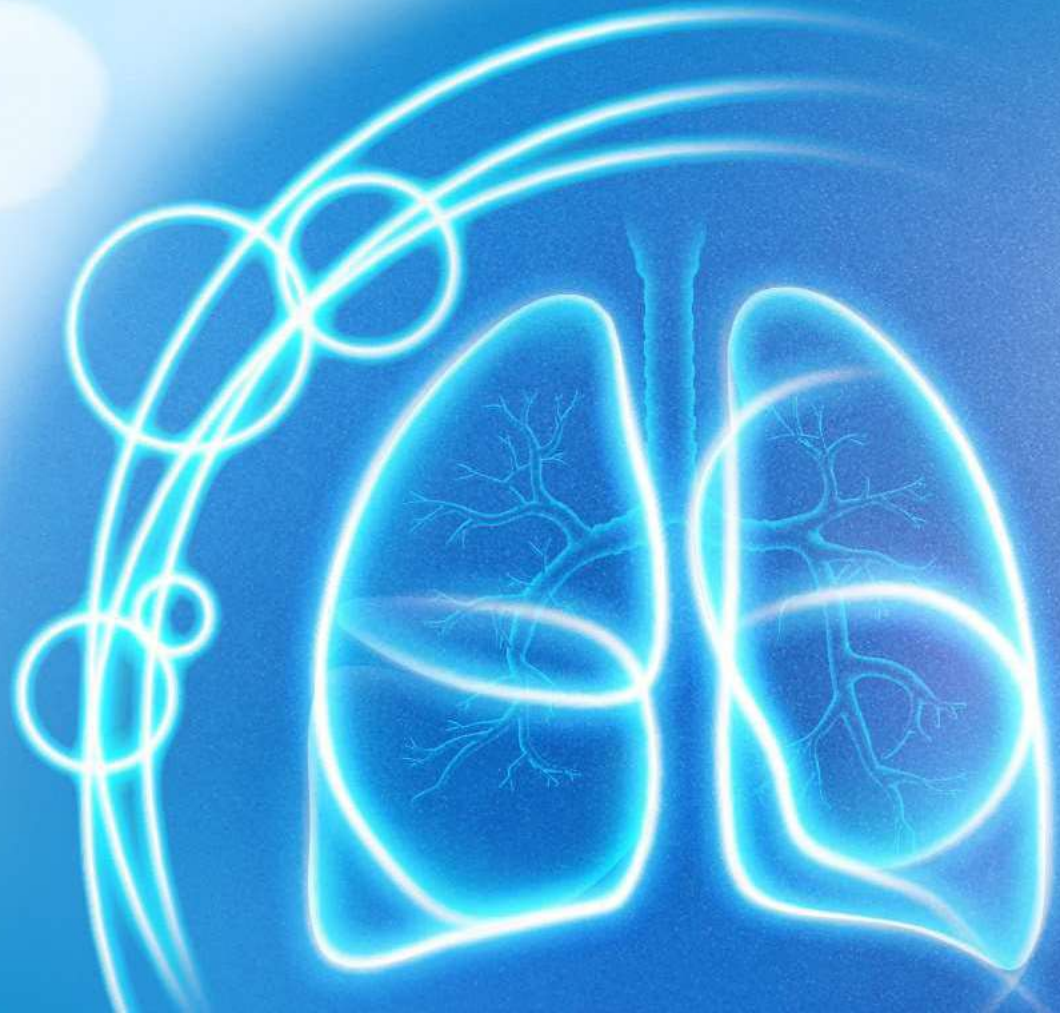
# COPD, how we do this in Primary Care!



# Presenter Disclosure

FAMILY PHYSICIAN airways group

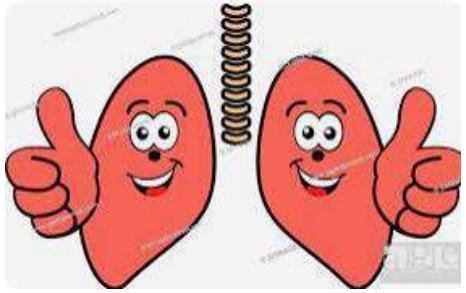
- **Faculty:** Alan Kaplan MD CCFP(EM) FCFP
- Chair Family Physician Airways Group of Canada
- Vice President, Respiratory Effectiveness Group
- Past Chair of Special Interest Focused Practice, College of Family Physicians in Respiratory Medicine.
- Honorary Professor of Primary Care Respiratory Research, OPRI
- Regional Primary Care Cancer Lead, Central Region, Ontario
- **Relationships with commercial interests:**
  - **Grants/Research Support:** none
  - **Speakers Bureau/Honoraria:** ALK, Astra Zeneca, Boehringer Ingelheim, GSK, Idorsia, Merck Frosst,, Moderna, Pfizer, Sanofi, Trudel, Valeo.
  - **Consulting Fees:** ALK**,** Astra Zeneca, GSK, Idorsia, Trudel, Merck, Moderna, Pfizer, Sanofi, Trudel, Valeo
  - **Other:**

    Member of Health Canada Section on Allergy and Respiratory Therapeutics.

    Member of Public Health Agency of Canada section on Respiratory Surveillance

Ontario Health
Cancer Care Ontario

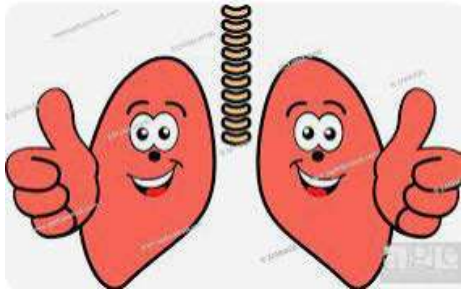
# Disclosure of Financial Support



- **This program has received no financial support**
- **This program has received no in-kind support**

- **Potential for conflict(s) of interest:**
- **The speaker has received honoraria from multiple companies that make COPD medications and vaccines**

# Mitigating Potential Bias



Potential sources of bias identified in the preceding 2 slides have been mitigated as follows:

- Information/recommendations provided in the following program will be evidence- and/or guideline-based and opinions of the speaker will be identified as such.
- Current Canadian and International guidelines are referenced.

# Statistics of note

COPD

## 300 and 400 million

Chronic obstructive pulmonary disease (COPD) affects between 300 and 400 million people globally, making it the third leading cause of death worldwide.

COPD

## 45% of the public

45% of the public could not correctly identify COPD as a lung disease despite the fact that it is the third leading cause of death worldwide and kills more people yearly than lung and breast cancer combined.

COPD

## 600 million

The worldwide prevalence of COPD is likely to increase to 600 million cases by 2050, with the greatest increase among women and in low- and middle-income countries.

https://respiratoryhealth.org/copd

# We are #11 worldwide

| Ranking | | P | A | H | D | E | SCORE |
|---|---|---|---|---|---|---|---|
| 1 | Australia | 17 | 15 | 12 | 10 | 17 | **71.5** |
| 2 | United Kingdom | 18 | 17 | 11 | 8 | 18 | **71.1** |
| 3 | Finland | 15 | 15 | 13 | 9 | 18 | **70.7** |
| 4 | Estonia | 15 | 14 | 13 | 10 | 17 | **69.3** |
| 5 | Spain | 16 | 15 | 14 | 7 | 17 | **68.8** |
| 6 | Slovakia | 13 | 15 | 13 | 10 | 17 | **68.4** |
| 7 | Italy | 13 | 14 | 15 | 9 | 17 | **67.7** |
| 8 | Japan | 15 | 12 | 13 | 10 | 17 | **66.4** |
| 9 | France | 11 | 15 | 13 | 9 | 18 | **66.3** |
| 10 | Sweden | 12 | 15 | 12 | 8 | 19 | **66.2** |
| 11 | Canada | 12 | 14 | 12 | 9 | 17 | **65.7** |
| 12 | Ireland | 12 | 16 | 11 | 9 | 18 | **65.6** |

### Weighting and Scoring

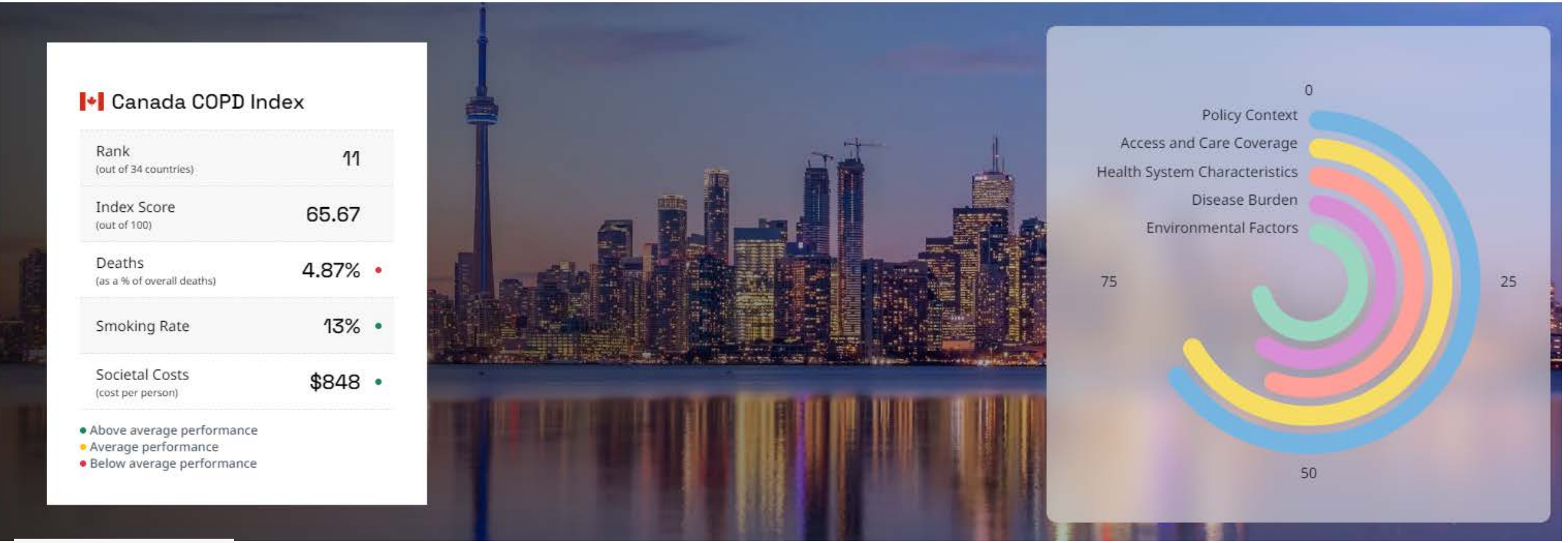
Following normalisation, country scores for each indicator category were averaged and then multiplied by 10 to give a score out of 100 points. The following weights were applied to each indicator category when calculating the overall Index score for each country:

| | |
|---|---|
| Policy Context | 21 % |
| Access and Care Coverage | 20 % |
| Health System Characteristics | 22.5 % |
| Disease Burden | 15.5 % |
| Environmental Factors | 21 % |

- The Copenhagen Institute for Futures Studies, with the support of an independent, expert steering committee, has developed the **COPD Index**, a unique data tool for **assessing both country health systems' approach to preventing and managing COPD**

https://respiratoryhealth.org/copd

# How do we rate worldwide for COPD outcomes?




CANADIAN THORACIC SOCIETY

Canada scores significantly above average in the Policy Context category, with strong tobacco control policies and relatively strong COPD care guidelines and practices.

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https://respiratoryhealth.org/copd/country/canada

# Learning Objectives

Explore how the risk of future exacerbations, mortality, and cardiopulmonary outcomes will change your approach to symptomatic patients with COPD

Highlight how new and emerging evidence and guideline recommendations are advancing patient outcomes

Identify how practical strategies for patient management are creating new pathways for care

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# Differential Diagnosis of COPD

Figure 2.3

| Diagnosis | Suggestive Features |
|---|---|
| COPD | Symptoms slowly progressive<br>History of tobacco smoking or other risk factors |
| Asthma | Variable airflow obstruction<br>Symptoms vary widely from day to day<br>Symptoms worse at night/early morning<br>Allergy, rhinitis, and/or eczema also present<br>Often occurs in children<br>Family history of asthma |
| Congestive heart failure | Chest X-ray shows dilated heart, pulmonary edema<br>Pulmonary function tests indicate volume restriction, not airflow obstruction |
| Bronchiectasis | Large volumes of purulent sputum<br>Commonly associated with bacterial infection<br>Chest X-ray/HRCT shows bronchial dilation |
| Tuberculosis | Onset at all ages<br>Chest X-ray shows lung infiltrate<br>Microbiological confirmation<br>High local prevalence of tuberculosis |
| Obliterative bronchiolitis | Can occur in children<br>Seen after lung or bone marrow transplantation<br>HRCT on expiration shows hypodense areas |
| Diffuse panbronchiolitis | Predominantly seen in patients of Asian descent<br>Most patients are male and nonsmokers<br>Almost all have chronic sinusitis<br>Chest X-ray & HRCT show diffuse small centrilobular nodular opacities & hyperinflation |

*These features tend to be characteristic of the respective diseases, but are not mandatory. For example, a person who has never smoked may develop COPD (especially in LMICs where other risk factors may be more important than cigarette smoking).*

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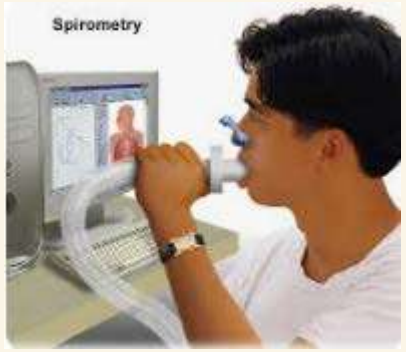
GLOBAL INITIATIVE FOR CHRONIC OBSTRUCTIVE LUNG DISEASE™




# Considerations in Performing Spirometry

Figure 2.4

| | |
|---|---|
| **PREPARATION** | • Spirometers should produce hard copy or have a digital display of the expiratory curve to permit detection of technical errors or have an automatic prompt to identify an unsatisfactory test and the reason for it<br>• The supervisor of the test needs training in optimal technique and quality performance<br>• Maximal patient effort in performing the test is required to avoid underestimation of values and hence errors in diagnosis and management |
| **PERFORMANCE** | • Spirometry should be performed following national and/or international recommendations[a]<br>• The expiratory volume/time traces should be smooth and free from irregularities<br>• The pause between inspiration and expiration should be less than one second<br>• The recording should go on long enough for a volume plateau to be reached, which may take more than 15 seconds in severe disease<br>• Both FVC and FEV1 should be the largest value obtained from any of three technically satisfactory curves and the FVC and FEV1 values in these three curves should vary by no more than 5% or 150 mL, whichever is greater<br>• The FEV1/FVC ratio should be taken from the technically acceptable curve with the largest sum of FVC and FEV1 |
| **BRONCHODILATION** | • Possible dosage protocols are 400 mcg short-acting beta$_2$-agonist, 160 mcg short-acting anticholinergic, or the two combined[b]; FEV1 should be measured 10-15 minutes after a short-acting beta$_2$-agonist is given, or 30-45 minutes after a short-acting anticholinergic or a combination of both classes of drugs<br>• Patients already on bronchodilator treatment, in whom spirometry is requested for monitoring purposes do not need to stop their regular treatment for spirometry |
| **EVALUATION** | • Spirometry measurements are evaluated by comparison of the results with appropriate reference values based on age, height and sex<br>• The presence of a post-bronchodilator FEV1/FVC < 0.7 confirms the presence of non-fully reversible airflow obstruction |

[a]Miller *et al.* Eur Respir J 2005; 26(2): 319; [b]Pellegrino *et al.* Eur Respir J 2005; 26(5): 948.

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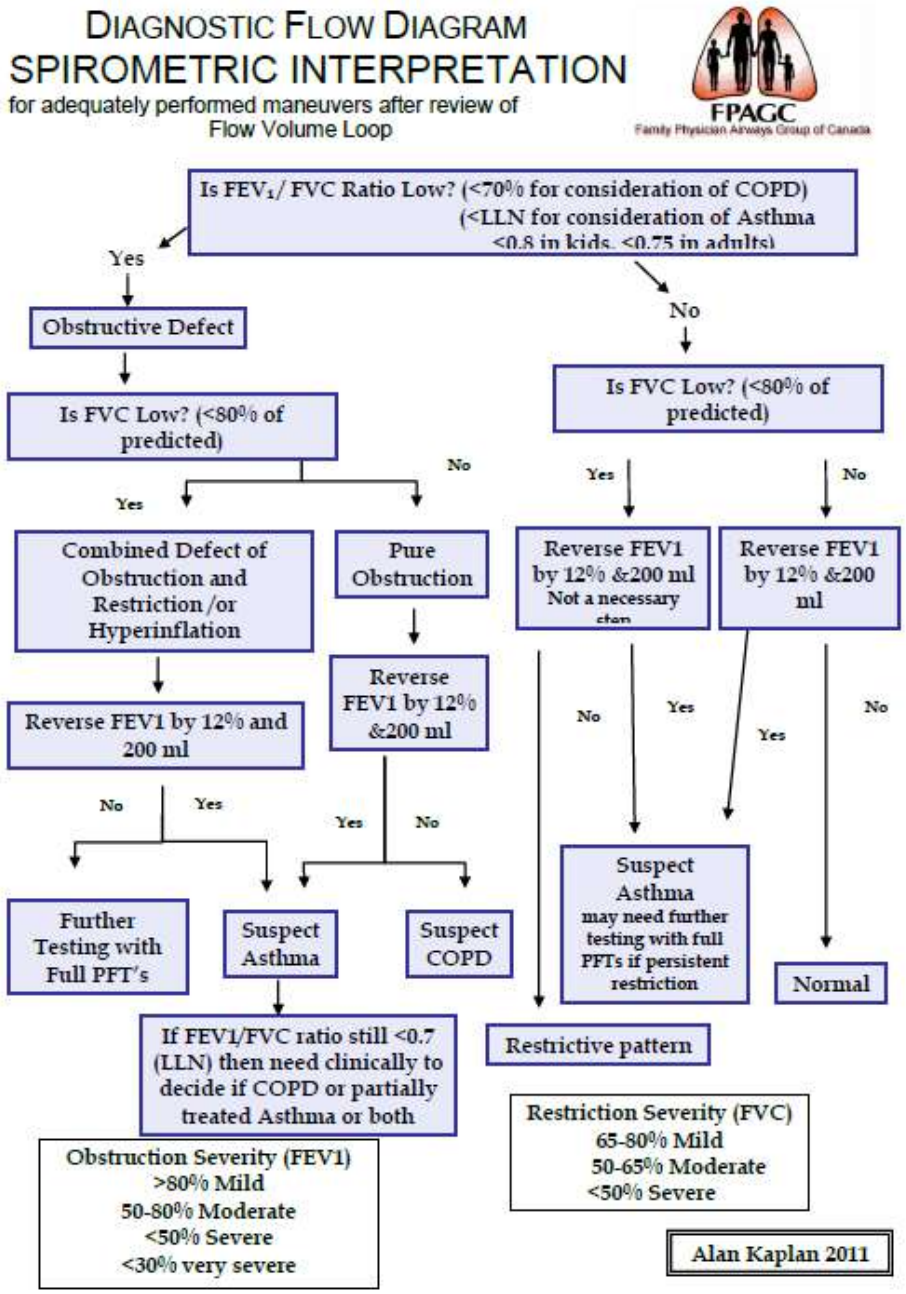
www.fpagc.com
Tools section



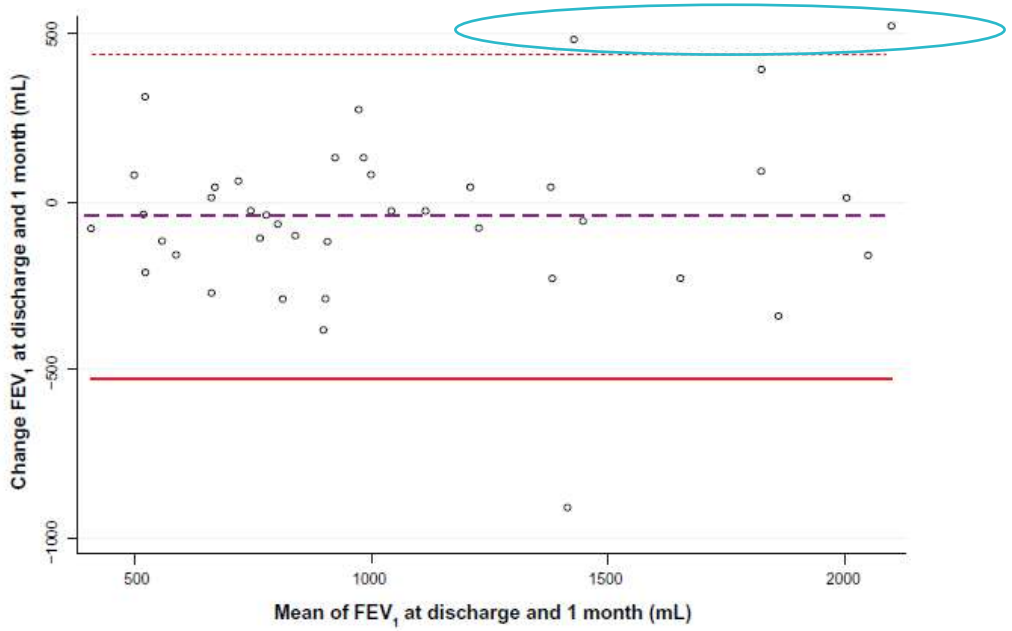



Figure 2 Difference between $FEV_1$ at 1 month and $FEV_1$ at discharge from hospital for each patient. Central line is observed average agreement. Upper and lower lines are 95% limits of agreement.
**Note:** N = 41.

Diagnosis does not change doing it acutely,
Severity may change, however

False positive diagnosis from doing spirometry close to an acute exacerbation is **not** a clinical problem.(2/41 were no longer obstructed, so it can happen!)

International Journal of COPD
Dovepress
open access to scientific and medical research
Open Access Full Text Article
ORIGINAL RESEARCH

# Spirometry for patients in hospital and one month after admission with an acute exacerbation of COPD

This article was published in the following Dove Press journal:
International Journal of COPD
13 October 2011
Number of times this article has been viewed

**Table 1** Patients with COPD according to GOLD spirometry criteria at hospital discharge

| | Discharge | 1 month | *P* value |
|---|---|---|---|
| $FEV_1$ | 1.04 (0.51) | 1.08 (0.48) | 0.26 |
| FVC | 2.09 (0.89) | 2.18 (0.81) | 0.12 |
| $FEV_1$/FVC | 0.50 (0.11) | 0.50 (0.12) | 1.00 |
| $FEV_1$ % predicted | 38.7 (14.4) | 40.6 (14.3) | 0.18 |
| **Classification ($FEV_1$ % predicted)** | | | |
| Moderate (50 to <80) | 10 | | |
| Mild | | 0 | |
| Moderate | | 8 | |
| Severe | | 2 | |
| Severe (30 to <50) | 18 | | |
| Moderate | | 4 | |
| Severe | | 11 | |
| Very severe | | 2 | |
| Very severe (<30) | 13 | | |
| Severe | | 6 | |
| Very severe | | 6 | |

**Notes:** Spirometry measures and GOLD severity classification at discharge and at 1 month. Results are mean (SD) or counts. N = 41. One 'severe' and one 'very severe' patient at discharge no longer met GOLD criteria at 1 month (see text).

Rea H, Kenealy T, Adair J, Robinson E, Sheridan N. Spirometry for patients in hospital and one month after admission with an acute exacerbation of COPD. *Int J Chron Obstruct Pulmon Dis.* 2011;6:527-32. doi: 10.2147/COPD.S24133. Epub 2011 Oct 14. PMID: 22069364; PMCID: PMC3206769.

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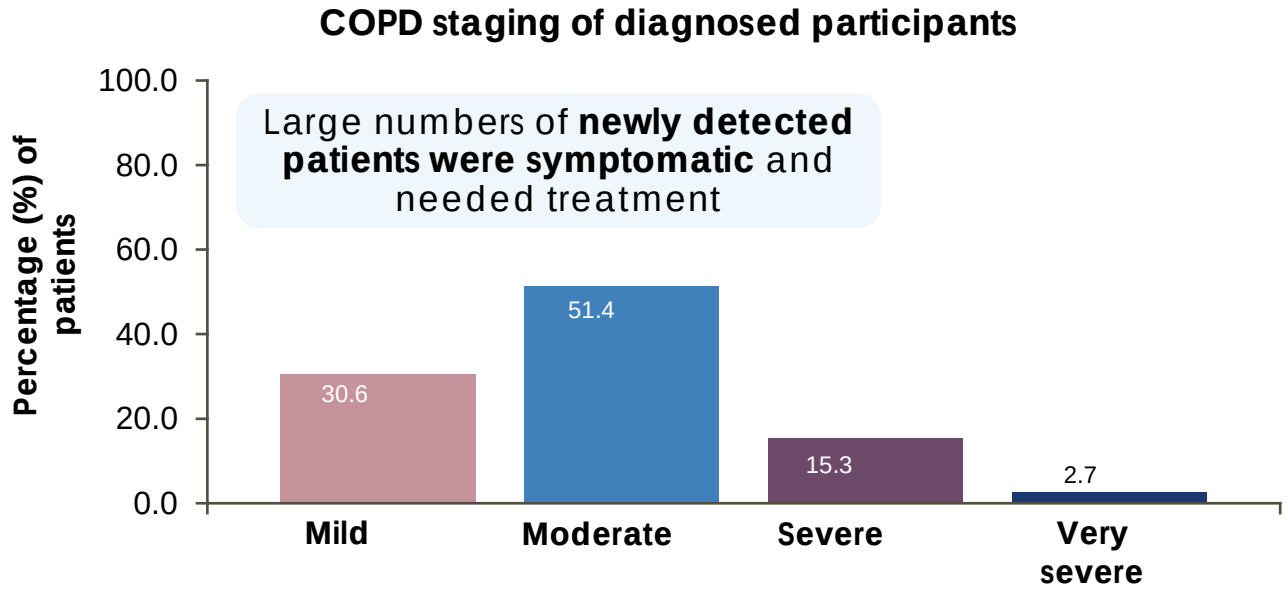
# Prevalence of COPD Underdiagnosis in the Primary Care Setting

- 1960 patients aged 40+ (mean age 56.7 years) who were registered in a primary care practice participated
- 299 of participants had a $FEV_1$/FVC below the fifth percentile of the predicted value and were given 200 µg of salbutamol to complete post-BD spirometry 15 minutes later
  - 211 participants had airflow obstruction present post-BD

**81.4% participants (149/183) diagnosed with COPD did not have a prior COPD diagnosis**




COPD was **largely underdiagnosed without spirometry:** only patients with severe disease ($FEV_1$ <50% predicted) had been diagnosed and treated

BD: bronchodilator; $FEV_1$: forced expiratory volume in 1 second; FVC: forced vital capacity.

