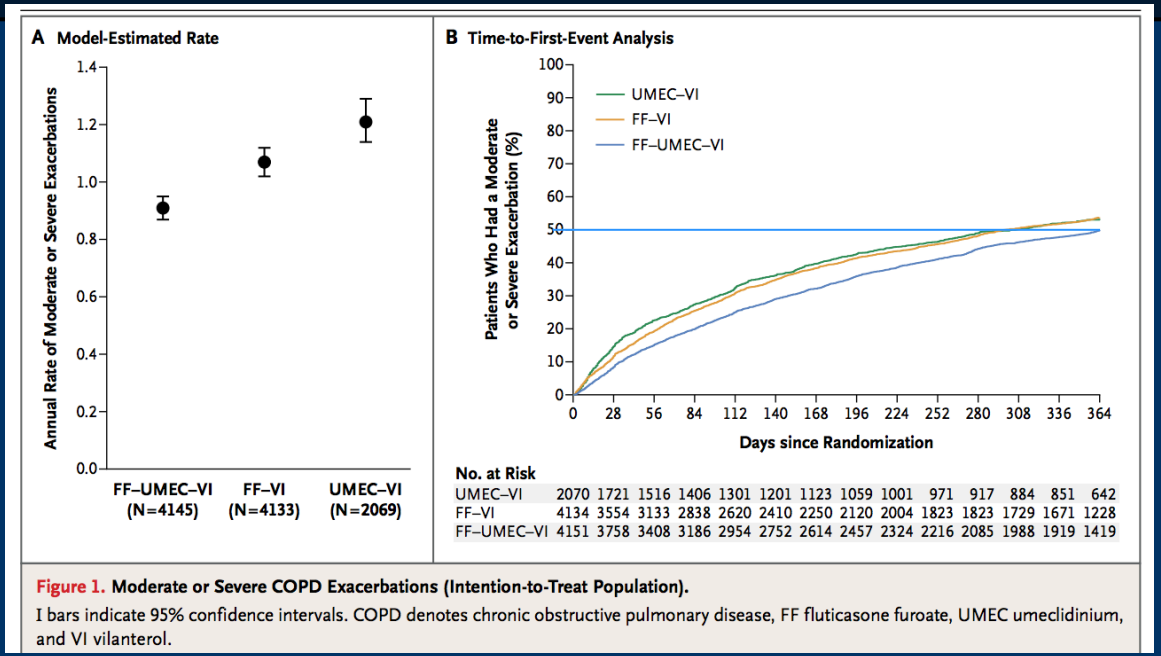


Figure 1. Moderate or Severe COPD Exacerbations (Intention-to-Treat Population).

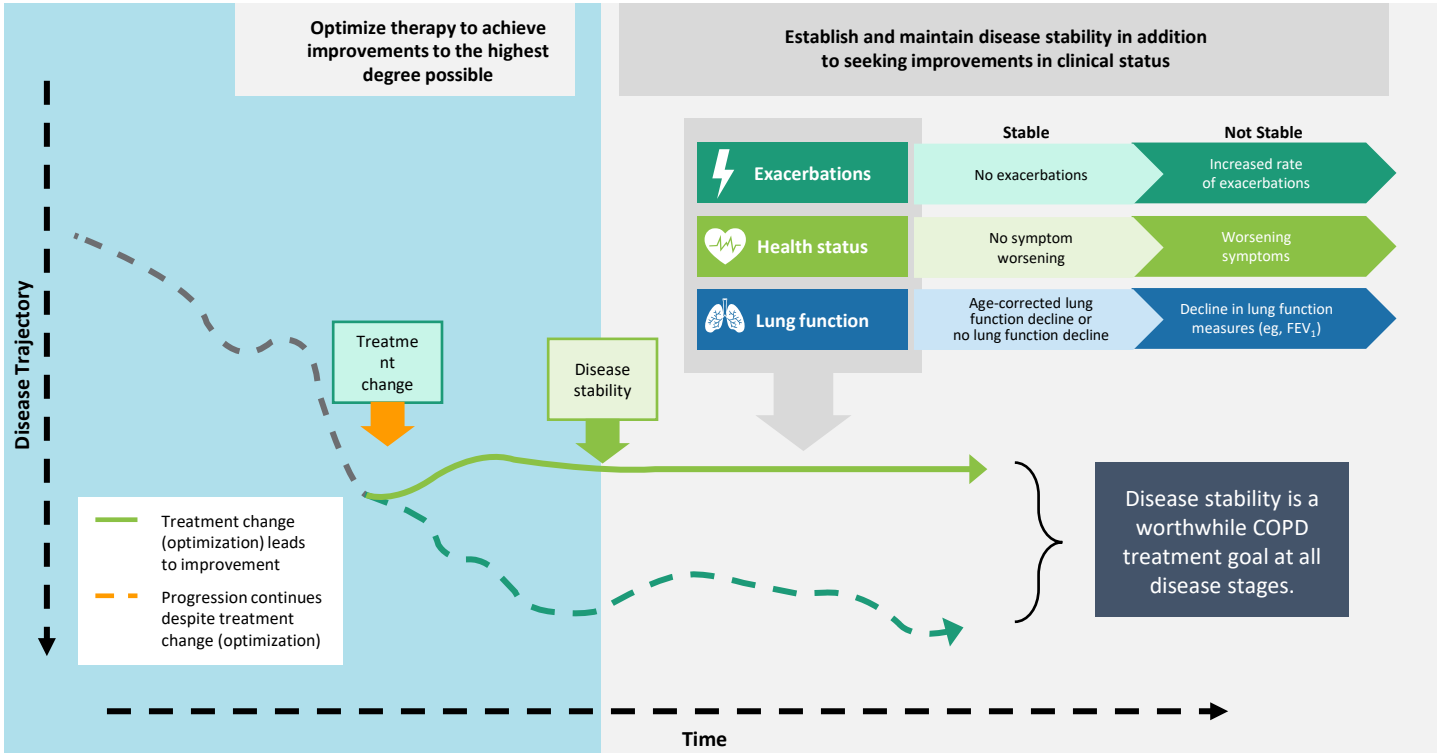
I bars indicate 95% confidence intervals. COPD denotes chronic obstructive pulmonary disease, FF fluticasone furoate, UMEC umeclidinium, and VI vilanterol.

Persistent exacerbations in patients on maximal (triple-therapy) single inhaler and under "best care" in a clinical trial

Only 37% of U.S. COPD patients were following GOLD recommended maintenance regimens3

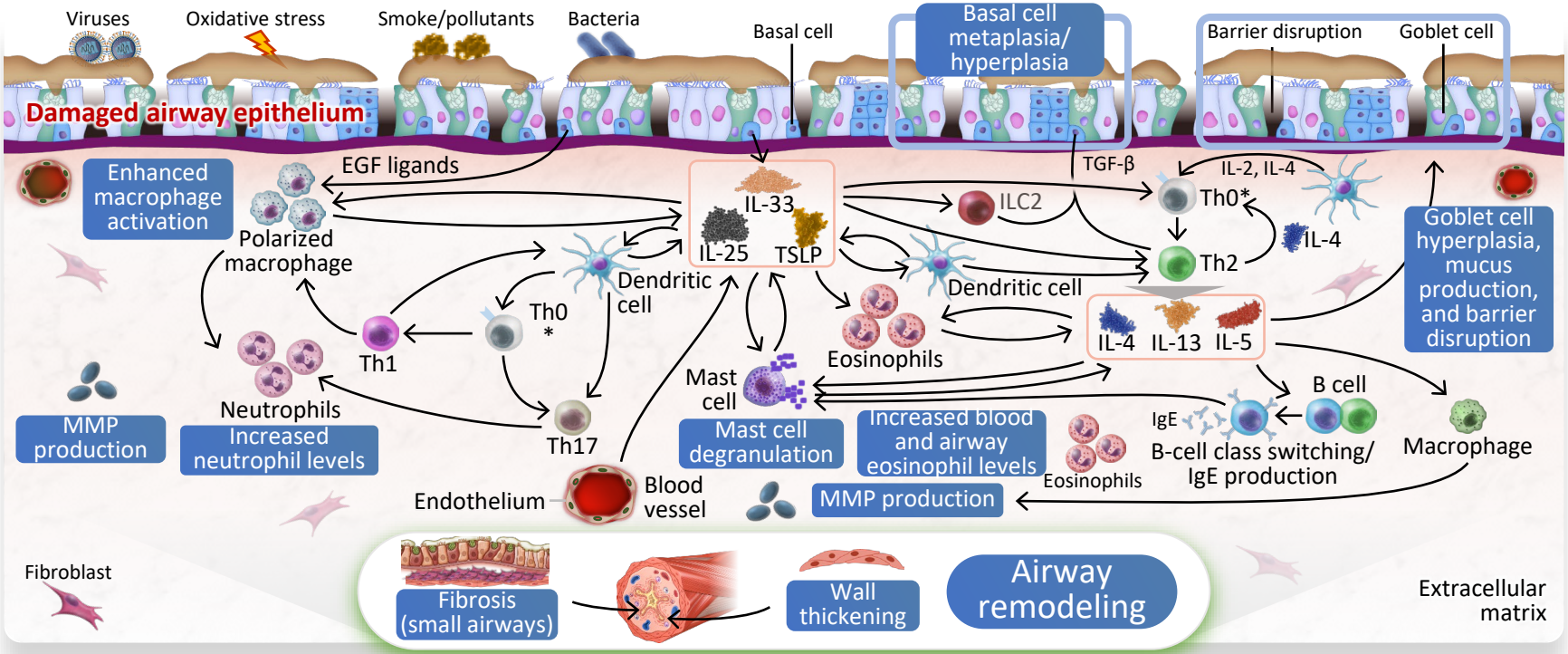
48% did not receive maintenance medication3

Idealized Target: Disease Activity/ Stability



Singh D, et al. *Am J Respir Crit Care Med*. 2025;211:452-463.

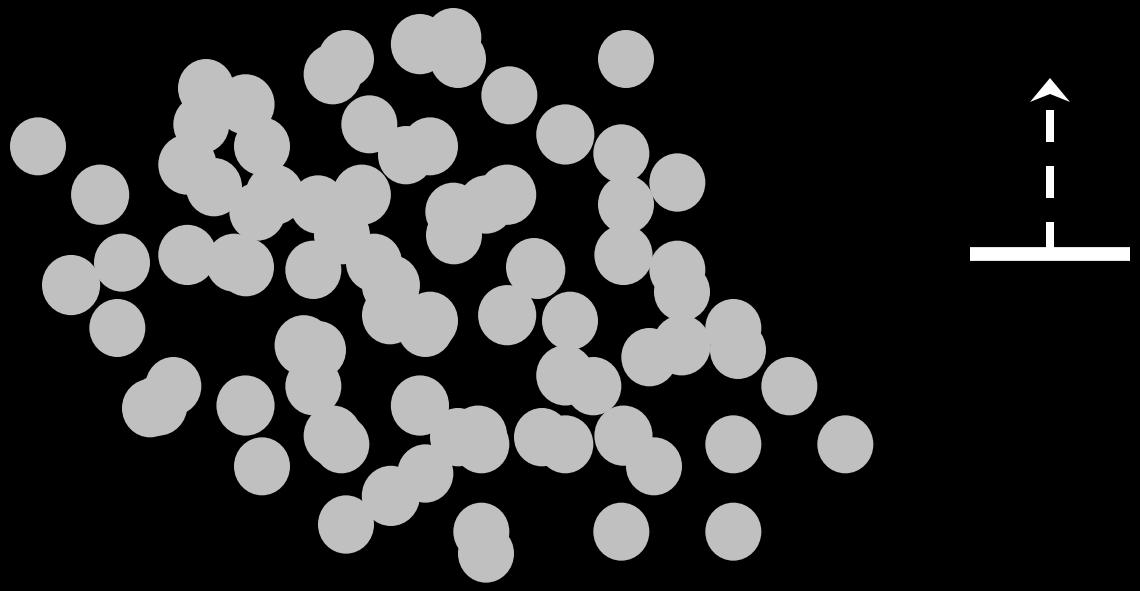
Variation in COPD Pathophysiology: Type 1/3 and Type2 Inflammation: Opportunity for Precision Tx



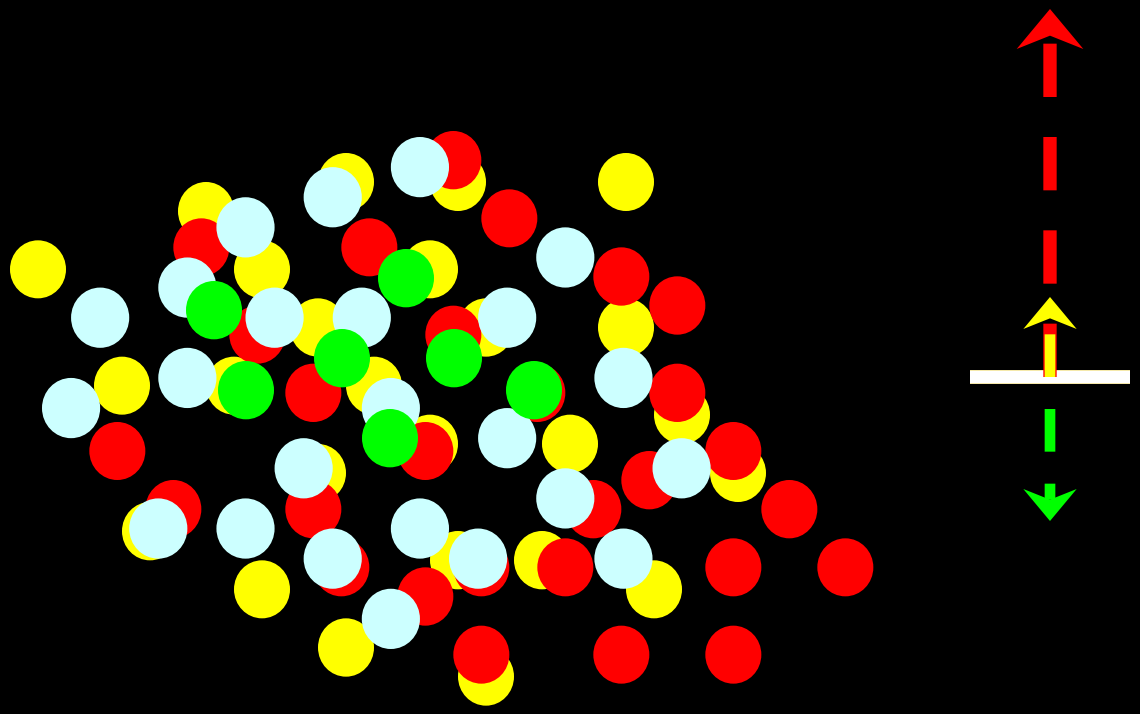
EGF, epidermal growth factor; IgE, immunoglobulin E; IL, interleukin; ILC2, group 2 innate lymphoid cell; MMP, matrix metalloproteinase; TGF-β, transforming growth factor beta; Th, T helper cell; TSLP, thymic stromal lymphopoietin.
*T-cell differentiation takes place in lymph nodes and is included in the schematic for the purposes of illustration only.
COPD is a complex heterogeneous disease. Not all pathophysiological processes may be specific to COPD.

1. Linden D, et al. *Eur Respir Rev*. 2019;28(151):180063. 2. Papi A, et al. *Am J Respir Crit Care Med*. 2006;173(10):1114-1121. 3. Ruysseveldt E, et al. *Front Allergy*. 2021;2:787128. 4. Aghapour M, et al. *Am J Respir Cell Mol Biol.* 2018;58(2):157-169.5. Yousuf A, et al. *J Allergy Clin Immunol Pract*. 2019;7(5):1405-1416. 6. Zhu J, et al. *Annu Rev Immunol*. 2010;28:445-489. 7. Liu M, et al. *Front Pharmacol*. 2021;12:695957. 8. Doyle AD, et al. *Eur Respir J*. 2019;53(5):1801291. 9. Arora S, et al. *Immunobiology*. 2018;223(4-5):383-396. 10. Barnes PJ. *J Clin Invest*. 2008;118(11):3546-3556. 11. Poto R, et al. *Cells*. 2022;11(10):1720. 12. Dey S, et al. *Am J Physiol Lung Cell Mol Physiol*. 2022;322:L64-L83.13. Vremec D, et al. *Blood*. 2007;109(3):1165-1173. 14. Freeman CM, Curtis JL. *Am J Respir Cell Mol Biol*. 2017;56(2):152-159. 15. Christopoulou ME, et al. *Int J Mol Sci*. 2023;24(4):3786.

Traditional Non-precision Assessment of An Intervention



Response to an Intervention Using a Precision Paradigm



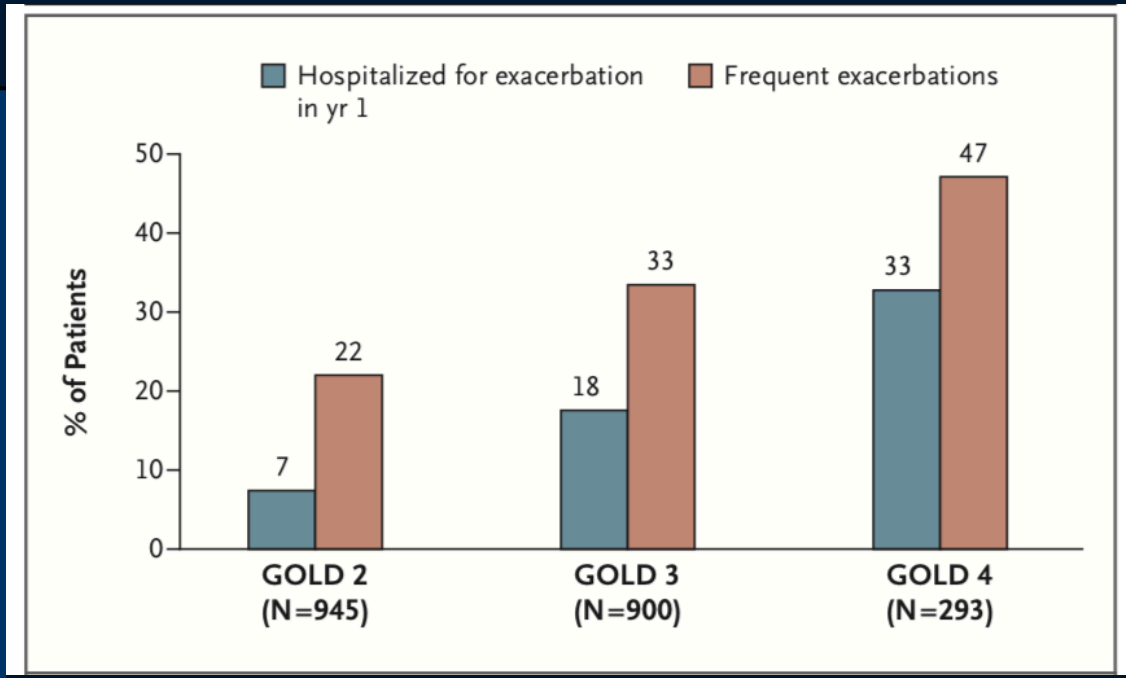
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Susceptibility to Exacerbation in Chronic Obstructive Pulmonary Disease

John R. Hurst, M.B., Ch.B., Ph.D., Jørgen Vestbo, M.D., Antonio Anzueto, M.D., Nicholas Locantore, Ph.D., Hana Müllerova, Ph.D., Ruth Tal-Singer, Ph.D., Bruce Miller, Ph.D., David A. Lomas, Ph.D., Alvar Agusti, M.D., Ph.D., William MacNee, M.B., Ch.B., M.D., Peter Calverley, M.D., Stephen Rennard, M.D., Emiel F.M. Wouters, M.D., Ph.D., and Jadwiga A. Wedzicha, M.D., for the Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) Investigators*

ABSTRACT



"Since moderate COPD is much more prevalent than very severe COPD, the overall burden of exacerbations may be greater in moderate disease."

Decline in FEV_1 in Patients With Frequent Exacerbations and Smokers

Average Decline in FEV_1 % Predicted Per Year Over 3 Years*

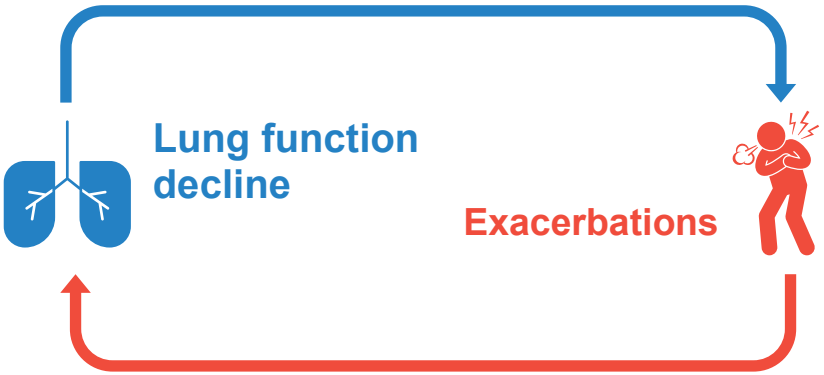
	Smokers			Ex-Smokers		
	N	Mean	95% CI P-Value	N	Mean	95% CI P-Value
Frequent exacerbations	22	-4.10	(-4.40, -3.80) <0.0001	29	-2.80	(-3.1, -2.5) <0.0001
Infrequent exacerbations	19	-3.15	(-3.55, -2.75) 0.002	27	-0.85	(-1.1, -0.5) 0.3

* Random effects modeling for COPD patients, smokers and ex-smokers separately, by exacerbation status. Adjusted for sex, age, smoking status, baseline FEV_1 (% predicted).

Makris D, et al. Resp Med. 2007;101:1305-1312. Reproduced with permission from Elsevier.

Summary: Lung Function Decline and Exacerbations are Interconnected and Have a High Impact on Patients With COPD

Lung function decline is associated with increasing frequency and severity of exacerbations[1]



Exacerbations contribute to progressive and potentially irreversible lung damage[2]

Exacerbations and declining lung function are associated with:

- Increased dyspnoea[3]
- Impaired physical activity[4,5]
- Reduced quality of life[3]
- Hospitalisation and medical costs[6]
- Death[7,8]

COPD=chronic obstructive pulmonary disease.

1. Hurst JR, et al. *N Engl J Med*. 2010;363(12):1128-1138. 2. Hansel TT, Barnes PJ. *Lancet*. 2009;374(9691):744-755. 3. de la Loge C, et al. *Chronic Obstr Pulm Dis*. 2016;3(2):519-538. 4. Hurst JR, et al. *Eur J Intern Med*. 2020;73:1-6. 5. Alahmari AD, et al. *Eur Respir J*. 2016;48(2):340-349. 6. Ozkaya S, et al. *Clinicoecon Outcomes Res*. 2011;3:15-18. 7. Suissa S, et al. *Thorax*. 2012;67(11):957-963. 8. Boutou AK, et al. *Eur Respir J*. 2013;42(3):616-625.

IMPACT of PRIOR EXACERBATIONS in MODERATE COPD on FUTURE RISK

ORIGINAL ARTICLE

Natural History of Chronic Obstructive Pulmonary Disease Exacerbations in a General Practice–based Population with Chronic Obstructive Pulmonary Disease

Kieran J. Rothnie[1,2], Hana Müllerová[3], Liam Smeeth[2], and Jennifer K. Quint[1,2]

[1]Respiratory Epidemiology, Occupational Medicine and Public Health, National Heart and Lung Institute, Imperial College London, London, United Kingdom; [2]Faculty of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London, United Kingdom; and [3]Respiratory Epidemiology, GlaxoSmithKline R&D, Uxbridge, United Kingdom

ORCID ID: 0000-0003-4279-1624 (K.J.R.).

- 99,574 COPD patients from UK Clinical Practice Research Database
  - mean 67 yo
  - 70% GOLD 2/3
  - 52% smoker
- 10 years of follow-up, 2004 - 2015

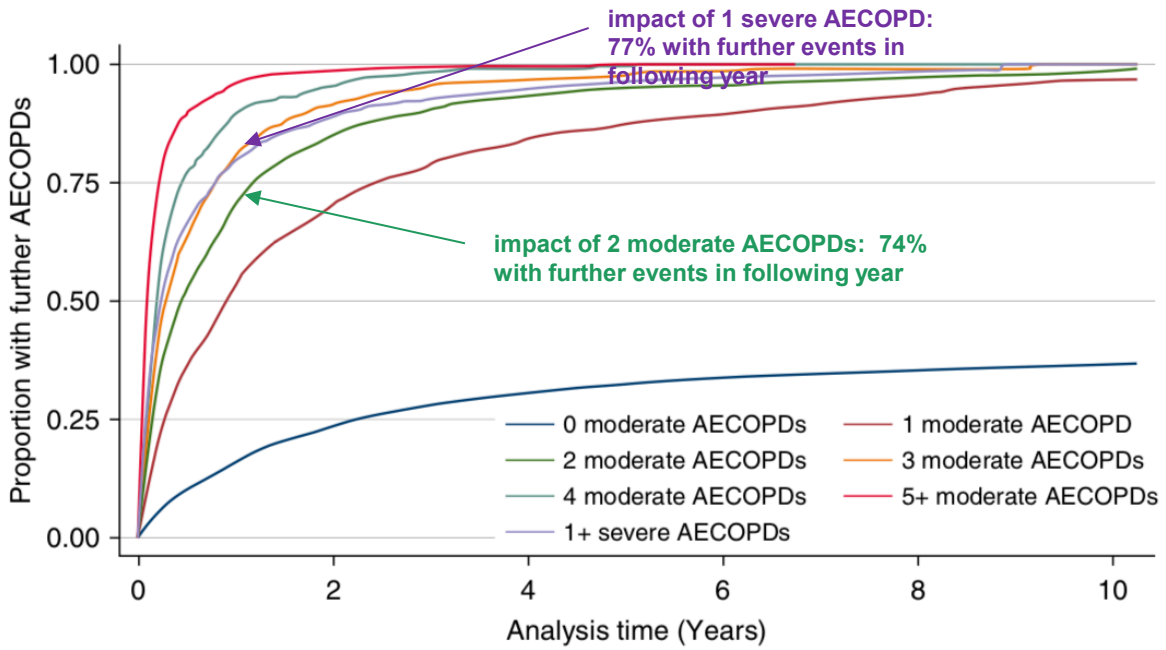
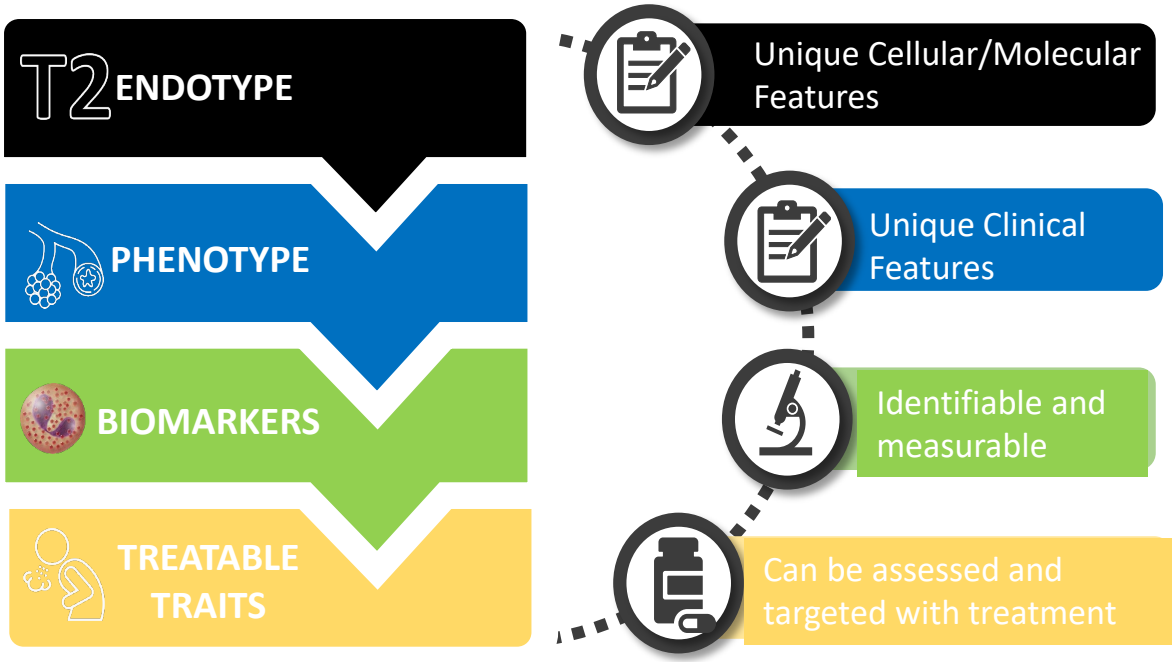


Figure 1. Time to first acute exacerbation of chronic obstructive pulmonary disease (AECOPD) by baseline AECOPD frequency and severity, established patients with chronic obstructive pulmonary disease.

Treatable Traits Strategy as the Basis for Targeted Therapeutic Intervention[1–4]



A treatable trait is defined as a **"therapeutic target** identified by **phenotypes** or **endotypes** through a **validated biomarker"**[4]

1. Garudadri S, et al. *Ann Am Thorac Soc*. 2018;15:S234–S238 2. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Updated 2025. Accessed Feb 23, 2025. https://goldcopd.org/2025-gold-report/. 3. McDonald VM, et al. *Eur Respir J*. 2019;53:1802058. doi:10.1183/13993003.02058-2018. 4. McDonald VM, et al. *Arch Bronconeumol.* 2022;58:583-585. doi:10.1016/j.arbres.2021.07.003.

COPD Endotypes

COPD with type 1/type 3 inflammation[1,2] (ie, neutrophilic inflammation)	COPD with type 2 inflammation[1,3-5]
Elevated sputum neutrophils	Elevated blood/sputum eosinophils
Elevated Tc1/Th1/Th17 cells	Elevated Th2 cells
Elevated ILC3	Elevated ILC2
Elevated cytokines (eg, IL-1β, TNF-α)	Elevated type 2 cytokines (IL-4, IL-5, IL-13)
Poor response to corticosteroids	Responsive to inhaled corticosteroids

Majority of COPD patients

Up to ~30-40% of COPD patients[6,7]*

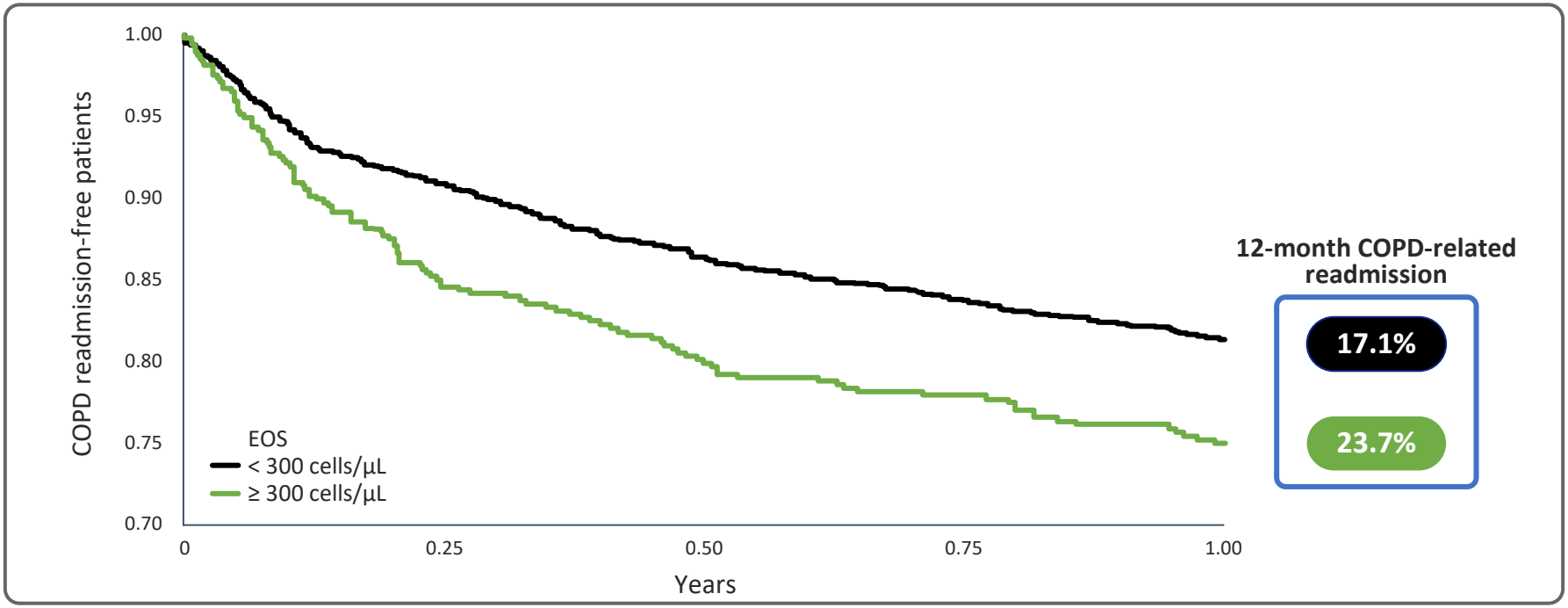
There is potential overlap in type 2 and type 1/type 3 inflammatory mechanisms driving COPD

*Based on sputum EOS ≥3% and blood EOS ≥2%.[6,7]

EOS, eosinophils; IL, interleukin; ILC, innate lymphoid cell; Tc, cytotoxic T cell; Th, T helper cell; TNF, tumor necrosis factor.

1. Barnes PJ. *Allergy.* 2019;74(7):1249-1256. 2. Chen L, et al. *PeerJ.* 2016;4:e2301. 3. Ghebre MA, et al. *J Allergy Clin Immunol.* 2018;141(6):2027-2036.e12. 4. Barczyk A, et al. *J Allergy Clin Immunol.* 2006;117(6):1484-1492. 5. Christenson SA, et al. *Am J Respir Crit Care Med.* 2015;191(7):758-766. 6. Singh D, et al. *Eur Respir J.* 2014;44(6):1697-1700. 7. Leigh R, et al. *Eur Respir J.* 2006;27(5):964-971.

COPD With Elevated EOS Is Associated With Higher Hospital Readmission



Retrospective, observational, cohort study to examine COPD-related hospital admission between January 2011 and December 2016 at Intermountain Healthcare facility (serving Utah, Idaho, and Wyoming). Final sample size was 2,445 unique patients hospitalized with COPD exacerbation with blood EOS counts.

Hegewald MJ, et al. *Int J Chron Obstruct Pulmon Dis*. 2020;15:2629-2641.

GOLD Recommends Blood Eosinophils as a Biomarker to Help Guide Therapeutic Choices in COPD[1]

Elevated blood eosinophils are:

Associated with:

- Response to ICS treatment*
- Increased exacerbation risk
- Increased rate of lung function decline†
- Greater risk of future COPD development‡

Correlated with:

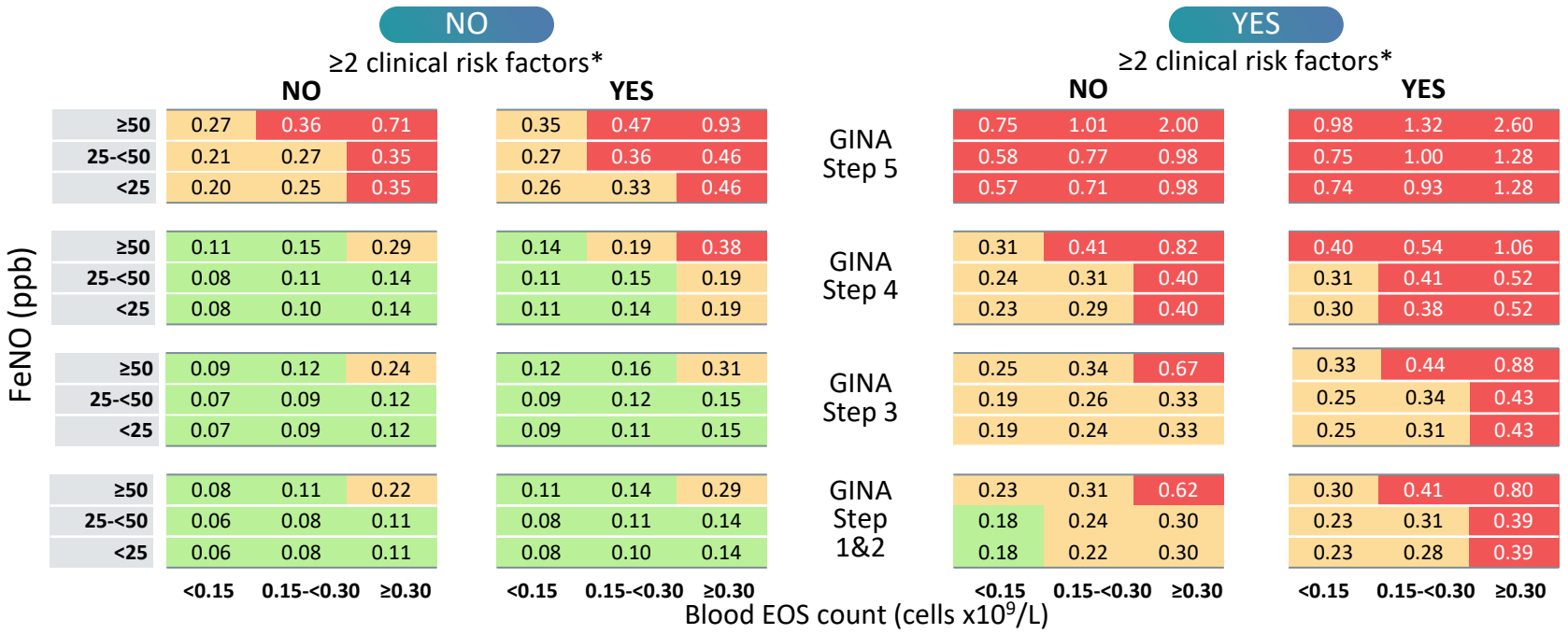
- Elevated lung eosinophil numbers
- Presence of higher levels of markers of type 2 inflammation in the airways

*GOLD strongly favors the use of ICS in patients with blood eosinophils ≥300 cells/µL. The threshold of <100 cells/µL can be used to identify patients with a low likelihood of treatment benefit with ICS. †In patients on low-dose ICS. ‡Results obtained in a study of 359,456 South Korean adults with no history of physician-diagnosed asthma or COPD.[2]

GOLD, Global Initiative for Chronic Obstructive Lung Disease; ICS, inhaled corticosteroids.

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Updated 2025. Accessed Feb 23, 2025. https://goldcopd.org/2025-gold-report/ 2. Park HY, et al. *Eur Respir J*. 2021;58(4):2003823.

Asthma: FeNO and Blood EOS Are Independently and Additively Associated With the Risk of Exacerbations



Systematic review of RCTs was used to create a prototype risk scale. Cell numbers represent the predicted annual asthma attack rate if treatment is not changed.
*Risk factors as defined by GINA include poor symptom control, low lung function, adherence issues, reliever overuse, intubation or intensive care unit admission for asthma previously, comorbidities, and environmental exposures
Couillard S, et al. *Thorax*. 2022;77(2):199-202.

What Are Biologics[1-3]

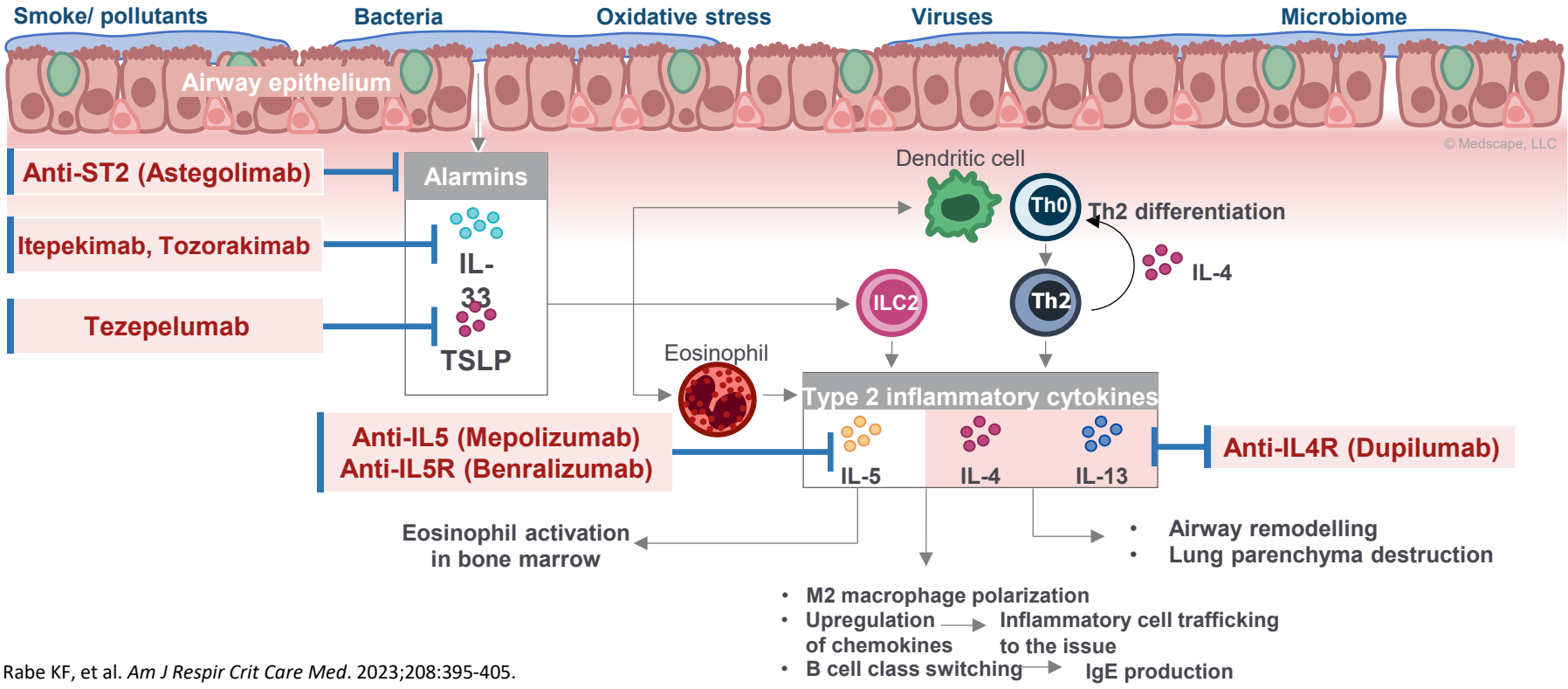
- Biological products are used to diagnose, prevent, treat, and cure disease/medical conditions
  - Generally large complex molecules
  - Highly selective
  - Produced with biotechnology through a living system
    - Microorganism, plant cell, and animal cell
- Regulated by FDA
- Composed of any combination of proteins, nucleic acids, or sugars
- Therapeutic proteins, blood/tissue products, monoclonal antibodies, vaccines, and gene therapy
- May be heterogenous mixtures that are not precisely defined
- Highly specific with low levels of toxicity
- Production and regulation are difficult
  - Processes complicated
    - Sensitive to small changes
  - Tend to be heat sensitive and susceptible to microbial contamination
  - Expensive
- Can trigger immune responses
- Most are injections
  - Self-injection or IV infusion

1. FDA. https://www.fda.gov/files/drugs/published/Biological-Product-Definitions.pdf. Accessed Feb 24, 2025 2. Martins AC, et al. *Biomedicines.* 2022; 10(9):2325. 3. Plitcha J, et al. *Front Immunol*. 2023;14:1207641

Biologics in COPD

- Why do we need them & What are they?
- TH2 cytokine targeting biologics
- Alarmins and non-TH2 targets
- Practical aspects of biologics use

Biologics Targeting TH2 Inflammatory Pathways in COPD



Rabe KF, et al. *Am J Respir Crit Care Med*. 2023;208:395-405.

COPD Biologic and New Treatment Landscape

- IL, interleukin; PDE, phosphodiesterase; Ph, phase; POC, proof-of-concept; R, receptor; ST2, interleukin 1 receptor-like 1; TSLP, thymic stromal lymphopoietin.

ORIGINAL ARTICLE

Dupilumab for COPD with Blood Eosinophil Evidence of Type 2 Inflammation

S.P. Bhatt, K.F. Rabe, N.A. Hanania, C.F. Vogelmeier, M. Bafadhel, S.A. Christenson, A. Papi, D. Singh, E. Laws, N. Patel, G.D. Yancopoulos, B. Akinlade, J. Maloney, X. Lu, D. Bauer, A. Bansal, R.M. Abdulai, and L.B. Robinson, for the NOTUS Study Investigators*

BOREAS

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 20, 2023 VOL. 389 NO. 3

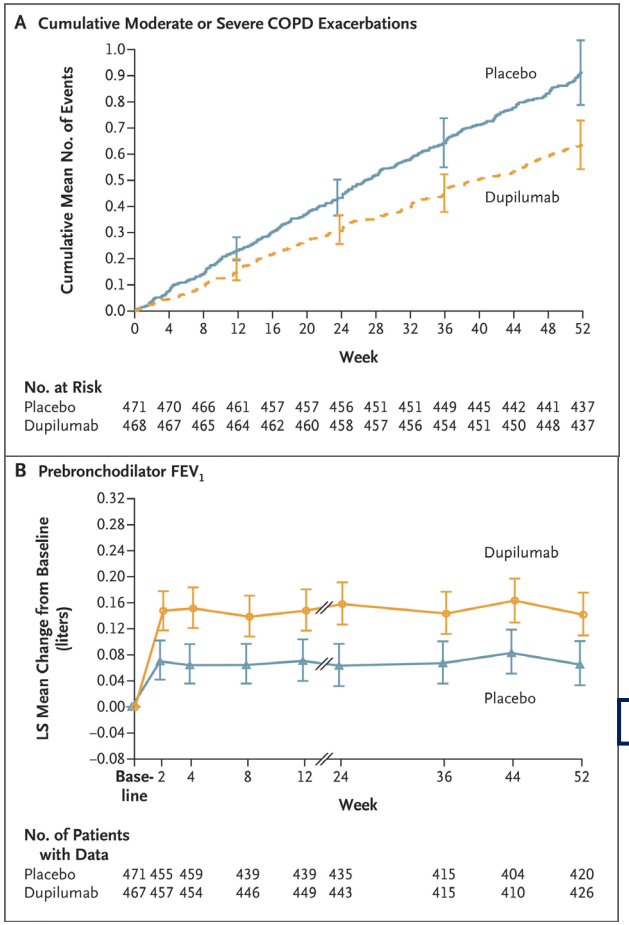
Dupilumab for COPD with Type 2 Inflammation Indicated by Eosinophil Counts

S.P. Bhatt, K.F. Rabe, N.A. Hanania, C.F. Vogelmeier, J. Cole, M. Bafadhel, S.A. Christenson, A. Papi, D. Singh, E. Laws, L.P. Mannent, N. Patel, H.W. Staudinger, G.D. Yancopoulos, E.R. Mortensen, B. Akinlade, J. Maloney, X. Lu, D. Bauer, A. Bansal, L.B. Robinson, and R.M. Abdulai, for the BOREAS Investigators*

NOTUS

Dupilumab

- Reduces signaling of IL-4 and IL-13 by binding to the IL-4 receptor
- BOREAS/NOTUS (n =935/939)
  - Annualized rate of moderate or severe AECOPD (Week 52; **primary end point)**
  - 10 pack year smoking history
  - triple therapy for ≥ 3 months
  - ≥ 2 moderate or ≥ 1 severe exacerbation
  - Chronic bronchitis
  - FEV1 > 30% pred.
  - No history of asthma
  - Blood Eos: ≥ 300/µL at screening



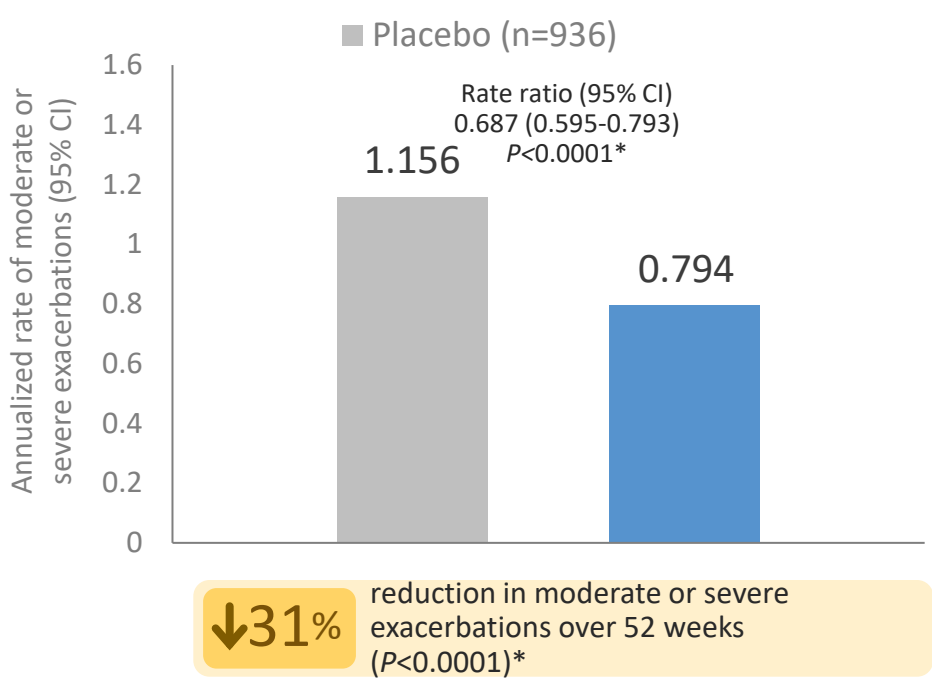
Exacerbations: 30% reduction

NOTUS: 34% reduction

Similar in NOTUS

1. Bhatt SP, et al. *N Engl J Med*. 2023;389(3):205-214. 2. Bhatt SP, et al. *N Engl J Med*. 2024;390(24):2274-2283.

BOREAS and NOTUS: Pooled Primary Endpoint



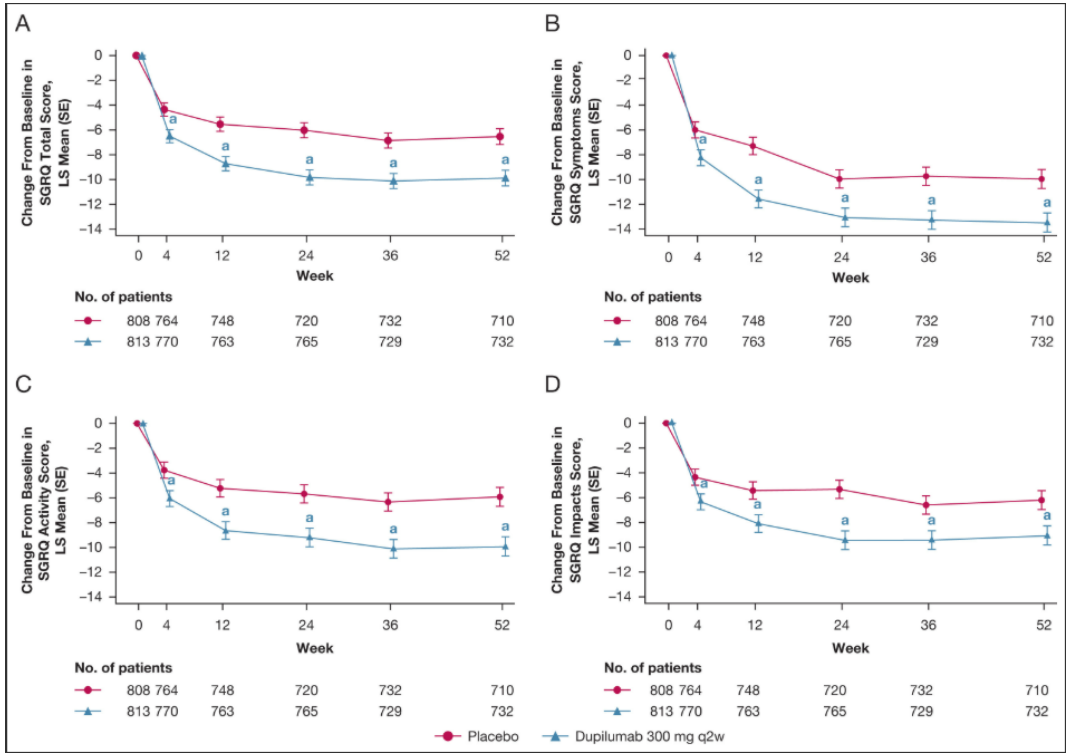
Annualized rate of moderate or severe COPD exacerbations over 52-week treatment period

Dupilumab	0.794
Placebo	1.156
Difference (95% CI)	0.687 (0.595-0.793)
P value*	<0.0001

*Nominal *P* value.
CI, confidence interval.
Bhatt SP, et al. Lancet Respir Med 2025

Dupilumab – Patient Related Outcome SGRQ

- BOREAS and NOTUS pooled analysis[2]
  - Significant improvements in St. George's Respiratory Questionnaire total and domain scores
  - Safety similar between dupilumab and PBO



1. Bhatt SP, et al. *Respir Med*. 2025;236:107846. 2. Bhatt SP, et al. *Chest*. 2025; Published online January 31, 2025. doi:10.1016/j.chest.2025.01.029.

ORIGINAL ARTICLE

Mepolizumab to Prevent Exacerbations of COPD with an Eosinophilic Phenotype

MATINEE

F.C. Sciurba,[1] G.J. Criner,[2] S.A. Christenson,[3] F.J. Martinez,[4] A. Papi,[5] N. Roche,[6] J. Bourbeau,[7] S. Korn,[8] M. Bafadhel,[9] M.L.K. Han,[10] S. Kolterer,[11] K. Miller,[12] D. Mouneimne,[13] J. Fletcher,[13] B. Mayer,[14] J. Min,[15] and I.D. Pavord,[16] for the MATINEE Study Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 26, 2017 VOL. 377 NO. 17

Mepolizumab for Eosinophilic Chronic Obstructive Pulmonary Disease

METREX/METREO

I.D. Pavord, P. Chanez, G.J. Criner, H.A.M. Kerstjens, S. Korn, N. Lugogo, J.-B. Martinot, H. Sagara, F.C. Albers, E.S. Bradford, S.S. Harris, B. Mayer, D.B. Rubin, S.W. Yancey, and F.C. Sciurba

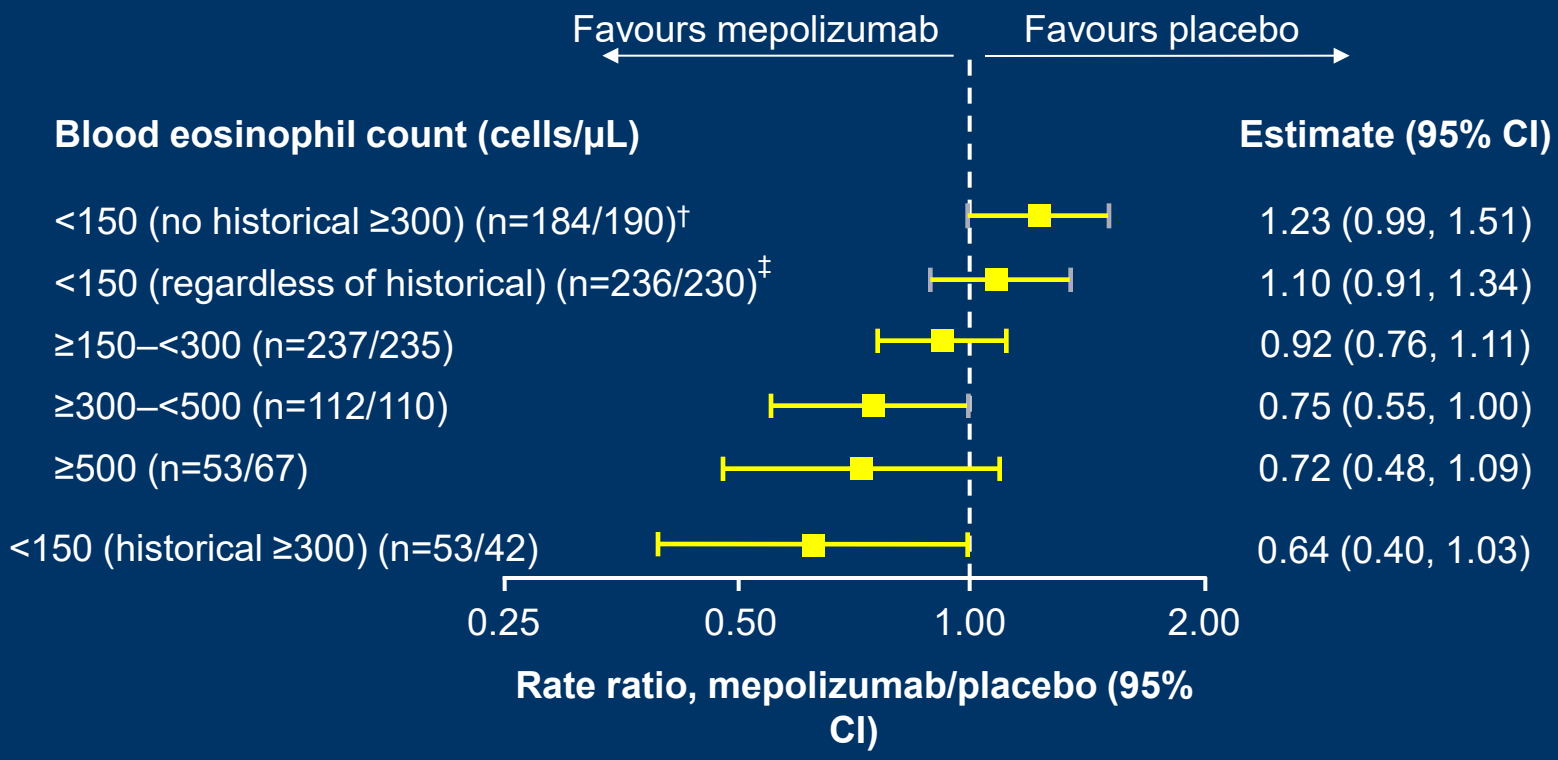
Anti-IL-5 Biologic: Mepolizumab (Anti-IL-5)

- METREX and METREO[1]
  - Eligibility
    - » 10 pack year smoking history
    - » Triple therapy x3 months
    - » ≥ 2 moderate or ≥ 1 severe exacerbation
    - » Current diagnosis of asthma excluded
    - » Blood Eos:
      - ≥ 150 cells/µL at screening OR ≥300cells/µL during previous year
- 18% reduction in exacerbations in METREX, 20% reduction not significant in METREO
- Mixed effect in symptom scores

- Post hoc analysis of METRX/METREO[2]
  - Eos ≥ 300 cells/µL and chronic bronchitis
  - 24% decrease in annualized exacerbation rate vs PBO
  - 39% decrease in exacerbations requiring ED visit/hospitalization vs PBO
- MATINEE
  - Eos ≥ 300 cells/µL, with or without chronic bronchitis
  - 21% decrease in annualized exacerbation rate
  - Safety similar to PBO
- FDA approved in May 2025[3]

1. Pavord ID, et al. *N Engl J Med*. 2017;377(17):1613-1629. 2. Criner GJ, et al. *Am J Respir Crit Care Med* 2024;209:A1203. 3. GSK press release: https://us.gsk.com/en-us/media/press-releases/us-fda-accepts-gsk-s-submission-for-the-use-of-nucala-mepolizumab-in-copd/#

METREX and METREO: Annual rate of moderate/severe exacerbations by blood eosinophil categories at screening

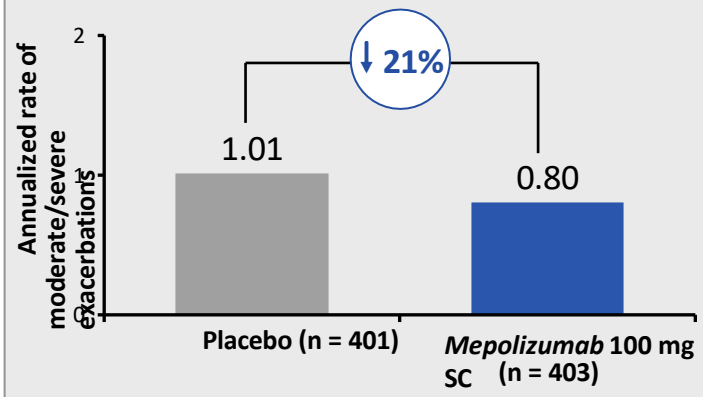


*Moderate exacerbation: requiring either SCS and/or antibiotics; severe exacerbation: requiring hospitalisation/resulting in death; †data from METREX mITT population patients without an eosinophilic phenotype; ‡post hoc analysis of METREX mITT-All and METREO mITT includes patients with an eosinophil count ≥300 cells/μL in previous year; all others are the METREX mITT-Eos plus METREO mITT

MATINEE Primary Endpoint: *Annualized rate of moderate/severe exacerbations up to Week 104*

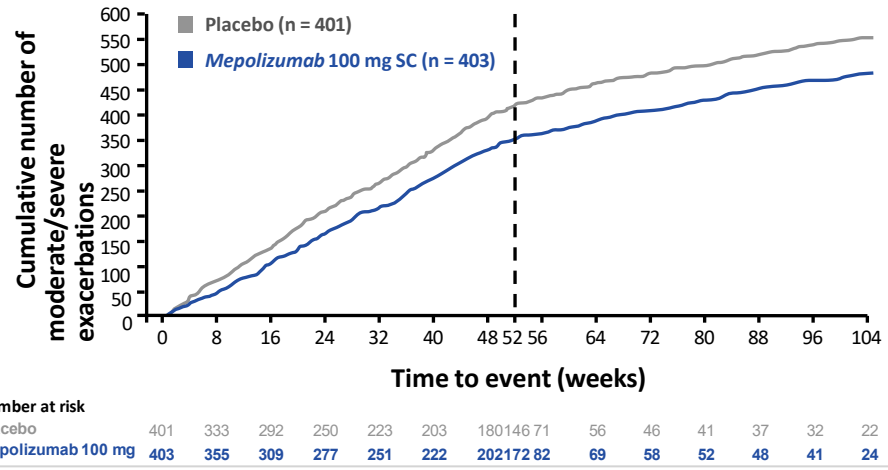
Primary Endpoint

Annualized rate of moderate/severe exacerbations[a] up to Week 104



The difference between *Mepolizumab* and placebo was maintained throughout the 104-week period

Cumulative number of moderate/severe exacerbations[a]



Number at risk

Placebo	401	333	292	250	223	203	180	146	71	56	46	41	37	32	22
Mepolizumab 100 mg	403	355	309	277	251	222	202	172	82	69	58	52	48	41	24

The mITT population was the primary population for assessing efficacy and included all randomized patients who received ≥1 dose of investigational product, with analysis according to randomized treatment group.

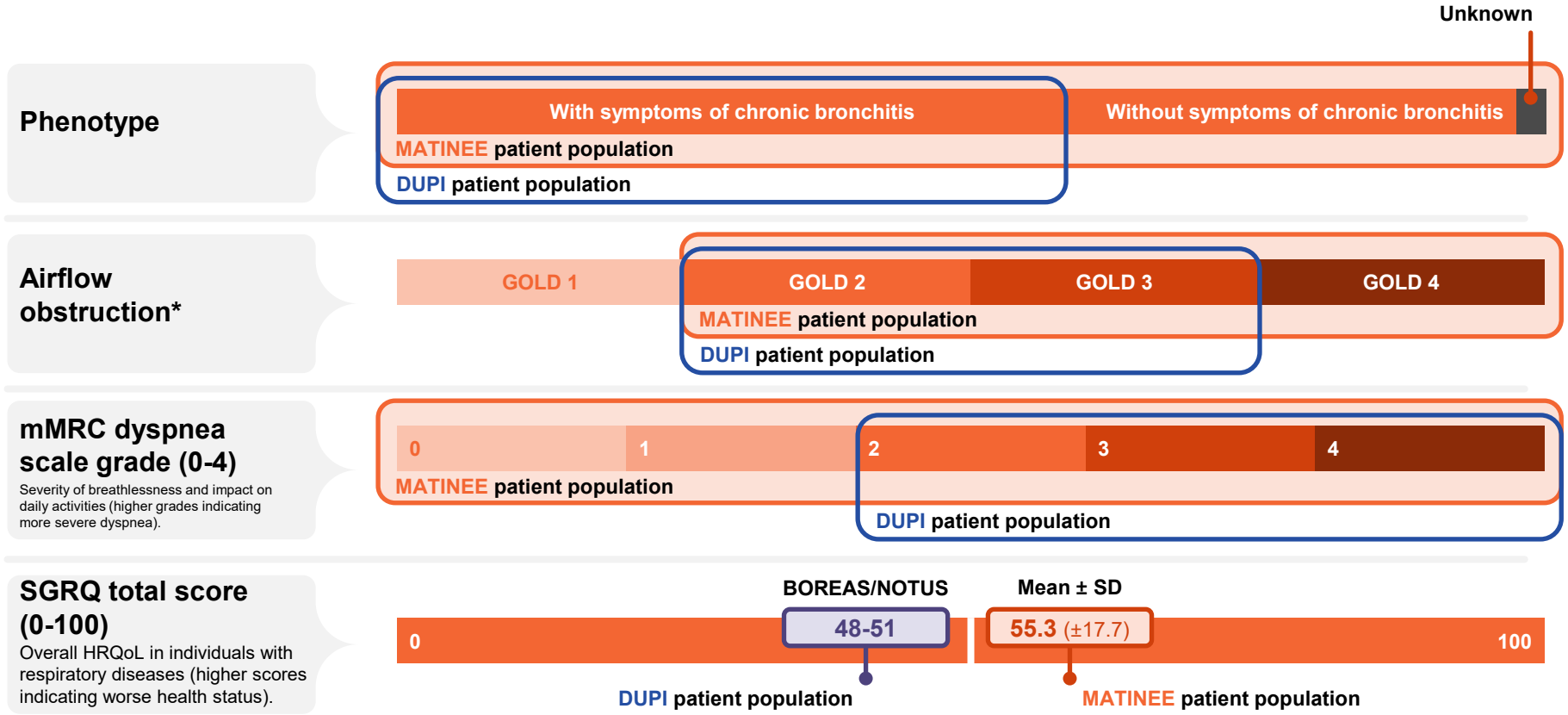
[a]Moderate and severe exacerbations: 'Moderate' defined as treated with systemic corticosteroids and/or antibiotics; 'severe' defined as requiring hospitalization ≥24 hours or resulting in death.

CI = confidence interval; mITT = modified intention-to-treat; RR = rate ratio.

Sciurba F et al. *N Egl J Med*. 2025;392:1710-1720.

- 35% reduction in severe exacerbation (ED visit or hospitalization)
- 31% reduction is AER in patients with Chronic Bronchitis only

MATINEE (mepo) vs. NOTUS/BOREAS (dupi) More inclusive COPD Patient Population



*Inclusion criteria were GOLD 2 and GOLD 3; a small number of GOLD 4 and GOLD 1 patients were included in the patient population.
COPD, chronic obstructive pulmonary disease; HRQoL, health-related quality of life; mMRC, modified Medical Research Council; SD, standard deviation; SGRQ, St. George's Respiratory Questionnaire.

References: 1. Bhatt SP, et al. *Resp. Med.* 2025;236:107846. 2. https://clinicaltrials.gov/study/NCT04133909 3. https://clinicaltrials.gov/study/NCT03930732 4. https://clinicaltrials.gov/study/NCT04456673 5. Drazen JM, et al. *N Eng J Med.* 2018;378(26):2533-2534.

Anti-IL-5 Biologic: Benralizumab (Anti-IL-5Rα)

- GALATHEA and Terranova[1]
  - Eligibility
    - » 10 pack year smoking history
    - » Dual or Triple Therapy
    - » ≥ 2 moderate or ≥ 1 severe exacerbation
    - » Symptomatic: MMRC ≥ 1
    - » Current diagnosis of asthma excluded
    - » Blood Eos:
      - ≥ 220/µL at baseline
- **No significant change in exacerbations**
- Improved lung function

- Post-hoc analysis:[2]
  - After initial exacerbation
    - » 60% reduction in exacerbations within 30 days
    - » 42% reduction in exacerbations within 90 days
- RESOLUTE: Enhanced for Exacerbation frequency/high EOS Repeat phase 3 trial
- AstraZeneca press release September 17, 2025

The RESOLUTE Phase III trial of FASENRA (benralizumab), despite showing numerical improvement, did not achieve statistical significance in the primary endpoint in patients with chronic obstructive pulmonary disease (COPD).

1. Criner GJ, et al. *N Engl J Med*. 2019;381(11):1023-1034. 2. Singh D, et al. *Int J Chron Obstruct Pulmon Dis*. 2023;18:1595-1599. 3. Clinical trials. Clinical trials.gov. https://clinicaltrials.gov/study/NCT04053634. accessed Feb 28, 2025.

Déjà vu - Comparison of Asthma Biologics

Exacerbations (OCS requiring)

Treatment	Rate Ratio (95% CI)
Omalizumab	0.52 (0.37-0.73)
Mepolizumab	0.45 (0.36-0.55)
Reslizumab	0.43 (0.33-0.55)
Benralizumab	0.59 (0.51-0.68)
Dupilumab 200 mg	0.52 (0.41-0.66)
Dupilumab 300 mg	0.54 (0.43-0.68)

AQLQ

Treatment	Difference (95% CI)
Omalizumab	0.26 (0.05-0.47)
Mepolizumab	0.35 (0.08-0.62)
Reslizumab	0.28 (0.17-0.39)
Benralizumab	0.23 (0.11-0.35)
Dupilumab 200 mg	0.29 (0.15-0.44)
Dupilumab 300 mg	0.26 (0.12-0.40)

FEV_1 (Pre-BD)

Treatment	Difference, L (95% CI)
Omalizumab	0.06 (0.02-0.10)
Mepolizumab	0.10 (0.01-0.18)
Reslizumab	0.12 (0.08-0.16)
Benralizumab	0.13 (0.08-0.19)
Dupilumab 200 mg	0.14 (0.08-0.19)
Dupilumab 300 mg	0.13 (0.08-0.18)

If we do not take a head-to-head approach, we will end up prescribing the treatment with the most effective marketing.

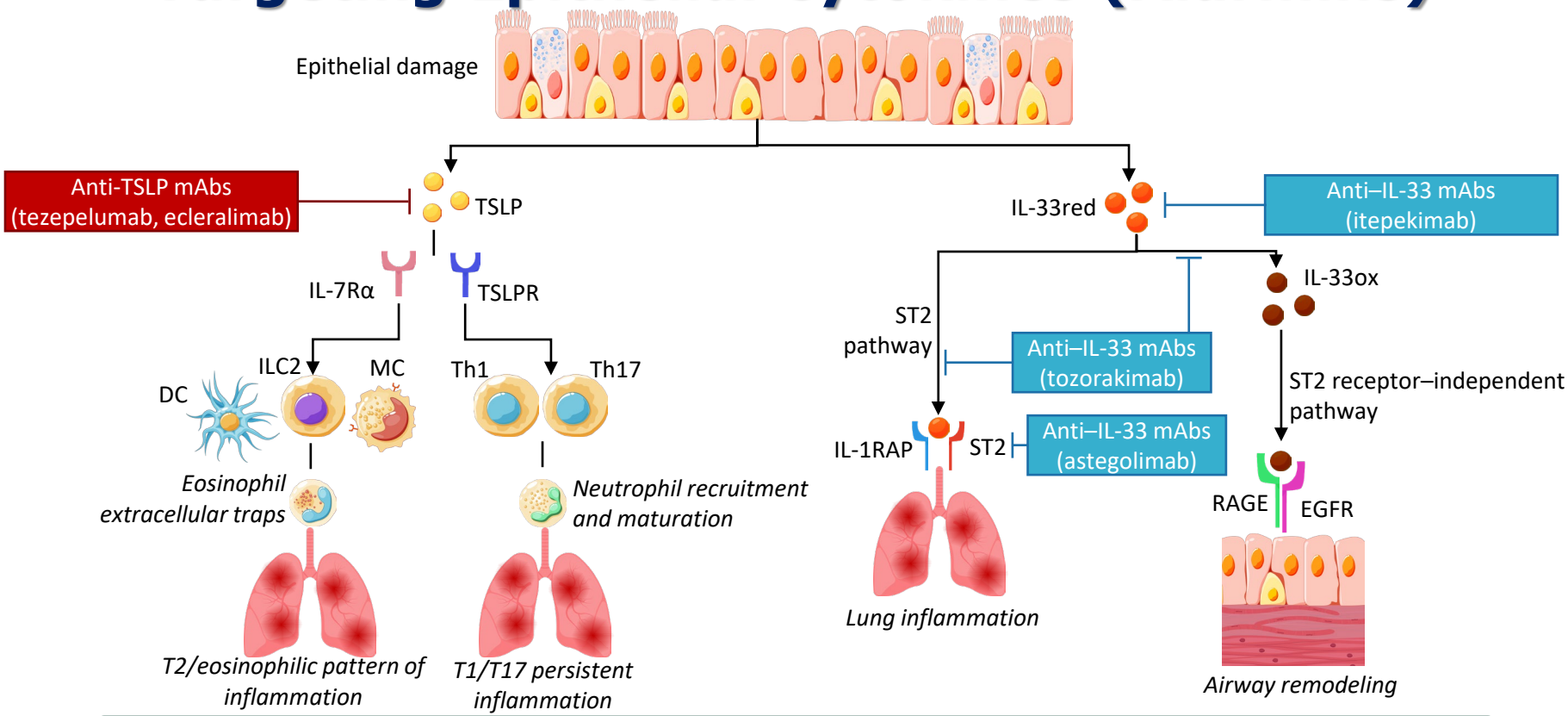
J. Drazen

ICER Report 2018 & Drazen N Engl J Med 2018

Biologics in COPD

- Why do we need them & What are they?
- TH2 cytokine targeting biologics
- Alarmins and non-TH2 targets
- Practical aspects of biologics use

Targeting Epithelial Cytokines (Alarmins)

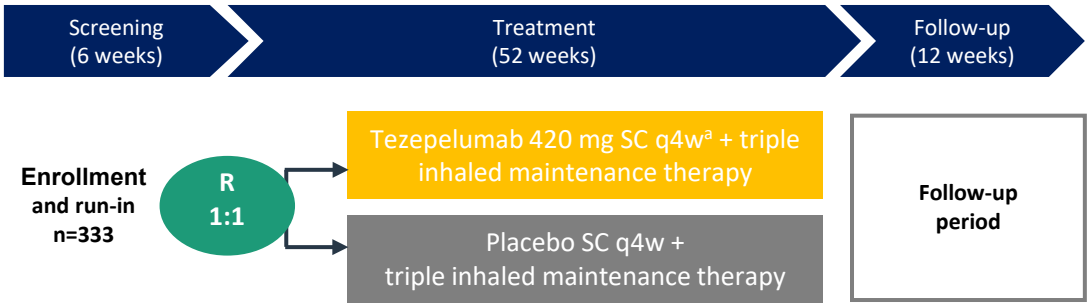


Upstream targeting of alarmins enables inhibition of *both* Type 1 and 2 responses.

DC, dendritic cell; EGFR, epidermal growth factor receptor; ILC, type 2 innate lymphoid cells; mAbs, monoclonal antibodies; MC, mast cell; Th, T helper; RAGE, receptor for advanced glycation end profuct; TSLP, thymic stromal lymphopoietin. Cazzola M, Hanania NA. *Int J COPD.* 2023;18:1333-1352.

Tezepelumab Phase 2a COURSE: Study Design

52-week, randomized, placebo-controlled, double-blind, multicenter study in adults with moderate-to-severe COPD



Primary end point

Annualized rate of moderate or severe COPD exacerbations for 52 weeks

- **Secondary end points:**
  - Annualized rate of severe COPD exacerbations for 52 weeks
  - Change from baseline to Week 52 in pre-BD FEV_1, SGRQ, and CAT total scores
  - Safety

Key eligibility criteria

- **Inclusion criteria:**
  - Aged 40–80 years
  - Moderate-to-severe COPD (CAT >15)
  - ≥2 Moderate or severe COPD exacerbation in the previous year despite receiving stable triple inhaled maintenance therapy (ICS+LABA+LAMA)
- No exclusions were based on BEC or chronic bronchitis
- Current asthma or a history of asthma or significant pulmonary diseases other than COPD was excluded

[a]Twice the approved dosing for tezepelumab.

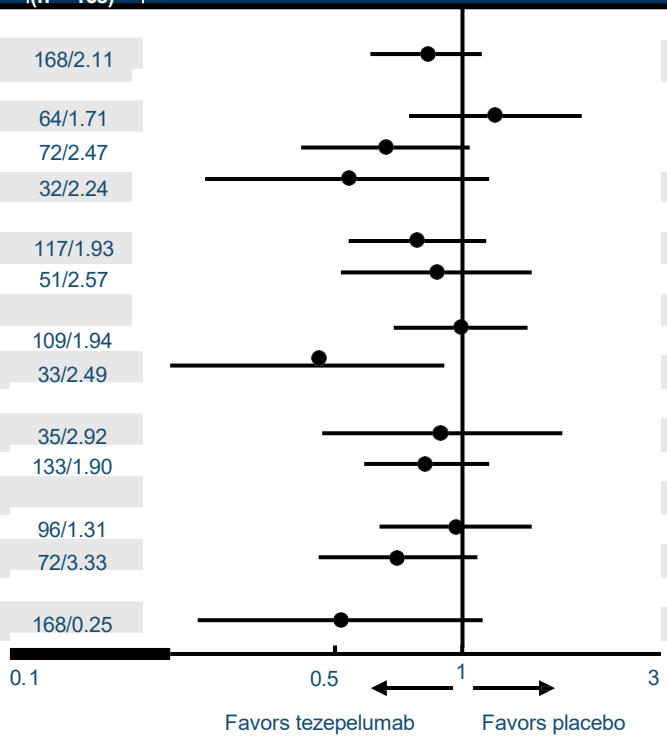
BD, bronchodilator; BEC, blood eosinophil count; CAT, COPD Assessment Test; FEV_1, forced expiratory volume in 1 second; ICS, inhaled corticosteroids; LABA, long-acting β_2 agonist; LAMA, long-acting muscarinic antagonist; q4w, every 4 weeks; R, randomization; SC, subcutaneous; SGRQ, St George's Respiratory Questionnaire.

Singh D, et al. *ATS* 2024. Poster 705.