1. Bednarek et al. Thorax. 2008;63:402-07.

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# Screening


**Screening for Chronic Obstructive Pulmonary Disease: A Targeted Evidence Update for the U.S. Preventive Services Task Force**

*Evidence Synthesis, No. 215*

Investigators: Jennifer S. Lin, MD, MCR, Elizabeth M. Webber, MS, and Rachel G. Thomas, MPH.

Rockville (MD): Agency for Healthcare Research and Quality (US); 2022 May.
Report No.: 21-05287-EF-1

USPSTF issued a D Recommendation **against** screening for COPD in asymptomatic adults (defined as individuals who do not recognize or report respiratory symptoms)

- Although they found that screening for COPD could accurately identify persons with COPD, they determined that, based on the included evidence, early detection of COPD did not alter the course of the disease or improve patient outcomes
- Did not support screening as a means to improve smoking cessation rates or the uptake of other recommended preventive services.
- Case finding = Screening for symptoms; THAT WORKS!

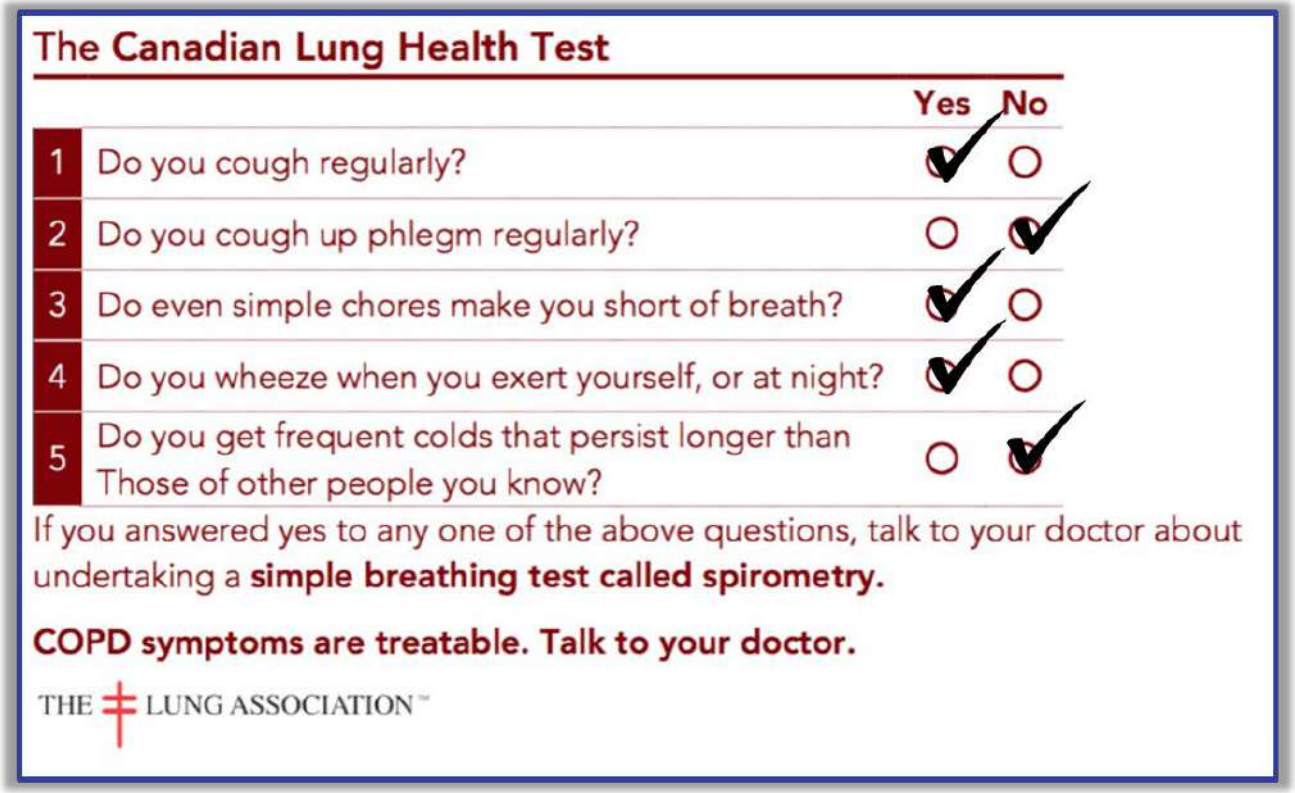
# What is MILD COPD?

- Mild COPD = GOLD 1 (More than or equal to 80% $FEV_1$) spirometric description
- Mild COPD is mild wrt symptoms,
  - ie., GOLD Group A
- Mild is infrequent exacerbations,
  (0-1 per year and no hospitalizations)
  - ie. GOLD Group A

| CLASSIFICATION OF AIRFLOW LIMITATION SEVERITY IN COPD (BASED ON POSTBRONCHODILATOR $FEV_1$) | | |
|---|---|---|
| **In patients with $FEV_1/FVC < 0.70$:** | | |
| GOLD 1: | Mild | $FEV_1 \geq 80\%$ predicted |
| GOLD 2: | Moderate | $50\% \leq FEV_1 < 80\%$ predicted |
| GOLD 3: | Severe | $30\% \leq FEV_1 < 50\%$ predicted |
| GOLD 4: | Very severe | $FEV_1 < 30\%$ predicted |

# What is EARLY COPD?

- Making a diagnosis before too much lung has been lost
  - Continued exposure stopped (eg smoking)
  - Prevention of exacerbations, more to come
- Before symptoms….GOLD only describes COPD as symptomatic, so no
- BUT, before diagnosis the patient is suffering, so need to LOOK for symptoms
  - Not screening with spirometry, but screening for symptoms in those at risk



**The Canadian Lung Health Test**

| | | Yes | No |
|---|---|---|---|
| 1 | Do you cough regularly? | ✓ | ○ |
| 2 | Do you cough up phlegm regularly? | ○ | ✓ |
| 3 | Do even simple chores make you short of breath? | ✓ | ○ |
| 4 | Do you wheeze when you exert yourself, or at night? | ✓ | ○ |
| 5 | Do you get frequent colds that persist longer than Those of other people you know? | ○ | ✓ |

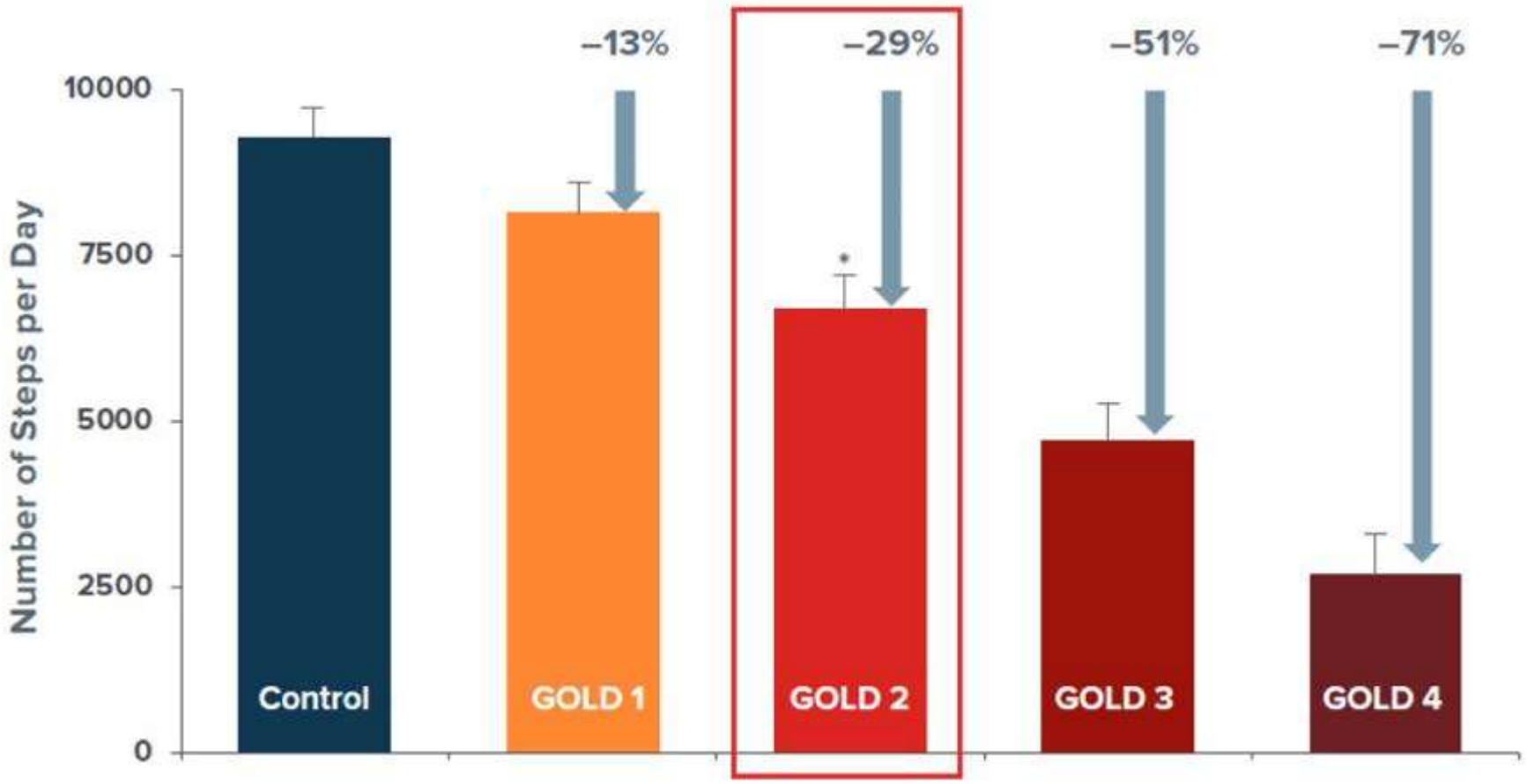
If you answered yes to any one of the above questions, talk to your doctor about undertaking a **simple breathing test called spirometry.**

**COPD symptoms are treatable. Talk to your doctor.**

THE LUNG ASSOCIATION™

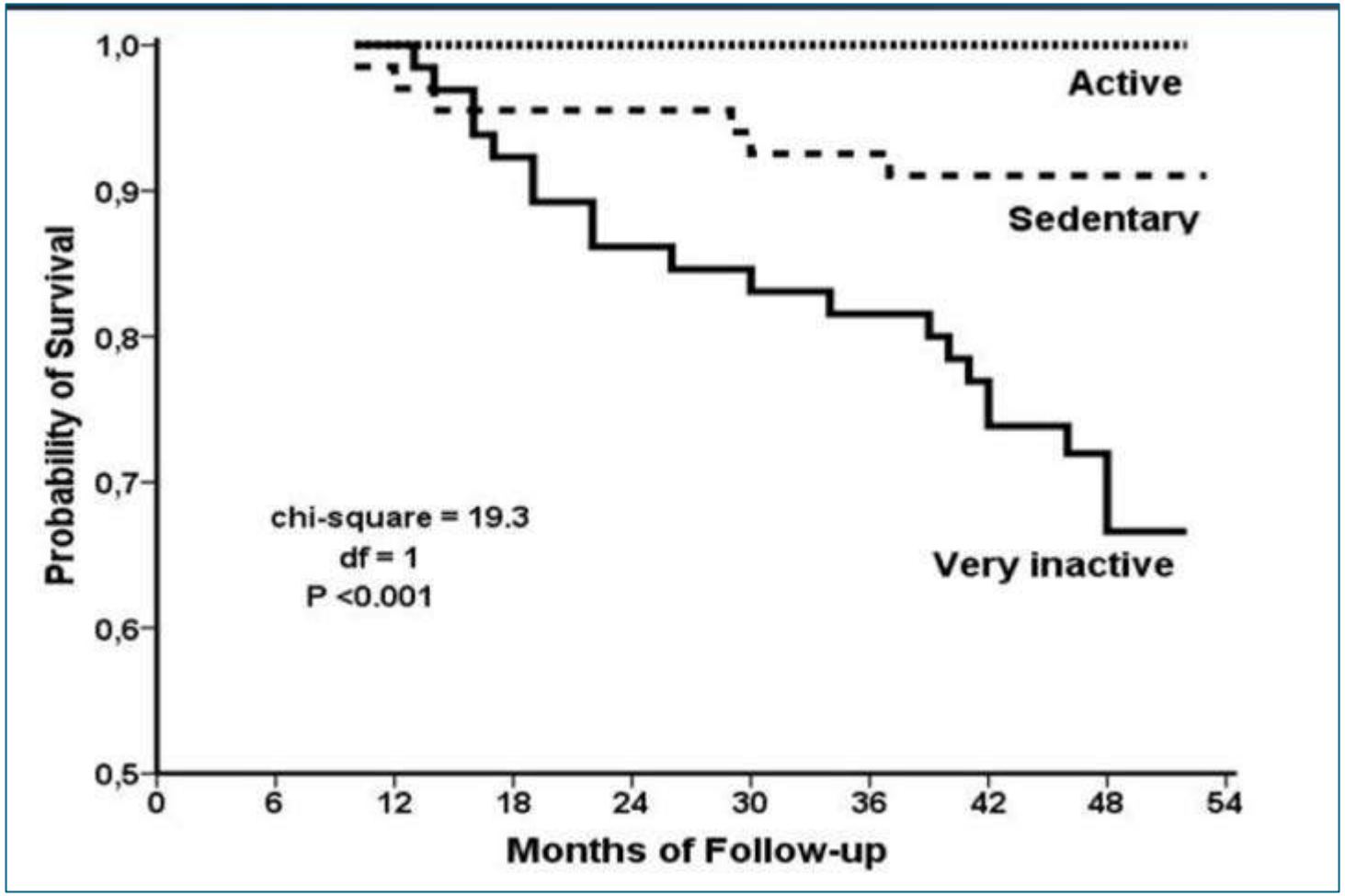
# COPD; does early diagnosis matter?

# Even early disease, esp at GOLD 2, can lead to reduced physical activity!




Troosters T, et al. *Respir Med.* 2012;104:1005-1011.

# Physical Activity and Mortality




Survival curve vs Physical Activity

Mortality risk based on Physical Activity:

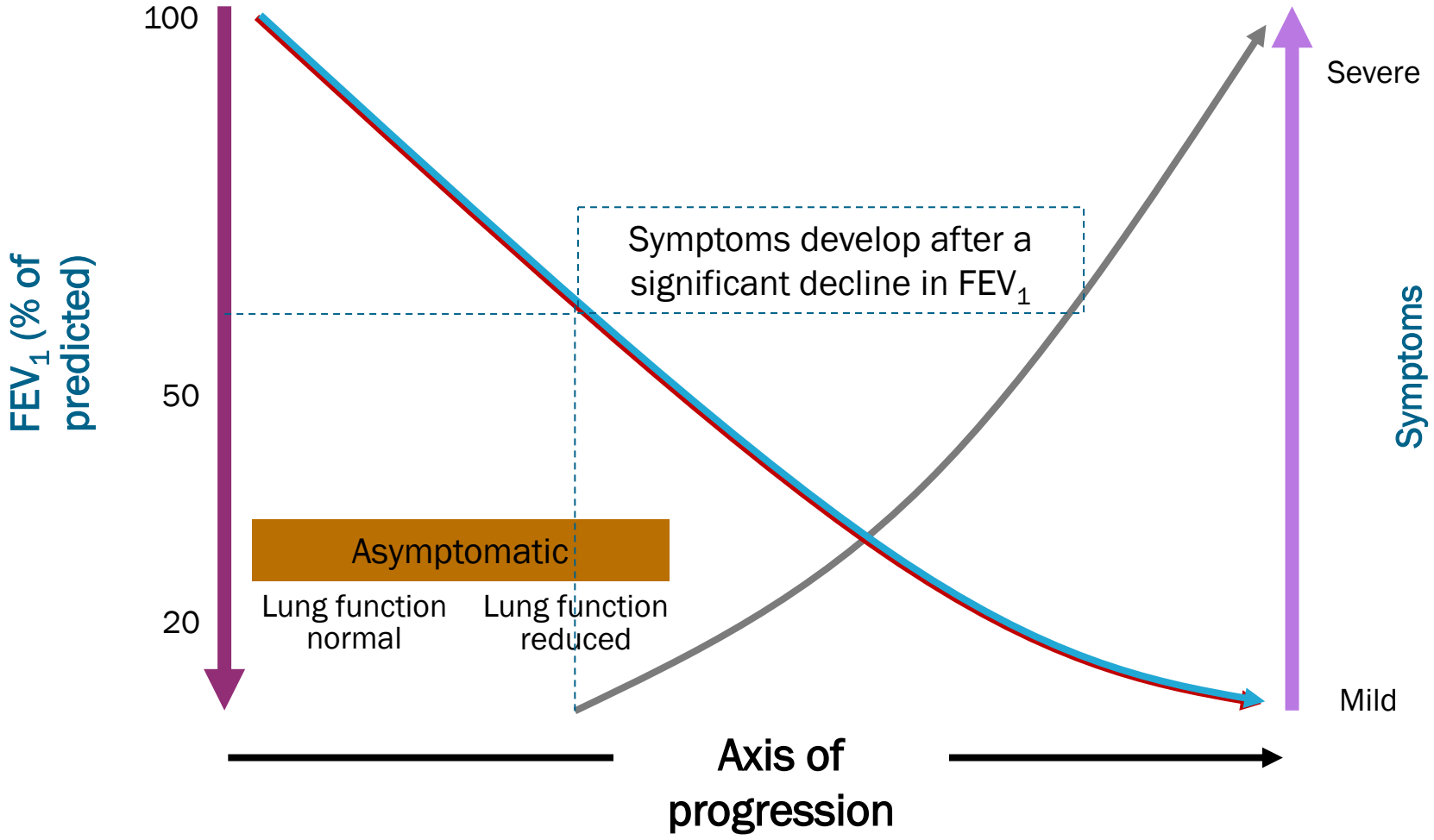
0% Active (baseline)

9% if Sedentary

31% if Very Inactive

Waschki B, et al. *Chest.* 2011;140:331-342.

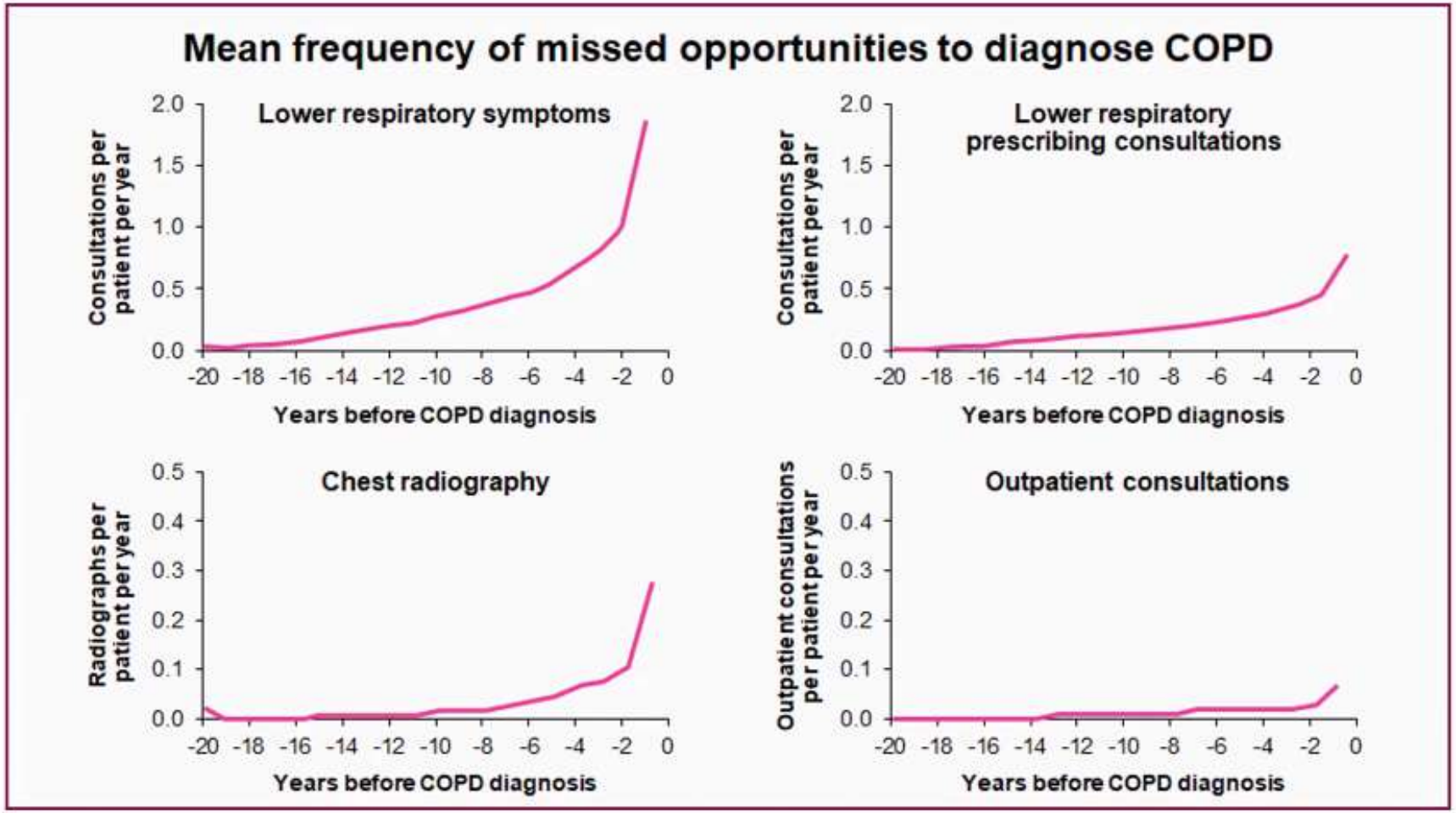
# The Importance of Earlier Diagnosis




$FEV_1$, forced expiratory volume in 1 second

Sutherland ER, Cherniack RM. *N Engl J Med.* 2004;350:2689

# We can make a diagnosis earlier, if we think about it!!



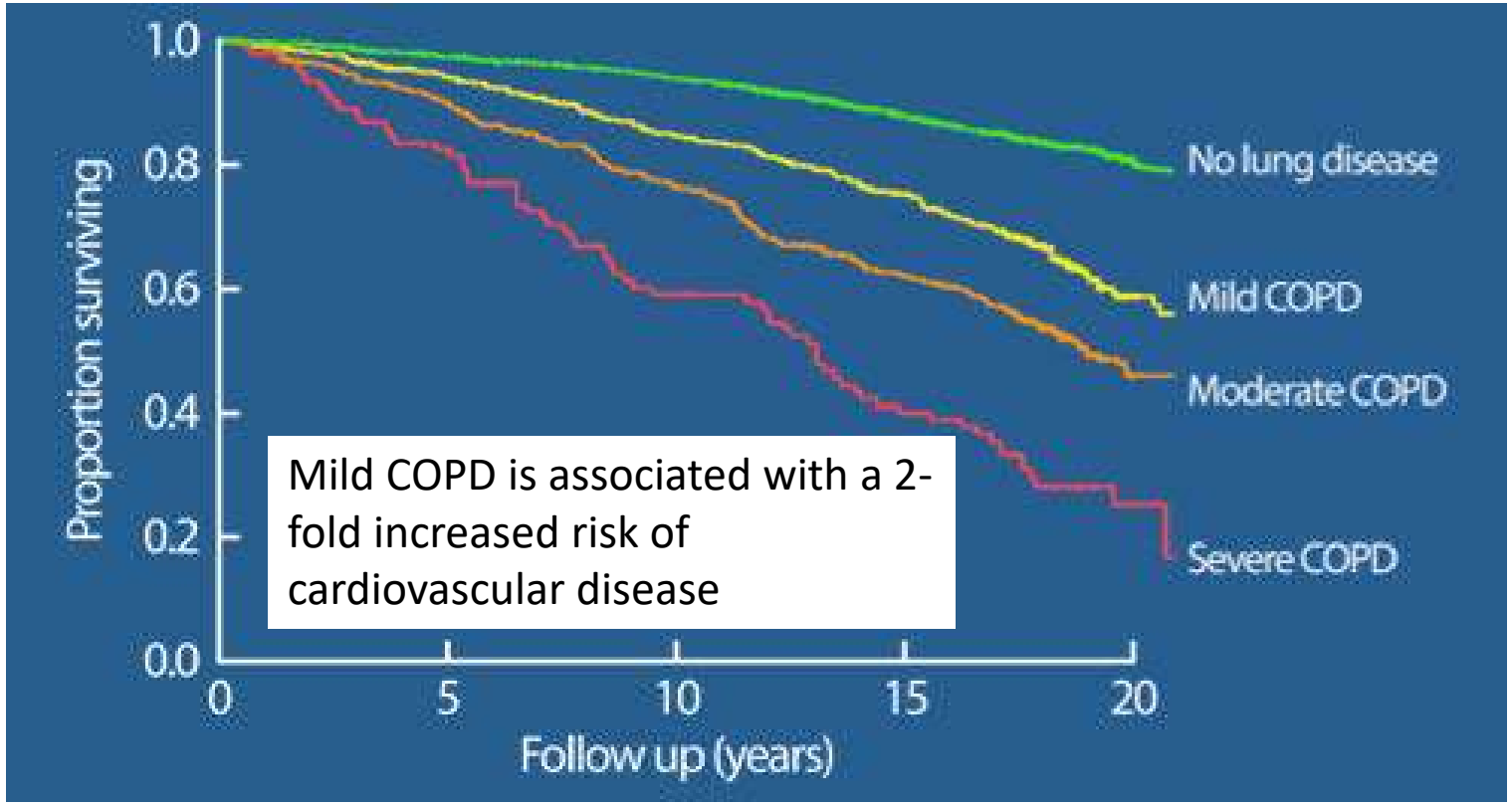

In the **5 years before** diagnosis of COPD:

- **85%** with lower respiratory consultation
- **68%** with lower respiratory prescription
- **40%** prescribed oral steroids
- **55%** prescribed antibiotics

Jones RC, Price D, Ryan D, Sims EJ, von Ziegenweidt J, Mascarenhas L, Burden A, Halpin DM, Winter R, Hill S, Kearney M, Holton K, Moger A, Freeman D, Chisholm A, Bateman ED; Respiratory Effectiveness Group. Opportunities to diagnose chronic obstructive pulmonary disease in routine care in the UK: a retrospective study of a clinical cohort. Lancet Respir Med. 2014 Apr;2(4):267-76. doi: 10.1016/S2213-2600(14)70008-6. Epub 2014 Feb 13. PMID: 24717623.

# Decreased Survival EVEN in Mild Disease!

- Although airflow obstruction is still minimal, physiologic changes in mild COPD lead to progressive morbidity and reduced life-expectancy




*Ofir et al Am J Respir Crit Care Med* 2013; Chin *et al Am J Respir Crit Care Med* 2013; Elbehairy *et al Drug Review 2013 in press*
Mannino *et al. Thorax.* 2003; Ekberg-Aronsson *et al. Respir Research.* 2005; Mannino *et al. Respir Med.* 2006

# Cardiovascular-Related Mortality in Mild-to-Moderate COPD

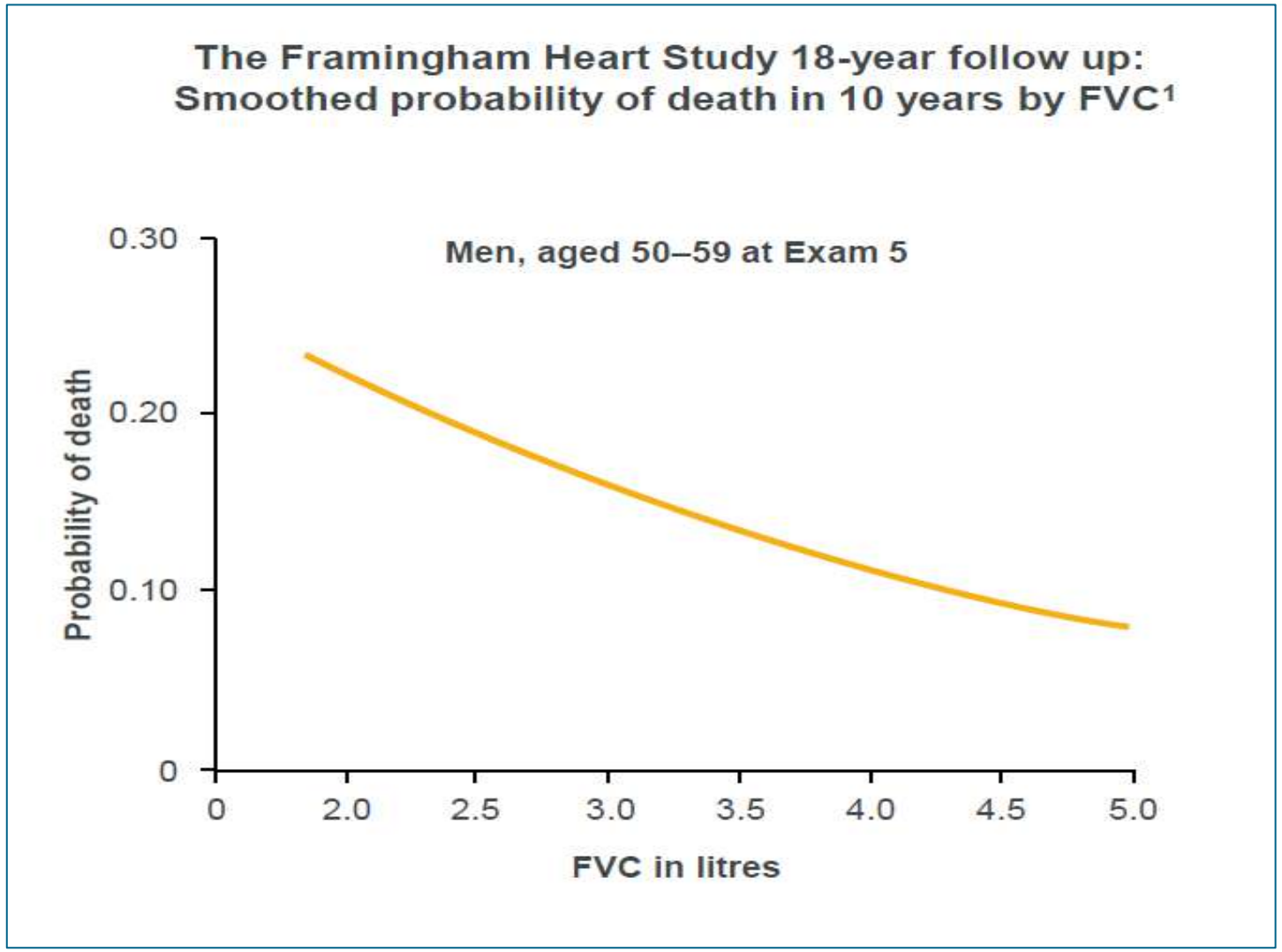
## Underlying Cause of Death Among 1242 Decedents in the Study

| | Deaths | Underlying cause of death (%)* | | | |
|---|---|---|---|---|---|
| | | Respiratory | Lung cancer | Cardiac | Other |
| GOLD 3 or 4† | 92 | 31.5 | 23.9 | 13.0 | 31.5 |
| GOLD 2 | 232 | 3.5 | 25.4 | 27.6 | 43.5 |
| GOLD 1 | 137 | 0.7 | 18.3 | 24.8 | 56.2 |
| Restricted | 150 | 1.3 | 7.3 | 39.3 | 52.0 |
| GOLD 0 | 204 | 0.5 | 8.3 | 35.3 | 55.9 |
| Normal | 427 | 0.5 | 6.3 | 30.2 | 63.0 |

From the Atherosclerosis Risk on Communities (ARIC) study 1986–1989 and follow-up through 1997.
*Based on International Classification of Disease, Ninth Revision (ICD-9) codes to classify death as respiratory (ICD-9 490-496), lung cancer (ICD-9 162), cardiovascular (ICD-9 410-429), or other (all others).
†GOLD stage 3 or 4 ($FEV_1$/FVC <0.70 and $FEV_1$ <50% predicted), GOLD stage 2 ($FEV_1$/FVC <0.70 and $FEV_1$ ≥50 to <80% predicted), GOLD Stage 1 ($FEV_1$/FVC <0.70 and $FEV_1$ ≥80%), restricted ($FEV_1$/FVC ≥0.70 and FVC <80% predicted), GOLD stage 0 (presence of respiratory symptoms in the absence of any lung function abnormality), and no long disease.

FVC, forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease. Mannino DM, et al. *Respir Med*. 2006;100:115-22.

# COPD Is a CVD Risk Factor: Framingham data from 1975!




Ashley F, et al. *Ann Intern Med.* 1975;82:739-745.

# How does an earlier diagnosis make a difference

- Patients quality of life is actually better when they understand what is wrong
- Smoking cessation can be attempted with more vigour!
  - Motivational interviewing better when it affects them personally
- Other exposures removed?
- Prevent exacerbations by vaccinating
  - Now a high-risk group
- Moderate effect of AECOPD by providing action plans
- Can we prevent further lung loss and prevent disability/Stability vs continued deterioration?
- Nutrition advice
- CV protection
- Bone protection
- Bronchodilate to efficacy for symptoms
  - This may just be a SABD prn?

Adapted from Early Diagnosis of COPD Does Matter, IPCRG desktop helper: /https://www.ipcrg.org/sites/ipcrg/files/content/attachments/2020-03-04/IPCRG_Desktop_Helper_Early_Diagnosis_COPD.pdf

# Nonpharmacological Recommendations

| | | |
|---|---|---|
| **Smoking Cessation** | o<br>o | Crucial<br>Pharmacotherapy to aid |
| **Immunization** | o | Six, can you think of them? |
| **Physical Activity** | o<br>o<br>o | ↓ level associated with reduced quality of life (QOL), ↑ rates of hospitalization/mortality<br>Can be enhanced with optimizing bronchodilators<br>Full Pulmonary Rehabilitation |
| **Inhaler technique** | o | Meds do not work if they do not get to the lungs! |
| **Action Plan** | o | Act within 48 hours of worsening may prevent exacerbations |

Global Initiative for Chronic Obstructive Lung Disease (GOLD).
*Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease (2018 Report)*.
Global Initiative for Chronic Obstructive Lung Disease (GOLD), 2018. http://www.goldcopd.org

# 5As

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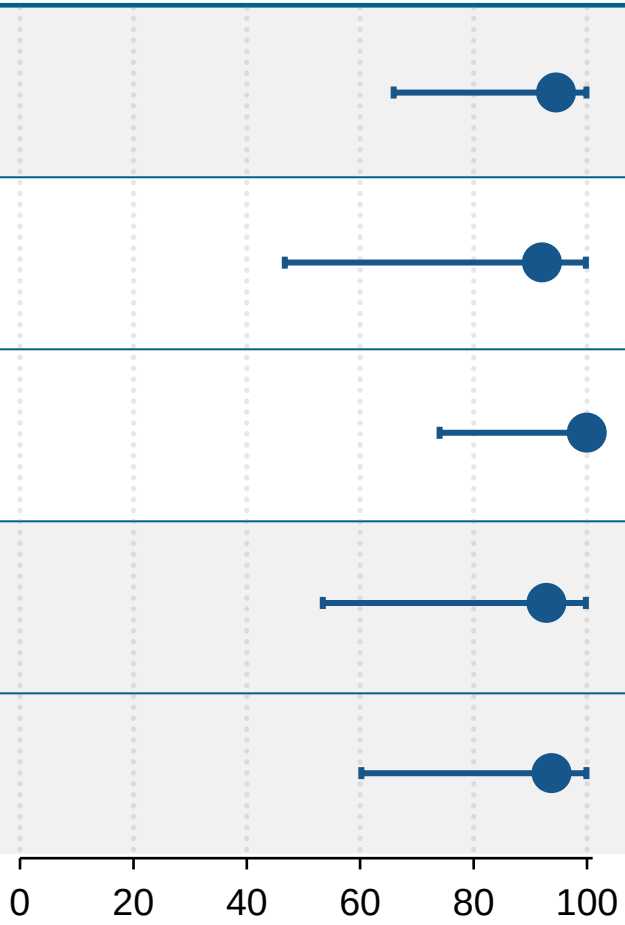
# RSV Adjuvanted is highly efficacious in older adults at increased risk of severe RSV disease, including those with comorbidities

| | *Number of events* | | **Vaccine efficacy** (95% CI) against RSV-LRTD |
|---|---|---|---|
| | *AREXVY N=12,466* | *Placebo N=12,494* | |
| **≥1 pre-existing comorbidity of interest** | 1 | 18 | **94.6%** (65.9, 99.9) |
| ≥1 cardiorespiratory condition | 1 | 12 | **92.1%** (46.7, 99.8) |
| ≥1 endocrine metabolic condition | 0 | 13 | **100%** (74.0, 100) |
| **Pre-frail** (gait speed test: 0.4–0.99 m/s) | 1 | 14 | **92.9%** (53.4, 99.8) |
| **70–79 years of age** | 1 / 4,487 | 16 / 4,487 | **93.8%** (60.2, 99.9) |




CI, confidence interval; LRTD, lower respiratory tract disease.

Papi A et al. N Engl J Med 2023;388(7):595–608.

# But, Zoster risk and ICS

Chronic Obstructive Pulmonary Diseases:
Journal of the COPD Foundation®

COPD FOUNDATION

Brief Report

## Increased Herpes Zoster Risk With Inhaled Corticosteroid Use for Those With Chronic Obstructive Pulmonary Disease

Barbara P. Yawn, MD, MSc[1] Elisabeth Callen, PhD, PStat[2] Gabriela Gaona-Villarreal, MPH[2] Asif Shaikh, MD, DrPH, MPH[3] Wilson D. Pace, MD[2]

**Table 1. Relative Risk and Hazard Ratio for Herpes Zoster Episodes by Inhaled Corticosteroid Exposure Duration: Prevalence and Inception Cohorts**

| ICS Duration | All With COPD N | No HZ During Observation Period n, (%) | HZ During Observation Period n, (%) | Unadjusted RR Long-Term vs. Short-Term/No | Adjusted HR[a] |
|---|---|---|---|---|---|
| **HZ in COPD Matched Prevalent Cohort Including Asthma (N=242,623)** | | | | | |
| ICS 24+ Months | 81,159 | 79,950 (98.5) | 1209 (1.49)[b] | 2.40 (2.2–2.6) | 2.57 (2.55–2.60) |
| ICS <3 Months/No ICS | 161,464 | 160,466 (99.4) | 998 (0.62) | | |
| **HZ in COPD Matched Inception Cohort Including Asthma (N=147,279)** | | | | | |
| ICS 24+ Months | 73,933 | 72,695 (98.3) | 1238 (1.70)[b] | 2.42 (2.3–2.8) | 2.55 (2.52–2.58) |
| ICS <3 Months/No ICS | 73,346 | 72,855 (99.3) | 491 (0.67) | | |

[a]Adjusted for age at index, index year, number of steroid bursts, gender, race, ethnicity, smoking status, BMI, and Carlson-Deyo Score
[b]$p<.001$ for ICS 24+ months versus ICS <3 months/no ICS for prevalent and incidence cohorts

HZ=herpes zoster; COPD=chronic obstructive pulmonary disease; ICS=inhaled corticosteroid; RR=relative risk; HR=hazard ratio; BMI=body mass index

Message: Only use ICS when appropriate and Vaccinate for Shingles!!

Yawn BP, Callen E, Gaona-Villarreal G, Shaikh A, Pace WD. Increased herpes zoster risk with inhaled corticosteroid use for those with chronic obstructive pulmonary disease. Chronic Obstr Pulm Dis. 2024; 11(3): 303-306. doi: http://doi.org/10.15326/jcopdf.2023.0478

# Felix's Case

Felix is a 61-year-old male with moderate-to-severe COPD (diagnosed 6 years ago), HTN, T2DM, and dyslipidemia.

**Treatment regimen**

- LAMA plus SABA prn
- Lisinopril, 30 mg once a day
- Atorvastatin, 40 mg once a day
- Metformin, 500 mg 3 times a day with meals
- Salbutamol 100 mcg PRN

**COPD-specific test results**

- $FEV_1$/FVC: 57%
- $FEV_1$: 45% of predicted

,

. Gets SOB walking with spouse on level ground

(mMRC 2)


DPI, dry powdered inhaler; $FEV_1$, forced expiratory volume in 1 second; FVC, forced vital capacity; HTN, hypertension; prn, as needed; PRN, as needed; T2DM, type 2 diabetes mellitus.

CANADIAN JOURNAL OF RESPIRATORY, CRITICAL CARE, AND SLEEP MEDICINE
https://doi.org/10.1080/24745332.2023.2231451

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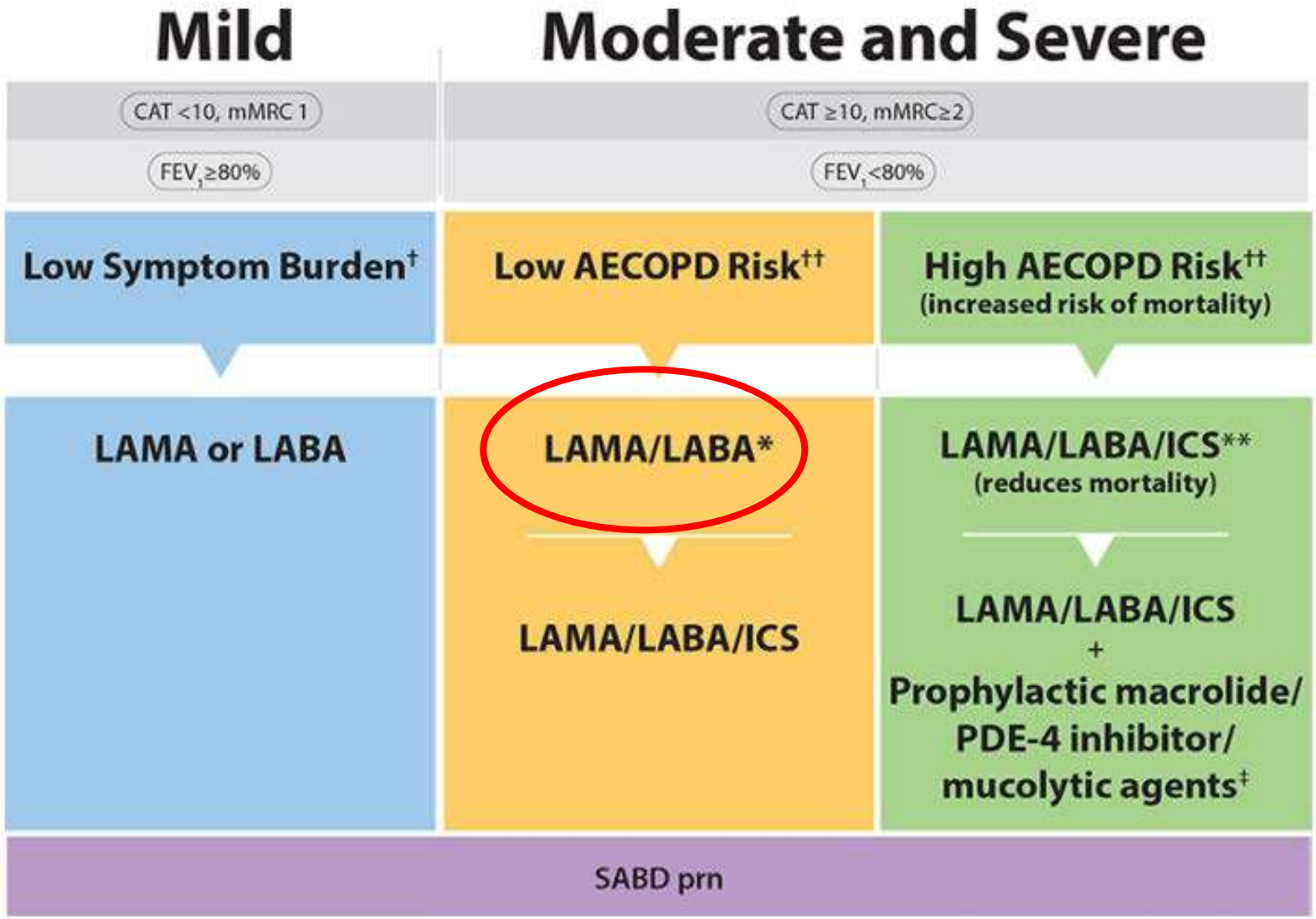
CTS GUIDELINES AND POSITION PAPERS

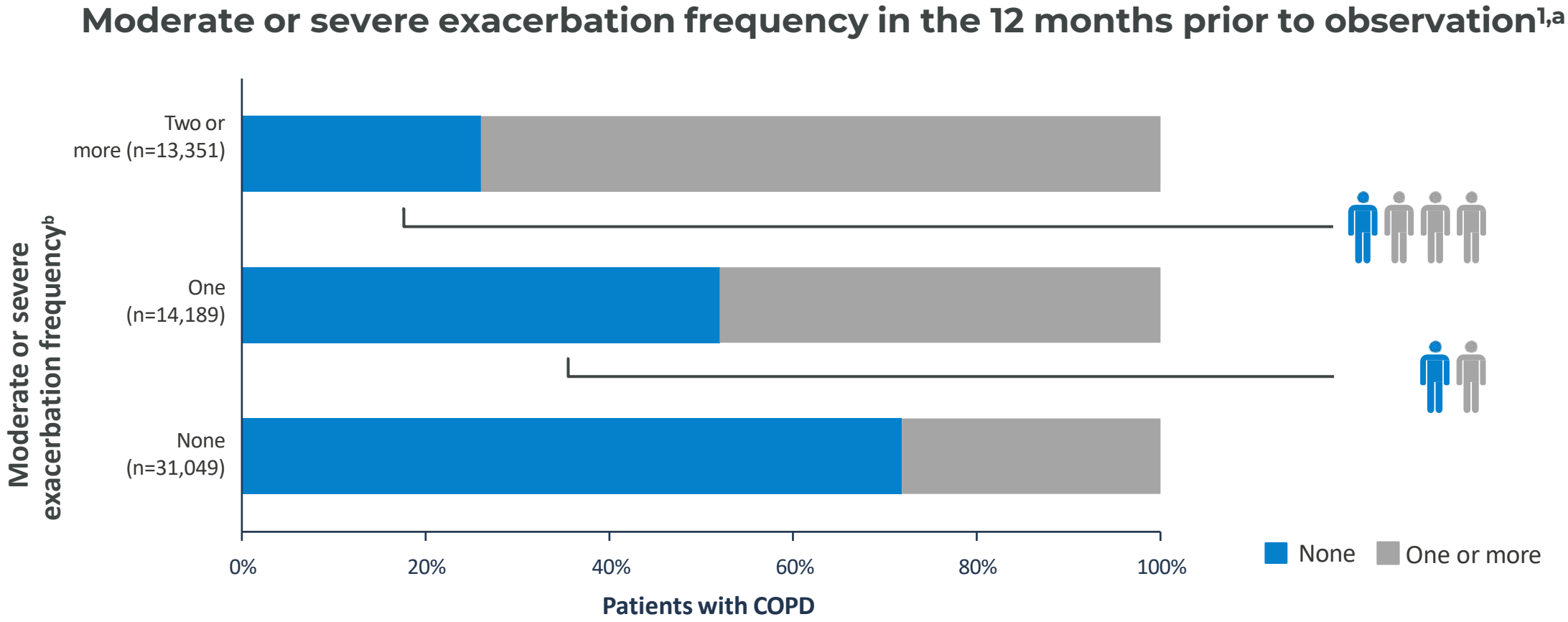
## 2023 Canadian Thoracic Society Guideline on Pharmacotherapy in Patients with Stable COPD

Jean Bourbeau[a*], Mohit Bhutani[b*], Paul Hernandez[c*], Shawn D. Aaron[d], Marie-France Beauchesne[e], Sophie B. Kermelly[f], Anthony D'Urzo[g], Avtar Lal[h], François Maltais[i], Jeffrey D. Marciniuk[j], Sunita Mulpuru[d], Erika Penz[k], Don D. Sin[l], Anne Van Dam[h], Joshua Wald[k], Brandie L. Walker[l] and Darcy D. Marciniuk[c*]




Bourbeau J, Bhutani M, Hernandez P, Aaron SD, Beauchesne MF, Kermelly SB, D'Urzo A, Lal A, Maltais F, Marciniuk JD, Mulpuru S, Penz E, Sin DD, Van Dam A, Wald J, Walker BL, Marciniuk DD. 2023 Canadian Thoracic Society Guideline on Pharmacotherapy in Patients With Stable COPD. Chest. 2023 Nov;164(5):1159-1183. doi: 10.1016/j.chest.2023.08.014. Epub 2023 Sep 9. PMID: 37690008.

# Patients With COPD Are Susceptible to Exacerbations, Even Without a History of Exacerbations




Note: although the definition and classification of exacerbations have been updated in the 2023 GOLD report, exacerbation severity refers to an earlier definition and classification to align with the published data.

[a]Retrospective observational cohort study that evaluated risk factors associated with exacerbation frequency in 58,589 patients with COPD identified in the UK Clinical Practice Research Datalink; [b]Moderate and severe exacerbation episodes were recorded over a 12-month follow-up period.

GOLD, Global Initiative for Chronic Obstructive Lung Disease.