Tezepelumab Reduces Annualized Rate of Moderate or Severe COPD Exacerbations: Phase 2a COURSE[1]

The annualized rate of moderate or severe COPD exacerbations over 52 weeks was 1.75 for tezepelumab versus 2.11 for placebo (rate ratio 0·83 [90% CI 0·64–1·06]; p=0·10)
****the primary endpoint was not met**

	Patient s/Rate		Rate Ratio (95% CI)
	Tezepelumab (n = 165)	Placebo (n = 168)	
Moderate or severe COPD exacerbations			
Overall	165/1.75	168/2.11	0.83 (0.61-1.11)
BEC, cells per mcL			
<150	73/2.04	64/1.71	1.19 (0.75-1.90)
150 to <300	68/1.64	72/2.47	0.66 (0.42-1.04)
≥300	24/1.20	32/2.24	0.54 (0.25-1.15)
Smoking status			
Former	110/1.51	117/1.93	0.78 (0.54-1.13)
Current	55/2.23	51/2.57	0.87 (0.52-1.45)
FeNO level, ppb			
<25	117/1.93	109/1.94	0.99 (0.69-1.43)
≥25	26/1.15	33/2.49	0.46 (0.22-0.98)
Previous severe exacerbation at randomization			
Yes	30/2.61	35/2.92	0.89 (0.47-1.71)
No	135/1.57	133/1.90	0.82 (0.59-1.15)
Number of previous exacerbations at randomization			
Two	96/1.26	96/1.31	0.96 (0.64-1.45)
At least three	69/2.33	72/3.33	0.70 (0.46-1.07)
Severe COPD exacerbations			
Overall	165/0.13	168/0.25	0.52 (0.24-1.11)

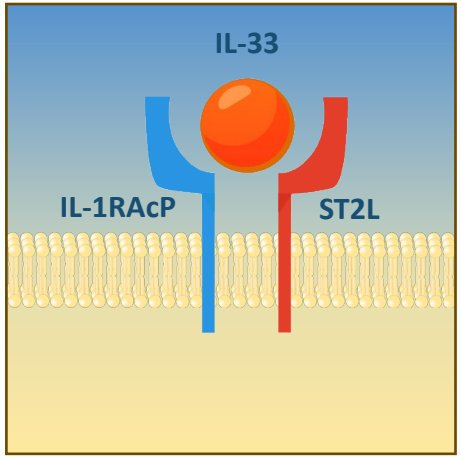


Phase 3 study (EMBARK/ JOURNEY) ongoing

1. Singh D et al. *Lancet Respir Med.* 2025;13:47-58.

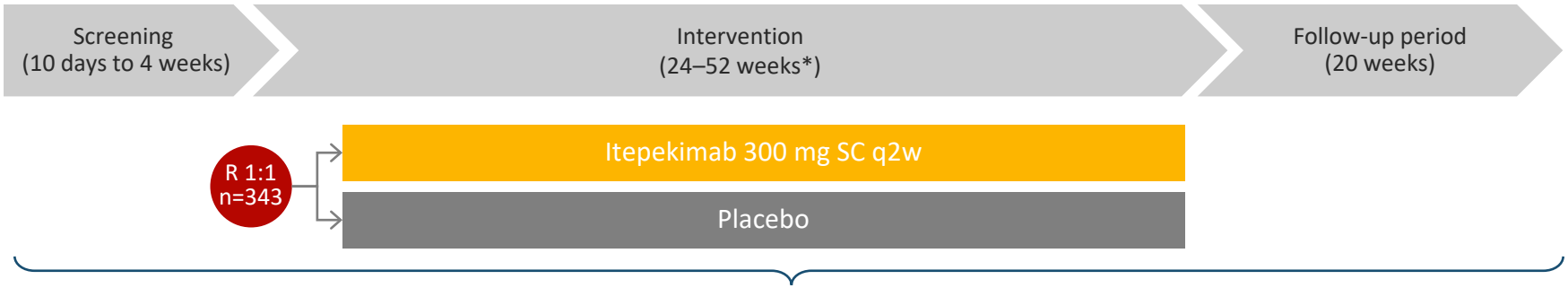
Anti-IL-33/ST2 Therapies Currently in Phase 3

Biologic	Therapeutic Target
Itepekimab	IL-33
Tozorakimab	IL-33
Astegolimab	ST2 (IL-33 receptor)



: Itepekimab (anti IL-33) Phase 2a POC [1,2]

Randomized, double-blind, multicenter, parallel-group, placebo-controlled, Phase 2a study (NCT03546907)



Background therapy + rescue medication (albuterol/salbutamol or levalbuterol/levosalbutamol) as necessary

All patients received standard-of-care background controller therapy for 3 months before randomization at a stable dose for ≥1 month prior to screening†

Study Population

- Moderate-to-severe COPD
- Current or non-current smokers with a smoking history of ≥10 packs/year
- Independent of blood eosinophils
- Age 40–75 years
- A history of ≥2 moderate exacerbations or ≥1 severe exacerbation in the last 12 months

Primary Endpoint

Annualized rate of moderate-to-severe AECOPD during the treatment period

The use of Itepekimab in COPD is currently under clinical investigation, and its safety and efficacy have not been fully regulated by any regulatory authority.

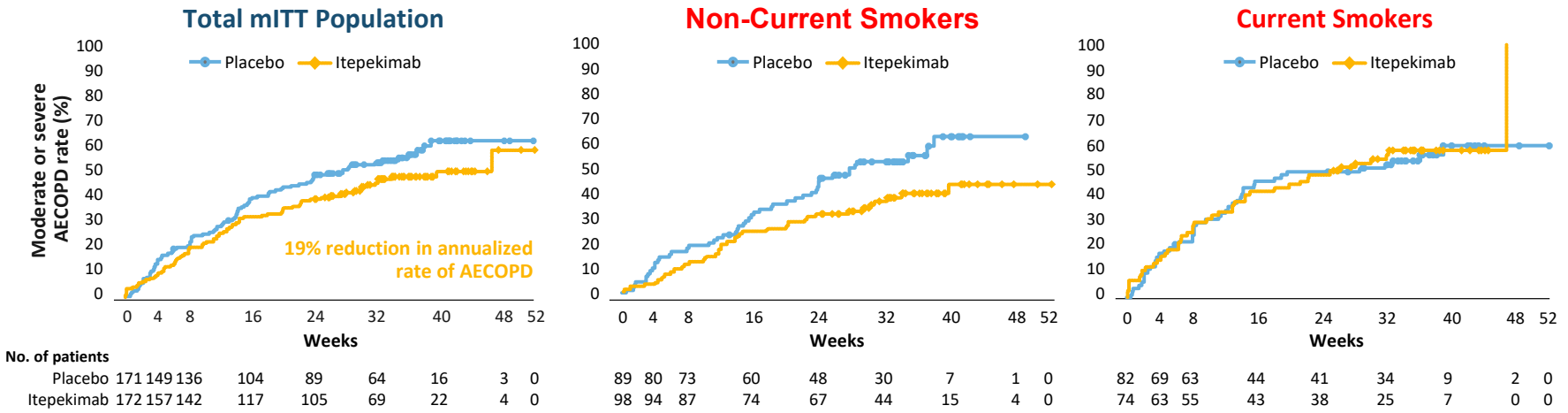
AECOPD, acute exacerbations of COPD; COPD, chronic obstructive pulmonary disease; ICS, inhaled corticosteroids; LABA, long-acting beta agonist; LAMA, long-acting muscarinic antagonist; q2w, every 2 weeks; R, randomization; SC, subcutaneous.

*Patients received treatment for up to a maximum of 52 weeks or until the last randomized patient received a minimum of 24 weeks of study drug. †Background maintenance therapy was defined as double therapy (LABA+LAMA, LABA+ICS, LAMA+ICS) or triple therapy (LAMA+LABA+ICS).

1. Rabe KF, et al. Lancet Respir Med. 2021;9:1288-1298. 2. ClinicalTrials.gov. NCT03546907. Accessed April 25, 2025. https://clinicaltrials.gov/ct2/show/NCT03546907.

Itepekimab Numerically Reduced the Annualized Rate of AECOPD

Time to First Moderate or Severe AECOPD



Moderate-to-Severe AECOPD Events			
RR vs placebo (95% CI)	0.81 (0.61–1.07)	0.58 (0.39–0.85)	1.09 (0.74–1.61)
P value vs placebo	*0.13*	*0.0061*	*0.65*

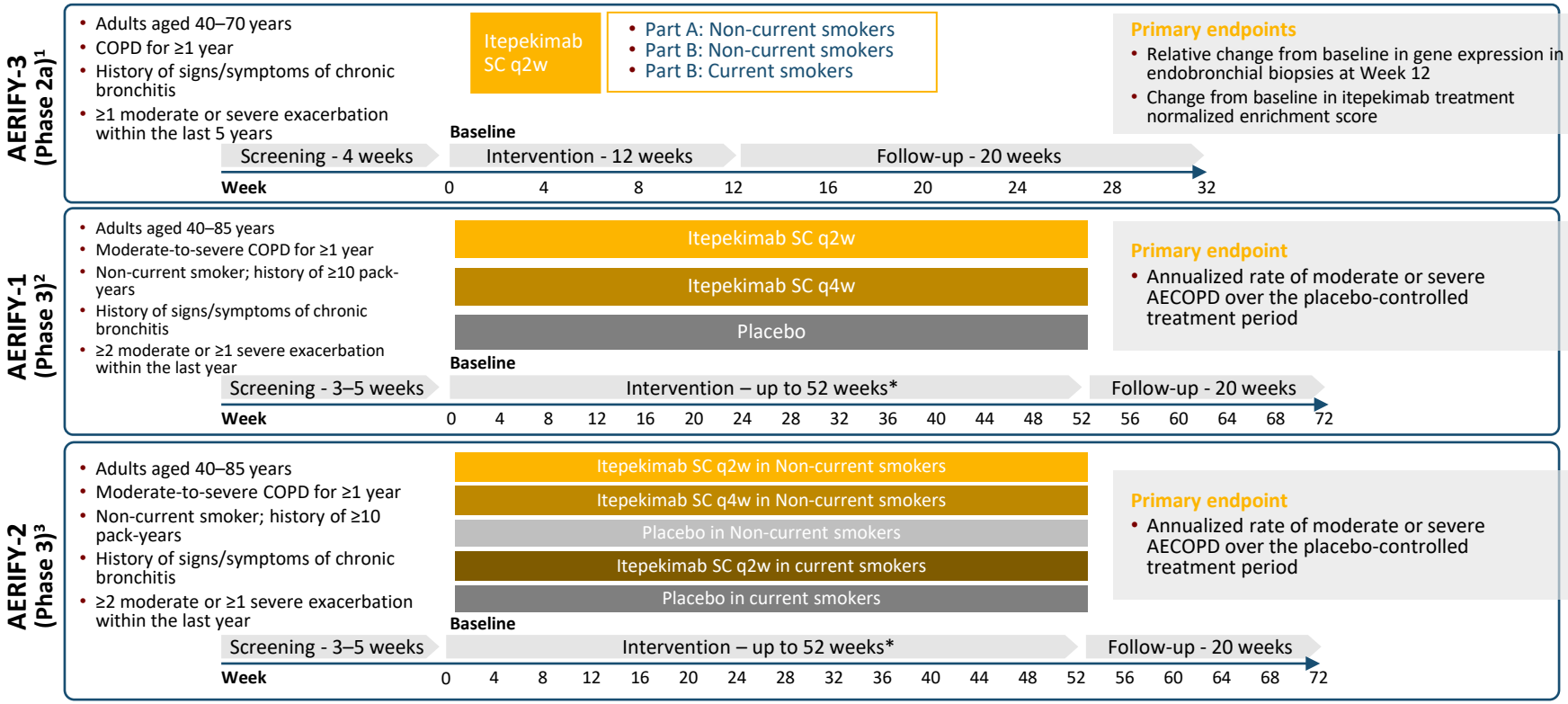
The Subgroup analysis revealed that itepekimab reduced exacerbation rates by 42% (*P=0.0061*) in non-current smokers with COPD

AECOPD, acute exacerbation of COPD; CI, confidence interval; COPD, chronic obstructive pulmonary disease; mITT, modified intent-to-treat; RR, relative risk.

P values are nominal (unadjusted for multiple comparisons) unless otherwise specified.

Rabe KF, et al. Lancet Respir Med. 2021;9:1288-1298.

Recently Completed Itepekimab Clinical Trials



AECOPD, acute exacerbation of COPD; COPD, chronic obstructive pulmonary disease; q2w, every 2 weeks; q4w, every 4 weeks; SC, subcutaneous.
*Patients received treatment for up to a maximum of 52 weeks or until the last randomized patient received a minimum of 24 weeks of study drug.
1. ClinicalTrials.gov. NCT05326412. Accessed April 25, 2025. https://clinicaltrials.gov/ct2/show/NCT05326412. 2. ClinicalTrials.gov. NCT04701983. Accessed April 25, 2025. https://clinicaltrials.gov/ct2/show/NCT04701983. 3. ClinicalTrials.gov. NCT04751487. Accessed April 25, 2025. https://clinicaltrials.gov/ct2/show/NCT04751487.

AERIFY-1 and AERIFY-2: Efficacy and Safety of Itepekimab for COPD

Press Release: Itepekimab met the primary endpoint in one of two COPD phase 3 studies

May 30,2025

Reduction of COPD Exacerbations

	AERIFY-1		AERIFY-2	
	24 weeks	52 weeks	24 weeks	52 weeks
Itepekimab Q2W	30%	27%*	18%	2%
Itepekimab Q4W	34%	21%*	21%	12%
Placebo	–	–	–	–

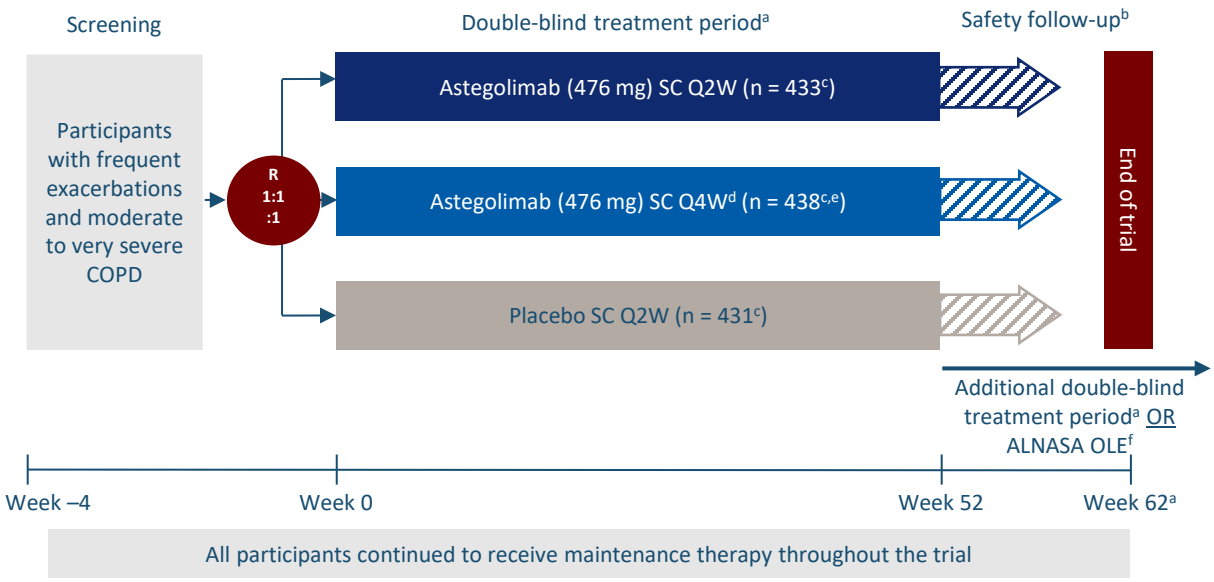
*Formal significance testing was only performed at 52 weeks in the Phase 3 trials, with significance achieved for both the every two-week arm and every four-week arm in AERIFY-1

Itepekimab every two weeks (AERIFY-1: n=375; AERIFY-2: n=326), every four weeks (AERIFY-1: n=377; AERIFY-2: n=303), or placebo (AERIFY-1: n=375; AERIFY-2: n=324),

www.sanofi.com/en/media-room/press-releases/2025/2025-05-30-05-00-00-3090818

Astegolimab (Anti-ST2): ALIENTO (phase 2B) and ARNASA (phase 3) RCT in Pts With COPD

A Phase IIb, randomised, double-blind, placebo-controlled trial (NCT05037929) conducted at 191 sites across 24 countries



Primary endpoint:

- Annualised rate of moderate or severe COPD exacerbations over 52 weeks

Key secondary endpoints[g]:

- Change in SGRQ-C total score
- Change in post-bronchodilator FEV_1
- Annualised rate of severe exacerbations (>24 h hospitalisation or death)
- Change in E-RS:COPD total score
- Proportion of participants with decrease from baseline of ≥4 points in SGRQ-C total score
- Safety, including adverse events

.

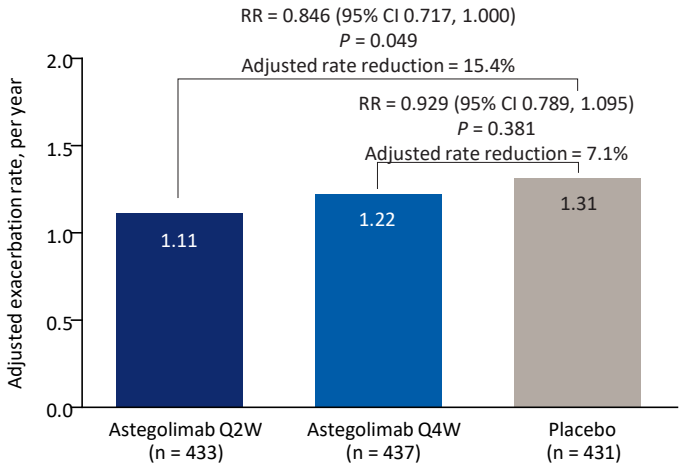
Clinicaltrials.gov. https://clinicaltrials.gov/study/NCT05037929. Accessed 8 September 2025.
Greening N et al, ERS 2025

Inclusion:

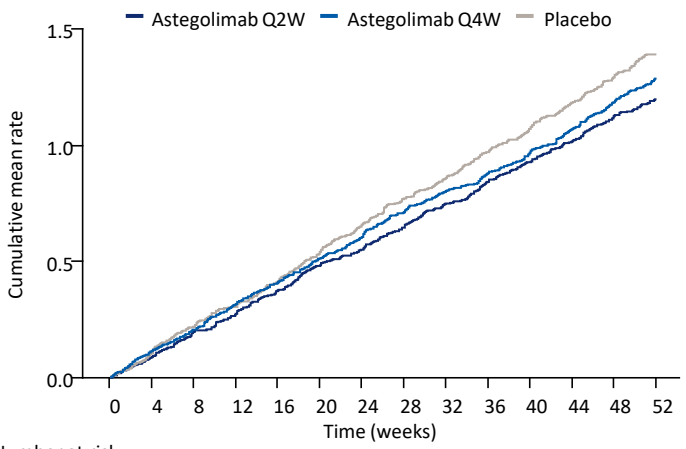
- Frequent exacerbator
- Chronic bronchitis
- Independent of Eos
- Independent of Smoking status

Efficacy: Primary Endpoint - Aliento (mITT population)

Annualised rate of moderate or severe COPD exacerbations over 52 weeks[a]



Cumulative mean rate of moderate or severe COPD exacerbations[a]



Number at risk

Placebo	431	430	421	416	407	404	396	390	387	383	378	372	368	329
Astegolimab Q4W	437	436	431	422	419	416	413	402	394	389	382	380	376	325
Astegolimab Q2W	433	431	424	419	413	410	403	396	392	388	384	380	374	333

Moderate exacerbation:
- New or increased COPD symptoms that led to treatment with systemic corticosteroids and/or antibiotics for ≥3 days

Severe exacerbation:
- New or increased COPD symptoms that led to hospitalisation for >24 hours or death

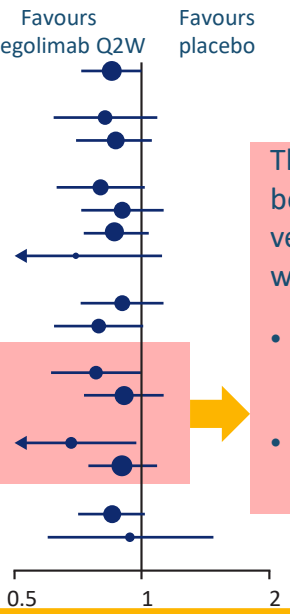
There was a statistically significant reduction of 15.4% in the annualised rate of moderate or severe exacerbations versus placebo in the astegolimab Q2W arm[b]

[a]Analyses are adjusted by stratification factors; [b]The difference in rates was not statistically significant for the Q4W arm versus placebo.
CI, confidence interval; COPD, chronic obstructive pulmonary disease; mITT, modified intent-to-treat; Q2W, every 2 weeks; Q4W, every 4 weeks; RR, rate ratio
Greening N et al. ERS 2025.

Efficacy: Primary Endpoint Subgroup Analysis (astegolimab Q2W vs placebo; mITT population)

Selected prespecified subgroup analyses of the primary endpoint, Q2W vs placebo[a]

Baseline characteristic	Placebo n	Astegolimab Q2W n	RR	95% CI	*P*-value
All participants	431	433	0.85	(0.72, 1.00)	0.049
Smoking status					
Current smoker	150	149	0.82	(0.62, 1.09)	0.169
Former smoker	281	284	0.87	(0.70, 1.06)	0.168
Baseline blood EOS					
<150 cells/µL	206	228	0.80	(0.63, 1.02)	0.068
≥150 cells/µL	225	205	0.90	(0.72, 1.13)	0.369
<300 cells/µL	386	371	0.87	(0.73, 1.04)	0.121
≥300 cells/µL	45	62	0.69	(0.43, 1.12)	0.137
Baseline chronic bronchitis					
Yes	230	232	0.90	(0.72, 1.13)	0.380
No	201	201	0.79	(0.62, 1.01)	0.061
Number of COPD exacerbations[b]					
>2	135	136	0.78	(0.61, 1.00)	0.049
2	296	296	0.91	(0.73, 1.13)	0.389
Prior hospitalisation for COPD[c]					
Yes	89	88	0.68	(0.48, 0.97)	0.034
No	342	345	0.90	(0.75, 1.09)	0.278
Baseline COPD triple therapy					
Yes	346	338	0.85	(0.71, 1.02)	0.075
No	84	94	0.94	(0.60, 1.48)	0.791



There was a greater treatment benefit with astegolimab Q2W versus placebo in participants with:

- More frequent exacerbations **(RR 0.78 [95% CI 0.61, 1.00])**
- Prior hospitalisation **(RR 0.68 [95% CI 0.48. 0.97])**

Pre-specified subgroup analyses showed a generally consistent treatment benefit in favour of astegolimab Q2W versus placebo

[a]Analyses are adjusted by stratification factors; [b]Number of exacerbations in a 12-month period in the 24 months prior to screening; [c]Hospitalisation for COPD within the 12 months prior to screening.
CI, confidence interval; COPD, chronic obstructive pulmonary disease; EOS, eosinophils; mITT, modified intent-to-treat; Q2W, every 2 weeks; RR, rate ratio.
Greening N et al. ERS 2025

ALIENTO and ARNASA[a]: Comparison of Topline Efficacy Results (mITT)

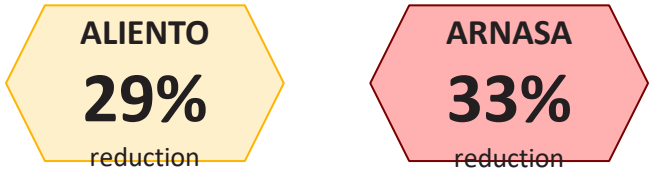
Adjusted rate reductions for astegolimab Q2W vs placebo[b]

Primary endpoint:

Annualised rate of moderate or severe COPD exacerbations

Key secondary endpoint:

Annualised rate of severe COPD exacerbations



OR for proportion of participants with a decrease of ≥4 points in SGRQ-C:
1.2 in ALIENTO and **1.5 in ARNASA**

The ALIENTO results are numerically consistent with results from ARNASA, despite ARNASA not meeting statistical significance for the primary endpoint

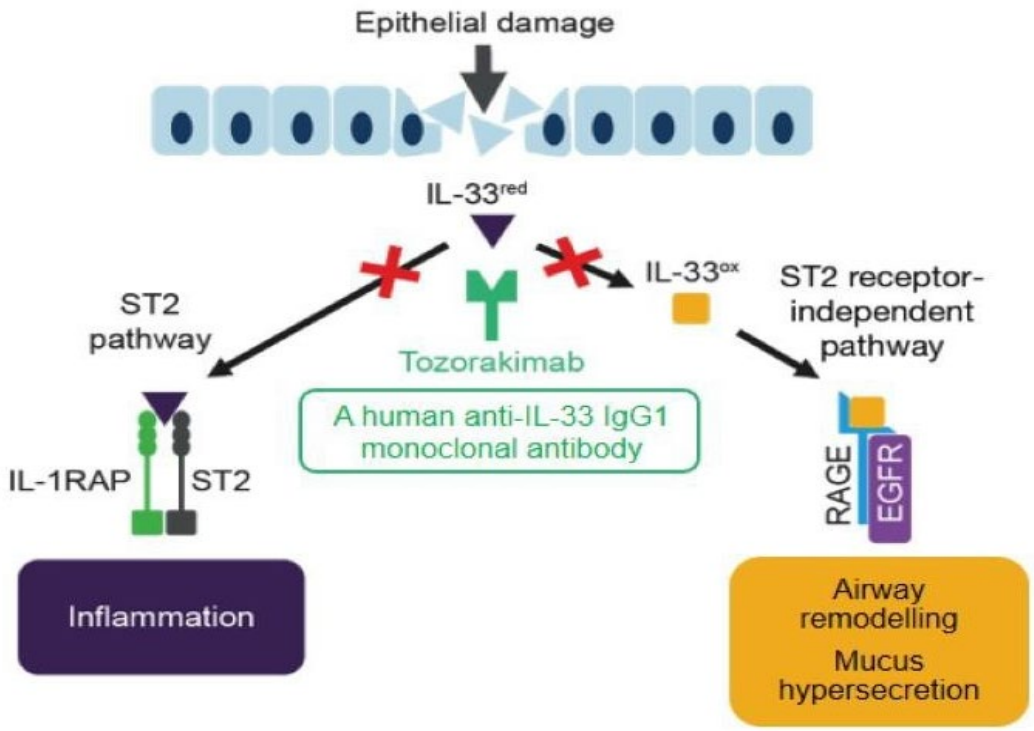
These findings were obtained in two broad populations of participants with COPD, regardless of their blood EOS level, current or former smoking status or chronic bronchitis status at baseline

The results, including a clinically meaningful reduction in severe exacerbations that lead to hospitalisation or death, may help address the unmet need in COPD

[a]ARNASA: primary population, N=1375; NCT05595642.

[b]Analyses are adjusted by stratification factors in both trials, with the number of moderate or severe COPD exacerbations within the 12 months prior to screening as an additional covariate in ARNASA.
COPD, chronic obstructive pulmonary disease; EOS, eosinophils; mITT, modified intent-to-treat; OR, odds ratio; Q2W, every 2 weeks; SGRQ-C, St George's Respiratory Questionnaire for COPD.
Greening N et al. ERS 2025

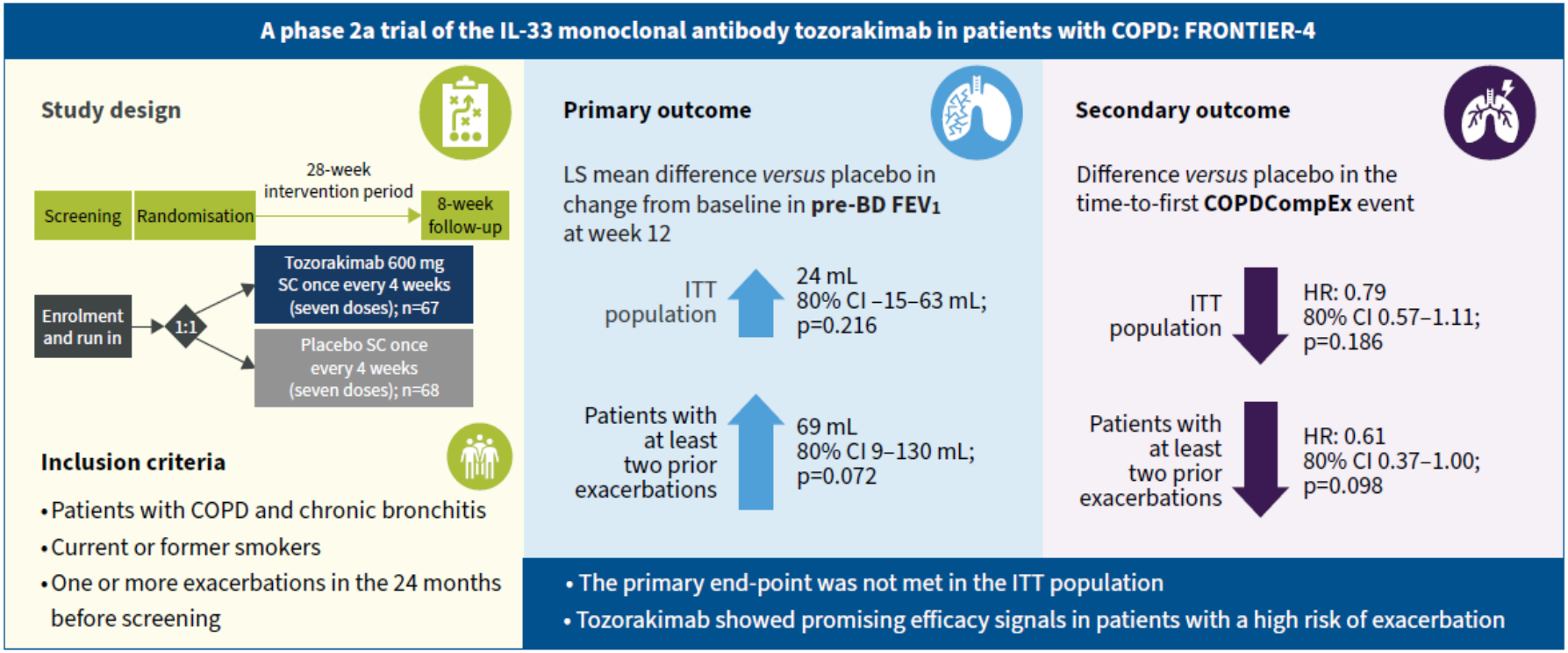
Tozorakimab (Anti- IL-33)



Singh D, et al. Presented at 2024 ERS Congress, Strickson S, et al. Eur Respir J. 2022;62:2202210..

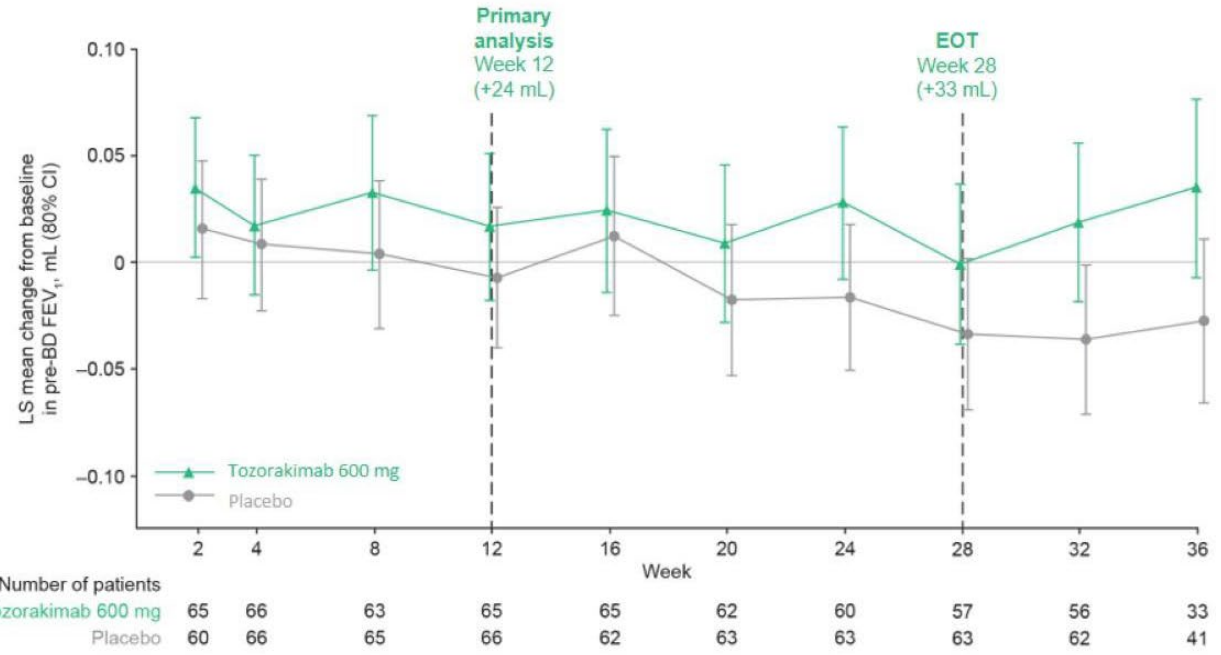
FRONTIER-4 (phase 2a): Effects of Tozorakimab Treatment on Lung Function in Patients With COPD

N=135



Singh D, et al. Eur Respir J 2025; 66: 2402231

FRONTIER-4: Effects of Tozorakimab Treatment on Lung Function in Patients With COPD



LS mean difference vs placebo in pre-BD FEV_1 at week 12, mL (80% CI):
24 (−15, 63); $p = 0.216$

BD, bronchodilator; CI, confidence interval; EOT, end of treatment; FEV_1, forced expiratory volume in 1 second; ITT, intention-to-treat; LS, least-squares

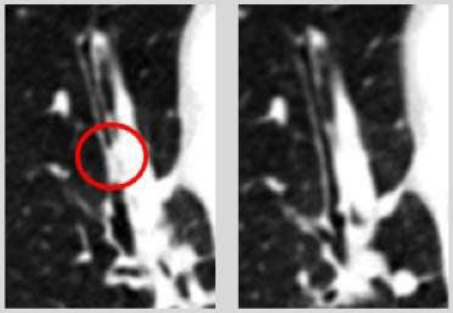
Singh D, et al. Presented at *2024 ERS Congress*.

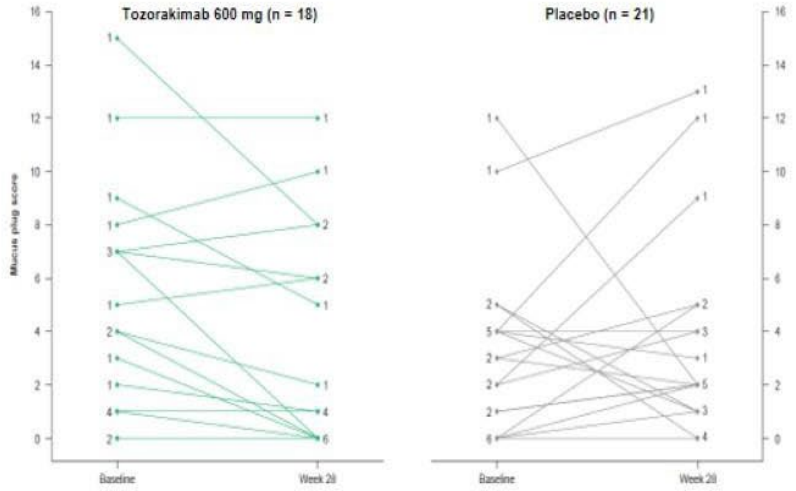
Effect of Tozorakimab on Mucus Plugging

- In the CT sub-study (n=39 had a CT scan performed at both baseline and week 28), mucus plugging was assessed in each of the 18 lung segments, resulting in a total mucus score of 0-18 per timepoint
- Mean baseline mucus scores were 4.4. and 3.1 for tozorakimab (n=18) and placebo (n=21), respectively

- Mucus plug score was reduced in patients receiving tozorakimab versus placebo (LS mean difference vs placebo in the change from baseline at week 28: −1.5; 80% CI: −3.0, 0.0; p=0.097)
- This result was further supported in a *post-hoc* non-parametric analysis stratified by baseline score category (p=0.0312)

Mucus plug in RB3 airway
Example CT images from FRONTIER-4





Each line may represent more than one patient. Annotated numbers indicate the number of patients at each data point
In a *post hoc* analysis, the change from baseline in mucus score was compared between treatment groups using a van Elteren test stratified for baseline mucus score subgroup (zero, low [1–3] and high [4–18]).
CT, computed tomography; RB3, right upper lobe anterior segment 3

Singh D, et al. Presented at *2024 ERS Congress*.

COPD Biologic and New Treatment Landscape

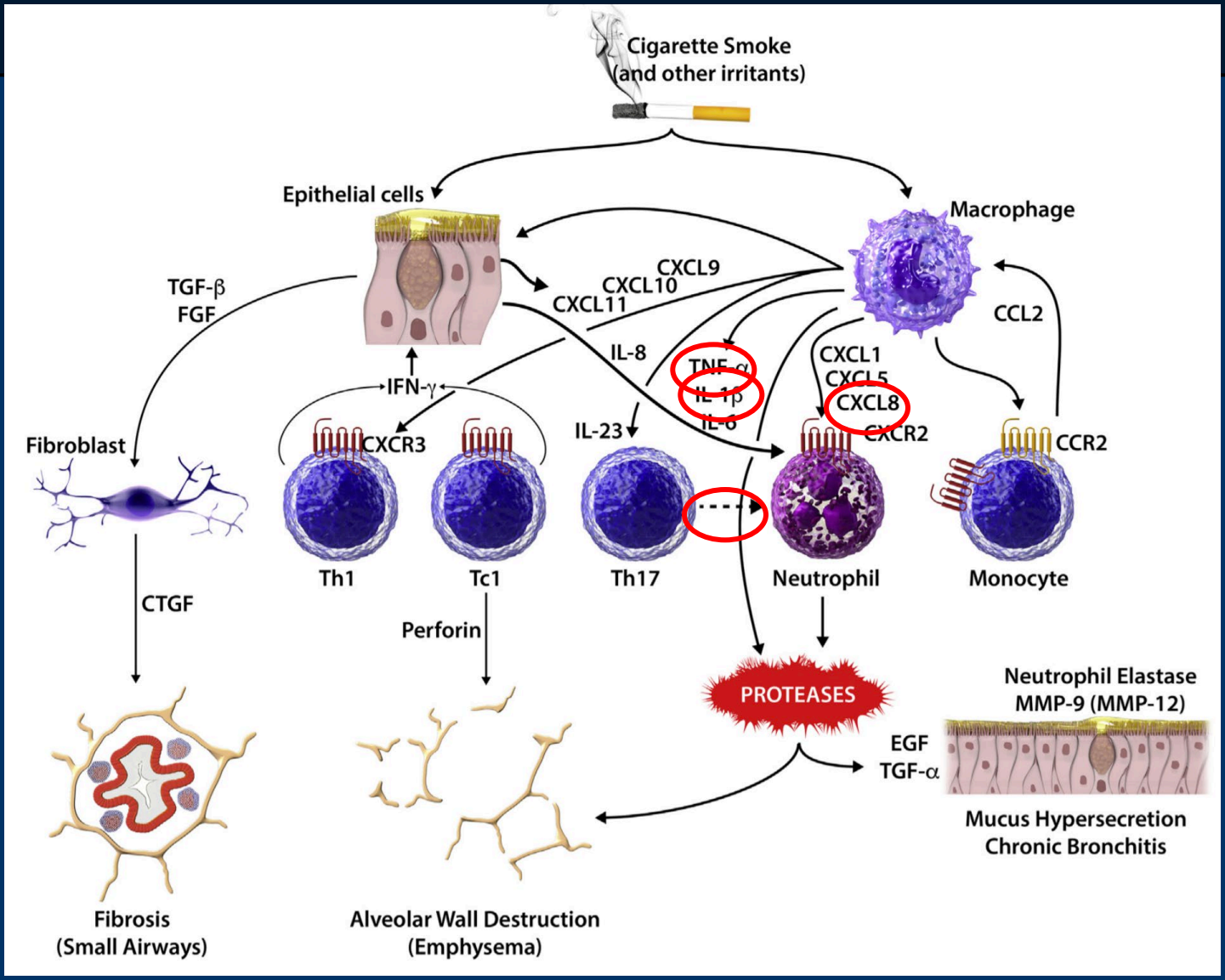
- IL, interleukin; PDE, phosphodiesterase; Ph, phase; POC, proof-of-concept; R, receptor; ST2, interleukin 1 receptor-like 1; TSLP, thymic stromal lymphopoietin.

Biologic Safety Considerations

Biologic	Adverse Effects/Warnings
Benralizumab	• Rare: Hypersensitivity reactions • Parasitic and helminthic infections
Dupilumab	• Rare: Hypersensitivity reactions; conjunctivitis and keratitis in patients with atopic dermatitis • Parasitic and helminthic infections, eosinophilic conditions
Omalizumab	• **Black box warning:** ~0.1 to 0.2% risk for anaphylaxis in clinical trials and postmarketing reports* • Parasitic and helminthic infections, Churg-Strauss syndrome and hypereosinophilic syndrome, serum sickness, cardiovascular and cerebrovascular disorders
Mepolizumab	• Rare: Hypersensitivity reactions and activation of herpes zoster • Parasitic and helminthic infections
Reslizumab	• **Black box warning:** ~0.3% risk for anaphylaxis in clinical trials† • Parasitic and helminthic infections
Tezepelumab	• Rare: Hypersensitivity reactions. • Parasitic and helminthic infection, infections, serious cardiac events

Genentech USA, Inc.; 2003; Mepolizumab [prescribing information]. Philadelphia, PA: GlaxoSmithKline, LLC; 2015; Reslizumab [prescribing information]. West Chester, PA: Teva Respiratory, LLC; 2016; Tezepelumab-ekko [prescribing information]. Thousand Oaks, CA: Amgen, Inc. and AstraZeneca; 2021.

Other pathways in COPD



Anti-IL-17α
Not Reported

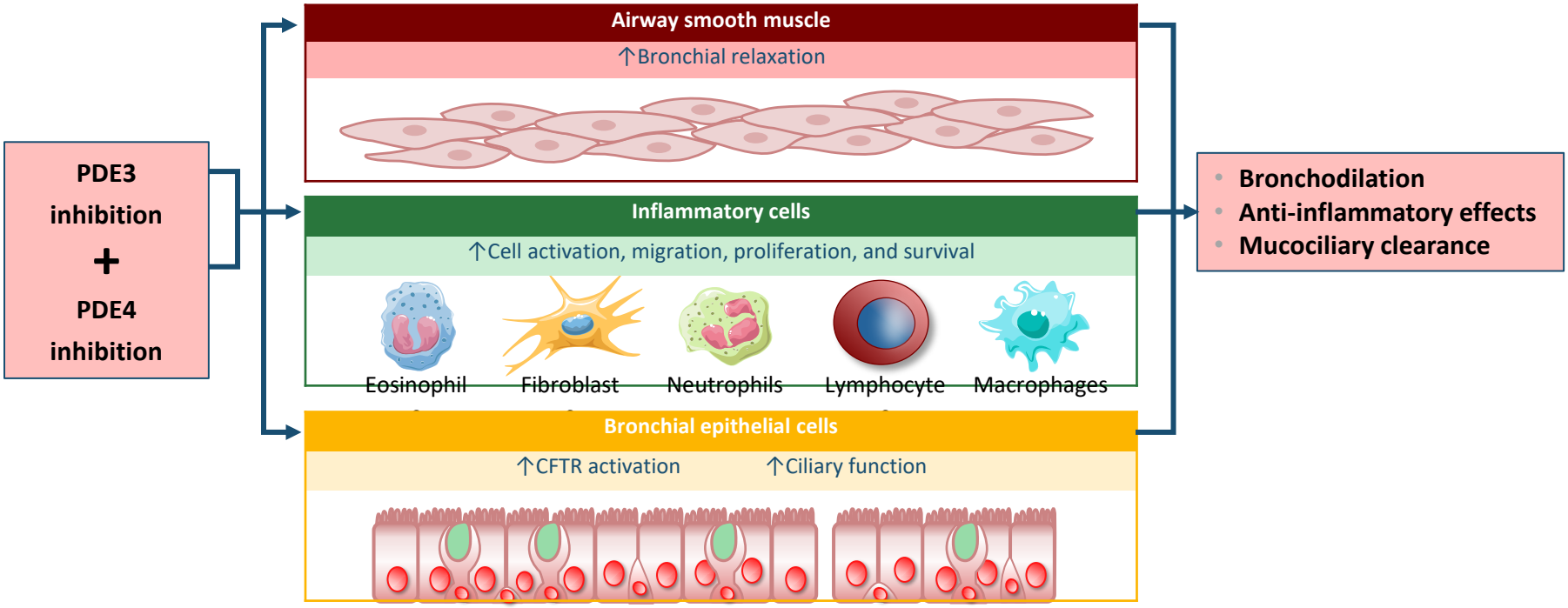
Anti-IL8
-Improved TDI (28% vs. 11%)
-negative FEV_1
-Exacerbation not evaluated

Infliximab & Etancercept TNFα
Negative CRQ, exacerbation prevention and treatment

Canakinamab IL-1β
Negative SGRQ, exacerbation prevention and FEV_1

Pavord. J Allergy Clin Immunol 2018

Targeting PDE3 and PDE4 in COPD



CFTR, cystic fibrosis transmembrane conductance regulator; PDE, phosphodiesterase enzymes.
Donohue JF, et al. *Int J Chron Obstruct Pulmon Dis.* 2023;18:1611-1622.

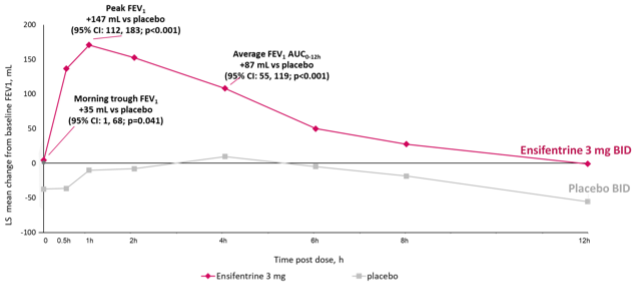
Ensifentrine, a Novel Phosphodiesterase 3 and 4 Inhibitor for the Treatment of Chronic Obstructive Pulmonary Disease

Randomized, Double-Blind, Placebo-controlled, Multicenter Phase III Trials (the ENHANCE Trials) #NOT_A_BIOLOGIC

Antonio Anzueto[1,2], Igor Z. Barjaktarevic[3], Thomas M. Siler[4], Tara Rheault[5], Thomas Bengtsson[6], Kathleen Rickard[5], and Frank Sciurba[7]; for the ENHANCE investigators

Figure 1. Week 12 FEV_1 Profiles

a) ENHANCE-1 (N=760)



b) ENHANCE-2 (N=789)

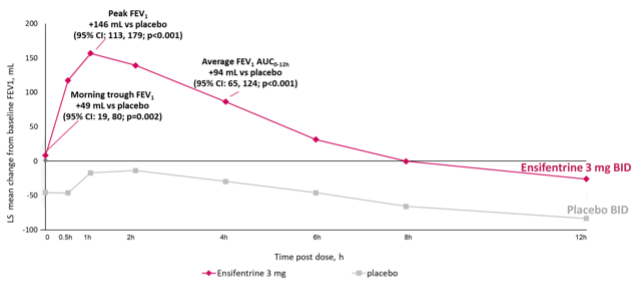
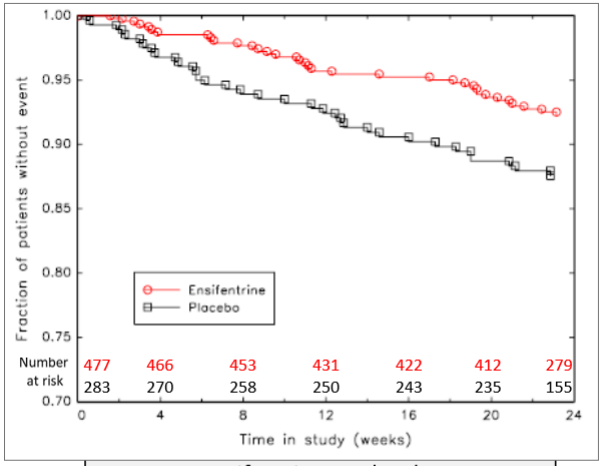


Figure 2. Time to First Moderate/Severe COPD Exacerbation

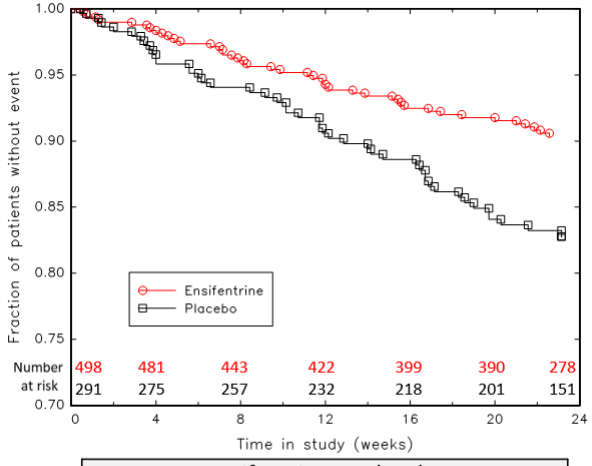
- Ensifentrine significantly delayed the time to first moderate/severe COPD exacerbation in both trials.

a) ENHANCE-1 (N=760)



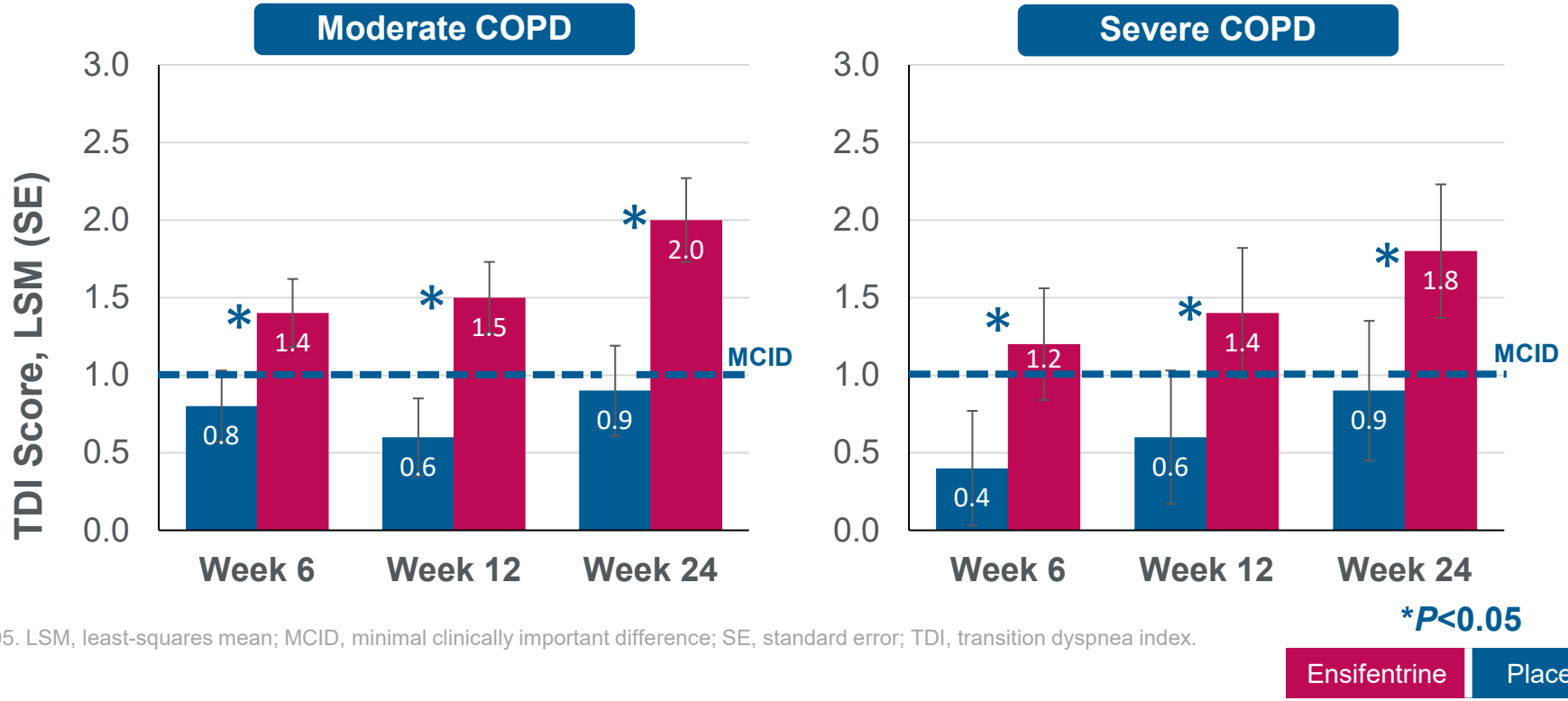
Ensifentrine vs Placebo	
Hazard ratio (95% CI)	0.62 (0.39, 0.97)
Risk Reduction	38%
p value	0.038

b) ENHANCE-2 (N=789)



Ensifentrine vs Placebo	
Hazard ratio (95% CI)	0.58 (0.38, 0.87)
Risk Reduction	42%
p value	0.009

Change in TDI scores vs placebo by GOLD Stage at All Time Points



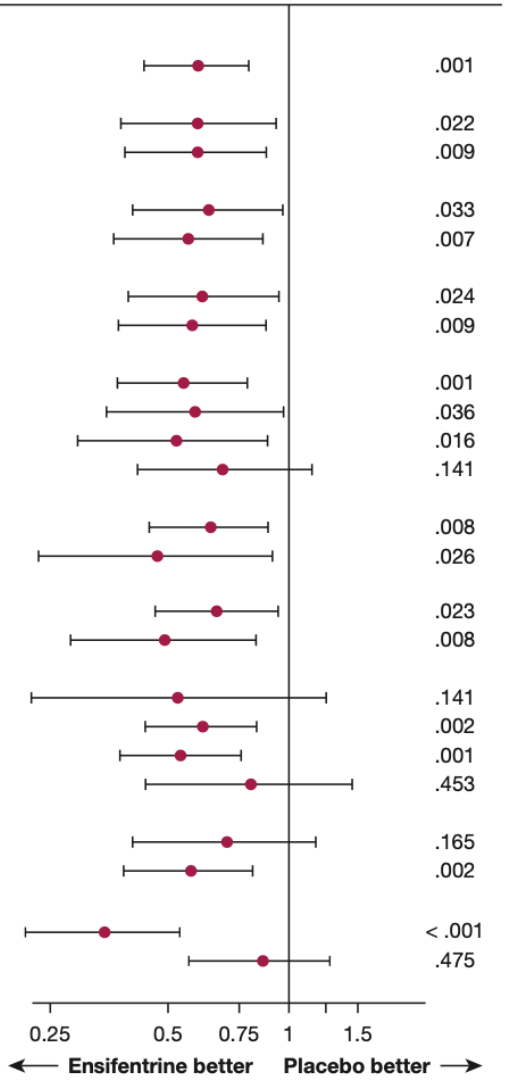
*p<0.05. LSM, least-squares mean; MCID, minimal clinically important difference; SE, standard error; TDI, transition dyspnea index.

Bon Chest 2024

Mahler. *Expert Rev Respir Med. 2024*

Ensifentrine Pooled Subgroup Analysis of Time to First Exacerbation

	Ensifentrine		Placebo			
	Events/No	(%)	Events/No	(%)	HR (95% CI)	*P* Value
Primary analysis						
mITT	84/975	(8.6)	81/574	(14.1)	0.59 (0.44-0.81)	.001
Age y						
≤ 64	38/443	(8.6)	35/257	(13.6)	0.58 (0.37-0.93)	.022
≥ 65	46/532	(8.6)	46/317	(14.5)	0.58 (0.38-0.87)	.009
Sex						
Male	43/518	(8.3)	39/305	(12.8)	0.62 (0.40-0.96)	.033
Female	41/457	(9.0)	42/269	(15.6)	0.55 (0.36-0.85)	.007
Smoking status						
Former	41/431	(9.5)	38/251	(15.1)	0.60 (0.39-0.94)	.024
Current	43/544	(7.9)	43/323	(13.3)	0.57 (0.37-0.87)	.009
Background medication						
On background	52/606	(8.6)	54/352	(15.3)	0.54 (0.37-0.78)	.001
LABA	27/282	(9.6)	29/181	(16.0)	0.57 (0.34-0.97)	.036
LAMA	25/324	(7.7)	25/171	(14.6)	0.51 (0.29-0.88)	.016
No background	32/369	(8.7)	27/222	(12.2)	0.68 (0.41-1.14)	.141
ICS use						
Nonuser	70/811	(8.6)	61/456	(13.4)	0.63 (0.44-0.88)	.008
User	14/164	(8.5)	20/118	(16.9)	0.46 (0.23-0.91)	.026
History of chronic bronchitis[a]						
With	60/707	(8.5)	51/405	(12.6)	0.65 (0.45-0.94)	.023
Without	24/268	(9.0)	30/169	(17.8)	0.48 (0.28-0.82)	.008
Baseline eosinophils						
< 100 cell/μL	10/182	(5.5)	11/107	(10.3)	0.52 (0.22-1.24)	.141
≥ 100 cells/μL	74/791	(9.4)	70/467	(15.0)	0.60 (0.43-0.83)	.002
< 300 cells/μL	60/745	(8.1)	62/434	(14.3)	0.53 (0.37-0.76)	.001
≥ 300 cells/μL	24/228	(10.5)	19/140	(13.6)	0.79 (0.43-1.45)	.453
Previous exacerbation (≤ 15 mo)						
Yes	29/220	(13.2)	26/136	(19.1)	0.69 (0.40-1.17)	.165
No	55/755	(7.3)	55/438	(12.6)	0.56 (0.38-0.81)	.002
COPD severity						
Moderate	26/559	(4.7)	40/307	(13.0)	0.34 (0.21-0.56)	< .001
Severe	56/410	(13.7)	41/267	(15.4)	0.86 (0.58-1.29)	.475

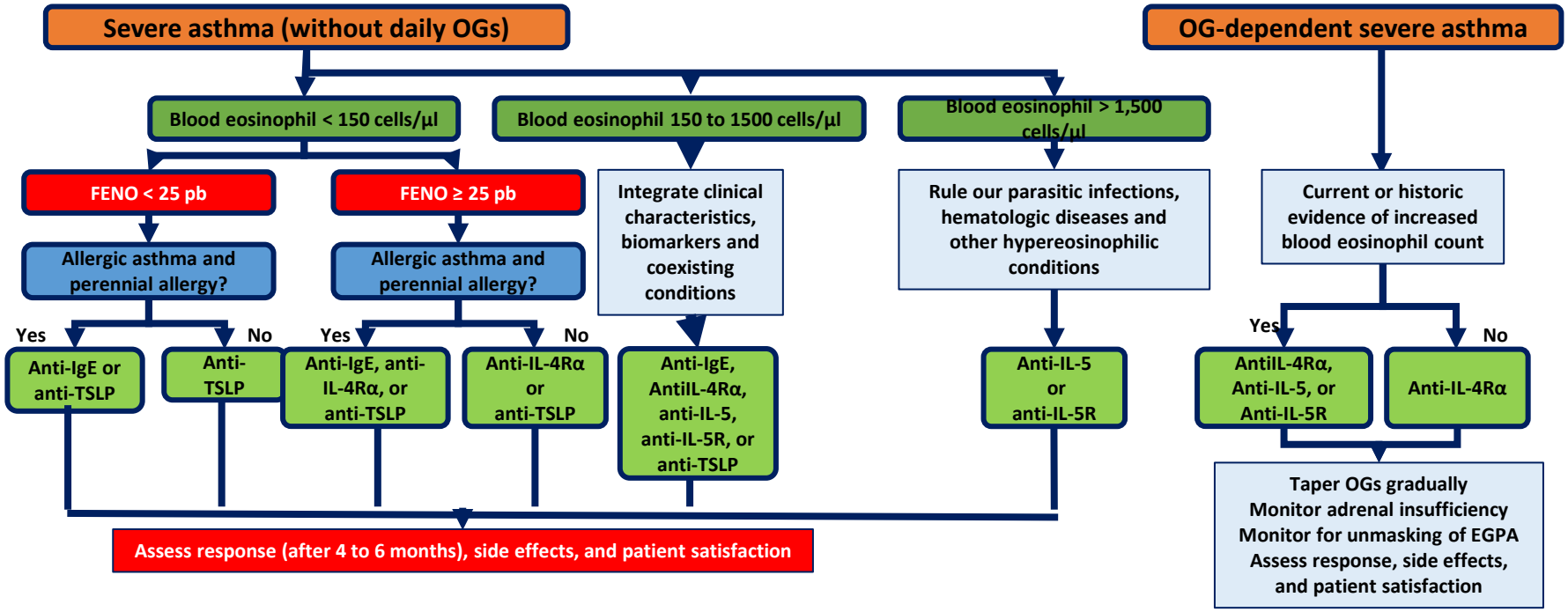


Sciurba Chest 2025

Biologics in COPD

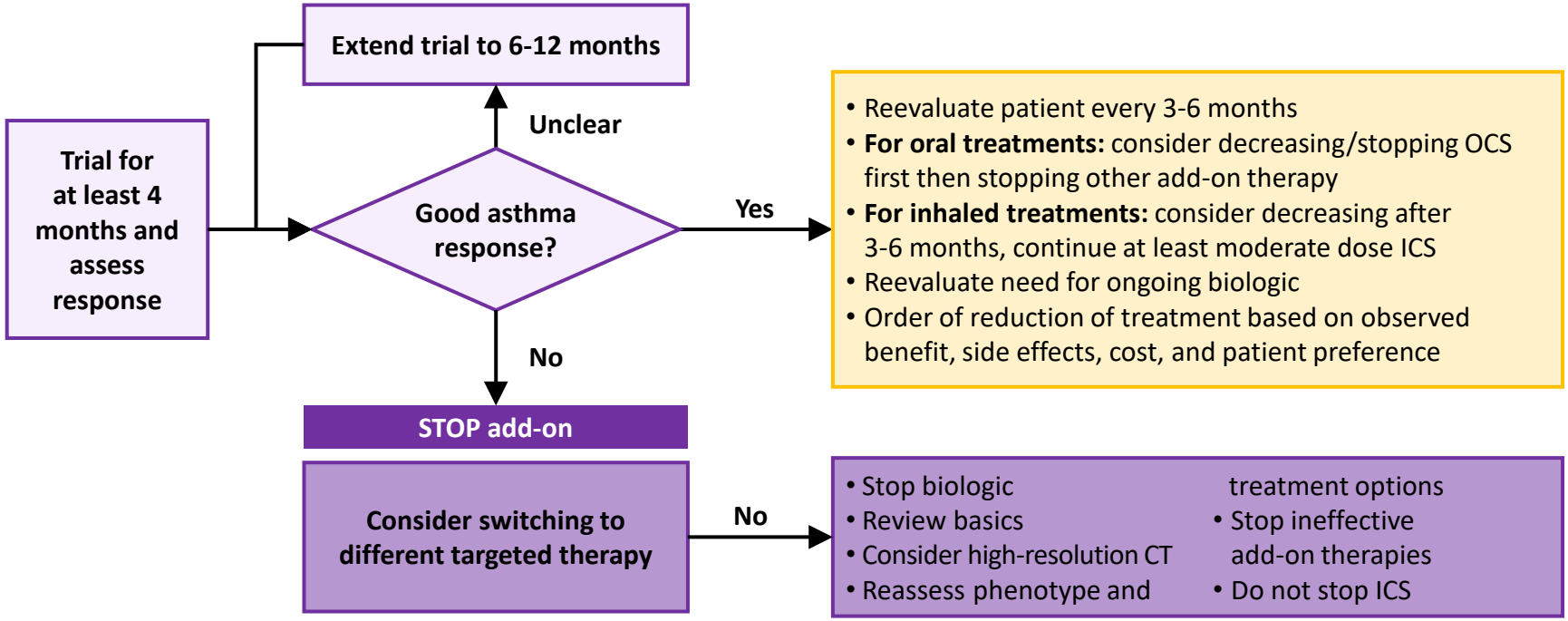
- Why do we need them & What are they?
- TH2 cytokine targeting biologics
- Alarmins and non-TH2 targets
- Practical aspects of biologics use

Lessons from Asthma: Phenotypic and Biomarker Approach for the Choice of Biologics



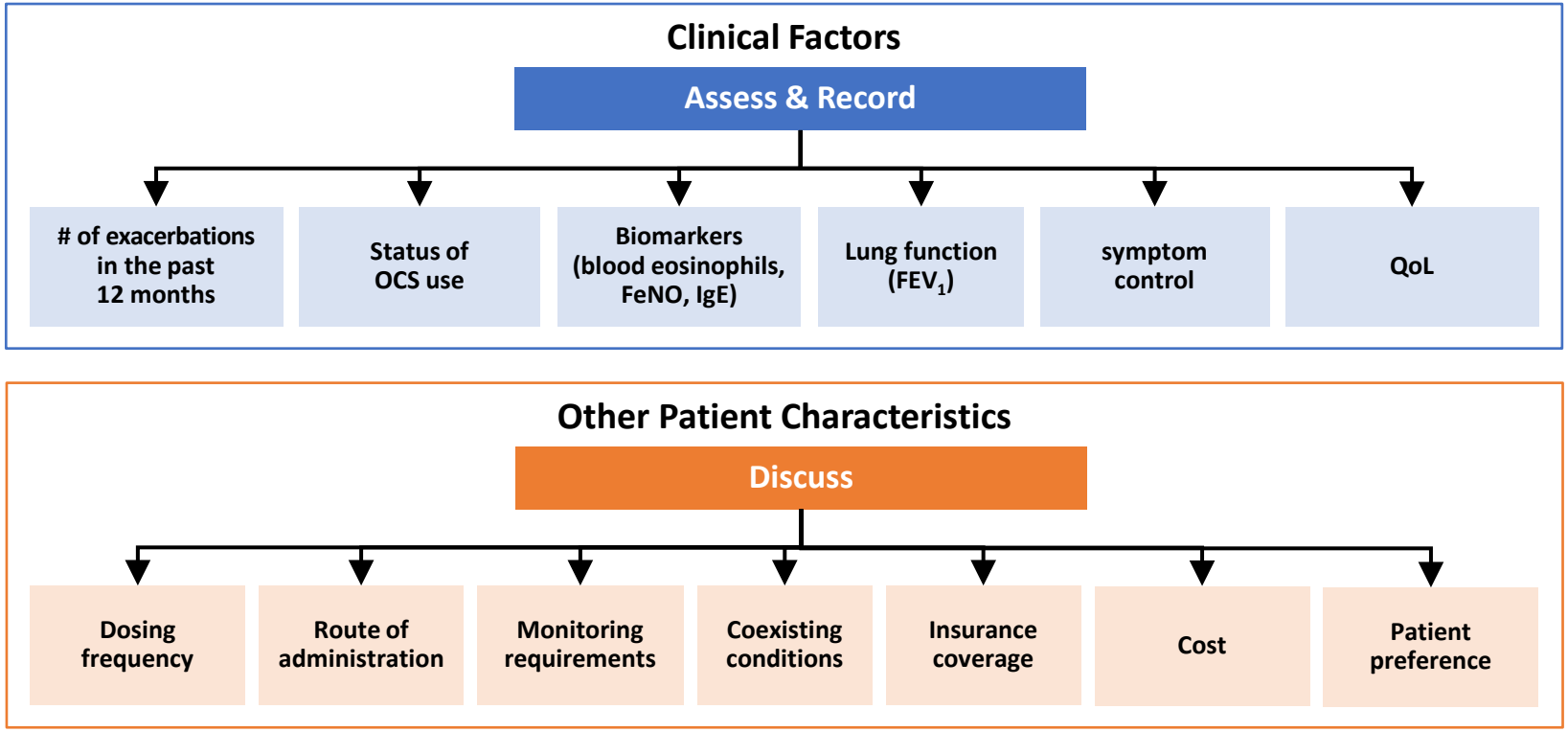
Brusselle G, et al. *N Eng J Med*. 2022;386:157-171.

Lessons from Asthma: GINA Recommendations for Implementing a Trial of Biologic Therapy



Global Initiative for Asthma. *Global Strategy for Asthma Management and Prevention (2024 update).* https://ginasthma.org/2024-report. Accessed March 21, 2025.

Factors Determining Biologic Selection



Key Challenges and Future Opportunities

- **Patient selection**: Ongoing research aims to refine biomarkers and identify clinical traits that predict biologic responders
- **Addressing different disease types:** Effectiveness may vary by smoking status and inflammatory phenotype, highlighting the need for a personalized approach
- **Earlier intervention/ Impact on disease progression :** Biologics could be introduced earlier to slow lung function decline or limit airway remodeling, not just manage late-stage symptoms. Cost and NNT considerations.
- **Rescue therapy:** Investigating biologic use during exacerbations for targeted, acute-phase treatment

Key Takeaways- Biologics in COPD

- A precision approach is required, taking individual variability into account, including the emerging phenotypes and endotypes
- Chronic inflammation in asthma and COPD can include both type 1/type 3-Th17 inflammation and type 2 inflammation
- Potential pathways in type 2 inflammation for therapeutic intervention are Available and in development for COPD
- Clinical Trials in non-TH2 pathways continue
- Experience with asthma has revealed barriers specific to biologics
- Treatable traits and shared decision making are important in tailoring each treatment regimen

Dr. Stephanie Christenson is an Associate Professor at the University of California, San Francisco in the Division of Pulmonary, Critical Care, Allergy, and Sleep Medicine. She serves as an attending physician on the Pulmonary Consult Service and in the Pulmonary Clinic. Dr. Christenson obtained her undergraduate degree at University of Wisconsin, Madison and her medical degree at the Medical College of Wisconsin. She completed her residency training as well as a year of research training in computational biology at Boston Medical Center. She then came to UCSF for fellowship in Pulmonary and Critical Care Medicine where she also obtained a Master's in Clinical Research, after which she joined faculty.

Dr. Christenson's research program integrates her expertise in genomics/bioinformatics and clinical research to study chronic airway disease and the associated risk factors. Her research emphasizes innovative computational tools, systems biology approaches, and 'omics biomarkers to better inform our understanding of the biology underlying clinical traits and outcomes in asthma, smoking, and COPD. Dr. Christenson also serves in multiple leadership roles for multi-center studies and advises industry on trials of biologic and inhaled therapies for COPD. Leadership roles include co-director of the Genetics and Genomics Subcommittee for the multi-center SPIROMICS and SOURCE studies, the UCSF site PI for the American Lung Association (ALA) Airway Clinical Research Consortium, and Disease Study Site PI for the NHGRI-funded Multi-Omics in Health and Disease (MOHD) Consortium.

Diagnosis and Case Finding in COPD

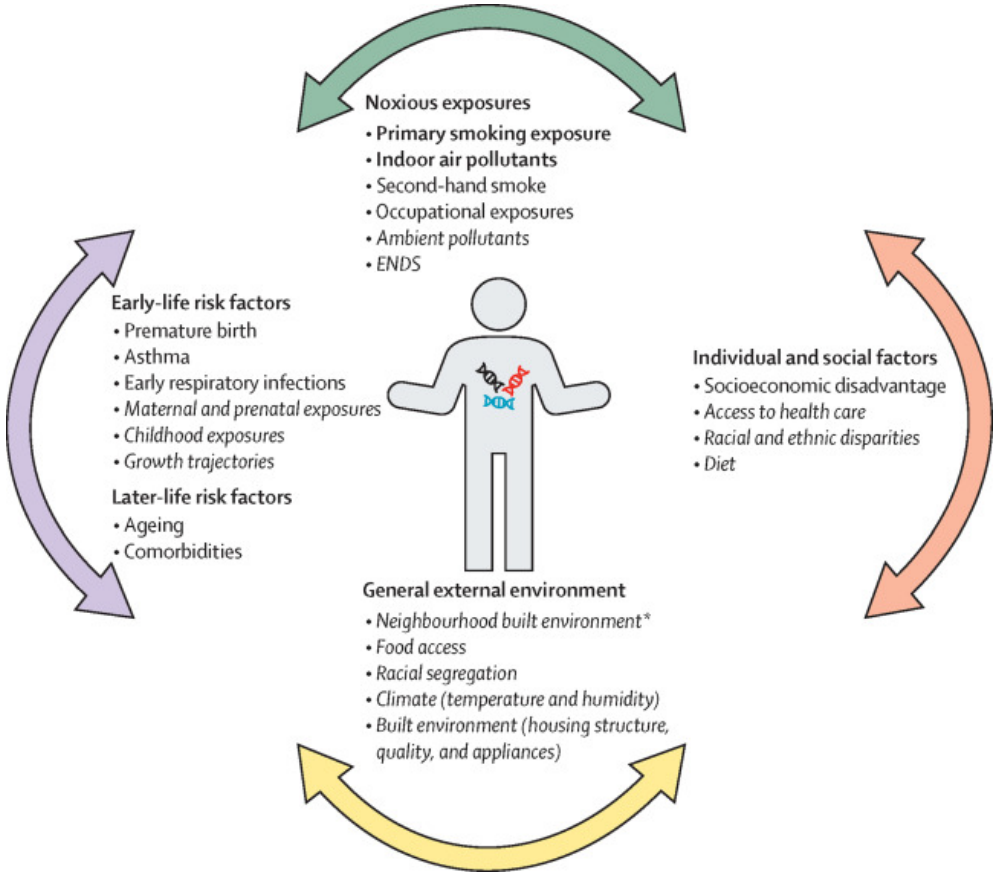
Stephanie Christenson, MD MAS

University of California, San Francisco

Disclosures

- I have the following relationships with ACCME defined ineligible companies:
  - AstraZeneca: Consulting/Advisory Board, Speaker (non-branded)
  - GSK: Consulting/Advisory Board, Speaker (non-branded)
  - Sanofi: Consulting/Advisory Board, Speaker (non-branded)
  - Regeneron: Consulting/Advisory Board, Speaker (non-branded)
  - Verona: Consulting /Advisory Board
  - Apogee Therapeutics: Consulting/Advisory Board
  - Devpro Pharma: Advisory Board
  - Uniquity Bio: Consulting/Advisory Board and Research Funding (contract)
  - Amgen: Advisory Board
  - Kymera Therapeutics: Advisory Board
  - Genentech: Consulting/Advisory Board
  - Gilead: Advisory Board
  - Abbvie: Consulting
- I **WILL NOT** discuss off-label use and/or investigational use of any drugs or devices.