1. Reproduced from Müllerová H, et al. Risk factors for acute exacerbations of COPD in a primary care population: a retrospective observational cohort study. *BMJ Open.* 2014;4:e006171,

# Elevated risk of CV event or all-cause death already present following first exacerbation in incident COPD population

| Time period | No. of first CV events of any type | Person-years of follow up | Adjusted* HR (95% CI) |
|---|---|---|---|
| After the onset of the first exacerbation (moderate or severe) | | | |
| **1–7 days** | 33 | 43 | **15.2 (10.3, 22.4)** |
| 8–14 days | 20 | 42 | 9.3 (5.8, 15.1) |
| 15–30 days | 16 | 91 | 3.9 (2.3, 6.4) |
| 31–180 days | 49 | 704 | 1.6 (1.2, 2.2) |
| 181–365 days | 38 | 640 | 1.5 (1.1, 2.1) |
| After the onset of the second exacerbation (moderate or severe) | | | |
| **1–7 days** | 21 | 20 | **22.3 (14.3, 34.6)** |
| 8–14 days | 6 | 20 | 6.5 (2.9, 14.6) |
| 15–30 days | 9 | 43 | 4.6 (2.4, 8.9) |
| 31–180 days | 31 | 289 | 2.6 (1.8, 3.7) |
| 181–365 days | 12 | 226 | 1.3 (0.7, 2.3) |

**Clinical relevance**

- Underlines the need to evaluate cardiopulmonary risk even in newly diagnosed patients
- Supports the hypothesis that preventative treatment early in the disease trajectory may be beneficial
- Reducing exacerbation frequency may reduce cardiopulmonary risk

Unexposed: the time period prior to the first exacerbation and the time period post 365 days following an exacerbation. *Adjusted for baseline covariates

Table adapted from Swart et al: Hazard ratios for time to the composite outcome (non-fatal severe CV event or all-cause death), comparing exposed periods in the 365 days following a first and second exacerbation of COPD to the non-exposure period. CI, confidence interval; CV, cardiovascular; HR, hazard ratio

Swart KM, et al. Respir Res 2023;24:293

# How to reduce risk of exacerbations in these non-frequent exacerbators?

- Vaccinate
- Smoking cessation
- Exercise
- Medication adherence and inhaler technique
- Pharmacotherapy adjustment?
    - LABA/LAMA
    - Triple?
- CV pharmacotherapy: statins, ACE/ARB…

# KRONOS: The Only COPD Study to Assess the Effect of Triple Therapy on Patients Irrespective of Exacerbation History

**Population**

Moderate to very severe COPD **with no requirement for history of exacerbations** within the past year

- **74%** had **no exacerbations**
- **88%** had **no severe exacerbations** and 1 or 0 moderate exacerbations

**Primary endpoints**

- **$FEV_1$ $AUC_{0-4}$**
- Change from baseline in trough (pre-dose) $FEV_1$[a]

**Secondary endpoints**[b]

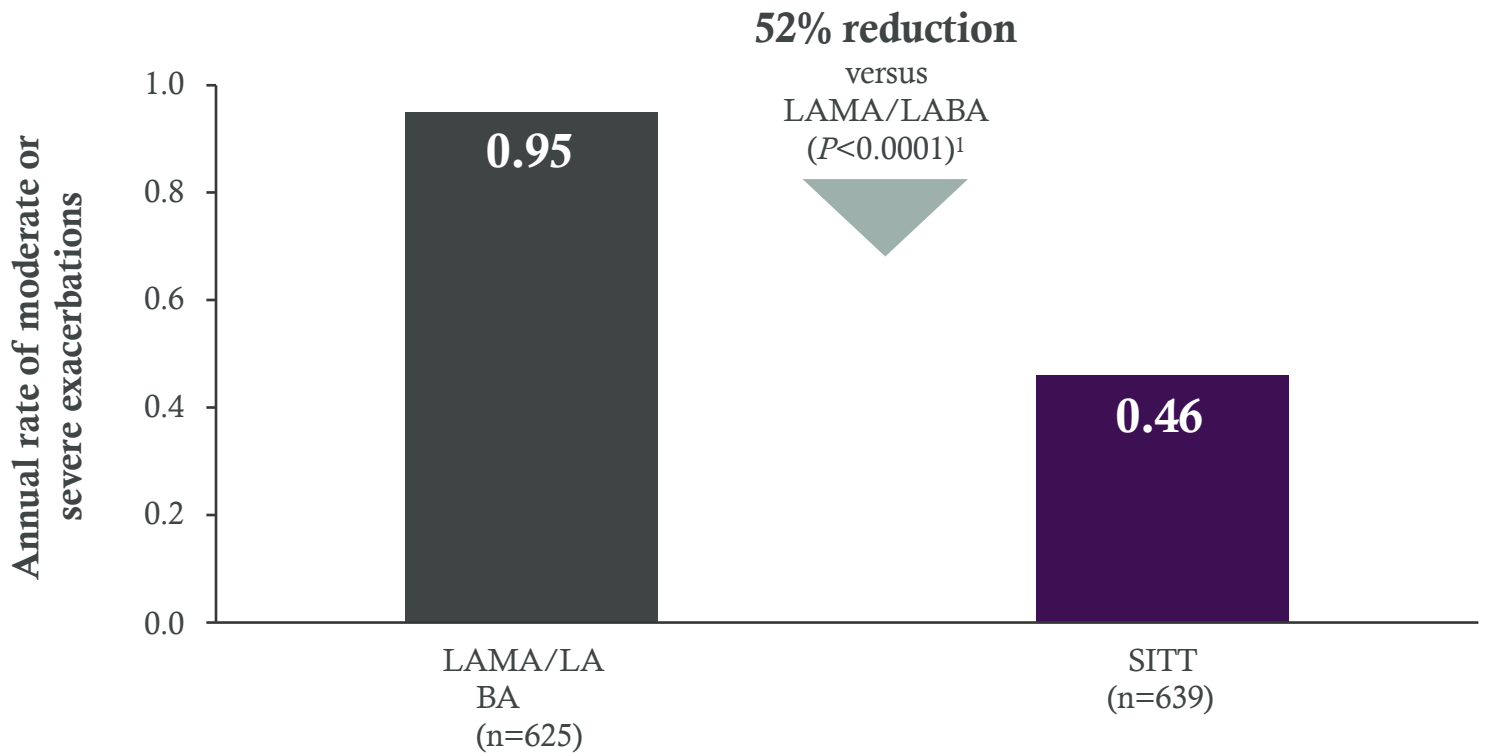
- **Rate of moderate or severe COPD exacerbations over 24 weeks**
- Change from baseline in TDI focal score (units)[a]
- Change from baseline in SGRQ total score (units)[a]
- Change from baseline in average daily use of rescue salbutamol[a]

[a]Over 24 weeks; [b]Not representative of all the secondary endpoints.

$AUC_{0-4}$, area under the curve from 0-4 hours; $FEV_1$, forced expiratory volume in 1 second; SGRQ, St. George's Respiratory Questionnaire; TDI, Transition Dyspnea Index.

1. Ferguson GT, et al. *Lancet Respir Med*. 2018;6(10):747–758.

# BUD/GLY/FORM Prevented Moderate or Severe Exacerbations vs LAMA/LABA Even in Patients Not Reporting Exacerbations in the Last Year[1]




**NNT=3**

Prevent **1** moderate/severe exacerbation for every **3** patients treated for 1 year with **BUD/GLY/FORM** versus LAMA/LABA (95% CI: 2-4)[1,2]

Note: although the definition and classification of exacerbations have been updated in the 2023 GOLD Report, exacerbation severity refers to an earlier definition and classification to align with the published data; KRONOS co-primary endpoints: change from baseline in morning pre-dose trough $FEV_1$ over 24 weeks vs LAMA/LABA pMDI (22 mL; *P*=0.0139); $FEV_1$ $AUC_{0-4}$ vs ICS/LABA pMDI (104 mL; *P*<0.0001) and ICS/LABA DPI (91 mL; *P*<0.0001).[1]

$AUC_{0-4}$, area under the curve from 0 to 4 h; BUD, budesonide; CI, confidence interval; DPI, dry powder inhaler; $FEV_1$, forced expiratory volume in 1 second; FORM, formoterol fumarate dihydrate; GOLD, Global Initiative for Chronic Obstructive Lung Disease; GLY, glycopyrronium; ICS, inhaled corticosteroid; ICS/LABA, budesonide/formoterol fumarate dihydrate; LABA, long-acting beta-2 agonist; LAMA, long-acting muscarinic antagonist; LAMA/LABA, glycopyrronium/formoterol fumarate dihydrate; NNT, number needed to treat; pMDI, pressurized metered-dose inhaler; SITT, single-inhaler triple therapy.

1. Ferguson GT, et al. *Lancet Respir Med*. 2018;6(10):747–758; 2. Martinez FJ, et al. *Int J Chron Obstruct Pulmon Dis.* 2021;16:179–189.

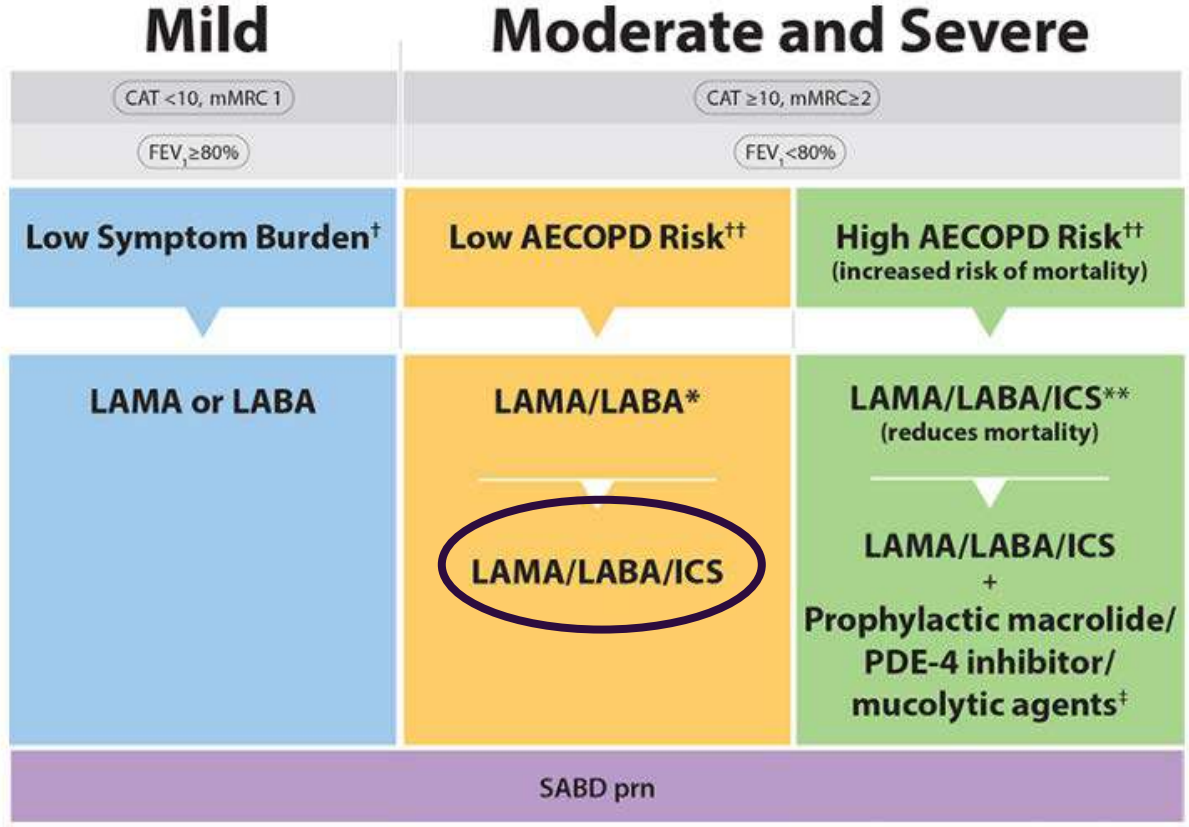
# What if he is still dyspneic?

First make sure there is not another reason:

Anemia

CV disease, angina, heart failure

Fitness?



# Felix's Case, years later..

Felix is a 61-year-old male with moderate-to-severe COPD (diagnosed 6 years ago), HTN, T2DM, and dyslipidemia.

6 months ago, he was stepped up to dual therapy due to continued dyspnea and a moderate exacerbation.

**Treatment regimen**

- LABA/LAMA of your choice
- Lisinopril, 30 mg once a day
- Atorvastatin, 40 mg once a day
- Metformin, 500 mg 3 times a day with meals
- Salbutamol 100 mcg PRN

**COPD-specific test results**

- $FEV_1$/FVC: 57%
- $FEV_1$: 45% of predicted

He had a viral infection a few months ago and 'just isn't the same'

He is not able to do the same activities as a few months ago and that he has been using his reliever more often. Gets SOB walking with spouse

(mMRC 2)


DPI, dry powdered inhaler; $FEV_1$, forced expiratory volume in 1 second; FVC, forced vital capacity; HTN, hypertension; prn, as needed; PRN, as needed; T2DM, type 2 diabetes mellitus.

# Acute Exacerbations of COPD (AECOPD)

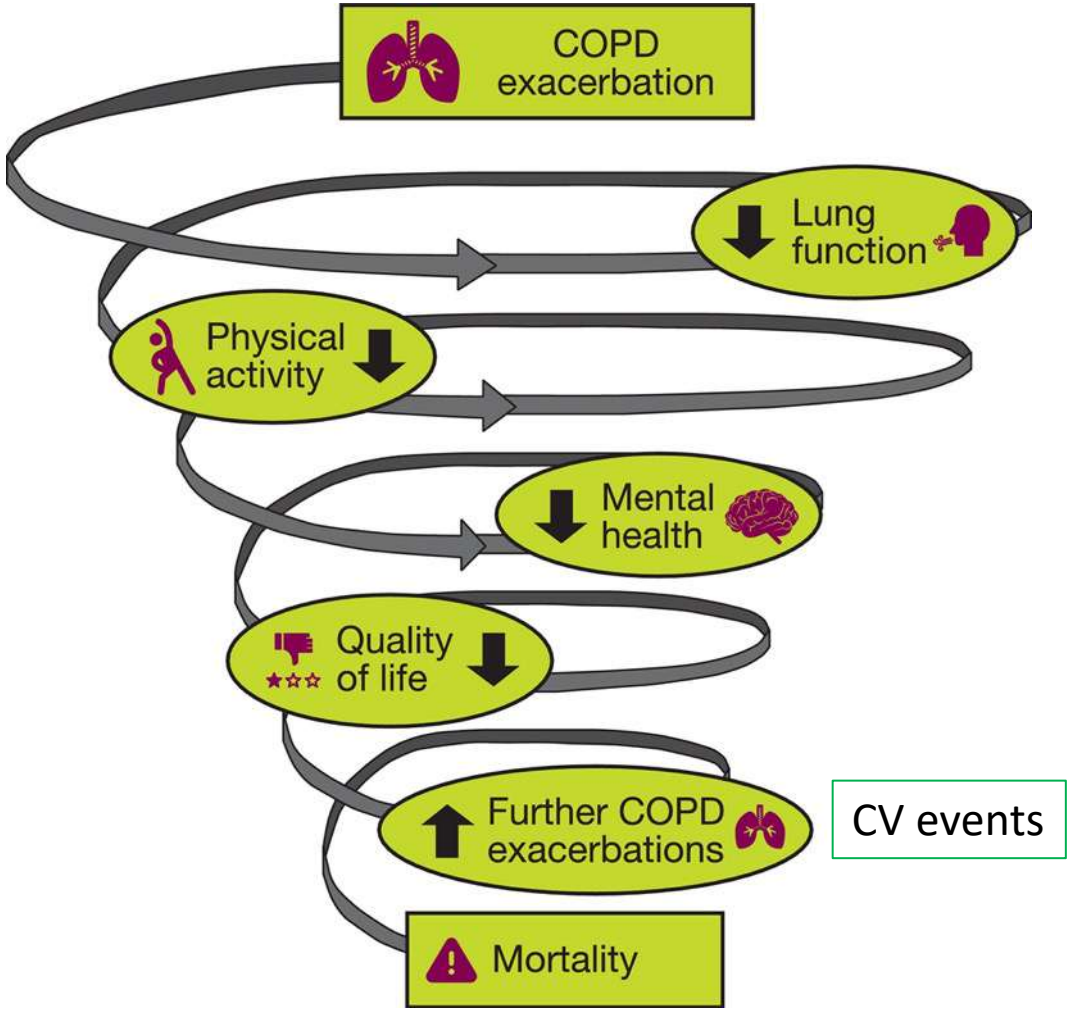
A COPD exacerbation is defined as:

- A worsening of respiratory symptoms beyond the normal day to day variability and
- May require use of antibiotics and systemic corticosteroids and/or healthcare services
- Second leading cause of Hospital admissions in Canada

| Mild | Moderate | Severe |
|---|---|---|
| Worsening or new respiratory symptoms without a change in prescribed medicines | Requires prescription of antibiotic and/or oral corticosteroid | Requires a hospital admission or Emergency Department visit |

Bourbeau J et al. CTS position statement: Pharmacotherapy in patients with COPD - An update. Canadian Journal of Respiratory, Critical Care, and Sleep Medicine 1(4): 222-241; Oct 2019

# Negative Impact of Exacerbations

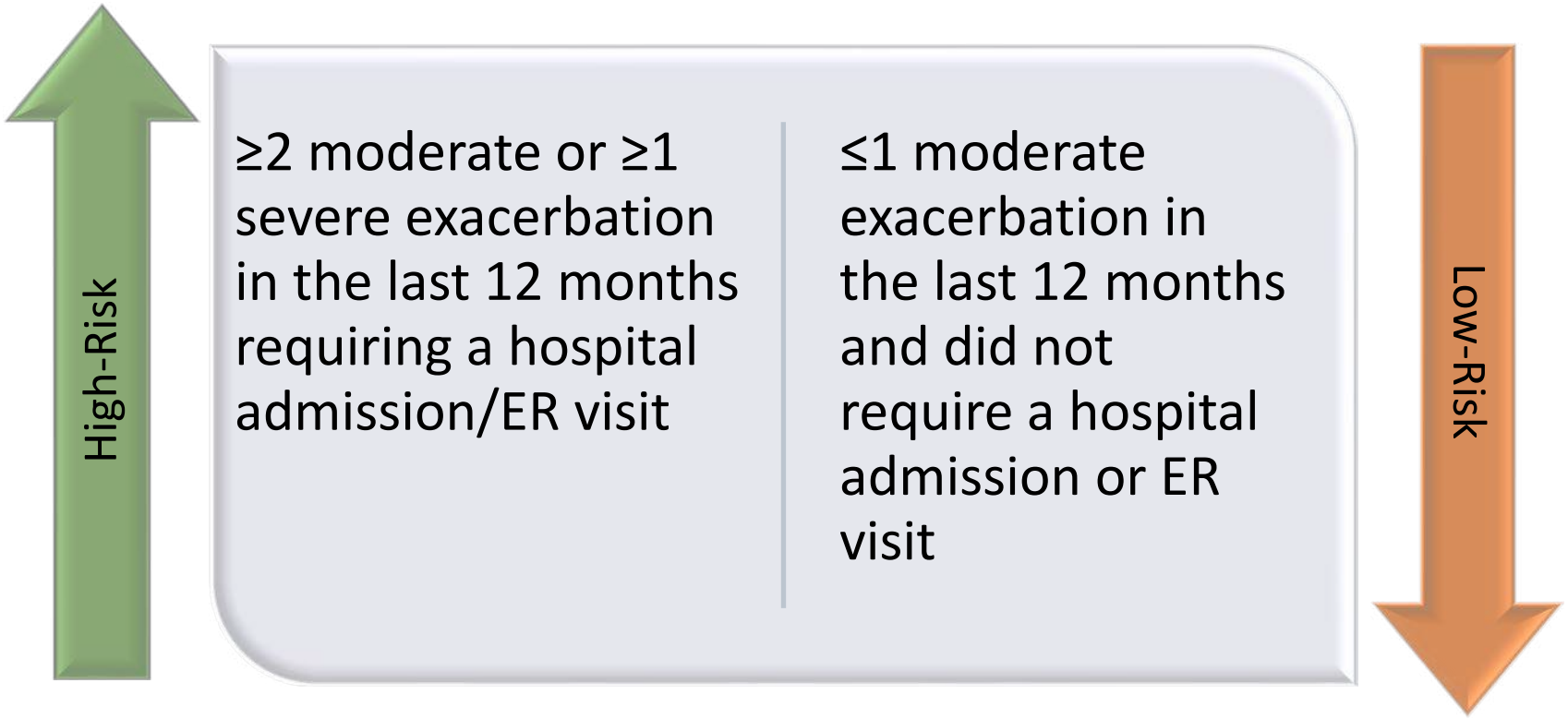



- Exacerbations have negative consequences:
  - Decreased lung function
  - Increased risk of future exacerbations
  - Decreased health-related QoL
  - Impaired activity
  - Increased risk of depression and anxiety
  - Moderate to severe exacerbations increased mortality risk

Hurst J et al. Eur J Int Med 2020;73(March):1-6.

# Who is considered a ‘Frequent Exacerbator’ Phenotype?

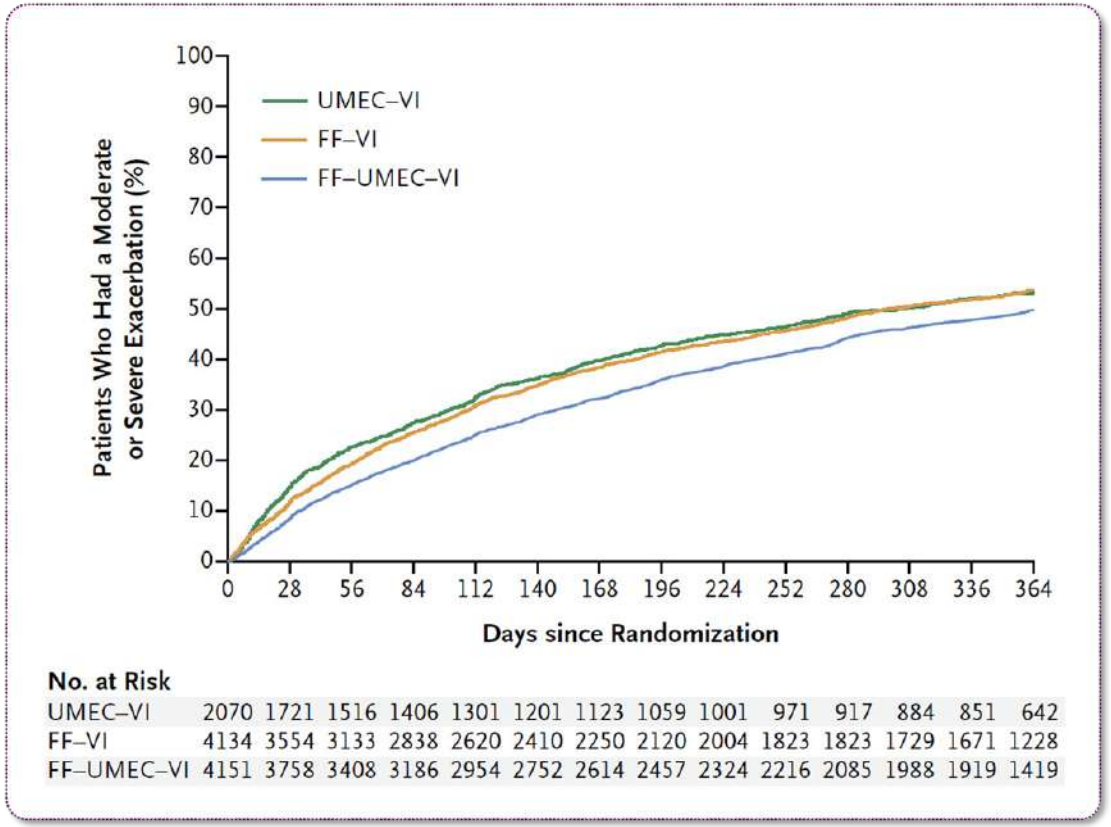
- CTS Guidelines classify patients at high- or low-risk of future exacerbations




Bourbeau J et al. CTS position statement: Pharmacotherapy in patients with COPD - An update. Canadian Journal of Respiratory, Critical Care, and Sleep Medicine 1(4): 222-241; Oct 2019

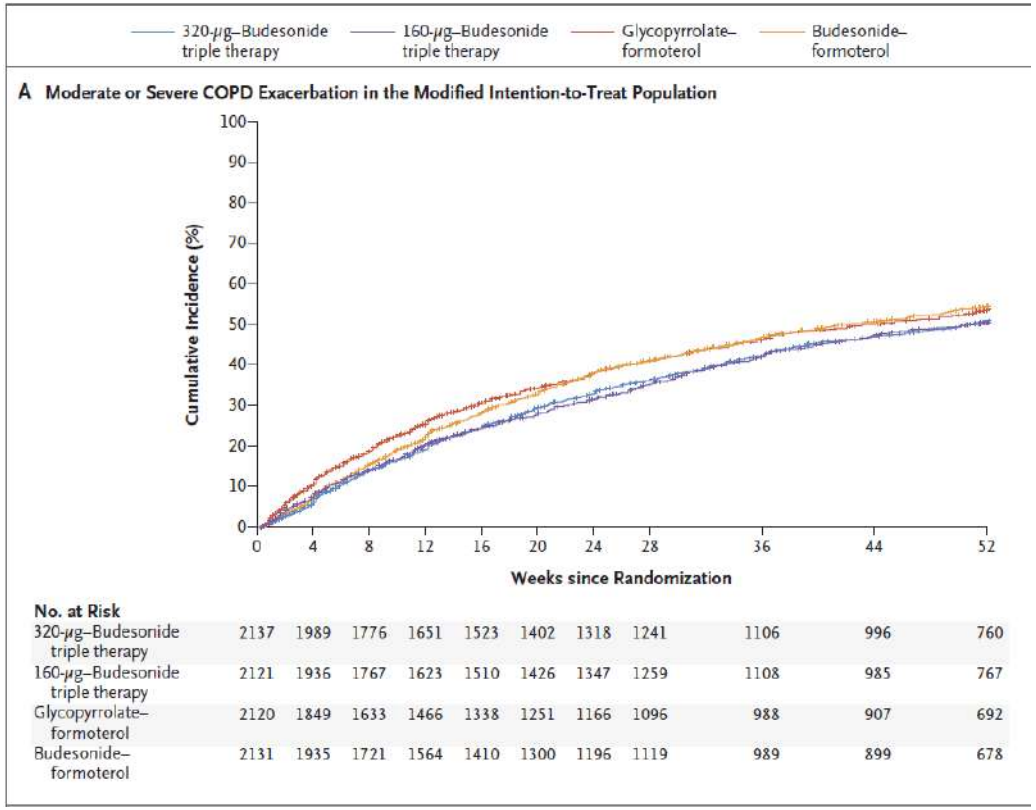
# Triple therapy (ICS/LABA/LAMA) reduces exacerbations vs duals

**IMPACT**




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

**ETHOS**



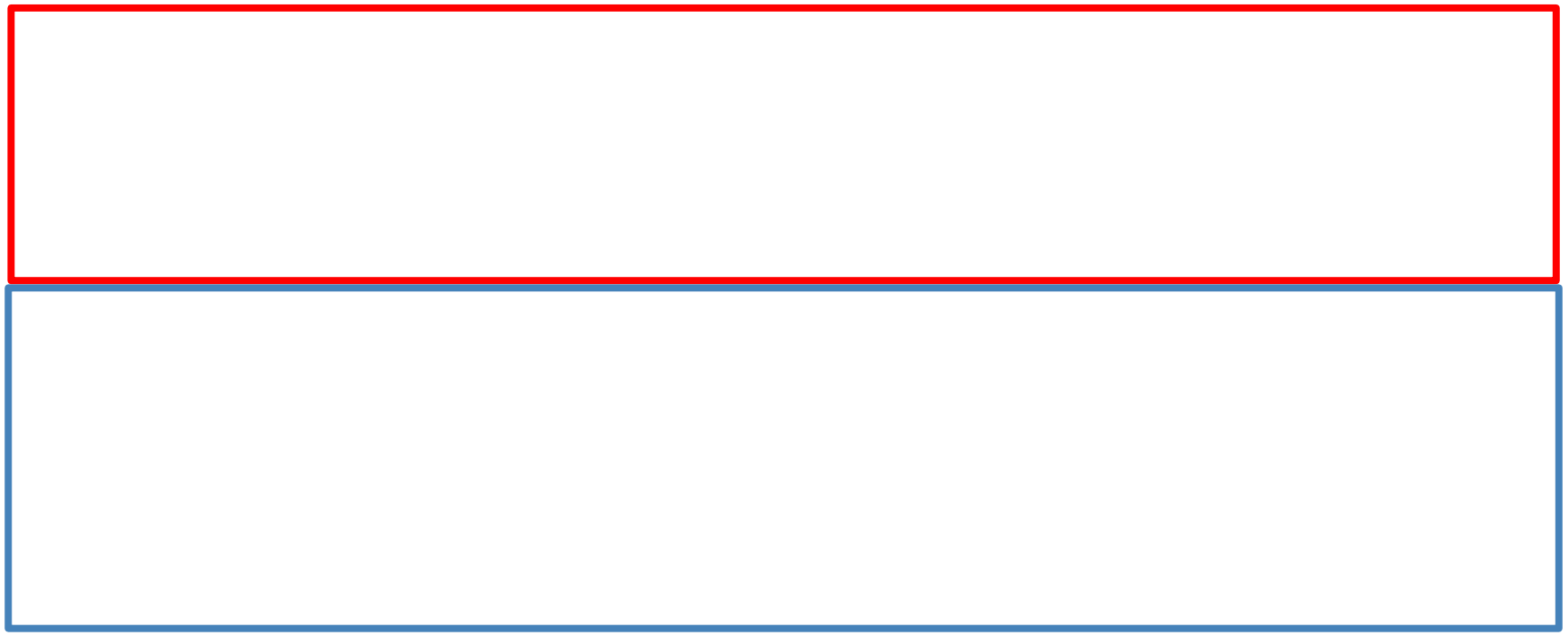

Rabe KF, N Engl J Med. 2020 Jul 2;383(1):35-48.

# But, need to balance with the side effects of ICS in COPD

| | Randomised controlled trial | Observational study | Systematic review |
|---|---|---|---|
| Pneumonia | X | X | X |
| Tuberculosis | | X | |
| Bone fracture | (no effect on fracture risk) | X | X |
| Skin thinning/ easy bruising | X | | |
| Cataract | | X | |
| Diabetes | | X | |
| Oropharyngeal candidiasis | X | X | X |

Price D. Prim Care Respir J 2013; 22: 92-100.

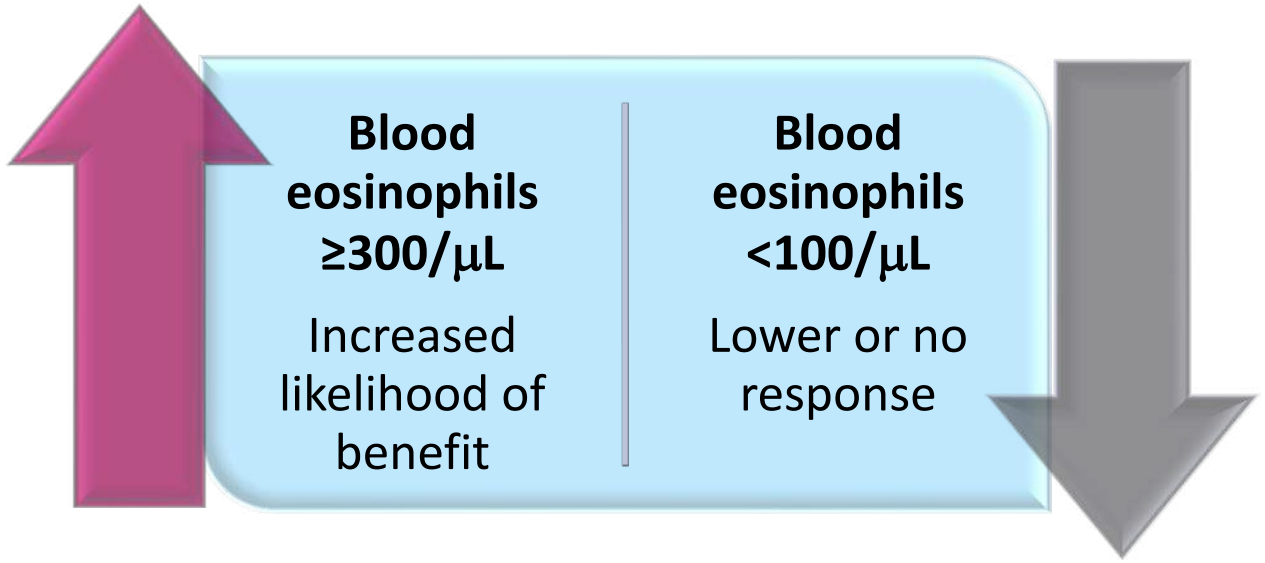
# What about Inhaled Corticosteroids, what is their place?



# Peripheral Blood Eosinophils in COPD

- Blood eosinophil ≥300/μL in patients with previous AECOPD may be useful to predict a favorable response to ICS combination inhaler

**Likelihood of reduction of exacerbation with ICS-containing regimens**



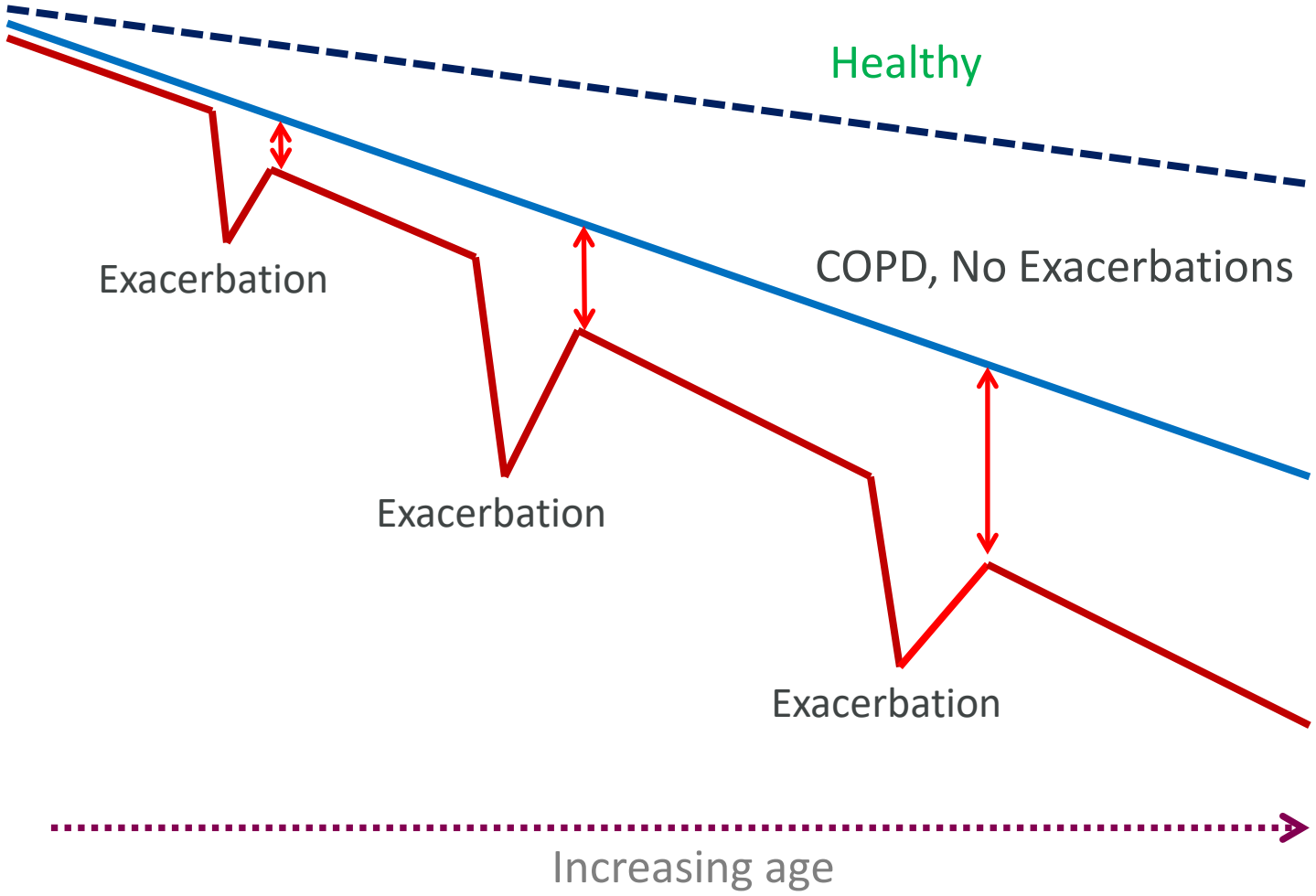

Ordered Items
CBC With Differential/Platelet; Blood Drawing

| TESTS | RESULT | FLAG | UNITS | REFERENCE INTERVAL | LAB |
|---|---|---|---|---|---|
| **CBC With Differential/Platelet** | | | | | |
| WBC | 6.6 | | x10E3/uL | 3.4 - 10.8 | 01 |
| **RBC** | **4.07** | **Low** | x10E6/uL | 4.14 - 5.80 | 01 |
| Hemoglobin | 15.6 | | g/dL | 13.0 - 17.7 | 01 |
| Hematocrit | 45.5 | | % | 37.5 - 51.0 | 01 |
| **MCV** | **112** | **High** | fL | 79 - 97 | 01 |
| **MCH** | **38.3** | **High** | pg | 26.6 - 33.0 | 01 |
| MCHC | 34.3 | | g/dL | 31.5 - 35.7 | 01 |
| RDW | 14.2 | | % | 12.3 - 15.4 | 01 |
| Platelets | 256 | | x10E3/uL | 150 - 379 | 01 |
| Neutrophils | 57 | | % | Not Estab. | 01 |
| Lymphs | 32 | | % | Not Estab. | 01 |
| Monocytes | 8 | | % | Not Estab. | 01 |
| Eos | 2 | | % | Not Estab. | 01 |
| Basos | 1 | | % | Not Estab. | 01 |
| Neutrophils (Absolute) | 3.7 | | x10E3/uL | 1.4 - 7.0 | 01 |
| Lymphs (Absolute) | 2.1 | | x10E3/uL | 0.7 - 3.1 | 01 |
| Monocytes(Absolute) | 0.5 | | x10E3/uL | 0.1 - 0.9 | 01 |
| Eos (Absolute) | 0.1 | | x10E3/uL | 0.0 - 0.4 | 01 |
| Baso (Absolute) | 0.0 | | x10E3/uL | 0.0 - 0.2 | 01 |
| Immature Granulocytes | 0 | | % | Not Estab. | 01 |
| Immature Grans (Abs) | 0.0 | | x10E3/uL | 0.0 - 0.1 | 01 |

AECOPD – Acute exacerbation chronic obstructive pulmonary disease

Bourbeau J et al. CTS position statement: Pharmacotherapy in patients with COPD - An update. Canadian Journal of Respiratory, Critical Care, and Sleep Medicine 1(4): 222-241; Oct 2019

# Impact of AE-COPD

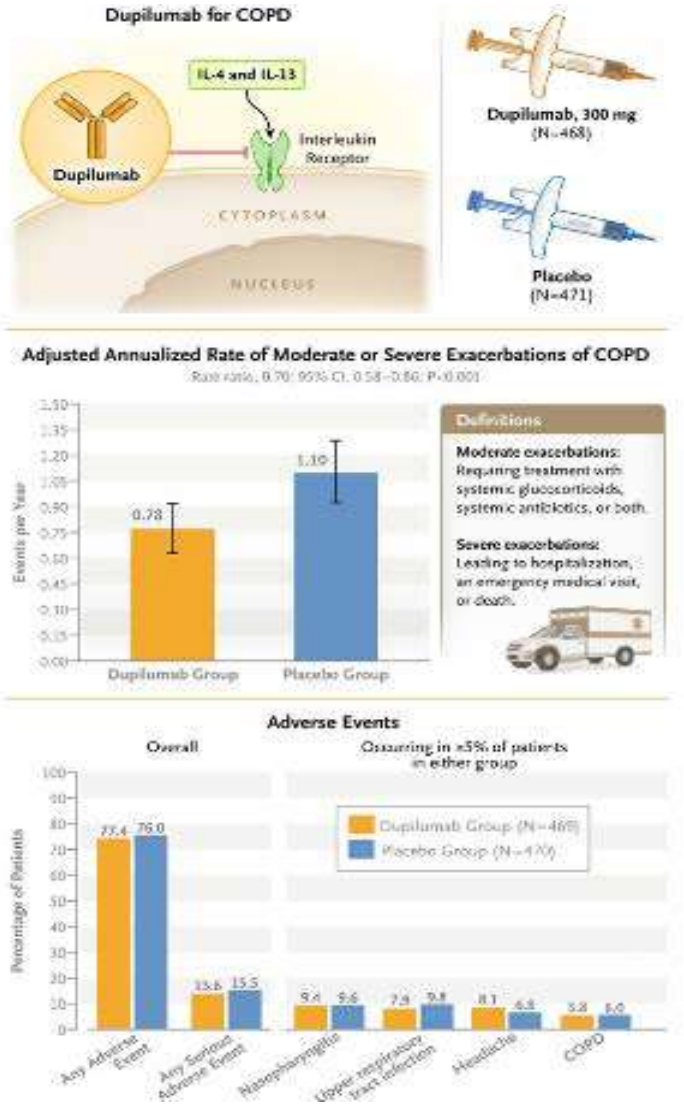



In-hospital mortality: **2.5% to 25%**
Those who survive: **25% - 55% will be re-admitted**
Die within 1year: **25% to 50%**

- Greater decline in lung function – rapid progression of the disease
- Increases symptoms and worsens quality of life
- Increases mortality
- Increases economic costs

# What is New in COPD Management? Biologics for COPD Exacerbators

The NEW ENGLAND JOURNAL of MEDICINE




## Dupilumab for COPD with Type 2 Inflammation Indicated by Eosinophil Counts

**Authors**: Surya P. Bhatt, M.D., M.S.P.H., Klaus F. Rabe, M.D., Ph.D., Nicola A. Hanania, M.D., Claus F. Vogelmeier, M.D., Jeremy Cole, M.D., Mona Bafadhel, M.D., Ph.D., Stephanie A. Christenson, M.D., +15, for the BOREAS

- **Conclusions:** Among patients with COPD who had type 2 inflammation as indicated by elevated blood eosinophil counts (≥300) and had the chronic bronchitis phenotype, those who received dupilumab had:
- fewer exacerbations,
- better lung function
- Better quality of life,
- less severe respiratory symptoms than those who received placebo.

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

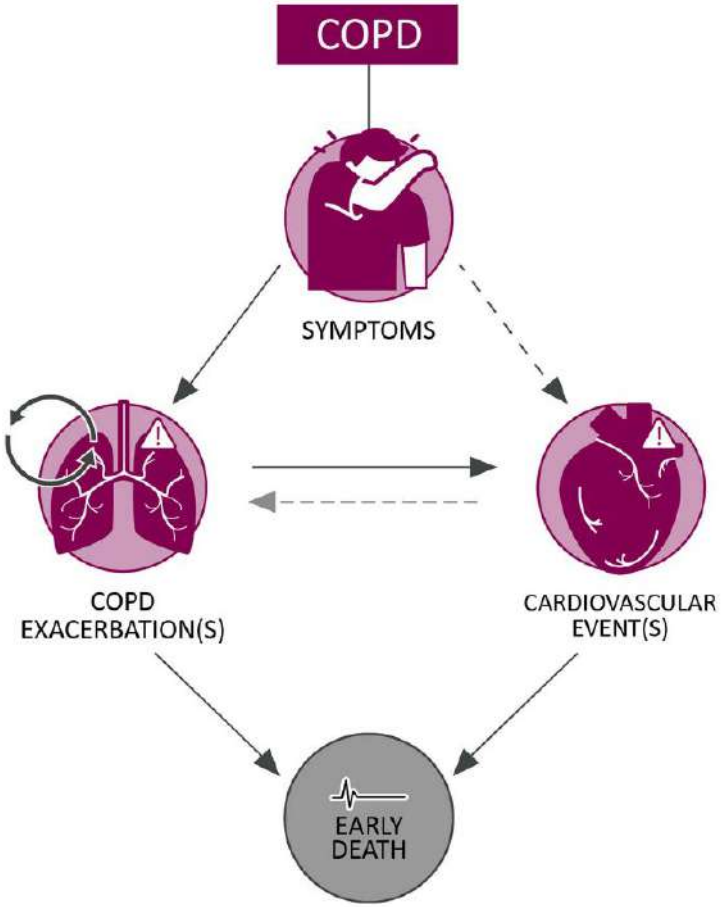
# Cardiopulmonary Risk

Adv Ther (2024) 41:2151–2167
https://doi.org/10.1007/s12325-024-02855-4

REVIEW

**Implications of Cardiopulmonary Risk for the Management of COPD: A Narrative Review**

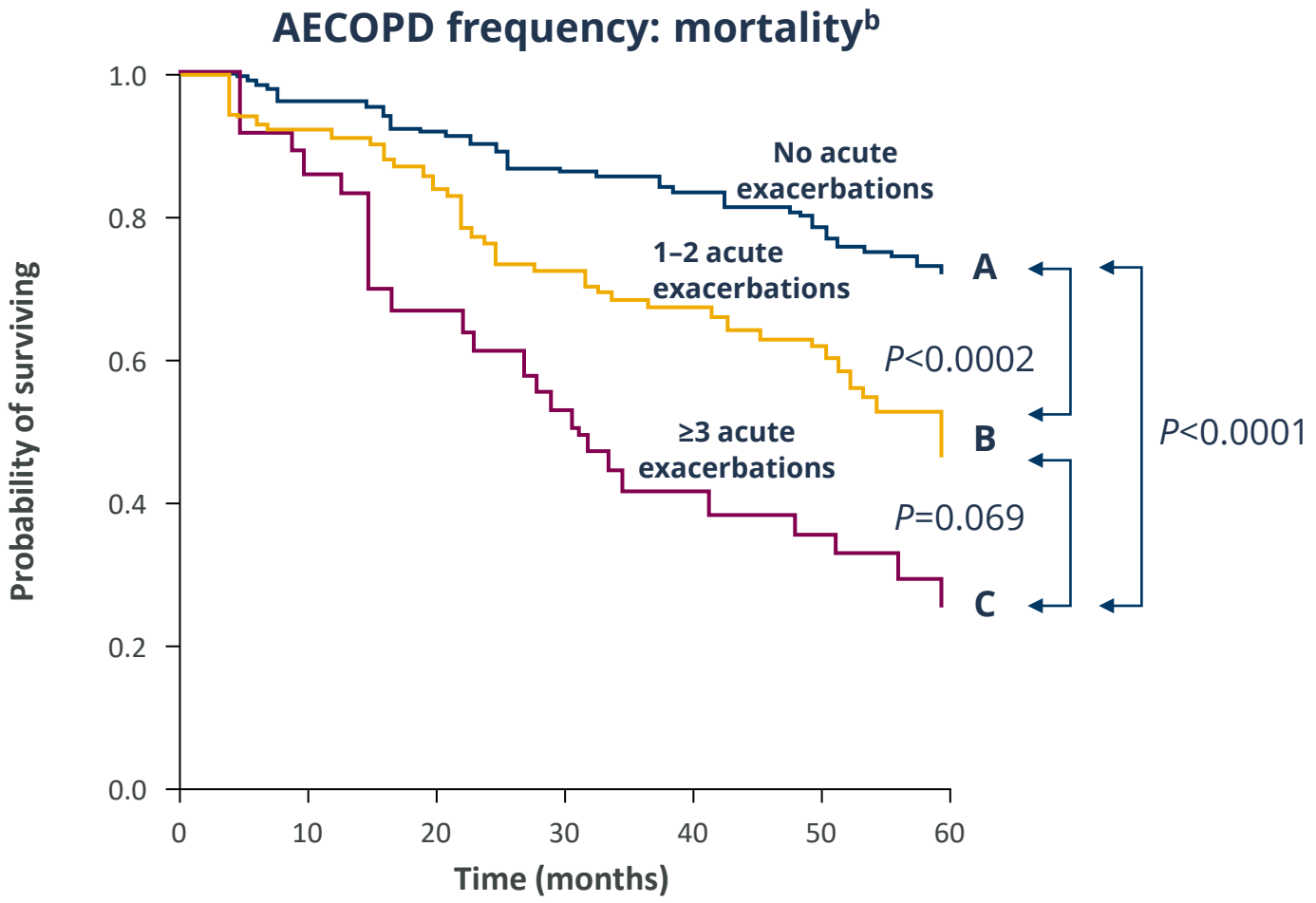
Dave Singh · MeiLan K. Han · Nathaniel M. Hawkins · John R. Hurst · Janwillem W. H. Kocks · Neil Skolnik · Daiana Stolz · Jad El Khoury · Chris P. Gale




Cardiopulmonary Risk:
'The risk of serious respiratory and/or cardiovascular events in patients with COPD. These include, but are not limited to, COPD exacerbations, myocardial infarction, stroke, heart failure decompensation, arrhythmia and death due to any of these events.'

Singh D, Han MK, Hawkins NM, Hurst JR, Kocks JWH, Skolnik N, Stolz D, El Khoury J, Gale CP. Implications of Cardiopulmonary Risk for the Management of COPD: A Narrative Review. Adv Ther. 2024 Jun;41(6):2151-2167. doi: 10.1007/s12325-024-02855-4. Epub 2024 Apr 25. PMID: 38664329; PMCID: PMC11133105.

# Severe Acute[a] Exacerbations of COPD Have an Independent Negative Impact on Patient Prognosis




Patients with **≥3 acute exacerbations** had the highest mortality with a **4.3-times greater risk of death** vs those with no exacerbations

[a]An acute exacerbation of COPD was defined as any sustained increase in respiratory symptomatology compared with the baseline situation requiring modification of regular medication and hospital treatment; [b]Kaplan-Meier survival curve by frequency of exacerbations in patients with COPD.

AECOPD, acute exacerbation of COPD.

# Cardiopulmonary Deaths Are a Common Cause of Mortality in Patients With COPD

Across five studies in patients with COPD,[1,a] up to **39%** of deaths were due to **CV causes**[2]


| n | EUROSCOP[2] | ISOLDE[3] | LHS III[4] | TORCH[5] | UPLIFT[1,6] |
|---|---|---|---|---|---|
| Study size | 1277 | 751 | 5887 | 6184 | 5993 |
| Total deaths | 18 | 68 | 731 | 911 | 941 |
| CV-related deaths | 7 | 22 | 163 | 237[c] | 151[c] |

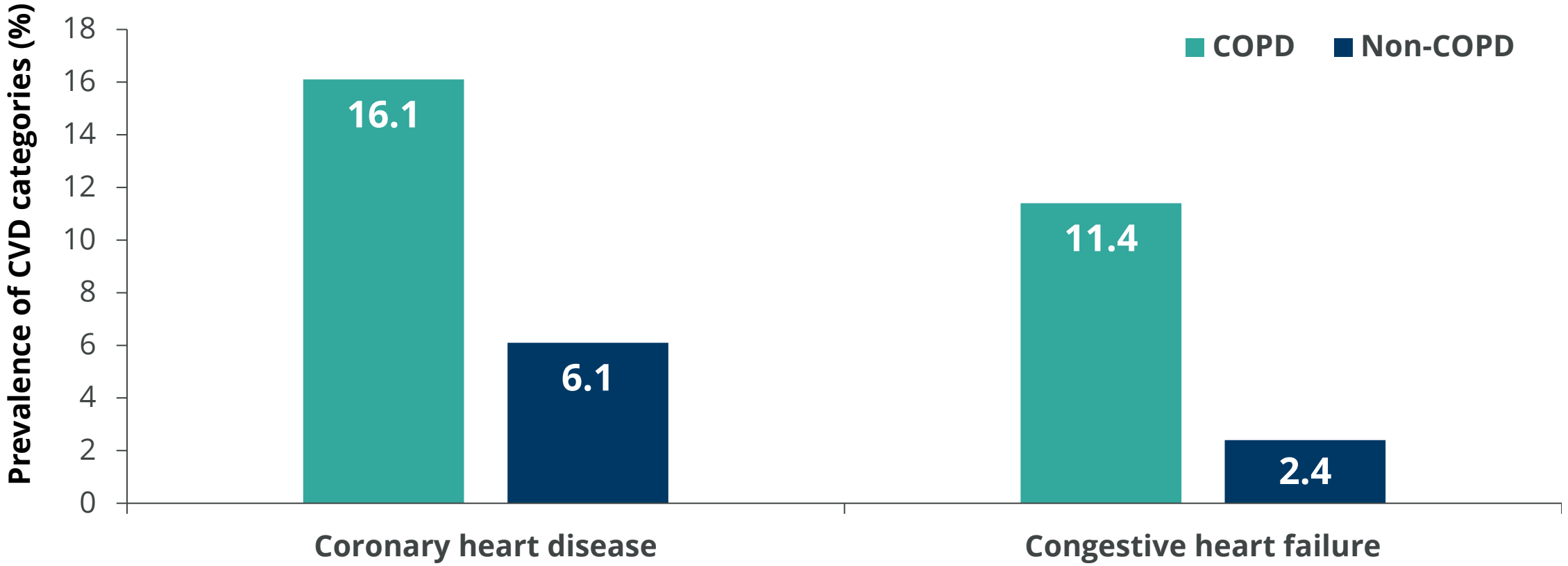
[a]Trial participants were followed for 3 to ~14 years[1]; [b]Data from five large COPD trials; percentage of total deaths from CV causes was calculated based on the percentages of death for each cause and total number of deaths in each study; [c]Number of CV-related deaths was calculated based on the percentage of CV-related deaths and total number of deaths in the study.