The COPD Exposome

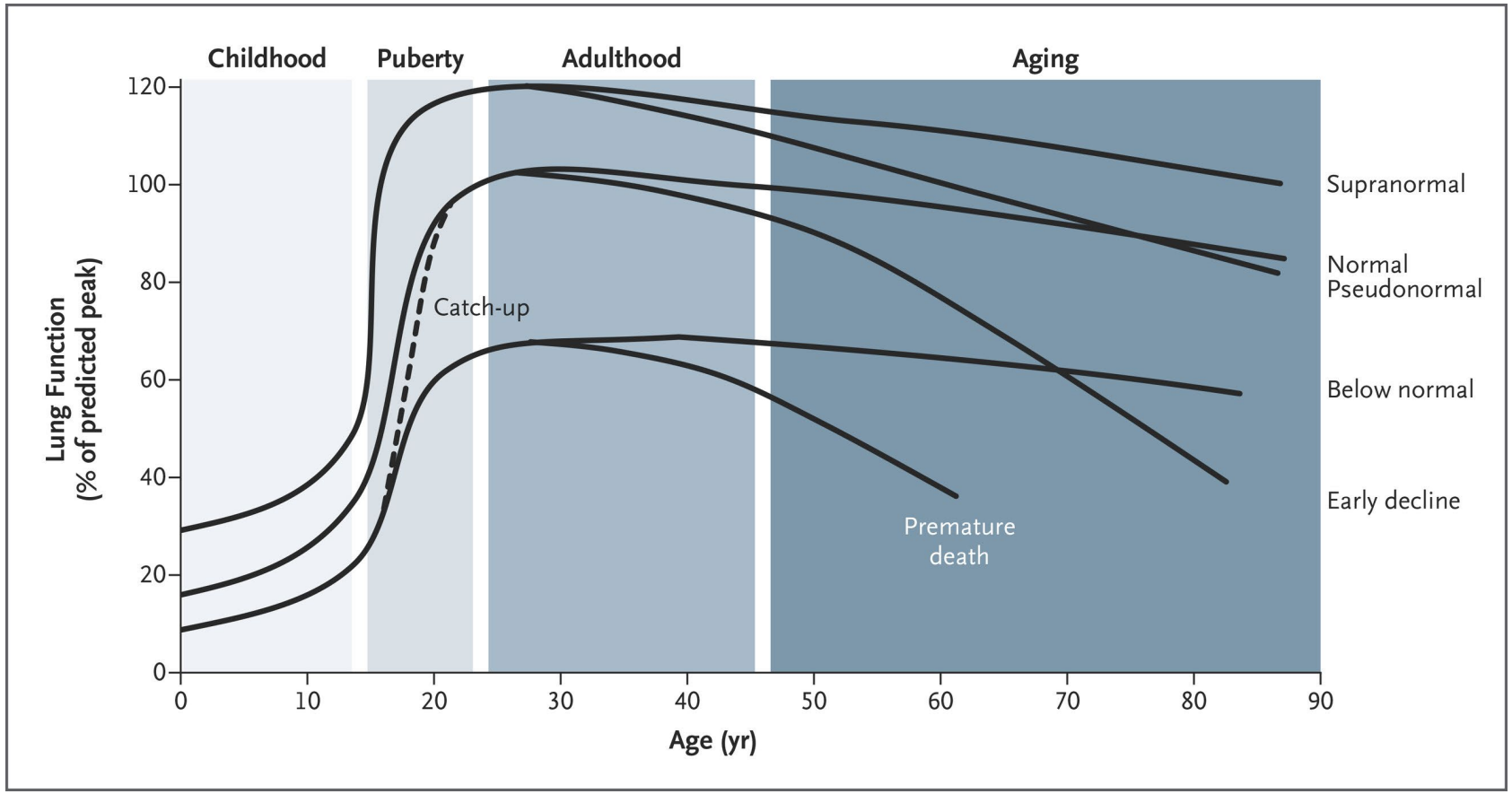


2023 GOLD Report COPD Definition:

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

Christenson et al, Lancet. 2022
GOLD 2026

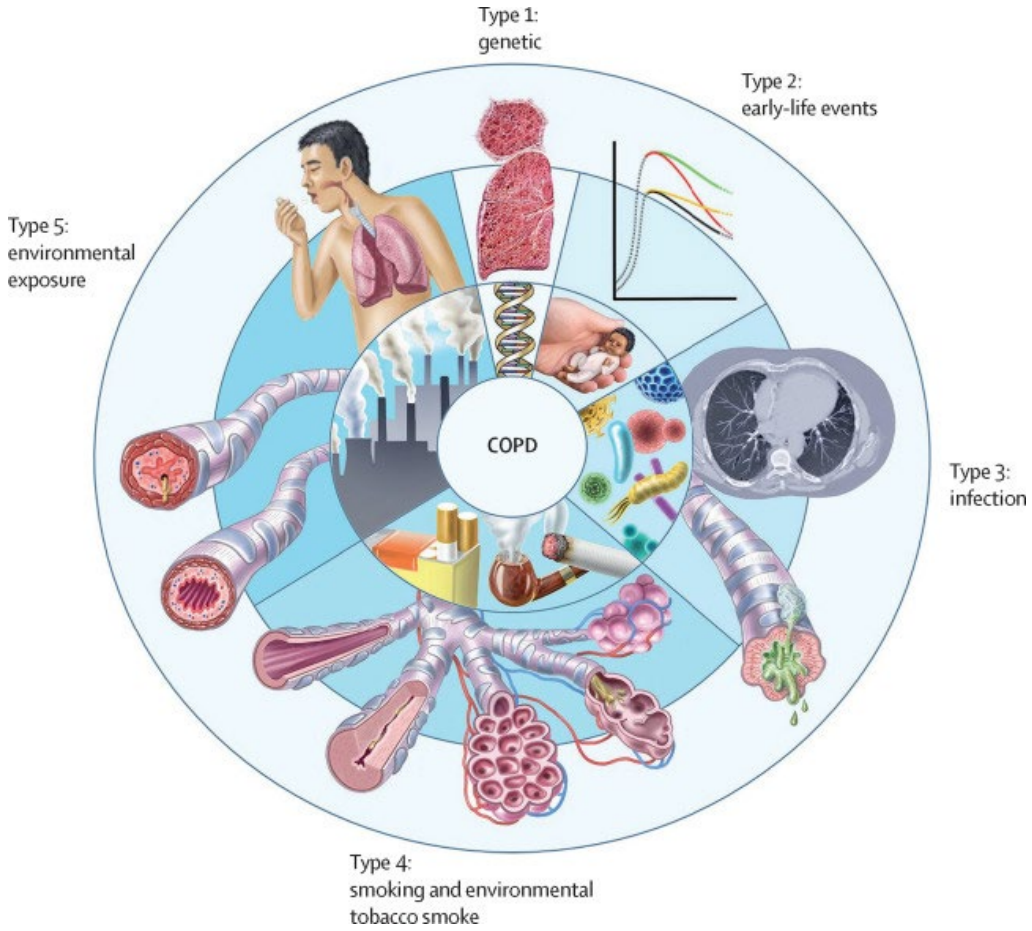
Lung Function Trajectories



Agusti et al, NEJM. 2019

COPD Etiotypes

Lancet Commission

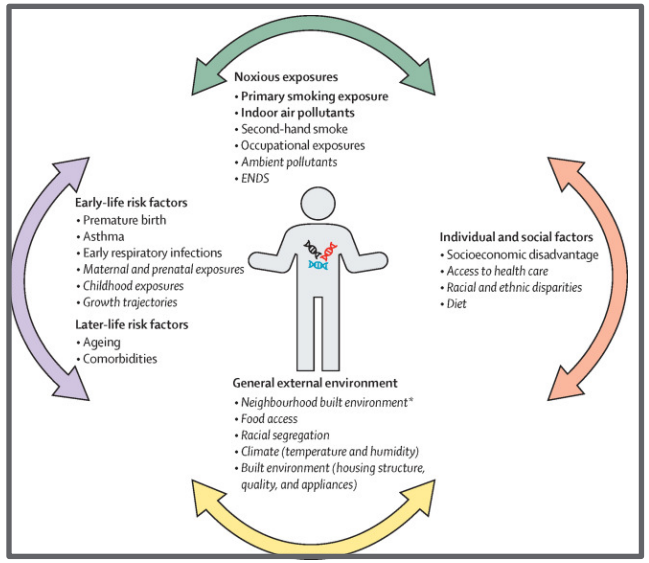


GOLD Report

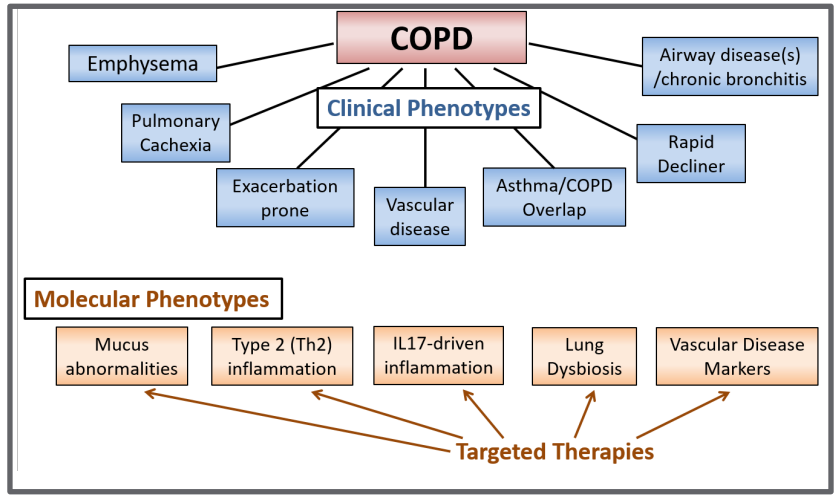
Classification	Description
Genetically determined COPD (COPD-G)	Alpha-1 antitrypsin deficiency (AATD) Other genetic variants with smaller effects acting in combination
COPD due to abnormal lung development (COPD-D)	Early life events, including premature birth and low birthweight, among others
Environmental COPD	
Cigarette smoking COPD (COPD-C)	• Exposure to tobacco smoke, including *in utero* or via passive smoking • Vaping or e-cigarette use • Cannabis
Biomass and pollution exposure COPD (COPD-P)	Exposure to household pollution, ambient air pollution, wildfire smoke, occupational hazards
COPD due to infections (COPD-I)	Childhood infections, tuberculosis-associated COPD, HIV-associated COPD
COPD & asthma (COPD-A)	Particularly childhood asthma
COPD of unknown cause (COPD-U)	

Stolz, et al. Lancet Commission 2022
GOLD Report 2026

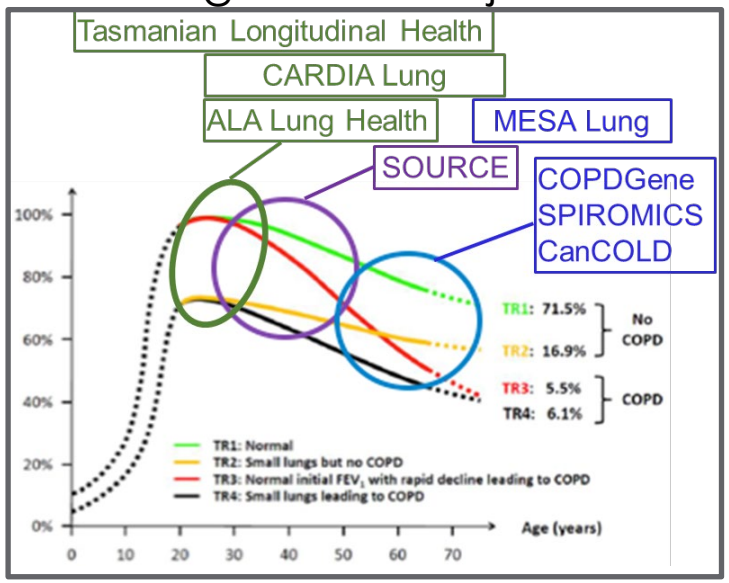
Heterogeneous Risk Factors



Heterogeneous Disease Manifestations



Heterogeneous Trajectories



Christenson et al, Lancet. 2022
Lange et al, NEJM. 2016

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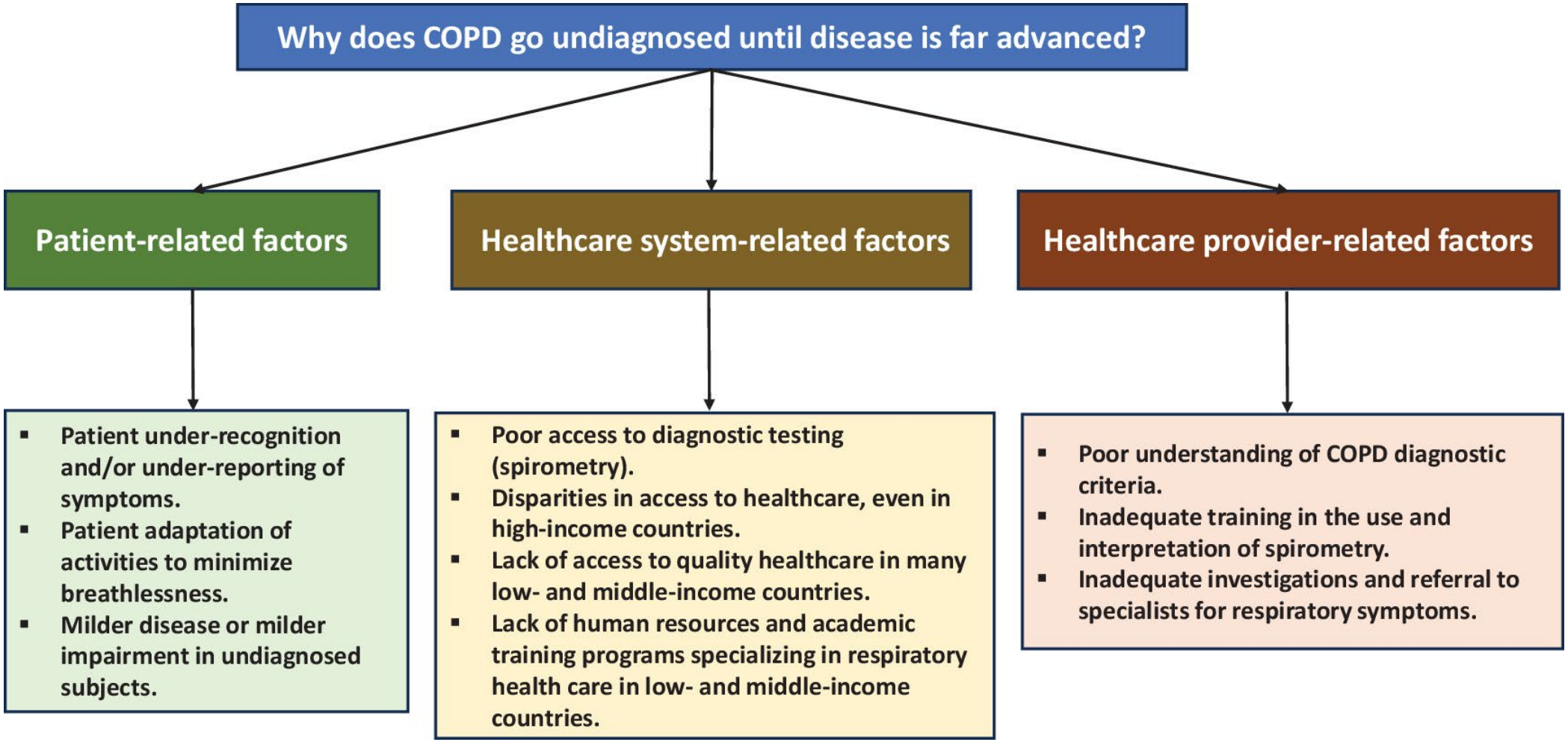
COPD Prevalence

Estimated COPD Prevalence According to Different Sources

Figure 1.1

	GBD 2019[a]	GBD 2021[b]	Population-based study 2019[c]	Other sources 2020[d]
Prevalence (%)	2.6	2.5	10.3	10.6
Number of cases (per million)	212	213	392	479

References: [a]Safiri et al. BMJ 2022;378:e069679; [b]Wang et al. Respir Res 2025;26:2; [c]Adeloye et al. Lancet Respir Med 2022;10:447–458; [d]Boers et al. JAMA Netw Open 2023;6:E2346598.



Aaron SD et al. Early Diagnosis and Treatment of Chronic Obstructive Pulmonary Disease: The Costs and Benefits of Case Finding. AJRCCM. Feb 2024

USPSTF Asymptomatic COPD Screening

Evidence update of 2016 recommendations

1. **Benefits of early detection and treatment**
   - reviewed three new medication trials: SUMMIT, PINNACLE, UPLIFT
     - inhaled therapies reduce exacerbations in moderate symptomatic COPD→Not generalizable to Asymptomatic Individuals
   - Reviewed 13 new non-pharmacologic trials in mild/moderate COPD→Mixed Data
2. **Harms of screening and treatment**
   - Reviewed 8 new studies→ No substantial harm
   - Opportunity Cost: $$ of additional medical services after positive screening

*****Conclusion: Benefit and Harm are minimal***

GOLD 2026: The case for universal spirometry

- *"Increasing evidence highlights the remarkable variability in pulmonary function both within individuals over time and between individuals across the life course."*
- *"**Mapping individual trajectories**…could allow people to serve as their own controls [similar to pediatric growth charts], enabling earlier identification of deviations from expected patterns."*
- *"Articulating this concept underscores the potential for future prevention strategies to **MAINTAIN LUNG HEALTH** before overt disease develops."*

USPSTF JAMA May 2022
GOLD 2026

Case Finding In COPD

Case-Finding

Targets only those who have unexplained respiratory symptoms, or specific risk factors for COPD

Active Case-Finding

- Proactively searching for individuals at higher risk of the condition
- Positive questionnaire responses or risk prediction too; *(sometimes paired with peak flow or micro-spirometer assessment)* → Targeted for spirometry

Opportunistic Case-Finding

- ID individuals when presenting for healthcare unrelated to the condition they are being screened for
- Example: Do spiro when presenting for lung cancer screening

Clinical Indicators for Considering a Diagnosis of COPD

Figure 2.1

Consider the diagnosis of COPD, and perform spirometry, if any of these clinical indicators are present:
(these indicators are not diagnostic themselves, but the presence of multiple key indicators increases the probability of the presence of COPD; in any case, spirometry is required to establish a diagnosis of COPD)

Dyspnea that is	Progressive over time Worse with exercise Persistent
Recurrent wheeze	
Chronic cough	May be intermittent and may be non-productive
Recurrent lower respiratory tract infections	
History of risk factors	Tobacco smoke (including popular local preparations) Smoke from home cooking and heating fuels Occupational dusts, vapors, fumes, gases and other chemicals Host factors (e.g., genetic factors, developmental abnormalities, low birthweight, prematurity, childhood respiratory infections etc.)

GLOBAL INITIATIVE FOR CHRONIC OBSTRUCTIVE LUNG DISEASE™

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JAMA | Original Investigation

Discriminative Accuracy of the CAPTURE Tool for Identifying Chronic Obstructive Pulmonary Disease in US Primary Care Settings

Fernando J. Martinez, MD, MS; MeiLan K. Han, MD, MS; Camden Lopez, MS; Susan Murray, ScD; David Mannino, MD; Stacey Anderson, MPH; Randall Brown, MD, MPH; Rowena Dolor, MD; Nancy Elder, MD, MPH; Min Joo, MD, MPH; Irfan Khan, MD; Lyndee M. Knox, PhD; Catherine Meldrum, PhD; Elizabeth Peters, BSN, RN; Cathie Spino, ScD; Hazel Tapp, PhD; Byron Thomashow, MD; Linda Zittleman, MPH; Barry Make, MD; Barbara P. Yawn, MD, MSc, MPH; for the CAPTURE Study Group

- cross-sectional multi-center study assessed CAPTURE tool in **4325 US primary care patients** to screen for clinically significant COPD
- **clinically significant COPD:**
  - post-BD FEV1/FVC <0.7
  - FEV1 <60% predicted **OR** self-reported acute respiratory illness in the last 12 months.

For each question, place an X in the box with the answer that is best for you. There are no right or wrong answers, only answers which are right for you.

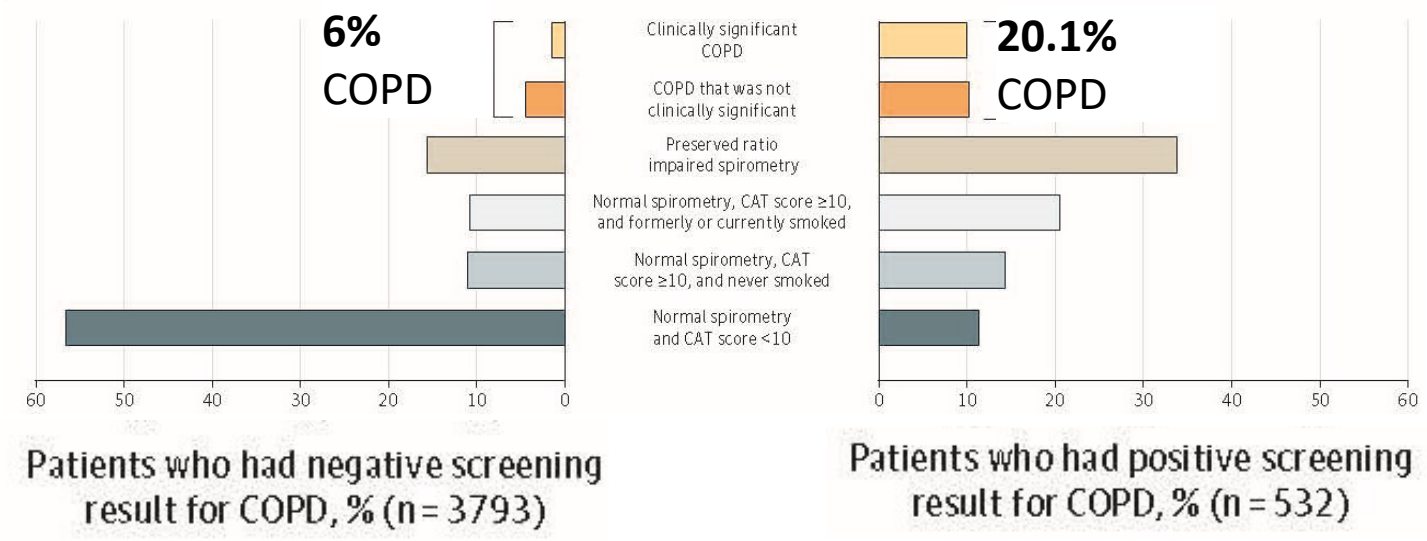
Please answer each question	No (0 points)	Yes (1 point)
1. Have you ever lived or worked in a place with dirty or polluted air, smoke, second-hand smoke, or dust?	☐	☐
2. Does your breathing change with the seasons, weather, or air quality?	☐	☐
3. Does your breathing make it difficult to do such things as carry heavy loads, shovel dirt or snow, jog, play tennis, or swim?	☐	☐
4. Compared to others your age, do you tire easily?	☐	☐
5. In the past 12 months, how many times did you miss work, school, or other activities due to a cold, bronchitis, or pneumonia?	None (0 points) ☐	Once (1 point) ☐ / 2 or more (2 points) ☐

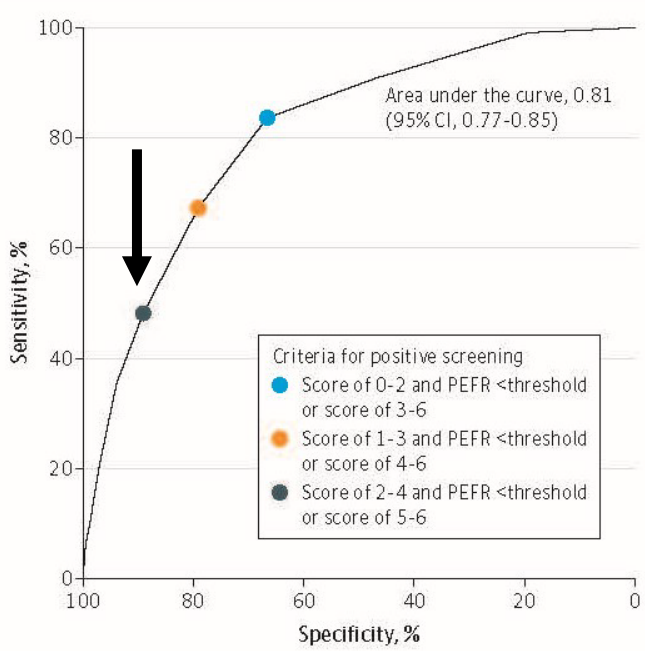
Total Score (0-6): _____

Total Score (check ONLY one box based on above score)		RECOMMENDED ACTION:
0 or 1 ☐		A. Low likelihood of COPD based on CAPTURE: No further testing recommended at this time
2, 3, or 4 Record Highest Peak Flow (highest of 3): _____ L/min	(check one based on highest Peak Flow) Females ≥ 250 L/min Males ≥ 350 L/min ☐	B. Consider rescreening or reassessing in 12 months
	Females < 250 L/min Males < 350 L/min ☐	C. Evaluation including spirometry recommended
5 or 6 ☐		D. Significant likelihood of COPD: Evaluation including spirometry recommended

CAPTURE Study: JAMA 2023

12.3%: Positive screening test
2.5%: clinically significant COPD





***only **48.2% sensitive** but was **88.6% specific** for clinically significant COPD*

Martinez et al. *JAMA* Feb 2023

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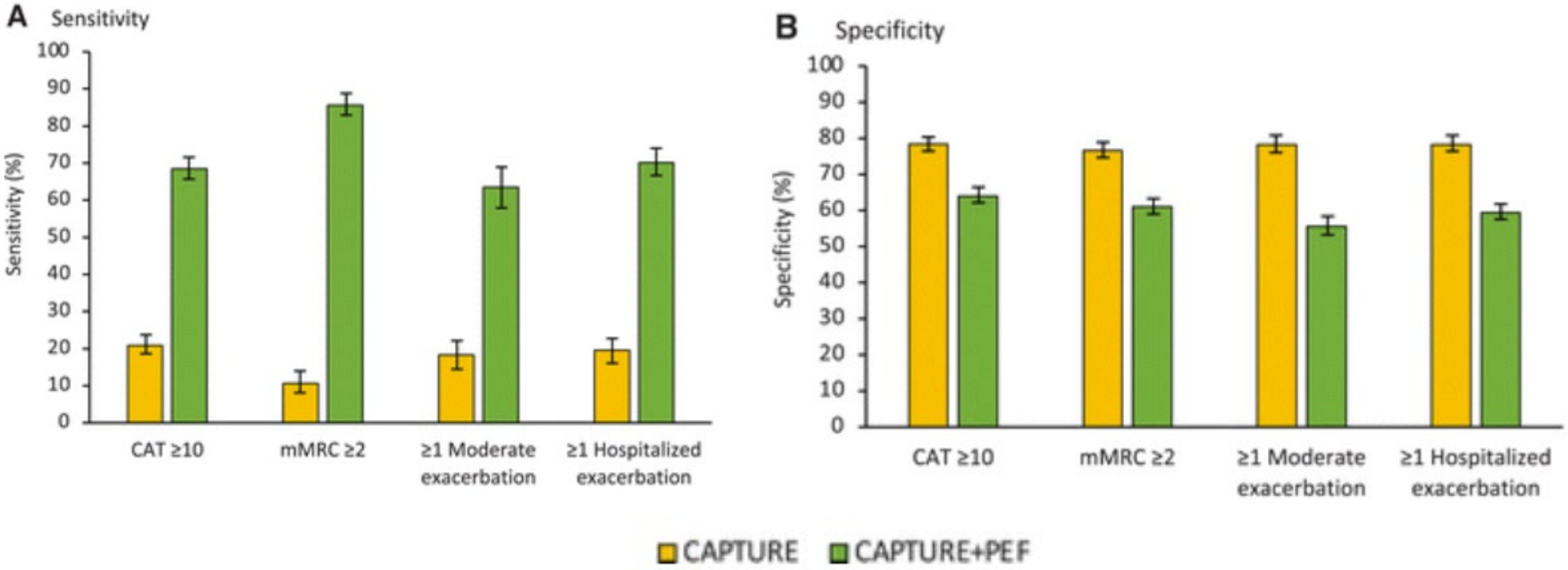
American Journal of Respiratory and Critical Care Medicine

Use of CAPTURE to Identify Individuals Who May or May Not Require Treatment for Chronic Obstructive Pulmonary Disease

Yun Li [1], Fuqiang Wen [2], Qianli Ma [3], Rongchang Chen [4], Yongchang Sun [5], Tiantian Liu [6], Chenjuan Gu [6], Shuling Hu [6], Jie Song [6], Chris Compton [7], Jinping Zheng [1], Show All...



The NEW ENGLAND JOURNAL of MEDICINE

Early Diagnosis and Treatment of COPD and Asthma — A Randomized, Controlled Trial

S.D. Aaron, K.L. Vandemheen, G.A. Whitmore, C. Bergeron, L.-P. Boulet, A. Côté, R.A. McIvor, E. Penz, S.K. Field, C. Lemière, I. Mayers, M. Bhutani, T. Azher, M.D. Lougheed, S. Gupta, N. Ezer, C.J. Licskai, P. Hernandez, M. Ainslie, G.G. Alvarez, and S. Mulpuru, for the UCAP Investigators*

Background

- Up to 70% of persons with COPD or asthma remain undiagnosed
- Undiagnosed patients have:
  - Worse disease-specific and overall quality of life
  - Greater healthcare utilization
  - Poorer work productivity
- Global health burden of COPD and asthma likely underestimated

Study Objective

To determine whether early diagnosis coupled with specialist-directed treatment of undiagnosed COPD or asthma:

- Reduces healthcare utilization for respiratory illness
- Improves health outcomes

The NEW ENGLAND JOURNAL of MEDICINE

Early Diagnosis and Treatment of COPD and Asthma — A Randomized, Controlled Trial

Intervention Details

- Day of randomization visit with pulmonologist/educator
- Follow-up visit at 4 months
- Guideline-based pharmacologic treatment
- Non-pharmacologic interventions:
  - Disease education
  - Action plans (35%)
  - Exercise advice (61%)
  - Weight management (22%)
  - Inhaler technique training
  - Smoking cessation support

Participant Characteristics

- Mean age: 63 years
- ~60% male
- Balanced diagnosis:
  ~50% asthma, ~50% COPD
- Most had mild-to-moderate airflow obstruction
- Smoking Status:
  ~25% current, ~48% former
- **High** baseline **symptom burden** (CAT score ~17.5)

Aaron SD et al. Early Diagnosis and Treatment of COPD and Athma- A Randomized Controlled Trial. NEJM. June 2024

The NEW ENGLAND JOURNAL of MEDICINE

Early Diagnosis and Treatment of COPD and Asthma — A Randomized, Controlled Trial

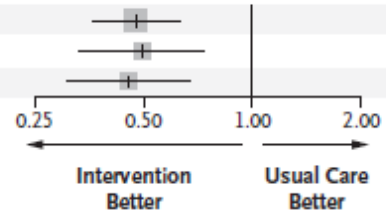
Results

Respiratory Treatments During Trial

Treatment†	Intervention (N=253)	Usual Care (N=255)
	number (percent) of participants	
No respiratory treatments during the entire trial period	19 (7.5)	92 (36.1)
SABA only	15 (5.9)	35 (13.7)
LAMA	32 (12.6)	27 (10.6)
LABA	0	11 (4.3)
ICS	56 (22.1)	32 (12.5)
LTRA	1 (0.4)	2 (0.8)
LAMA + LABA	34 (13.4)	6 (2.4)
LABA + ICS	101 (39.9)	53 (20.8)
LAMA + LABA + ICS	29 (11.5)	9 (3.5)
Supplemental oxygen at home	3 (1.2)	1 (0.4)
Short-course systemic glucocorticoid	13 (5.1)	7 (2.7)

Incidence Rate Ratio for Healthcare Utilization Events

Group	Intervention	Usual Care	Incidence Rate Ratio (95% CI)	P Value
	no. of participants/events per person-yr			
Overall	253/0.53	255/1.12	0.48 (0.36–0.63)	<0.001
Asthma subgroup	123/0.61	127/1.23	0.49 (0.33–0.73)	
COPD subgroup	130/0.46	128/1.01	0.46 (0.31–0.67)	



Secondary Outcomes

Outcome	Intervention	Usual Care	Mean Difference (95% CI)*
SGRQ total score†			
Change over 12 mo — points	−10.2	−6.8	−3.5 (−6.0 to −0.9)
CAT total score‡			
Change over 12 mo — points	−3.8	−2.6	−1.3 (−2.4 to −0.1)
Prebronchodilator FEV_1§			
Change over 12 mo — percentage points	4.7	1.5	3.2 (1.5 to 4.9)
SF-36 total score¶			
Change over 12 mo — points	4.4	2.5	1.9 (−0.4 to 4.2)

Aaron SD et al. Early Diagnosis and Treatment of COPD and Athma- A Ranomized Controlled Trial. NEJM. June 2024

The NEW ENGLAND JOURNAL of MEDICINE

Early Diagnosis and Treatment of COPD and Asthma — A Randomized, Controlled Trial

Conclusions:

- Case-finding approach successfully identified adults with undiagnosed COPD/asthma
- Specialist-directed care reduced ***respiratory healthcare utilization*** by 52%
- Both care approaches improved **symptoms** and ***quality of life***
- Early intervention showed clinically meaningful improvements in ***lung function***

Key Implications for Clinical Practice:

- **Early diagnosis matters**: Case-finding in symptomatic adults yields clinical benefits
- **Specialist care advantage** but with **Primary care benefits**
- **Disease modification potential**: Early intervention may preserve lung function
- **Patient-centered outcomes**: Both approaches improved quality of life

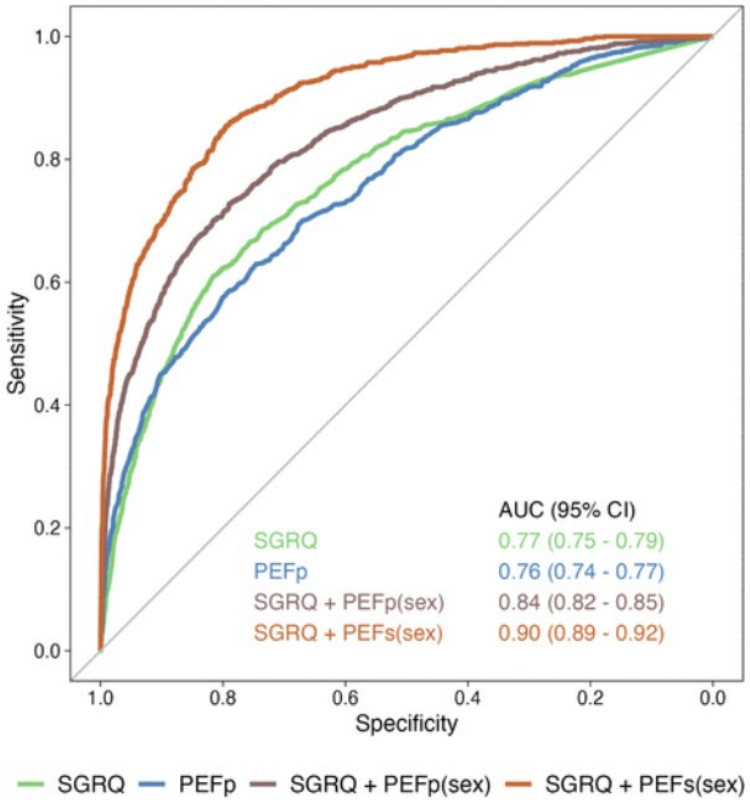
Limitations:

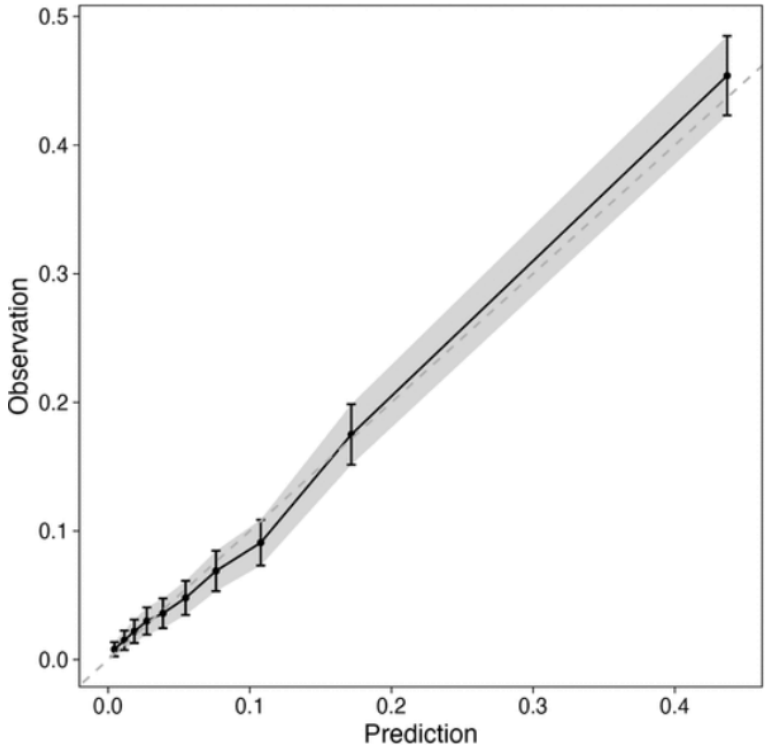
- **Demographics:** ***Older*** population (Mean age 63) and needed ***telephone*** accessRequired telephone access (potential selection bias)
- **Resource intensive case-finding**: ~27,000 interviews to identify 595 undiagnosed cases
- **Limited generalizability**: Canadian healthcare system only
- **Specialist access concerns**: May not be feasible in resource-constrained settings

American Journal of Respiratory and Critical Care Medicine

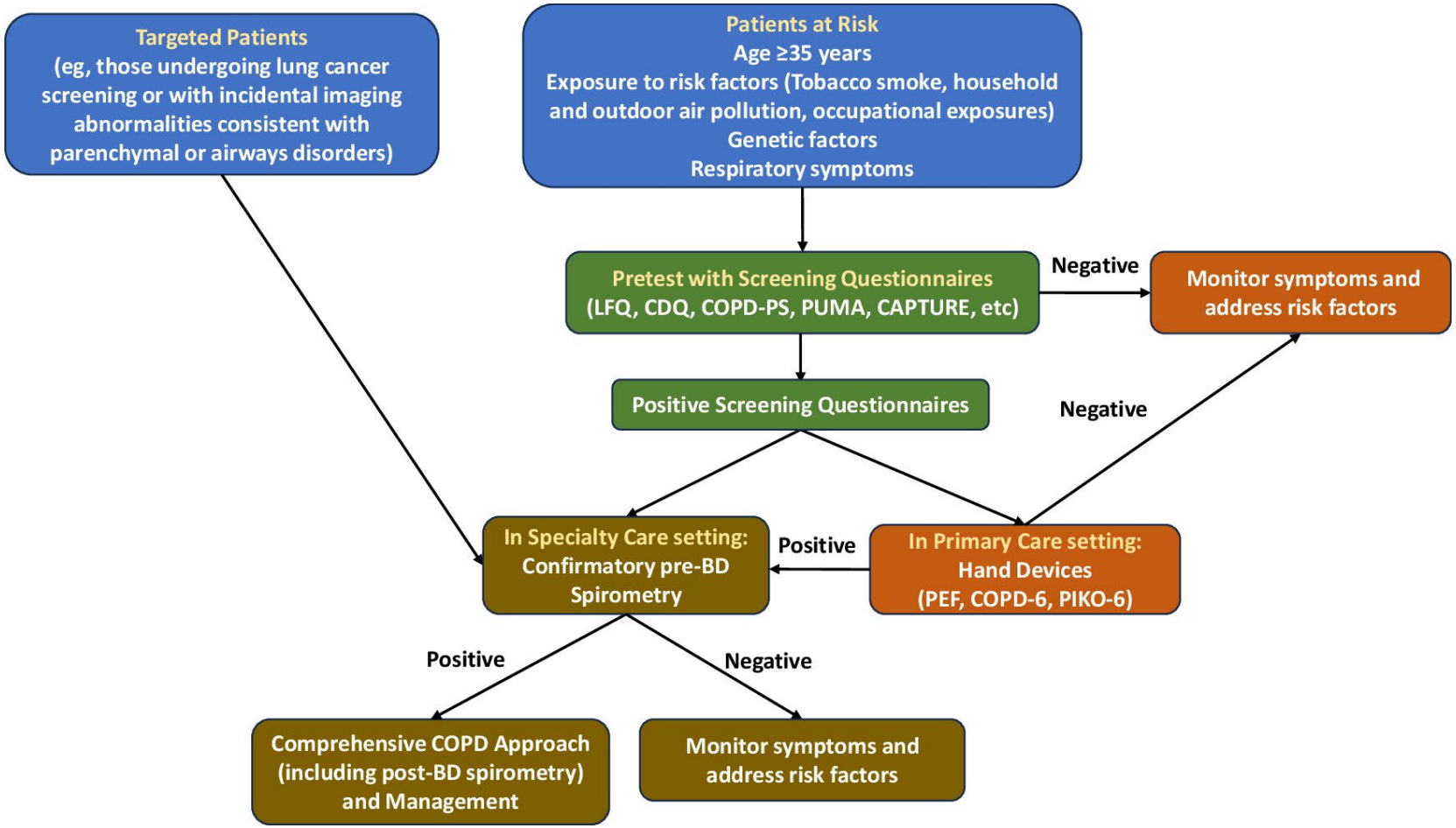
Population-Based Screening for Chronic Obstructive Pulmonary Disease Using the St. George's Respiratory Questionnaire in Resource-Limited Settings

William Checkley [1,2], Mingling Yang [1,2], Nicole M. Robertson [1,2], Arun K. Sharma [3], Ram K. Chandyo [5], Laxman Shrestha [3], Santa K. Das [4], Bruce Kirenga [6], Patricia Alupo [6], Gonzalo Gianella [7], Trishul Siddharthan [2,8], Show





Case Finding In COPD



Aaron SD et al. Early Diagnosis and Treatment of Chronic Obstructive Pulmonary Disease: The Costs and Benefits of Case Finding. AJRCCM. Feb 2024

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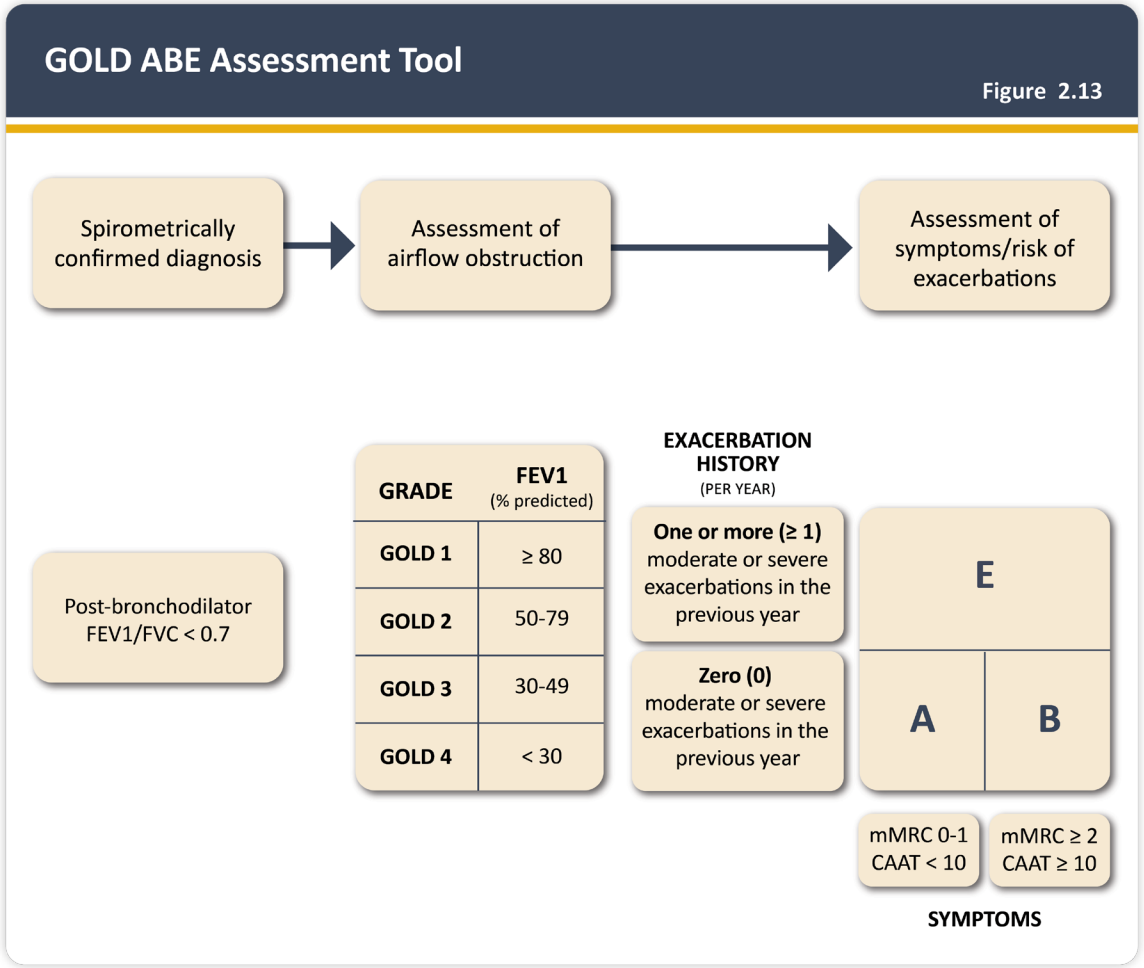
COPD Assessment



COPD Treatable Traits: Symptoms

Medical Research Council (MRC) Dyspnea Scale

1 I only get breathless with strenuous exercise

2 I get short of breath when hurrying on the level or walking up a slight hill

3 I walk slower than people of the same age on the level or have to stop for breath when walking at my own pace

4 I stap for breath after walking about 100 meters or after a few minutes on the level

5 I am too breathless to leave the house or I am breathless when dreasing or undreasing

How is your COPD? Take the COPD Assessment Test™ (CAT)

This questionnaire will help you and your healthcare professional measure the impact COPD (Chronic Obstructive Pulmonary Disease) is having on your wellbeing and daily life. Your answers, and test score, can be used by you and your healthcare professional to help improve the management of your COPD and get the greatest benefit from treatment.

For each item below, place a mark (X) in the box that best describes you currently. Be sure to only select one response for each question.

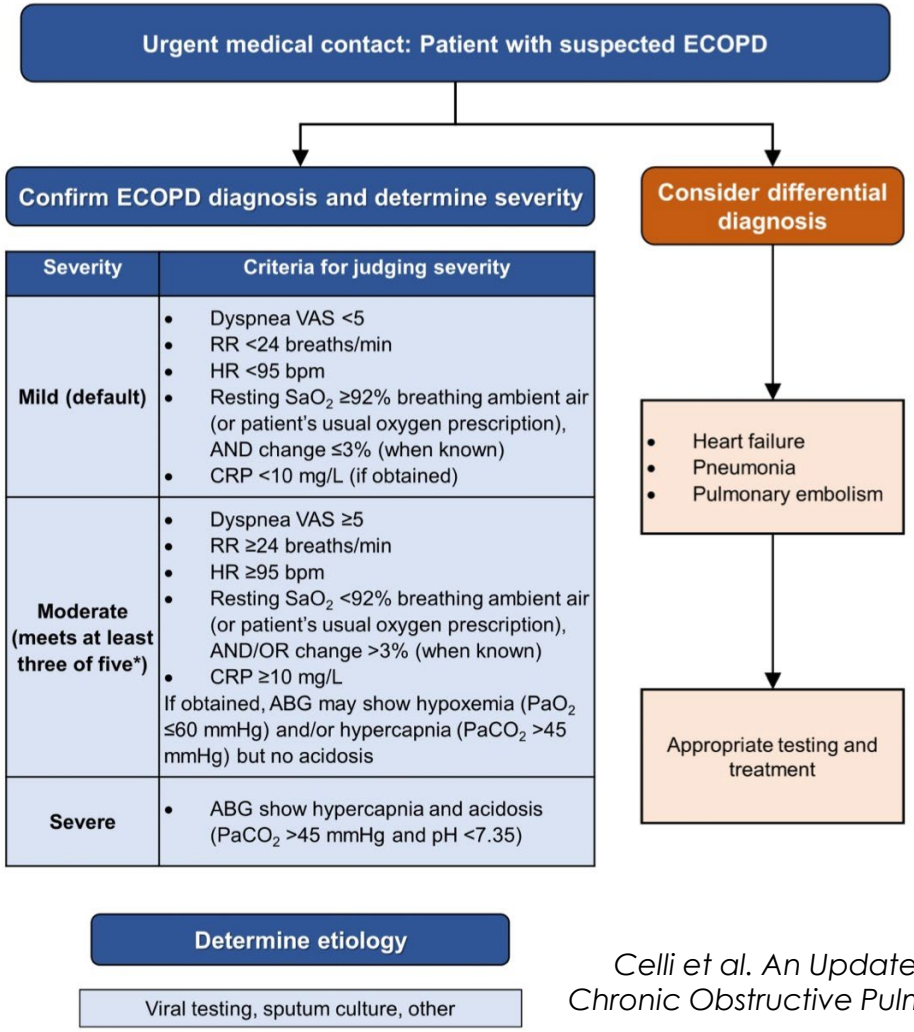
Example: I am very happy 0 X 2 3 4 5 I am very sad

		SCORE
I never cough	0 1 X 3 4 5	I cough all the time	2
I have no phlegm (mucus) in my chest at all	0 X 2 3 4 5	My chest is completely full of phlegm (mucus)	1
My chest does not feel tight at all	0 X 2 3 4 5	My chest feels very tight	1
When I walk up a hill or one flight of stairs I am not breathless	0 1 X 3 4 5	When I walk up a hill or one flight of stairs I am very breathless	2
I am not limited doing any activities at home	0 1 2 3 4 X	I am very limited doing activities at home	5
I am confident leaving my home despite my lung condition	0 1 2 3 X 5	I am not at all confident leaving my home because of my lung condition	4
I sleep soundly	0 1 2 3 X 5	I don't sleep soundly because of my lung condition	4
I have lots of energy	0 1 2 3 X 5	I have no energy at all	4

TOTAL SCORE 23

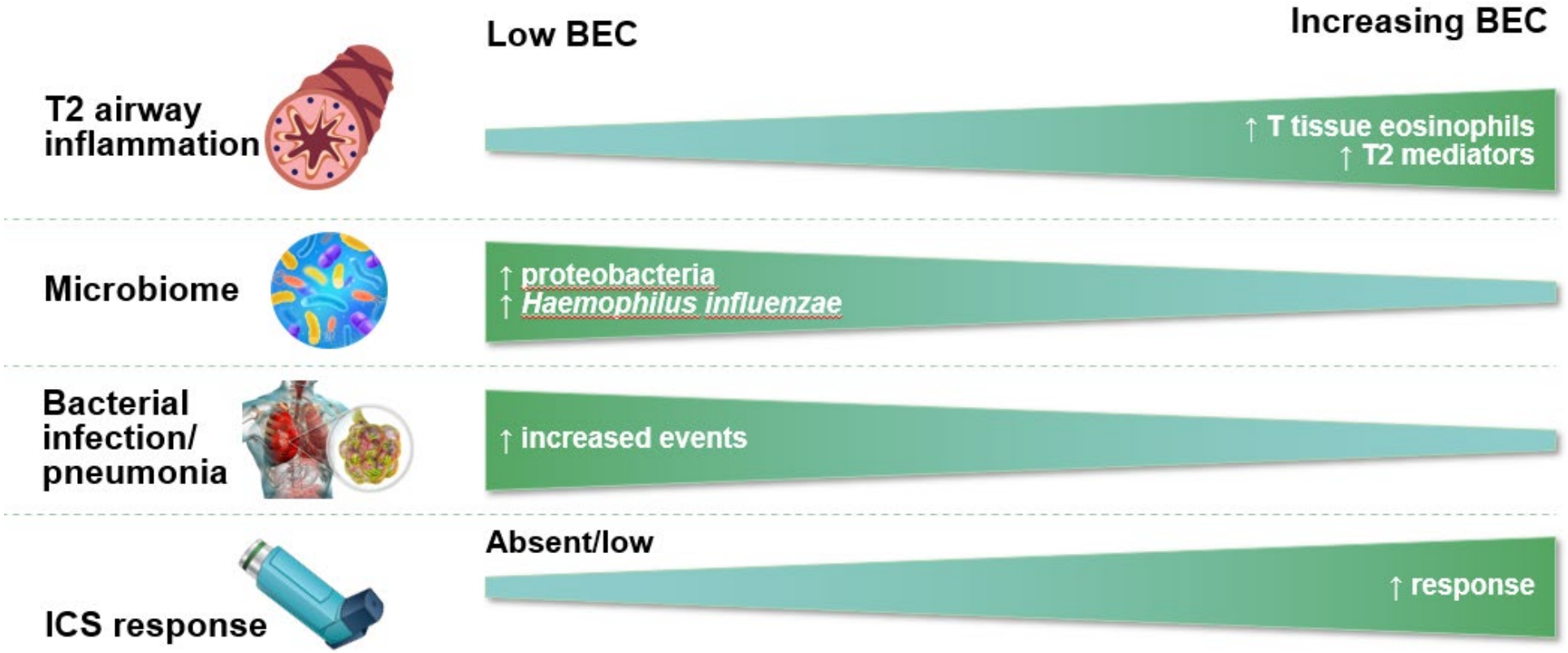
COPD Treatable Traits: Exacerbations

ROME Proposal for Classifying Exacerbations



Celli et al. An Updated Definition and Severity Classification of Chronic Obstructive Pulmonary Disease Exacerbations: The Rome Proposal. AJRCCM Sept 2021

COPD Treatable Traits: Type 2 Inflammation



Singh, D, et al. AJRCCM 2022; 206: 17-24.

Conclusions

- COPD is a heterogeneous disease. Genetics and Heterogeneous exposures throughout the lifecourse (including but not limited to tobacco smoking) contribute to COPD diagnosis and presentation.
- Lung function trajectories that lead to the manifestation of COPD vary across individuals
- COPD is underdiagnosed due to a combination of patient- and healthcare related factors
- While broadly screening asymptomatic individuals is not yet feasible or widely recommended; Screening patients at-risk for disease ("Case-Finding") may identify many previously undiagnosed cases and improve outcomes
- Screening with a combination of validated questionnaire and Peak Flow/Micro-Spirometer provides the best validity compared to gold standard spirometry
- COPD diagnosis requires post-Bronchodilator spirometry; identifying treatable traits (exacerbations, symptoms, T2 inflammation (eos)) requires further assessment

Laura C. Myers, M.D., M.P.H., is a Research Scientist I (Assistant Professor level) at Kaiser Permanente Northern California and a pulmonary intensivist in the Diablo Service Area. She obtained her medical degree in 2012 from Harvard Medical School and a Master's in Public Health in 2018 from Harvard Chan School of Public Health. She completed fellowships in Pulmonary/Critical Care Medicine and Patient Quality and Safety at Massachusetts General Hospital. Her research focuses on protecting vulnerable populations with chronic lung disease from the negative health effects of environmental exposures, such as poor air quality and heat. She has special interest in the negative health effects of wildfire smoke and making communities more resilient in the face of a changing climate. She manages a portfolio of funded research projects and is actively implementing interventions at scale within the Kaiser member population.

COPD Epidemiology

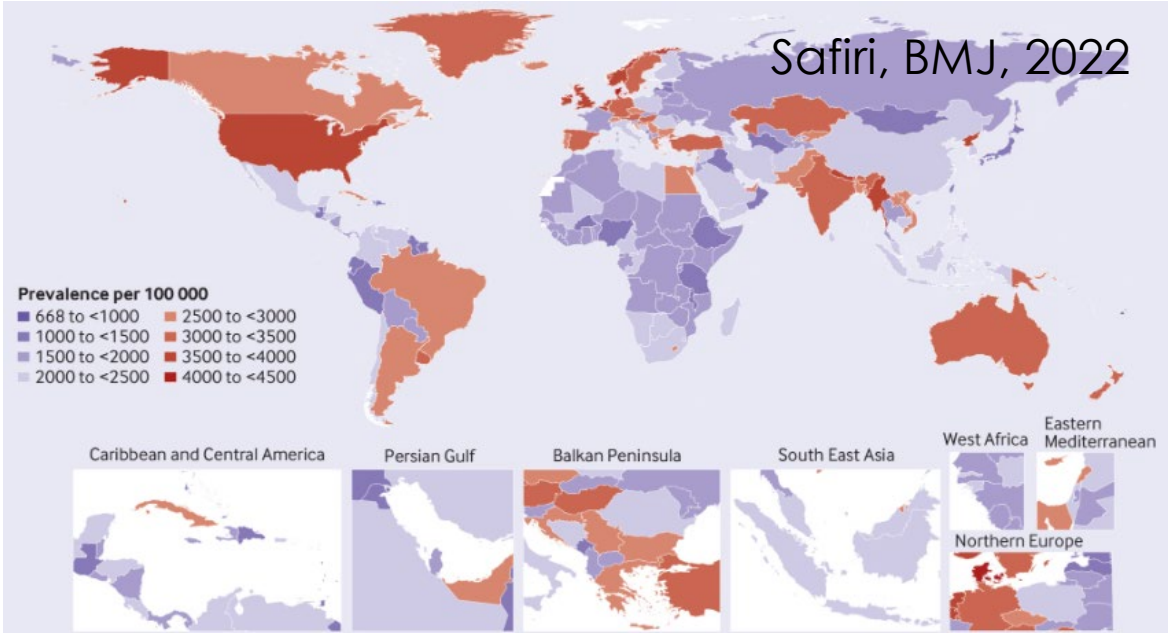
Laura Myers MD MPH

Kaiser Permanente Northern California

- I do not have conflicts of interest.
- I **WILL NOT** discuss off-label use and/or investigational use of any drugs or devices.

Global Burden of COPD

- ~213 million prevalent cases worldwide
- 3.7 million deaths annually
- Smoking is the predominant risk factor but others include air pollution, work place exposures, genetics (Alpha1AT)



https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd)

Global Trend in COPD

- Projected to reach 600 million cases by 2050

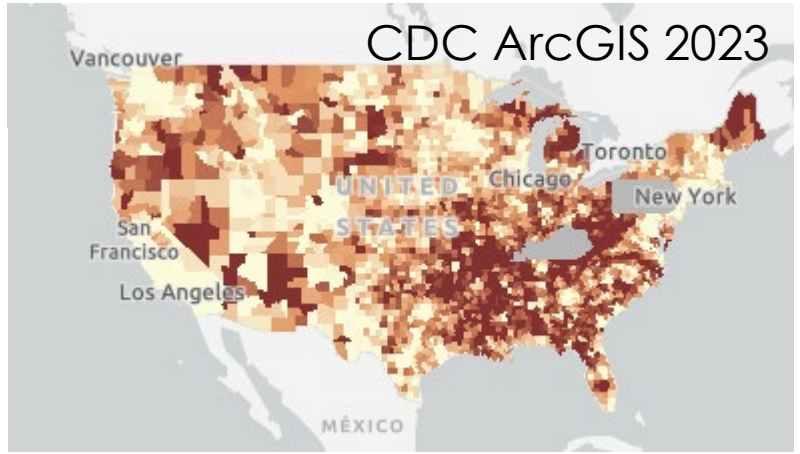
Table. Global Projected COPD Prevalence, Cases, and Relative Change From 2020 to 2050 by Sex

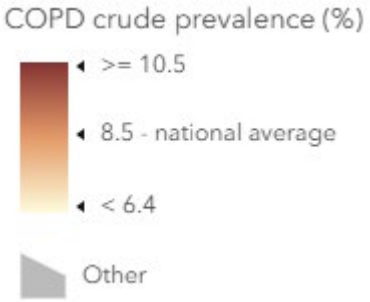
Sex	2020	2030	2040	2050
Female				
Prevalence, %	7.8	8.1	8.34	8.33
Cases, No.	176 776 887	210 351 803	240 030 181	260 106 028
Relative change in prevalence, %	NA	3.8 (vs 2020)	2.5 (vs 2030)	−0.12 (vs 2040); 6.4 (vs 2020)
Relative change in cases, %	NA	19.0 (vs 2020)	14.1 (vs 2030)	8.4 (vs 2040); 47.1 (vs 2020)
Male				
Prevalence, %	13.4	12.5	11.6	10.6
Cases	303 080 615	322 532 353	333 145 741	331 449 760
Relative change in prevalence, %	-NA	−6.7 (vs 2020)	−7.2 (vs 2030)	−8.6 (vs 2040); −20.9 (vs 2020)
Relative change in cases, %	NA	6.4 (vs 2020)	3.3 (vs 2030)	−0.5 (vs 2040); 9.4 (vs 2020)
Global				
Prevalence, %	10.6	10.3	9.7	9.5
Cases, No.	479 857 502	532 884 156	573 175 922	591 555 788
Relative change in prevalence, %	NA	−2.8 (vs 2020)	−5.8 (vs 2030)	−2.1 (vs 2040); −10.4 (vs 2020)
Relative change in cases, %	NA	11.0 (vs 2020)	7.6 (vs 2030)	3.2 (vs 2040); 23.3 (vs 2020)

Boers, JNO, 2023

COPD Burden across the United States

- Overall prevalence 8.5% (more common in women)
- More common in rural areas; highest prevalence in Appalachia and Southeast U.S.
- COPD is the 5th leading cause of death
  - ~141,700 deaths in 2023
- ~$24B annual medical costs

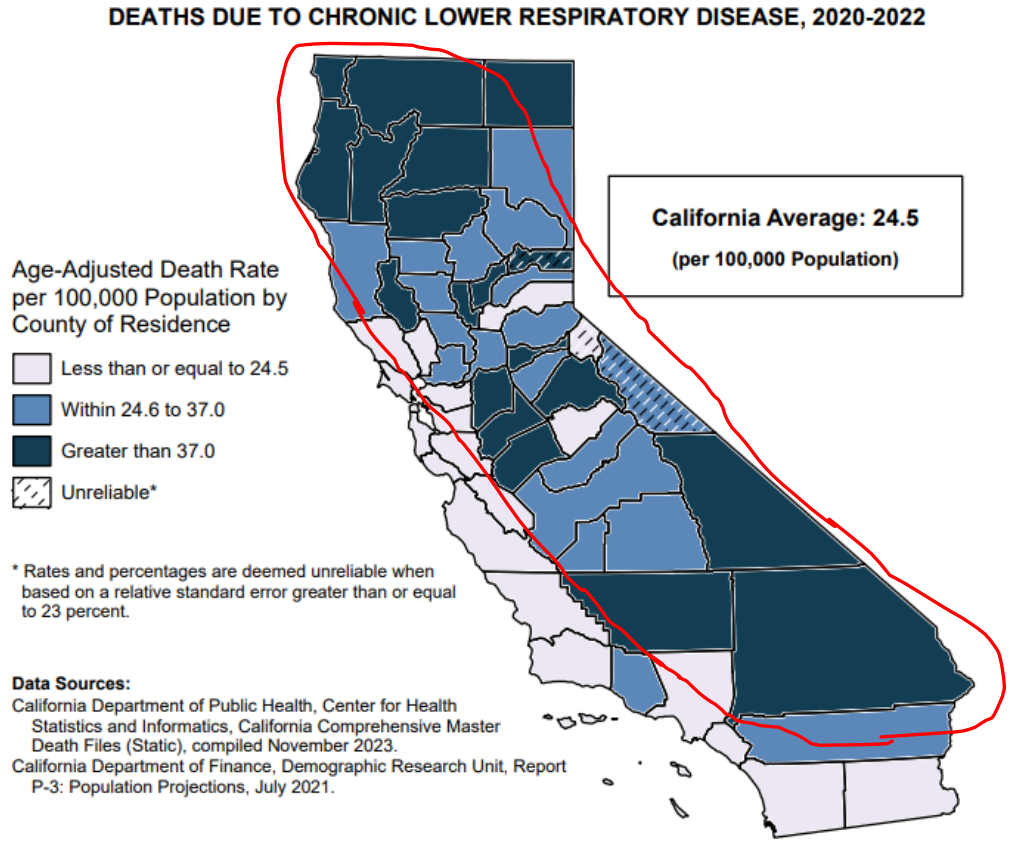




CDC, 2023

COPD Burden in California

COPD by the Numbers in California	
Adults diagnosed with COPD [5]	1,413,761
COPD prevalence [5]	4.6%
COPD mortality [3]	11,210
Annual cost of COPD treatment [4]	$2.4 Billion
Workdays lost to COPD [4]	2,128,980
Medicare hospitalizations [2]	11,505



Social Determinants of Health and COPD

- People are more likely to develop COPD who experience
  - Poverty
  - Air pollution
  - Less green space
  - Less access to healthy foods
  - More chronic stress
  - More violent crime
  - Poorer housing quality

- In SPIROMICS cohort, racial residential segregation is adversely associated with COPD morbidity among urban Black individuals

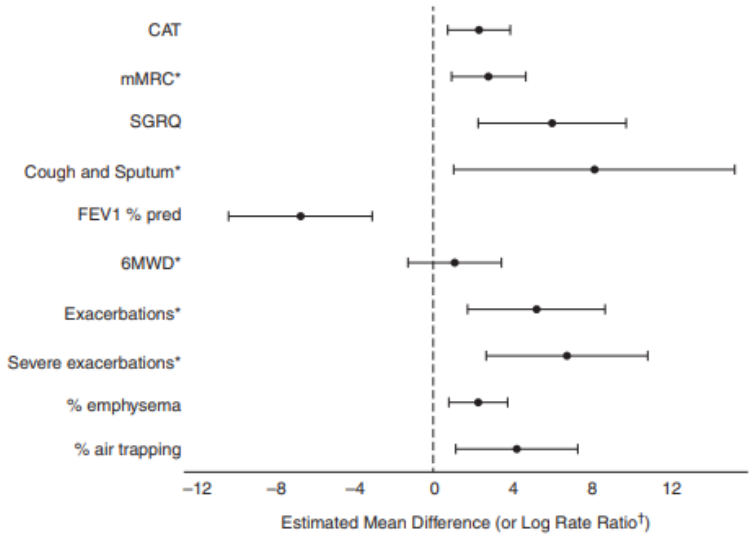


Figure 2. Black participants with or at risk of chronic obstructive pulmonary disease living in segregated neighborhoods have worse chronic obstructive pulmonary disease outcomes than their counterparts living in nonsegregated neighborhoods. Above demonstrates the estimated mean difference (or the log incidence rate) and 95% confidence intervals of respiratory morbidity/computed tomography scan findings (or exacerbations) for Black participants residing in tracts with isolation ≥0.6 (vs. isolation <0.6), adjusting for age, sex, smoking status, pack-years, obesity, marital status, occupational exposure, and total population size. In exacerbation models, participant total follow-up days in the study was specified as offset. *Estimated mean differences were rescaled to fit the chart: multiplied by 10 for mMRC, Cough and Sputum, any exacerbation (log rate), and severe exacerbation (log rate); multiplied by 1/10 for 6MWD. †For any exacerbation and severe exacerbation, the point estimate and 95% confidence interval represents the log rate ratio (multiplied by 10 to fit the chart's scale). 6MWD = 6-minute-walk distance; CAT = COPD Assessment Test; COPD = chronic obstructive pulmonary disease; mMRC = modified Medical Research Council; SGRQ = St. George's Respiratory Questionnaire.

Woo et al, AJRCCM 2021

Disparities in Outcomes & Access

- Worse COPD outcomes attributed to multiple factors (low income, reduced access to care

- Lower SES was consistently and strongly linked with poorer COPD outcomes across all measured domains among Kaiser NorCA members.
- Black race was associated with greater disease severity and a higher risk of acute exacerbations but this was explained by differences in SES.

Table 2 Socioeconomic status, race—ethnicity and chronic obstructive pulmonary disease severity

	COPD severity score			BODE score		
SES indicator	**Model 1**	**Model 2**	**Model 3**	**Model 1**	**Model 2**	**Model 3**
Race						
White	Referent	Referent	Referent	Referent	Referent	Referent
Black	1.5 (0.5 to 2.4)	1.0 (0.04 to 1.9)	0.7 (−0.2 to 1.6)	0.4 (0.03 to 0.8)	0.1 (−0.2 to 0.5)	0.07 (−0.3 to 0.4)
Asian	−1.5 (−3.5 to 0.6)	−0.5 (−2.5 to 1.5)	−0.5 (−2.5 to 1.5)	−0.2 (−1.1 to 0.6)	0.3 (−0.5 to 1.1)	0.5 (−0.3 to 1.2)
Hispanic	−0.5 (−1.7 to 0.7)	−0.9 (−2.1 to 0.2)	−1.1 (−2.2 to 0.1)	−0.1 (−0.6 to 0.4)	−0.3 (−0.8 to 0.1)	−0.3 (−0.8 to 0.1)
Other	0.4 (−1.6 to 2.3)	−0.2 (−2.1 to 1.6)	−0.4 −2.3 to 1.4)	0.4 (−0.3 to 1.2)	0.08 (−0.6 to 0.8)	0.06 (−0.7 to 0.8)
Education						
Less than high school	N/A	2.0 (1.0 to 2.9)	1.8 (0.9 to 2.7)	N/A	1.1 (0.7 to 1.4)	1.0 (0.6 to 1.3)
Some college	N/A	1.4 (0.6 to 2.3)	1.3 (0.4 to 2.0)	N/A	0.7 (0.4 to 1.0)	0.6 (0.3 to 1.0)
College degree+	N/A	Referent	Referent	N/A	Referent	Referent
Income						
Low	N/A	3.6 (2.3 to 4.9)	3.4 (2.1 to 4.7)	N/A	1.9 (1.4 to 2.4)	1.7 (1.2 to 2.2)
Medium	N/A	1.4 (0.5 to 2.3)	1.4 (0.5 to 2.2)	N/A	0.8 (0.4 to 1.1)	0.7 (0.4 to 1.0)
High	N/A	Referent	Referent	N/A	Referent	Referent

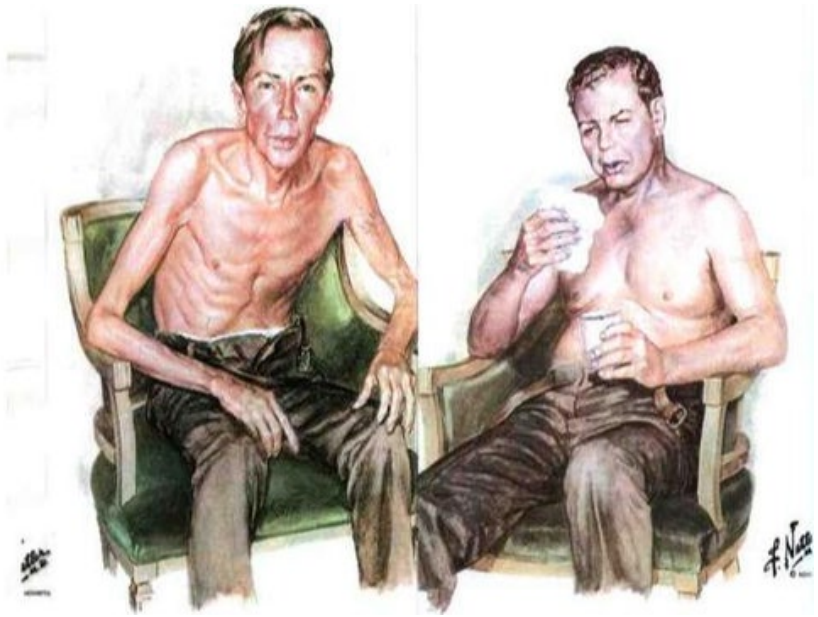
Educational attainment categories are less than high school, some college, college degree or graduate school; income categories are low (<US$20 000), medium (US$20 000—80 000), high (>US$80 000) and missing.
Higher COPD severity scores and BODE scores=poorer status.
Multivariable linear regression analysis—all results are mean difference compared to referent group (95% CIs).
Model 1=impact of race, adjusting for age and sex; model 2=impact of race, educational attainment and household income, adjusting for age and sex; model 3=race, educational attainment and household income, adjusting for age and sex; also including additional covariates (smoking history, occupational exposures on longest held job, body mass index and comorbidities—see Methods).

J Epi Comm Health, 2011

Heterogeneity of COPD

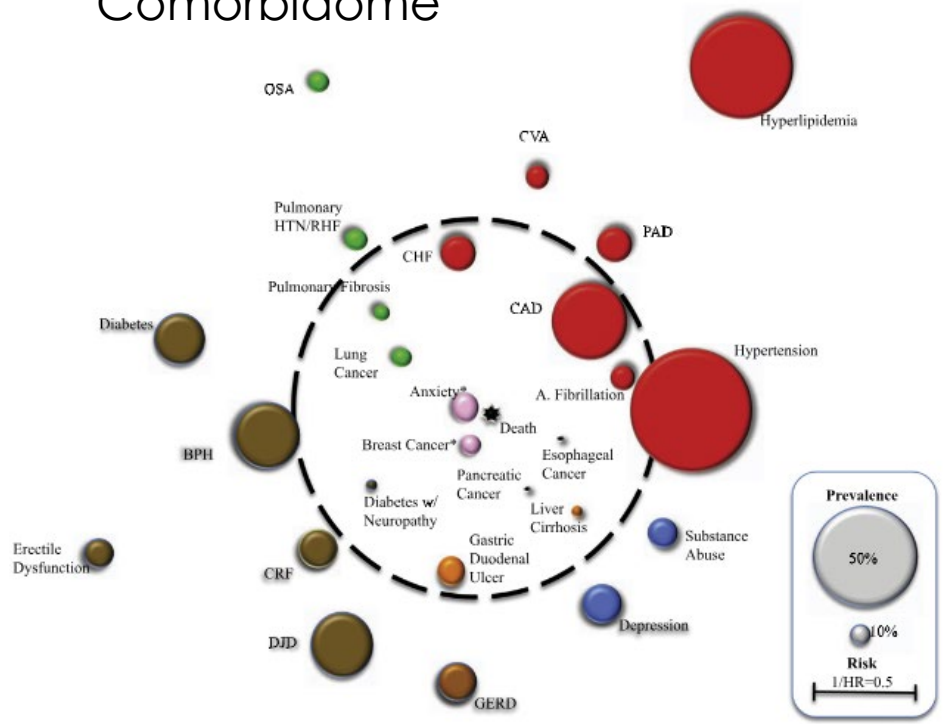
- Chronic Bronchitis: daily productive cough; airway predominant
- Emphysema-predominant: alveolar destruction, dyspnea,
- Frequent Exacerbator: ≥2 exacerbations/year
- Asthma–COPD Overlap
- Eosinophilic COPD
- Alpha-1 Antitrypsin Deficiency: early-onset emphysema

Historical image of "Pink puffer vs Blue bloater"



The Comorbidity Burden in COPD

"Comorbidome"



Divo, AJRCCM, 2012

Phenotypes within COPD using clustering analysis

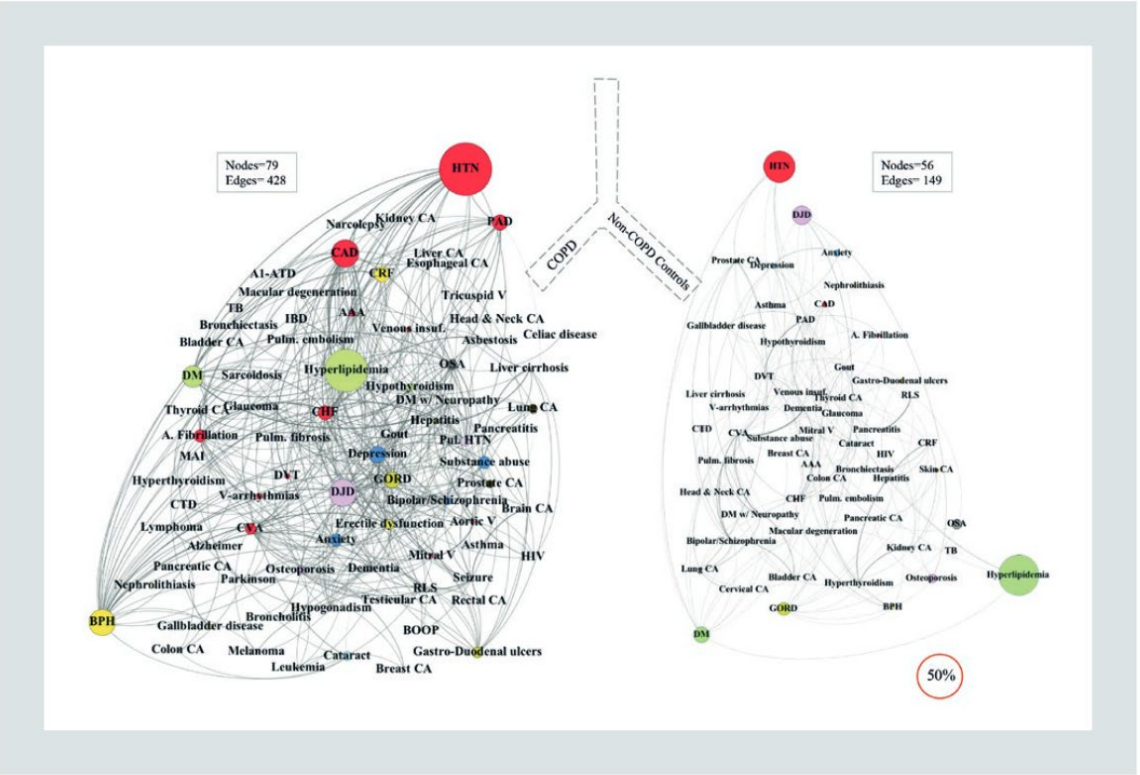


FIGURE 5. Graphical visualization of the BODE COPD comorbidities Network. COPD network (shown on the right) is compared to a control group shown on the left. Each node represents a comorbidity and its size corresponds to its prevalence. Links between nodes exist if the Pearson's correlation (Φ) has a p-value of < 0.001 *(reproduced with permission from Divo et al. Eur Respir J. 2015;46:640-50[15]).*
A. fibrillation: atrial fibrillation; BPH: benign prostatic hypertrophy; CAD: coronary artery disease; CHF: congestive heart failure; CVA: cerebrovascular accident; DJD: degenerative joint disease; DM: diabetes mellitus; GORD: gastro-oesophageal reflux disease; HTN: hypertension; OSA: obstructive sleep apnoea; PAD: peripheral artery disease.

Divo et al. Eur Respir J. 2015

Multimorbidity in COPD

- COPD patients with comorbid illnesses have worse outcomes
- COPD as a disease is not limited to the lungs so maybe we should view it as full-body disease

Summary

- COPD is common, costly
- Prevalence of COPD varies across the U.S., counties of CA and across socioeconomic status
- COPD is a heterogeneous disease (or collection of diseases)

References

1. GOLD 2024 Pocket Guide to COPD.
2. Kim V, Criner GJ. Am J Respir Crit Care Med. 2013;187(3):228-237.
3. Makita H et al. Thorax. 2007;62:932-937.
4. Hurst JR et al. N Engl J Med. 2010;363:1128-1138.
5. Postma DS, Rabe KF. N Engl J Med. 2015;373:1241-1249.
6. Sandhaus RA et al. Chronic Obstr Pulm Dis. 2016;3(3):668-682.

Dr Ghimire is a Clinical Professor and the division chief for the PCCSM at UCSF Fresno. His clinical interest are in obstructive airway disease mainly COPD and Cystic Fibrosis. He also serves as the Director of Adult CF center at UCSF Fresno.

Updates on the treatment algorithm of COPD - GOLD 2026

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Clinical Professor, UCSF

Division of Pulmonary, Critical care & Sleep Medicine, UCSF Fresno

Disclosures

- I have the following relationships with ACCME defined ineligible companies:
- **PI**
  - **AERIFY-1**
  - **AERIFY-2**
- I **WILL NOT** discuss off-label use and/or investigational use of any drugs or devices.

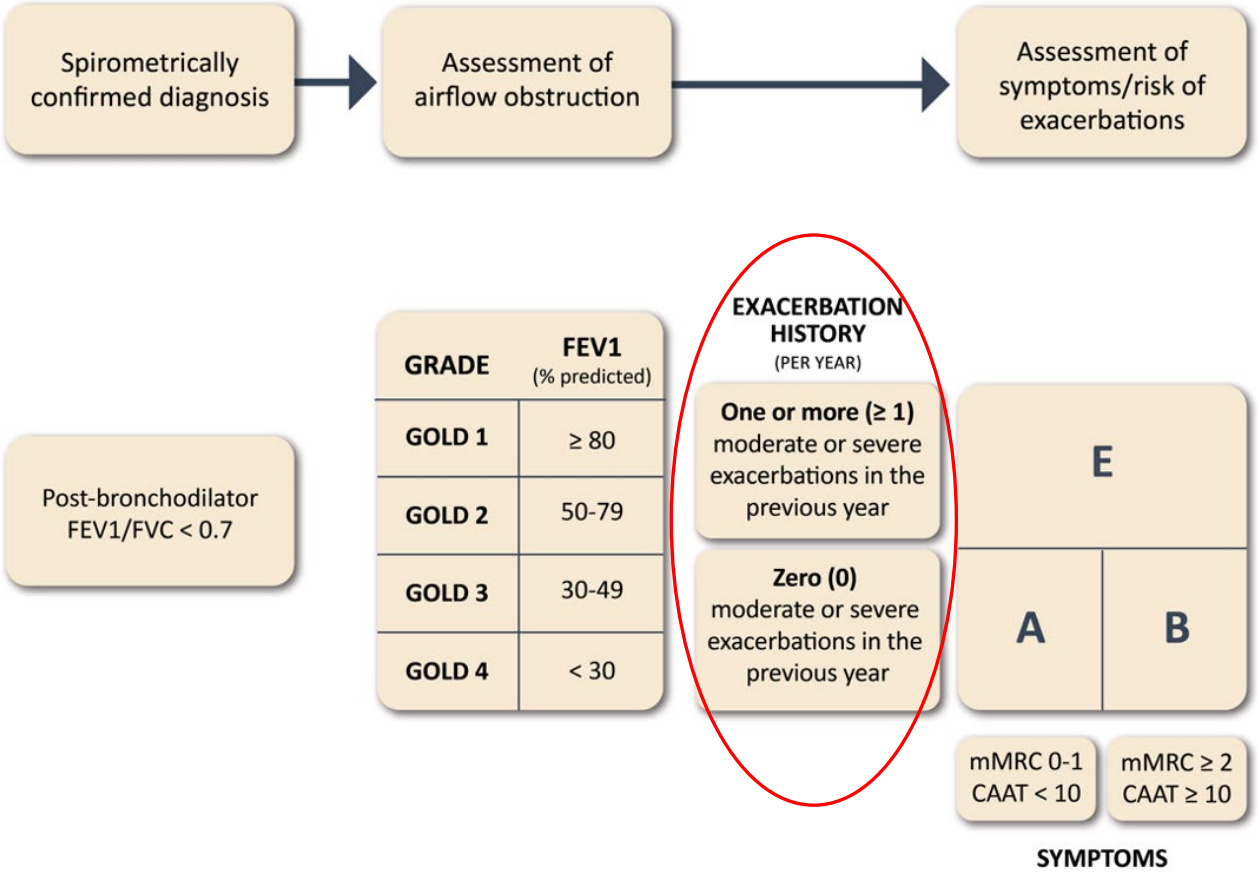
Outline

- Describe key updates from GOLD 2026 report.
- Discuss and apply the GOLD 2026 initial and follow up treatment algorithm
- Utilize blood eosinophil count as a key biomarker to guide treatment decisions
- Formulate a treatment strategy for patients already on ICS

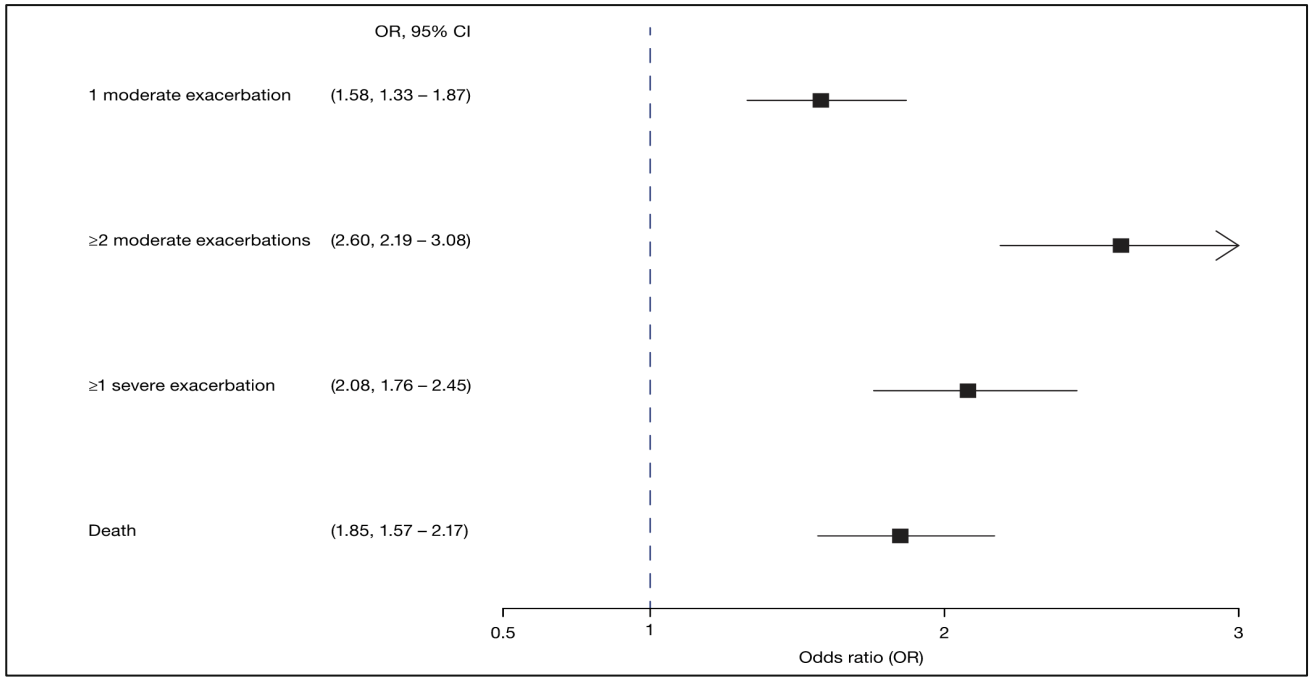
GOLD 2026 - Key updates on management of COPD

- **Criteria** for defining Gold A, B, and E have been modified
- A new concept of **disease activity** is introduced
- Emphasizes the importance of addressing **multimorbidity**

Every exacerbation counts – *ABE classification*



Every exacerbation counts



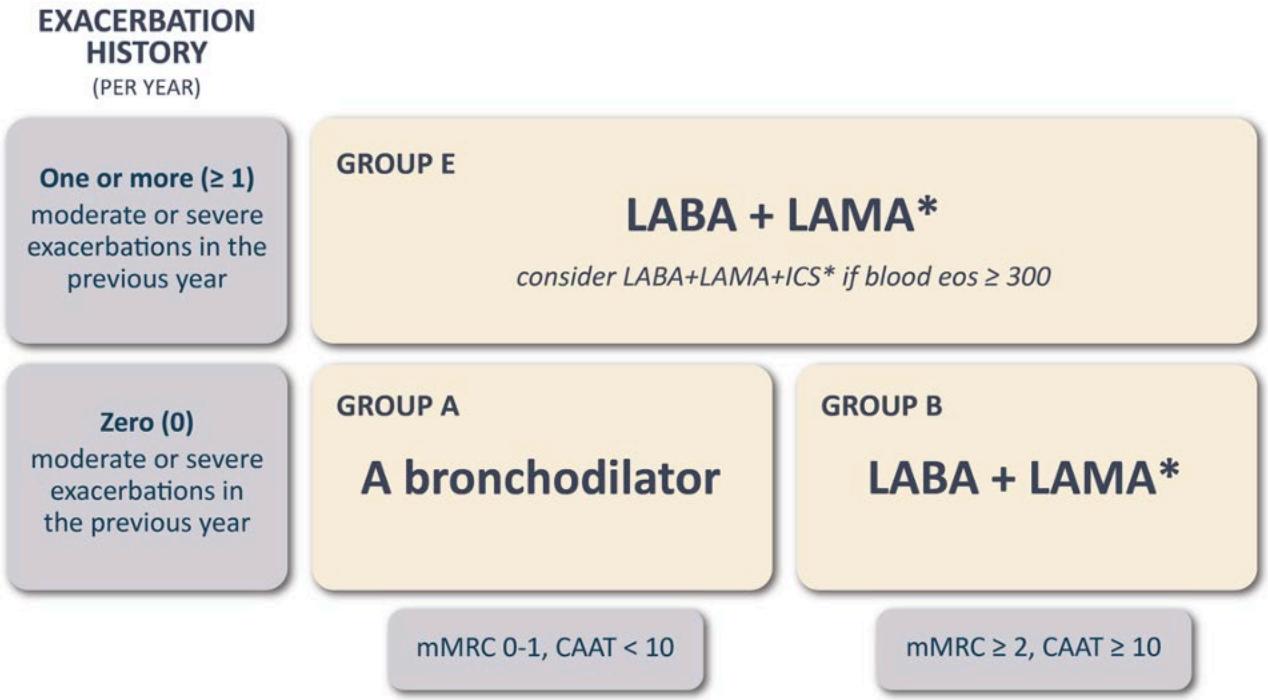
Odds ratio for exacerbation and death after 3 year follow up in GOLD B0 and B1

Lokke et al, Int J COPD, 2022

Low disease activity is a key objective in COPD

Disease activity - A biological pathway that causes the pathological outcome of the disease and are potentially reversible with treatment.

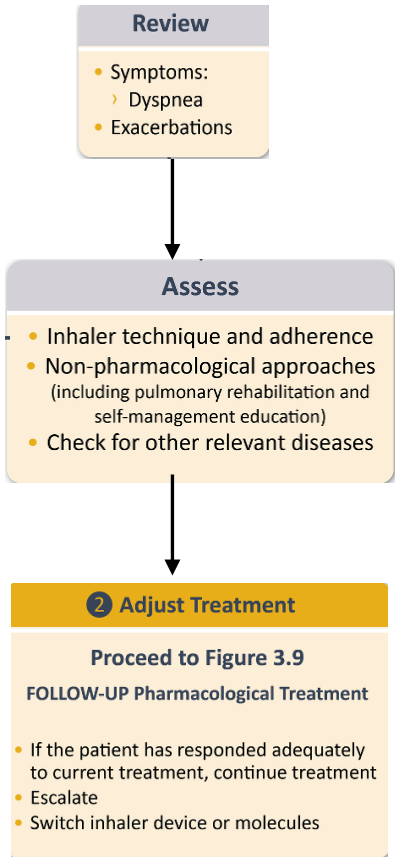
Initial treatment – *dual bronchodilator is the mainstay of treatment*

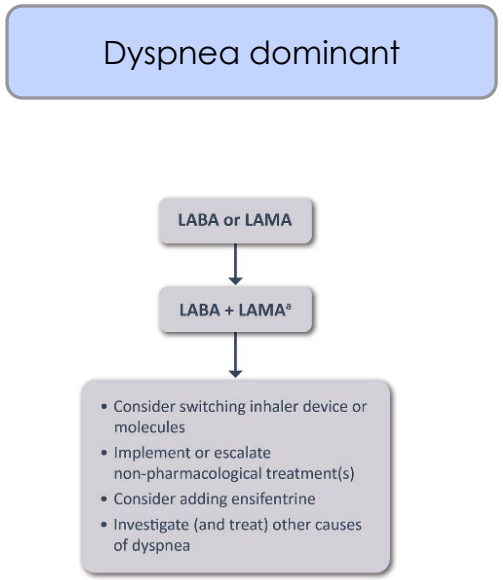


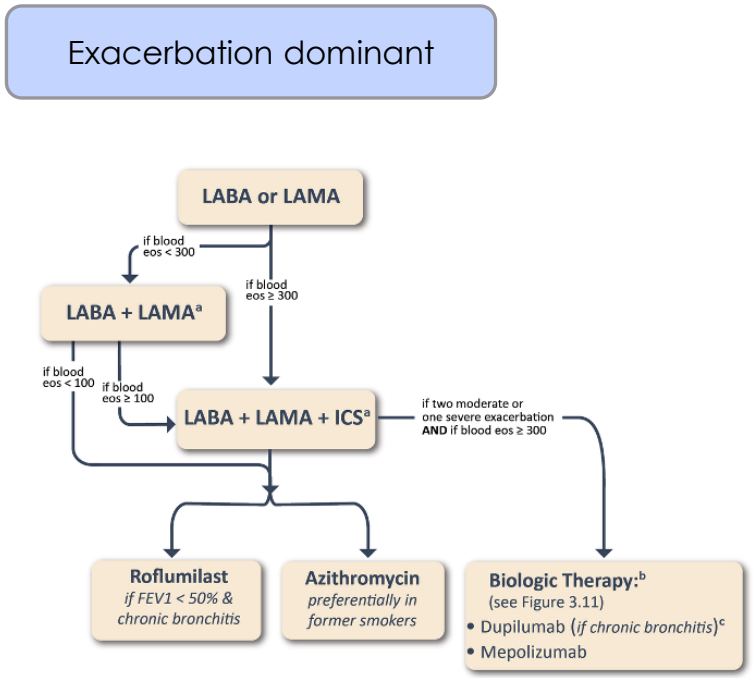
*A single device inhaler improves adherence and outcomes

GOLD 2026 report
Lin et al, Front Pharmacol 2023

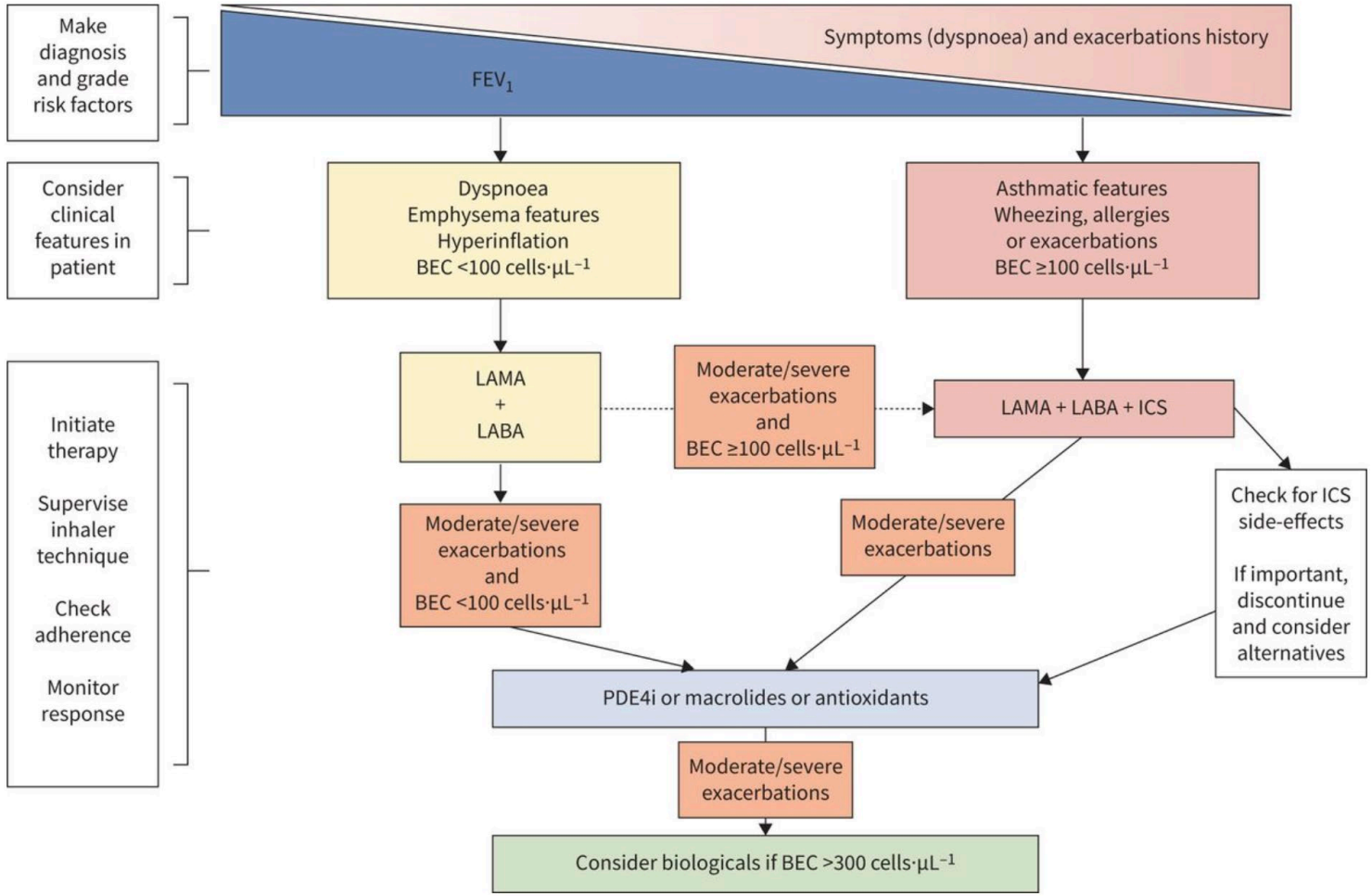
Follow up - *a phenotype driven approach*







Alternative algorithm



Celli et al, ERJ, 2023

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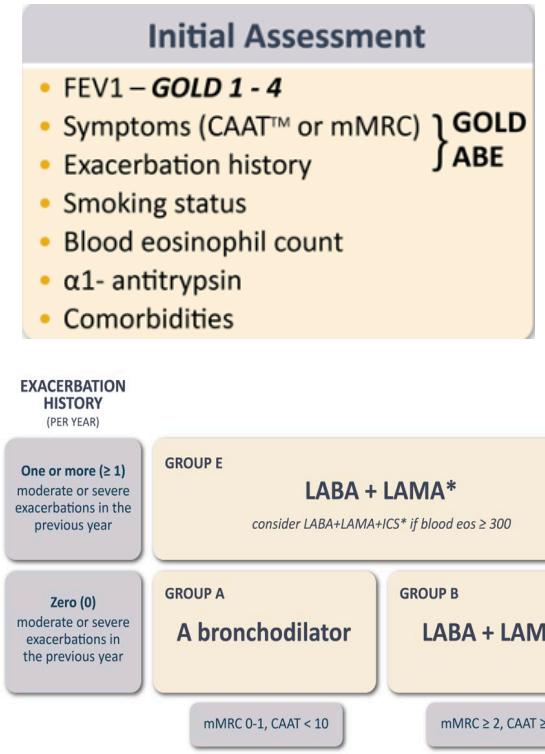
Patient cases

Case 1- *initial treatment*

- 59 yr old male presents with progressive dyspnea on exertion. He has h/o 40 pky of smoking, currently smokes half pack daily. h/o Meth abuse.
  - CAT 12, mMRC 2
  - 0 exacerbations in last 12 months
  - Spirometry FEV1/FVC: 0.63, FEV1 58%
  - Blood eosinophils :105
  - Alpha-1 antitrypsin level – wnl
  - Comorbidities – BMI 42, HTN, Type 2 DM
- Initial treatment
  - **Group B**
  - **LABA+LAMA**

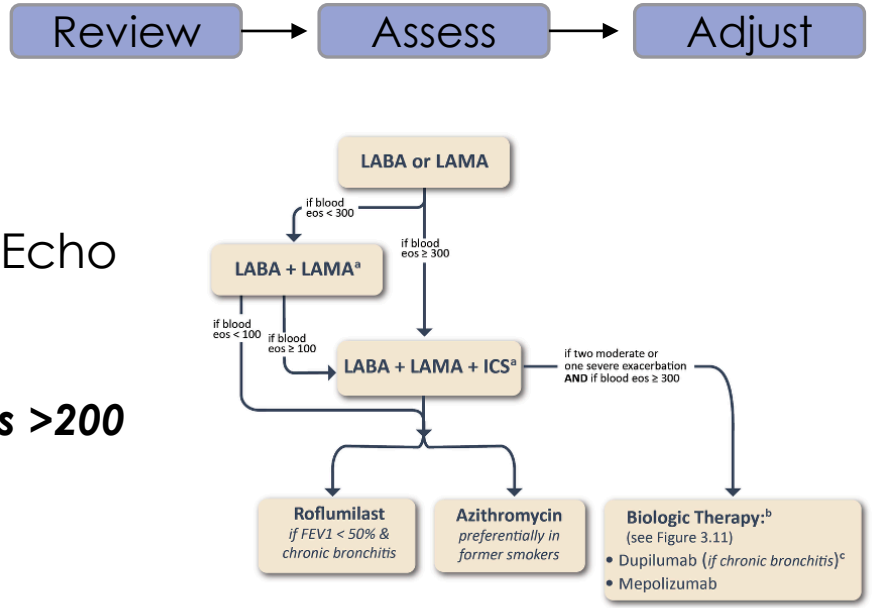


Case 1 - *6 month follow up*

- Patient did well on LABA+LAMA combination and during the 1st follow. During the 2nd follow, up he reported one urgent care visit for worsening shortness of breath which was treated with prednisone and antibiotics. Currently, he is nearly back to his baseline (mMRC - 2). Eosinophils during exacerbation was 110.

- Treatment plan
  - **Roflumilast or Azithromycin or** *add an ICS*
  - Smoking cessation
  - Screen for sleep apnea, check NT- proBNP & 2 D Echo

Current smokers – beneficial effects seen when eosinophils >200 cell per microL



Exacerbation with low eosinophils

Azithromycin	Roflumilast
Former smoker	Agnostic to smoking status
Older patients with milder disease	Chronic bronchitis
Oxygen use	Eosinophils >150 cell/microL
Hearing loss (25%)	GI side effects

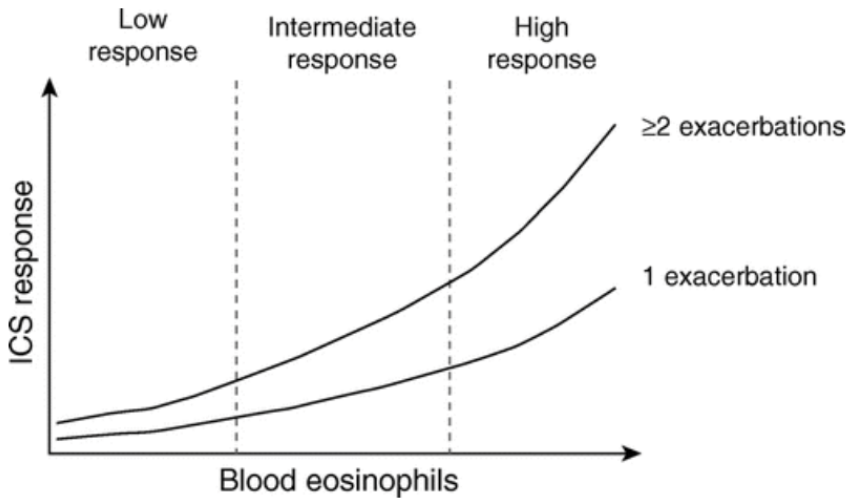
Han et al, AJRCCM 2014
Martinex et al, AJRCCM, 2018

Guidance on initiation of ICS

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



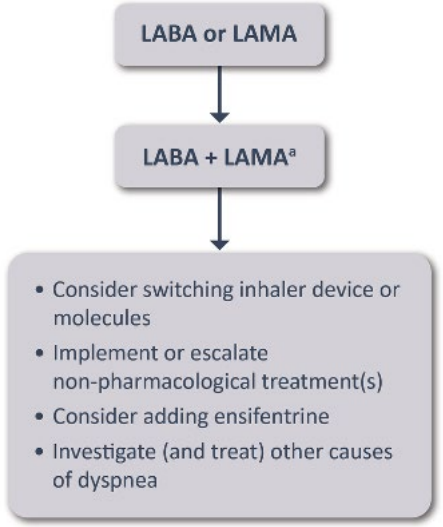
GOLD report 2026
Singh AJRCCM, 2021

Case 1 - *2 yr follow up*

- Patient reports decreasing exercise capacity, tiredness and worsening dyspnea on exertion, intermittent cough with clear sputum, quit smoking for 9 months but resumed. Gained 15 lbs.

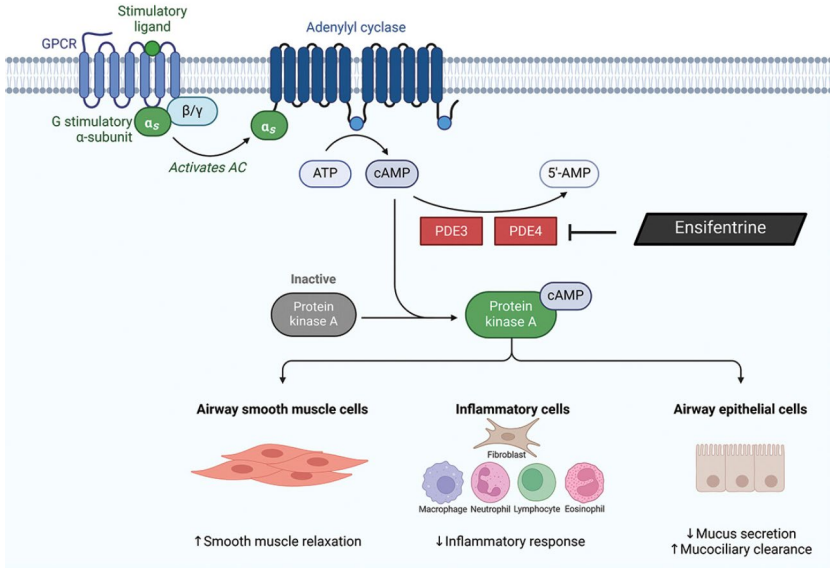
- Treatment plan
  - ESS -12, order 2D echo
  - **Ensifentrine**

- 3 month follow up – no significant change
  - Moderate OSA – waiting for CPAP
  - EF 45-50%, Grade 2 DD , Mild PH – pending RHC/LHC



Ensifentrine – *a bronchodilator, PDE3/PDE4 inhibitor*

- ENHANCE -1, ENHANCE -2
- FEV1 = 52%, Age 40-80, median 65
- Nebulized Ensifentrine 3 mg bid vs placebo for 24 weeks, 5:3 ratio
- Results:
  - Improved Average FEV1 – 87 ml & 94 ml
  - Improved QOL (SGRQ) (not in ENHANCE -2)
- Baseline inhalers in placebo
  - LAMA – 30%
  - LABA – 14%
  - LABA+ICS – 17%
- Supported by Verona pharma

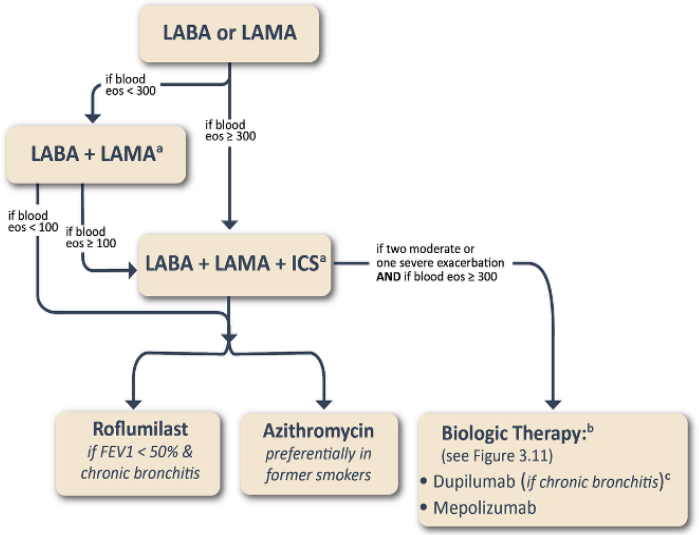


Anzueto et al, AJRCCM 2023

Case 2 - *biologics*

- 67-year-old female with COPD referred to you by PCP because of frequent hospitalization and worsening respiratory. She was discharged 3 weeks ago on supplemental oxygen. Quit smoking 4 years ago after an MI.
  - Spirometry – Ratio 58, FEV1 45%
  - CAT 28, mMRC 2
  - Blood eosinophils – baseline 156, exacerbation 200-400
  - Comorbidities : CAD s/p CABG X 2, A fib s/p ablation
  - Was on triple therapy (single device)

- Treatment plan:
  - **Dupilumab**
  - **Mepolizumab**



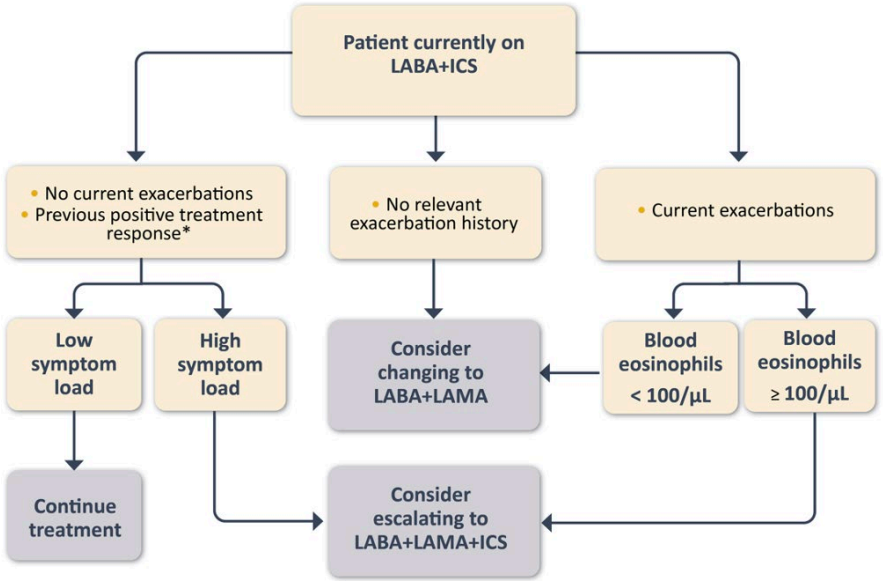
FDA approved biologics for COPD with high eosinophils

Dupilumab (Anti IL-4R)	Mepolizumab (Anti IL-5)
Chronic bronchitis	Emphysema & chronic bronchitis
Eosinophils – *300 cells/microL at screening*	Eosinophils – *300 cells/microL at screening & 150 cells/microL in prior year*
Reduction in exacerbations - 30%-34%	Reduction in exacerbations - 21%
Increase FEV1	No effect in FEV1
Improved quality of life (SGRQ)	Comparable quality of life (SGRQ)

Bhatt et al, NEJM 2024
Sciurba et al, NEJM 2025

Case 3 - *patient on combination LABA+ ICS*

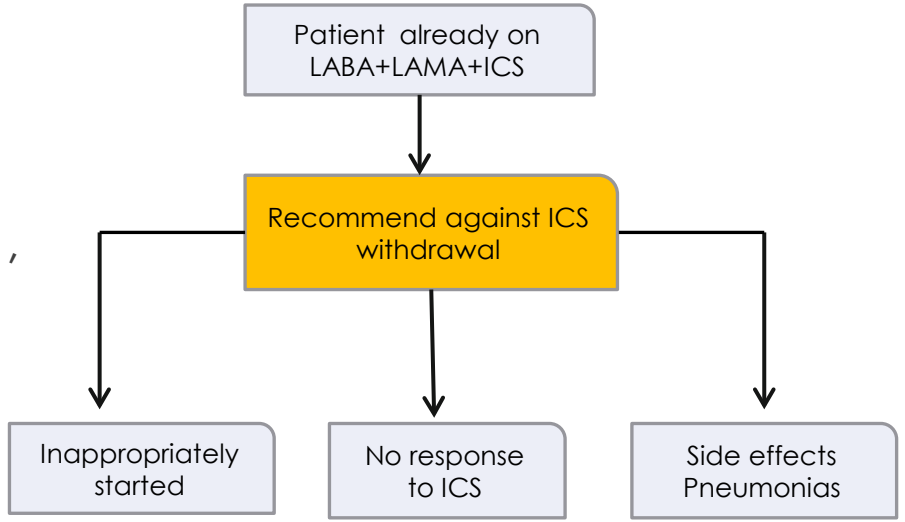
- 72-year-old ex smoker (30 PKY, quit 10 year ago) referred to establish care after moving to the city.
  - FEV1/FVC ratio 0.6, FEV1 65% predicted.
  - CAT 8, mMRC 1, no previous exacerbations, eosinophils 110
  - Currently on high dose LABA/ICS
- Treatment choices
  - Switch to LABA+LAMA
  - Reduce ICS dose



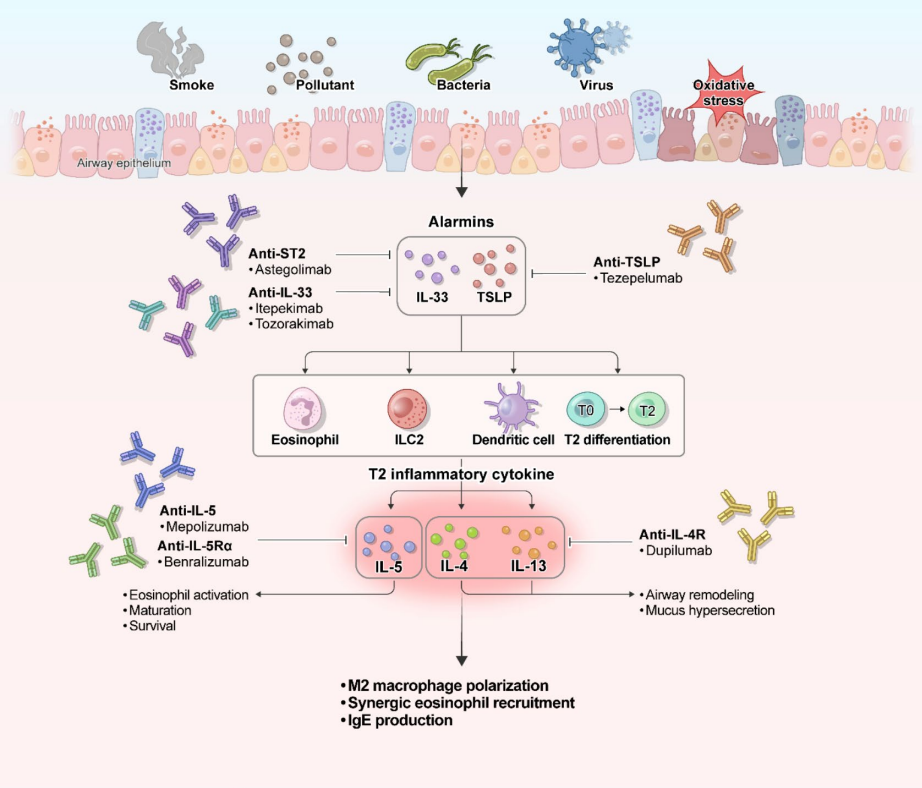
*Patient previously had exacerbations and responded to LABA+ICS treatment

Case 4 - *Patients on combination LABA+LAMA+ICS*

- 72-year-old ex smoker,(30PKY, quit 10 years ago), BMI 19 referred to establish care with pulmonary.
  - FEV1/FVC ratio 0.6, FEV1 65% predicted.
  - CAT 8, mMRC 1, one exacerbations 2 years ago , eosinophils during exacerbation 120
  - Currently on LABA/LAMA/ICS
- Treatment choice
  - Continue same treatment
  - Watch for side effects *(older patients with low BMI and exacerbations– high risk for pneumonia)*



Emerging therapies – *advancing phenotype driven approach to therapy*



Pathway	Drug	Study	Completion
Anti- TSLP	*Tezepelumab*	EMBARK JOURNEY	2029
Anti IL-33	*Itepekimab*	AERIFY-1 AERIFY-2	Completed
	Tozorakimab	OBERON TITIANA	3/2026
Anti-ST2	Astegolimab	ARNASA	Completed

Choi, Tub Res Dis 2026 in press

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Take home points

- A single moderate exacerbation warrants treatment escalation
- COPD management should target low disease activity with goal of no exacerbations.
- Ensifentrine can be added to treat persistent dyspnea in COPD
- Dupilumab and Mepolizumab are FDA approved biologics for COPD with TH2 inflammation.
- COPD patients should be actively screened and managed for multimorbidity.
- Emerging biologics will expand the phenotype driven therapy in COPD

Thank You

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Dr. Ehteshami Afshar's clinical expertise lies in the management of complex pulmonary conditions and sleep-related respiratory disorders, with a particular focus on patients with neuromuscular diseases. She diagnoses and treats acute and chronic respiratory failure requiring noninvasive home mechanical ventilation, sleep-related respiratory disorders including sleep apnea, and airway disease including asthma and chronic obstructive pulmonary disease (COPD). She also provides care for critically ill patients in the intensive care units (ICU).

Home Oxygen and Non-Invasive Ventilation in COPD

Solmaz Ehteshami Afshar, MD, MSc

Division of Pulmonary, Critical Care Medicine
Stanford University

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Objectives

- Understand the evidence behind oxygen and NIV use in COPD patients
- Understand the indications to initiate LTOT and/or NIV in COPD patients
- Understand the CMS criteria for RAD/NIV in COPD patients

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Long Term Oxygen Therapy

GOLD 2026 Guideline for Oxygen Therapy

- According to the **GOLD 2026 Report**, LTOT is indicated for stable patients with:
- **Group A: Severe Resting Hypoxemia**
  - PaO2≤55 mmHg OR
  - SpO2≤88%
- confirmed twice over a three-week period;

- **Group B: Moderate Hypoxemia with Complications**
  - PaO2 between **55–60** mmHg
  - **AND** evidence of:
    - Pulmonary hypertension
    - Peripheral edema suggesting Congestive heart failure
    - Polycythemia (hematocrit >55%)

Nocturnal Oxygen Therapy Trial (NOTT), 1980

Entry criteria
- Clinical diagnosis of chronic obstructive lung disease
- Hypoxemia
  - $Pa_{O_2} \leq 55$ mm Hg
  - $Pa_{O_2} \leq 59$ plus one of the following:
    - Edema
    - Hematocrit $\geq 55\%$
    - P pulmonale on ECG: 3 mm in leads II, III, aVf
- Lung function*
  - $FEV_1/FVC < 70\%$ after inhaled bronchodilator
  - TLC $\geq 80\%$ predicted
  - Age > 35

Exclusion criteria
- Previous O_2 therapy: 12 h/d for 30 days during previous 2 months
- Other disease that might be expected to influence mortality, morbidity, compliance with therapy, or ability to give informed consent

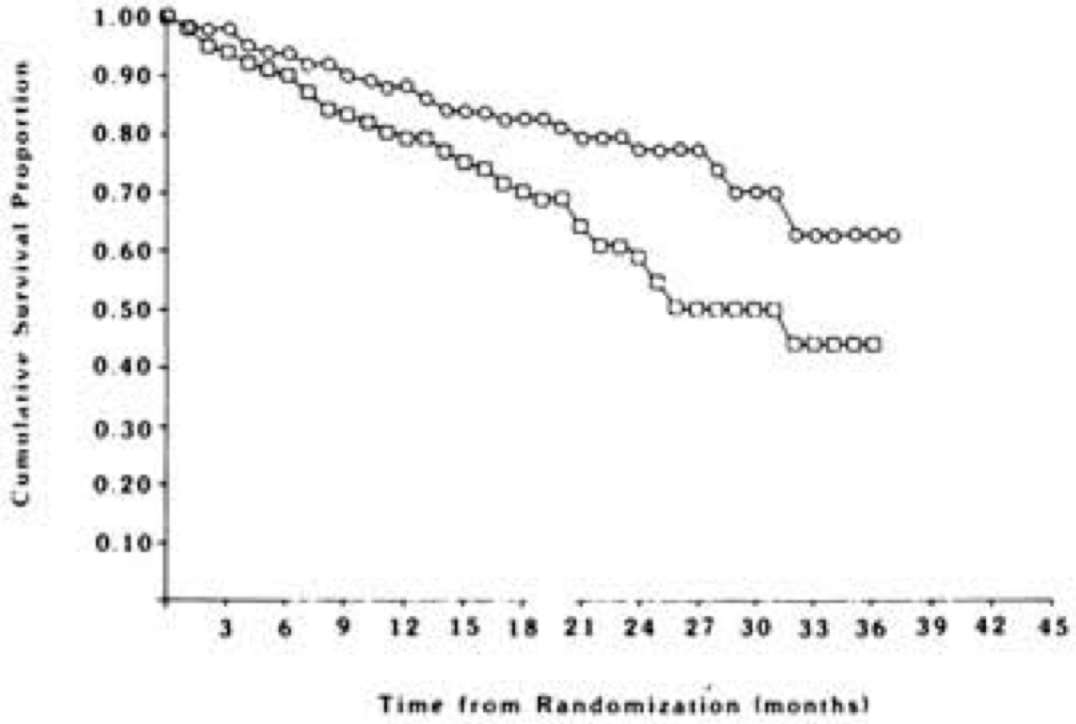
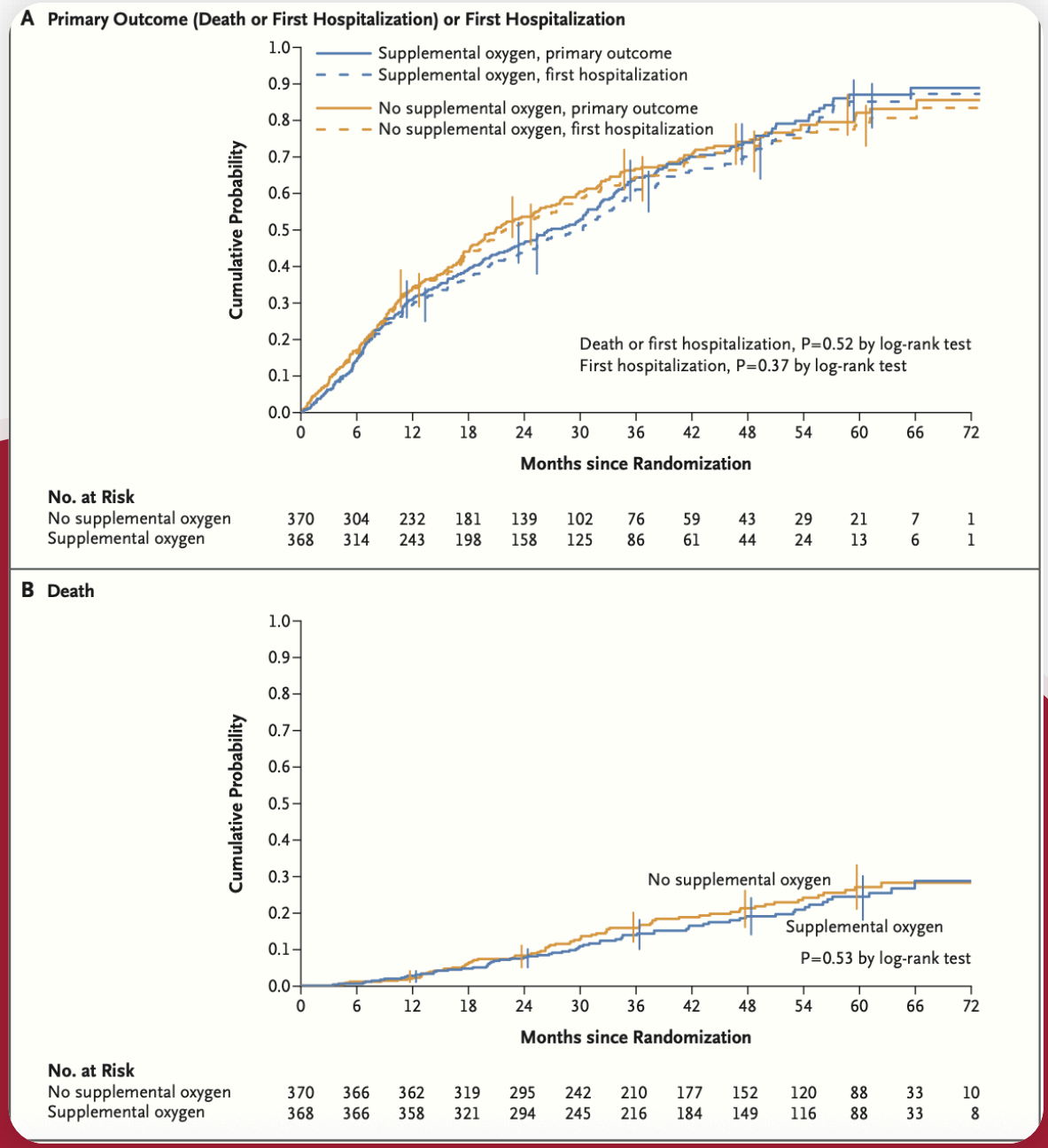


Figure 2. Overall mortality. Ordinate is fraction of patients surviving; abscissa is time from randomization or duration of treatment. Open circles represent continuous O_2 therapy group; squares represent nocturnal O_2 therapy group. Of the total group, 80 nocturnal O_2 and 87 continuous O_2 therapy patients were followed for 12 months, and 29 nocturnal O_2 and 37 continuous O_2 therapy patients were followed for 24 months.

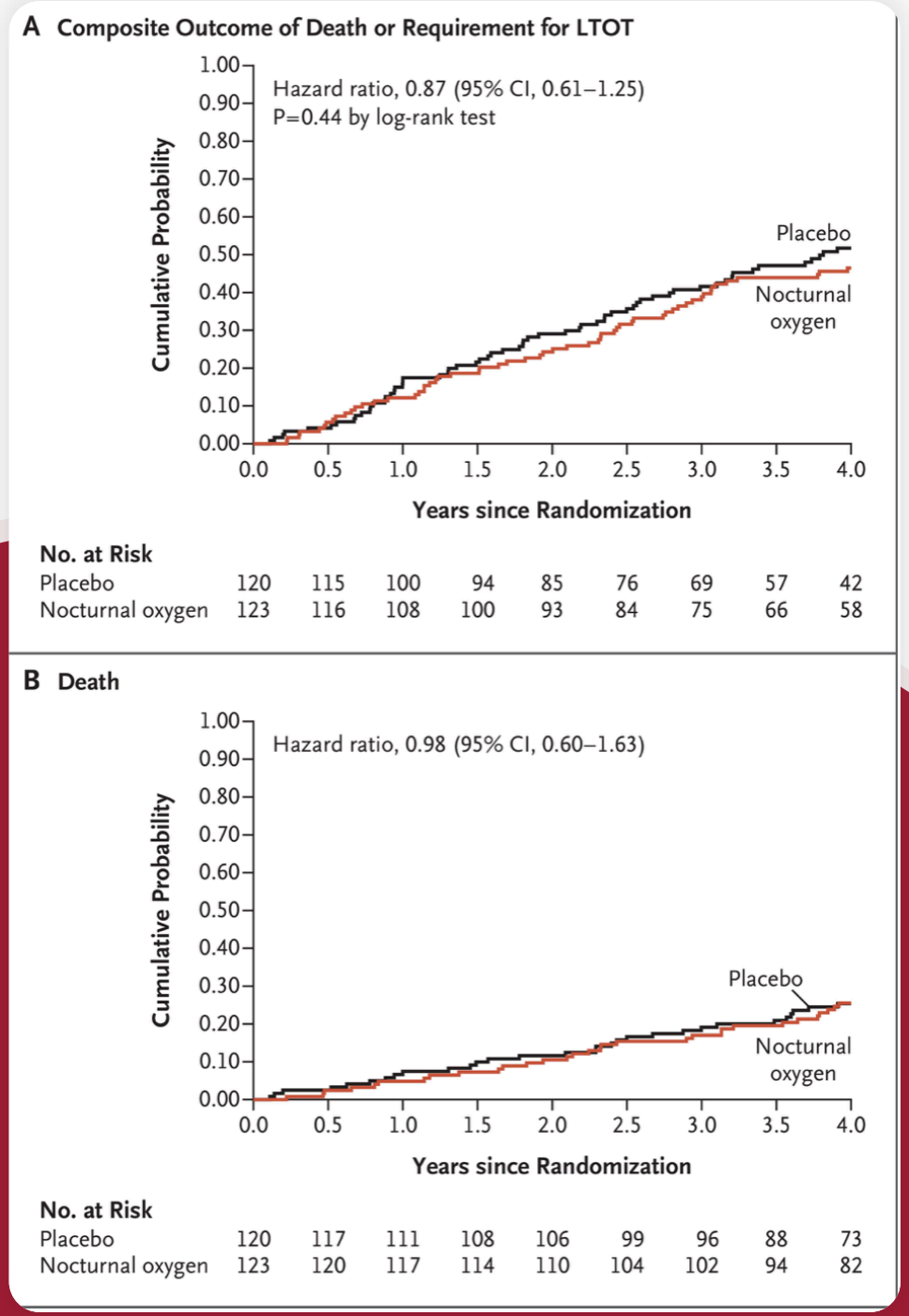
Ann Intern Med. 1980 Sep;93(3):391-8.

Long-Term Oxygen for COPD with Moderate Desaturation (LOTT)



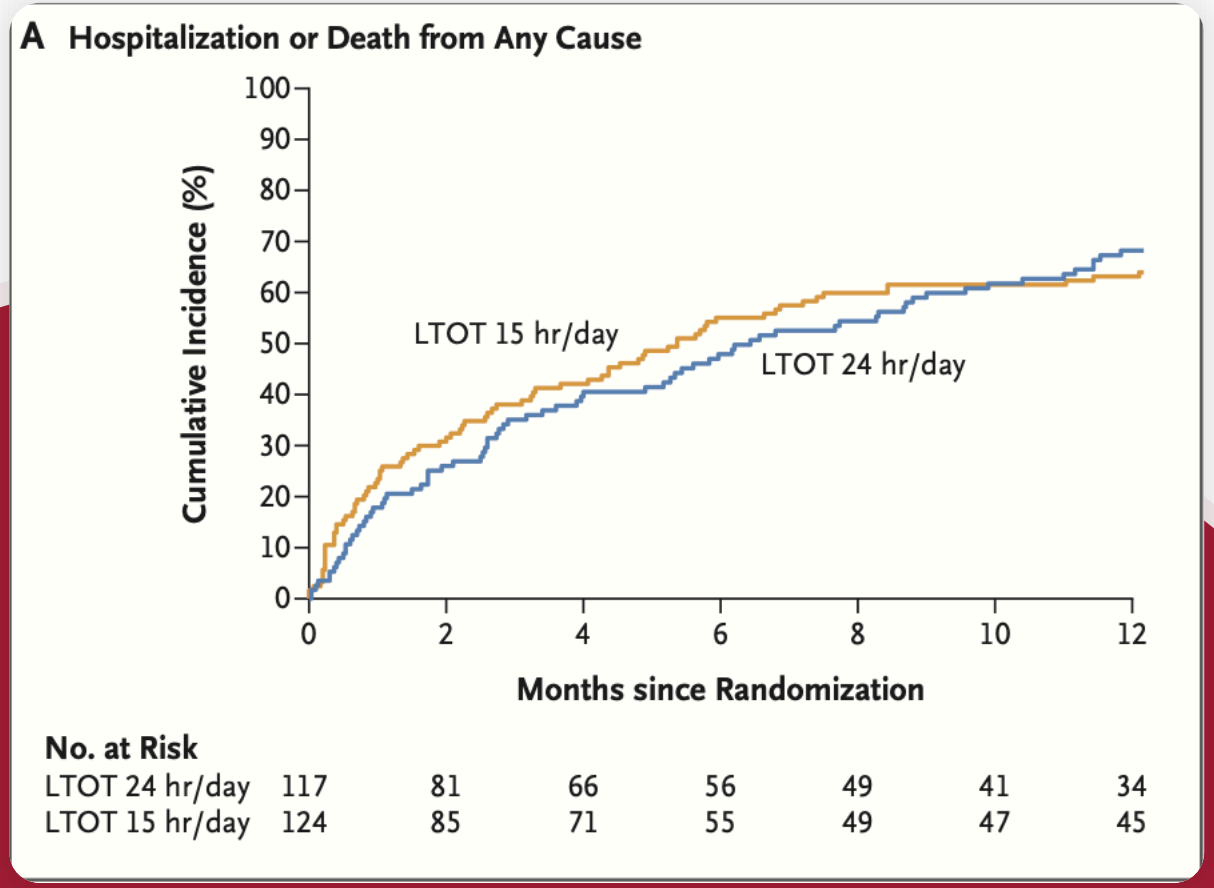
N Engl J Med 2016;375:1617-27.

Randomized Trial of Nocturnal Oxygen in Chronic Obstructive Pulmonary Disease (INOX)



N Engl J Med 2020;383:1129-1138

Long-Term Oxygen Therapy for 24 or 15 Hours per Day in Severe Hypoxemia



N Engl J Med 2024;391:977-88

ATS recommendations

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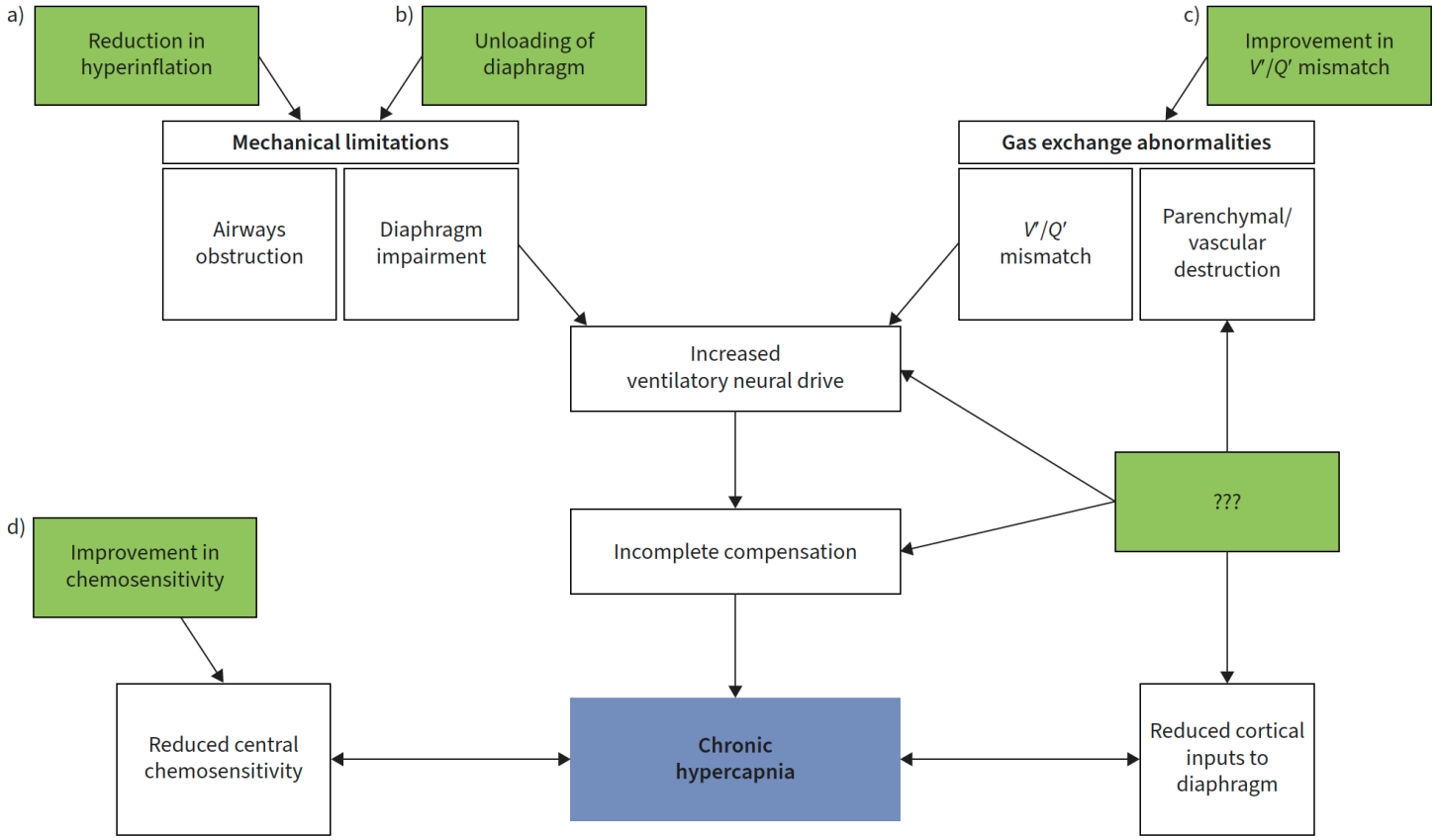
Table 4. Summary of ATS Recommendations

Question	ATS Recommendation	Strength of Recommendation and Level of Evidence
COPD		
Question 1: Should long-term oxygen be prescribed for adults with COPD who have severe* chronic resting room air hypoxemia?	In adults with COPD who have severe chronic resting room air hypoxemia, we recommend prescribing LTOT for at least 15 h/d.	Strong recommendation, moderate-quality evidence
Question 2: Should long-term oxygen be prescribed for adults with COPD who have moderate† chronic resting room air hypoxemia?	In adults with COPD who have moderate chronic resting room air hypoxemia, we suggest not prescribing LTOT.	Conditional recommendation, low-quality evidence
Question 3: Should ambulatory oxygen be prescribed for adults with COPD who have severe exertional room air hypoxemia?	In adults with COPD who have severe exertional room air hypoxemia, we suggest prescribing ambulatory oxygen.	Conditional recommendation, moderate-quality evidence

Am J Respir Crit Care Med Vol 202, Iss 10, pp e121–e141, Nov 15, 2020

Noninvasive mechanical ventilation (NIV)

Mechanisms of NIV in hypercapnic COPD



McCartney A, et al. Eur Respir Rev 2022; 31: 220069

NIV improve mortality

- Baseline PaCO2 ≥ 51.9 mmHg (mean 58.5 mmHg)
- No exacerbation within 4 weeks
- NIV targeted to reduce PaCO2 by at least 20% or < 48 mmHg
- Mean IPAP 21.6 cmH2O, EPAP 4.8 cmH2O, backup rate 16.1 breaths/min
- 1-year mortality 12% in NIV group vs 33% in control group

	3 months	6 months	9 months	12 months
Overall	0·8 (3·5)	2·1 (5·7)	0·9 (4·0)	2·6 (8·6)
Non-invasive positive pressure ventilation group	0·2 (1·1)	1·4 (4·7)	1·3 (4·9)	2·2 (10·2)
Control group	1·5 (4·9)	3·0 (6·9)	0·4 (1·9)	3·1 (5·4)

Values are mean (SD).

Table 2: **Emergency hospital admissions per patient by follow-up period and treatment group**

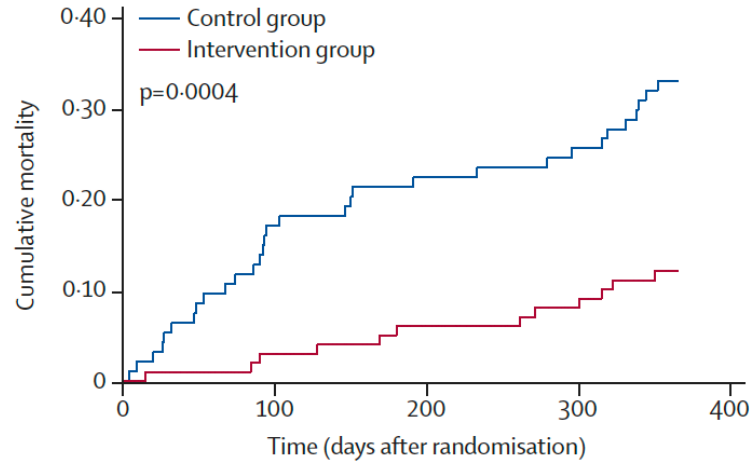


Figure 2: **Kaplan-Meier estimate of cumulative all-cause mortality during the first year after randomisation (primary outcome)**
The p value results from a log-rank test of the between-group difference.

Kohnlein et al. Lancet Respir Med. 2014 Sep;2(9):698-705.

NIV post exacerbation

Baseline PaCO2 > 53 mmHg (mean 59.0 mmHg)

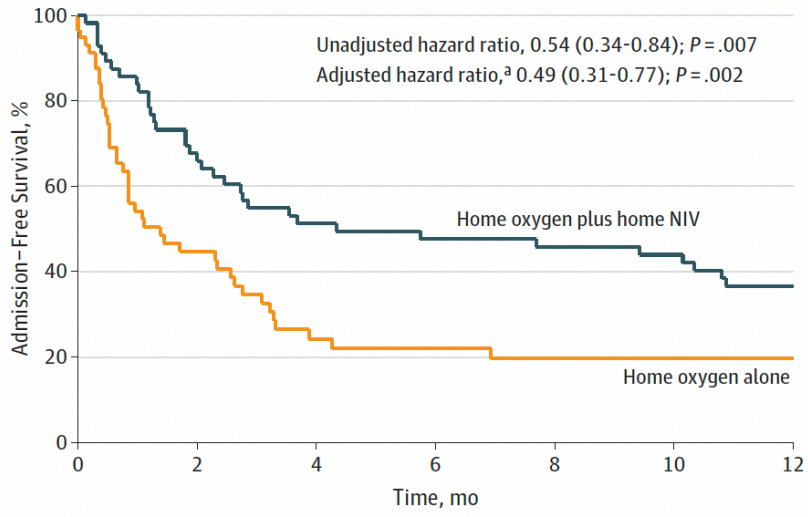
Persistent hypercapnia after acute COPD exacerbation (2-4 weeks after resolution of respiratory acidemia)

NIV targeted to reduce PaCO2 by 3.75 – 7.5 mmHg overnight

Mean IPAP 24 cmH2O, EPAP 4 cmH2O, backup rate 14 breaths/min

Mean time to readmission or death 4.3 months in NIV group vs 1.4 months in control group

Figure 2. Kaplan-Meier Survival Plot of Time to Readmission or Death From Randomization to the End of Trial Follow-up at 1 Year



No. at risk							
Home oxygen plus home NIV	57	37	28	26	25	24	16
Home oxygen alone	59	23	11	10	8	8	6

The median follow-up times were 8.1 months (interquartile range, 2.3-12.6 months) for the home oxygen therapy alone group and 12.2 months (interquartile range, 8.9-12.9 months) for the home oxygen therapy plus home noninvasive ventilation (NIV) group.

[a] Adjusted for number of chronic obstructive pulmonary disease readmissions within past year, prior use of long-term oxygen therapy, age, and body mass index.

Murphy et al. JAMA. 2017;317(21):2177-2186.

Timing of NIV initiation matters

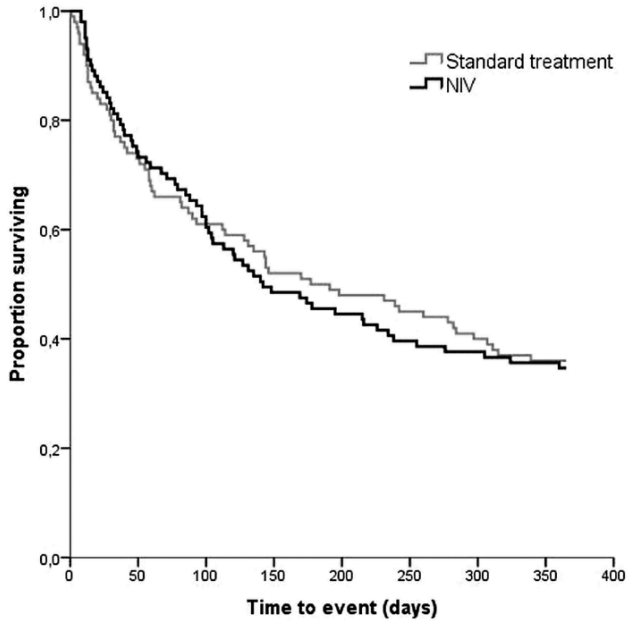


Figure 2 Kaplan–Meier plot of time to event (readmission for respiratory cause or death) in patients randomised to non-invasive positive pressure ventilation (NIV) and standard treatment.

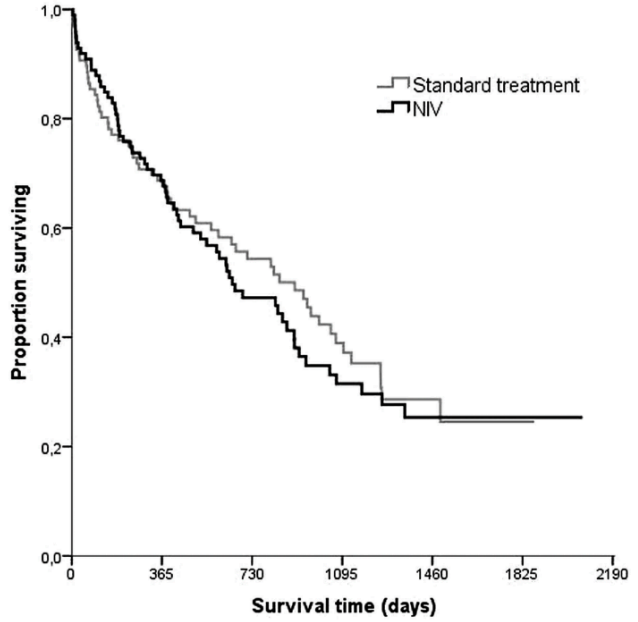
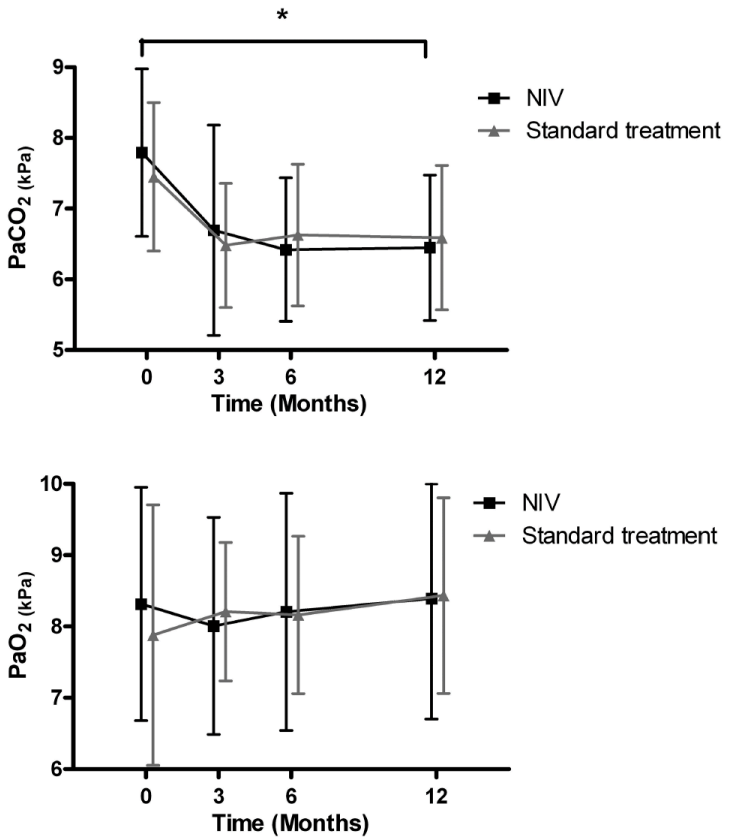


Figure 3 Kaplan–Meier plot of long-term survival curves of patients randomised to non-invasive positive pressure ventilation (NIV) and standard treatment. Because of small numbers of patients followed up after 3 years, the right-hand end of the survival plots remains uncertain.



Struik et al. Thorax. 2014;69:826-34

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Where to Start High Intensity NIV?

Table 2 Gas exchange

	Home, N=23			Hospital, N=26			Adjusted mean difference in change home versus in-hospital (95% CI)
	Baseline	3 months	6 months	Baseline	3 months	6 months	6 months–baseline
$PaCO_2$, kPa	7.3±0.9	6.7±0.9*	6.4±0.8**	7.4±1.0	6.5±0.5*	6.4±0.6**	0.04 (–0.31 to 0.38)
PaO_2, kPa	6.8±1.3	7.5±1.5	7.6±1.2	7.3±1.5	8.1±1.4*	8.0±1.2	–0.18 (–0.85 to 0.49)
HCO_3^-, mmol/L	33.1±3.8	30.8±3.2*	29.8±2.9*	33.6±4.2	30.2±2.1*	29.7±2.8**	0.2 (–1.5 to 1.2)

Data are shown as mean±SD. A positive mean difference means an increase from baseline to 6 months for the home compared with the in-hospital group.
Compared with baseline within the group: *p<0.05 and **p<0.001.
HCO_3^-, bicarbonate; kPa, kilopascal; $PaCO_2$, partial arterial carbon dioxide pressure; PaO_2, partial arterial oxygen pressure.

Table 4 Ventilatory settings

	Home, N=25			Hospital, N=28		
Group	Baseline	3 months	6 months	Baseline	3 months	6 months
IPAP, cm H_2O	21.0±2.8	22.1±2.9*	23.6±2.3*	24.3±3.6†	24.7±3.3†	25.7±3.4*†
EPAP, cm H_2O	4.5±0.8	4.6±0.9	4.6±0.9	5.7±1.2†	5.8±1.2†	6.0±1.3†
IPAP–EPAP, cm H_2O	16.5±2.6	17.5±2.5*	19.0±2.1*	18.6±3.3†	18.9±2.8†	19.7±2.7*
BURR, breaths/min	13.5±2.5	13.8±2.2	13.9±2.0	15.6±2.9†	15.3±2.9†	15.4±3.0†

*Significant increase from baseline to 3 months or from 3 months to 6 months.
†Significant difference between the groups at equal time points.
BURR, backup respiratory rate; EPAP, expiratory positive airway pressure;IPAP, inspiratory positive airway pressure.

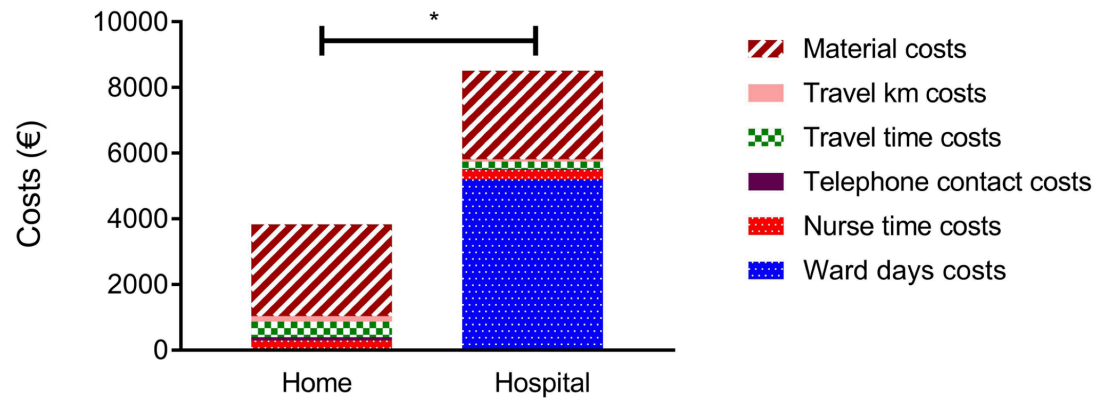

Figure 4 Costs (€) of NIV initiation hospital versus at home. Represented as median costs (€). Material: costs of the ventilator, telemedicine material and material/device for transcutaneous measurements; travel km: costs for travel kilometres of the specialised respiratory nurse; travel time: costs for travel time to the patients of the specialised respiratory nurse; telephone contact: costs for the time spend by the respiratory nurse to have telephone contact with the patients; nurse time: costs of the time spend by the specialised nurse directly with the patient; ward days: costs of the ward days. *p< 0.001. NIV, non-invasive ventilation.

Duiverman Thorax. 2020 Mar;75(3):244–252

Summary of ATS recommendations:

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Summary of recommendations chronic hypercapnic respiratory failure due to COPD (FEV1/FVC <0.70; resting PaCO2 > 45 mm Hg; not during exacerbation):

1. We **suggest** the use of NIV in addition to usual care for patients with **chronic stable hypercapnic COPD**.
2. We suggest that patients with chronic stable hypercapnic COPD undergo **screening** for OSA before initiation of long-term NIV.
3. We **suggest not** initiating long-term NIV during an admission for acute-on-chronic hypercapnic respiratory failure, favoring instead reassessment for NIV at 2–4 weeks after resolution.
4. We suggest not using an in-laboratory overnight polysomnogram (PSG) to titrate NIV in patients with chronic stable hypercapnic COPD who are initiating NIV.
5. We suggest NIV with targeted normalization of PaCO2 in patients with hypercapnic COPD on long-term NIV.

Macrea et al. Am J Respir Crit Care Med. 2020; 202(4): 74–87

Older version of CMS criteria to Qualify for NIV: COPD

ABG with $PaCO_2$ ≥ 52 mmHg (awake and on prescribed FiO_2)

AND

Sleep oximetry with oxygen saturation ≤ 88% for ≥ 5 cumulative minutes on 2 L/min O_2 or prescribed FiO_2 (whichever is higher)

AND

OSA and CPAP treatment have been considered and ruled out
(formal sleep testing not required)

E470 = Bilevel S

Conversion from S to ST

Situation 1 (after period of initial use of E0470):

ABG with $PaCO_2$ worsening ≥ 7 mmHg vs original ABG (awake and on prescribed FiO_2)

AND

Facility-based PSG on E470 with oxygen saturation ≤ 88% for ≥ 5 cumulative minutes (not caused by OSA – AHI < 5)

E471 = Bilevel ST

Situation 2 (no sooner than 61 days after initial use of E0470):

ABG with $PaCO_2$ ≥ 52 mmHg (awake and on prescribed FiO_2)

AND

Sleep oximetry on E470 with oxygen saturation ≤ 88% for ≥ 5 cumulative minutes on 2 L/min O_2 or prescribed FiO_2 (whichever is higher)

Courtesy of Dr. Singh

NEW CMS Qualifying Criteria for NIV for COPD

Baseline

ABG with $PaCO_2 \geq$ 52 mmHg (awake and on prescribed FiO_2)

AND

Sleep apnea not predominant cause of hypercapnia (formal sleep testing not required)

Additional Requirements: Stability, HI-NIV, Risk

No new/↑ in >1 resp symptom (cough, sputum production/purulence, wheezing, dyspnea) for ≥2 d and no change in meds for ≥2 wk **or** $PaCO_2$ ≥52 mmHg for ≥2 wk after hosp for + resolution of AECOPD requiring NIV

E471 = Bilevel S/T VAPS

AND

IPAP ≥15 cmH_2O, BUR ≥14/min (i.e., HI-NIV) by 6 mo

Intolerant of HI-NIV **or** BUR medically inappropriate

E470 = Bilevel S

FiO_2 ≥36% or 4L NC **or** vent support ≥8 hr/d **or** requirement for alarms + internal battery **or** unlikely to achieve clinical improvement criteria with E0470 or E0471

E0465, E0466, E0467, or E0468 = home vents (in volume-targeted mode)

Acute on chronic resp failure

Post-hosp D/C if
required vent within 24-hr prior to D/C
and deemed to be at risk of AECOPD
or ↑ $PaCO_2$ after D/C

E470 or E0471 **OR** E0465, E0466, E0467, or E0468 = home vents (in volume-targeted mode) if needs exceed E0470 or E0471

Courtesy of Dr. Singh

Continued Coverage Requirements

both devices:

- Evaluations by end of month 6 AND during months 7–12
- Adherence threshold: ≥4 h/24h on ≥70% of days (30-day period at 6-month eval; then each paid rental month)

RAD (6-month eval requires ≥1 clinical outcome):

- $PaCO_2$ normalize <46, OR stabilize rising $PaCO_2$, OR 20% $PaCO_2$ reduction, OR symptom improvement

HMV (6-month eval):

- adherence only (no separate physiologic outcome requirement specified)

Summary

- **Who** truly benefits from long-term oxygen therapy and/or NIV?
- **What** is the evidence behind these recommendations?
- **How** to operationalize that with current ATS guideline and the updated CMS coverage pathway?

Thank you

- Michelle Cao , MD
- Gaurav Singh , MD
- CTS leadership

Dr. Chopra received his medical degree from the University of Cincinnati. He subsequently completed his Internal Medicine Residency Banner University Medical Center Phoenix and Pulmonary Critical Care Fellowship at Banner University Medical Center Tucson. He then went to complete an Interventional Pulmonary Fellowship at Penn State. His clinical focus includes robotic bronchoscopy, rigid bronchoscopy and endobronchial valve placement. He is passionate about teaching bronchoscopy and pleural procedure to pulmonary and critical care fellows. He currently serves as Assistant Professor of Medicine at the University of Arizona College of Medicine - Tucson.

Hype, Hope and Hard Truths: Endobronchial Valves in COPD

Madhav Chopra MD

Assistant Professor

University of Arizona College of Medicine-Tucson

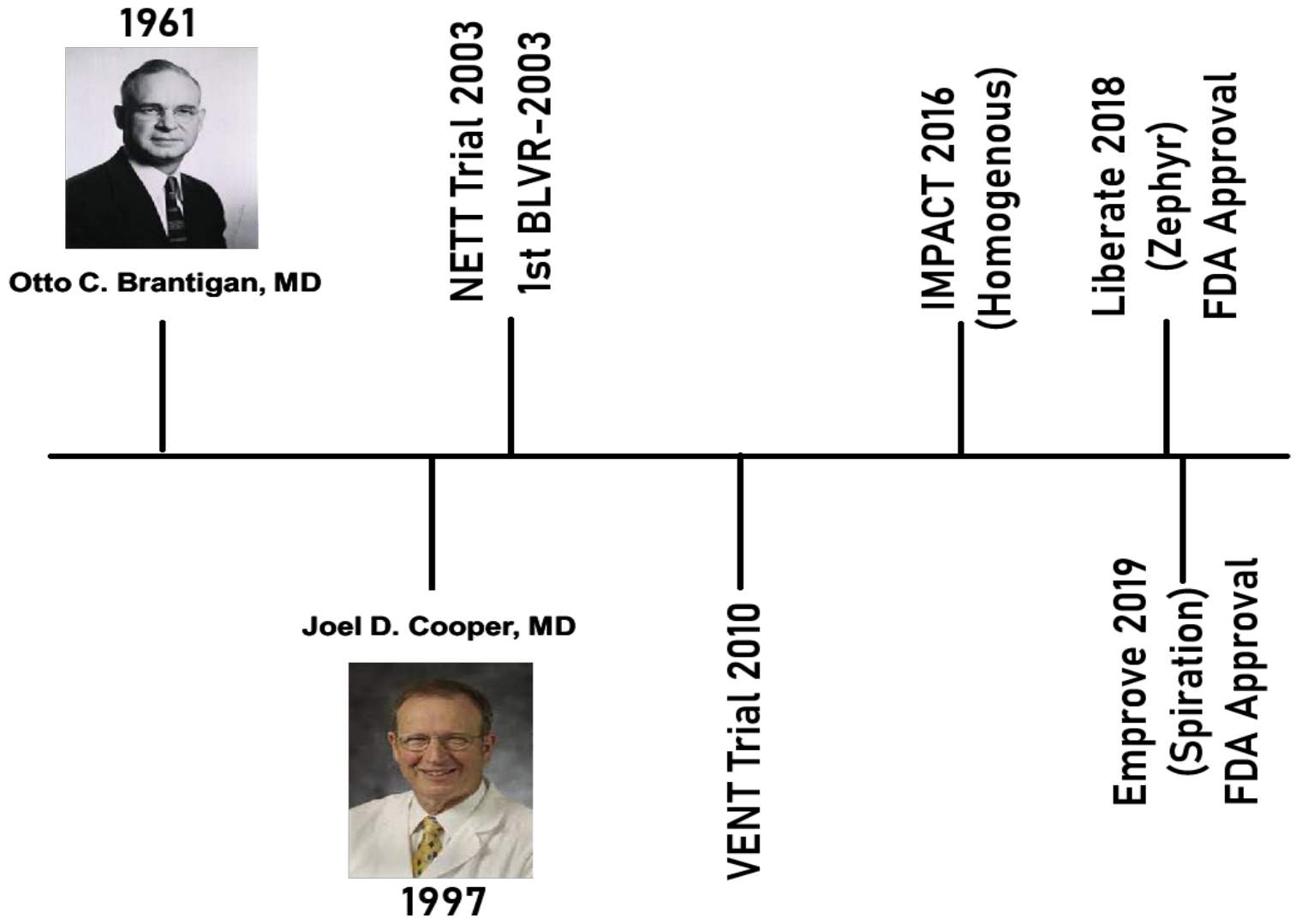
Disclosures

- I have the following relationships with ACGME defined ineligible companies: **None**
- I **WILL NOT** discuss off-label use and/or investigational use of any drugs or devices.