CV, cardiovascular; EUROSCOP, European Respiratory Society Study on Chronic Obstructive Pulmonary Disease; ISOLDE, Inhaled Steroids in Obstructive Lung Disease in Europe; LHS, Lung Health Study; TORCH, Towards a Revolution in COPD Health; UPLIFT, Understanding Potential Long-Term Impacts on Function with Tiotropium.

1. Berry CE, Wise RA. *COPD*. 2010;7(5):375–382; 2. Pauwels RA, et al. *N Engl J Med*. 1999;340(25):1948–1953; 3. Burge PS, et al. *BMJ*. 2000;320(7245):1297–1303; 4. Anthonisen NR, et al. *Ann Intern Med*. 2005;142(4):233–239; 5. McGarvey LP, et al. *Thorax*. 2007;62(5):411–415; 6. Tashkin DP, et al. *N Engl J Med*. 2008;359(15):1543–1554.

# Patients With COPD Are at Elevated Risk of Having CV Conditions[1–4]

Prevalence of **CVD categories in COPD** (n=958) **versus non-COPD** (n=17,384) populations[3,a,b]




[a]Data from the adult file of the 2002 National Health Interview Survey; [b]$P<0.0001$ for all variables (Wald chi-squared test).

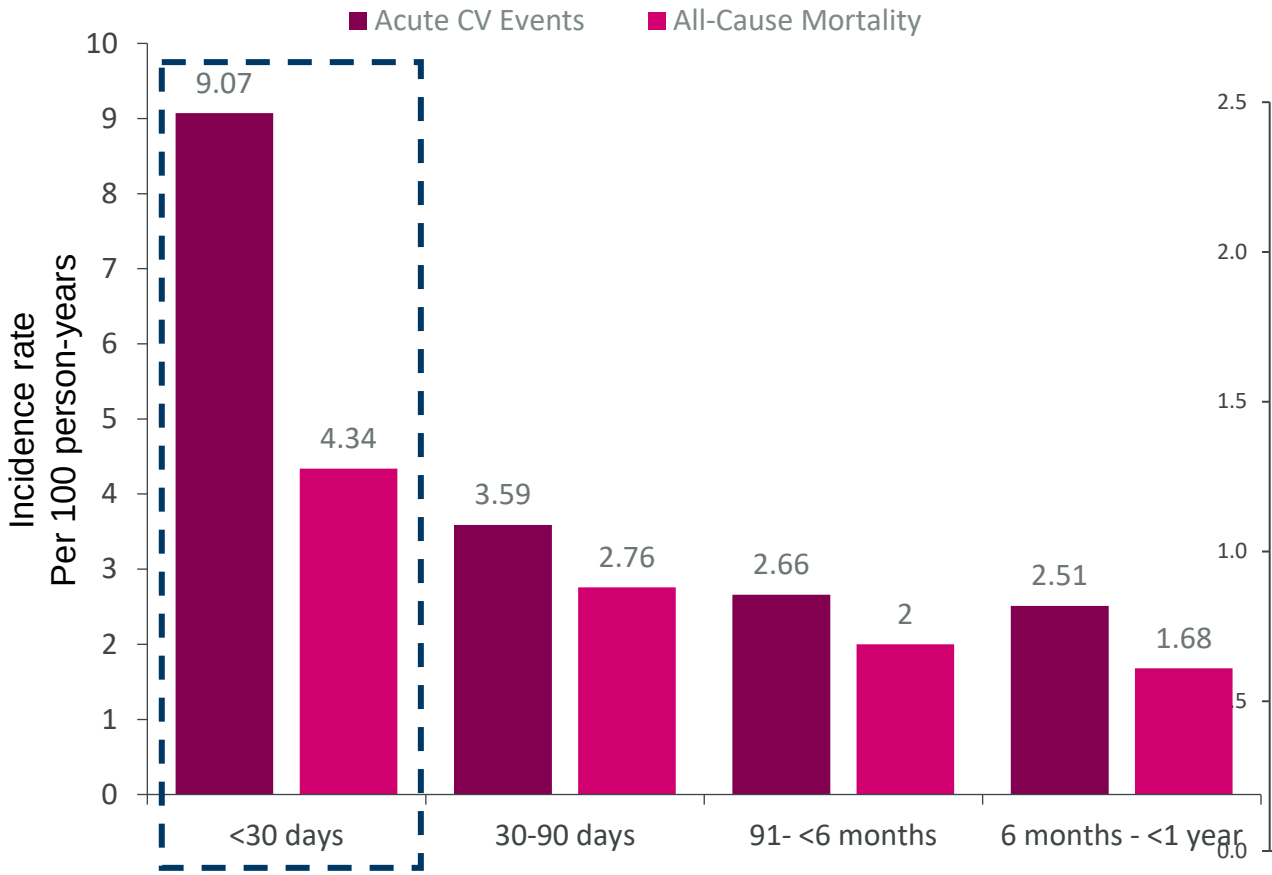
CV, cardiovascular; CVD, cardiovascular disease.

1. Müllerova H, et al. *Chest.* 2013;144(4):1163–1178; 2. Finkelstein J, et al. *Int J Chron Obstruct Pulmon Dis.* 2009;4:337–349; 3. Chen W, et al. *Lancet Respir Med.* 2015;3(8):631–639; 4. Williams MC, et al. *Thorax.* 2014;69(8):718–723.

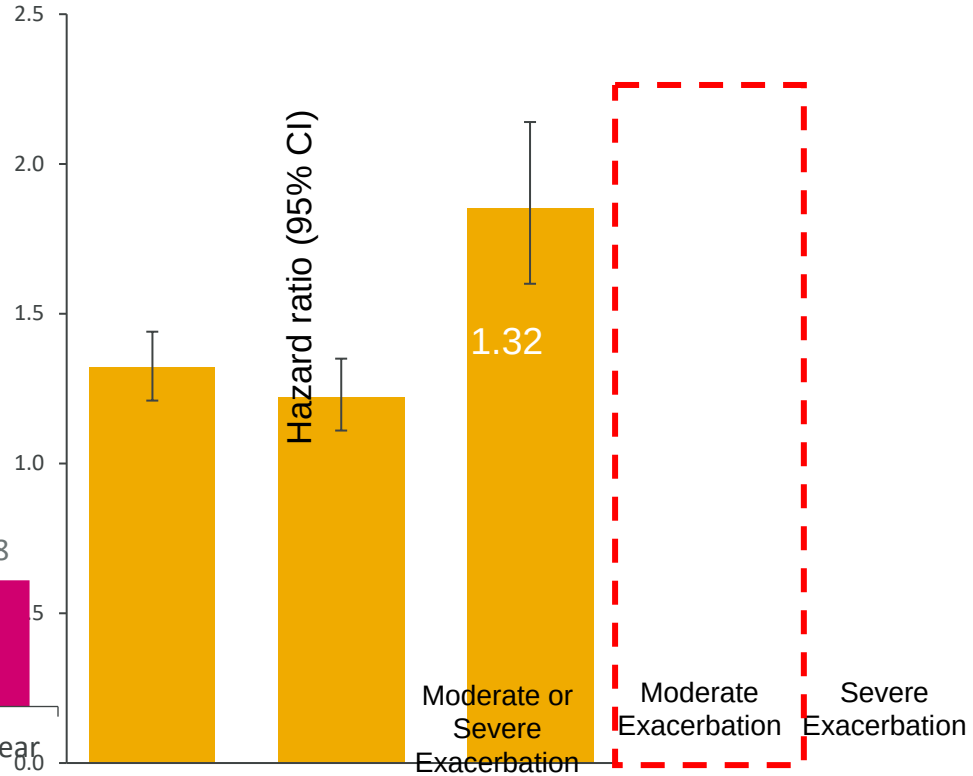
# Cardiopulmonary and All-Cause Mortality Risk is Highest Within 30 Days of a COPD Exacerbation (EXACOS-CV US)

EXACOS-CV

## Risk of an Acute CV Event[a] and All-Cause Mortality is Highest within 30 Days of a COPD Exacerbation, but persists…




## Even a Moderate Exacerbation Increases the Risk of a CV Event within 30 Days



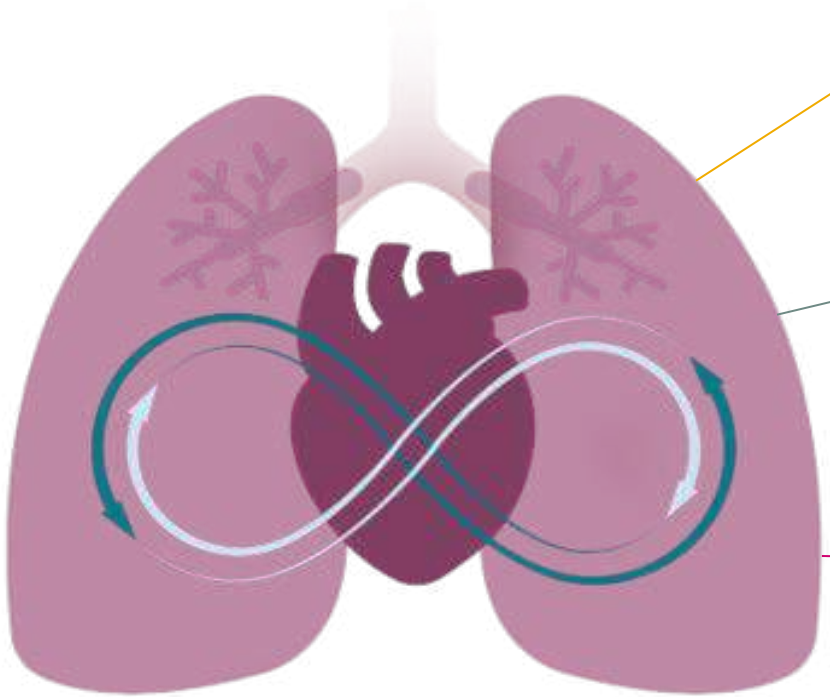

A retrospective cohort study of 355,978 patients with COPD between January 1, 2012 and December 31, 2019 using the US healthcare claims database that compared the incidence of acute CV events following an AECOPD to incidence in the absence of an AECOPD, by time since AECOPD and severity of AECOPD. Acute CV events were hospitalizations for myocardial infarction, ischemic stroke, unstable angina, acute heart failure, pulmonary embolism, cardiac arrhythmias, CV-related death, and cardiac arrest.



Pollack M et al., CHEST. 2023: P5264. Daniels K et al. *Am J Respir Crit Care Med.* 2023;207:A3331.

# How May COPD Exacerbations Elevate Patients' Cardiopulmonary Risks?

**Exacerbations** amplify three drivers of cardiopulmonary risk in patients with COPD, contributing to an increased risk of heart and lung events[1–3]

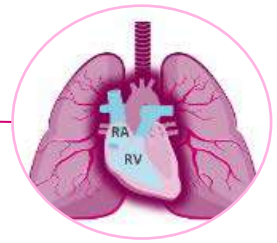


### Inflammation[2]

COPD lung inflammation **drives systemic inflammation**, promoting atherosclerotic damage in the heart and vasculature

### Hyperinflation[4,5]

Hyperinflation compresses the heart, **reducing cardiac output**[5]




### Hypoxemia[3]

Hypoxemia can lead to pulmonary hypertension and **right heart failure**

RA, right atrium; RV, right ventricle.

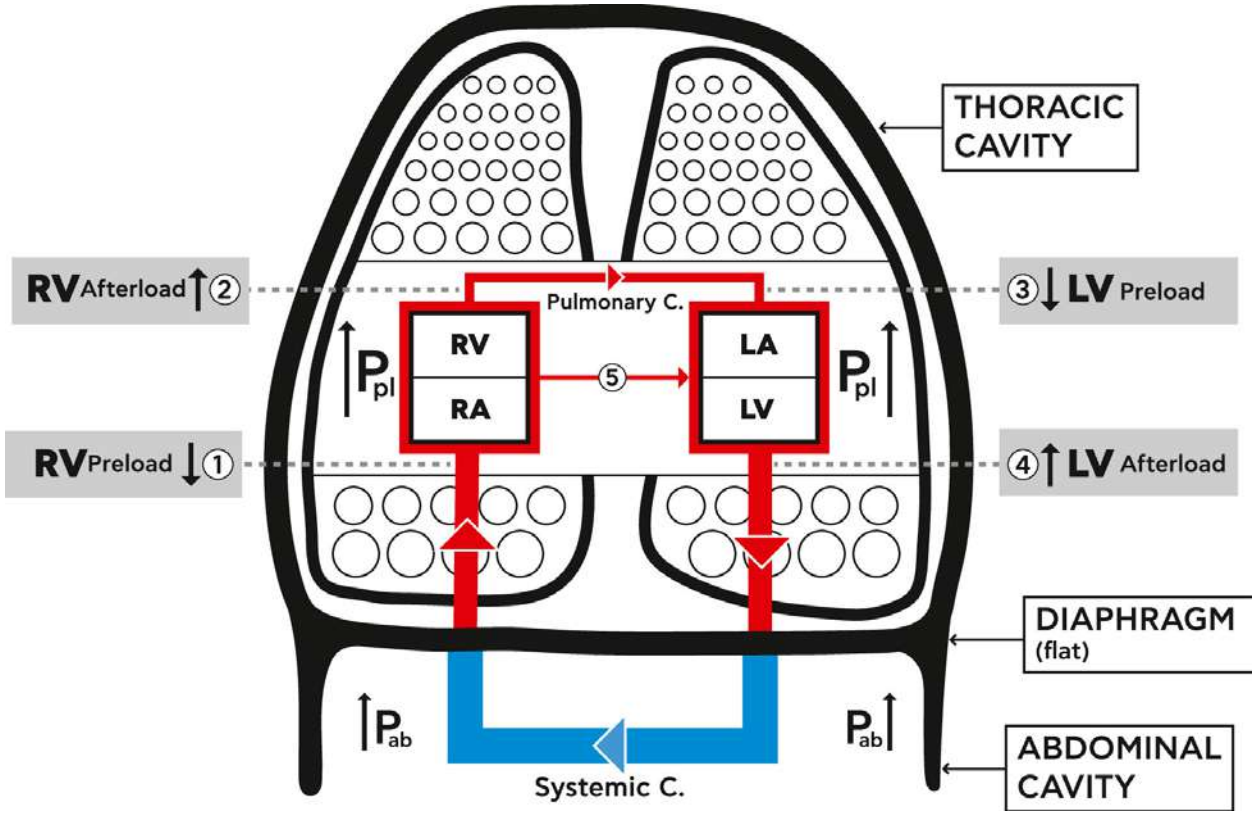
1. Verhoeff K and Mitchell JR. *Adv Physiol Educ*. 2017;41:348–353; 2. Aisanov Z et al. *J Thorac Dis*. 2020;12:2791–2802; 3. Kent BD et al. *Int J Chron Obstruct Pulmon Dis.* 2011;6:199–208; 4. O'Donnell D et al. *COPD Res Pract*. 2015;1:1–12; 5. Solidoro P et al. *Front Med*. 2022;9:816843:1–9.

PULMONOLOGY

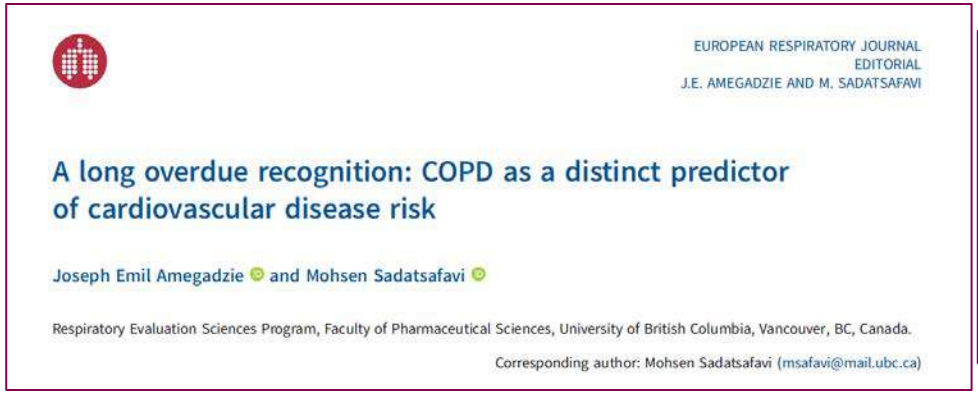
# By deflating the lungs pulmonologists help the cardiologists. A literature review

**Lung hyperinflation affects the function of the CVS by**

- reducing venous blood return
- increasing pulmonary vascular resistance, and
- compressing the intra-thoracic cardiovascular parts




Siafakas N, Trachalaki A. By deflating the lungs pulmonologists help the cardiologists. A literature review. Pulmonology. 2023 Dec;29 Suppl 4:S86-S91. doi: 10.1016/j.pulmoe.2023.02.011. Epub 2023 Apr 6. PMID: 37031001.



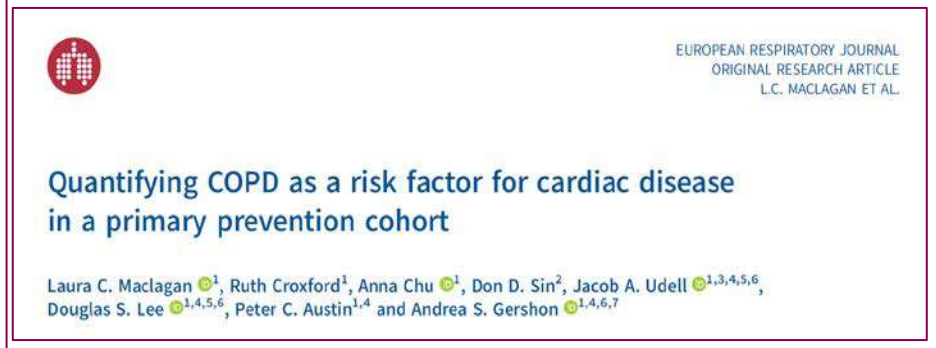
EUROPEAN RESPIRATORY JOURNAL
EDITORIAL
J.E. AMEGADZIE AND M. SADATSAFAVI

A long overdue recognition: COPD as a distinct predictor of cardiovascular disease risk

Joseph Emil Amegadzie and Mohsen Sadatsafavi

Respiratory Evaluation Sciences Program, Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada.

Corresponding author: Mohsen Sadatsafavi (msafavi@mail.ubc.ca)

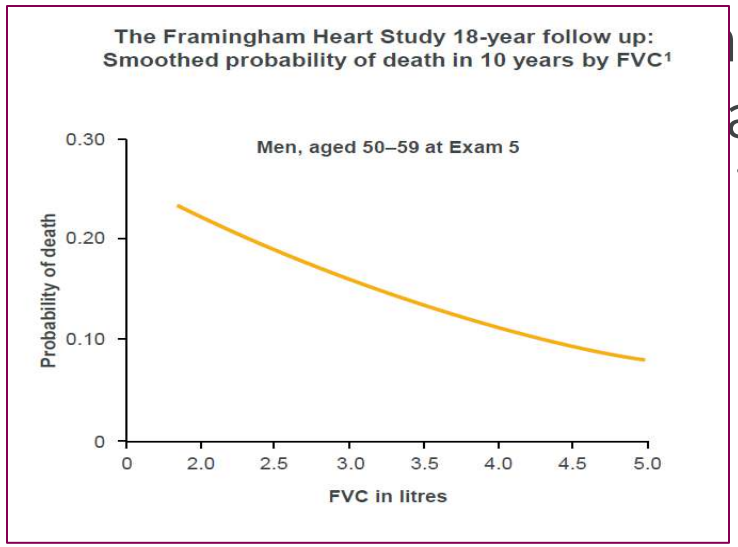


EUROPEAN RESPIRATORY JOURNAL
ORIGINAL RESEARCH ARTICLE
L.C. MACLAGAN ET AL.

Quantifying COPD as a risk factor for cardiac disease in a primary prevention cohort

Laura C. Maclagan[1], Ruth Croxford[1], Anna Chu[1], Don D. Sin[2], Jacob A. Udell[1,3,4,5,6], Douglas S. Lee[1,4,5,6], Peter C. Austin[1,4] and Andrea S. Gershon[1,4,6,7]

- In a large real-world population without CVD, people with physician-diagnosed COPD were 25% more likely to have a major CVD event, after adjustment for CVD risk and other factors.




ble to the rate in people
alls for more aggressive CVD
in the COPD population.

Ashley F, et al. Ann Intern Med 1975;82:739-745.

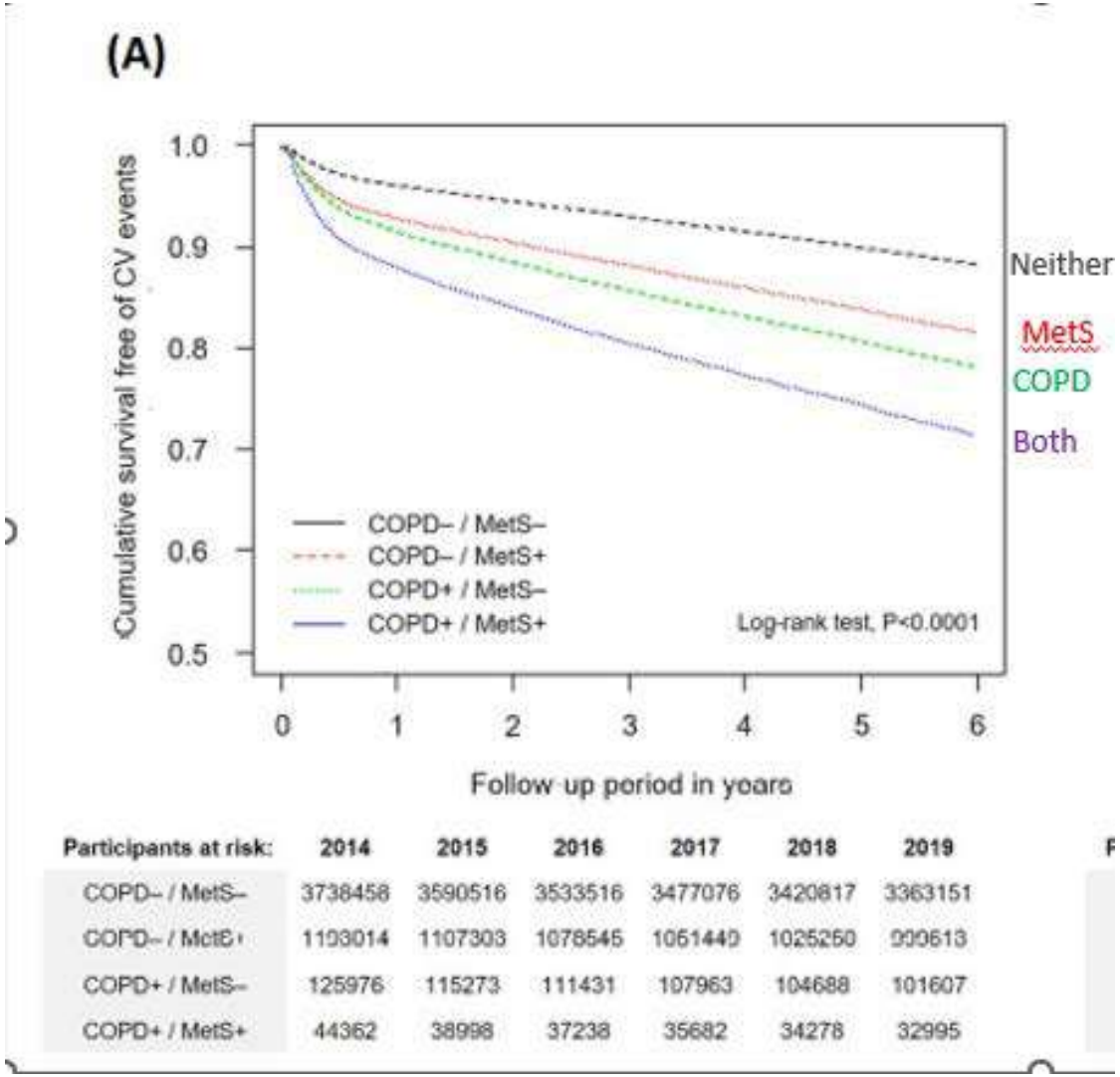
# COPD risk (additive to) and **Greater** than Metabolic Syndrome risk!