Objectives

- Review Bronchoscopic Lung Volume Reduction (BLVR)
- Discuss the Benefits of BLVR
- Identify the Risks and Limitations of BLVR
- Outline Strategies for Patient Selection for BLVR

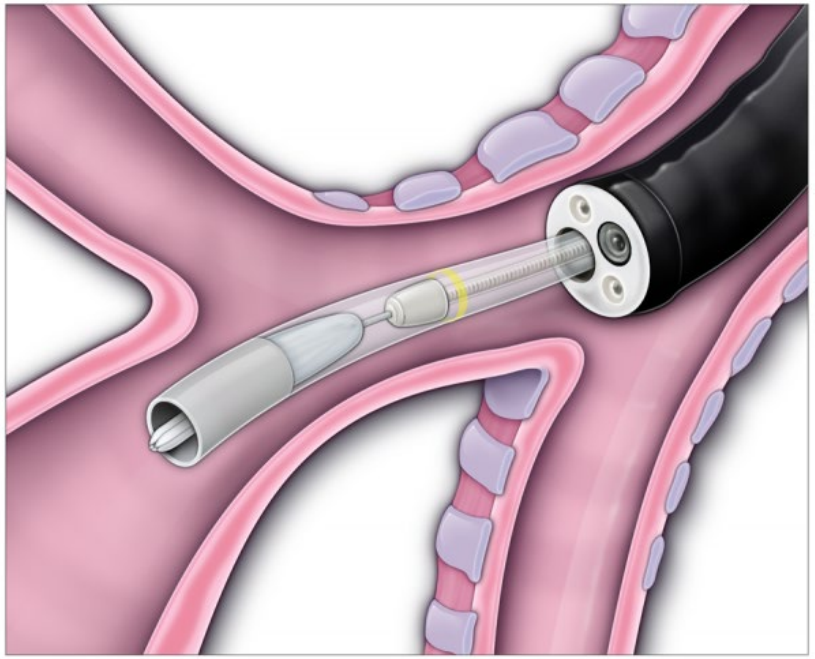
Brief History of Lung Volume Reduction

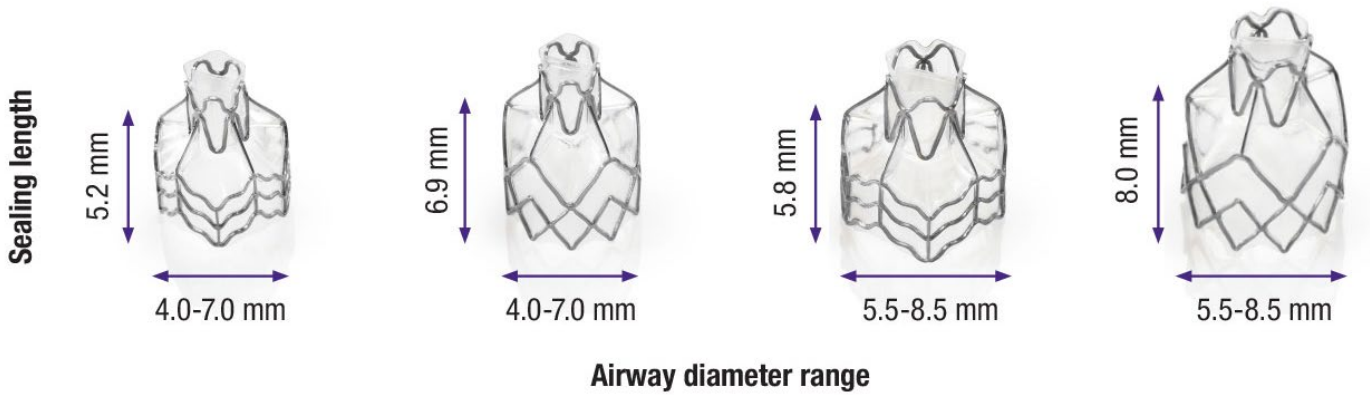


Endobronchial Valves (EBVs)

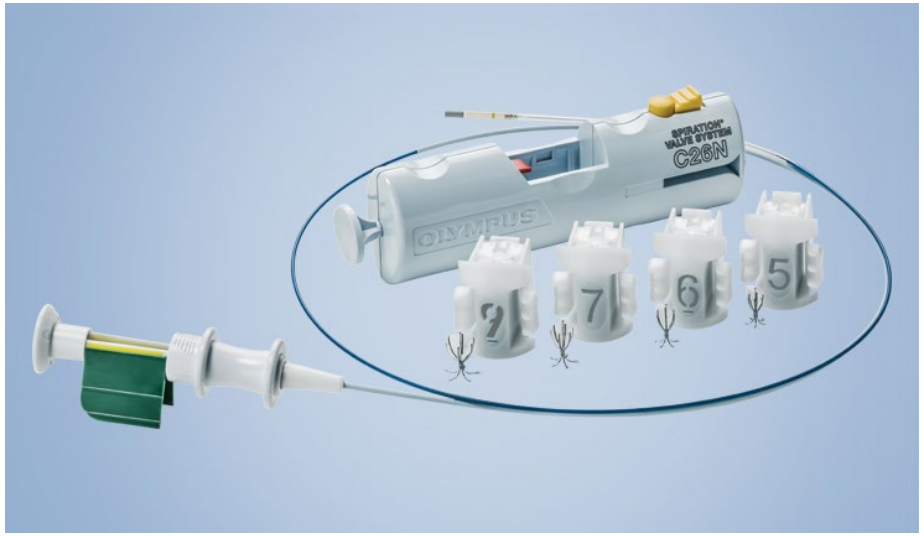
- EBVs are one-way valves that restrict expiratory flow from lung segments, reducing hyperinflation of treated downstream lung parenchyma
- Indicated for adult emphysema with lobar hyperinflation in regions with little or no collateral ventilation
- Deployed through flexible bronchoscopy using a delivery catheter and are retrievable
- There are Two FDA approved EBV systems for BLVR in COPD

EBVs





Zephyr valve system (Pulmonx; Palo Alto, CA)



Spiration valve system (Olympus; Redmond, WA)

EBVs

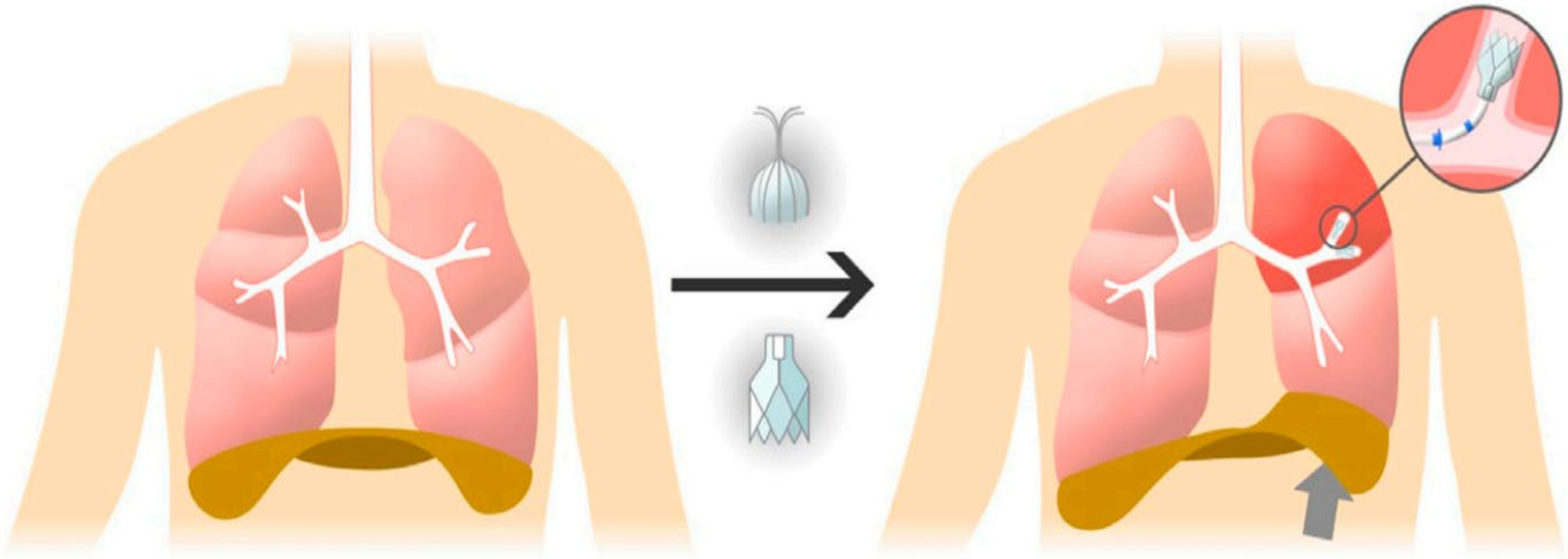
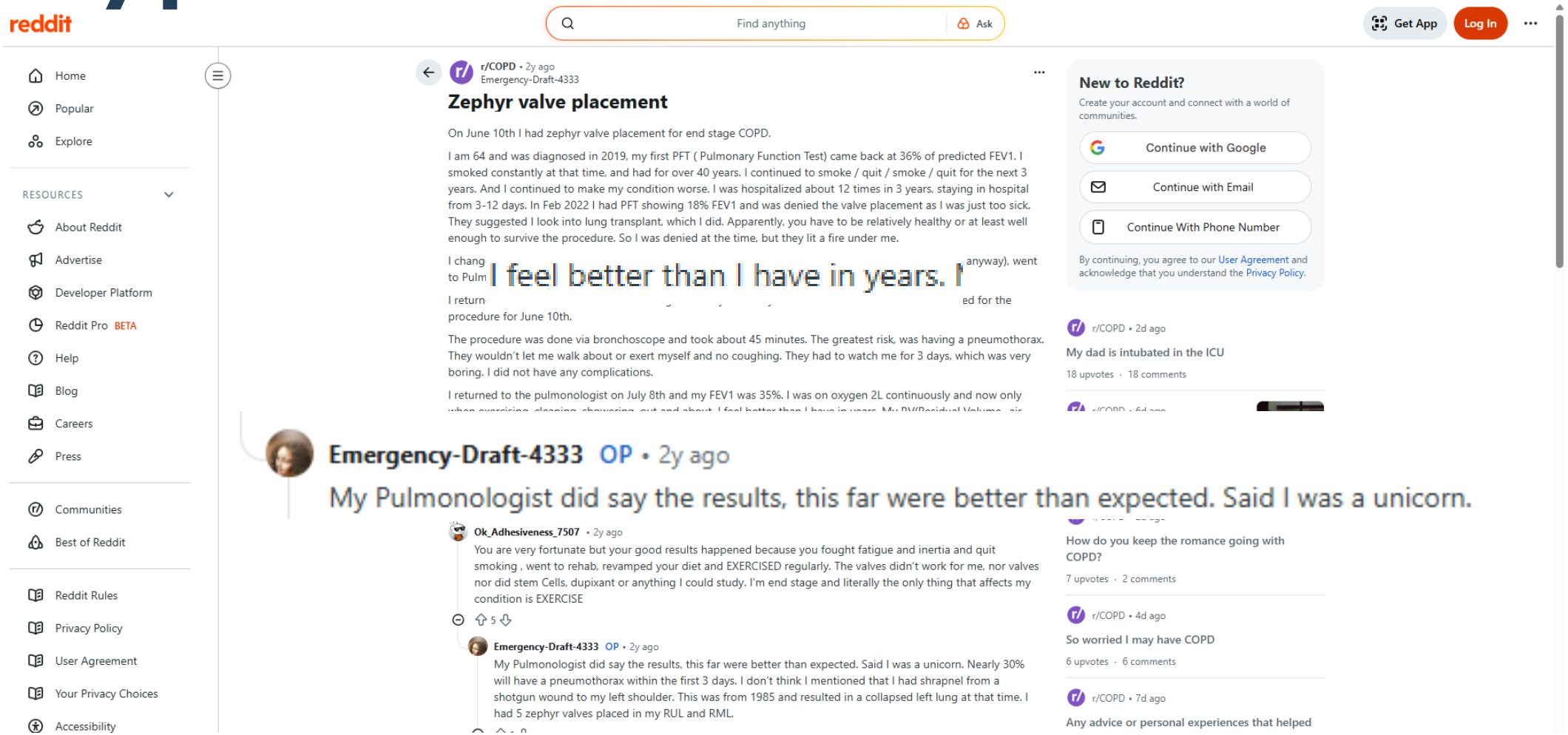


Figure 1. Effect of endobronchial valve (EBV) on target lung lobe and diaphragm. Before EBV placement, the left upper lobe is hyperinflated and the diaphragm is flattened because of trapped air within the lung (left). After EBV placement, the left upper lobe is deflated and the diaphragm is no longer flattened (right). Illustration courtesy of Arnon Brand, PhD.

Gesthalter YB, Maheshwari J. Bronchoscopic Lung Volume Reduction with Endobronchial Valves for Emphysema. ATS Sch. 2025 Jun;6(2):252-254.

Hype


reddit
Find anything
Ask
Get App
Log In
Home
Popular
Explore
RESOURCES
About Reddit
Advertise
Developer Platform
Reddit Pro BETA
Help
Blog
Careers
Press
Communities
Best of Reddit
Reddit Rules
Privacy Policy
User Agreement
Your Privacy Choices
Accessibility
r/COPD • 2y ago
Emergency-Draft-4333
Zephyr valve placement
On June 10th I had zephyr valve placement for end stage COPD.
I am 64 and was diagnosed in 2019, my first PFT (Pulmonary Function Test) came back at 36% of predicted FEV1. I smoked constantly at that time, and had for over 40 years. I continued to smoke / quit / smoke / quit for the next 3 years. And I continued to make my condition worse. I was hospitalized about 12 times in 3 years, staying in hospital from 3-12 days. In Feb 2022 I had PFT showing 18% FEV1 and was denied the valve placement as I was just too sick. They suggested I look into lung transplant, which I did. Apparently, you have to be relatively healthy or at least well enough to survive the procedure. So I was denied at the time, but they lit a fire under me.
I chang
anyway), went
to Pulm
I feel better than I have in years. I
I return
ed for the
procedure for June 10th.
The procedure was done via bronchoscope and took about 45 minutes. The greatest risk, was having a pneumothorax. They wouldn't let me walk about or exert myself and no coughing. They had to watch me for 3 days, which was very boring. I did not have any complications.
I returned to the pulmonologist on July 8th and my FEV1 was 35%. I was on oxygen 2L continuously and now only
Emergency-Draft-4333 OP • 2y ago
My Pulmonologist did say the results, this far were better than expected. Said I was a unicorn.
Ok_Adhesiveness_7507 • 2y ago
You are very fortunate but your good results happened because you fought fatigue and inertia and quit smoking , went to rehab, revamped your diet and EXERCISED regularly. The valves didn't work for me, nor valves nor did stem Cells, dupixant or anything I could study. I'm end stage and literally the only thing that affects my condition is EXERCISE
5
Emergency-Draft-4333 OP • 2y ago
My Pulmonologist did say the results, this far were better than expected. Said I was a unicorn. Nearly 30% will have a pneumothorax within the first 3 days. I don't think I mentioned that I had shrapnel from a shotgun wound to my left shoulder. This was from 1985 and resulted in a collapsed left lung at that time. I had 5 zephyr valves placed in my RUL and RML.
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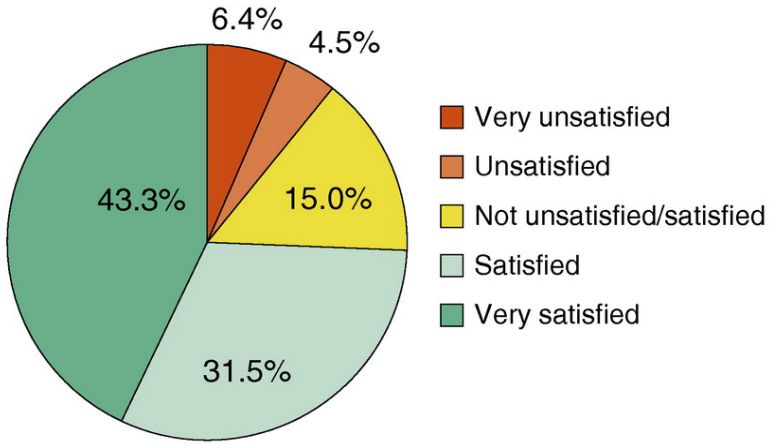
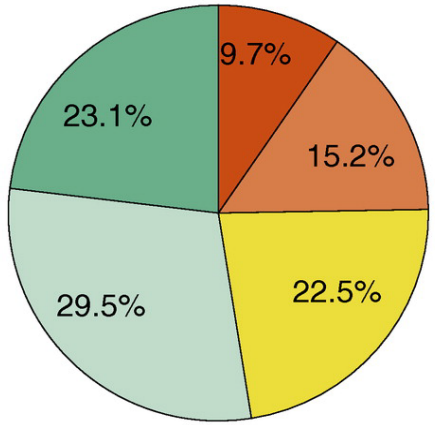
Continue with Google
Continue with Email
Continue With Phone Number
By continuing, you agree to our User Agreement and acknowledge that you understand the Privacy Policy.
r/COPD • 2d ago
My dad is intubated in the ICU
18 upvotes · 18 comments
How do you keep the romance going with COPD?
7 upvotes · 2 comments
r/COPD • 4d ago
So worried I may have COPD
6 upvotes · 6 comments
r/COPD • 7d ago
Any advice or personal experiences that helped

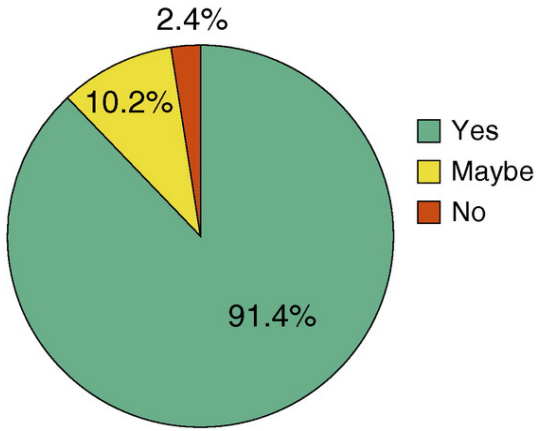
1) How satisfied are you with the treatment?



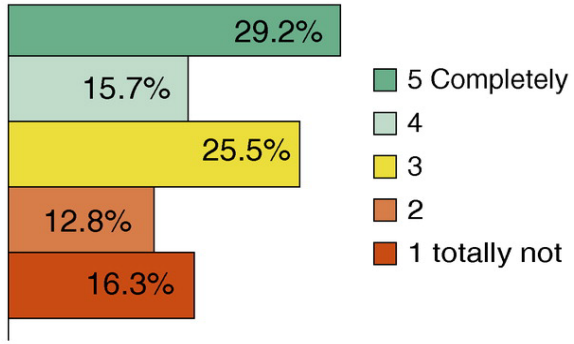
2) How satisfied are you with the reduction of your symptoms after treatment?



3) Would you recommend the treatment to other patients?



4) Does the result of the treatment fulfill your expectations?



Jorine E. Hartman; Karin Klooster; Nick H. T. ten Hacken; Marlies van Dijk; Dirk-Jan Slebos; Annals ATS 1868-74.

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HOPE-Physiological Benefits of BLVR

- Reduction in hyperinflation which leads to improved respiratory muscle mechanics and decreased work of breathing
- Decreased residual volume and total lung capacity with sustained improvements in gas transfer
- Redistribution of ventilation and perfusion to healthier lung regions, improving V-Q matching and overall lung efficiency
- Improved cardiac preload, contractility, and cardiac output without increasing pulmonary artery pressures

Global Initiative for Chronic Obstructive Lung Disease. 2025; American Journal of Respiratory and Critical Care Medicine. 2016. Valipour A, Slebos DJ, Herth F, et al ; Annals of the American Thoracic Society. 2020. Dransfield MT, Garner JL, Bhatt SP, et al.

Interventional Therapy in Stable COPD

Figure 3.22

Lung Volume Reduction Surgery	• Lung volume reduction surgery improves survival in patients with severe emphysema who have an upper-lobe and low post-rehabilitation exercise capacity **(Evidence A)**
Bullectomy	• In selected patients, bullectomy is associated with decreased dyspnea, improved lung function and exercise tolerance **(Evidence C)**
	• In appropriately selected patients with very severe COPD, lung transplantation has been shown to improve quality of life and functional capacity **(Evidence C)**
Bronchoscopic Interventions	• In select patients with advanced emphysema, bronchoscopic interventions reduce end-expiratory lung volume and improve exercise tolerance, health status and lung function at 6-12 months following treatment. Endobronchial valves **(Evidence A)**; Lung coils **(Evidence B)**; Vapor ablation **(Evidence B)**
Bronchoscopic Interventions	• In select patients with advanced emphysema, bronchoscopic interventions reduce end-expiratory lung volume and improve exercise tolerance, health status and lung function at 6-12 months following treatment. Endobronchial valves **(Evidence A)**; Lung coils **(Evidence B)**; Vapor ablation **(Evidence B)**
Bronchoscopic Interventions Under Study	• Phase III trials are currently being conducted to determine the efficacy of treatments for patients with refractory exacerbations and chronic bronchitis using cryospray, rheoplasty and targeted lung denervation technology

HOPE-Benefits of BLVR

A 68-year-old woman with severe emphysema and hyperinflation undergoes bronchoscopic lung volume reduction with endobronchial valves. At 6-month follow-up, which of the following outcomes is MOST likely compared to baseline?

A. Increase in FEV_1 by approximately 140 mL with no change in exercise capacity

B. Improvement in FEV_1, 6-minute walk distance, and St. George's Respiratory Questionnaire scores all exceeding minimal clinically important differences

C. Decreased residual volume with worsening quality of life scores

D. No significant change in lung function but improved exacerbation rates and no longer on supplemental oxygen

E. Improvement in FVC only, with no change in FEV_1 or exercise capacity

AJ RCCM. 2016. Valipour A, Slebos DJ, Herth F, et al ; Annals of the ATS. 2020. Dransfield MT, Garner JL, Bhatt SP, et

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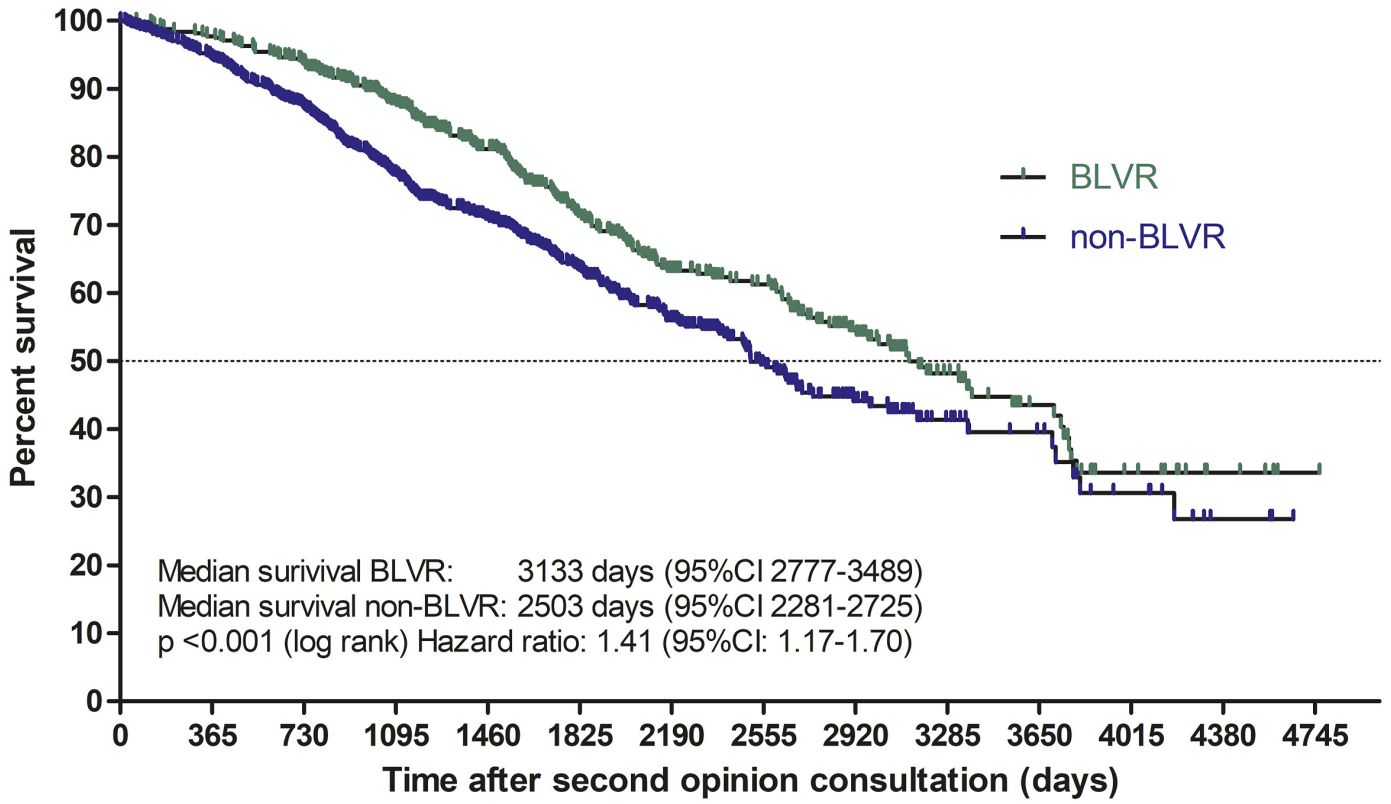
Does Lung Volume Reduction Surgery Improve Mortality?

Do Endobronchial Valves Improve Mortality?

Kaplan-Meier Plot



Numbers at risk(censored)

Year:	1	2	3	4	5	6	7	8	9	10	11	12	13
BLVR	483(0)	472(8)	445(61)	358(56)	277(51)	196(37)	139(19)	116(21)	83(28)	47(15)	28(8)	14(9)	5(4)	1(1)
non-BLVR	988(0)	934(33)	830(145)	599(99)	453(114)	298(74)	194(62)	115(40)	64(32)	29(9)	19(4)	11(7)	3(3)	

.Respir Med. 2022 May;196:106825. doi: 10.1016/j.rmed.2022.106825. Epub 2022 Mar 16. PMID: 35325741.

HARD TRUTHS- Contraindications

Structural Lung Disease	Presence of interlobar collateral ventilation
	Incomplete or absent fissure integrity (<90% complete on HRCT)
	Significant bronchiectasis
	Large bullae
	Pleural adhesions
Infectious/Inflammatory	Repeated infectious complications
	Active pulmonary infection
Malignancy	Suspicious pulmonary nodules requiring evaluation
	Active malignancy
Cardiovascular	Unstable cardiovascular comorbidities or LVEF <45%
	sPAP >45mm Hg
Functional Status	6-minute walking distance <100 m
Lung Function	Residual volume <150% of predicted
	Total lung capacity <100% of predicted
Arterial Blood Gas	Severe hypoxemia PaO_2 ≤45 mm Hg
	Severe hypercapnia $PaCO_2$ ≥50 mm Hg
Smoking Status	Active smoking or cessation 4 months or greater

Respiration; 2016. Slebos DJ, Shah PL, Herth FJ, Valipour A. ; Mayo Clinic Proceedings. 2023. Martin MJ, Dulohery Scrodin MM, Edell ES, et al.

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Complications

- **Pneumothorax-** Most common complication (18-27% of patients) **typically occurs within 72hours**. Upper lobe treatment has a 6-fold higher risk. High target lobe volume and high residual volume are independent risk factors for pneumothorax development.
  - -Risks can be minimized with the following ventilator settings low FIO2, minimal PEEP and reduce TV with placement of final valve
- -**Pneumonia-** occurs approximately 4-6% of patients, occurring distal to the valves. Valve removal maybe necessary in about half of these cases
- **COPD exacerbations requiring hospitalization-** occur most frequently within 90 days affecting approximately 8% of patients
- **Hemoptysis-** occurs in approximately 5-6% of patients, typically due to oozing from granulation tissue formation.
- **Mechanical Complications:**
  - Valve migration, aspiration, or expectoration (approximately 2-5% of patients)
  - Valve dislocation due to granulation tissue formation
- **Repeat Bronchoscopy-** is required in approximately 20-35%

The New England Journal of Medicine. 2010. Sciurba FC, Ernst A, Herth FJ, et al. ; Respirology. 2025. Jørgensen KH, Christensen TD, Titlestad IL, et al ; Journal of Thoracic Disease. 2018. Fiorelli A, D'Andrilli A, Bezzi M, et al.

A 64-year-old man with severe COPD underwent placement of four Endobronchial Valves in the Left Upper Lobe. Approximately, 48 hours after placement he had a pneumothorax. He underwent successful chest tube placement but was noted to have persistent air leak on waterseal10 days after endobronchial valve (EBV) placement for lung volume reduction. Despite chest tube drainage, the air leak continues. Which of the following is the MOST appropriate next step in management?

A. Instillation of Talc in the Chest Tube for Chemical Pleurodesis

B. Removal of 1-2 endobronchial valves

C. Place an additional chest tube or replace existing chest tube with a larger bore tube

D. Continue chest tube drainage for an additional 2 weeks before considering further intervention

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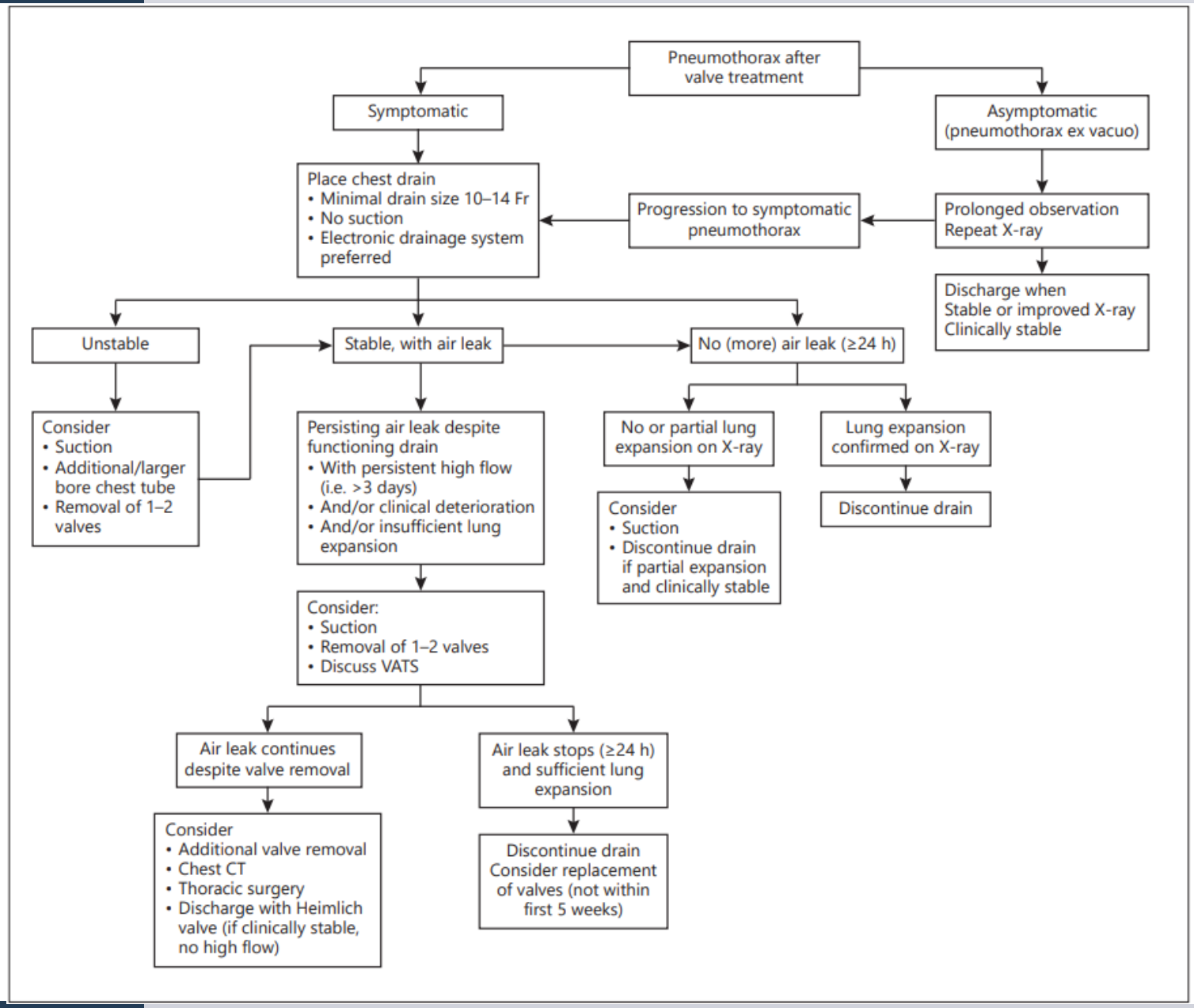

Respiration. 2021;100(10):969-978. doi: 10.1159/000516326.

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Minimum Criteria for Referral

1. Confirmed diagnosis of COPD
2. Non-smoking or willing to quit smoking
3. FEV_1 < 50% predicted
4. Breathless despite optimal medical management (mMRC≥2)

Patient Selection

Clinical and Physiological Criteria:

- **Symptomatic patients with GOLD stage 3 or 4 COPD ,severe emphysema and hyperinflation**
- Key physiological thresholds include residual volume >150/175% predicted, FEV_1 <50% predicted, and 6-minute walking distance >100 m
- Caution when ≥4 liters per minute supplemental oxygen, low or high BMI and moderate pulmonary hypertension

Patient Prerequisites:

- Optimal medical therapy, completed pulmonary rehabilitation, and be willing to quit smoking

Anatomical Requirements:

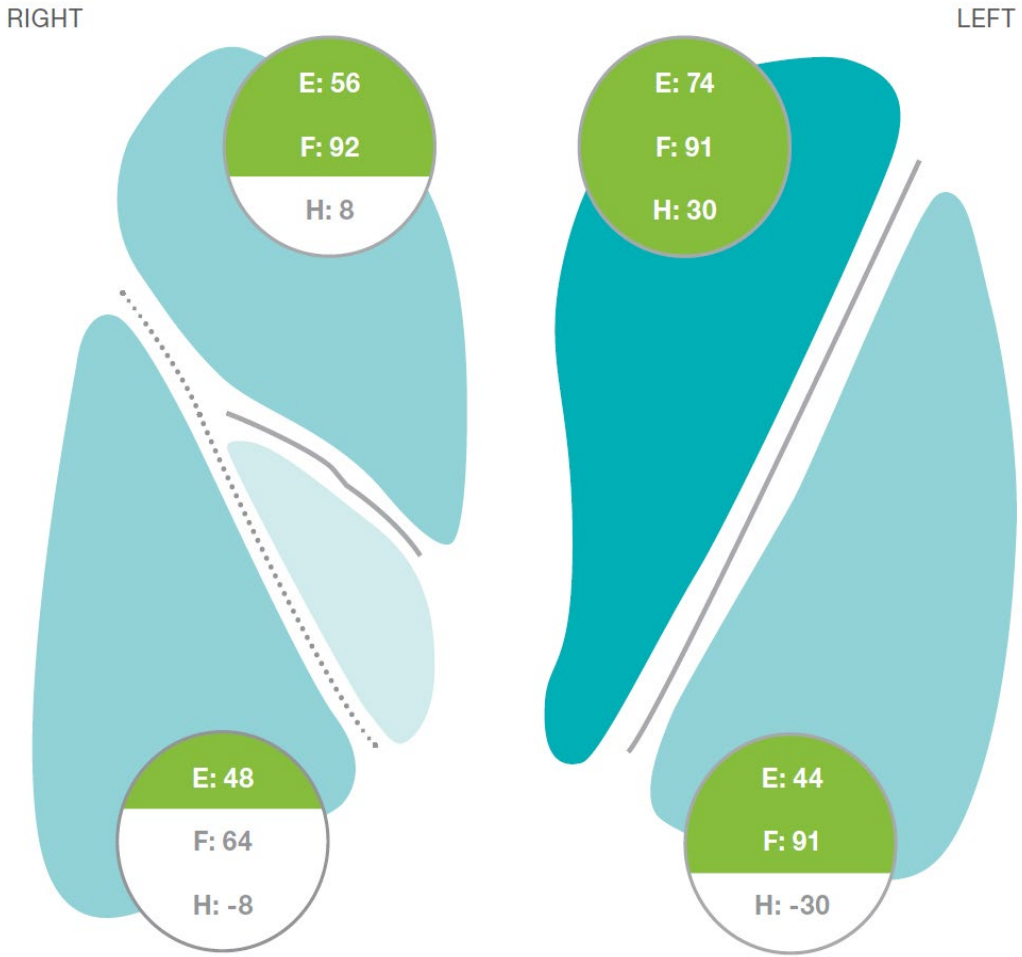
- Fissure integrity on high-resolution CT or physiological assessment using endoscopic balloon occlusion (Chartis system)
- Target lobe selection is based on quantitative CT analysis and ventilation-perfusion scintigraphy
- Airway anatomy considerations including shape, size and position of carina

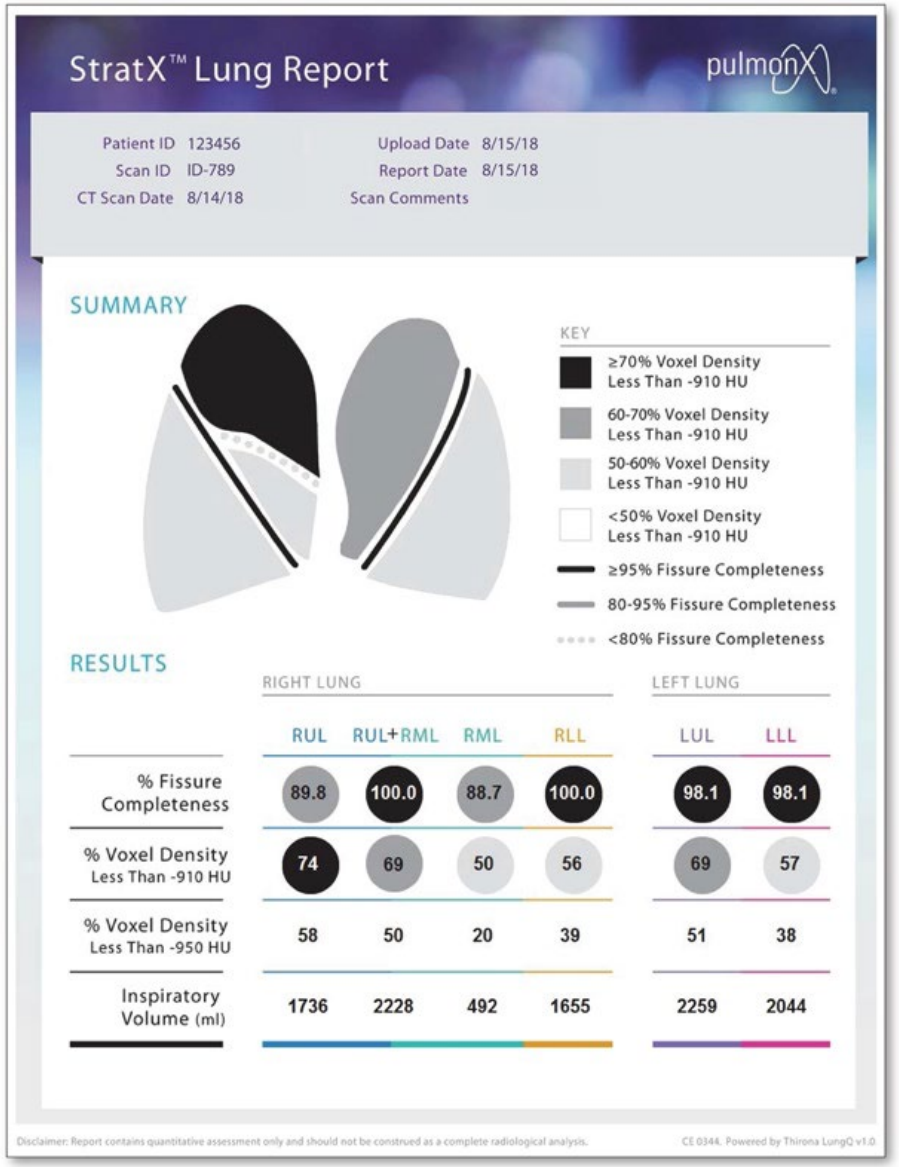
Respiration; International Review of Thoracic Diseases. 2025. Wahidi MM, Lentz RJ, Criner GJ, et al.

Patient Selection

- ❑ Medical history
  - ❑ Diagnosis of emphysema
  - ❑ BMI < 35 kg/m^2
  - ❑ Stable with ≤ 20mg prednisone (or equivalent) daily
  - ❑ Non-smoking
  - ❑ Collect any available imaging and lung function studies
  - ❑ Pulmonary Rehab
- ❑ 6MWD (100m–500m)
- ❑ Pulmonary Function Tests (post-bronchodilator)
  - ❑ Spirometry (FEV_1 15–45% predicted)
  - ❑ Body Plethysmography (RV ≥ 175%, TLC ≥ 100% for Heterogenous emphysema and RV ≥ 200% predicted, TLC ≥ 100% predicted for Homogeneous emphysema)
- ❑ Imaging
  - ❑ High Resolution CT (≤ 1.5mm slice thickness, TLC view)
  - ❑ Stratx and Select Scan
  - ❑ Perfusion Scan
- ❑ Arterial Blood Gas Levels collected on room air
  - ❑ Rule out severe hypercapnia PaCO2 ≥50 mm Hg
  - ❑ Rule out severe hypoxemia PaO2 ≤45 mm Hg
- ❑ Echocardiogram
  - ❑ Rule out congestive heart failure, LVEF <45%
  - ❑ Rule out uncontrolled pulmonary hypertension, sPAP >45mm Hg

CT Analysis





StratX™ Lung Report

pulmonX

Patient ID 123456
Scan ID ID-789
CT Scan Date 8/14/18
Upload Date 8/15/18
Report Date 8/15/18
Scan Comments

SUMMARY

KEY
- ≥70% Voxel Density Less Than -910 HU
- 60-70% Voxel Density Less Than -910 HU
- 50-60% Voxel Density Less Than -910 HU
- <50% Voxel Density Less Than -910 HU
- ≥95% Fissure Completeness
- 80-95% Fissure Completeness
- <80% Fissure Completeness

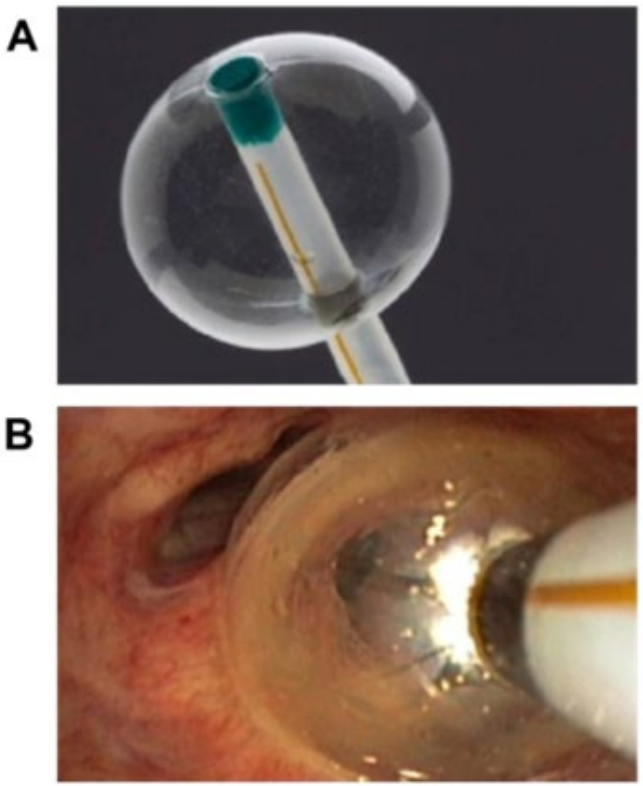
RESULTS

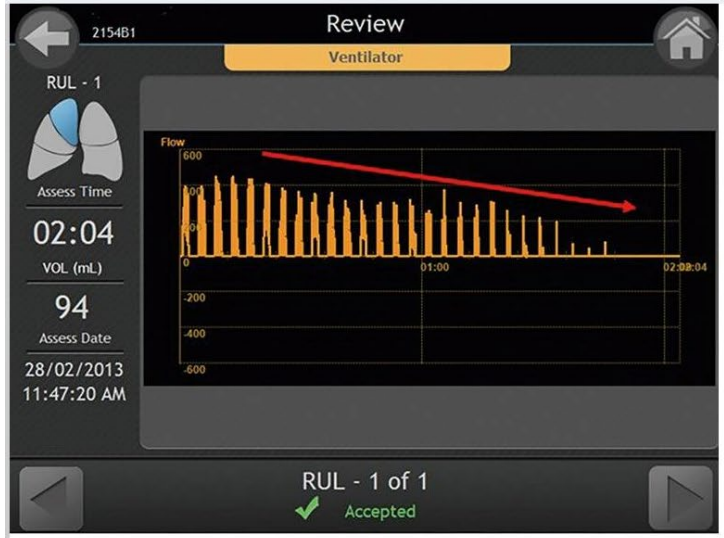
	RIGHT LUNG				LEFT LUNG	
	RUL	RUL+RML	RML	RLL	LUL	LLL
% Fissure Completeness	89.8	100.0	88.7	100.0	98.1	98.1
% Voxel Density Less Than -910 HU	74	69	50	56	69	57
% Voxel Density Less Than -950 HU	58	50	20	39	51	38
Inspiratory Volume (ml)	1736	2228	492	1655	2259	2044

Disclaimer: Report contains quantitative assessment only and should not be construed as a complete radiological analysis.

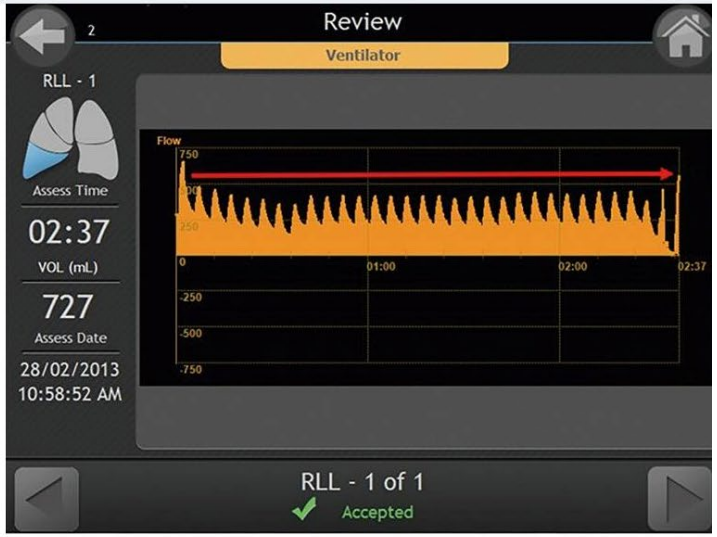
CE 0344. Powered by Thirona LungQ v1.0

CHARTIS





Collateral ventilation negative



Collateral ventilation positive

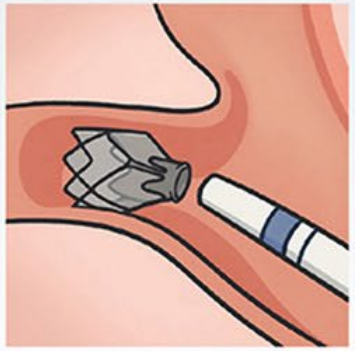
Respiration; International Review of Thoracic Diseases. 2025. Wahidi MM, Lentz RJ, Criner GJ, et al.

COPD

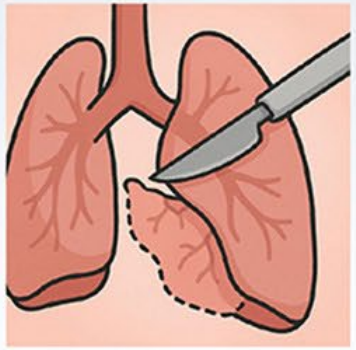
How Does a Comprehensive Approach to Lung Volume Reduction Encompassing Both Surgical and Endobronchial Treatment Translate Into Clinical Benefits?

STUDY DESIGN

- Prospective study of a comprehensive **lung volume reduction** (LVR) program in Belgium
- Assessed outcomes of patients with COPD that underwent bronchoscopic LVR with endobronchial valves (EBVs) (N = 73) or lung volume reduction surgery (LVRS) (N = 131)



EBV



LVRS

RESULTS

Transplant free survival:

- EBV vs usual care **(HR, 0.14; 95% CI, 0.04-0.44)**
- LVRS vs usual care (HR, 0.7; 95% CI, 0.45-1.2)

	EBV	LVRS	Usual Care
3-year mortality rate	8.2%	12.2%	17.7%
% transplant	1.4%	3.1%	8%

The findings of this study suggest that LVR programs should cover both surgical and bronchoscopic interventions to improve outcome and prognosis of patients with severe emphysema.

CHEST® Pulmonary

Janssens W, et al. *CHEST Pulmonary* | 2025
@journal_CHEST | https://doi.org/10.1016/j.chpulm.2025.100194

Post Procedure Management

BLVR VISIT PROTOCOLS

VISIT	ABG	TTE	QUESTIONNAIRES	PFT & 6MWT	CT CHEST	CXR
Initial	X	X	MMRC, SGRQ, BODE, CAT	X	X	
1 Week			MMRC			X
6 Week			MMRC		X	
3 Month			MMRC, SGRQ, BODE, CAT	X		
6 Month			MMRC	X		
1 Year			MMRC	X	X	

Respiration; International Review of Thoracic Diseases. 2025. Wahidi MM, Lentz RJ, Criner GJ, et al.

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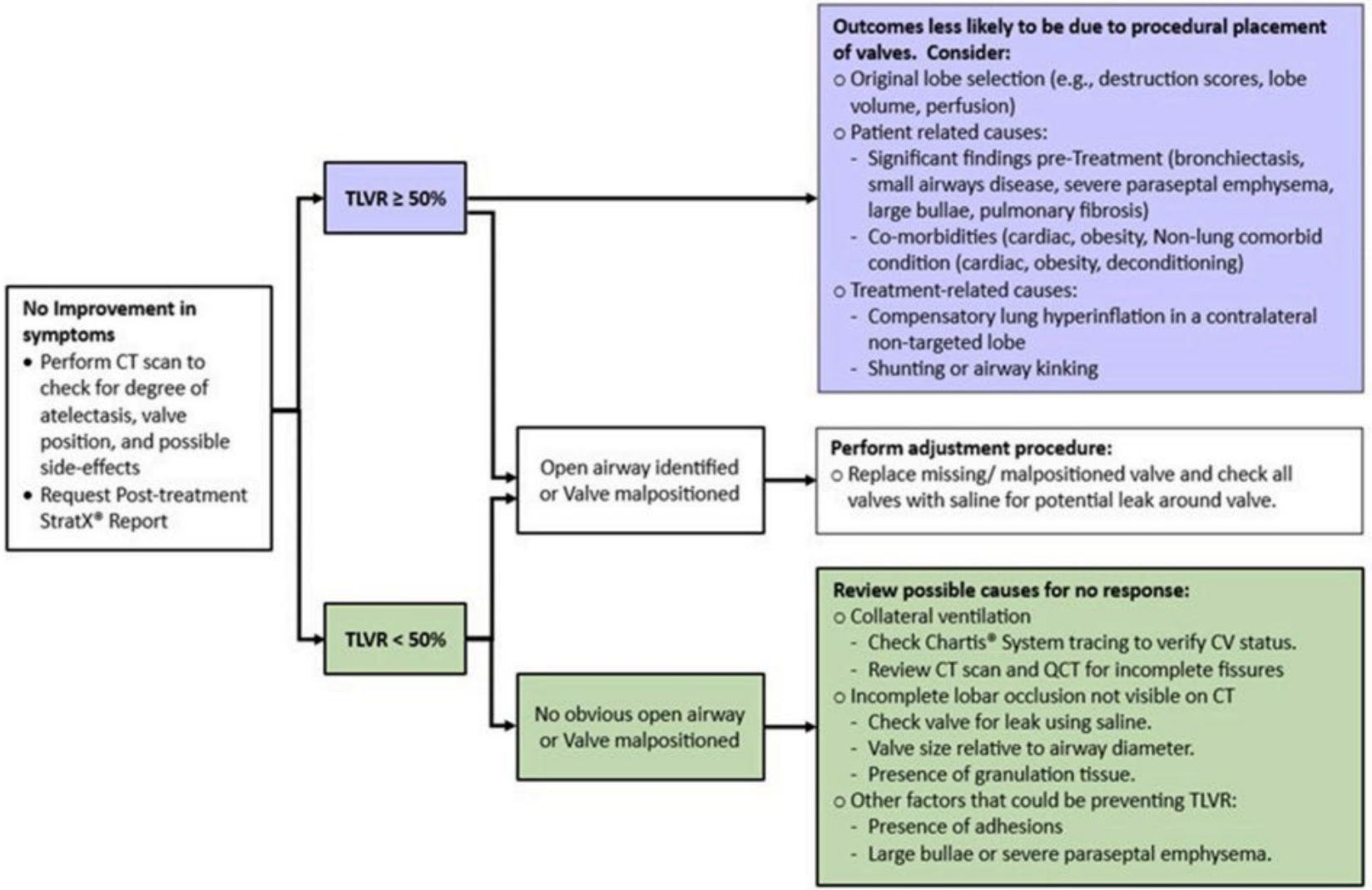


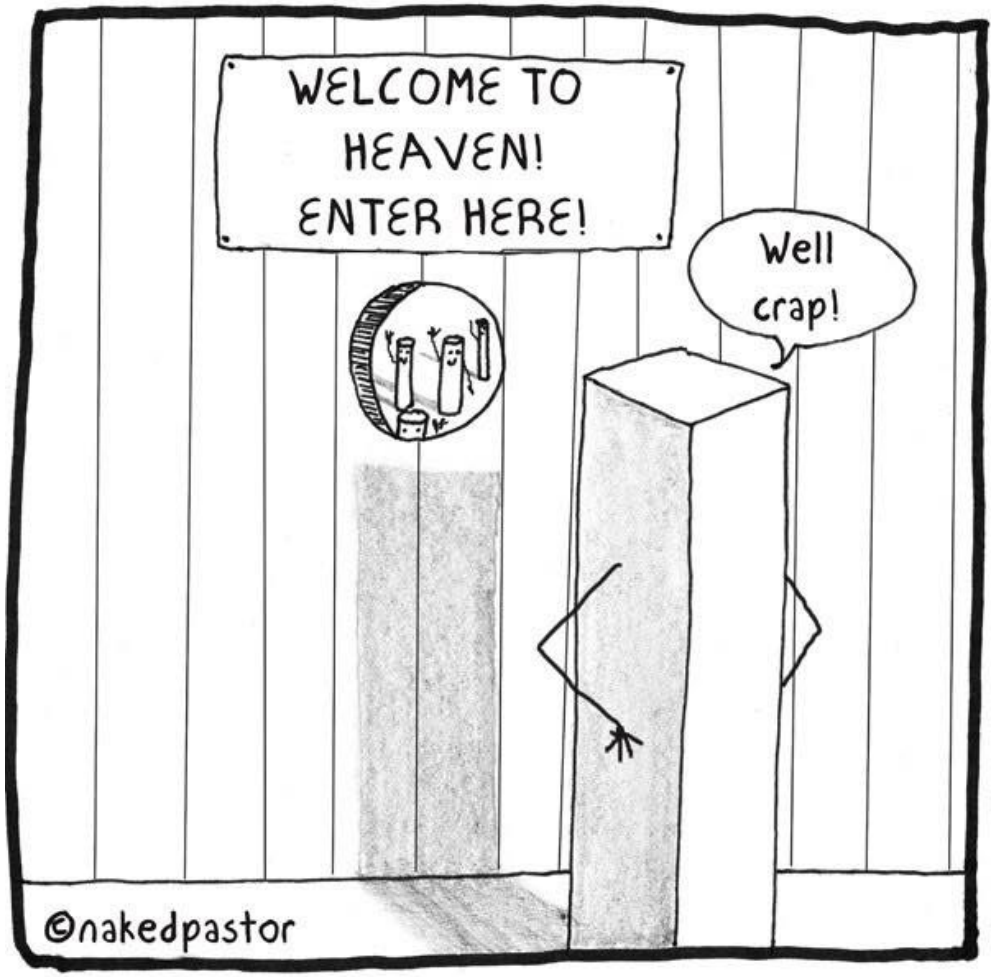
Fig. 6. Algorithm for managing inadequate response.

TAKE HOME POINTS

- The goal of BLVR is symptom improvement not complete lobar atelectasis
- Multidisciplinary review of clinical, radiological, and physiological data is essential
- Post-procedure hospital admission for a minimum of three nights
- An effective BLVR program requires oversight and a BLVR Nurse Coordinator can optimize patient care, safety, experience, efficiency, and overall outcomes
- Set reasonable expectations with patients regarding the benefits of BLVR

CHEST, Volume 159, Issue 5, 2090 - 2098

Questions?



Dr. Casaburi completed his undergraduate degree in electrical engineering, and (in 1971) a doctorate in biomedical engineering at Rensselaer Polytechnic Institute. He traveled to Los Angeles for post-doctoral bioengineering studies at the University of Southern California. Five years after joining the Department of Medicine faculty at Harbor-UCLA Medical Center, Dr. Casaburi pursued his medical degree at the University of Miami. Returning to Harbor-UCLA, he completed clinical training and rejoined the Division of Respiratory Medicine faculty. He served as Division Chief for six years and currently holds the rank of Distinguished Professor of Medicine at the UCLA School of Medicine.

Dr. Casaburi established the Rehabilitation Clinical Trials Center in 1999, dedicated to improving COPD patient's lives. He and co-workers have completed more than 80 clinical research studies, including three major NIH multicenter projects. He has presented over 800 invited lectures on respiratory physiology, exercise science, pulmonary rehabilitation, and COPD management. He has published more than 430 papers and 360 abstracts. His papers have received over 100,000 citations; his h-index is 107.

Dr. Casaburi is a Fellow of the American College of Chest Physicians, American Thoracic Society, European Respiratory Society and American Association of Cardiovascular and Pulmonary Rehabilitation. He received the 2020 European Respiratory Society Presidential Award and the 2021 Lifetime Achievement Award from the Pulmonary Rehabilitation Assembly of the ATS. He is a member of the Board of Directors of the COPD Foundation.

He currently serves as co-director of the Exercise Physiology and Respiratory Medicine Institute within the Lundquist Institute for Biomedical Innovation at Harbor-UCLA Medical Center.

Pulmonary Rehabilitation for COPD

Richard Casaburi, PhD, MD

Distinguished Professor of Medicine

Lundquist Institute at Harbor-UCLA Medical Center

Disclosures

- I have the following relationships with ACCME defined ineligible companies:
  - **Consultant for Inogen, Inc.**
- I **WILL NOT** discuss off-label use and/or investigational use of any drugs or devices.

ATS Journals | American Journal of Respiratory and Critical Care Medicine

Title: Pulmonary Rehabilitation Prolongs Life…And May Be Dying

Authors: Christopher L. Mosher, MD, MHS[1,2], Richard Casaburi, PhD, MD[3,4]

Editorial, in Press

Our message is that pulmonary rehabilitation program availability in the United States is shrinking when it should be expanding.

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Eras of Pulmonary Rehabilitation

- Pre-history –1950s Alvan Barach posits benefits of exercise for COPD
- The Dawn – 1969 Tom Petty organizes the first pulmonary rehabilitation program
- The Rise – 1970s-1980s Pulmonary rehabilitation programs expand
- The Rationale - 1990s Physiologic basis for pulmonary rehabilitation elucidated
- The Refinement - 2000s Small trials test rehabilitation enhancements
- The Mobilization – 2010s Enhancing physical activity is explored as a goal
- The Panic – 2020s Alternate modes explored to counter limited access

Saturday 11:40AM -12:10 PM: Aimee Kizziar and Julia Rigler Debate
"Virtual Pulmonary Rehabilitation is Ready for Prime Time"

Unequivocal Benefits in COPD

Pulmonary rehabilitation:

- improves exercise tolerance
- improves the symptom of dyspnea
- improves health-related quality of life

These benefits are generally of greater magnitude than for any other COPD therapy

Comparison of Benefits of Long-Acting Bronchodilators and Pulmonary Rehabilitation

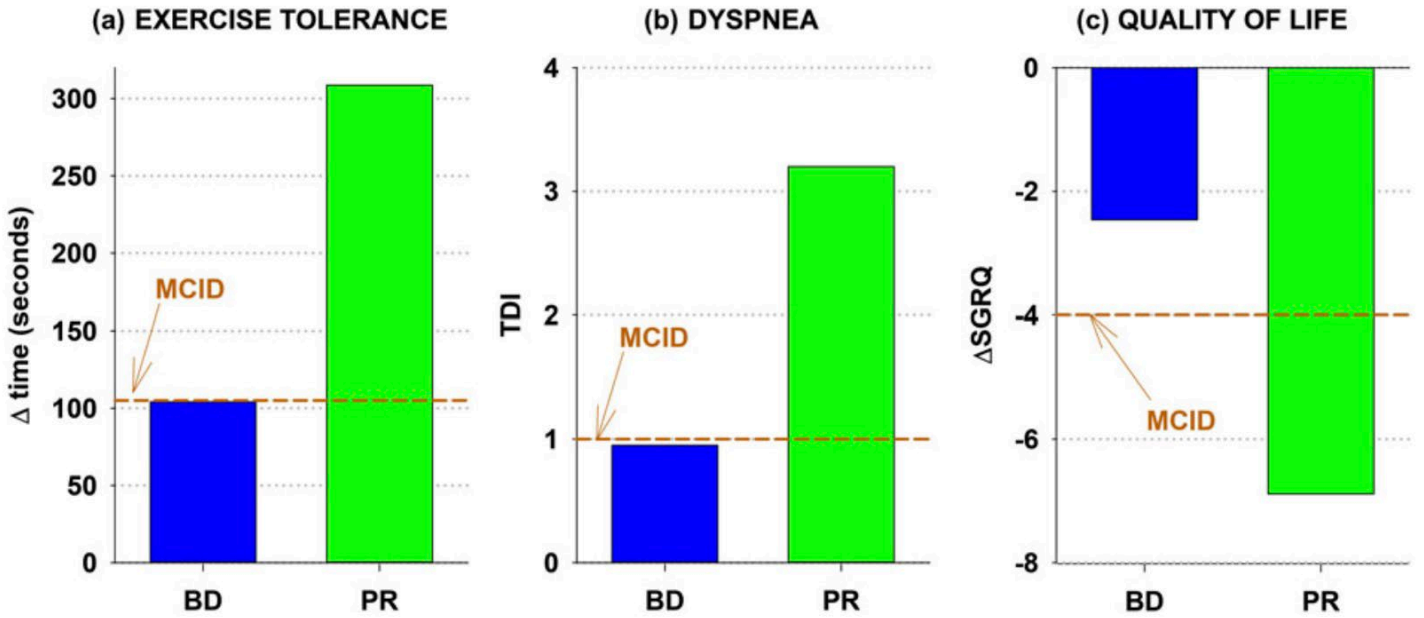
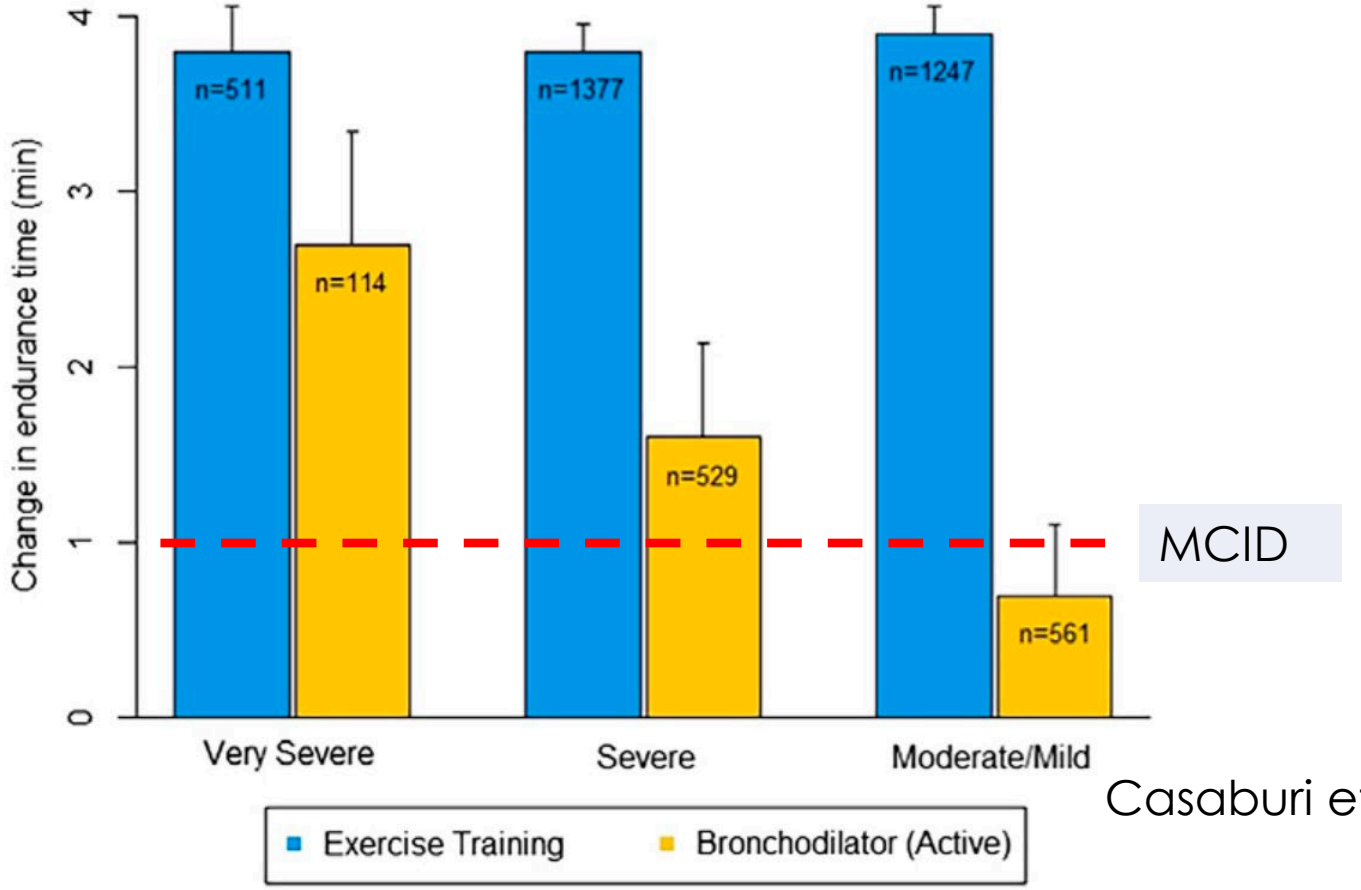


Figure 1. Semi-quantitative comparison of the benefits of pulmonary rehabilitation with inhaled long-acting bronchodilator administration (beta agonist or anti-cholinergic). (a) exercise tolerance improvement assessed by increase in exercise time in constant work rate cycle ergometer testing. (c) health-related quality of life improvement assessed by decrease in SGRQ total score. (b) dyspnoea reduction assessed by increase in Transitional Dyspnoea Index. The horizontal line in each panel represents the postulated MCID. See text for details of analysis.

Casaburi, JCOPD, 2018

Comparison of Rehabilitation and Bronchodilator on Constant Work Rate Exercise Tolerance in COPD
-Effect of Spirometric Severity-



Casaburi et al., Ann ATS, 2024

Additional Benefits of Pulmonary Rehabilitation…What's New?

- **The difficulty**: Evaluation of long-term benefits have traditionally been performed in randomized trials involving large subject groups and long durations
- Deep-pocket funders have been hard to find; NIH has generally declined to fund large pulmonary rehabilitation trials.
- **Electronic medical record** studies and **meta-analysis** are tools are now being used to evaluate these long-term benefits
- **Six recent studies published in high-profile journals**

Association between Initiation of Pulmonary Rehabilitation and Rehospitalizations in Patients Hospitalized with Chronic Obstructive Pulmonary Disease

Mihaela S. Stefan[1,2], Penelope S. Pekow[1,3], Aruna Priya[1,3], Richard ZuWallack[4], Kerry A. Spitzer[1], Tara C. Lagu[5,6], Quinn R. Pack[1,2,7], Victor M. Pinto-Plata[2,8], Kathleen M. Mazor[9], and Peter K. Lindenauer[1,2,10]

AJRCCM, 2021

- Observational cohort study of 197,376 patients 66 years or older hospitalized with a COPD exacerbation.
- 1.5% initiated pulmonary rehabilitation within 90 days of discharge.
- **Initiation of PR within 90 days of discharge was associated with a lower all- cause readmission rate at one year (56.4% vs 64.6%) and lower mean number of rehospitalizations (1.2 vs. 1.5; P <0.001).**

Association between Initiation of Pulmonary Rehabilitation and Rehospitalizations in Patients Hospitalized with Chronic Obstructive Pulmonary Disease

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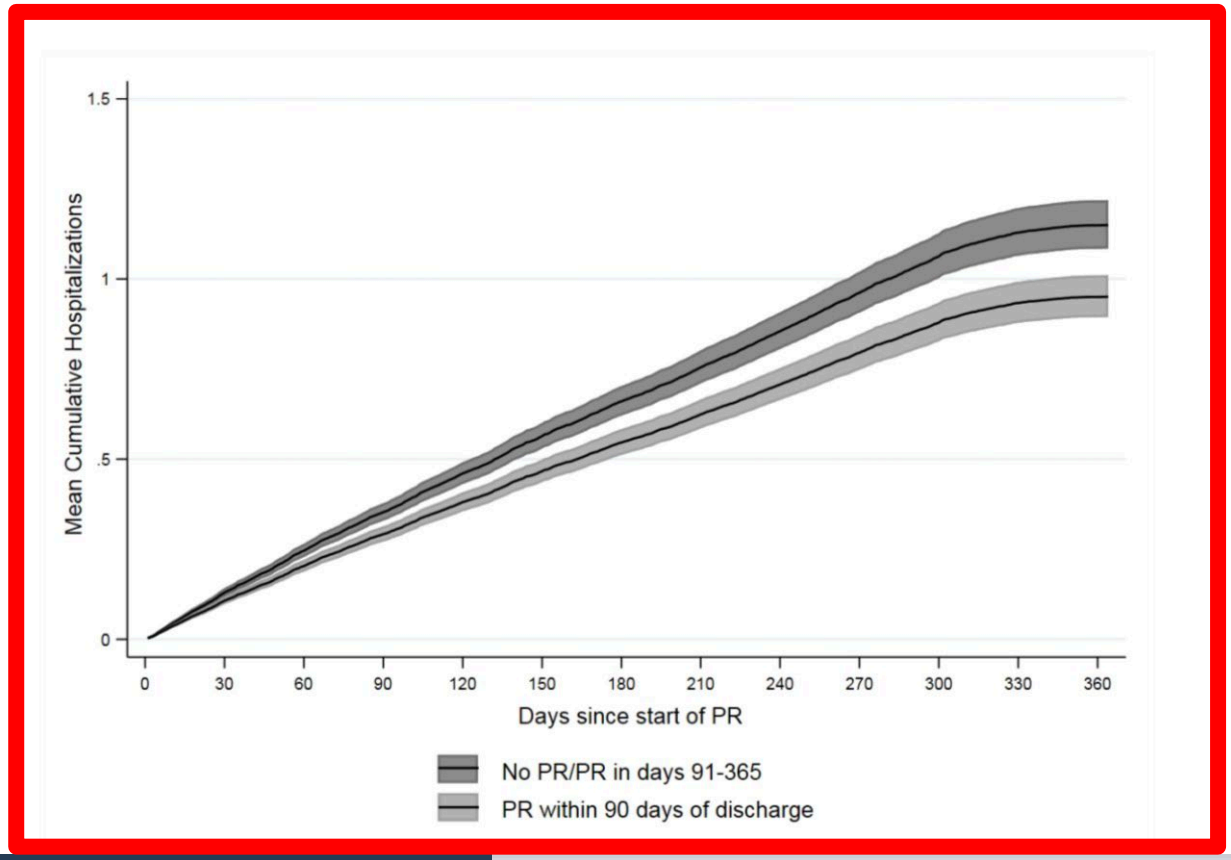
AJRCCM, 2021



In Propensity-Matched Analysis Hazard Ratio = 0.83

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JAMA Network | Open

Original Investigation | Pulmonary Medicine

Cost-effectiveness of Pulmonary Rehabilitation Among US Adults With Chronic Obstructive Pulmonary Disease

Christopher L. Mosher, MD, MHS; Michael G. Nanna, MD, MHS; Oliver K. Jawitz, MD, MHS; Vignesh Raman, MD, MHS; Norma E. Farrow, MD, MHS; Samia Aleem, MBBS, MHS; Richard Casaburi, MD, PhD; Neil R. MacIntyre, MD; Scott M. Palmer, MD, MHS; Evan R. Myers, MD, MPH

2022

- Analyzed Medicare data base of patients discharged after a COPD hospitalization
- Estimated cost-effectiveness of participation in PR vs. no participation on one-year costs
- Net cost *savings* per patient was $5721
- A single PR session would remain cost saving to $171 per session (vs. ~$56 current Medicare reimbursement)
- If willing to pay $50,000/QALY, PR would be cost-effective at $884 per session.

JAMA | Original Investigation

Association Between Initiation of Pulmonary Rehabilitation After Hospitalization for COPD and 1-Year Survival Among Medicare Beneficiaries

Peter K. Lindenauer, MD, MSc; Mihaela S. Stefan, MD, PhD; Penelope S. Pekow, PhD; Kathleen M. Mazor, EdD; Aruna Priya, MA, MSc; Kerry A. Spitzer, PhD, MPA; Tara C. Lagu, MD, MPH; Quinn R. Pack, MD, MSc; Victor M. Pinto-Plata, MD; Richard ZuWallack, MD

2020

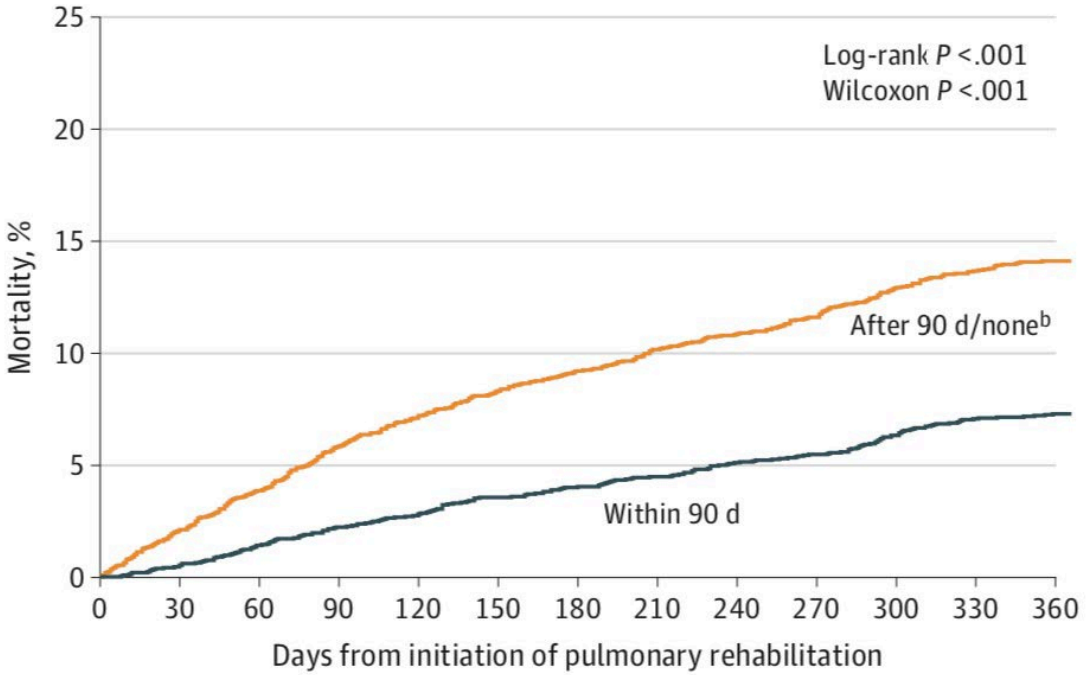
- Probed medical records of 197,376 US Medicare beneficiaries discharged after hospitalization for COPD in 2014.
- Compared mortality of the 2710 who initiated pulmonary rehabilitation within 3 months of discharge with later or no pulmonary rehabilitation.
- Created a propensity matched cohort from among the no rehabilitation group to match characteristics

JAMA | Original Investigation

Association Between Initiation of Pulmonary Rehabilitation After Hospita… Among Medic…

Peter K. Lindenauer, MD, MS
Aruna Priya, MA, MSc; Kerry
Victor M. Pinto-Plata, MD; R

Figure 3. One-Year Mortality After Initiation of Pulmonary Rehabilitation in the Propensity-Matched Cohort[a]



No. at risk

After 90 d/none[b]	2710	2538	2449	2361
Within 90 d	2709	2645	2591	2538

Hazard Ratio for Death in Rehabilitation Group = 0.63

Pulmonary Rehabilitation Is Associated With Decreased Exacerbation and Mortality in Patients With COPD

A Nationwide Korean Study

CHEST

2024

*Joon Young Choi, MD, PhD; Ki Uk Kim, MD, PhD; Deog Kyeom Kim, MD, PhD; Yu-Il Kim, MD, PhD; Tae-Hyung Kim, MD, PhD; Won-Yeon Lee, MD, PhD; Seong Ju Park, MD, PhD; Yong Bum Park, MD, PhD; Jin Woo Song, MD, PhD; Kyeong-Cheol Shin, MD, PhD; Soo-Jung Um, MD, PhD; Kwang Ha Yoo, MD, PhD; Hyoung Kyu Yoon, MD, PhD; Chang Youl Lee, MD, PhD; Ho Sung Lee, MD; Ah Young Leem, MD, PhD; Won-Il Choi, MD, PhD; Seong Yong Lim, MD, PhD; and Chin Kook Rhee, MD, PhD; on behalf of the Korean Pulmonary Rehabilitation Study Group**

- Among the 442,858 patients with COPD, 6,360 (1.43%) were prescribed pulmonary rehabilitation.
- The time to first moderate-to-severe exacerbation and severe exacerbation was significantly longer in the pulmonary rehabilitation group than the non-pulmonary rehabilitation group.
- The pulmonary rehabilitation group had a lower mortality than the non-pulmonary rehabilitation group: Hazard Ratio = 0.67 ($p < 0.001$)

Do pulmonary rehabilitation programmes improve outcomes in patients with COPD posthospital discharge for exacerbation: a systematic review and meta-analysis

Thorax
2023

Alex R Jenkins ,[1] Chris Burtin,[2,3] Pat G Camp,[4,5] Peter Lindenauer,[6] Brian Carlin, Jennifer A Alison,[8,9] Carolyn Rochester,[10,11] Anne E Holland[12,13,14]

- Seventeen studies of posthospital discharge pulmonary rehabilitation published 2015-2023 were included. Compared to usual care, pulmonary rehabilitation:
- Reduced hospital admissions (OR 0.48),
- Improved exercise capacity:
  - 6 min walk test, mean difference (MD) 57 m, ;
  - incremental shuttle walk test, MD 43 m,

Do pulmonary rehabilitation programmes improve outcomes in patients with COPD posthospital discharge for exacerbation: a systematic review and meta-analysis

Thorax
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- Improved health-related quality of life:
  - St. George's Respiratory Questionnaire, MD −8.7 points,
  - Chronic Respiratory Disease Questionnaire (CRQ)-
    - emotion, MD 1.0 points,
    - fatigue, MD 0.9 points
- Decreased dyspnea
  - CRQ- dyspnea MD 1.0 points,
  - modified Medical Research Council Dyspnea Scale, MD −0.3points

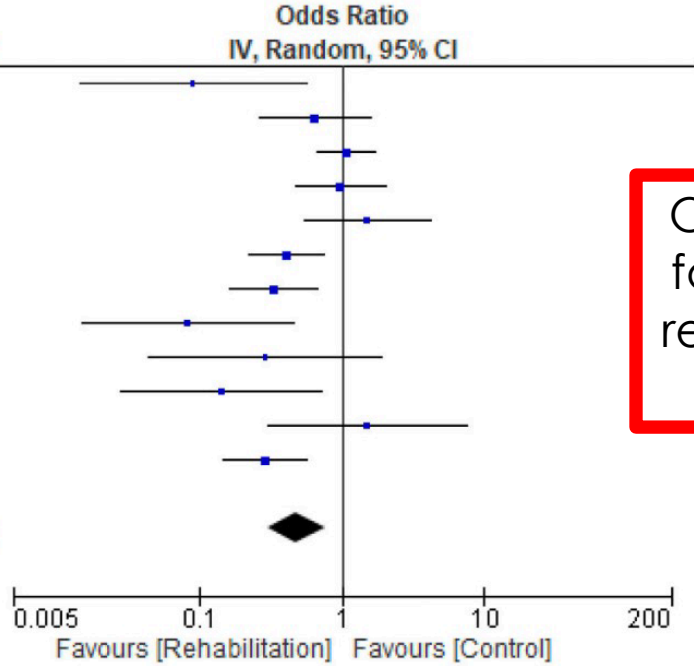
Do pulmonary rehabilitation programmes improve outcomes in patients with COPD posthospital discharge for exacerbation: a systematic review and meta-analysis

Thorax 2023

Study or Subgroup	Rehabilitation Events	Total	Control Events	Total	Weight	Odds Ratio IV, Random, 95% CI
Behnke 2000	3	14	9	12	4.5%	0.09 [0.01, 0.56]
Eaton 2009	11	47	16	50	9.5%	0.65 [0.26, 1.60]
Greening 2014	62	169	53	151	12.7%	1.07 [0.68, 1.69]
Kjaergaard 2020	25	70	22	61	10.8%	0.98 [0.48, 2.01]
Ko 2011	16	30	13	30	8.6%	1.49 [0.54, 4.14]
Ko 2016	44	90	63	90	11.6%	0.41 [0.22, 0.76]
Ko 2021	28	68	46	68	11.0%	0.33 [0.17, 0.67]
Man 2004	2	20	12	21	5.0%	0.08 [0.02, 0.45]
Murphy 2005	2	13	5	13	4.4%	0.29 [0.04, 1.90]
Seymour 2010	2	30	10	30	5.3%	0.14 [0.03, 0.72]
Tang 2019	3	20	4	38	5.4%	1.50 [0.30, 7.48]
Zhang 2020	47	85	72	89	11.1%	0.29 [0.15, 0.58]
Total (95% CI)		**656**		**653**	**100.0%**	**0.48 [0.30, 0.77]**
Total events	245		325			

Heterogeneity: $Tau^2 = 0.40$; $Chi^2 = 33.60$, $df = 11$ ($P = 0.0004$); $I^2 = 67\%$

Test for overall effect: $Z = 3.04$ ($P = 0.002$)



Odds Ratio for hospital readmission = 0.48

Comparison of odds of hospital re- admission (up to 12 months) following posthospital discharge pulmonary rehabilitation vs. no rehabilitation

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Pulmonary Rehabilitation is Associated with Increased 1-Year Survival in Stable COPD

Stephanie A. Robinson, PhD,[1,2] Paige A. Burns, MPH,[3] Emma Fitzelle-Jones, MPH,[3,4] David R. Gagnon, MD, MPH, PhD,[5,6] Marilyn L. Moy, MD, MSc[3,7,8]

AJRCCM, 2026, in press

- Retrospective cohort study of US Veterans with stable COPD who were referred to center-based PR
- Compared all-cause 1-year mortality among persons who attended 2 or more center-based PR sessions (engaged PR group) compared to persons who attended only 1 session (non-engaged PR group).
- The cohort of 23,621 participants with stable COPD was 96% male, mean
- age 70 years, white race 81.8%. The engaged group included 21,313 participants and the non-engaged group included 2,308.
- Median PR sessions attended in the engaged group was 16.
- 2,087 (8.8%) participants died within 1 year.