International Journal of Chronic Obstructive Pulmonary Disease Dovepress

ORIGINAL RESEARCH

## Risk of Cardiovascular Events Associated with Chronic Obstructive Pulmonary Disease and/or Metabolic Syndrome: A Large-Scale Nationwide Population-Based Cohort Study

Enkyu Noh[1,*], Hyungmin Jeong[1,*], In-So Cho[2], Min-Seok Chang[2], Iseul Yu[2], Sunmin Park[2], Ji-Ho Lee[2], Seok Jeong Lee[2], Won-Yeon Lee[2], Suk Joong Yong[2], Sang-Ha Kim[2]




| Participants at risk: | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 |
|---|---|---|---|---|---|---|
| COPD– / MetS– | 3738458 | 3590516 | 3533516 | 3477076 | 3420817 | 3363151 |
| COPD– / MetS+ | 1103014 | 1107303 | 1078545 | 1061440 | 1025260 | 990613 |
| COPD+ / MetS– | 125976 | 115273 | 111431 | 107963 | 104688 | 101607 |
| COPD+ / MetS+ | 44362 | 38998 | 37238 | 35682 | 34278 | 32995 |

Analysis of the outcomes and CV events or deaths was performed from 2014 to 2019. (5 million records)

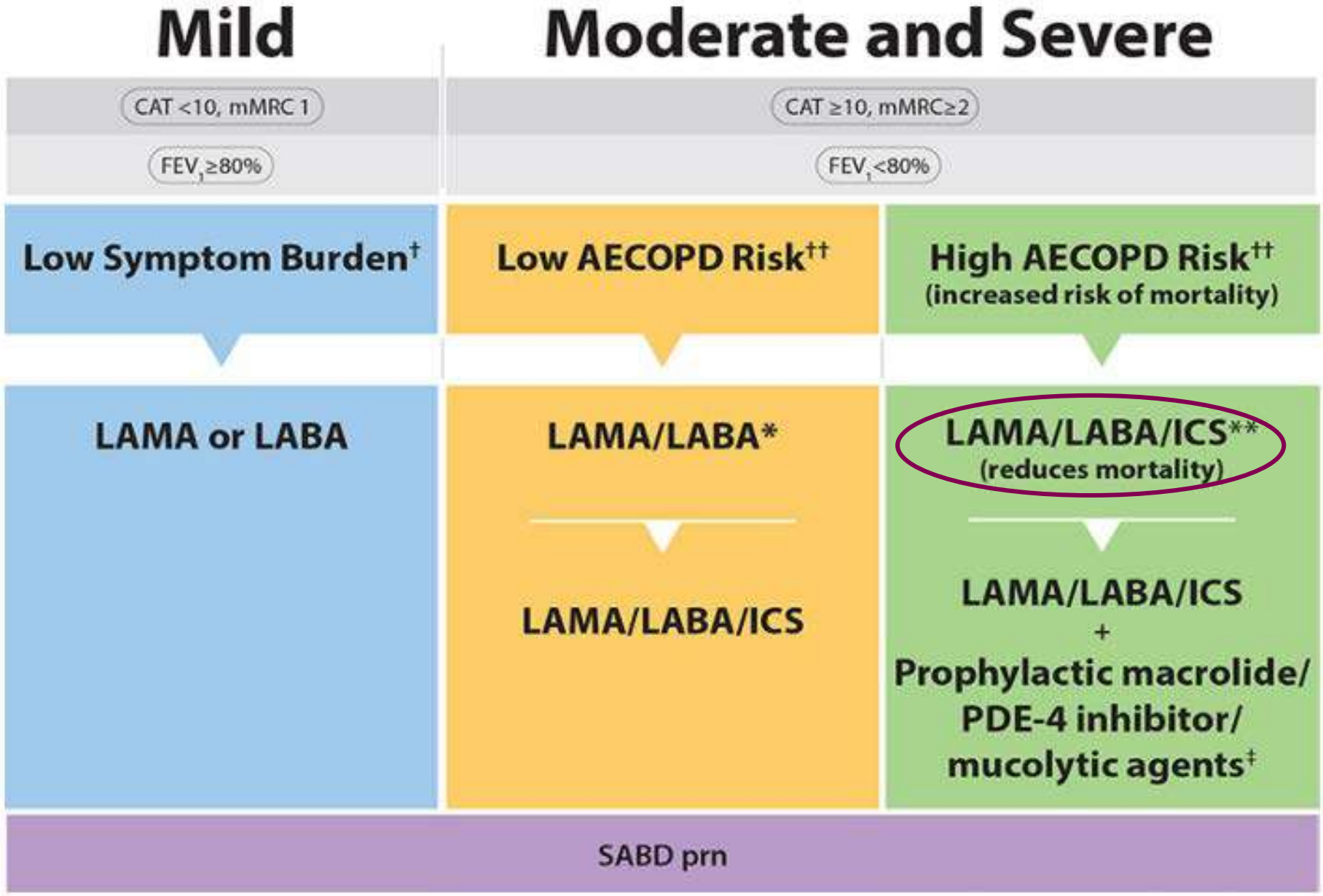
Noh E, Jeong H, Cho IS, Chang MS, Yu I, Park S, Lee JH, Lee SJ, Lee WY, Yong SJ, Kim SH. Risk of Cardiovascular Events Associated with Chronic Obstructive Pulmonary Disease and/or Metabolic Syndrome: A Large-Scale Nationwide Population-Based Cohort Study. Int J Chron Obstruct Pulmon Dis. 2024;19:1447-1456 https://doi.org/10.2147/COPD.S458779

# Model for how to approach Cardiopulmonary Risk

**Proposed steps to adapt key concepts of integrated multidisciplinary cardiometabolic care to a cardiopulmonary disease paradigm.**


ACEi = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; ASCVD = atherosclerotic cardiovascular disease; BP = blood pressure; CP = cardiopulmonary; CV = cardiovascular; COPD = chronic obstructive pulmonary disease; CP = cardiopulmonary; GLP-1 = glucagon-like peptide 1; RS = respiratory system; SGLT2i = sodium-glucose cotransporter-2 inhibitor; SITT = single inhaler triple therapy.

Hawkins NM , Kaplan A, Ko D, Penz E, Bhutani M. Is ‘cardiopulmonary’ the new ‘cardiometabolic’? Making a case for systems change in COPD. In Press




CANADIAN JOURNAL OF RESPIRATORY, CRITICAL CARE, AND SLEEP MEDICINE
https://doi.org/10.1080/24745332.2023.2211417
Taylor & Francis
CTS GUIDELINES AND POSITION PAPERS

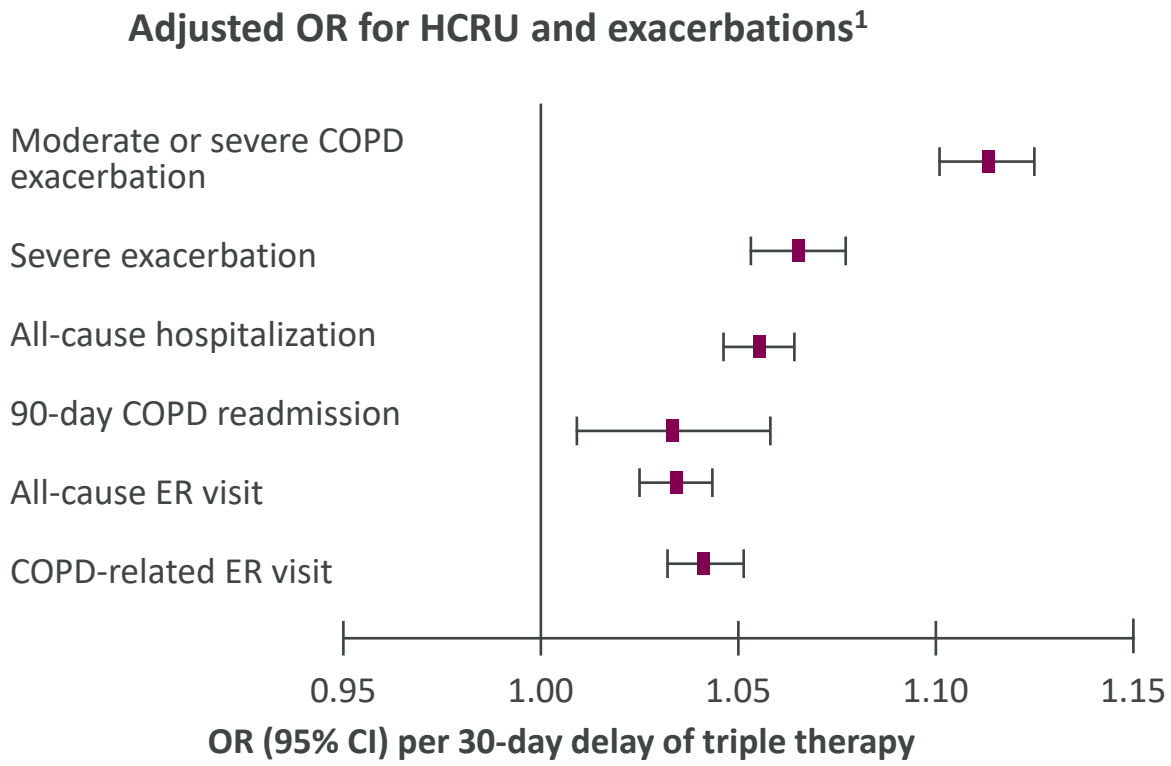
2023 Canadian Thoracic Society Guideline on Pharmacotherapy in Patients with Stable COPD

Jean Bourbeau[a], Mohit Bhutani[b], Paul Hernandez[c], Shawn D. Aaron[d], Marie-France Beauchesne[e], Sophie B. Kermelly[f], Anthony D'Urzo[g], Avtar Lal[h], François Maltais[i], Jeffrey D. Marciniuk[j], Sunita Mulpuru[k], Erika Penz[l], Don D. Sin[m], Anne Van Dam[n], Joshua Wald[o], Brandie L. Walker[p] and Darcy D. Marciniuk[q]

Bourbeau J, Bhutani M, Hernandez P, Aaron SD, Beauchesne MF, Kermelly SB, D'Urzo A, Lal A, Maltais F, Marciniuk JD, Mulpuru S, Penz E, Sin DD, Van Dam A, Wald J, Walker BL, Marciniuk DD. 2023 Canac
Thoracic Society Guideline on Pharmacotherapy in Patients With Stable COPD. Chest. 2023 Nov;164(5):1159-1183. doi: 10.1016/j.chest.2023.08.014. Epub 2023 Sep 9. PMID: 37690008.

# Prompt Initiation of Triple Therapy Reduces the Odds of Exacerbations

Each 30-day delay in initiating triple therapy was associated with an increase in the odds of another COPD exacerbation (PRIMUS)

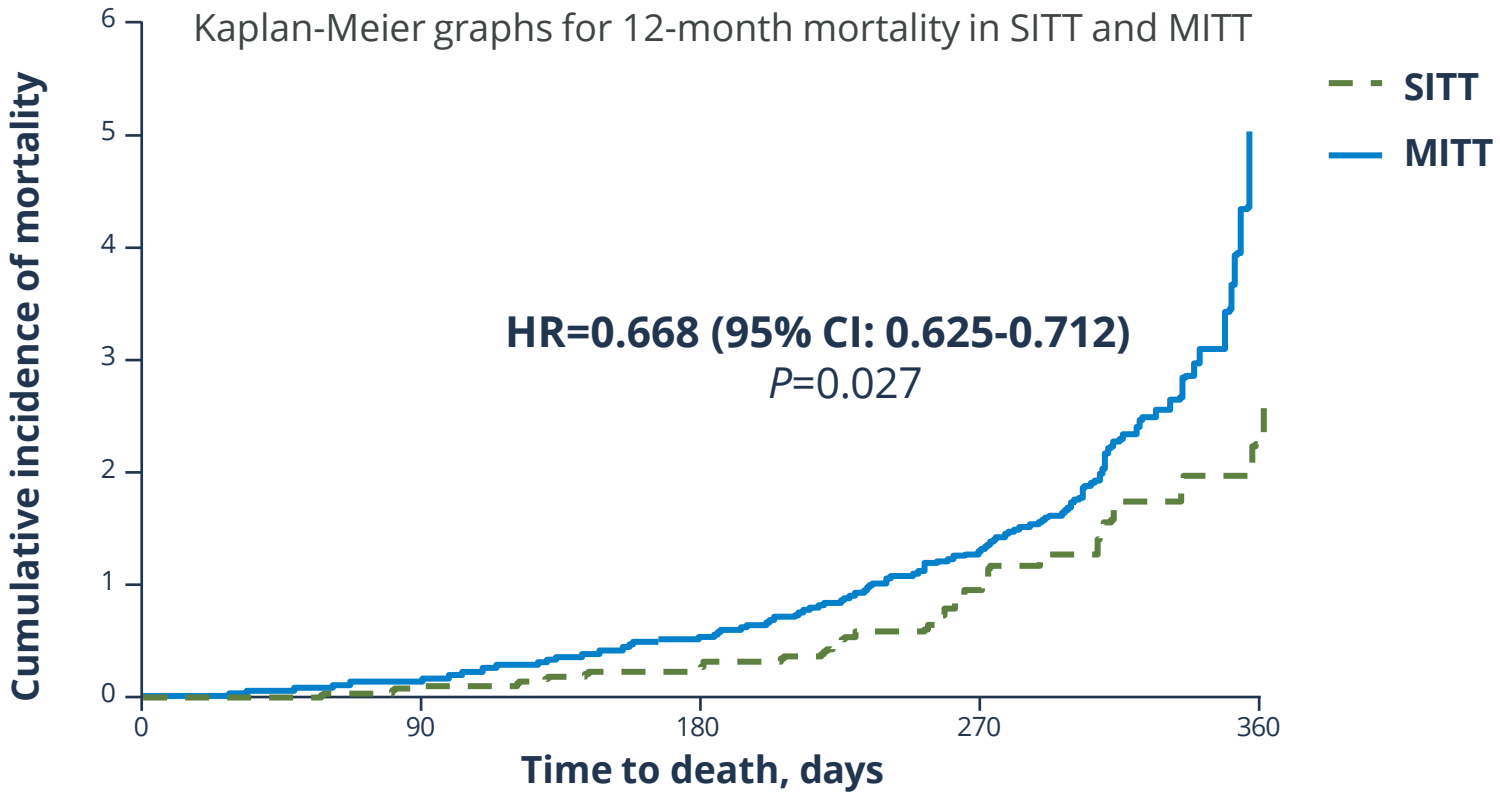



[a]1.. Tkacz J, et al. *Int J Chron Obstruct Pulmon Dis*. 2022;17:329-342.

# Triple Therapy With a Single Inhaler Lowers All-Cause Mortality Risk vs Triple Therapy Split Among Multiple Inhalers[1]

**SITT:**
3 agents contained in 1 device

**MITT:**
3 agents across 2 to 3 devices




Patients treated with SITT had ~**33% lower all-cause mortality risk** at 12-month follow-up[a,b]

[a]Adjusted for covariates: age, sex, body mass index, smoking status, time from diagnosis, $FEV_1$, eosinophil count, heart failure, renal failure, Charlson Comorbidity Index, and previous exacerbations;
[b]Although significant differences between SITT and MITT cohorts were found, secondary outcomes including all-cause mortality were not adjusted for persistence.

CI, confidence interval; $FEV_1$, forced expiratory volume in 1 second; HR, hazard ratio; MITT, multiple-inhaler triple therapy; SITT, single-inhaler triple therapy.

1. Bourbeau J, et al. *Chest.* 2023;164(5)1159-1183; 2. Alcázar-Navarrete B, et al. *Chest*. 2022;162(5):1017–1029.

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

Figure 3.17

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

Single inhaler triple therapy compared to dual LABD therapy relative risk reduction:

IMPACT: HR 0.72 (95% CI: 0.53, 0.99)[1a]
ETHOS: HR 0.51 (95% CI: 0.33, 0.80)[1b]

*RCT with pre-specified analysis
pulmonary rehabilitation across

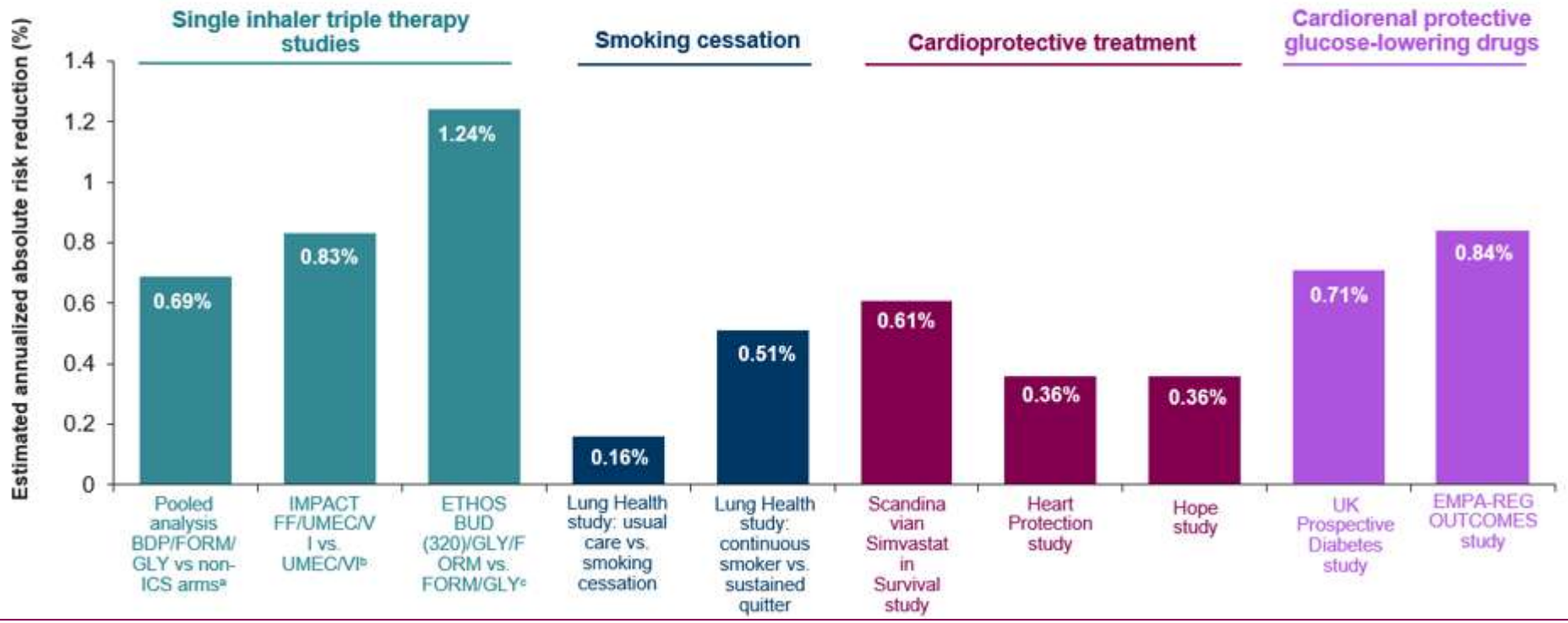
1. a) IMPACT trial (Lipson et al.
(2011) and b) Puhan et al. 2016
al. 2003)

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

2024 Teaching Slide Set

# In the appropriate patient: Reduction in Mortality!!

**Figure 2. Absolute reductions in all-cause mortality with SITT, smoking cessation, and secondary preventive CVD treatments. Adapted from Bourbeau et al.** (75,78–80)




Hawkins, N.M., Kaplan, A., Ko, D.T. et al. Is 'Cardiopulmonary' the New 'Cardiometabolic'? Making a Case for Systems Change in COPD. Pulm Ther (2024). https://doi.org/10.1007/s41030-024-00270-2

# Inhalation
# Fast or Slow?

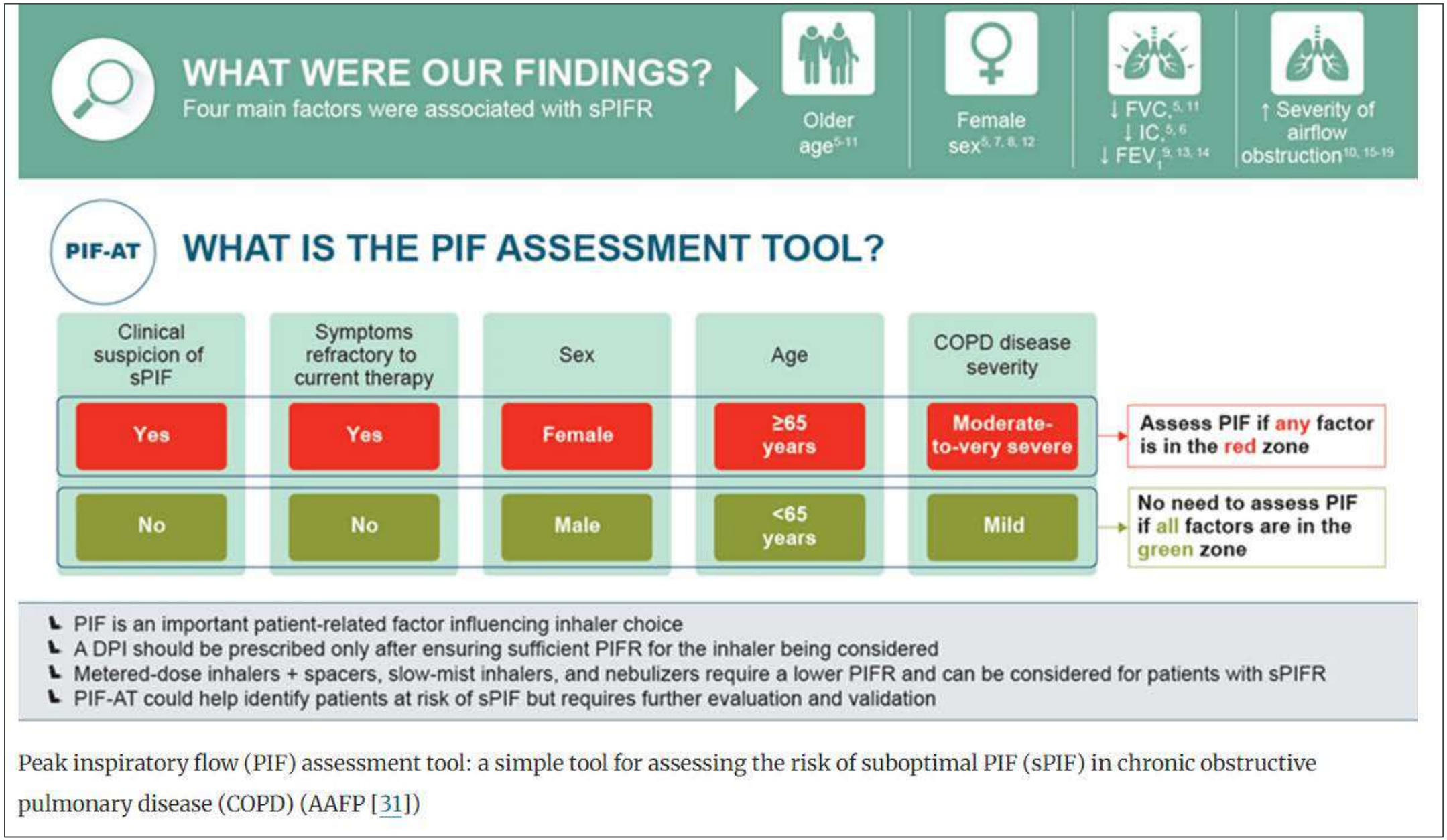

- **Energy from Device**
  - MDI: Metered Dose Inh
  - Soft mist inhaler
  - Nebulizers
  - Device produces aerosol
  - **INHALE SLOWLY**
- **Energy from patient**
  - DPI: Dry powder inhalers
  - Patient creates aerosol
  - **INHALE FORCEFULLY**

For both extremes:

Prepare properly

Empty lungs prior

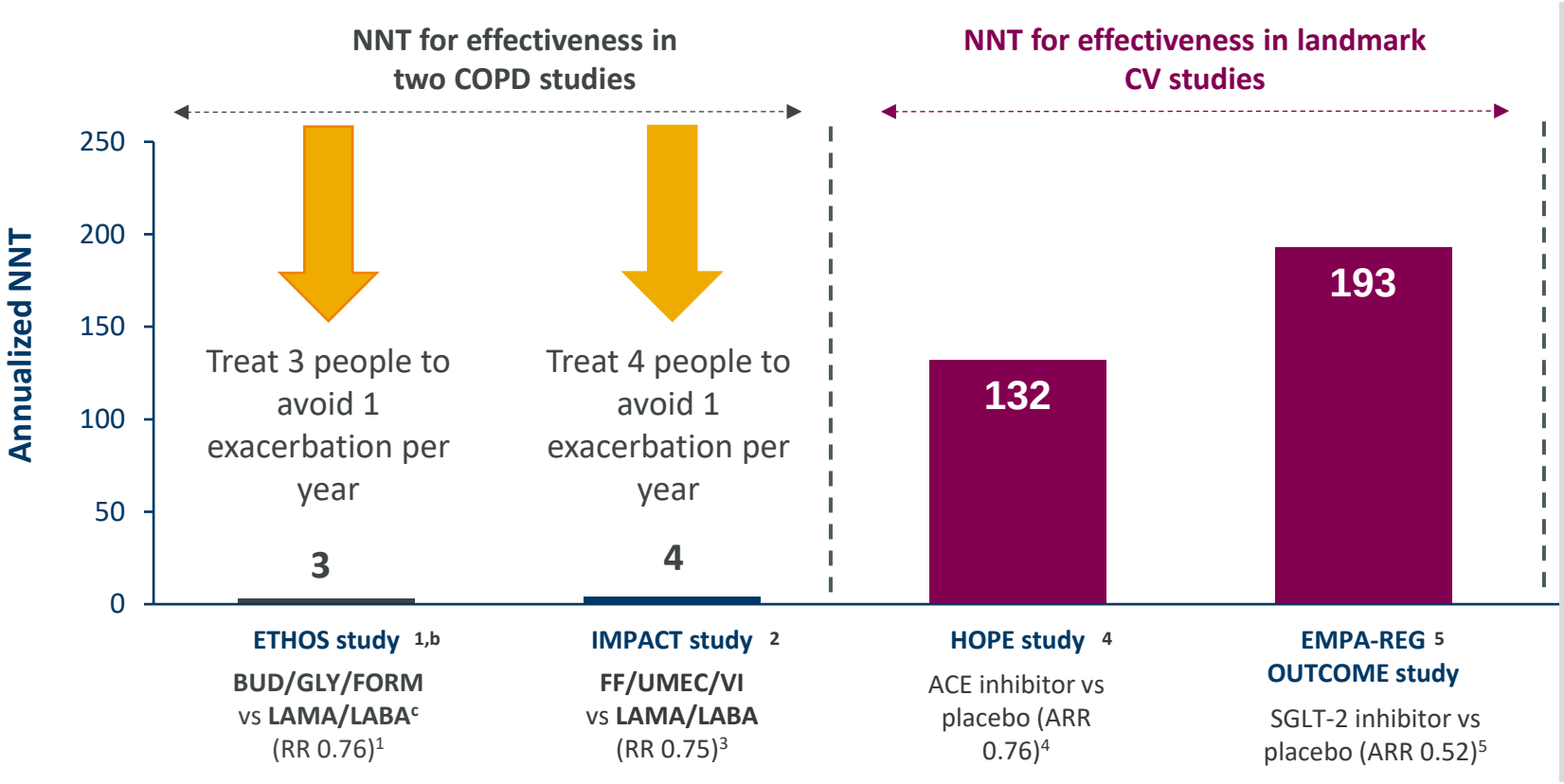
Hold breath after x 10 seconds




Peak inspiratory flow (PIF) assessment tool: a simple tool for assessing the risk of suboptimal PIF (sPIF) in chronic obstructive pulmonary disease (COPD) (AAFP [31])

Kaplan, A., van Boven, J.F.M. Switching Inhalers: A Practical Approach to Keep on UR RADAR. Pulm Ther 6, 381–392 (2020). https://doi.org/10.1007/s41030-020-00133-6

# Number Needed to Treat for Effectiveness[a] in COPD and Other Interventions[1–6]




NNTs are calculated from the estimated annualized ARR and represent the number of patients who need to be treated to prevent one additional bad outcome (ie, death); landmark CV studies included patients with coronary heart disease and/or diabetes mellitus at high risk of a CV event.