Pulmonary Rehabilitation is Associated with Increased 1-Year Survival in Stable COPD

Stephanie A. Robinson, PhD,[1,2] Paige A. Burns, MPH,[3] Emma Fitzelle-Jones, MPH,[3,4] David R. Gagnon, MD, MPH, PhD,[5,6] Marilyn L. Moy, MD, MSc[3,7,8]

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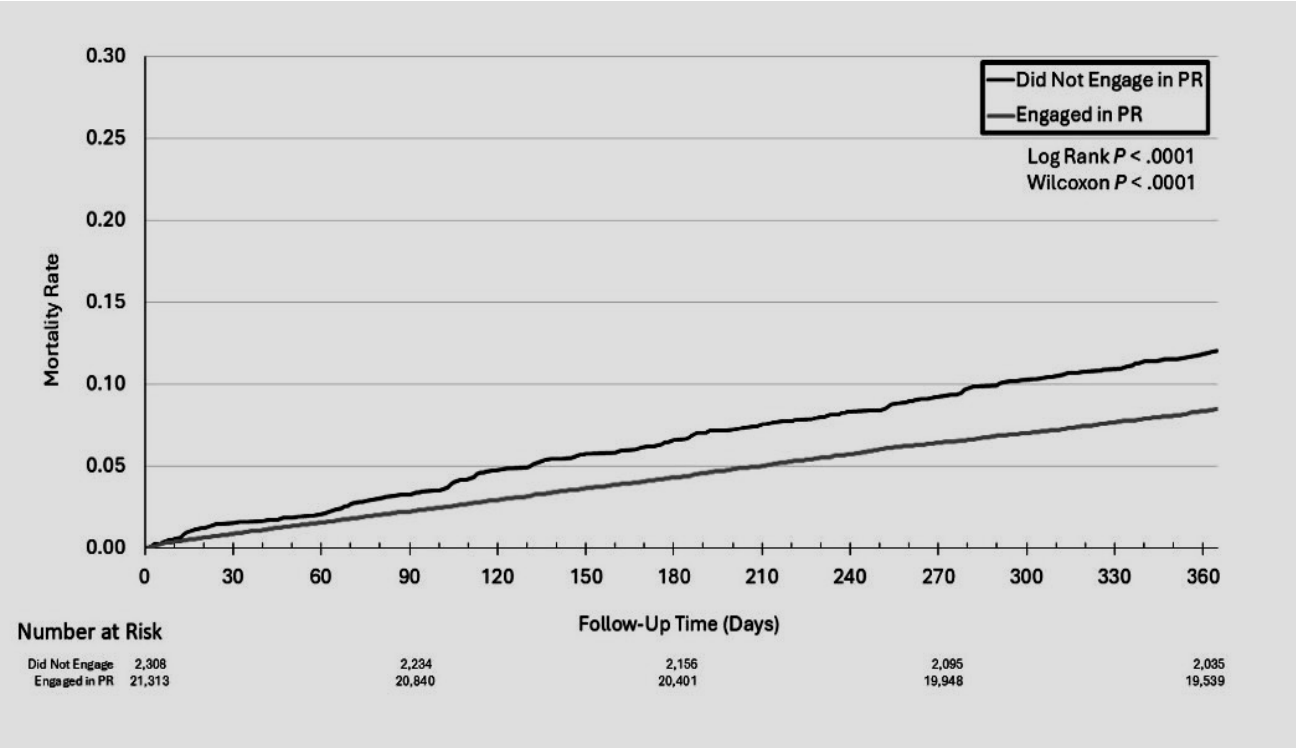

Those who engaged in pulmonary rehabilitation had a 26% lower 1-year mortality rate (HR: 0.74)

There was a significant trend of lower 1-year mortality with increasing number of pulmonary rehabilitation sessions

California Thoracic Society
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So…New Studies Demonstrating Additional Pulmonary Rehabilitation Benefits

- Decreased readmissions following a hospitalization
- Decreased mortality post-hospitalization and in stable COPD
- Highly cost-effective
- One might think that pulmonary rehabilitation would be reaching a golden age.
- This is unfortunately not the reality in the United States
- **Recent publications define the problem**

VIEWPOINT: TURNING THE AIR BLUE

An Alarming Loss of Pulmonary Rehabilitation Programs: Example from the U.S. Veterans Administration

Marilyn L. Moy[1,2] and Linda Nici[3,4]

AJRCCM, 2025

Number of VA sites offering in-center pulmonary rehabilitation was 122 in 2015 and 22 in 2022.

Pulmonary Rehabilitation Utilization in Older Adults with Chronic Obstructive Pulmonary Disease, 2013–2019

Surya P. Bhatt[1], Jordan Westra[2], Yong-Fang Kuo[2], and Gulshan Sharma[3]

[1]Division of Pulmonary, Allergy, and Critical Care Medicine, University of Alabama at Birmingham, Birmingham, Alabama; and [2]Department of Biostatistics and Data Science and [3]Division of Pulmonary and Critical Care Medicine, The University of Texas Medical Branch at Galveston, Galveston, Texas

Ann ATS, 2024

The use of pulmonary rehabilitation by Medicare beneficiaries with COPD has not changed meaningfully in the past decade and remains low.

JAMA Network Open™

Research Letter | Health Policy

Accessibility of Pulmonary Rehabilitation in the US

2024

Peter A. Kahn, MD, MPH, ThM; Walter S. Mathis, MD

For individuals living in rural and sparsely populated regions, access to PR programs was limited. with many regions (representing more than 14,000,000 people) necessitating more than a 1-hour drive to reach the nearest PR program

Access to Pulmonary Rehabilitation among Medicare Beneficiaries with Chronic Obstructive Pulmonary Disease

Gargya Malla[1,2,3], Sandeep Bodduluri[1,2], Vivek Sthanam[1,2], Gulshan Sharma[4], and Surya P. Bhatt[1,2]

[1]Division of Pulmonary, Allergy, and Critical Care Medicine, [2]UAB Lung Health Center, and [3]Department of Epidemiology, School of Public Health, University of Alabama at Birmingham, Birmingham, Alabama; and [4]Division of Pulmonary, Critical Care and Sleep Medicine, University of Texas Medical Branch, Galveston, Texas

Ann ATS, 2023

In a representative sample of Medicare beneficiaries, two-fifths of 10,376,949 adults with COPD overall, and eight in nine of those in rural areas, have poor access to pulmonary rehabilitation…defined as no program within 10 miles.

Equity in pulmonary rehabilitation delivery: a systematic review and meta-analysis

Anne E. Holland [1,2,3], Zahra Hamidah Eri Rusli[1,4], Murilo Rezende Oliveira[1,5], Jean Bremner[1], Sarah Rawlings[1,2] and Narelle S. Cox [1,3]

Eur Respir Rev, 2025

Place of residence (rurality, travel distance) was consistently associated with poor access and uptake. Uptake was lower for Black people than White people and in those of low socioeconomic status.

Sounding the Alarm
Seeking Solutions

California Thoracic Society
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EDITORIALS

Healing Pulmonary Rehabilitation in the United States

A Call to Action for ATS Members

C Garvey, RS Novitch, P Porte, R Casaburi

AJRCCM, 2019

…there is mounting concern that poor PR reimbursement in the United States may accelerate the decline in PR availability

EDITORIALS

Insufficient Patient Access to Pulmonary Rehabilitation: A Multifaceted Problem

Carolyn L. Rochester, M.D.

Ann ATS, 2023

…the scope and magnitude of deficit regarding PR program availability relative to the numbers of patients in need is likely much worse than that measured in the U.S. Medicare beneficiary population alone.
…The status quo is unacceptable.

VIEWPOINTS

Pulmonary Rehabilitation in Chronic Obstructive Pulmonary Disease

Medicine's Best-kept Secret That Could Save Medicare a Billion Dollars a Year

Christopher L. Mosher[1,2], Michael Belman[3], Chris Garvey[3], and Richard Casaburi[4]

Ann ATS, 2023

We propose the following strategies be considered to overcome disparities, barriers and inequities in access to pulmonary rehabilitation:

- **Develop solutions to overcome geographic and racial disparities in access to pulmonary rehabilitation**
- **Equitably reimburse pulmonary rehabilitation services**
- **Reduce healthcare costs by increasing access to pulmonary rehabilitation**
- **Focus initiatives on recently hospitalized patients and consider subsidizing transportation and co-payments to increase pulmonary rehabilitation access**
- **Prioritize pulmonary rehabilitation, particularly in Accountable Care Organizations and Medicare Advantage populations…**

EDITORIALS

Improving Pulmonary Rehabilitation Participation: It's Time to Examine the System

Valerie G. Press[1] and Linda Nici[2,3]

Ann ATS, 2024

Hospitalizations for COPD exacerbations may be a "teachable moment" for patients, healthcare providers, and payers to educate, support, and initiate referral to pulmonary rehabilitation.

Payment Reform as a Means of Achieving Justice

A Look at Pulmonary Rehabilitation Reimbursement

Derek R. Soled, MSc
Emilia Thurber, MD
Beret Amundson, MD
Scott Lew Schissel, MD, PhD
Boston, MA

Chest, 2021

Our proposals for payment reform are necessary to ensure the continued and increased adoption of PR and to help transform US health care into a system that achieves justice for historically marginalized patients.

ATS Journals | American Journal of Respiratory and Critical Care Medicine

Title: Pulmonary Rehabilitation Prolongs Life…And May Be Dying

Authors: Christopher L. Mosher, MD, MHS[1,2], Richard Casaburi, PhD, MD[3,4]

Editorial, in Press

Based on overwhelming evidence of effectiveness, the pulmonary community needs to voice support for, and increase referrals to, in-center PR programs. Professional organizations need to lobby for appropriate PR services reimbursement. Hopefully, new evidence of benefit will serve as a call-to-arms…and result in a robust, very much alive, treatment modality.

Dr. Brooks Kuhn is an Associate Professor in the Division of Pulmonary, Critical Care, and Sleep Medicine at the University of California, Davis School of Medicine, where he has established himself as a clinician and clinical researcher in chronic obstructive pulmonary disease (COPD) management, including the application of new technologies and novel approaches to care.

Dr. Kuhn earned his Master's degree in clinical research through the NIH-sponsored Mentored Clinical Research Training Program after completing his fellowship at UC Davis. His work with the UC Davis Critical Care Informatics Lab led to his designation as Dean's Fellow in Health Informatics, where he developed a predictive algorithm using natural language processing and machine learning to identify patients at high risk for severe COPD exacerbations.

As a clinical leader, Dr. Kuhn founded and now directs the UC Davis Comprehensive COPD Clinic, serving also as Medical Director of the UC Davis Pulmonary Clinics and Medical Director of the UC Davis Respiratory Care Department. In conjunction with our IP team, he engrained an endobronchial valve/interventional process through our COPD program. Working with a dedicated team of respiratory therapists, he has pioneered a remote patient monitoring program utilizing multiple devices to track high-risk patients and deliver early interventions, a model now replicated throughout the university system. His has been recognized with "Top Doc" designation in the Sacramento area for five consecutive years and won multiple teaching awards from residents and fellows.

As a translational researcher, Dr. Kuhn serves as an investigator on COPD and Alpha-1 Antitrypsin deficiency translational and industry led clinical trials, bridging the gap between clinical pulmonary medicine and health informatics.

As Clinical Lead for COPD/Asthma initiatives within UC Davis Population Health, Dr. Kuhn has impactful systems for high risk patients, including an automated air quality/wildfire preparedness system and a remote monitoring program.

Beyond UC Davis, Dr. Kuhn serves as President of the California Thoracic Society and is active working with the American Thoracic Society.

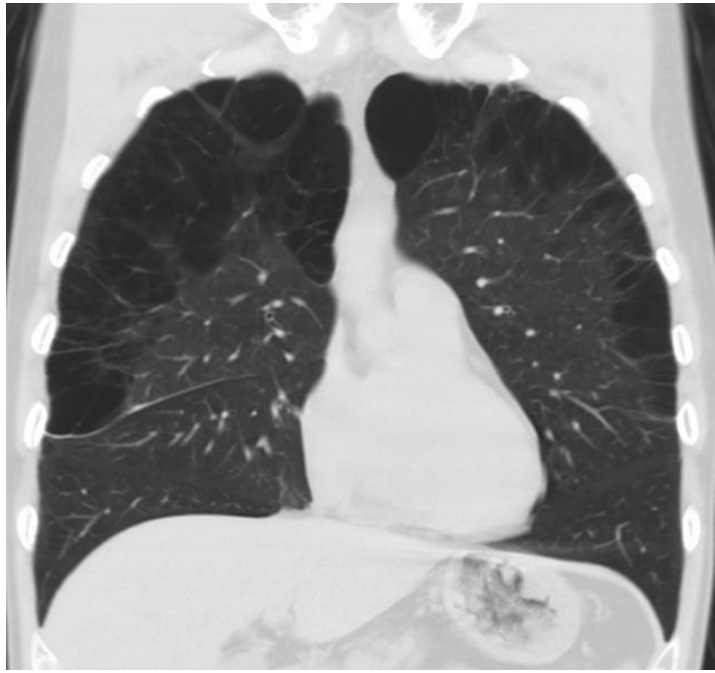
Ventilation Heterogeneity in COPD

Brooks Kuhn, MD, MAS

Associate Professor

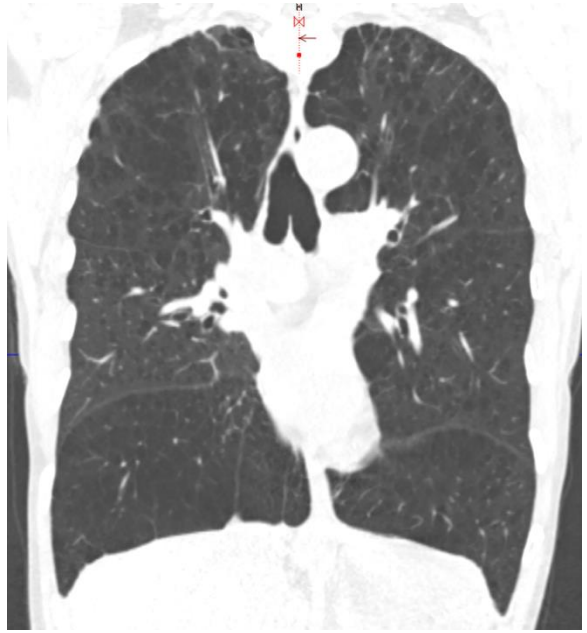
UC Davis

President (for 3 more day), California Thoracic Society

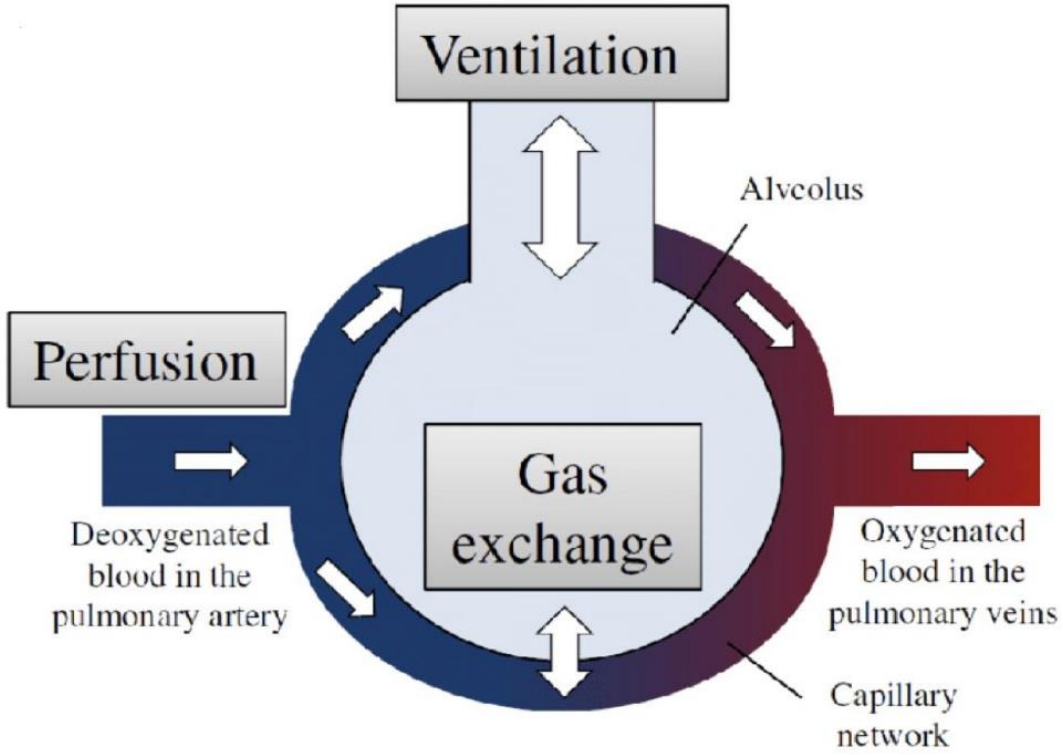


Disclosures

- I have the following relationships with ACCME defined ineligible companies: Consultant for Regeneron, Sanofi, Astra-Zeneca, Theravance.
- I **WILL NOT** discuss off-label use and/or investigational use of any drugs or devices.

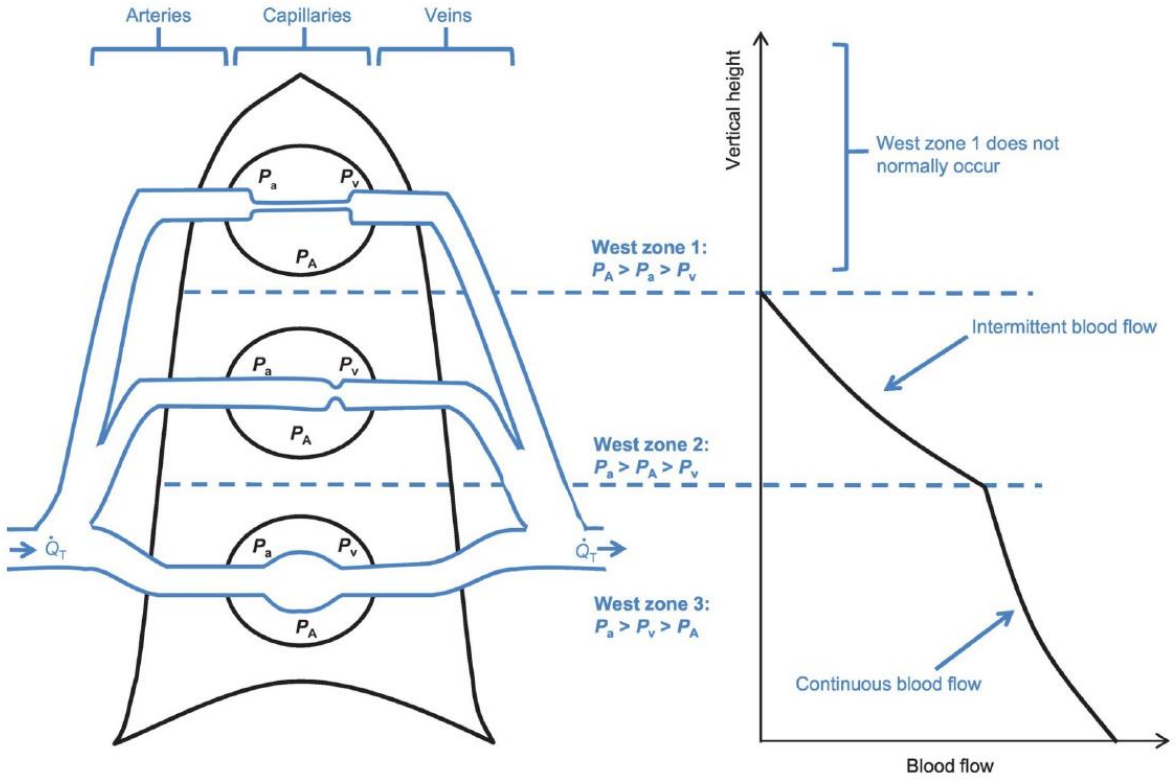


- **Ventilation (V):** flow of air into and out of the alveoli
- **Perfusion (Q)**: flow (or Quantity) of blood to the alveolar capillaries
- **V/Q**: collective effects of perfusion and ventilation
- **Ventilation heterogeneity:**
  - non-uniform distribution of air through the lungs (ie, inadequacies of V/Q matching)



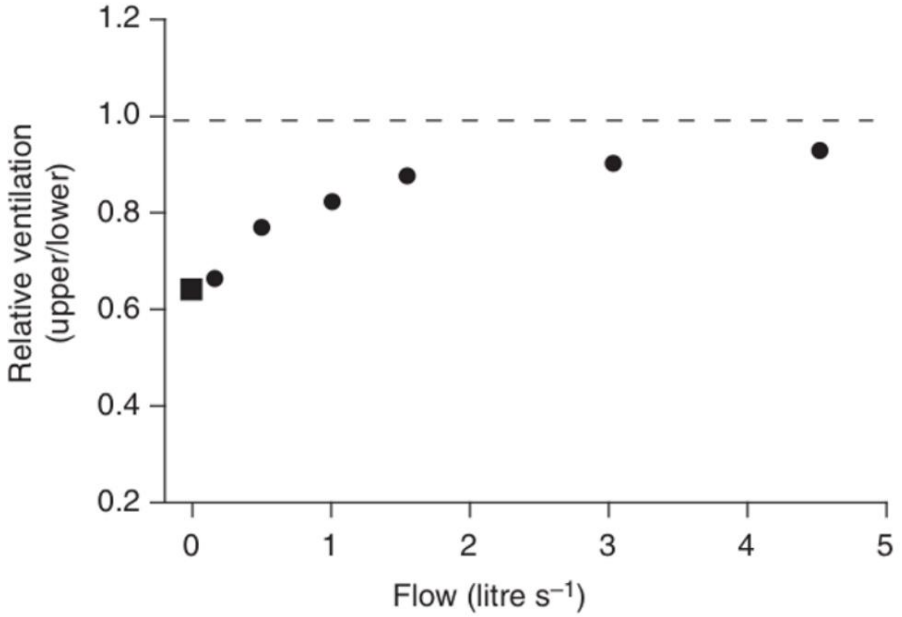
…but normal distribution is *homogeneous: Gravity*

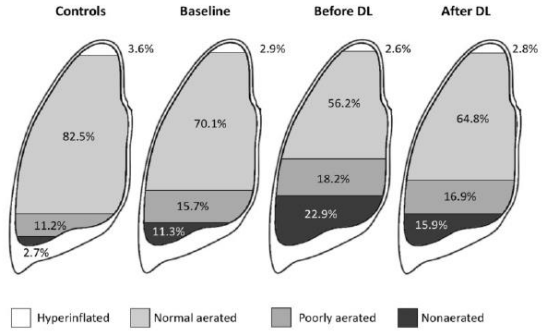
- Impacts both perfusion and ventilation
- **Perfusion:** hydrostatic pressure between the top and bottom of the lung
- **Ventilation:** differences in the pleural pressure at the apex vs the bottom
  - Less negative pleural pressure in the lower chest allows for higher compliance of lower lung alveoli and higher ventilation in the lower lungs



…but normal distribution is *homogeneous: Breathing Patterns*

- Airway and vessel architecture
  - Central receive more than periphery
- Breathing patterns
  - Faster flow rates shift more to upper zones
    - Intercostal breathing makes regional ventilation more homogenous
    - Diaphragmatic breathing augments regional ventilation inhomogeneity, worse at the base

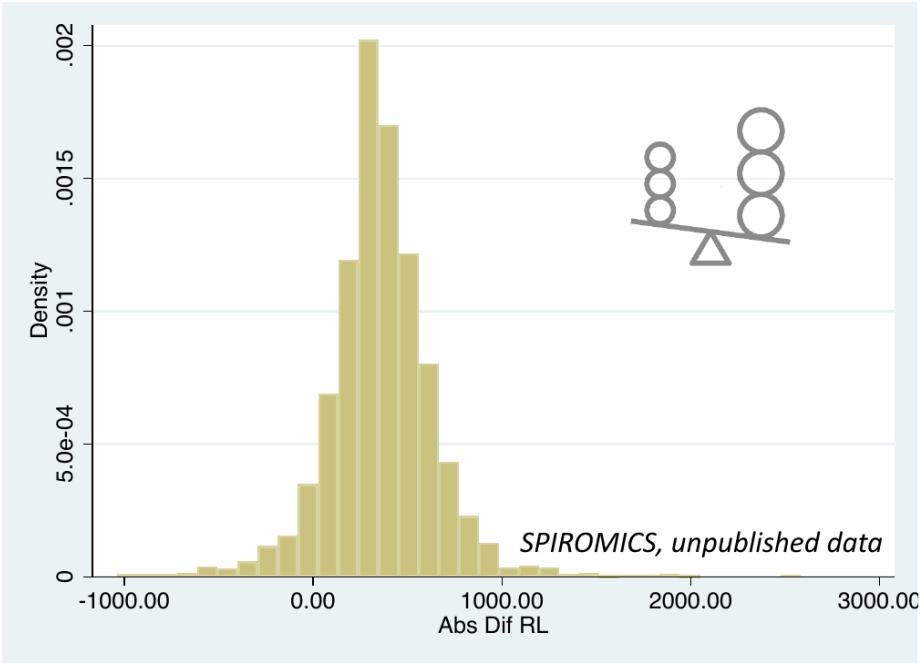




Bake B, J of Applied Physiology, 1974.
Sampson and Smaldone, J Appl Respiratory Physiology, 1984
Marshall, J Allergy Clin Immunology, 2021
Regli, Annals of Intensive Care, 2019

…but normal distribution is *homogeneous: Left vs Right*

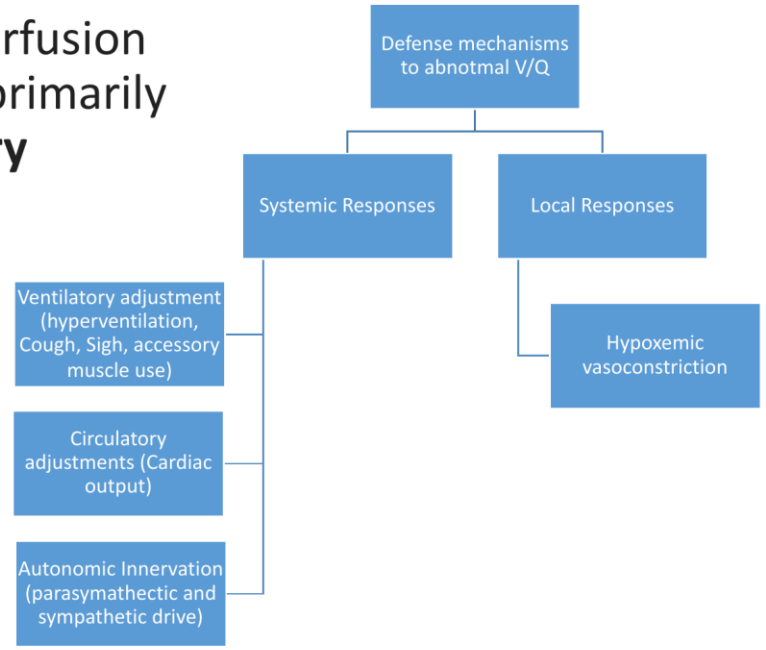
- Anatomic asymmetry
- Mean difference in volume 357 ml (+/- 291 mL) (SPIROMICS data)
- L and R lungs expand non-uniformly at higher lung volumes
  - Greater deposition in the L vs R at 70% and 85% TLC



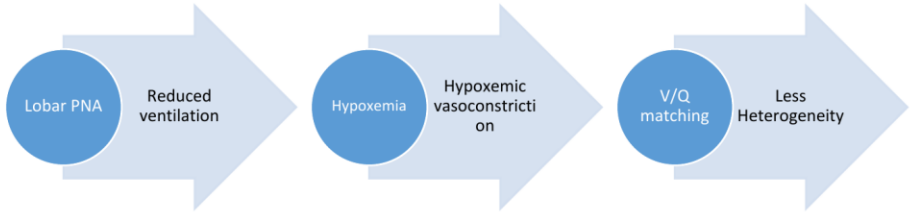
Bennet WD, J of Applied Physiology, 2000

Physiologic defense mechanisms

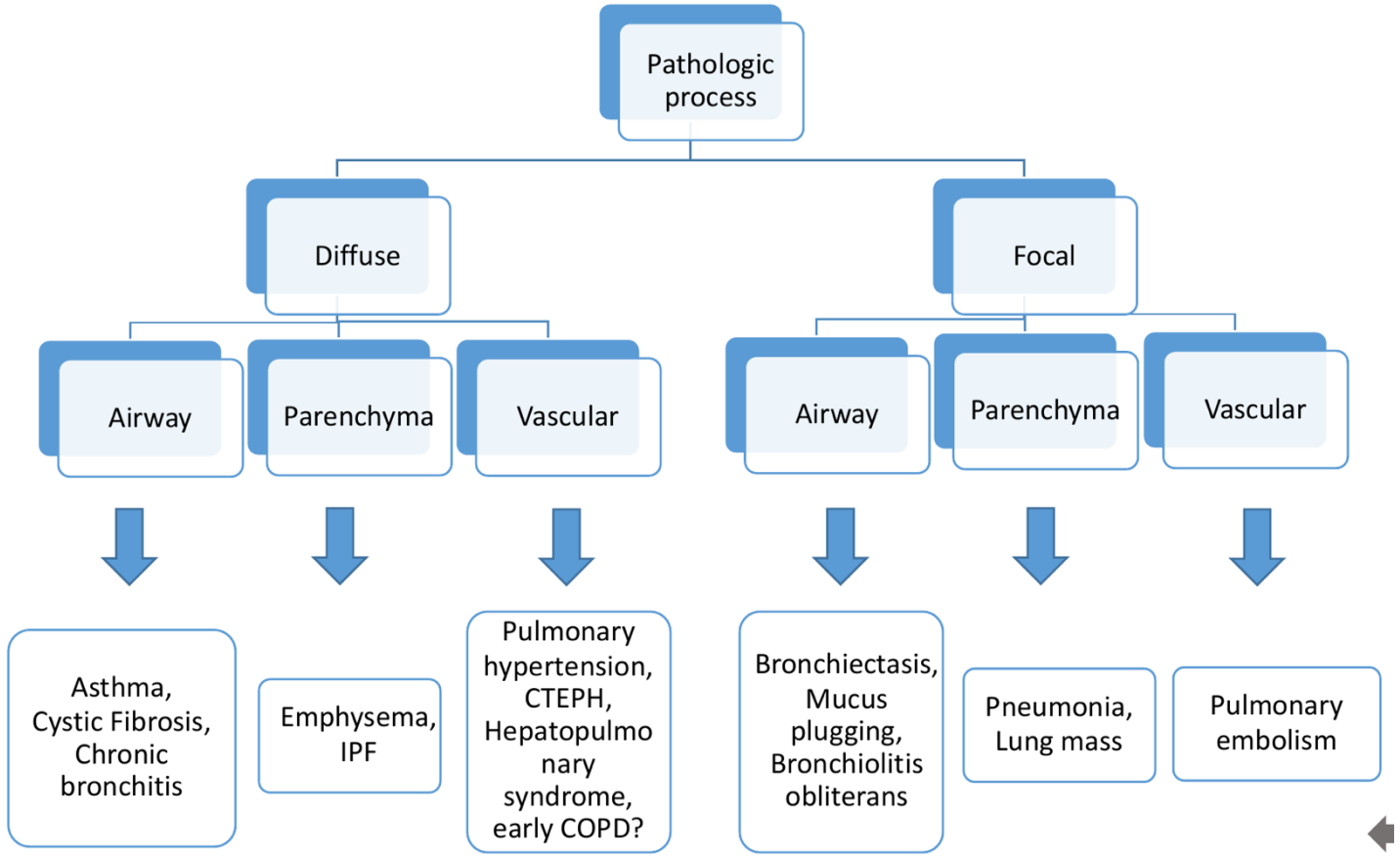
- The precise matching of ventilation to perfusion beyond that determined by anatomy, is primarily accomplished by **regulation of pulmonary vascular** and to a lesser extent airway **conductances**



- Example:



Ventilation Heterogeneity in Respiratory Pathology



Kuhn and Barjaktarevic, Frontiers, 2023

Clinical Significance of VH

Clinical significance of VH in Asthma

1. Heterogeneity **worsens with bronchoconstriction**
   - Minimal heterogeneity breaks the symmetry and leads to large clusters of poorly ventilated lung
   - The worsening of bronchoconstriction-caused VH is apparent whether assessed via imaging, MBW or oscillometry
2. Heterogeneity is a **predictor of disease severity**
   - VH (MBWT) worse in patients with poor or partly controlled asthma compared to well-controlled asthma
3. VH **worsens during the exacerbations**
4. Heterogeneity **predicts response to therapy**
   - *MBW and oscillometry indices improve* after initiation of combined ICS and LABA treatment
   - Patients who are well-controlled but have abnormal Sacin (MBWT) *may not tolerate stepping down* of their asthma inhaled regimens
   - BD-nonresponsive ventilation defects may help *distinguish airway inflammatio*n from non-inflammatory smooth muscle response, thus guiding treatment decisions
   - Higher VH (Hhe-3 MRI) severe phenotype with higher *Th-2 markers*

David Geffen School of Medicine

Venegas, Nature, 2005, Thompsn B, J Allergy Clin Immunology, 2013, Rutting et al. Current Opinion in Physiology 2021, Teague, Pediatric Pulm, 2021

Clincial Significance of VH in COPD

- In COPD, VH results from airway obstruction, air trapping, loss of lung elasticity, vascular abnormalities, and structural changes.
- Clinical significance of ventilation heterogeneity in asthma:
  - Heterogeneity worsens with bronchoconstriction.
  - It predicts disease severity.
  - It worsens during exacerbations.
  - It predicts response to therapy.

  Indices improve with ICS/LABA treatment.
  Abnormal MBW metrics may predict inability to step down therapy.
- Clinical evidence for ventilation heterogeneity in COPD:
  - Ventilation defect percent detected in smokers with mild emphysema before airflow obstruction.
  - Poorly communicating fraction (PCF) correlates with symptoms and exercise limitation.
  - Electrical impedance tomography distinguishes COPD from healthy lungs.
  - Perfusion heterogeneity is increased in COPD.
  - V/Q imbalance may precede airflow obstruction in early COPD.

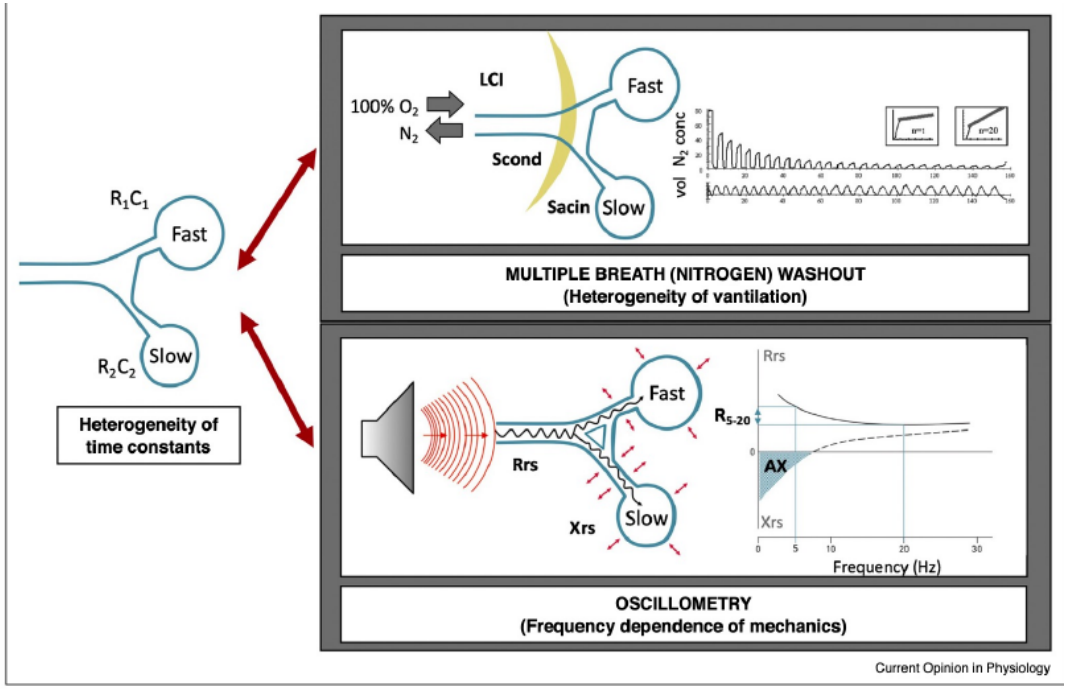
Measuring VH

- Gas washout techniques:
  - Single breath washout
  - Multiple breath washout

Pulmonary function testing:
- Poorly communicating fraction
- Impulse oscillometry

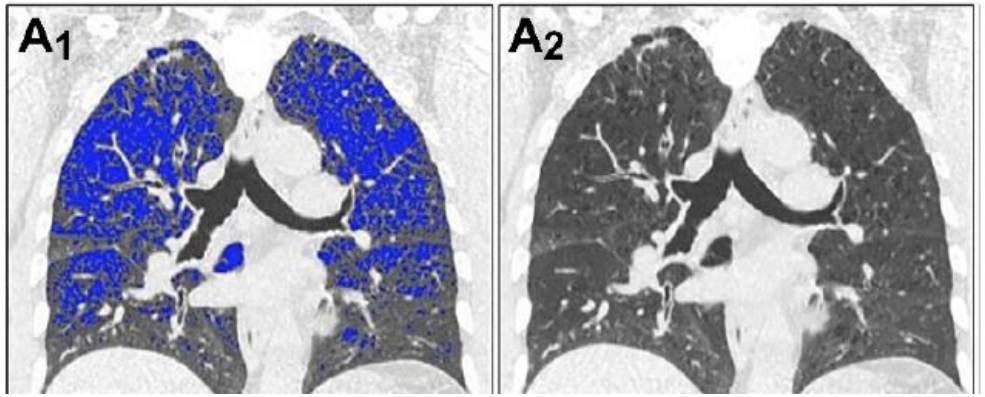
Imaging methods:
- Gamma camera scintigraphy
- CT-based quantitative imaging
- Functional respiratory imaging
- PET and Xe-enhanced CT
- Hyperpolarized gas MRI

Other:
- Electrical impedance tomography
- Inspired sinewave testing
- Molecular flow sensing.



Distribution of pathologic processes in COPD and VH

- • Homogeneous emphysema associated with more dynamic hyperinflation during exercise.
  - Air-trapping heterogeneity correlates better with pulmonary function than emphysema alone.
  - In SPIROMICS cohort, emphysema heterogeneity increases with extent of emphysema.
- SPIROMICS emphysema heterogeneity analysis:



VH in COPD

- Most heterogeneous group:
  - Younger
  - More female and more Black patients
  - Better FEV1 despite similar FVC
  - More often active smokers

However:
- No difference in longitudinal FEV1 decline, emphysema progression, or mortality.

- What ventilation heterogeneity assessment evaluates:

  - Temporal inhomogeneity of ventilation (gas washout).
  - Spatial distribution of structural lung disease.
  - Distribution of inhaled gas (functional imaging).
  - Regional V/Q mismatch.

Functional and anatomic assessments are not identical

VH Relevance

- Any regional compromise in ventilation or perfusion leading to V/Q mismatch may produce symptoms.

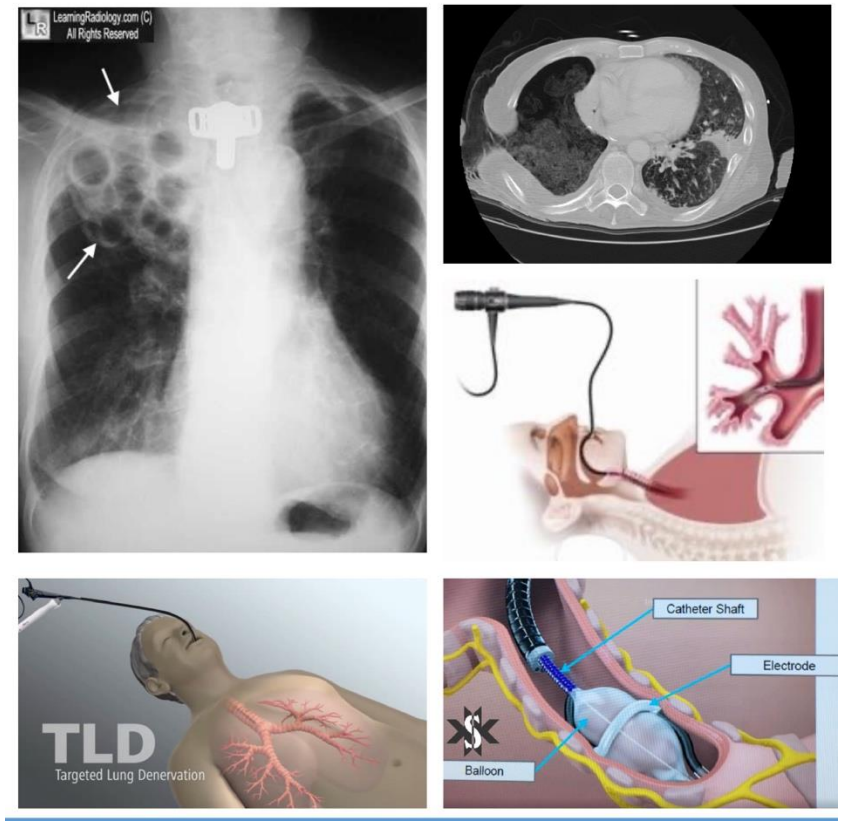
In some conditions homogeneous ventilation may also be disadvantageous if perfusion or diffusion abnormalities exist.

Ventilation Redistribtuion

Ventilation redistribution approaches:

Surgical:
- Plombage
- Bullectomy
- Eloesser flap

Endoscopic airway approaches:
- Targeted lung denervation
- Bronchial thermoplasty
- Endoscopic lung volume reduction.

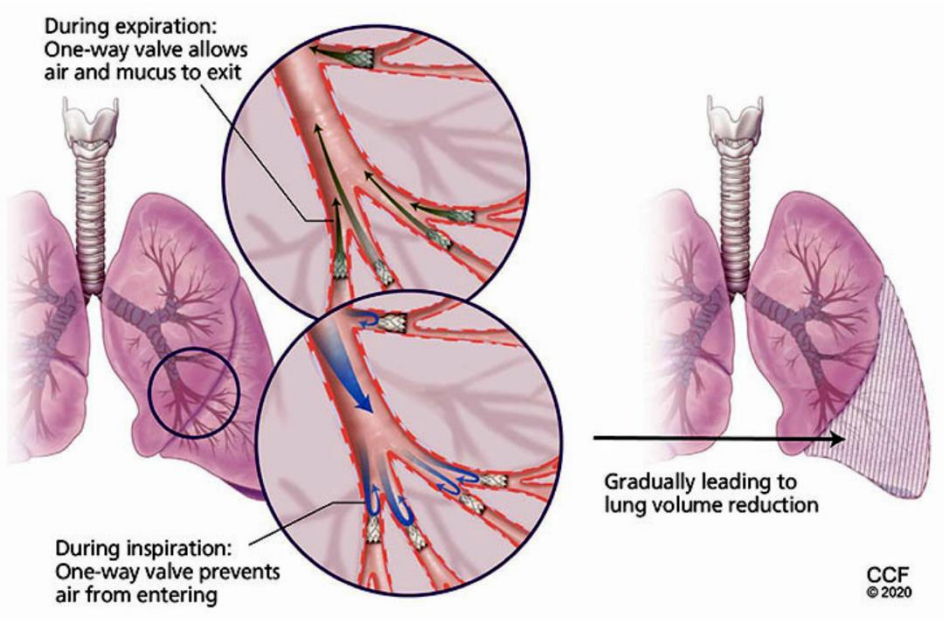


Lung volume reduction approaches

- Surgical or bronchoscopic lung volume reduction for advanced COPD with air trapping.
- Historically used for heterogeneous disease but can also benefit homogeneous disease (IMPACT trial).

Non-interventional approaches to address ventilation heterogeneity:

- Optimize inhaled drug delivery.
- Adjust inhaler technique and particle size.
- Supplemental oxygen considerations.
- PEEP adjustments and positioning strategies.



Opportunities to address VH with non-interventional approaches

- Optimize inhaled drug delivery
- Adjust inhaler technique and particle size.
- Supplemental oxygen considerations.
- PEEP adjustments and positioning strategies.

Summary:

- Heterogeneity is central to COPD pathophysiology.
- Ventilation heterogeneity arises from small airway disease, air trapping, and hyperinflation.
- Broader structural and vascular abnormalities also contribute.
- Improved tools to measure ventilation heterogeneity are important for future therapies.

Summary

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Dr. Russell Buhr grew up in the rural Willamette Valley of Oregon. He graduated with honors from Azusa Pacific University as a first-generation university student. He earned his MD at University of Southern California. He completed internal medicine residency and was Chief Resident at Georgetown, then pulmonary and critical care medicine fellowship at UCLA, where he concomitantly earned a PhD in Health Policy and Management. His research focuses on improving care delivery and health care policy for patients with airway disease in multiple contexts including among Medicare and Medicaid beneficiaries and within the Veterans Health Administration. He is an Assistant Professor of Medicine & Health Policy and Management at UCLA, and a Fellow of the American Thoracic Society, and the American College of Physicians.

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Genetics in COPD

From single gene mutations to polygenic risk: clinical overview and emerging frontiers

Russell G. Buhr, MD, PhD, FACP, ATSF
Assistant Professor of Medicine & Health Policy and Management

California Thoracic Society 2026 Conference

Learning Objectives

At the conclusion of this session, learners will be able to:

1. Synthesize the multilayered genetic architecture of COPD and critique the current limits of clinical translation for each layer
2. Critically appraise the ATS/ERS AATD testing gap and consider practice- or system-level interventions to close it
3. Analyze the RAPID trial, reconcile the CT density vs. FEV_1 controversy, and justify patient selection for augmentation therapy
4. Evaluate PRS clinical utility and equity implications, and propose a framework for responsible deployment across diverse populations
5. Integrate HDAC2 epigenomics and single-cell findings into a mechanistically coherent model of COPD pathogenesis with therapeutic implications

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I. Genetic Architecture of COPD

From Mendelian to polygenic to epigenetic

A Multilayered Genetic Architecture

Three Layers of Genetic Risk

- **Mendelian (rare, high-penetrance)**
  - AATD — the only proven single-gene cause
- **Polygenic (common variants)**
  - 80+ GWAS loci, each <1% variance — PRS aggregates them
- **Epigenetic**
  - HDAC2 impairment by cigarette smoke → steroid resistance

The Clinical Puzzle

- Only 20–30% of smokers develop significant COPD
- Heritability: 20–40% for FEV_1 and $FEV_{1:}FVC$
- Known GWAS loci explain ~5–10% of variance
- **Missing heritability: rare variants, structural variants, gene × environment, epigenetics**
- Goal: stratify risk, intercept early, deploy equitably

Refs: Zhou et al., AJRCCM 2013 (PMID 23972146); Hobbs et al., Nat Genet 2017 (PMID 28166215)

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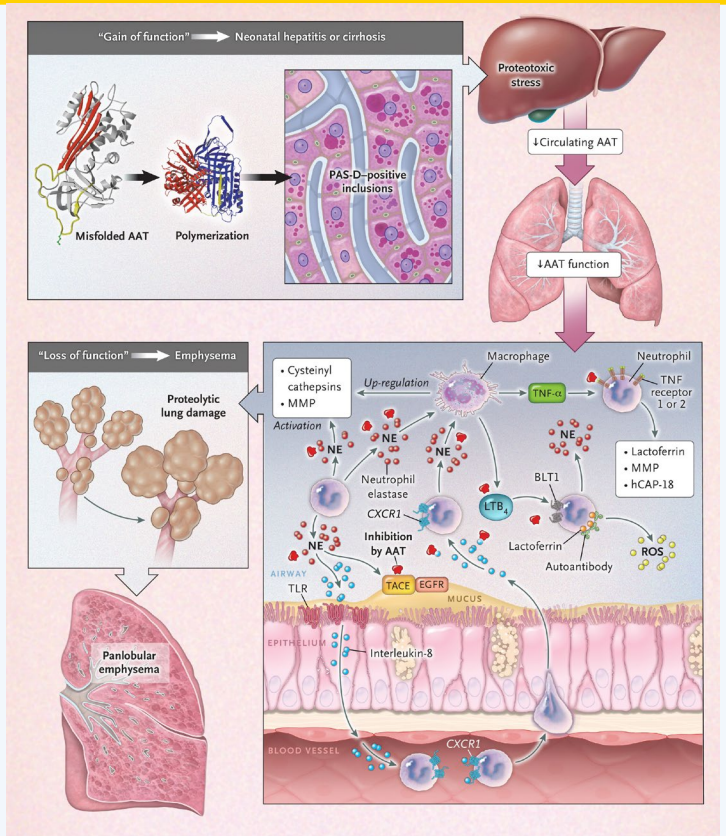
II. Alpha-1 Antitrypsin Deficiency

Pathophysiology · diagnosis · treatment · the implementation gap

AATD: Pathophysiology & Pi Nomenclature

- **SERPINA1 (chr 14q32) → AAT: primary serine protease inhibitor in lung epithelial lining fluid**
- Protease–antiprotease imbalance → unchecked neutrophil elastase → alveolar destruction
- Z-allele (E342K): protein misfolding → polymerization → hepatocyte accumulation → liver disease
- **Pi nomenclature (electrophoretic mobility):**
- PiMM = normal | PiZZ = <15% normal AAT → panlobular basilar emphysema
- PiMZ = 40–60% normal, intermediate risk | PiSZ = ~40–50%, uncertain COPD risk
- **CT clue: lower-lobe predominant emphysema — opposite of typical smoking-related distribution**



Refs: Strnad et al., N Engl J Med 2020 (PMID 32268028); Seixas & Marques, Appl Clin Genet 2021 (PMID 33790624)

The Underdiagnosis Problem: A 20-Year Implementation Failure

5-10%

of PiZZ individuals ever diagnosed

5-8 yr

mean diagnostic delay (up to 22 yrs reported)

- Average 3+ physicians before correct diagnosis; most common misdiagnosis: 'usual COPD' or asthma
- **ATS/ERS 2003: test ALL COPD patients regardless of age or smoking history**
- Barriers: low physician awareness, perceived futility, GINA life insurance gap
- **PFT-lab initiated buccal swab testing: OR = 35 for completion vs. standard referral**

Refs: Stoller, Chest 2005 (PMID 16236846); Gurevich, Chron Obs Pulm Dis 2021 (PMID 33290644)

Testing Algorithm & Counseling Essentials

Stepwise Diagnostic Algorithm

- **Step 1: Serum AAT level (all COPD patients)**
- <11 µmol/L (<57 mg/dL) = deficient threshold
- Caveat: acute-phase reactant — recheck if tested during illness
- **Step 2: SERPINA1 genotyping (S/Z alleles)**
- Full sequencing for discordant level/phenotype or pre-transplant
- **Cascade testing: offer to all first-degree relatives**

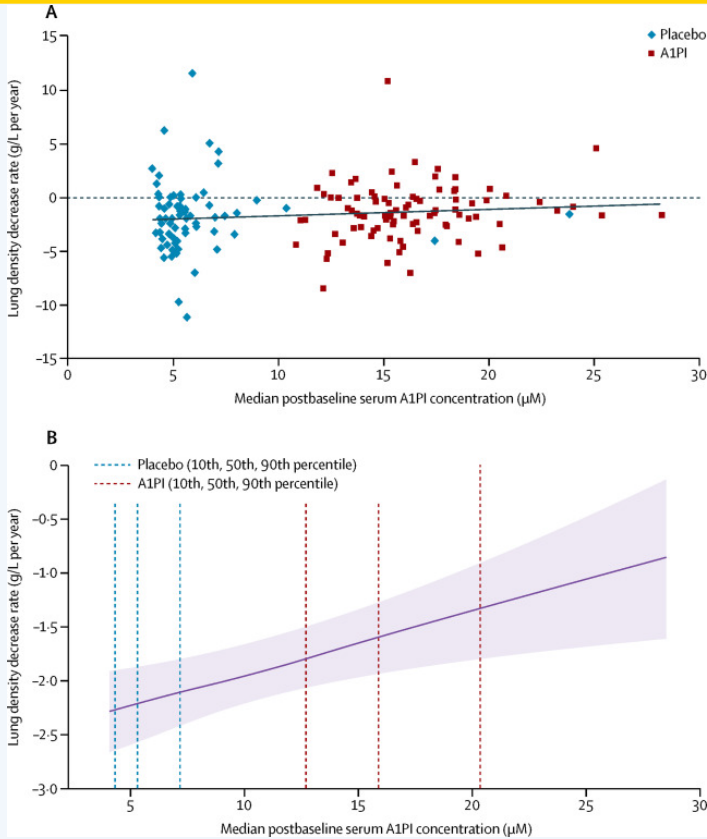
GINA & Genetic Counseling

- **GINA (2008) protects: health insurance, employment (≥15 employees)**
- **NOT protected: life, disability, long-term care insurance**
- Practical: counsel patients to secure life/disability coverage before testing if uninsured
- PiZZ confirmed: autosomal co-dominant — both parents obligate carriers, siblings 25% risk
- Smoking cessation imperative regardless of genotype

Refs: ATS/ERS AJRCCM 2003 (PMID 14522813); Sandhaus et al., JCOPDF 2016 (PMID 28848891); Hudson et al., NEJM 2008 (PMID 18565857)

Augmentation Therapy: Analyzing the RAPID Evidence

- **Mechanism: weekly IV pooled human AAT restores antiprotease 'shield' above the 11 µmol/L protective threshold**
- **RAPID (Chapman, Lancet 2015; n=180): CT lung density (PD15) — significant reduction in annual decline**
- FEV_1 decline: did not reach significance — ongoing regulatory and payer controversy
- RAPID-OLE: early treatment maintained CT benefit; delayed group partially caught up → supports early diagnosis
- **Candidacy: PiZZ (or PiSZ) with FEV1 ~30–65% and established emphysema on CT**
- Emerging pipeline: AAV gene therapy, Z-corrector small molecules (CFTR modulator analogy), mRNA augmentation



Refs: Chapman et al., Lancet 2015 (PMID 26026936); Dirksen et al., ERJ 2009 (PMID 19196813); Brantly, AJRCCM 2023 (PMID 37724887)

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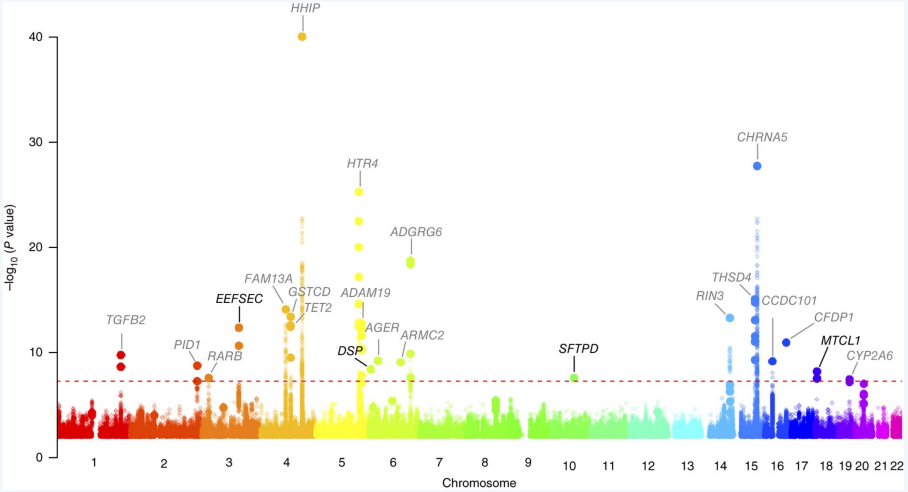
III. Common Variants, GWAS & PRS

From population genetics to clinical risk stratification

GWAS Landscape: 80+ Loci and Missing Heritability

- **Major cohorts: COPDGene, UK Biobank, TOPMed — ~320,000 participants**
- 80+ independent loci for COPD / FEV_1 / FEV_1:FVC
- **Top replicated loci:**
- HHIP (4q31): Hedgehog signaling — lung development, AT2 identity, exacerbation risk
- FAM13A (4q22): beta-catenin — airway epithelial proliferation
- CHRNA3/5 (15q25): nicotinic receptor — smoking intensity AND emphysema (MR challenge)
- **Known loci explain ~5–10% of variance — missing heritability remains open**



Refs: Hobbs et al., Nat Genet 2017; (PMID 28166215) Wain et al., Nat Genet 2017 (PMID 28166213); Zhao et al., Nat Commun 2020 (PMID 33057025)

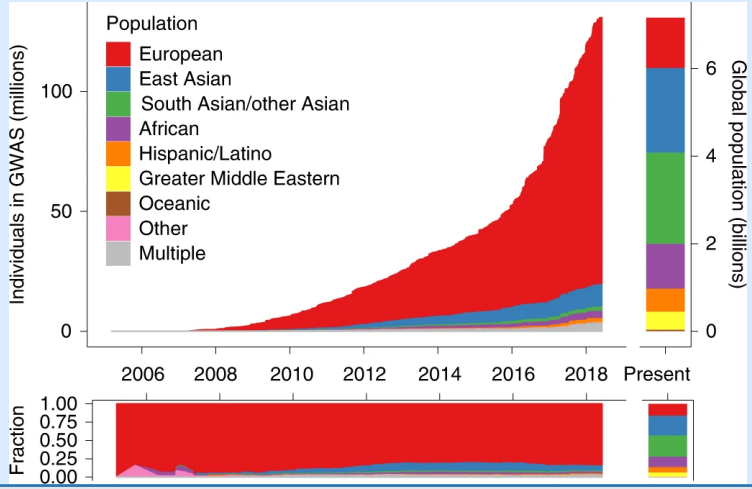
Polygenic Risk Scores: Promise and the Equity Gap

Clinical Performance

- **Moll et al., Lancet Respir Med 2020:**
- Top vs. bottom decile: OR 7.99 for COPD (European cohorts)
- PRS + clinical factors: AUC 0.80 vs. 0.76 without PRS
- **Zhang et al., JAMA 2025:**
- PRS + Lung Function Questionnaire detects undiagnosed COPD in primary care
- Theoretical framework: PRS-guided early intervention before spirometric decline

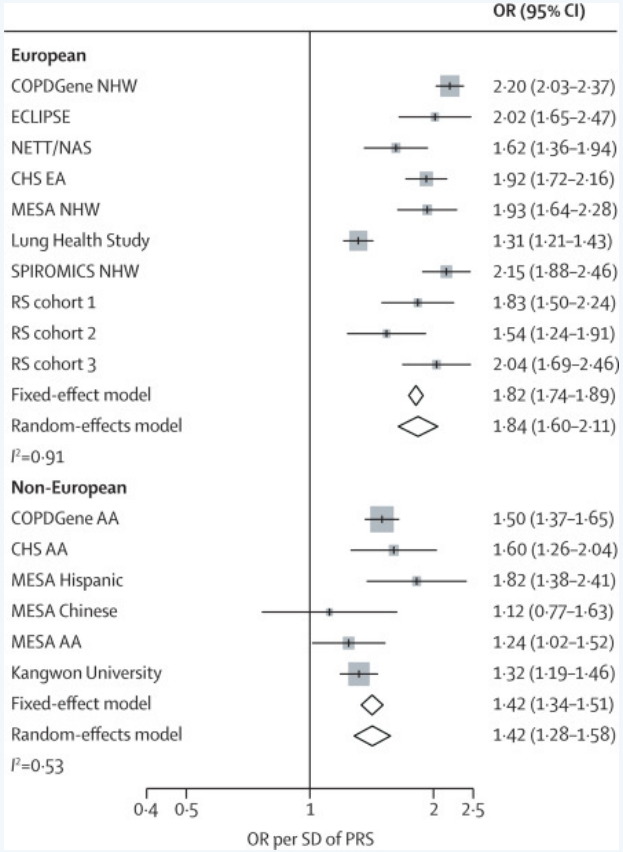
The Equity Problem

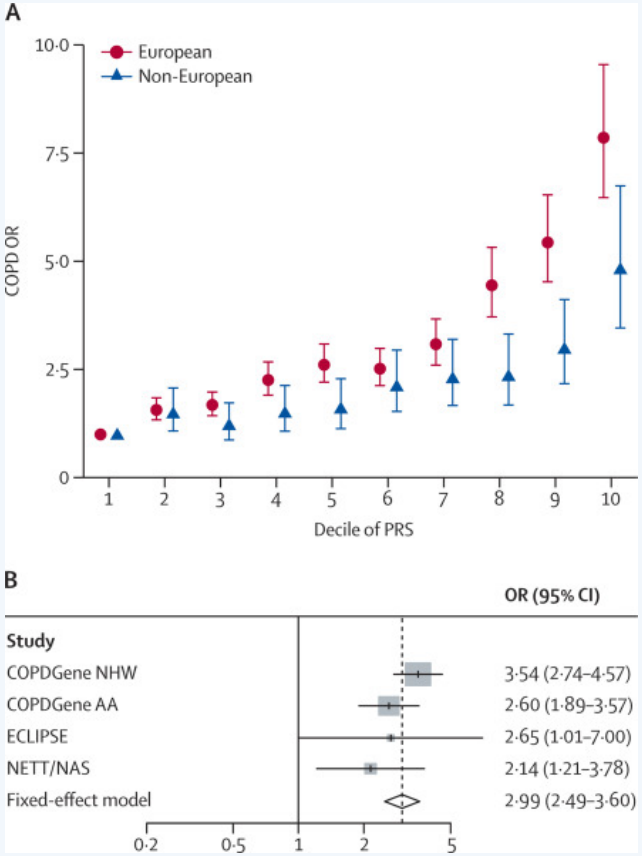
- **>80% of GWAS participants are European ancestry**
- Same PRS — European OR 7.99 vs. Non-European OR 4.83



Refs: Moll et al., Lancet Respir Med 2020 (PMID 32649918); Zhang et al., JAMA 2025 (PMID 39841442); Martin et al., Nat Genet 2019 (PMID 30926966)

PRS Risk Stratification — Moll et al., Lancet Respir Med 2020



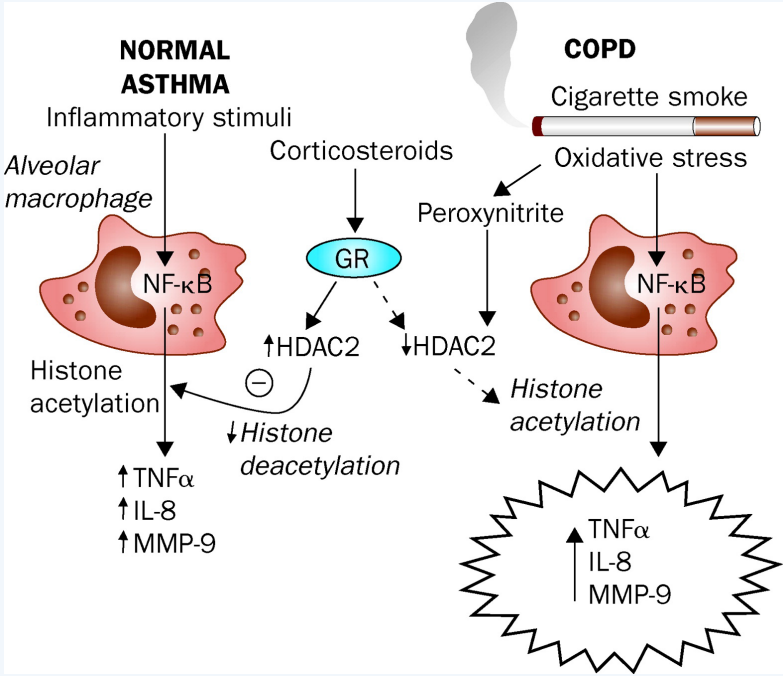


IV. Epigenetics & Emerging Biology

HDAC2 · single-cell transcriptomics · therapeutic implications

HDAC2 and Corticosteroid Resistance: Mechanism to Therapy

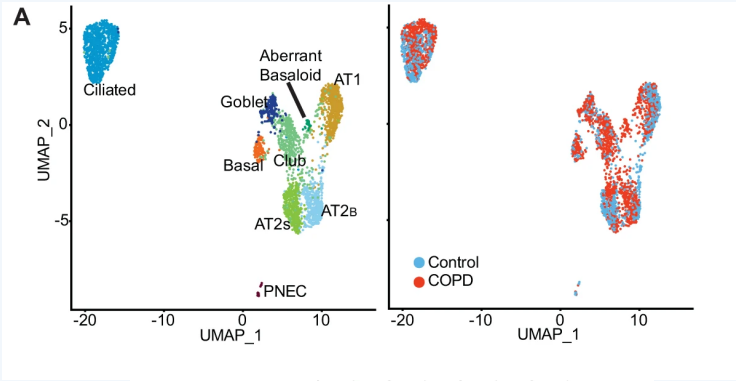
- **Normal ICS mechanism: GR–corticosteroid complex recruits HDAC2 → deacetylates histones at inflammatory gene promoters → transcriptional silencing**
- Cigarette smoke + oxidative stress → HDAC2 oxidation, nitrosylation → ubiquitin-proteasome degradation
- **Result: histones remain hyperacetylated → NF-κB target genes constitutively open → clinical steroid resistance**
- HDAC2 activity inversely correlates with COPD severity and ICS responsiveness (Ito, NEJM 2005)
- **Therapeutic implication: low-dose theophylline restores HDAC2 via oxidative stress reduction — mechanistic basis for ICS + theophylline combination**
- Nrf2 activators (sulforaphane) under investigation as HDAC2-protective antioxidants



Refs: Barnes, Lancet 2004 (PMID 15001333); Ito et al., N Engl J Med 2005 (PMID 15888697); Yao et al, AJP Lung Cell Mol Bio 2012 (PMID 22842217)

Single-Cell RNA-Seq: Resolving COPD Cellular Heterogeneity

- **scRNA-seq resolves disease-associated cell states masked by bulk RNA-seq averages**
- **Sauler et al., Nat Commun 2022 — Human COPD lung cell atlas:**
- AT2B subpopulation: highly expresses HHIP (validates GWAS locus at single-cell resolution), metabolically aberrant in COPD
- Capillary endothelial CXCL12/CXCR4 axis → sustained alveolar inflammation
- **Zhang et al., Nat Genet 2026 — 141 subjects, 1.5M nuclei:**
- Regenerative AT2 states peak in early COPD then decline → potential therapeutic window
- Profibrotic cell states expand with progression; spatial co-localization in disease niches
- **GWAS × scRNA-seq convergence on HHIP/AT2B: population genetics and cell biology independently pointing to the same target**

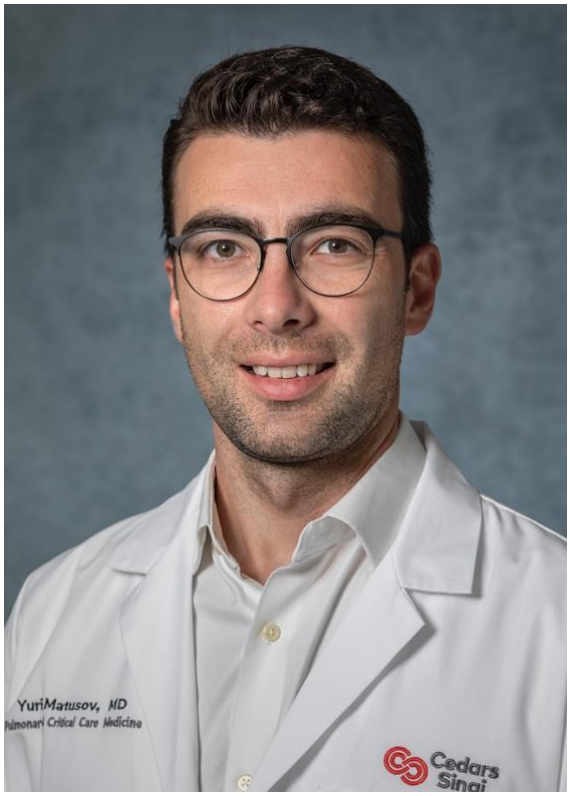


Refs: Sauler et al., Nat Commun 2022 (PMID 35078977); Zhang et al., Nat Genet 2026 (PMID 41578022); Begum et al., AJRCCM 2023

Key Take-Home Messages

- **Test every COPD patient for AATD — the knowledge-to-practice gap is a systems problem; PFT-lab buccal swab testing is a proven lever**
- **RAPID trial: CT density benefit is real; FEV1 controversy persists — endpoint choice in rare-disease trials is itself a lesson**
- PRS achieves OR ~8 top vs. bottom decile but performs meaningfully worse in non-European populations — responsible deployment requires equity-aware frameworks
- **HDAC2 loss is the molecular basis of steroid resistance; scRNA-seq reveals a therapeutic window in early COPD that closes with progression**
- GINA protects health insurance and employment — not life, disability, or LTC insurance; counsel patients before testing

Questions?



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Pulmonary hypertension in COPD

Yuri Matusov, MD, FACP, ATSF

Cedars Sinai Medical Center

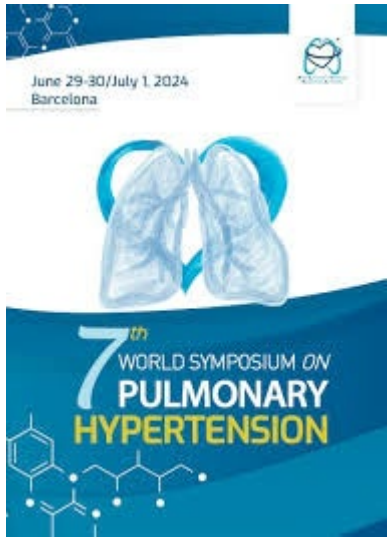
Disclosures

- I have the following relationships with ACCME defined ineligible companies:
- **Research funding from Tenax, Aerovate. Consultancy for United Therapeutics.**
- I **WILL** discuss off-label use and/or investigational use of some drugs or devices.

Objectives

- Describe the continuum of COPD associated with pulmonary vascular phenotype physiology
- Understand the epidemiology of PH associated with COPD
- Interpret the data of PH therapies in COPD-PH
- Discuss current trials for COPD-PH

Current definitions and classifications



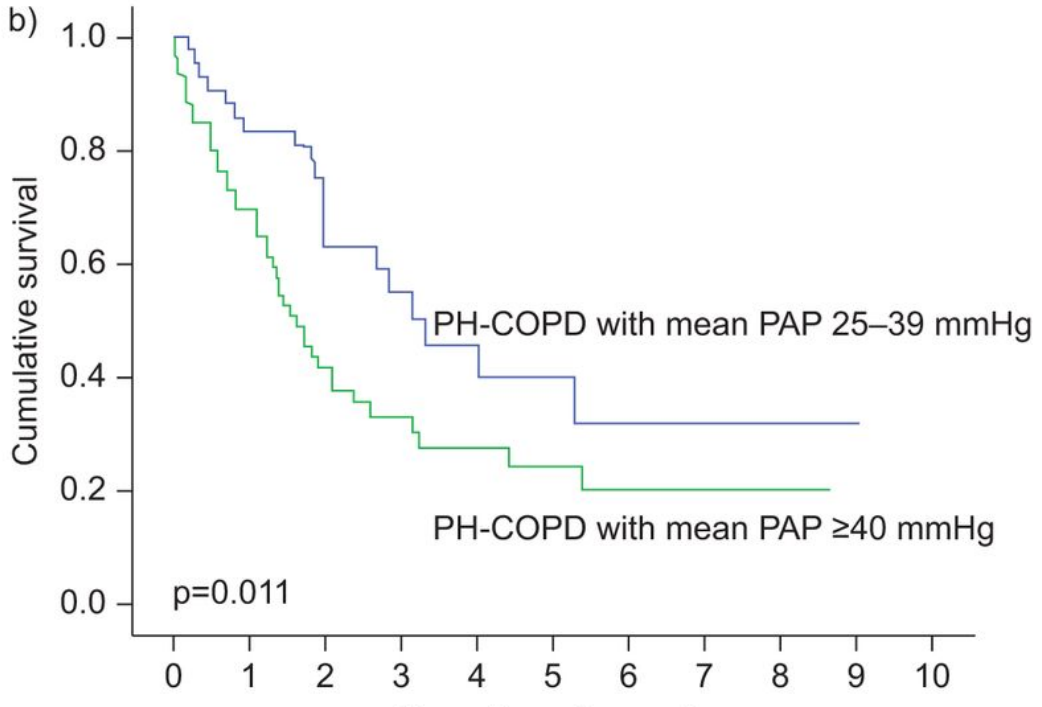
PH	mPAP >20 mmHg
Pre-capillary PH	mPAP >20 mmHg PAWP ⩽15 mmHg PVR >2 WU
Isolated post-capillary PH (ipcPH)	mPAP >20 mmHg PAWP >15 mmHg PVR ⩽2 WU
Combined post- and pre-capillary PH (cpcPH)	mPAP >20 mmHg PAWP >15 mmHg PVR >2 WU

Group 1: PAH
1.1 Idiopathic
1.1.1 Long-term responders to calcium channel blockers
1.2 Heritable[#]
1.3 Associated with drugs and toxins[#]
1.4 Associated with:
1.4.1 connective tissue disease
1.4.2 HIV infection
1.4.3 portal hypertension
1.4.4 congenital heart disease
1.4.5 schistosomiasis
1.5 PAH with features of venous/capillary (PVOD/PCH) involvement
1.6 Persistent PH of the newborn
Group 2: PH associated with left heart disease
2.1 Heart failure:
2.1.1 with preserved ejection fraction
2.1.2 with reduced or mildly reduced ejection fraction
2.1.3 cardiomyopathies with specific aetiologies[¶]
2.2 Valvular heart disease:
2.2.1 aortic valve disease
2.2.2 mitral valve disease
2.2.3 mixed valvular disease
2.3 Congenital/acquired cardiovascular conditions leading to post-capillary PH
Group 3: PH associated with lung diseases and/or hypoxia
3.1 COPD and/or emphysema
3.2 Interstitial lung disease
3.3 Combined pulmonary fibrosis and emphysema
3.4 Other parenchymal lung diseases[+]
3.5 Nonparenchymal restrictive diseases:
3.5.1 hypoventilation syndromes
3.5.2 pneumonectomy
3.6 Hypoxia without lung disease (*e.g.* high altitude)
3.7 Developmental lung diseases
Group 4: PH associated with pulmonary artery obstructions
4.1 Chronic thromboembolic PH
4.2 Other pulmonary artery obstructions[§]
Group 5: PH with unclear and/or multifactorial mechanisms
5.1 Haematological disorders[f]
5.2 Systemic disorders: sarcoidosis, pulmonary Langerhans cell histiocytosis and neurofibromatosis type 1
5.3 Metabolic disorders[##]
5.4 Chronic renal failure with or without haemodialysis
5.5 Pulmonary tumour thrombotic microangiopathy
5.6 Fibrosing mediastinitis
5.7 Complex congenital heart disease

Kovacs, Montani ERJ 2024

Pulmonary hypertension in COPD is common and not associated with severity of COPD

- ASPIRE registry (n=101)
- mPAP ≥40 associated with lower resting SpO2, lower CI, lower DLCO, worse FC – but not
  - FEV1%pred
  - Hypercapnia
  - Smoking status
  - Symptom duration
  - Cardiometabolic comorbidities
  - PCWP
  - Emphysema score or distribution on CT
  - PA/Ao ratio



Hurdman, Kiely, ERJ 2013

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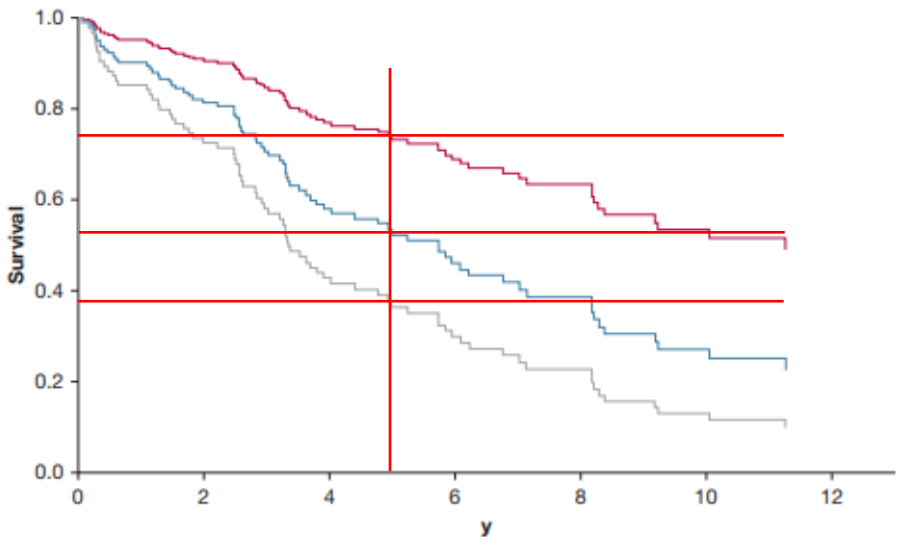
Pulmonary hypertension in COPD is common and prognostically relevant – even when not severe

- 142 COPD patients who underwent clinically indicated RHC 2005-2018
- PH:
  - mPAP ≥ 25 mmHg
  - mPAP 21-24 mmHg + PVR ≥ 3 WU
- Severe PH:
  - mPAP ≥ 35 mmHg
  - mPAP ≥ 25 mmHg + CI < 2 L/min/m^2
- 84% of patients had PH;
- 52% had severe PH

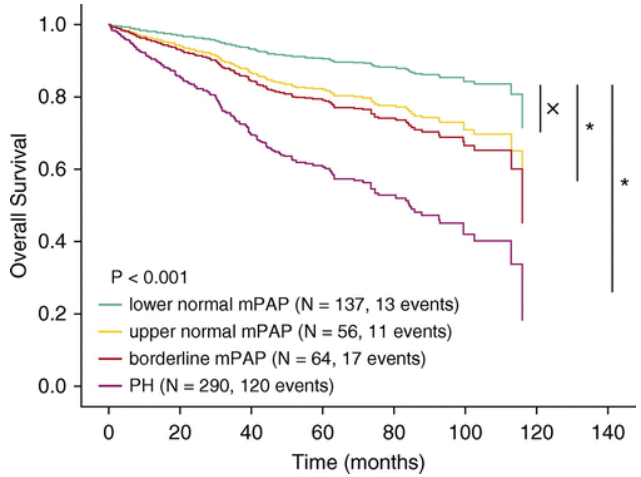


At risk:						
GOLD 1-2 and nonsevere PH	42	41	23	18	14	9
GOLD 1-2 and severe PH or GOLD 3-4 and nonsevere PH	70	52	28	20	14	9
GOLD 3-4 and severe PH	30	18	11	7	4	2

Kovacs, Olschewski CHEST 2022

Mild pulmonary hypertension is prognostically relevant

- 547 pts followed over time, mortality adjusted for age and comorbidities



5 year survival:

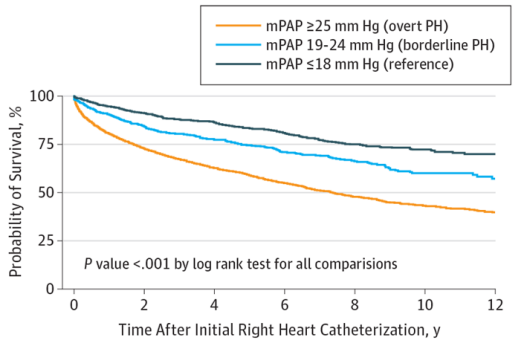
92% mPAP ≤17 mmHg

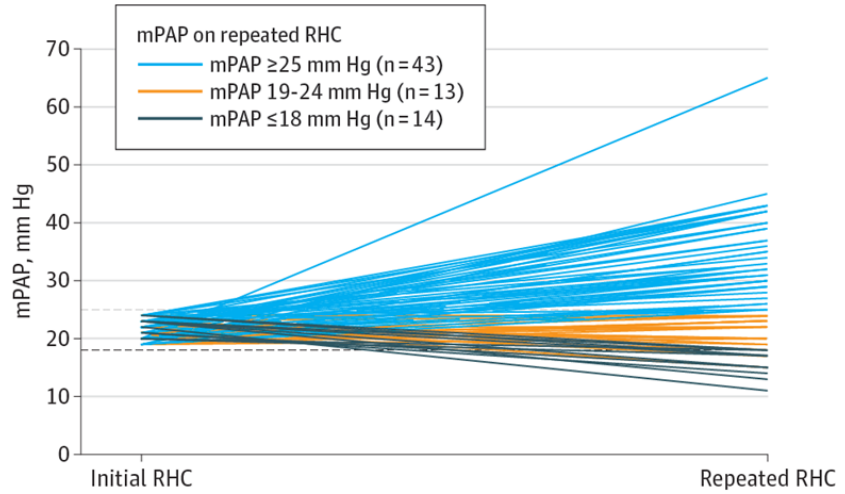
79% mPAP 17-20 mmHg

71% mPAP 20-24.9 mmHg

58% mPAP ≥ 25 mmHg

- And mild PH tends to progress over time





Douschan, Olschewski. AJRCCM 2017

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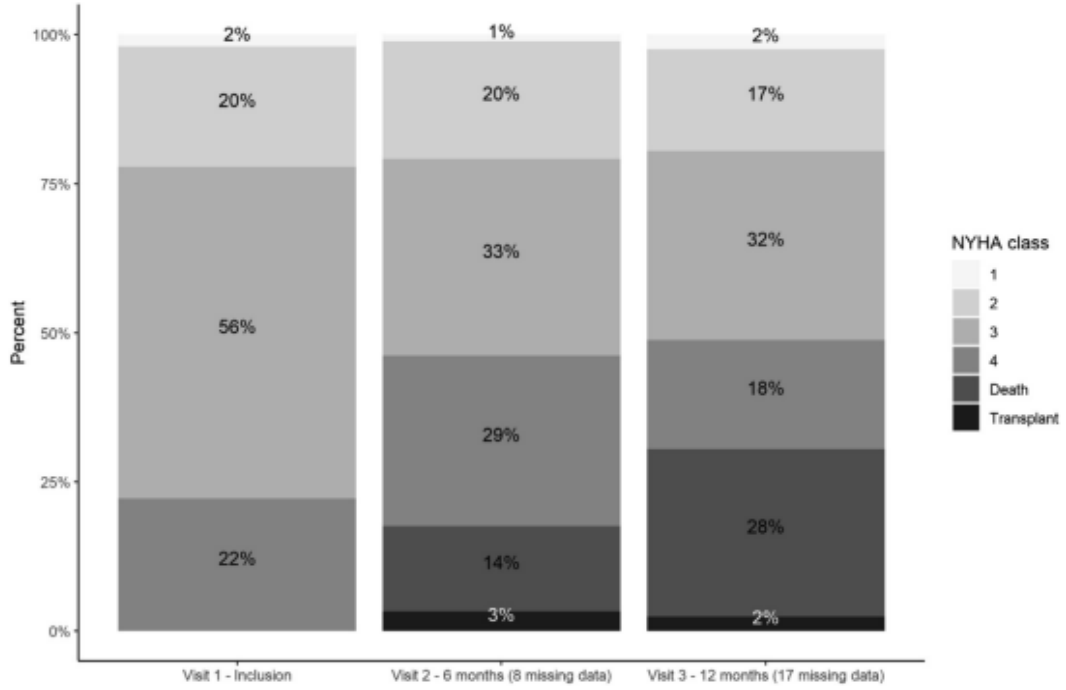
COPD-PH quickly clinically progresses over time

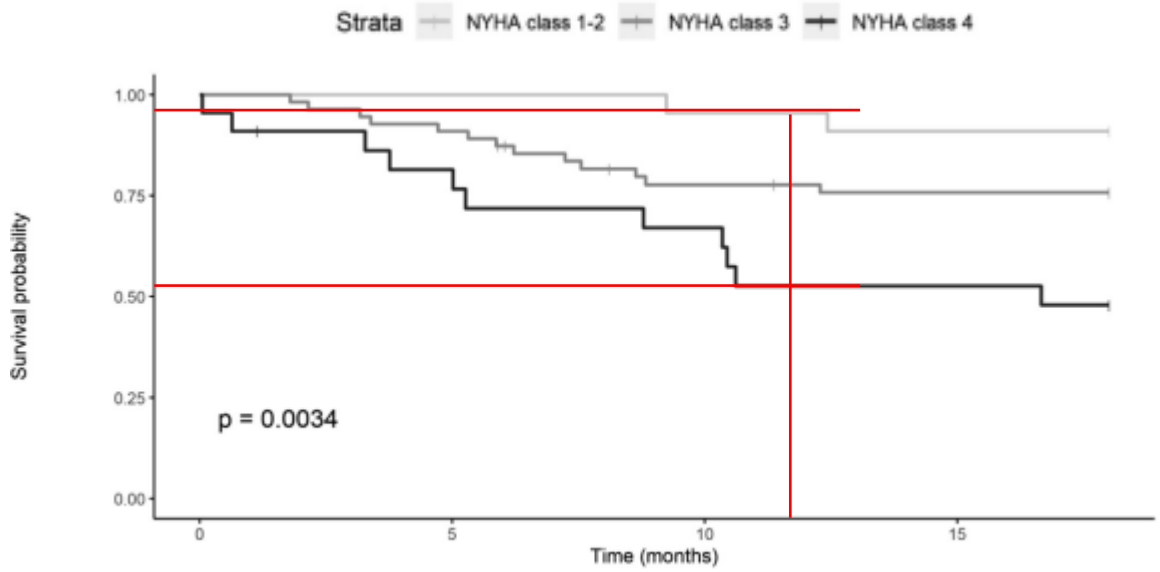
French PH registry of COPD-PH 2012-2016, n=99, mPAP ≥ 35mmHg

- Median mPAP 42 mmHg, PCWP 11mmHg, PVR 6.3 WU



22% FC I-II

19% FC I-II
28% died
2% transplanted



Dauriat, Mal. JHLT 2021

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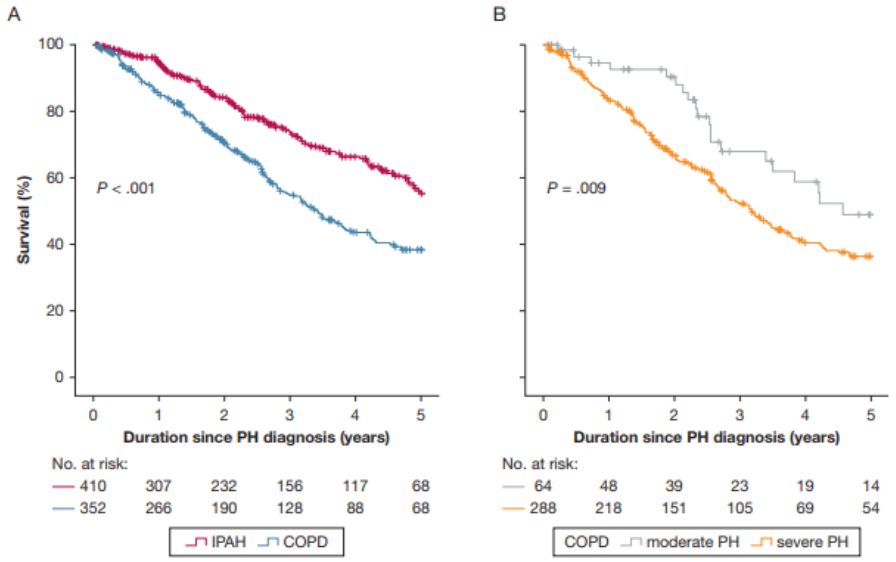
Mortality in COPD-PH may be *worse* than in PAH

- COMPERA registry data of
  - Idiopathic PAH
  - Moderate COPD-PH (mPAP 25-34 or 21-24 + PVR ≥ 3)
  - Severe COPD-PH (mPAP ≥35 or mPAP >25 + CI < 2)
- Similar hemodynamic abnormalities with substantially worse survival in COPD-PH
- All treated with PH therapy (most PDE5i alone)
- Response to PH therapy predicted improved survival



Survival	IPAH	COPD-PH
1 year	94%	86%
3 year	74%	55%
5 year	57%	38%

Vizza, Grunig. CHEST 2021

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Quick summary, so far

- PH in the context of COPD is often categorized as WSPH group 3, although hemodynamically and prognostically is similar or worse than WSPH group 1
- The prevalence of PH in COPD is somewhere around 40%
- Development of PH in COPD is not associated with severity of COPD
- Even *mild* PH in COPD is strongly associated with reduced functional capacity (worsening over time), QoL, increased hospitalizations and healthcare utilization, and mortality

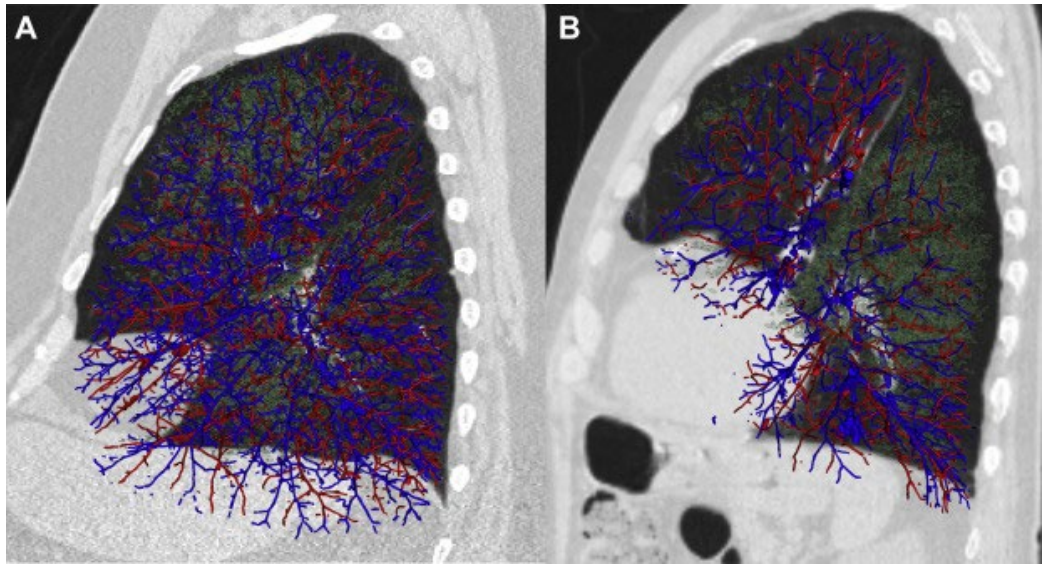
Pulmonary vascular phenotype– *not necessarily in severe COPD*

- **Pulmonary vascular phenotype of COPD**
  - Low DLCO
  - Cardiovascular exercise limitation
  - Absence of hypercapnia
  - Moderate airflow limitation
  - Mild-moderate emphysema on CT
  - Severe PH
- Some patients previously classified as 'PAH' actually had pulmonary vascular phenotype of COPD (with relatively mild COPD)

Shlobin, Channick. ERJ 2024
Hoeper, Halank. Lancet Respir Med 2022
Collins, Stickland. CHEST 2026

Pulmonary vascular morphology changes in COPD

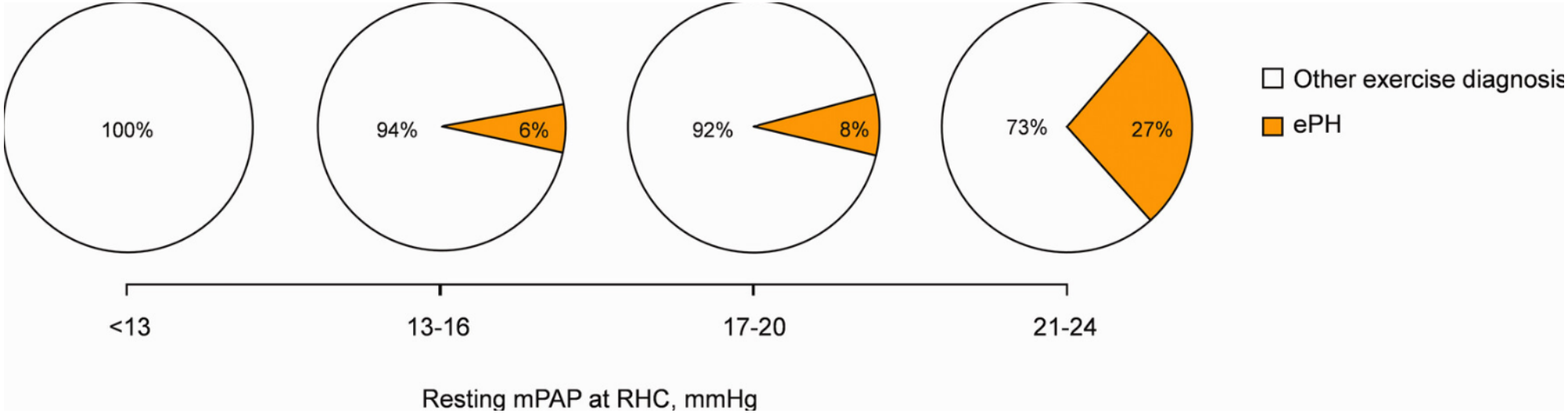
- COPDGene: Longitudinal observational study of >3000 ever-smokers with/without COPD
- Pulmonary artery pruning (lower ratio of small artery volume to total lung artery volume) associated with faster progression of radiographic emphysema and spirometric decline
- Pruning is associated with clinically significant increase in RV volume and mortality – even in mild-moderate COPD



Washko, San Jose Estepar. AJRCCM 2019
Pistenmaa, San Josee Estepar. CHEST 2021

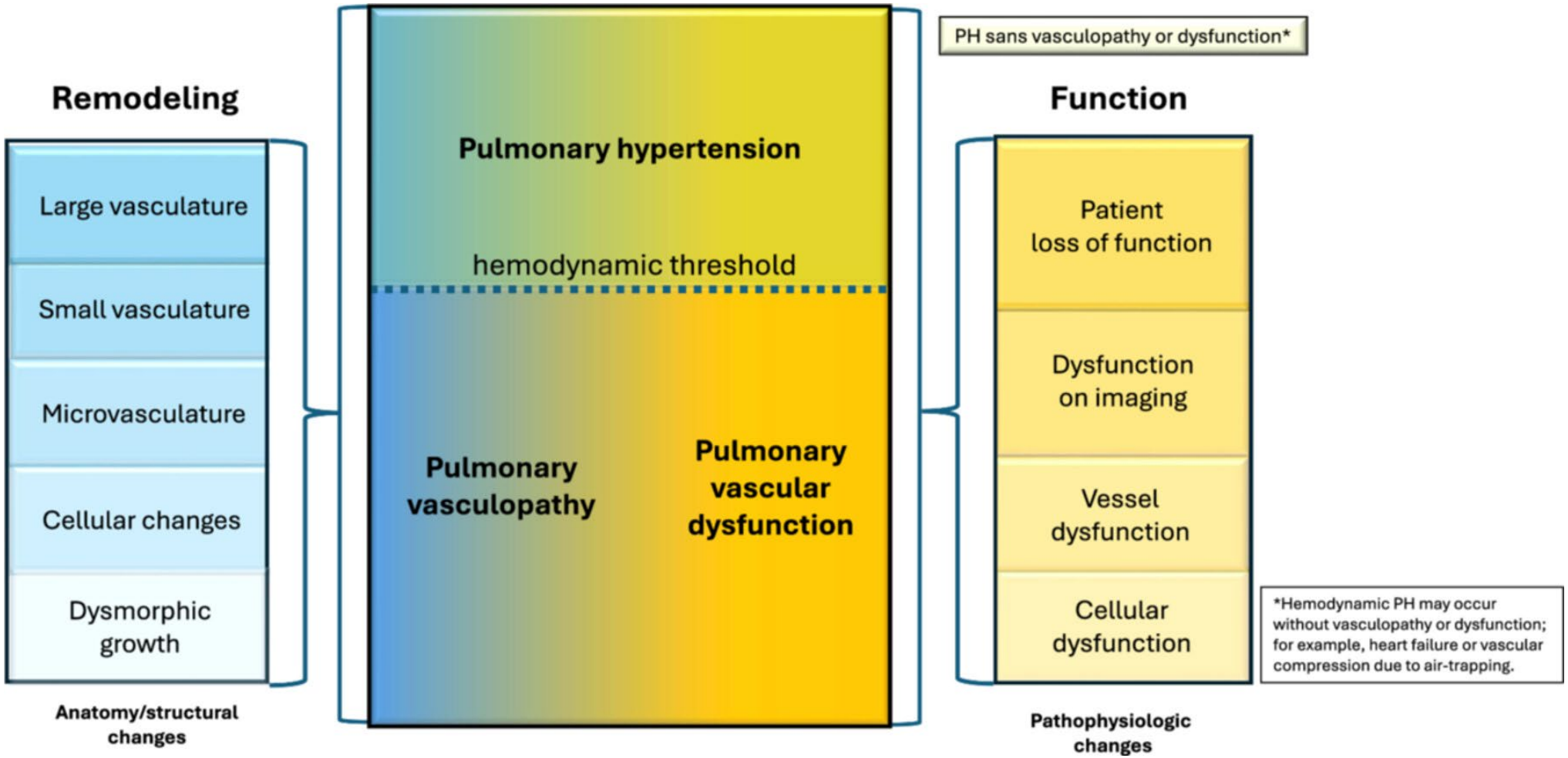
Pulmonary vascular compliance changes in COPD

- Impaired PA relaxation and excess vasoconstriction in COPD → rise in PAP, PVR
- In patients with 'normal' PA pressures → abnormal response to exercise, decrease in exertional tolerance, and increase in mortality



Oliveira, Systrom. Pulm Circ 2017

Pulmonary vascular abnormalities may exist even *without* PH in COPD



Nathan, Nikkho. Pulm Circ 2025

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Quick summary

- A substantial number of patients with COPD develop pulmonary vascular abnormalities
- These vascular abnormalities may be morphologic (e.g., pruning) and functional (e.g., impaired compliance)
- Pulmonary vascular abnormalities are directly associated with reduced functional capacity, inappropriate response to exercise, impaired QoL, and increased mortality – even when mild and below the threshold of PH
- There may be value in doing exercise RHC challenges on patients with COPD who have normal resting pulmonary hemodynamics
- Vascular changes are not proportional to severity of COPD, but may contribute to progression of emphysema

RCTs in COPD-PH have been limited

First author, year [reference]	Lung disease	Study design	Subjects n	Therapy	Results	Comments
COPD trials						
Vitulo, 2017 [167]	COPD-PH	RCT	28	Sildenafil (n=18)	Decrease in PVR, improvement in BODE, D_{LCO} and quality of life	No adverse effect on oxygenation
Maron, 2022 [168]	COPD-PH	RCT	42	Tadalafil (n=28)	No change in PVR or mPAP at 6 months Improvement in shortness-of-breath questionnaire	No adverse effect on oxygenation
Nathan, 2024 [169]	COPD-PH	RCT	136	Inhaled treprostinil (n=66)	Decrease in 6MWD at 12 weeks	Study terminated due to increased SAE in the treated group

Shlobin, Channick. ERJ 2024

What happened with PERFECT?

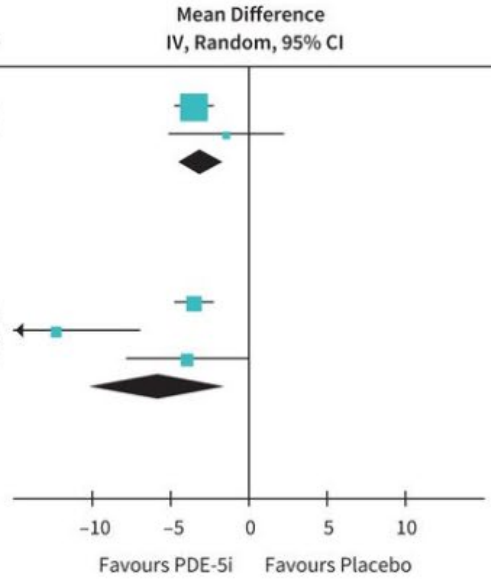
- Randomized, placebo controlled RCT of inhaled treprostinil for COPD-PH (mPAP ≥ 30 mmHg, PVR ≥ 4 WU) – actual was mPAP 43.5, PVR 7.4
- 12-week crossover study with primary endpoint of change in peak 6MWD
- Stopped early due to increased serious adverse events in treprostinil group
  - Maybe because the population was already so sick?
  - Maybe because of fragility of numbers?
- …but there were responders, and they had mPAP ≥40 mmHg, FEV1 >40%pred, DLCO >25% pred

Nathan, Waxman. ERJ 2024

PDE5i seem to trend toward benefit in meta-analyses

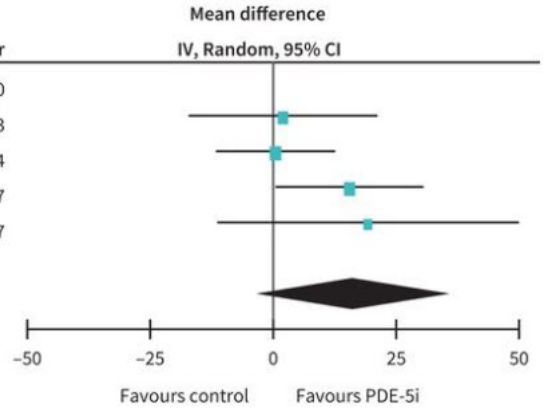
PA pressure

Study or subgroup	PDE-5i Mean (mmHg)	PDE-5i SD (mmHg)	PDE-5i Total	Control Mean (mmHg)	Control SD (mmHg)	Control Total	Weight	Mean Difference IV, Random, 95% CI	Year
1.2.1 mPAP									
Goudie et al. 2014	−3.5	2.12	55	0	4.12	56	86.2%	−3.50 (−4.72– −2.28)	2014
Vitulo et al. 2017	−3.84	3.87	18	−2.4	5.12	10	13.8%	−1.44 (−5.08–2.20)	2017
Subtotal (95% CI)			73			66	100.0%	**−3.21 (−4.61– −1.82)**	
Heterogeneity: Tau²=0.20; Chi²=1.11, df = 1 (P=0.29); I²=10%									
Test for overall effect: Z=4.52 (P<0.00001)									
1.2.2 sPAP									
Rao et al. 2010	−3.5	2.12	55	0	4.12	56	41.7%	−3.50 (−4.72– −2.28)	2010
Goudie et al. 2014	−4.7	4.11	12	7.6	8.77	13	26.1%	−12.30 (−17.60– −7.00)	2014
Shrestha et al. 2017	−9.87	7.84	30	−5.93	7.44	31	32.2%	−3.94 (−7.78– −0.10)	2017
Subtotal (95% CI)			97			100	100.0%	**−5.94 (−10.26– −1.62)**	
Heterogeneity: Tau²=11.28; Chi²=10.05, df=2 (P=0.007); I²=80%									
Test for overall effect: Z=2.69 (P=0.007)									



6MWD

Study or subgroup	PDE-5i Mean (m)	PDE-5i SD (m)	PDE-5i Total	Control Mean (m)	Control SD (m)	Control Total	Weight	Mean difference IV, Random, 95% CI	Year
Rao *et al.* 2010	191	127	15	39	87	18	5.5%	152.00 (76.20–227.80)	2010
Blanco *et al.* 2013	23	36.91	29	21	38.05	31	23.7%	2.00 (−16.97–20.97)	2013
Goudie *et al.* 2014	15.5	32.49	56	15	32.22	57	27.4%	0.50 (−11.43–12.43)	2014
Shrestha *et al.* 2017	48.13	25.79	30	32.59	32.96	31	25.9%	15.54 (0.71–30.37)	2017
Vitulo *et al.* 2017	8.1	35.9	18	−11.2	41.2	10	17.5%	19.30 (−11.15–49.75)	2017
Total (95% CI)			148			147	100.0%	**16.35 (−3.24, 35.94)**	
Heterogeneity: Tau²=327.98; Chi²=17.29, df=4 (p= 0.002); I²=77%									
Test for overall effect: Z=1.64 (p=0.10)									



Arif, Mehta. ERJ Open Research 2022

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…but the true clinical impact is uncertain

Treatment	PH outcomes		Clinical outcomes				
	Cardiopulmonary haemodynamic	RV function	Symptoms	Functional capacity	HRQoL	Hospitalisation	Survival
Oxygen (n=4)							
LTOT (n=8)	+	NA	NA	NA	NA	NA	+
NOT (n=2)	+/−	NA	NA	NA	NA	NA	0
CCBs (n=4)							
Nifedipine (n=3)	0	NA	+	NA	NA	NA	0
Felodipine (n=1)	+	NA	NA	0	NA	NA	NA
PH-targeted therapy (n=9)							
PDE type 5 inhibitors							
Sildenafil (n=5)	+	NA	+/−	+/−	+/−	NA	NA
Tadalafil (n=1)	+	NA	0	0	0	NA	NA
ERA							
Bosentan (n=2)	+/−	NA	+	+/−	+	NA	NA
Ambrisentan (n=1)	NA	+	+/−	0	NA	NA	NA

Arif, Mehta. ERJ Open Research 2022

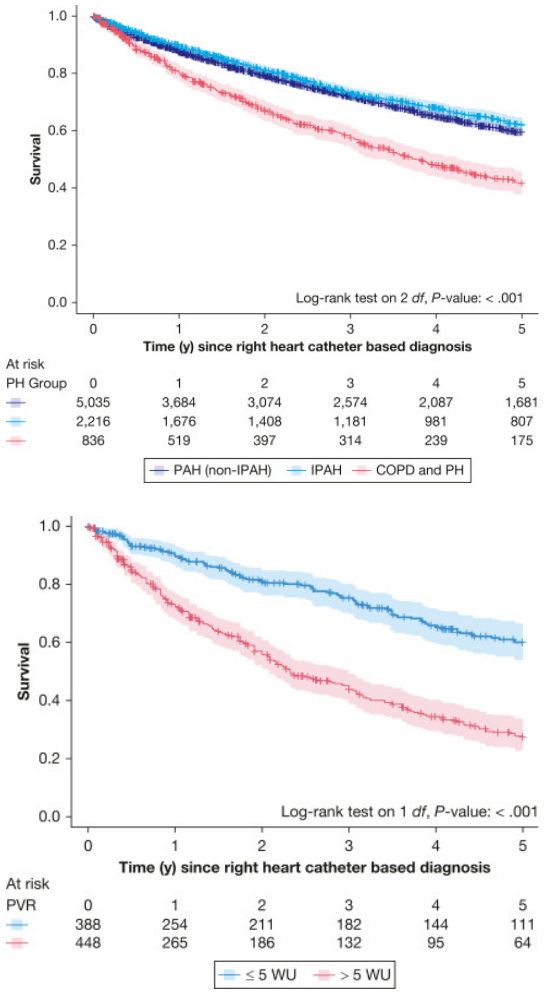
Previous studies have been limited by small numbers and inconsistent diagnostics – can we do better?

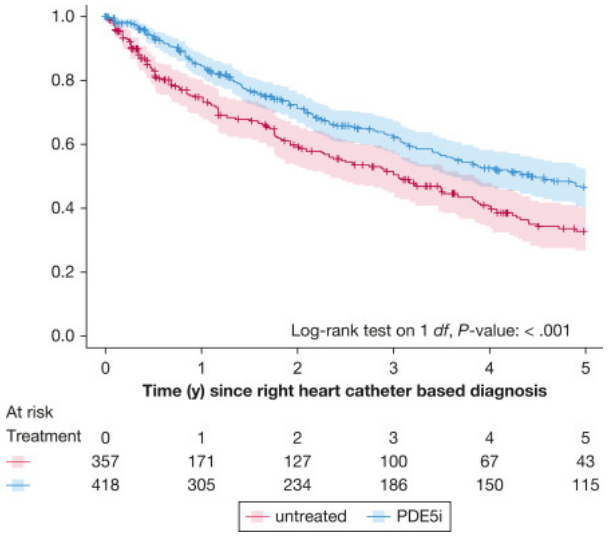
- 26981 patient PVRI GoDeep meta-registry – 836 pts with COPD-PH (by RHC)
- Median FEV1 51% pred, mPAP 35mmHg, PVR 5 WU, CI 2.5 L/min/m^2

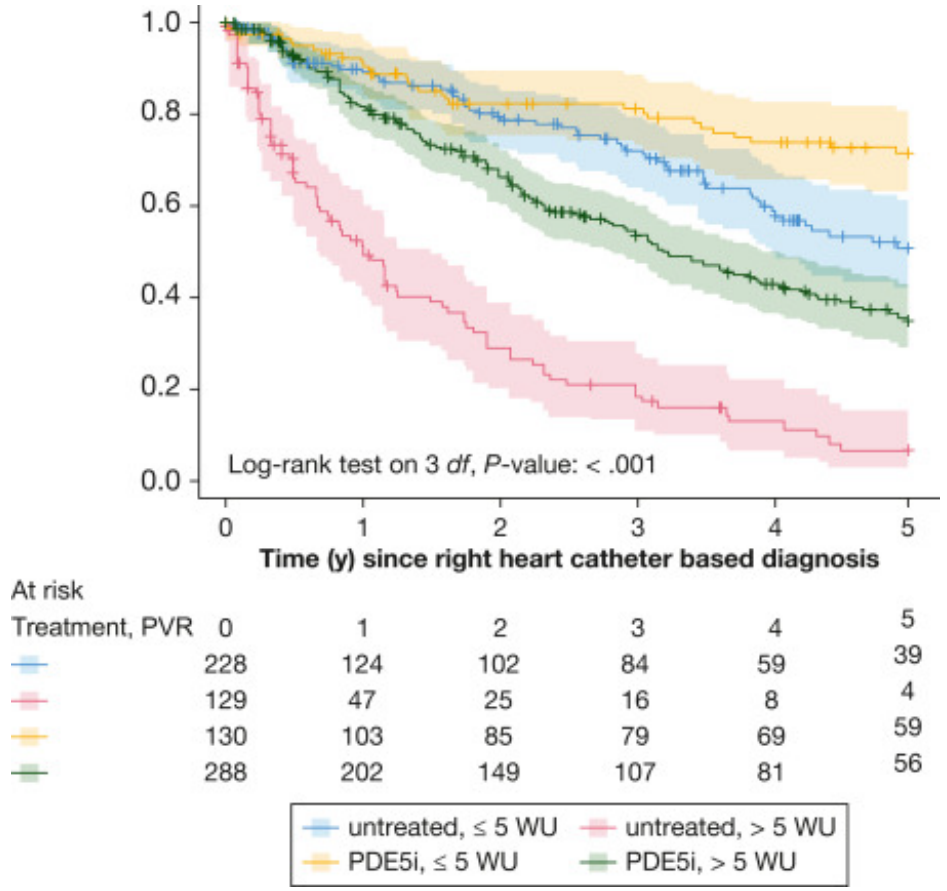
PVR	≤ 5 WU (N = 388)	> 5 WU (N = 448)	Overall (N = 836)
PDE5i	130 (34)	288 (64)	418 (50)
ERA	22 (5.7)	90 (20)	112 (13)
sGC stimulators	1 (0.26)	10 (2.2)	11 (1.3)
PGI2	46 (12)	60 (13)	106 (13)
PDE5i and ERA	16 (4.1)	71 (16)	87 (10)
ERA and PGI2	6 (1.5)	24 (5.4)	30 (3.6)
PDE5i and PGI2	21 (5.4)	47 (10)	68 (8.1)
PDE5i, ERA, and PGI2	4 (1)	21 (4.7)	25 (3)
≥ 1 PH drugs	160 (41)	319 (71)	479 (57)

Tello, Seeger. CHEST 2025

PDE5i use is associated with improved survival irrespective of PVR







Tello, Seeger. CHEST 2025

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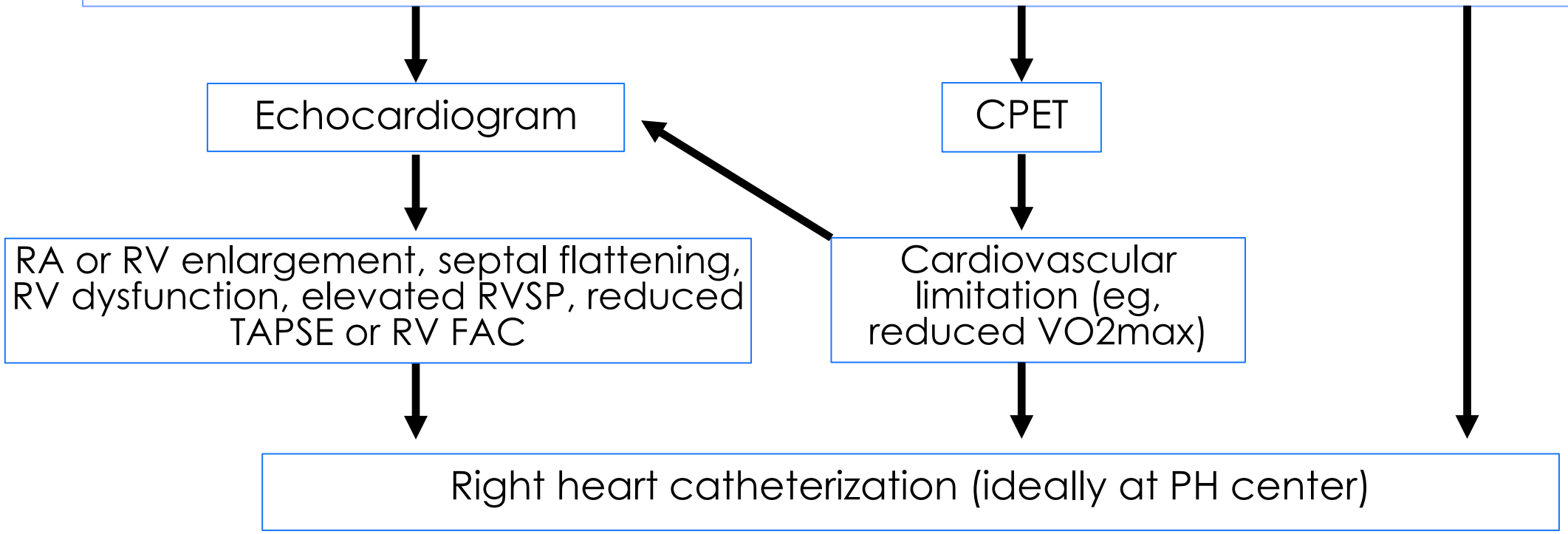
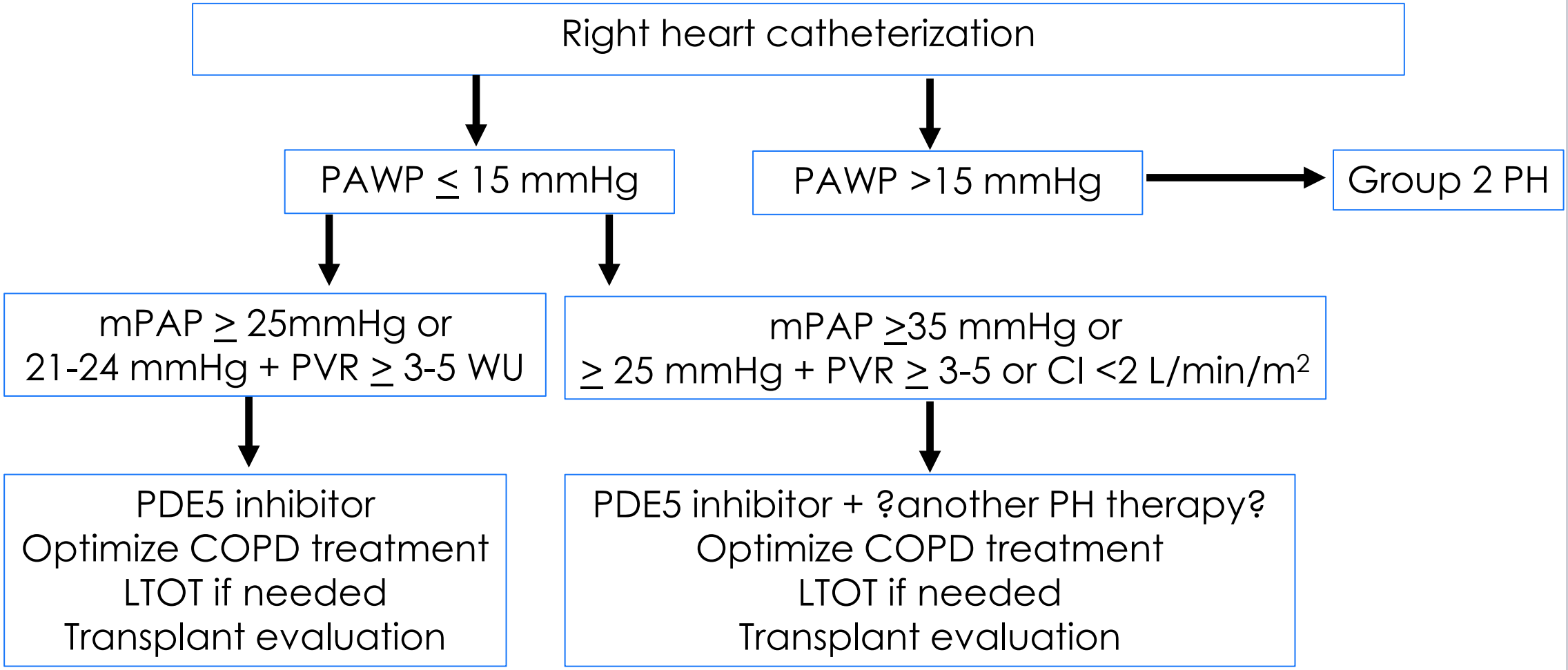
So, who should we screen?

- Dyspnea or exertional intolerance 'out of proportion' to spirometric or radiographic extent of COPD (or PA/Ao ratio >1 on CT)
- Reduction/decline in DLCO out of proportion to severity of obstruction
- Clinical evidence of RV dysfunction
- Absence of hypercapnia and presence of hypoxemia



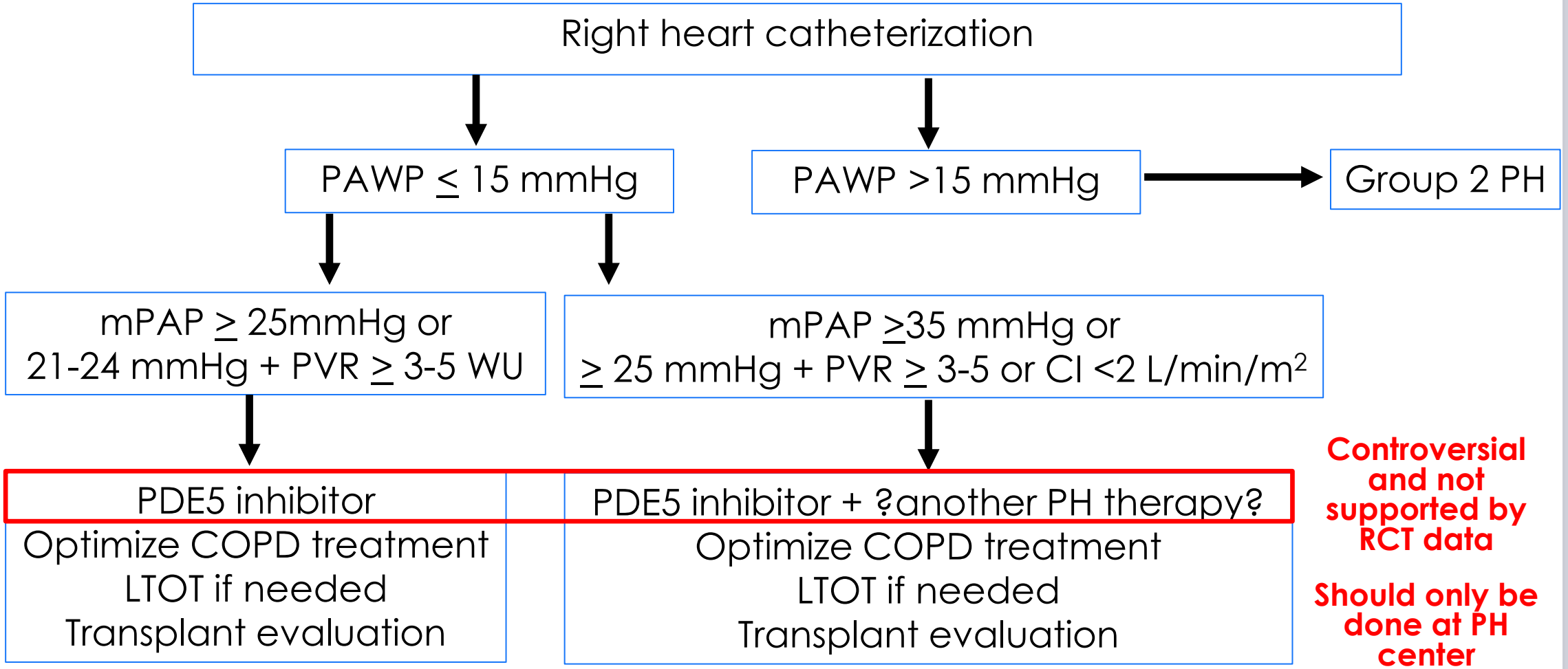
Shin, Nathan. Resp Med 2014
Higham, Morrell. ERJ 2001

How should we treat?



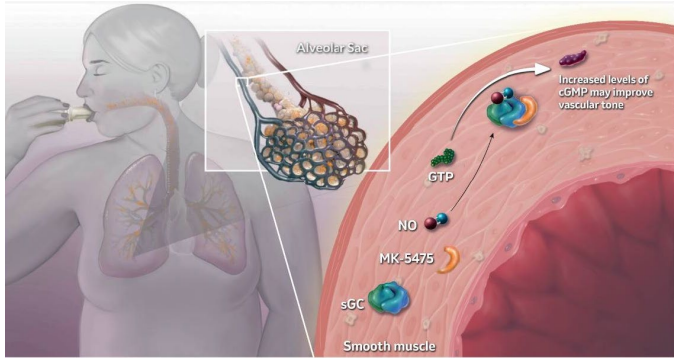
Tello, Seeger. CHEST 2025
Nathan, Nikkho. Pulm Circ 2025
Arif, Mehta. ERJ Open Research 2022

How should we treat?



Current active interventional trials in COPD-PH

- INSIGNIA-PH-COPD: placebo-controlled RCT of inhaled sGC stimulator (frespaciguat; MK5475) in PH-COPD (Merck; NCT05612035)
  - INSIGNIA-PAH – phase 2 PAH RCT demonstrated reduction in PVR with good AE profile
  - Phase 1 COPD-PH trial with ~15% placebo-controlled between-group reduction in PVR



- ERASE PH-COPD: placebo-controlled RCT of tadalafil for PH-COPD (AP-HP, France; NCT05844462)
- BETTER COPD-PH: placebo-controlled RCT of tadalafil for dyspnea in PH-COPD (VA; NCT05937854)

Humbert, Hoeper. ERJ 2024
Bajwa, Stoch. Int J COPD 2024

Unanswered questions

- Relationship between parenchymal changes and vasculopathy in COPD
- Which patients should undergo RHC
- How should COPD patients be phenotyped and can this phenotyping be used as a treatment endpoint (e.g., vascular pruning)?
- Which threshold of patients of COPD-PH benefit from PH therapy?
- Which subtypes of non-severe PH in COPD benefit from PH therapy?
- Is there value in treating exercise PH in COPD?
- What screening tools should be optimally used for PH in COPD?
- Etc.

Nathan, Nikkho. Pulm Circ 2025

Summary

- PH in COPD is common, unrelated to severity of COPD, underdiagnosed, and associated with impaired exertional tolerance, reduced quality of life, and reduced survival – even when mild
- Pulmonary vascular changes in a subset of patients with COPD begin early, are associated with progression of COPD and functional status, and affect clinical endpoints even before they meet criteria for 'PH'
- There is no robust prospective clinical trial data to support PH therapy in COPD, but a substantial body of observational and metadata studies support at least the use of PDE5 inhibitors – particularly with more advanced hemodynamic changes
- COPD-PH remains understudied, should be considered early in the diagnosis of COPD, and patients with COPD-PH deserve particular focus and early transplant evaluation

Thank you!

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Cedars Sinai

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Dr. Julia Maheshwari received her medical degree from New York University. She trained at Massachusetts General Hospital and subsequently at the University of California San Francisco, where she also completed subspecialty fellowship training in lung transplantation. Dr. Maheshwari founded and is now Medical Director of the UCSF Advanced COPD Clinic. She serves as an Assistant Professor at UCSF specializing in end-stage COPD and lung transplantation.

Lung Transplant for COPD

Julia Maheshwari, MD

Medical Director, Advanced COPD Clinic

Transplant Pulmonologist

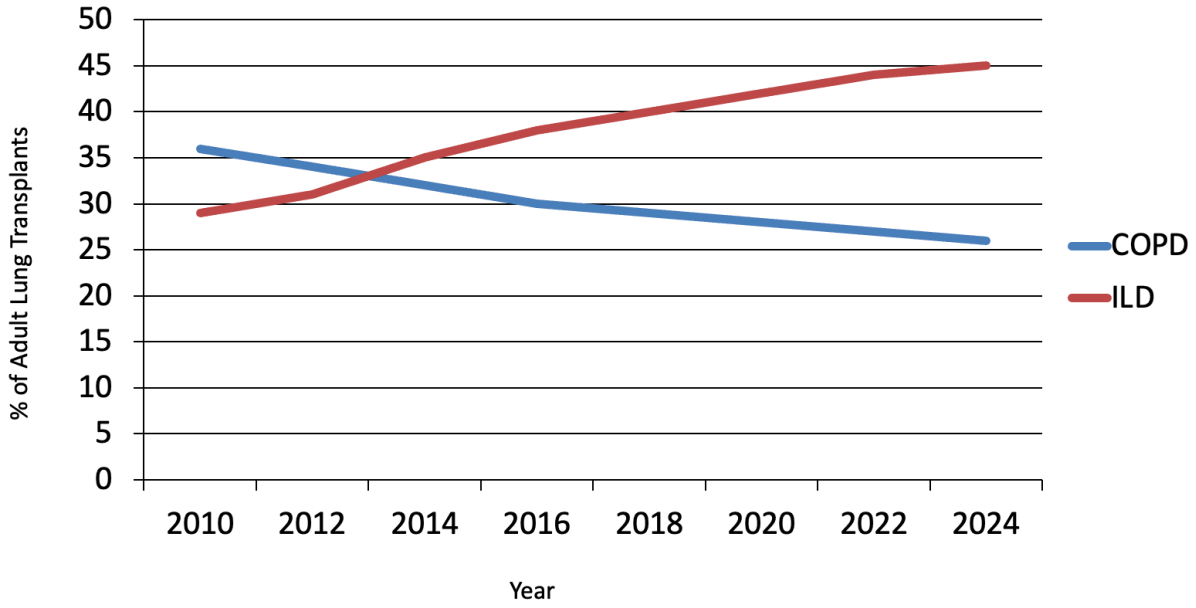
University of California, San Francisco

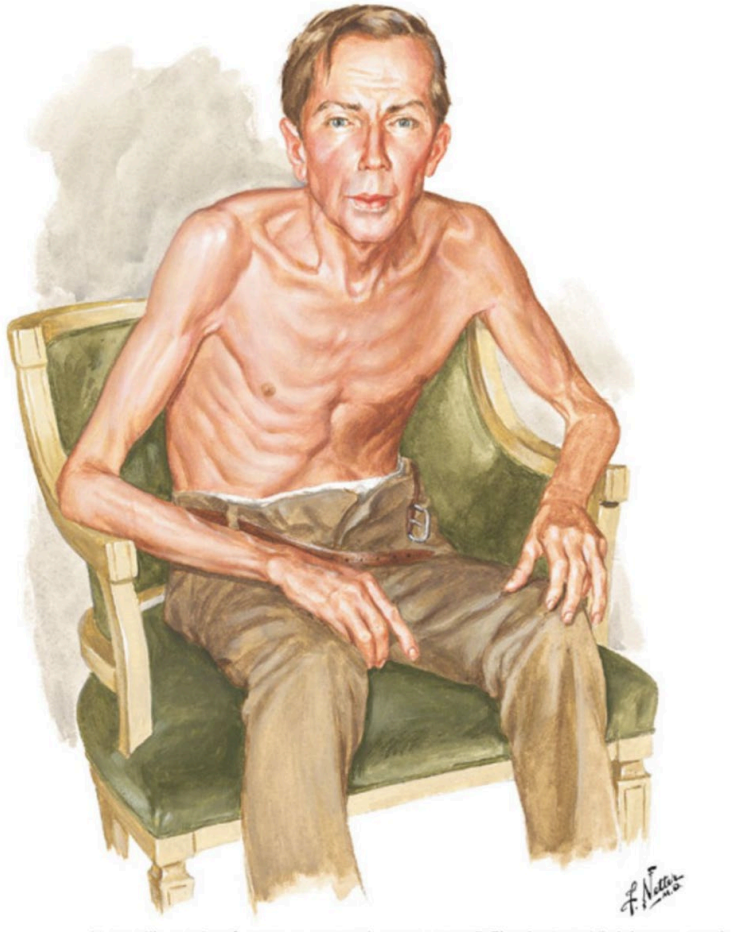
Disclosures

- I have no disclosures
- I will not discuss off-label use and/or investigational use of any drugs or devices

Lung Transplant for COPD

- 25% of adult lung transplants in 2023
- 600 lung transplants for COPD





Goals of Lung Transplantation

01

Increase survival

02

Reduce disability

03

Improve health-related quality of life

Outline

1. When To Refer?
2. When To List?
3. Single Or Double Lung Transplant?
4. Is There A Survival Benefit?

Prompts For Transplant Referral

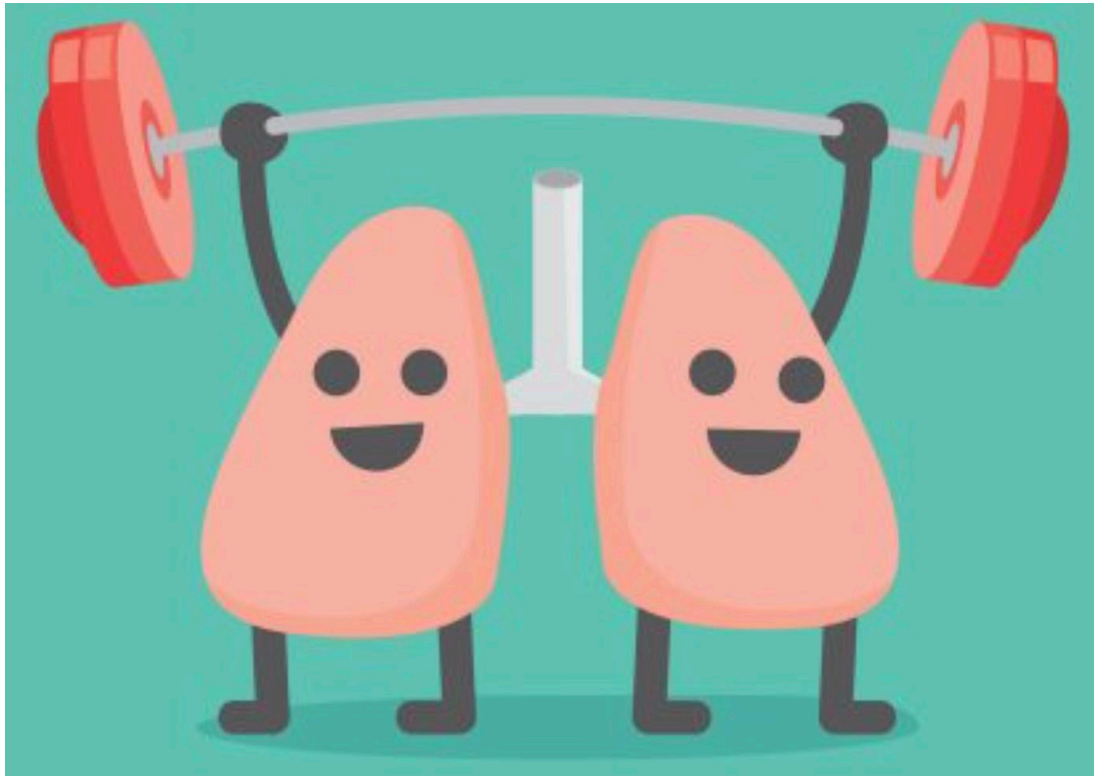
- BODE score 5-6 with any of the following:
  - Frequent exacerbations
  - Increase in BODE score > 1 over past 2 years
  - Pulmonary artery: aorta diameter > 1 on CT scan
  - FEV_1 20-25% predicted
- Progressive disease despite maximal treatment
- Poor quality of life unacceptable to patient
- Simultaneous referral to lung transplant and LVR is appropriate

Criteria For Transplant Listing

- Progressive disease despite maximal medical treatment
- $P_aCO_2 > 50$ mm Hg *or* $P_aO_2 < 60$ mm Hg
- At least one of the following:
  - BODE index ≥ 7
  - $FEV_1 < 20\%$ predicted
  - History of severe exacerbation(s)
  - Chronic hypercapnia
  - Moderate – severe pulmonary hypertension

Endobronchial Valves and Transplant

- Not a contraindication to lung transplant
- Provide more time before needing a transplant
- Allow patients to rehabilitate before transplant
  - Reverse frailty & sarcopenia



Absolute Barriers to Transplant

Malignancy with high risk of recurrence or death related to cancer
Limited functional status (non-ambulatory) with poor potential for post-transplant rehabilitation
Active substance use or dependence including current tobacco use, vaping, marijuana use, or IV drug use

Risk Factors for Transplant

Age > 65 years
BMI < 16 kg/m^2
Frailty
Hypoalbuminemia

Criteria for Transplant Listing

Patients with > 50% chance of death within the next 2 years

Patients with > 80% likelihood of 5-year post-transplant survival from a general medical perspective

Timing for Transplant in COPD Is Challenging

- Natural history of COPD can be protracted
- Gradual worsening in functional status and quality of life
- In COPD, survival without transplant can exceed median survival post-transplant

The BODE Index Debate

Table 2. Variables and Point Values Used for the Computation of the Body-Mass Index, Degree of Airflow Obstruction and Dyspnea, and Exercise Capacity (BODE) Index.*

Variable	Points on BODE Index			
	0	1	2	3
FEV_1 (% of predicted)†	≥65	50–64	36–49	≤35
Distance walked in 6 min (m)	≥350	250–349	150–249	≤149
MMRC dyspnea scale‡	0–1	2	3	4
Body-mass index§	>21	≤21		

The BODE Index Debate:

Pre-transplant BODE score

Predicted post-transplant survival

vs

Observed post-transplant survival

The BODE Index Debate

	Observed Kaplan–Meier post-transplant survival[#]	Expected survival according to BODE score						
		BODE score 4	BODE score 5	BODE score 6	BODE score 7	BODE score 8	BODE score 9	BODE score 10
1 yr	0.77 (0.65 – 0.89)	0.97 (0.96–0.98)	0.96 (0.95–0.97)	0.95 (0.93–0.96)	0.93 (0.90–0.95)	0.91 (0.86–0.94)	0.88 (0.81–0.93)	0.85 (0.74–0.91)
2 yrs	0.71 (0.58 – 0.84)	0.89 (0.87–0.91)	0.86 (0.81–0.89)	0.82 (0.75–0.87)	0.76 (0.66–0.83)	0.70 (0.56–0.80)	0.61 (0.44–0.75)	0.52 (0.31–0.70)
3 yrs	0.67 (0.54 – 0.80)	0.81 (0.77–0.85)	0.76 (0.69–0.81)	0.69 (0.59–0.77)	0.61 (0.47–0.72)	0.52 (0.34–0.66)	0.41[¶] (0.22–0.60)	0.31[¶] (0.12–0.31)
4 yrs	0.65 (0.51 – 0.79)	0.66 (0.59–0.72)	0.57 (0.47–0.66)	0.47 (0.34–0.59)	0.37[¶] (0.22–0.52)	0.26[¶] (0.12–0.44)	0.17[¶] (0.05–0.35)	0.09[¶] (0.01–0.27)
10 yrs	0.39 (0.21 – 0.57)	ND	ND	ND	ND	ND	ND	ND

- Survival benefit for patients with BODE score ≥ 7
- Improvement in HRQL for patients with BODE score 5-6

RGICAL TECHNIQUE I SURVIVAL

Single or Bilateral Lung Transplant?

REGIONAL VENTILATION AND PERFUSION AFTER LUNG TRANSPLANTATION IN PATIENTS WITH EMPHYSEMA*

PAUL M. STEVENS, M.D., PHILIP C. JOHNSON, M.D., ROBERT L. BELL, M.D., ARTHUR C. BEALL, JR., M.D., AND DANIEL E. JENKINS, M.D.

Abstract Serial ^{133}Xe ventilation and perfusion scans were done on two patients who underwent left-lung transplantation because of severe emphysema associated with alpha$_1$ antitrypsin deficiency. In both, perfusion of the implants increased to nearly 70 per cent of total and was accompanied by a decrease in ventilation and volume to about 30 per cent of total. Under these circumstances the implants functioned largely as physiologic shunts. The remaining emphysematous lung increased in volume and received most of the ventilation but very little of the total perfusion.

Patients with emphysema thus may be poor candidates for lung transplantation because the high vascular resistance and static compliance of the remaining emphysematous lung predispose it to further hypoperfusion and hyperinflation.

WITH one exception[1] all attempts at lung transplantation have failed within a month after surgery. The cause of death in these patients has been ascribed to unrelated disease,[2] intervening infections or "rejection" or both.[3,4] Because of methodologic limitations, little knowledge is available about the influence of physiologic abnormalities in the patient's remaining lung on the ultimate outcome.

Feasibility of unilateral lung homotransplantation has been based largely on experiments done in otherwise normal animals. Under these circumstances, adequate respiration is maintained by the animal's remaining lung until the transplant begins to function. Only rarely can an animal survive on only the transplanted lung after removal of his own remaining lung. In human beings, the situation is entirely different since the remaining lung may also be severely diseased — often with a process that

insufficiency (Table 1). Serum protein electrophoresis revealed decreased alpha$_1$ globulins. Immunodiffusion and immunoelectrophoresis confirmed that this was due to an alpha$_1$ antitrypsin deficiency.

Preoperative ^{133}Xe ventilation and perfusion scans were done with an Anger scintillation camera, but because of inability to move this camera to the transplantation suite, postoperative studies were done with collimating detectors directed at anatomically equivalent areas of the right and left chest posteriorly. In the first patient (W.W.), the availability of only two detectors necessitated repeated measurement during a single study since only one zone of each lung could be evaluated simultaneously. Thus, after an intravenous injection of approxi-

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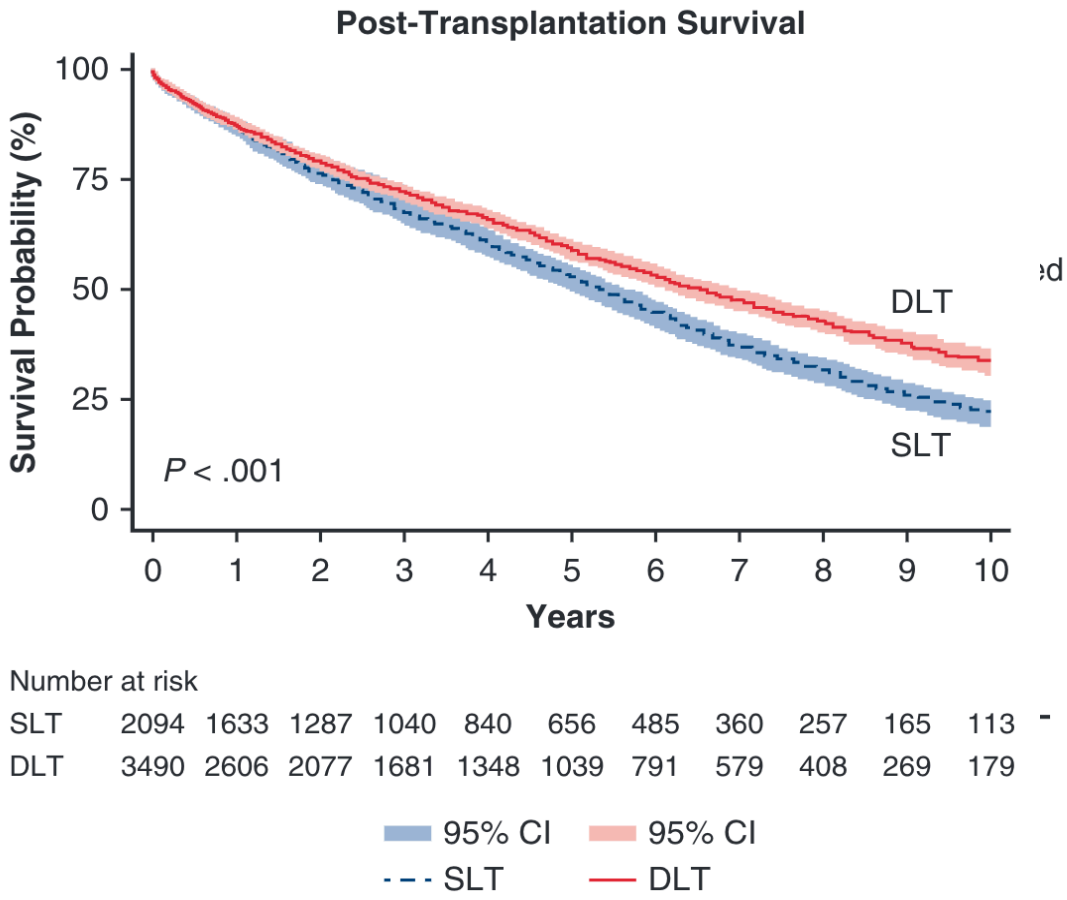
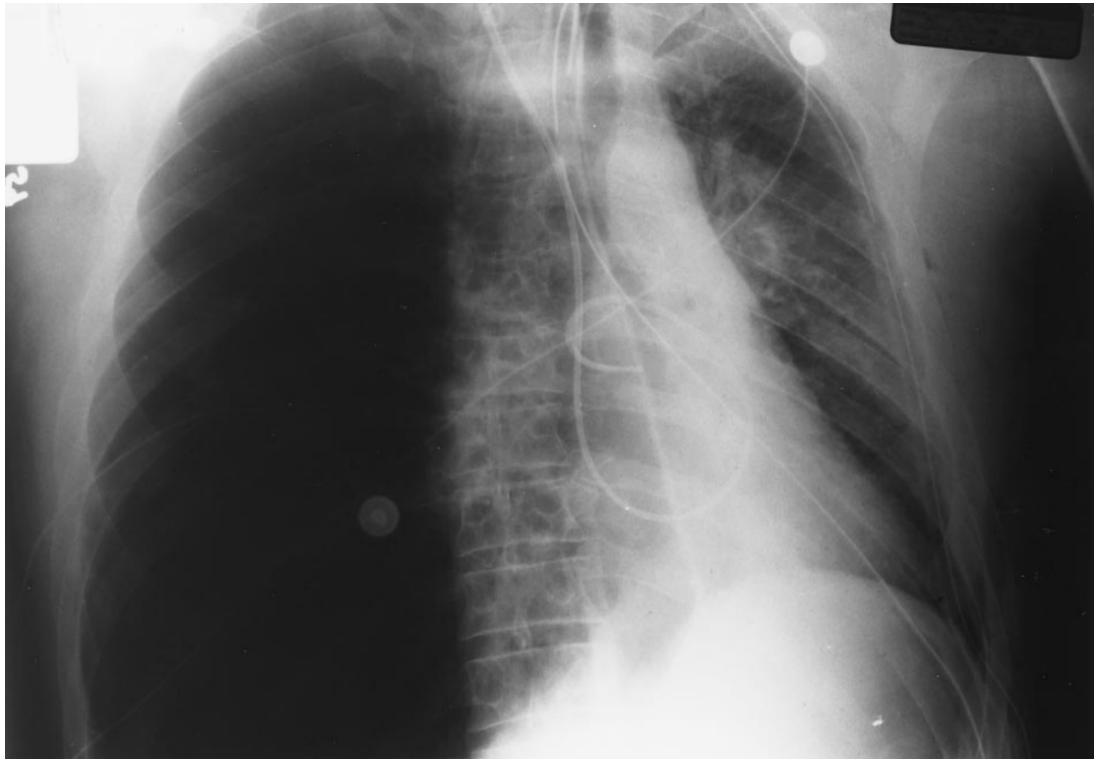
What About Single Lung Transplant?

- Allows for more lung transplants
- Reduces waitlist mortality

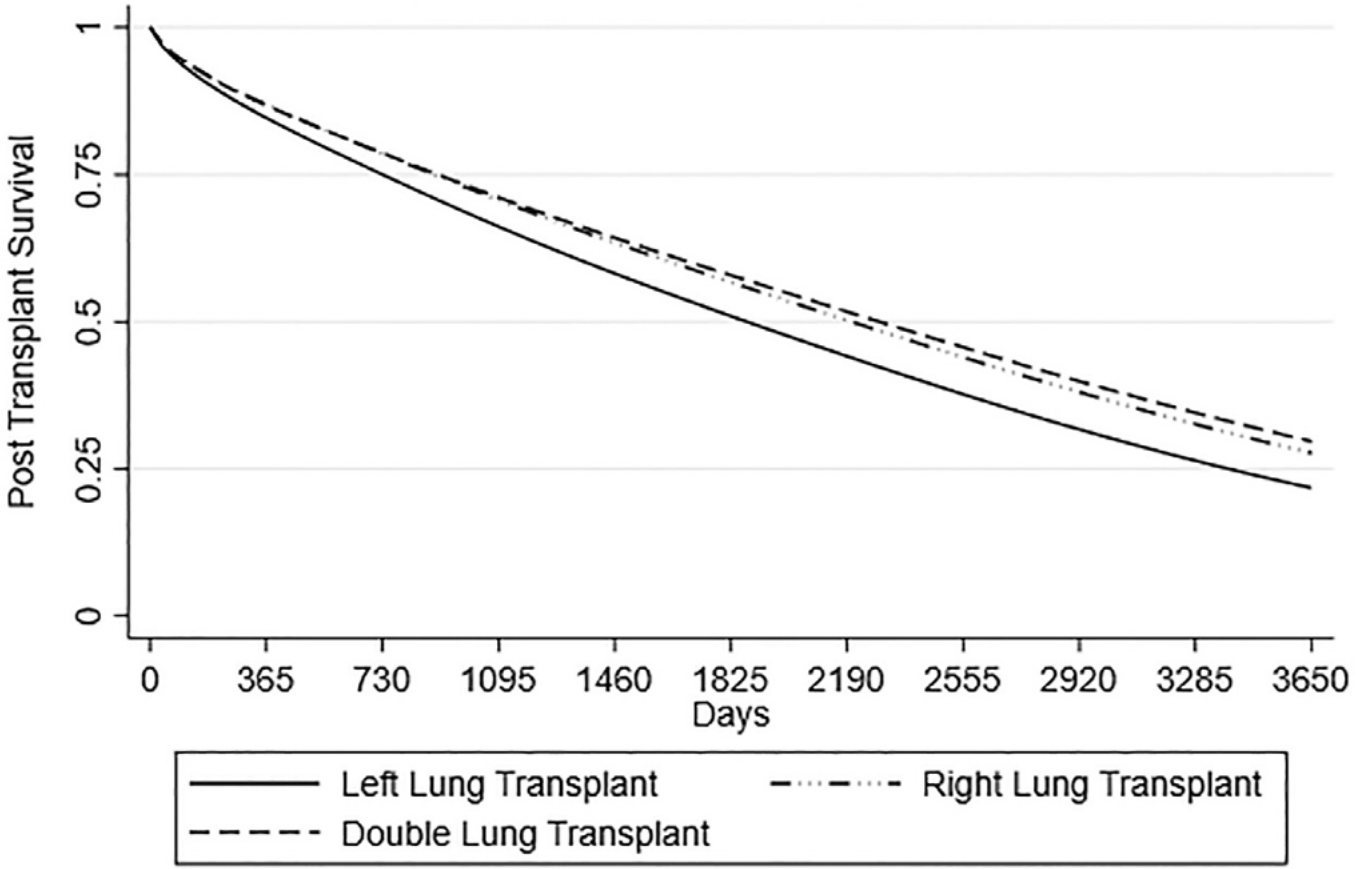


Complications with Single Lung Transplant

- Native lung hyperinflation
- Native lung cancer
- Less “lung reserve”



Does Laterality Matter For A Single?



Single or Bilateral Lung Transplant?

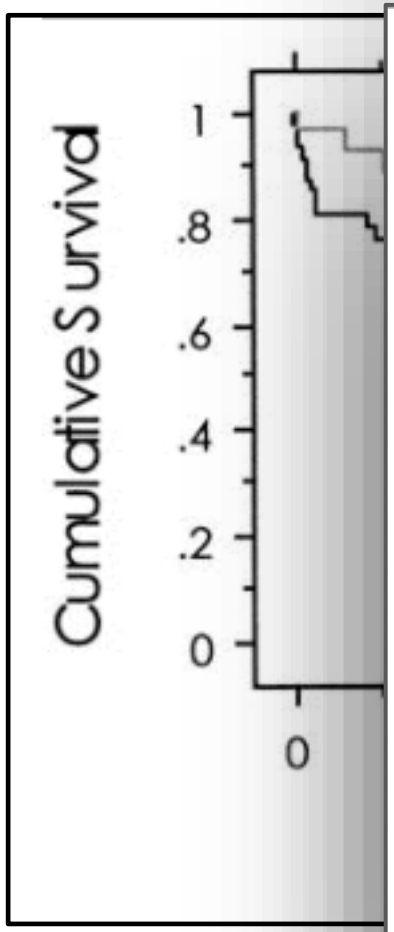
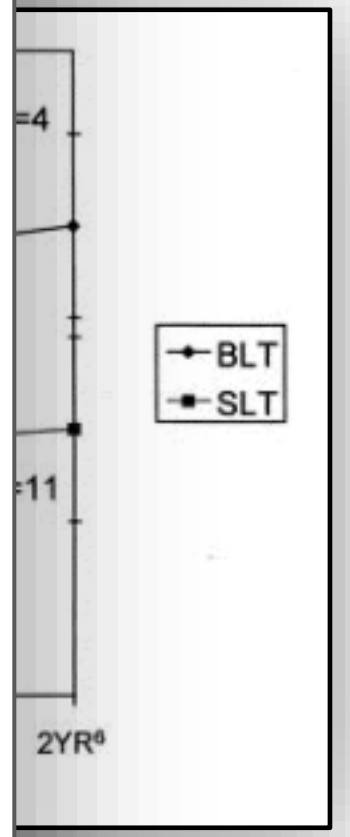


Table I. *Preoperative group demographics*

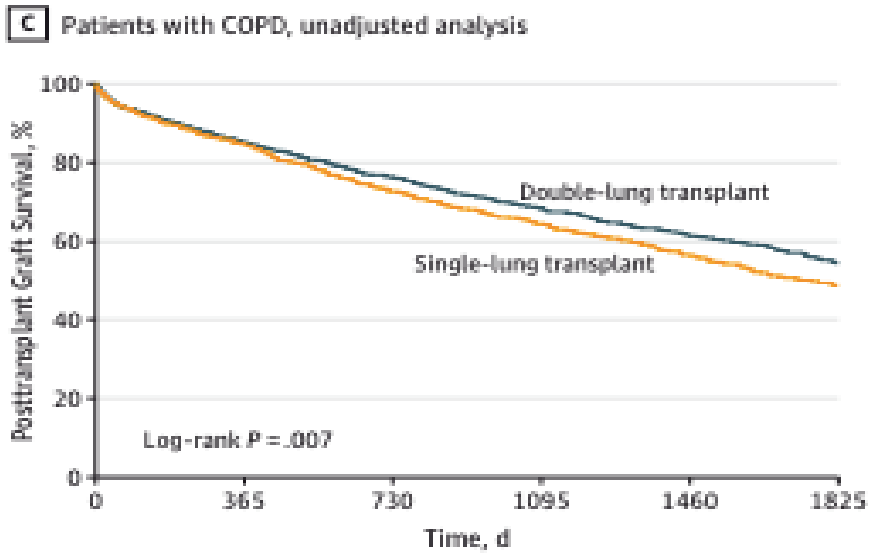
	BLT	*SLT*	*p Value*
Age	48.8 ± 9.7	55.3 ± 6.6	0.001
Sex (% male)	17/29 (58.6%)	13/47 (27.7%)	0.007
Pco_2 (mm Hg)	46.5 ± 11.9	49.3 ± 10.5	0.15 (NS)
PAP (mm Hg)	37.9 ± 11.2	35.8 ± 7.01	0.19 (NS)
FVC (L)	2.18 ± 0.75	1.76 ± 0.49	0.0097
FEV_1 (L)	0.6 ± 0.17	0.55 ± 0.18	0.096 (NS)
RV (L)	5.41 ± 2.1	5.13 ± 1.32	0.33 (NS)
6MWT (feet)	712.7 ± 238.1	677.1 ± 290.8	0.26 (NS)

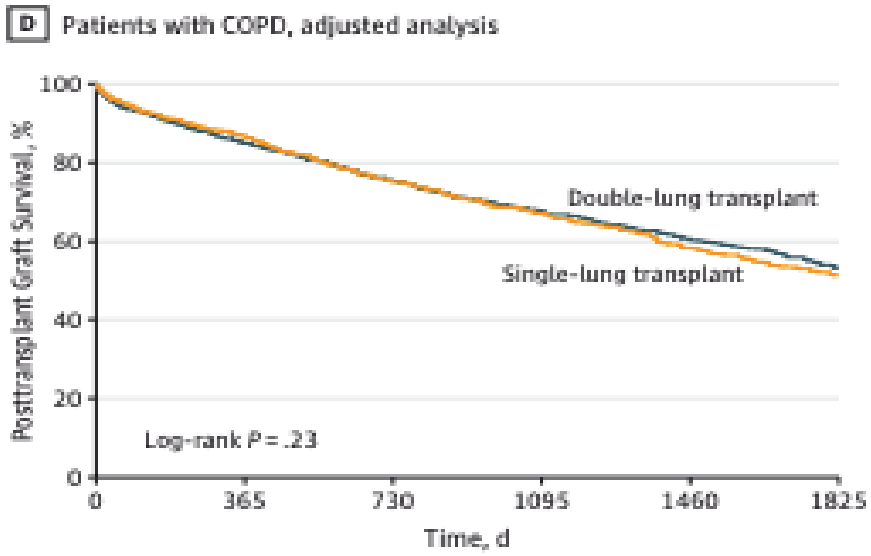
Data are shown as mean ± the standard deviation. *Pco_2*, Carbon dioxide tension; *PAP*, pulmonary artery pressure; *FVC*, forced vital capacity; *FEV_1*, volume exhaled in 1 second; *RV*, residual volume; *6MWT*, 6-minute walk test; *NS*, not significant. Pulmonary function test data were measured at the time of the initial evaluation and listing.