[a]Effectiveness for HOPE, EMPA-REG, AZD1222, and BNT162b2 is defined as mortality reduction. For ETHOS and IMPACT, effectiveness is defined in terms of exacerbation reduction; [b]On- and off-treatment deaths with additional vital status follow-up; [c]LAMA/LABA, glycopyrronium/formoterol fumarate dihydrate; [d]Efficacy and effectiveness are based on studies measuring prevention of mild-to-moderate COVID-19 infection; they were not designed to conclude on prevention of hospitalization, severe disease, or death, or on prevention of infection and transmission potential; [e]NNV represents the number of patients who need to be vaccinated to prevent one more case of COVID-19 as 1/ARR.[6]

ACE, angiotensin-converting enzyme; ARR, absolute risk reduction; BUD, budesonide; COVID-19, coronavirus disease 2019; CV, cardiovascular; FF, fluticasone furoate; FORM, formoterol fumarate dihydrate; GLY, glycopyrronium; LABA, long-acting beta-2 agonist; LAMA, long-acting muscarinic antagonist; mRNA, messenger RNA; NNT, number needed to treat; NNV, number needed to vaccinate; RR, relative risk; SARS-CoV-2, severe acute respiratory syndrome coronavirus-2; SGLT-2, sodium glucose co-transporter-2; UMEC, umeclidinium; VI, vilanterol.

1. Rabe KF, et al. *N Engl J Med*. 2020;383(1):35-48; 2. AstraZeneca. Data on file. Veeva Approval ID: REF-1849822; 3. Lipson DA, et al. *N Engl J Med*. 2018;378(18):1671-1680; 4. Yusuf S, et al. *N Engl J Med*. 2000;342(3):145–153; 5. Zinman B, et al. *N Engl J Med*. 2015;373(22):2117–2128; 6. Olliaro P, et al. *Lancet Microbe*. 2021;2(7):e279–e280.

# My take on all this?

- COPD is a CV disease
- Prevent exacerbations, use triple COPD therapy
- Prevent exacerbations: vaccinate
- BUT ALSO:
- Maximize CV protection in COPD patients
- Smoking cessation
- Optimize BP mgmt.
- Consider Statin
- Beta blocker when appropriate

# So, what factors increase Cardiopulmonary Risk? Or..How do I assess for risk?

Cardiac:
Smoking history
Hypertension
Diabetes
Hyperlipidemia
Family hx of cardiovascular disease
Obstructive Sleep apnea
Estrogen use
NSAID use
Chronic inflammation such as RA, Lupus, Psoriasis
Chronic kidney disease
Abnormal ECG
CT chest done, coronary calcification?
Peripheral vascular disease
Erectile dysfunction

Respiratory:
COPD phenotype
a) Frequent exacerbator
b) Type two inflammation
c) A1AT def?

Degree of lung function impairment
Depression/Antidepressants(?)
Productive cough
Vaccine status
Proximity from last exacerbation or viral resp infection

Both
Smoking
Oral steroid use/exposure

Biomarkers[1]?
BNP, Troponin, CRP

Kaplan, work in progress

1. Neumann JT, Twerenbold R, Weimann J, et al. Prognostic Value of Cardiovascular Biomarkers in the Population. JAMA. Published online May 13, 2024. doi:10.1001/jama.2024.5596

# To make the point….
# What comorbidities can you see from this CXR?

CHEST X-RAY

CLINICAL HISTORY: COPD.

IMPRESSION:

Stable right upper lobe granulomata. No active intrathoracic disease. No interval change.

This is not a patient of mine….

# COPD Comorbidities

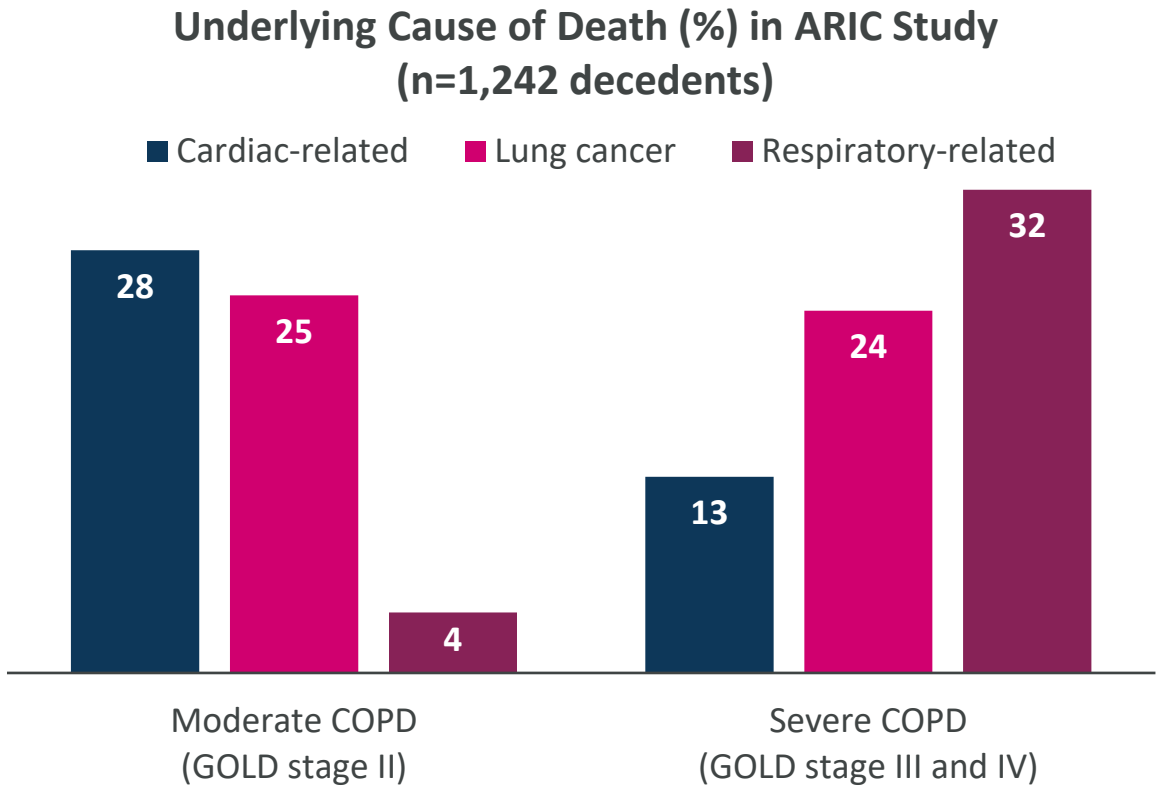
- Ischemic Heart Disease
- Congestive Heart Failure
- Arrhythmias
- Pulmonary Hypertension
- Lung Cancer
- Osteoporosis and Fractures
- Skeletal muscle dysfunction
- Cachexia
- Malnutrition
- Obesity
- Metabolic disorders
- Glaucoma
- Cataracts
- Depression
- Anxiety and Panic disorders

# CV Comorbidities in Patients With COPD Significantly Increases Risk of Death and Are More Likely Cause of Death in Moderate

**The presence of CV comorbidities** increases the **risk of mortality** in patients with COPD*

Patients with **moderate COPD** are more likely **to die from CV disease** than patients with **severe COPD**

| Increase in Mortality Risk vs COPD Alone (%)* | |
|---|---|
| COPD + Ischemic Heart Disease | 27% - 50% ↑ |
| COPD + Atrial Fibrillation | 56% ↑ |
| COPD + Diabetes | 54% - 70% ↑ |
| COPD + Heart Failure | 30% - 90% ↑ |




*Data show risk of mortality for patients with COPD and each comorbidity versus COPD alon

Rabe K et al. *Eur Respir Rev*. 2018;27:180057; Mannino DM et al. *Respir Med*. 2006;100:115–12

# Comorbidities and COPD Treatment Rules

The presence of comorbidities should not alter COPD treatment

Comorbidities should be treated per usual standards regardless of the presence of COPD

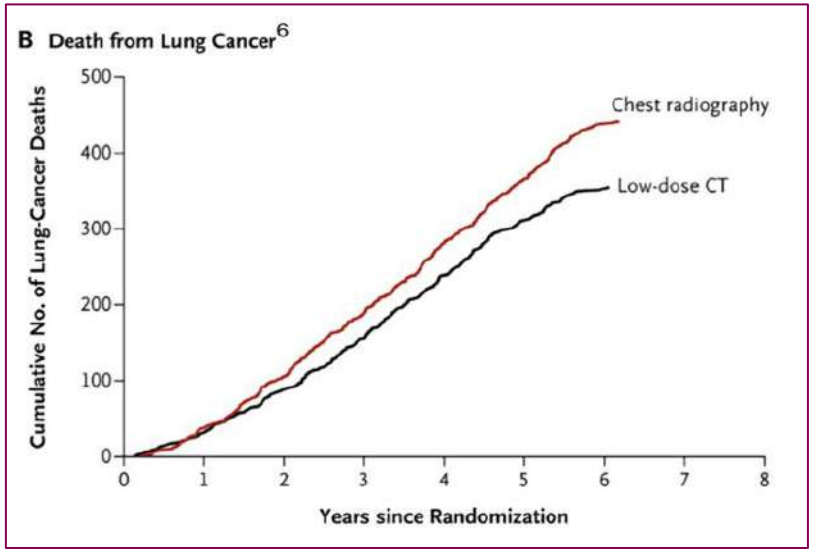
Treat COPD like a CV disease and be aggressive with CV risk management!

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease (2021 Report). Global Initiative for Chronic Obstructive Lung Disease (GOLD), 2021. http://www.goldcopd.org.

# Evidence for Screening People at High Risk for Lung Cancer

## Evidence from the National Lung Screening Trial (NLST):

- The NLST was a randomized controlled trial with over 50,000 participants ages 55–74 at the time of randomization
- It compared people at high risk of getting lung cancer who got screened with an LDCT scan to people who got a chest X-ray
- Screening with LDCT resulted in a 20% relative reduction in lung cancer mortality over 6 years




Patients with COPD have a HIGHER risk than smokers of equal amount without COPD!

**COMMON RISK FACTORS FOR DEVELOPMENT OF LUNG CANCER**

- Age > 55
- Smoking history > 30 pack years
- Presence of emphysema by CT scan
- Presence of airflow limitation $FEV_1/FVC < 0.7$
- BMI < 25 kg/m²
- Family history of lung cancer

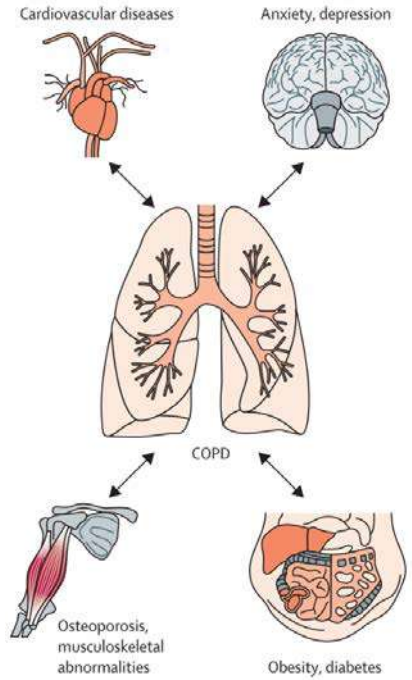

Aberle D, Adams A, Berg C, Black W, Clapp J, Fagerstrom R, et al. Reduced lung cancer mortality with low-dose computed tomographic screening. *N Engl J Med*. 2011 Aug;365(5):395–409.


Ontario Health
Cancer Care Ontario

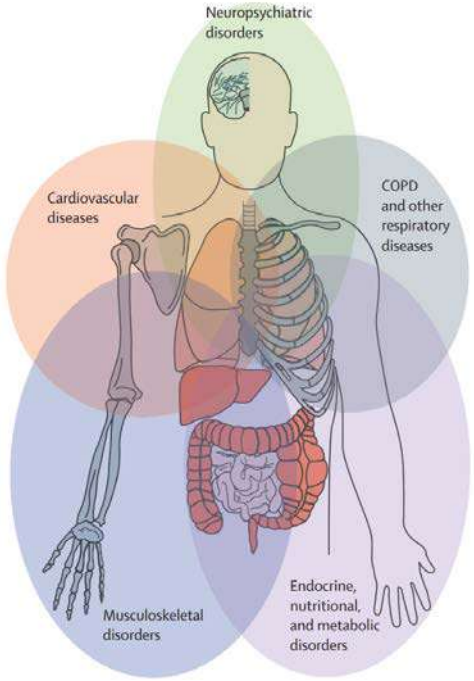
# Approaches to treatment of COPD and Multimorbidity

## COPD as a single disease

## COPD as a single disease with comorbidities




## *COPD in the context of multimorbidity*




$FEV_1$, forced expiratory volume in 1 second; FVC, forced vital capacity

Fabbri et al. 2023

# Quick way to assess/recognize your high-risk COPD patients?

1. Exacerbation

   (Frequency and type)

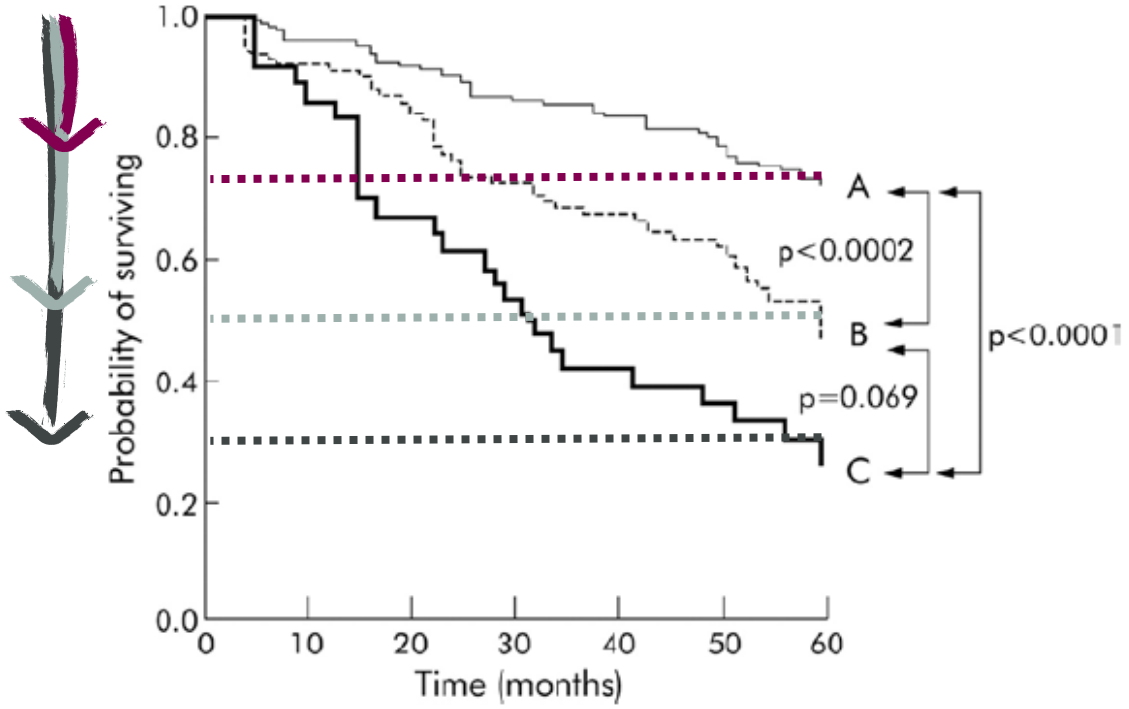
2. FEV1<80%

3. CAT > 10

4. mMRC >2

# Exacerbations and mortality

Kaplan-Meier survival curves by frequency of exacerbations in patients with COPD




**GROUP A= NO EXACERBATIONS**

**GROUP B= 1–2 EXACERBATIONS***

**GROUP C= ≥ 3 EXACERBATIONS***

*Exacerbations requiring hospital management

Soler-Cataluña et al. Thorax. 2005;60:925-931.

Global Strategy for Diagnosis, Management and Prevention of COPD

# Classification of Severity of Airflow Limitation in COPD

**$FEV_1$** Forced Expiratory Volume in 1 second

| Classification of Severity of Airflow Limitation in COPD (Based on Post-Bronchodilator $FEV_1$) | | |
|---|---|---|
| In patients with $FEV_1/FVC < 0.70$: | | |
| GOLD 1: | Mild | $FEV_1 \geq 80\%$ predicted |
| GOLD 2: | Moderate | $50\% \leq FEV_1 < 80\%$ predicted |
| GOLD 3: | Severe | $30\% \leq FEV_1 < 50\%$ predicted |
| GOLD 4: | Very Severe | $FEV_1 < 30\%$ predicted |



Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for prevention, diagnosis and management of COPD. 2013.
FEV, forced expiratory volume in one second; FVC, forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease

Your Name: Alan Kaplan

Today's Date: July 23, 2022

CAT COPD Assessment Test

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

**CAT 8 X 5 = 40**
**< 10 IS GOOD**

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 **X** 2 3 4 5 | I cough all the time | |
| I have no phlegm (mucus) in my chest at all | **X** 1 2 3 4 5 | My chest is completely full of phlegm (mucus) | |
| My chest does not feel tight at all | 0 **X** 2 3 4 5 | My chest feels very tight | |
| When I walk up a hill or one flight of stairs I am not breathless | 0 **X** 2 3 4 5 | When I walk up a hill or one flight of stairs I am very breathless | |
| I am not limited doing any activities at home | **X** 1 2 3 4 5 | I am very limited doing activities at home | |
| I am confident leaving my home despite my lung condition | **X** 1 2 3 4 5 | I am not at all confident leaving my home because of my lung condition | |
| I sleep soundly | **X** 1 2 3 4 5 | I don't sleep soundly because of my lung condition | |
| I have lots of energy | 0 **X** 2 3 4 5 | I have no energy at all | |

**TOTAL SCORE** 4



Your Name: Alan Kaplan

Today's Date: Sept. 23, 2022

CAT COPD Assessment Test

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

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 2 3 **X** 5 | I cough all the time | |
| I have no phlegm (mucus) in my chest at all | 0 1 2 **X** 4 5 | My chest is completely full of phlegm (mucus) | |
| My chest does not feel tight at all | 0 1 2 3 **X** 5 | My chest feels very tight | |
| When I walk up a hill or one flight of stairs I am not breathless | 0 1 2 3 4 **X** | When I walk up a hill or one flight of stairs I am very breathless | |
| I am not limited doing any activities at home | 0 1 2 3 **X** 5 | I am very limited doing activities at home | |
| I am confident leaving my home despite my lung condition | 0 1 2 **X** 4 5 | I am not at all confident leaving my home because of my lung condition | |
| I sleep soundly | 0 1 2 3 4 **X** | I don't sleep soundly because of my lung condition | |
| I have lots of energy | 0 1 2 3 **X** 5 | I have no energy at all | |

**TOTAL SCORE** 32

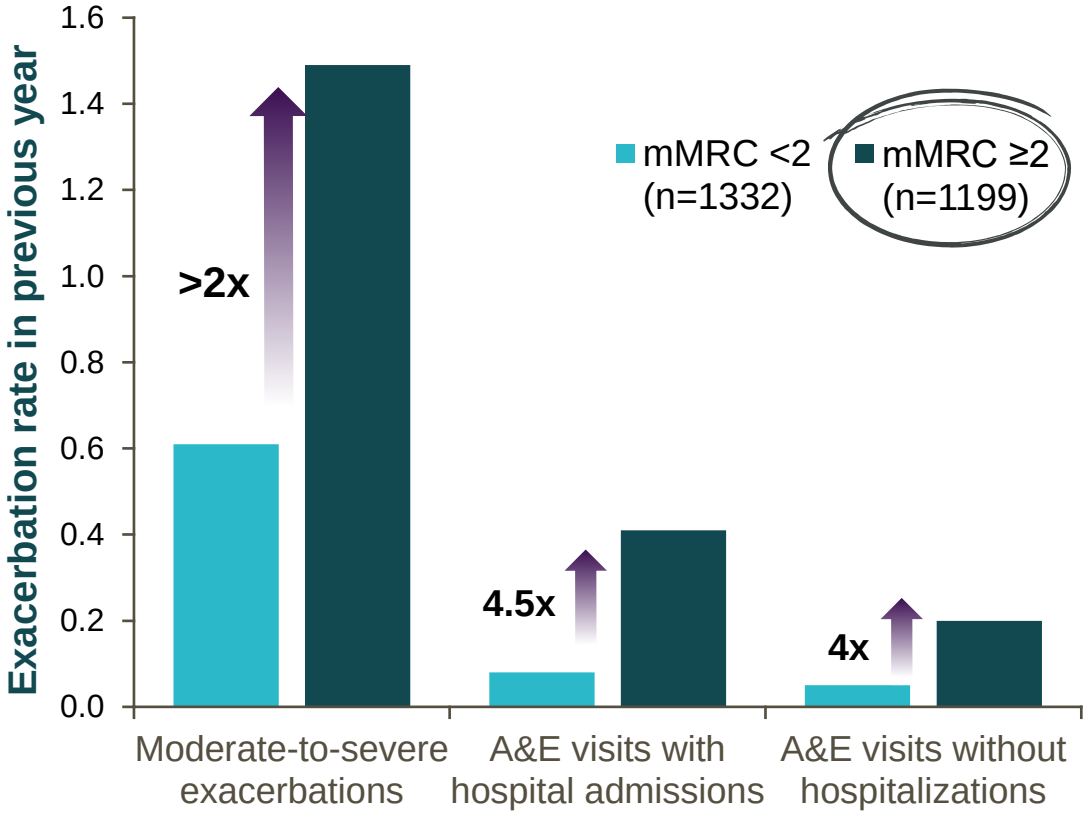
# mMRC ≥ 2 Predicts Worse Outcomes

| GRADE | DESCRIPTION OF BREATHLESSNESS |
|---|---|
| 0 | I only get breathless with strenuous exercise |
| 1 | I get short of breath when hurrying on level ground or walking up a slight hill |
| 2 | On level ground, I walk slower than people of the same age because of breathlessness, or have to stop for breath when walking at my own pace |
| 3 | I stop for breath after walking about 100 yards or after a few minutes on level ground |
| 4 | I am too breathless to leave the house or I am breathless when dressing |

**GRADE 2 = MODERATE COPD**

An mMRC score of 1 or more suggests significant symptoms
Adapted from Stenton C. Occup Med (Lond) 2008; 58(3):226–7

## A PAN-EUROPEAN CROSS-SECTIONAL RETROSPECTIVE COHORT STUDY, STRATIFYING PATIENTS BY LEVELS OF DYSPNEA[1]




Adapted from Punekar et al. Pulm Ther. 2016;2:59–72.

1. Punekar et al. Pulm Ther. 2016;2:59–72.

A&E, accident and emergency; mMRC, modeified Medical Research Council

# ABCs for COPD


- A for Airway clearance
- B for adequate Bronchodilation
- C for Corticosteroids when appropriate/CAT score
- D for Depression and Anxiety screening along with other Comorbidities
- E for Exacerbation prevention including vaccination
- E for Exercise to ensure PR done when appropriate

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- YOU ARE ALL INVITED TO JOIN THE FPAGC!
- NO COST, check out our website….

for4kids@gmail.com