Single or Bilateral Lung Transplant?

- 3174 patients with COPD who underwent single or double lung transplantation between 2005-2012





No. at risk

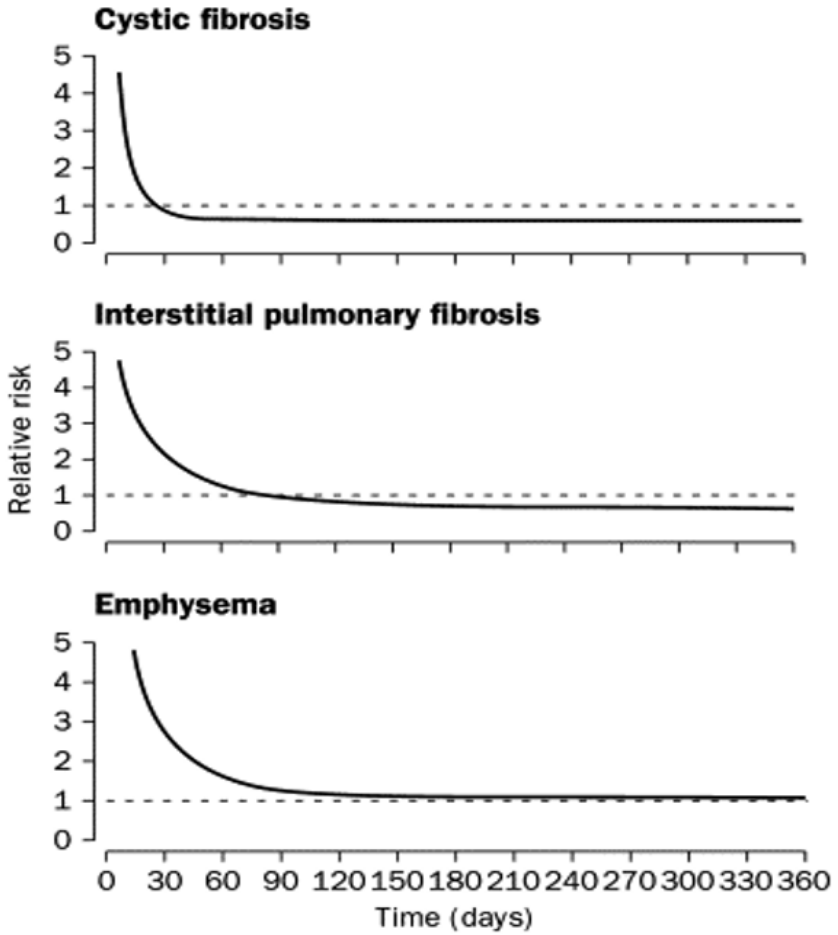
Single-lung transplant	1299	947	698	521	365	234
Double-lung transplant	1875	1326	955	667	438	274

Snapshot From Today

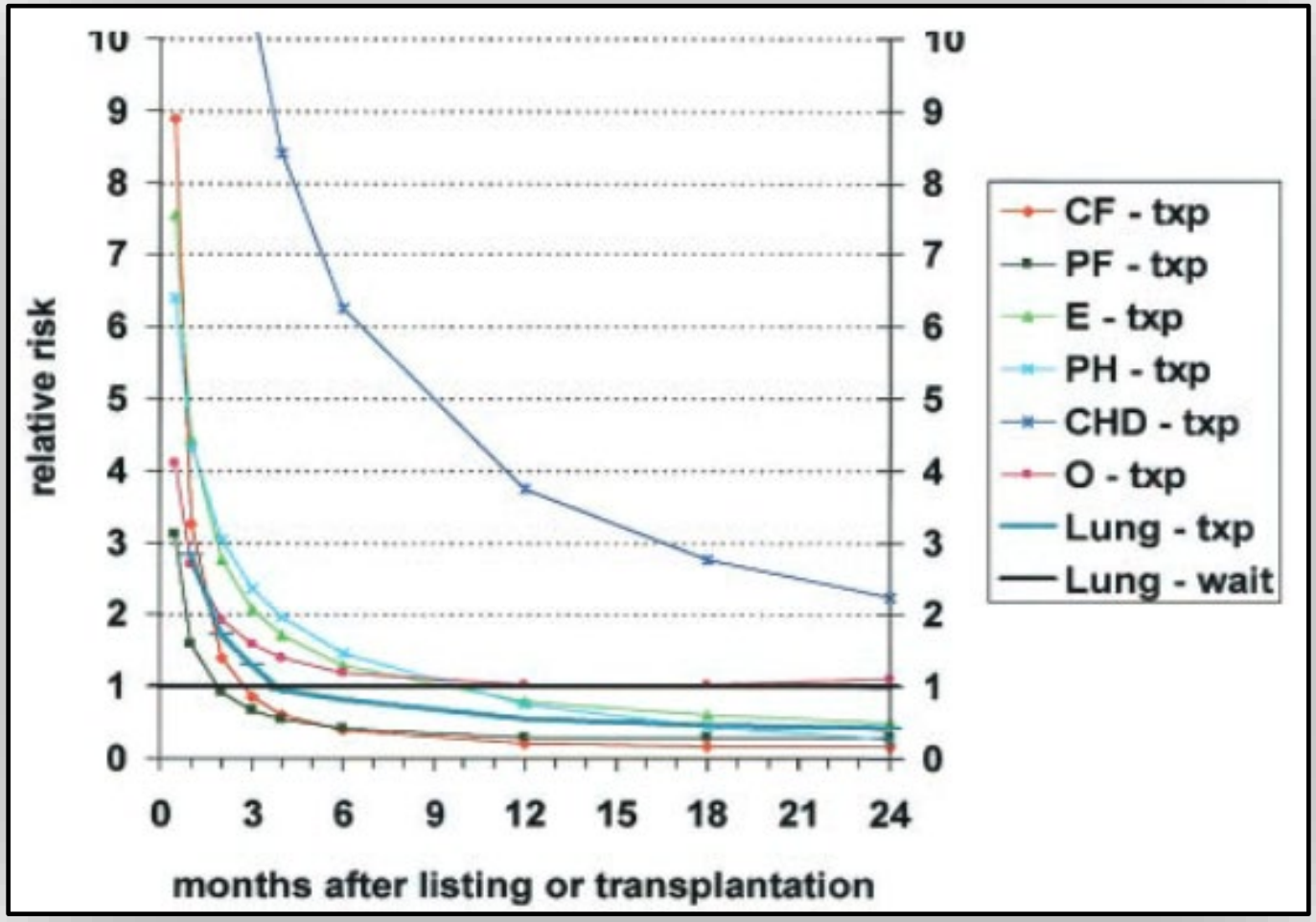
- Majority of lung transplants for COPD are bilateral

- Factors such as age, frailty, CAD, renal disease may support single

Does Transplant Confer A Survival Benefit?



Does Transplant Confer A Survival Benefit?



Why Might It Be Hard To Tell?

- Protracted disease course
- Able to function w/reduced QOL
- Similar life expectancy & median survival
- Difficult to compare post-transplant with patients still on waitlist
- Variable follow-up period, limited number of patients
- Studies include early lung transplantation, premature listing of COPD patients at start
- Changes in organ allocation algorithms over study periods

Does Transplant Confer A Survival Benefit?

Variables	Registration (*n* = 8,182) Hazard Ratio (95% CI)	*P* Value	Transplantation (*n* = 5,873) Hazard Ratio (95% CI)	*P* Value
Age (per 10-yr increase)	1.29 (1.19–1.40)	<0.001	1.15 (1.09–1.21)	<0.001
Female sex	1.08 (0.96–1.21)	0.21	1.02 (0.95–1.09)	0.65
Period of listing		<0.001		<0.001
1987–1995	1		1	
1996–1998	1.03 (0.89–1.19)		0.91 (0.83–0.99)	
1999–2001	0.79 (0.68–0.91)		0.80 (0.73–0.89)	
2002–2004	0.64 (0.50–0.81)		0.62 (0.54–0.71)	
α_1-Antitrypsin deficiency	0.58 (0.49–0.70)	<0.001	1.03 (0.96–1.13)	0.57
Functional status class*		<0.001		0.003
I, II	1		1	
III	1.43 (1.24–1.64)		1.02 (0.92–1.12)	
IV	2.47 (1.78–2.43)		1.36 (1.14–1.62)	
Diabetes	1.18 (0.85–1.65)	0.33	1.41 (1.08–1.83)	0.02
Oxygen required at rest	2.68 (2.20–3.27)	<0.001	0.91 (0.84–0.99)	0.02
Six-minute-walk distance < 150 ft	1.79 (1.46–2.20)	<0.001	1.07 (0.93–1.23)	0.35
Continuous mechanical ventilation	7.30 (3.61–14.60)	<0.001	2.04 (1.44–2.89)	<0.001
FEV_1 (per 10% of predicted)	0.62 (0.57–0.68)	<0.001	1.0 (0.97–1.03)	0.95
FVC (per 10% of predicted)	0.77 (0.74–0.80)	<0.001	1.0 (0.98–1.03)	0.81
PAPs (per 10-mm Hg increase)	1.18 (1.12–1.24)	<0.001	1.02 (0.98–1.07)	0.36
PCWP (per 10-mmHg increase)	1.30 (1.16–1.45)	<0.001	1.0 (0.92–1.09)	0.95
Body mass index† (per 5-point increase)	0.80 (0.75–0.85)	<0.001	1.01 (0.97–1.05)	0.56
Single lung transplantation	—	—	1.30 (1.19–1.43)	<0.001

Definition of abbreviations: PAPs = systolic pulmonary artery pressure; PCWP = pulmonary capillary wedge pressure.
* Functional status classes range from I to IV, with IV indicating that the patient experiences symptoms even at rest.
† The body mass index is the weight in kilograms divided by the square of the height in meters.

Summary

- Goals of lung transplant in COPD:
  - Prolong survival
  - Reduce disability
  - Improve health-related quality of life
- Refer early
- The "right" time to list can be challenging to pinpoint
- Ideal surgical technique is not clear, though mostly bilateral currently
- Transplant may not prolong survival, but it can increase quality of life

References

- 1. Lahzami S, Bridevaux PO, Soccal PM, Wellinger J, Robert JH, Ris HB, et al. Survival impact of lung transplantation for COPD. Eur Respir J. 2010;36(1):74-80. Epub 2009/12/10. doi: 10.1183/09031936.00087809. PubMed PMID: 19996194.
- 2. Reed RM, Cabral HJ, Dransfield MT, Eberlein M, Merlo CA, Mulligan MJ, et al. Survival of Lung Transplant Candidates With COPD: BODE Score Reconsidered. Chest. 2018;153(3):697-701. Epub 2017/10/22. doi: 10.1016/j.chest.2017.10.008. PubMed PMID: 29054348; PubMed Central PMCID: PMCPMC5989634.
- 3. Pirard L, Marchand E. Reassessing the BODE score as a criterion for listing COPD patients for lung transplantation. Int J Chron Obstruct Pulmon Dis. 2018;13:3963-70. Epub 2018/12/24. doi: 10.2147/COPD.S182483. PubMed PMID: 30573956; PubMed Central PMCID: PMCPMC6292230.
- 4. Fishman A, Martinez F, Naunheim K, Piantadosi S, Wise R, Ries A, et al. A randomized trial comparing lung-volume-reduction surgery with medical therapy for severe emphysema. N Engl J Med. 2003;348(21):2059-73. Epub 2003/05/22. doi: 10.1056/NEJMoa030287. PubMed PMID: 12759479.
- 5. Stevens PM, Johnson PC, Bell RL, Beall AC, Jr., Jenkins DE. Regional ventilation and perfusion after lung transplantation in patients with emphysema. N Engl J Med. 1970;282(5):245-9. Epub 1970/01/29. doi: 10.1056/NEJM197001292820504. PubMed PMID: 4903105.
- 6. Levine SM, Anzueto A, Peters JI, Cronin T, Sako EY, Jenkinson SG, et al. Medium term functional results of single-lung transplantation for endstage obstructive lung disease. Am J Respir Crit Care Med. 1994;150(2):398-402. Epub 1994/08/01. doi: 10.1164/ajrccm.150.2.8049821. PubMed PMID: 8049821.
- 7. Yusen RD, Edwards LB, Dipchand AI, Goldfarb SB, Kucheryavaya AY, Levvey BJ, et al. The Registry of the International Society for Heart and Lung Transplantation: Thirty-third Adult Lung and Heart-Lung Transplant Report-2016; Focus Theme: Primary Diagnostic Indications for Transplant. J Heart Lung Transplant. 2016;35(10):1170-84. Epub 2016/10/25. doi: 10.1016/j.healun.2016.09.001. PubMed PMID: 27772669.
- 8. Bavaria JE, Kotloff R, Palevsky H, Rosengard B, Roberts JR, Wahl PM, et al. Bilateral versus single lung transplantation for chronic obstructive pulmonary disease. J Thorac Cardiovasc Surg. 1997;113(3):520-7; discussion 8. Epub 1997/03/01. doi: 10.1016/S0022-5223(97)70365-9. PubMed PMID: 9081097.
- 9. Pochettino A, Kotloff RM, Rosengard BR, Arcasoy SM, Blumenthal NP, Kaiser LR, et al. Bilateral versus single lung transplantation for chronic obstructive pulmonary disease: intermediate-term results. Ann Thorac Surg. 2000;70(6):1813-8; discussion 8-9. Epub 2001/01/13. doi: 10.1016/s0003-4975(00)01970-6. PubMed PMID: 11156077.
- 10. Sundaresan RS, Shiraishi Y, Trulock EP, Manley J, Lynch J, Cooper JD, et al. Single or bilateral lung transplantation for emphysema? J Thorac Cardiovasc Surg. 1996;112(6):1485-94; discussion 94-5. Epub 1996/12/01. doi: 10.1016/s0022-5223(96)70007-7. PubMed PMID: 8975840.
- 11. Thabut G, Christie JD, Ravaud P, Castier Y, Brugiere O, Fournier M, et al. Survival after bilateral versus single lung transplantation for patients with chronic obstructive pulmonary disease: a retrospective analysis of registry data. Lancet. 2008;371(9614):744-51. Epub 2008/03/04. doi: 10.1016/S0140-6736(08)60344-X. PubMed PMID: 18313503.
- 12. Schaffer JM, Singh SK, Reitz BA, Zamanian RT, Mallidi HR. Single- vs double-lung transplantation in patients with chronic obstructive pulmonary disease and idiopathic pulmonary fibrosis since the implementation of lung allocation based on medical need. JAMA. 2015;313(9):936-48. Epub 2015/03/04. doi: 10.1001/jama.2015.1175. PubMed PMID: 25734735.
- 13. Bennett DT, Zamora M, Reece TB, Mitchell JD, Cleveland JC, Jr., Grover FL, et al. Continued Utility of Single-Lung Transplantation in Select Populations: Chronic Obstructive Pulmonary Disease. Ann Thorac Surg. 2015;100(2):437-42. Epub 2015/07/05. doi: 10.1016/j.athoracsur.2015.03.024. PubMed PMID: 26141775.
- 14. Hull TD, Leya GA, Axtell AL, Moonsamy P, Osho A, Chang DC, et al. Lung transplantation for chronic obstructive pulmonary disease: A call to modify the lung allocation score to decrease waitlist mortality. J Thorac Cardiovasc Surg. 2021. Epub 2022/01/13. doi: 10.1016/j.jtcvs.2021.11.086. PubMed PMID: 35016781.
- 15 Yonan NA, el-Gamel A, Egan J, Kakadellis J, Rahman A, Deiraniya AK. Single lung transplantation for emphysema: predictors for native lung hyperinflation. J Heart Lung Transplant. 1998;17(2):192-201. Epub 1998/03/26. PubMed PMID: 9513858.
- 16. Weill D, Torres F, Hodges TN, Olmos JJ, Zamora MR. Acute native lung hyperinflation is not associated with poor outcomes after single lung transplant for emphysema. J Heart Lung Transplant. 1999;18(11):1080-7. Epub 1999/12/22. doi: 10.1016/s1053-2498(99)00079-0. PubMed PMID: 10598731.
- 17. Hosenpud JD, Bennett LE, Keck BM, Edwards EB, Novick RJ. Effect of diagnosis on survival benefit of lung transplantation for end-stage lung disease. Lancet. 1998;351(9095):24-7. Epub 1998/01/20. doi: 10.1016/S0140-6736(97)06405-2. PubMed PMID: 9433425.
- 18. Stavem K, Bjortuft O, Borgan O, Geiran O, Boe J. Lung transplantation in patients with chronic obstructive pulmonary disease in a national cohort is without obvious survival benefit. J Heart Lung Transplant. 2006;25(1):75-84. Epub 2006/01/10. doi: 10.1016/j.healun.2005.06.025. PubMed PMID: 16399534.
- 19. De Meester J, Smits JM, Persijn GG, Haverich A. Listing for lung transplantation: life expectancy and transplant effect, stratified by type of end-stage lung disease, the Eurotransplant experience. J Heart Lung Transplant. 2001;20(5):518-24. Epub 2001/05/10. doi: 10.1016/s1053-2498(01)00241-8. PubMed PMID: 11343978.
- 20. Charman SC, Sharples LD, McNeil KD, Wallwork J. Assessment of survival benefit after lung transplantation by patient diagnosis. J Heart Lung Transplant. 2002;21(2):226-32. Epub 2002/02/09. doi: 10.1016/s1053-2498(01)00352-7. PubMed PMID: 11834351.
- 21. Vock DM, Durheim MT, Tsuang WM, Finlen Copeland CA, Tsiatis AA, Davidian M, et al. Survival Benefit of Lung Transplantation in the Modern Era of Lung Allocation. Ann Am Thorac Soc. 2017;14(2):172-81. Epub 2016/10/26. doi: 10.1513/AnnalsATS.201606-507OC. PubMed PMID: 27779905; PubMed Central PMCID: PMCPMC5427730.
- 22. Thabut G, Ravaud P, Christie JD, Castier Y, Fournier M, Mal H, et al. Determinants of the survival benefit of lung transplantation in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2008;177(10):1156-63. Epub 2008/03/04. doi: 10.1164/rccm.200708-1283OC. PubMed PMID: 18310481.
- 23. Eskander A, Waddell TK, Faughnan ME, Chowdhury N, Singer LG. BODE index and quality of life in advanced chronic obstructive pulmonary disease before and after lung transplantation. J Heart Lung Transplant. 2011;30(12):1334-41. Epub 2011/07/26. doi: 10.1016/j.healun.2011.06.006. PubMed PMID: 21782467.

California Thoracic Society
ATS Chapter Serving California and Arizona

Krystal works in the UC Davis University of California Asthma Network (UCAN) and Reversible Obstructive Airways Disease (ROAD) as an RT Coordinator and Case Manager. She received her Graduate Degree in Respiratory Care from Boise State University in 2020. Krystal is currently working on population health initiatives for asthma and COPD and received the Mallickrodt Literary Award in 2025 from the AARC for her publication on integrating RT case managers into COPD clinical care. She is also on the editorial board for Respiratory Care Reports.

Population Health Approach in COPD

Krystal Craddock, MSc, RRT, RRT-NPS, AE-C, RRT-ACCS, FAARC

UC Davis UCAN/ROAD Clinic
UC Davis Population Health

Disclosures

- I have the following relationships with ACCME defined ineligible companies:
- Fisher & Paykel, Sentec, Electromed, Therevance Biopharma
- **I WILL NOT** discuss off-label use and/or investigational use of any drugs or devices.

Objectives

- Discuss aspects of population health approaches in COPD care.
- Review outcomes and barriers to population health interventions.

Why a population health approach in COPD?

COPD – Burden on Patients

- COPD remains both under and over diagnosed.[1]
  - Challenge the diagnosis
- Pharmacologic and non-pharmacologic therapies of COPD can reduce symptoms, frequency, and severity of exacerbations and provide beneficial effects on lung function decline and mortality.[2]
  - Are patients on the right therapy?
  - Can they use their devices correctly?
  - Are the treatments affordable?
  - Do they have access?
  - Are they able to be mobile and socialize?
- Morbidity increases with age
  - Physician visits, ED visits, and hospitalizations
  - Comorbidities are seen in an earlier age

1. Lamprecht et al., 2015
2. GOLD, 2025

Office of Population Health & Accountable Care

- Implement UCDH's mission by engaging our patients & community
- Work to keep patients healthier at home
- Redesigning care pathways that meet & optimize patient care needs

Reversible Obstructive Airway Disease (ROAD) Program

Purpose

Improve outcomes for COPD patients through education and transition of care support

Focus Areas

Comprehensive **inpatient education** on COPD management, medications, and recognizing exacerbations

Personalized learning

One-on-one bedside education

Enrollment

Patients flagged at admission via EHR screening or provider referral

Staffing Model

Respiratory therapists trained as COPD case managers

Post-Discharge Support

Direct phone access to ROAD team

Referral to pulmonary rehabilitation and clinic for ongoing self-management

Impact

Readmission rates cut by more than half from 16% to 11.8%

Average length of stay reduced from 7.6 days to 5.6 days

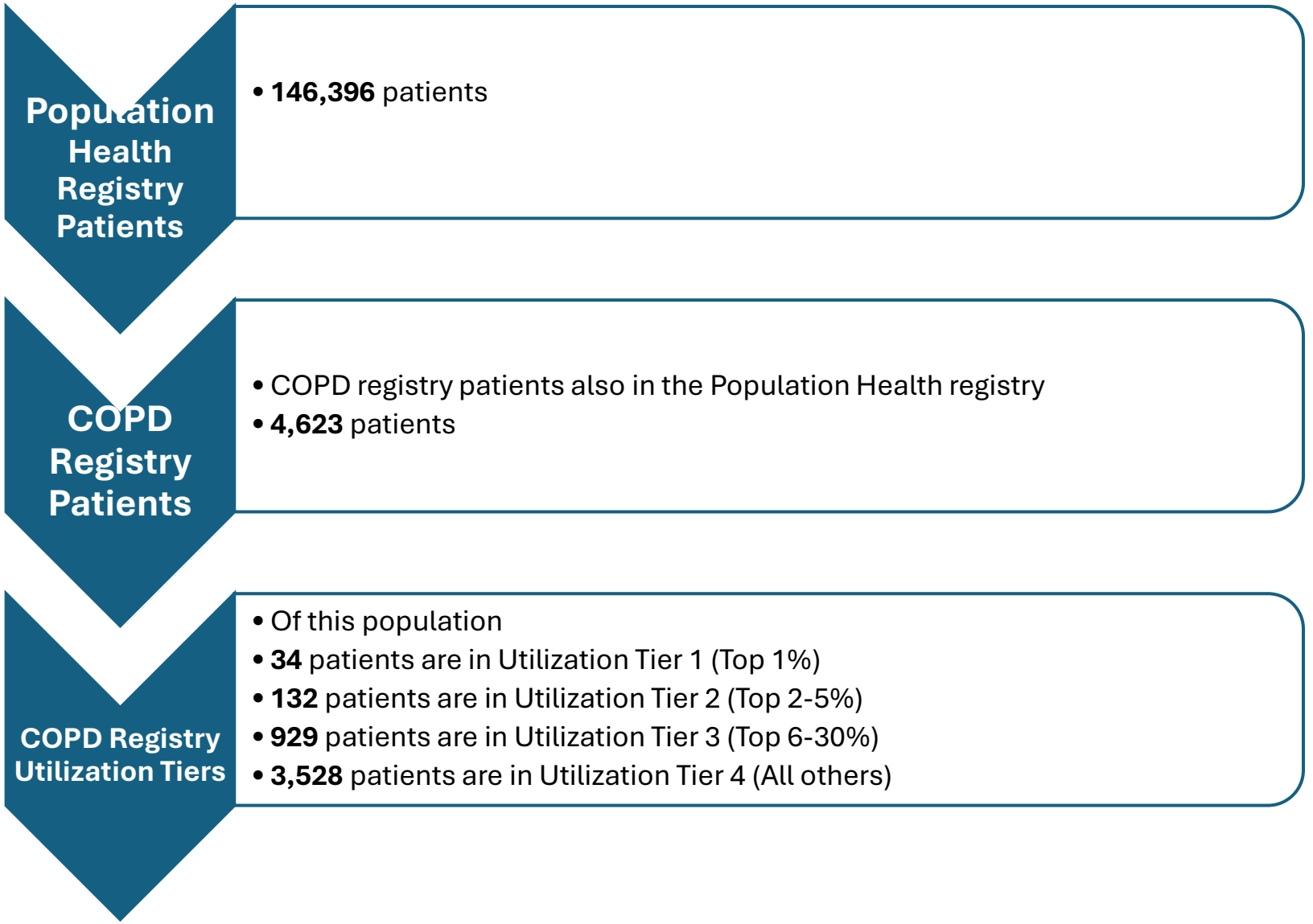
Comprehensive COPD Clinic

- Led by COPD-specialized physicians and respiratory therapists
- Offering advanced therapies, such as endobronchial valves and biologics
- Currently seeing >600 COPD patients/year

…but treating COPD exacerbations after the fact.

COPD Population Health – The Beginning

COPD Population and Utilization Tiers



Population Health Registry Patient: Active patient with at least one clinic visit in last two years at UCDH or attributed to a commercial or government contracted program with UCDH

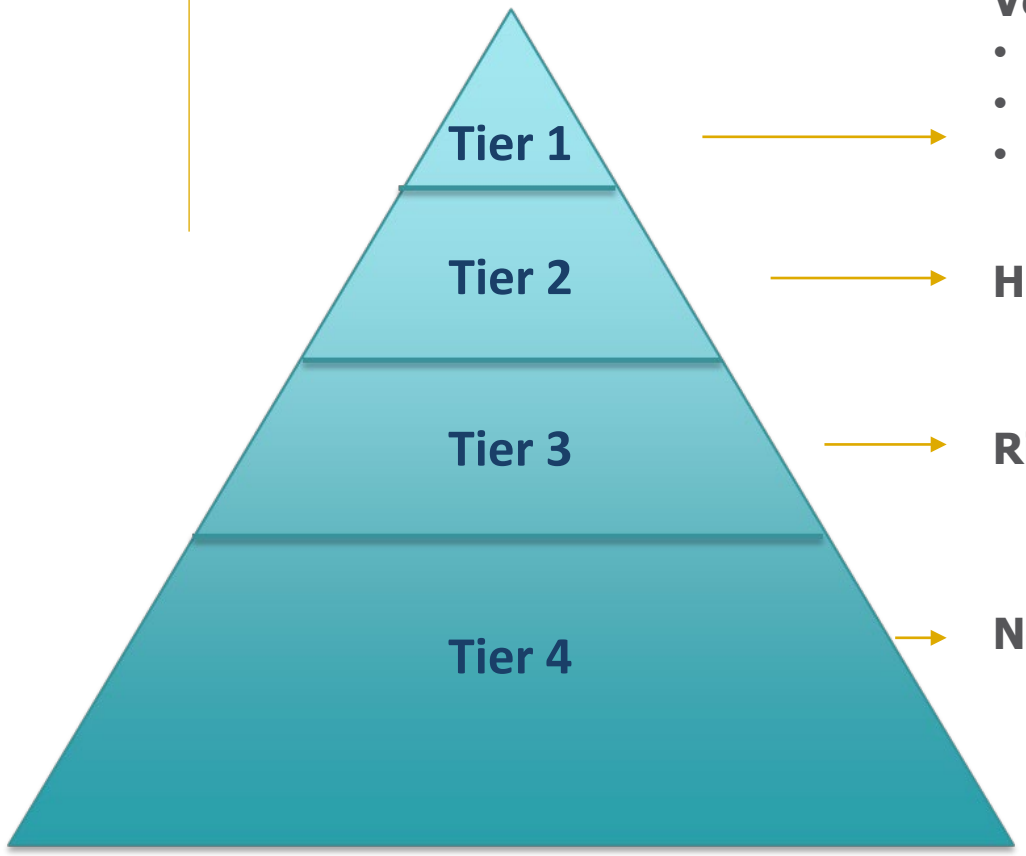
COPD Registry Patient: Active patient has COPD diagnosis in the last three years

COPD Registry Utilization Tiers: Defined by Medicare spending and average Anthem spending for Medical/Surgery bed days, ICU bed days, ED visits

Data pulled on 2/7/2022

Patient-Aligned Care Management

Tiered Level of Care interventions are modified based on patient risk factors, SDOH and goals.



Very High-Risk Patients
- 1A Super Complex
- 2A Multiple Active Complex Conditions
- 3A Primarily One Complex Condition

High Risk Patients

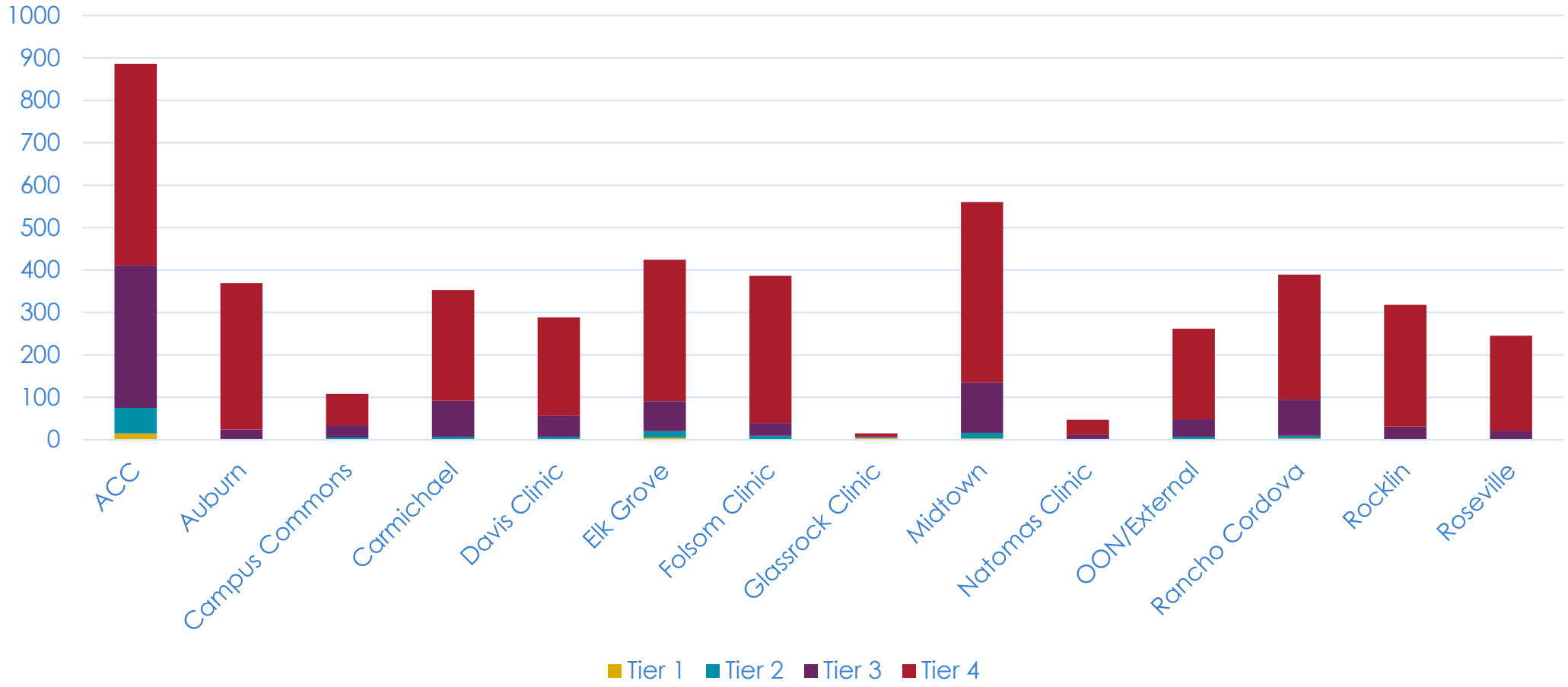
Rising Risk Patients

Normal/ Low Risk Patients

~2-6K patients at UCDH depending on patient factors (appropriateness for care management) and our team bandwidth and skills to expand reach (accounting for patient complexity, staffing level, feasibility)

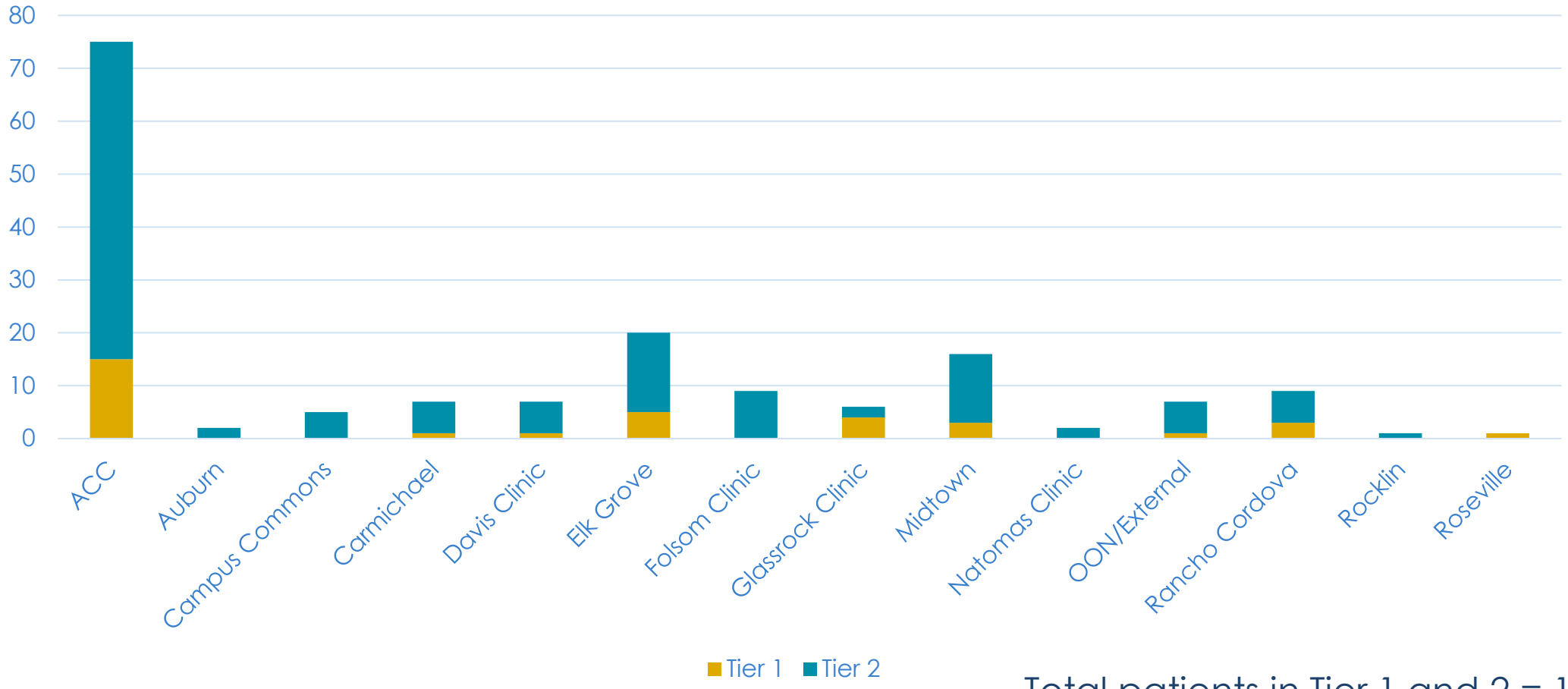
*Intake screening of patients that would most benefit from interventions based on complexity index score to even out panel size workloads *

COPD registry patients by clinic



COPD Registry Utilization Tiers:
Defined by Medicare spending and average Anthem spending for Medical/Surgery bed days, ICU bed days, ED visits

Utilization/Expenditure Tier 1 and 2 COPD registry patients by clinic



Total patients in Tier 1 and 2 = 166

COPD Registry Utilization Tiers:
Defined by Medicare spending and average Anthem spending for Medical/Surgery bed days, ICU bed days, ED visits

Chart Reviews

- Clinicians reviewed >100 charts from population health, ROAD, and non-UCD ED/hospitalized patients.
  - Research common themes
  - What should our focus be on?

Domain	Intervention	Work Group
Access	Cost-optimized medications	Medication Management
Diagnosis and Management	Spirometry, COPD management guidelines in EHR	COPD Specialty
Diagnosis and Management	Action plan	COPD Specialty
Home Services	Medication management and assistance program	Medication Management
Home Services	Dedicated care coordination	COPD Specialty/care coordination

COPD Population Health – Implementation

COPD Care Management (CM) Program

Goal

- To reduce COPD/Asthma exacerbations leading to an emergency department visit or hospital admission and improve outpatient care.

Target Population

- **High-risk:** COPD/Asthma patients, who has ≥ 60% population health risk score, had an ED or hospitalization in the last 12 months
- **Acute Decline:** COPD/Asthma patients experienced respiratory-related exacerbation in the last two weeks

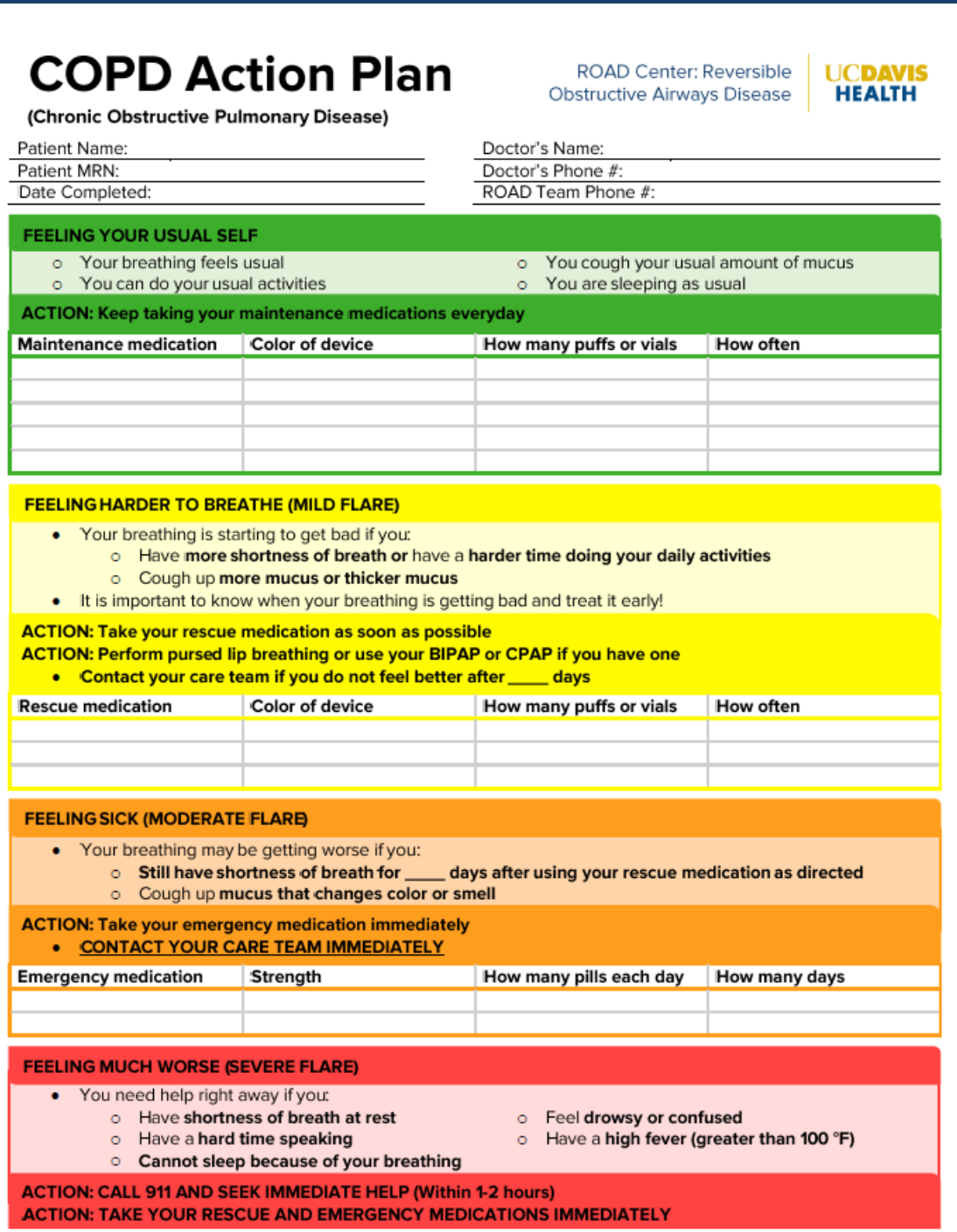
Eligibility Requirement

- Active patient established a primary care provider at UC Davis Health
- Active COPD or Asthma registry patient
- Patient ≥ 18 years old
- Open to make changes

Care Manager will outreach to eligible patients via telephone encounter

COPD Care Management

- Assessment and Chart Review
  - Challenge the diagnosis
  - Review past/current treatments
  - Communicate with PCP
- Education
  - Disease
  - Medications
  - Action plan
- Referrals
  - PFTs
  - COPD clinic
  - Pulmonary Rehab
  - Access to transportation, food, and other necessary resources



COPD Action Plan

(Chronic Obstructive Pulmonary Disease)

ROAD Center: Reversible Obstructive Airways Disease

UC DAVIS HEALTH

Patient Name: | Doctor's Name:
Patient MRN: | Doctor's Phone #:
Date Completed: | ROAD Team Phone #:

FEELING YOUR USUAL SELF

- Your breathing feels usual
- You can do your usual activities
- You cough your usual amount of mucus
- You are sleeping as usual

ACTION: Keep taking your maintenance medications everyday

Maintenance medication	Color of device	How many puffs or vials	How often

FEELING HARDER TO BREATHE (MILD FLARE)

- Your breathing is starting to get bad if you:
  - Have **more shortness of breath or** have a **harder time doing your daily activities**
  - Cough up **more mucus or thicker mucus**
- It is important to know when your breathing is getting bad and treat it early!

ACTION: Take your rescue medication as soon as possible
ACTION: Perform pursed lip breathing or use your BIPAP or CPAP if you have one

- **Contact your care team if you do not feel better after ____ days**

Rescue medication	Color of device	How many puffs or vials	How often

FEELING SICK (MODERATE FLARE)

- Your breathing may be getting worse if you:
  - **Still have shortness of breath for ____ days after using your rescue medication as directed**
  - Cough up **mucus that changes color or smell**

ACTION: Take your emergency medication immediately

- **CONTACT YOUR CARE TEAM IMMEDIATELY**

Emergency medication	Strength	How many pills each day	How many days

FEELING MUCH WORSE (SEVERE FLARE)

- You need help right away if you:
  - Have **shortness of breath at rest**
  - Have a **hard time speaking**
  - **Cannot sleep because of your breathing**
  - Feel **drowsy or confused**
  - Have a **high fever (greater than 100 °F)**

ACTION: CALL 911 AND SEEK IMMEDIATE HELP (Within 1-2 hours)
ACTION: TAKE YOUR RESCUE AND EMERGENCY MEDICATIONS IMMEDIATELY

POC Spirometry

Goal:

To make point-of-care spirometry available in UC Davis Health primary care clinics to assist with the proper identification of the driver of dyspnea for COPD patients which will allow for proper treatment of their dyspnea and allow for avoidance of ED and hospital visits.

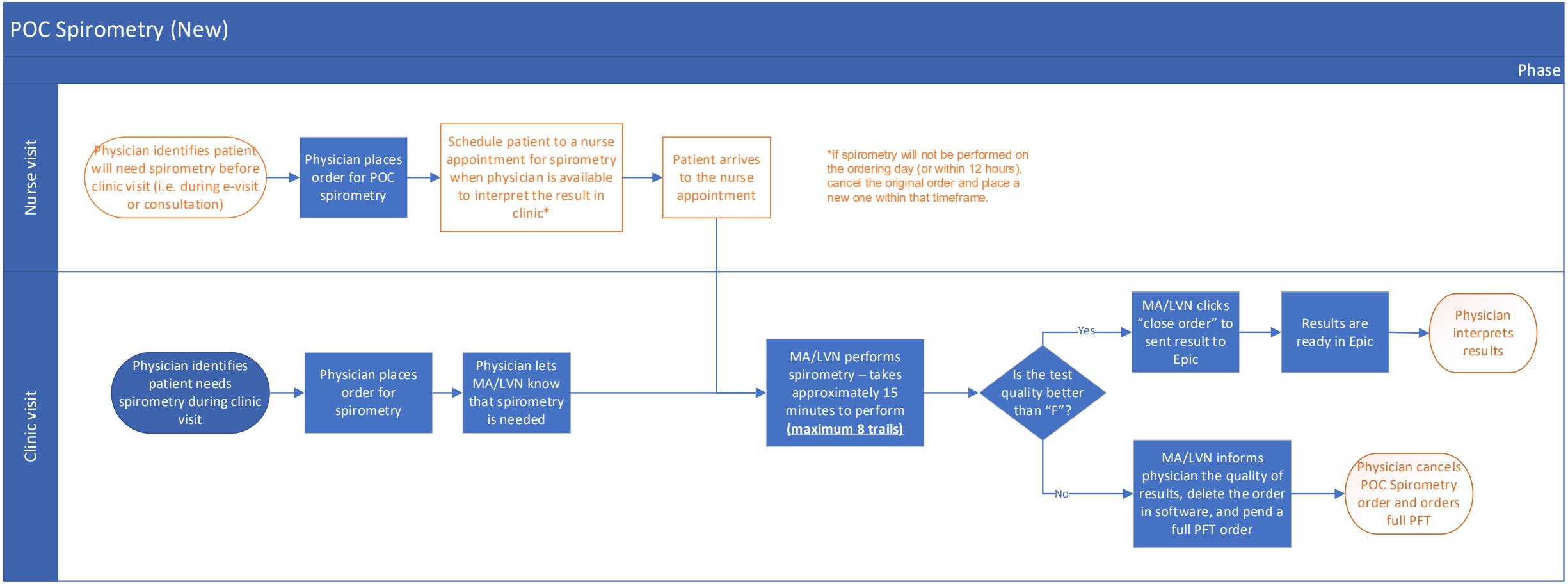
Pilot Clinics:

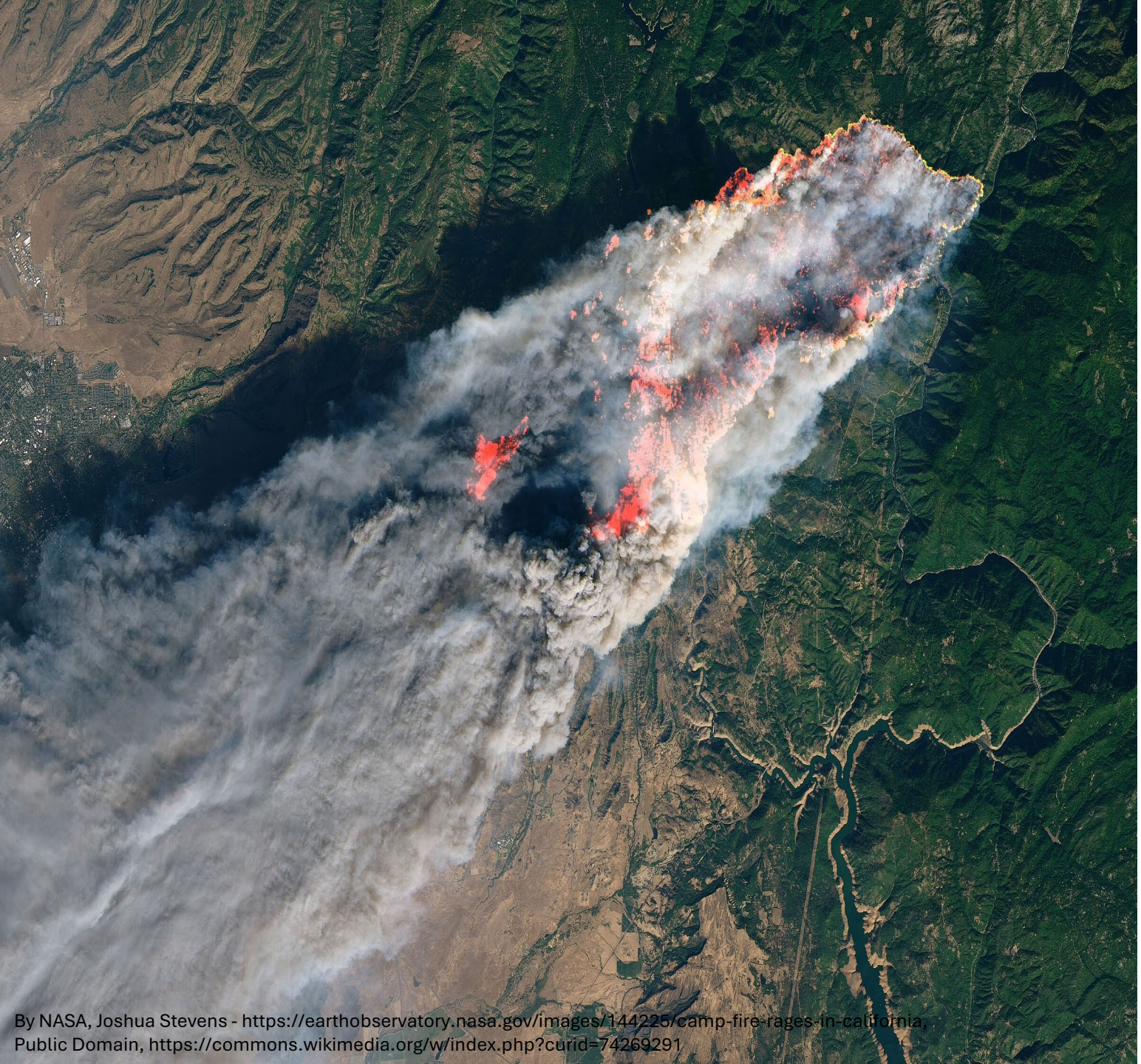
Folsom and Rocklin Clinics

Target Population:

All patients experiencing dyspnea or have expressed concerns about dyspnea in the pilot clinics.

POC Spirometry Workflow



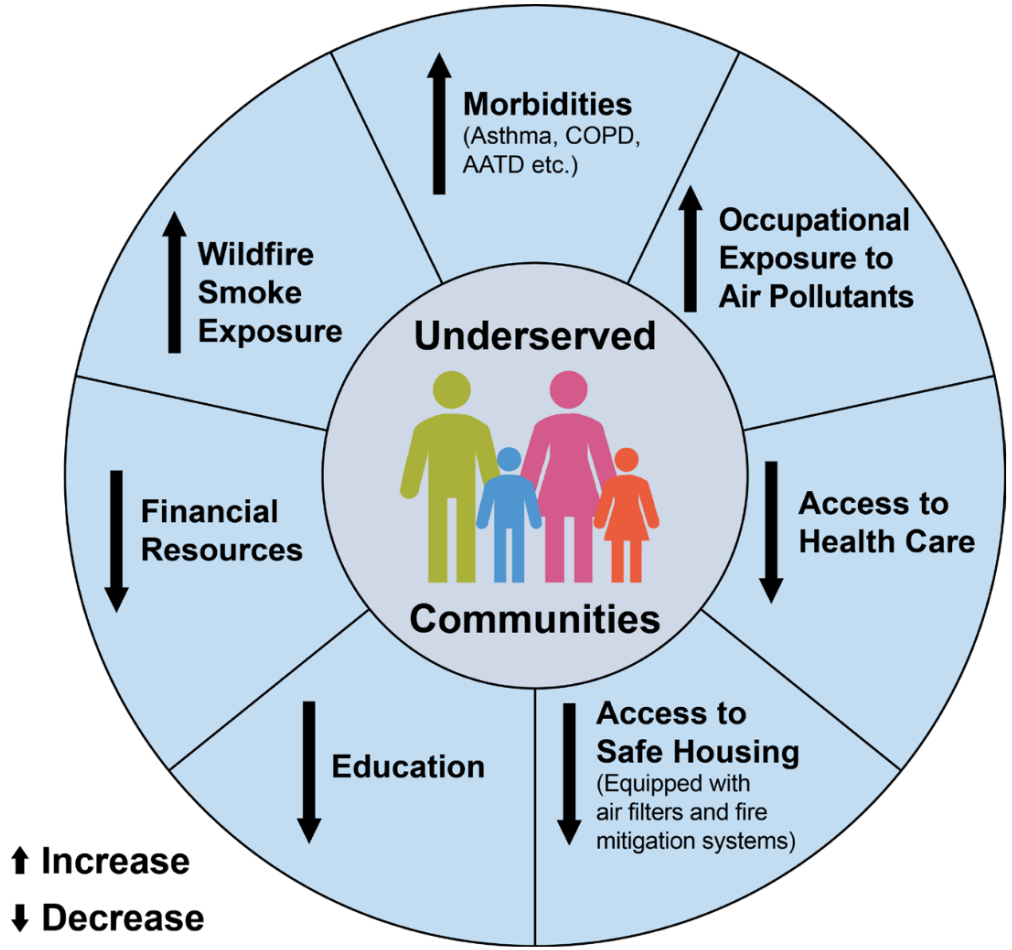


By NASA, Joshua Stevens - https://earthobservatory.nasa.gov/images/144225/camp-fire-rages-in-california, Public Domain, https://commons.wikimedia.org/w/index.php?curid=74269291

Camp Fire, 2018

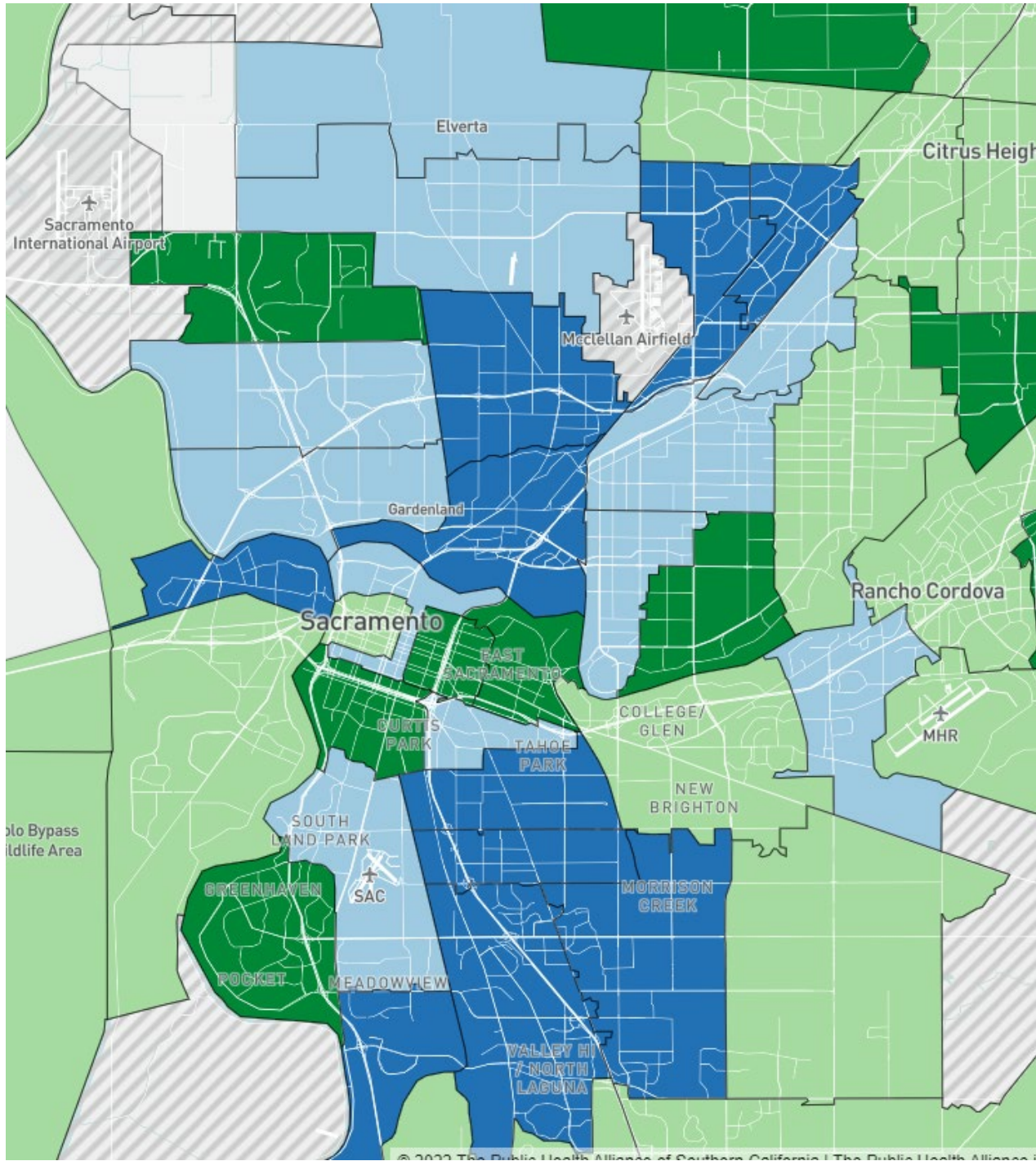
- Displaced more than 50,000 people, with 85 fatalities, and destroyed more than 18,000 structures
- Pivotal moment in the disease course of many patients with COPD with many ill effects:
  - Acute exacerbation
  - Persistent worsening of symptoms
  - Lack of access to healthcare
  - Lack of access to food and amenities
  - Difficulty maintaining air quality in home environment

Intersection of Negative Social Influences of Health and the Impact on Wildfires in Underserved Communities



Patient Population

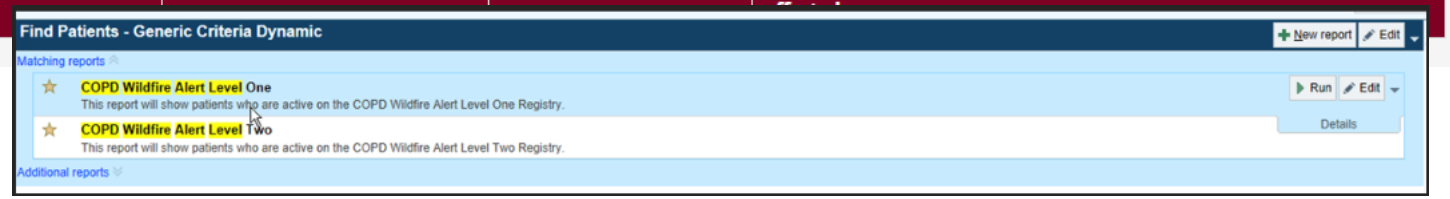
- Clinically At-Risk Population
- Underserved Patients
- Healthcare Utilization



EHR Air Quality Index Integration and Automated Electronic Alerts

AQI Basics for Ozone and Particle Pollution

Daily AQI Color	Levels of Concern	Values of Index	Description of Air Quality
Green	Good	0 to 50	Air quality is satisfactory, and air pollution poses little or no risk.
Yellow	Moderate	51 to 100	Air quality is acceptable. However, there may be a risk for some people, particularly those who are unusually sensitive to air pollution.
Orange	Unhealthy for Sensitive Groups	101 to 150	Members of sensitive groups may experience health effects. The general public is less likely to be affected.
Red	Unhealthy	151 to 200	Some members of the general public may experience health effects; members of sensitive groups may experience more serious health effects.
Purple	Very Unhealthy	201 to 300	Health alert: The risk of health effects is increased for everyone.
Maroon	Hazardous	301 and higher	Health warning of emergency conditions: everyone is more likely to be



EMR Alerts

Alert 1

Alert 2

Source: www.airnow.gov/aqi/aqi-basics/

Wildfires Disaster Guidance: Tips for Staying Healthy during Wildfires

Over the years fierce winds in Southern and Northern California have helped fuel disasterous wildfires. The Camp fire in 2018 has been the most deadly in California history. Other states including Utah, Montana and Arizona have also been challenged with wildfires near populated areas. Wildfire smoke can irritate the eyes, nose, throat, and lungs. It can cause coughing wheezing or difficulty in breathing.

Inhaling smoke can be especially dangerous to those with lung disease (such as asthma, COPD/ emphysema, and pulmonary fibrosis), heart disease, pregnant women, the elderly and children. These high-risk populations need to take special care and consider consulting with their healthcare providers regarding specific precautions. Inhaling smoke is not good for anyone. It can cause inflammation (swelling) of the airways and lungs, and can even make you more vulnerable to lung infections, such as COVID-19.

This fact sheet provides you with actions you can take to avoid adverse health effects from exposure to the smoke and ash from wildfires worldwide.

Here are 10 basic steps you can do to help stay safe, avoid smoke exposure, and protect your lungs from wildfire smoke:

1. **Stay indoors as much as possible** with windows and doors closed.
2. **Reduce strenuous physical activity.**
3. **Reduce other sources of indoor air pollution** such as smoking cigarettes, using a wood-burning stove, or frying meat. Do not vacuum anywhere in the house.
4. **Use central air conditioner or heater to filter the air:** A home's heater or air conditioner set to the fan mode may be able to filter out some of the particles by "re-circulating" the indoor air through the filter.
5. **Use air purifiers with HEPA filters.** Try to get an air purifier that has a HEPA ($PM_{2.5}$) filter. Note: do not use air cleaner devices that produce ozone such as "super oxygenators".
6. **When traveling in a vehicle,** keep windows closed, run the air conditioner, and set air to re-circulate to reduce smoke.
7. If you do have to go outside, wear a disposable respirator mask that is rated as **N95 or higher** to help reduce inhalation of particulates if properly fitted.

National Institute for Occupational Safety and Health (NIOSH) certified N95 masks filter at least 95% of airborne particles at the particle size of 0.3 microns (a size that can get into your lungs). A surgical or simple dust mask **will not** protect against particulate exposure. **None** of these masks protect against hazardous gas inhalation. Simple

cloth barriers, such as bandanas, do not filter out small airborne particles.

The following video demonstrates how to properly put on an N95 mask: https://m.youtube.com/watch?v=od_RaKdquek (from the Centers for Disease Control and Prevention).

1. **Consider evacuation** to areas with better air quality (a lower air quality index) especially if you have lung disease (such as with asthma, COPD, emphysema, cystic fibrosis and pulmonary fibrosis) or other high risk condition.
2. **Create a clean room in your home.** Use an interior room with fewer doors and windows and run an air conditioner and room air cleaner if available.
3. **If you have lung disease such as asthma or COPD, be sure** you are taking your maintenance ("daily controller") medications. Talk to your healthcare provider about whether you should take other medications or higher doses if you are having symptoms or cannot avoid some exposure.

How can I get current information regarding the air quality in my area?

There are several on-line resources that you can use to get information about air quality in your area.

Up to date air quality information may be found at https://airnow.gov.

The South Coast Air Quality Management District lists the following areas of direct smoke impacts: http://www.aqmd.gov/docs/default-source/air-quality/advisories/advisory1.pdf.

This fact sheet was adapted from Fire Dangers, Air Quality and Safety for Pulmonary Clinicians and Their Patients from the California Thoracic Society

Authors: Shazia Jamil, MD, W. Graham Carlos, MD, Lorriana Leard, MD, Angela Wang, MD, Lekshmi Santhosh, MD, John Balmes, MD, Nitin Seam, MD, Charles S. Dela Cruz, MD, PhD
Reviewers: Marianna Sockrider MD, DrPH, Allison Lambert, MD, MHS

Resources

American Thoracic Society
- https://thoracic.org/patients

AirNow
- https://www.airnow.gov/wildfire-potential/

Centers for Disease Control and Prevention
- https://www.cdc.gov/disasters/wildfires/smoke.html

California Department of Public Health
- https://www.cdph.ca.gov/Programs/EPO/Pages/Wildfire%20Pages/Wildfires--.aspx

South Coast Air Quality Management District
- http://www.aqmd.gov/home/air-quality/air-alerts

California Wildfires Statewide Recovery Resources
- http://wildfirerecovery.org/general-info/

California Environmental Protection Agency
- https://calepa.ca.gov/disaster/fire/

Enviromental Protection Agency (EPA)
- https://www.epa.gov/indoor-air-quality-iaq/air-cleaners-and-air-filters-home

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UC DAVIS HEALTH

Wildfire Evacuation Kit

RESPIRATORY MEDICATIONS

- ☐ Daily maintenance and rescue respiratory inhalers with spacer and/or nebulized medications.
- ☐ Emergency medications if prescribed (prednisone and antibiotics)
- ☐ Asthma or COPD Action Plan

NEBULIZER MACHINE WITH SUPPLIES

- ☐ Power cord/car charger/extra batteries
- ☐ Nebulizer medication cups with mouthpiece/facemask and tubing

OXYGEN AND SUPPLIES

- ☐ Portable oxygen concentrator (POC) or portable oxygen tanks
- ☐ Stationary concentrator
- ☐ Extra nasal cannulas and tubing
- ☐ Pulse oximeter to monitor oxygen levels.

CPAP/BIPAP OR NON-INVASIVE VENTILATION

- ☐ CPAP/BiPAP/NIV with power cord
- ☐ Mask, hose and an extra filter
- ☐ Distilled water for humidifier

AIRWAY CLEARANCE DEVICES

- ☐ Handheld oscillatory device (e.g., Aerobika, Acapella)
- ☐ Airway clearance vest with power cord

EMERGENCY CONTACTS		
HEALTHCARE	**NAME**	**PHONE**
Primary Care		
Pulmonary		
Pharmacy		
Alternate Pharmacy		
Medical Equipment		
RELATIONSHIP	**NAME**	**PHONE**

Preparation Tips

To prepare to evacuate your home due to a wildfire, make sure to take your respiratory supplies.

- ***Fill in emergency contact information and print this document to take with you.***
- *Have enough supplies to last several days.*
- *Pre-package a kit to have many of the items ready to go.*
- *Place items in a bag or backpack that is easy to grab.*
- *The goal is to continue your respiratory medications and therapies even when away from home.*

Local Evacuation Routes

CAL FIRE Incidents: sign up for text alerts about wildfires in your area and know your community's emergency response plan, evacuation orders and evacuation centers.

Find more information at:

https://incidents.readyforwildfire.org/

UC DAVIS HEALTH

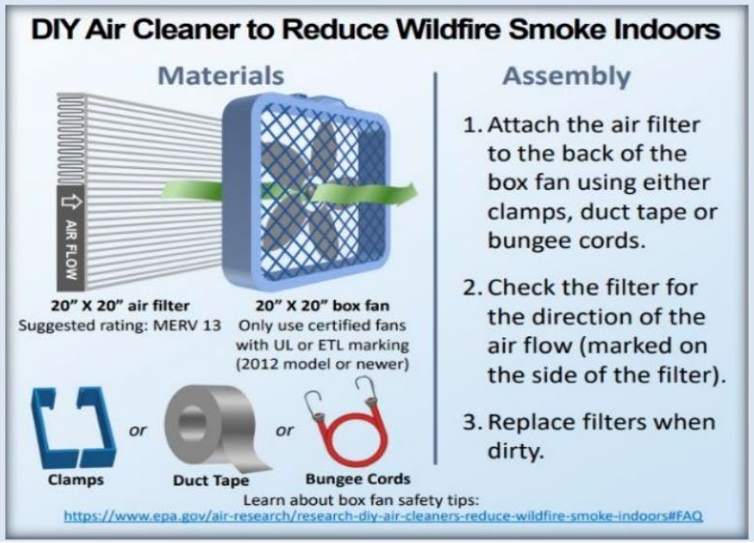
Improving Indoor Air Quality

Find information below on how to improve indoor air quality, create a clean room, and assemble a DIY box fan air cleaner.

EPA: Wildfire Smoke and Indoor Air Quality: How to Create a Clean Room
Click here for more information

DIY Box Fan Air Filter for Wildfire Smoke: UC Davis Agricultural Health & Safety
Click here for more information

Research on DIY Air Cleaners: Reduce Wildfire Smoke Indoors
Click here for more information



PG&E's Medical Baseline Program

Apply to obtain a backup battery to power your medical equipment here:

Community Wildfire Safety Program Support for Medical Baseline Customers

Find more information:

PG&E website

Cooling Centers

PG&E provides information on how to find a cooling center location by zip code

Cooling Center Locations

Find more information:

PG&E website

Patient Education Resources in PCP Offices

Wildfire Smoke Patient Education

Inhaling smoke can pose significant risks to those with pre-existing lung conditions (such as asthma, COPD, and pulmonary fibrosis), heart disease, diabetes and individuals who are immunocompromised or taking drugs that suppress the immune system. Also at risk are pregnant women, outdoor workers, those experiencing homelessness and those under 18 and over 65.

Wildfire smoke exposure can cause inflammation to the airways and lungs. If you are exposed to wildfire smoke, monitor for warning signs of a respiratory exacerbation (flare up).

Common signs and symptoms of a respiratory exacerbation may be as follows:

- Increased difficulty breathing, even at rest
- Increased wheezing, coughing and mucous production (thick, sticky, yellow/green)
- Chest tightness
- Increase in fatigue, lack of energy, irritability
- Increase in breathing rate and/or heart rate
- Skin tone changes (ashen or blue)

How to avoid smoke exposure

- Stay indoors with windows and doors closed.
- Use central air conditioner/heat or set to fan mode to filter indoor air.
- Limit strenuous physical activity.
- Reduce other sources of indoor air pollution (cigarette smoke, wood burning stove, frying food)
- Use air purifiers with HEPA filters and create a clean room in your home.
- When traveling in a vehicle, keep windows closed and set air to recirculate.
- Wear an N95 mask or higher if you must go outside.

In the event of an evacuation, be certain to pack your respiratory supplies as follows:

- ✓ Daily respiratory medications (inhalers with spacer, nebulized medications and nebulizer.
- ✓ Airway clearance devices (flutter valve, vest)
- ✓ Portable oxygen concentrator
- ✓ CPAP or BIPAP
- ✓ Asthma or COPD Action Plan

How to create a DIY air cleaner

1. Attach the air filter to the back of the box fan using either clamps, duct tape or bungee cords.
2. Check the air filter for the direction of the air flow (marked on the side of the filter).
3. Replace filters when dirty.

It is important to note that poor air quality is harmful to your health and should be avoided whenever possible. Take extra caution and consult your healthcare provider regarding specific precautionary

Additional Resources

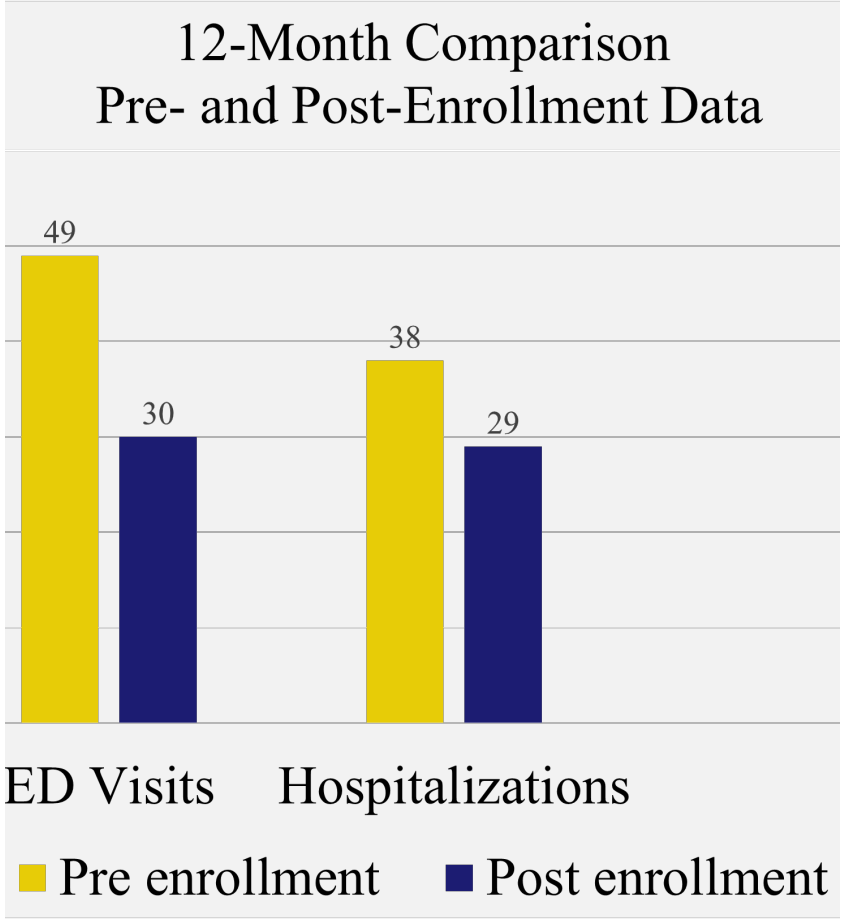
CDC recommendations:
How to use your N95
https://www.cdc.gov/niosh/topics/publicppe/use.html

Air quality data in your area: https://airnow.gov

COPD Population Health – Outcomes and Lessons Learned

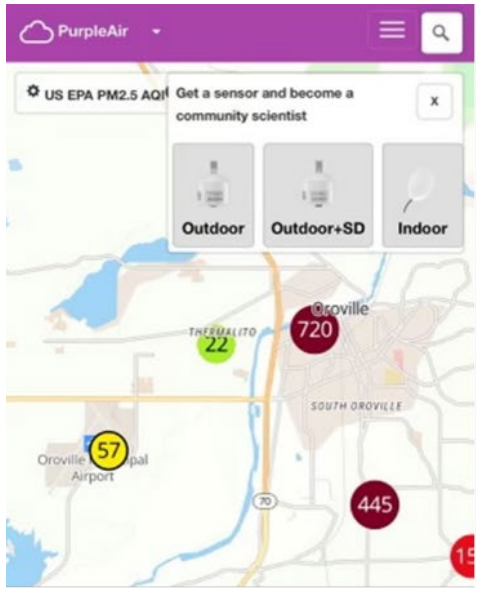
Outcomes

- A total of 70 patients were enrolled in the program with 67 enlisted between October 2022 to December 2023.
- The cohort, (37% male, mean age 73), included 54 patients with COPD, 5 with asthma, and 8 with asthma/COPD overlap.
- A 12-month comparison of pre-and post-enrollment data demonstrated a significant reduction in all-cause ED visits decreasing from 49 to 30 visits (39% reduction, p=.03).
- All-cause hospitalizations decreased from 38 to 29 (24% reduction, p=.31).
- Fifty-four patients completed a pre and post CAT with a mean decrease of 1, p=.23. MCID 2.
- Thirteen patients completed an ACT with a mean increase of 2.4, p=.03, MCID is 3.



Challenges Encountered

- Granularity of air quality data
- COPD diagnosis challenges (under and over-diagnosed)
- Institutional Support
  - Staffing
  - Analysts
  - IT Integration
- Local Support
  - Subject matter experts
  - Up-to-date community resources
- Studying/implementing around a natural disaster….
- Building collaborations with climate scientists, public health officials, and local communities



What We Achieved, What We Learned, Where We're Going

Key Results

- Positive clinical outcomes
- Enhanced care coordination
- Increased POC spirometry testing
- Improved patient preparedness and effective use of data integration for wildfires

Lessons Learned

- Data needs to be interpreted carefully
- Interdisciplinary collaboration is critical
- Tailored interventions work
- Infrastructure and staffing are key
- Change is a process

Next Steps

- Continue POC spirometry assessment leading to expanding.
- Expand COPD CM services
- Expand wildfire outreach to other patient groups

Thank you to our team!

- UC Davis Population Health COPD/Asthma Design Team
  - Reshma Gupta
  - Brooks Kuhn
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  - Nandini Sarma (now faculty!)
  - Jennifer Miller
  - Isaac Schwartzman

References

- Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease (2026 Report). Global Initiative for Chronic Obstructive Lung Disease; 2025. Accessed March 6, 2026. https://goldcopd.org/wp-content/uploads/2026/01/GOLD-REPORT-2026-v1.3-8Dec2025_WMV2.pdf.
- Lamprecht B, Soriano JB, Studnicka M, et al. Determinants of underdiagnosis of COPD in national and international surveys. Chest 2015; 148(4): 971-85 https://pubmed.ncbi.nlm.nih.gov/25950276.
- NASA, Joshua Stevens - https://earthobservatory.nasa.gov/images/144225/camp-fire-rages-in-california, Public Domain, https://commons.wikimedia.org/w/index.php?curid=74269291.