Updates in Obstructive Lung Diseases

Integrating Clinical Data and PFTs to Inform Management

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Disclosures

- Author (compensated), Merck Manuals (Merck & Co)
  - Editorially independent from Merck and Co’s commercial product lines

Objectives

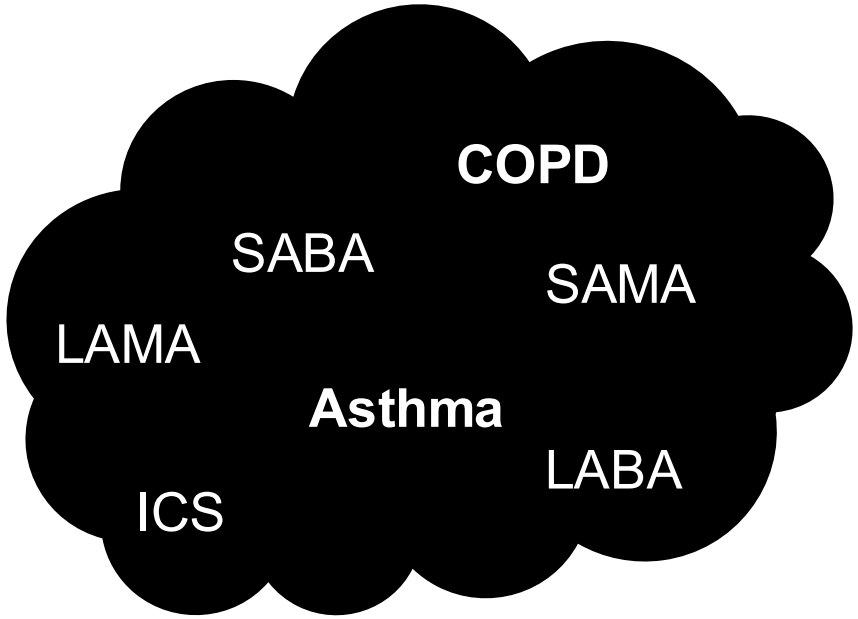
At the end of this session, participants will be able to:

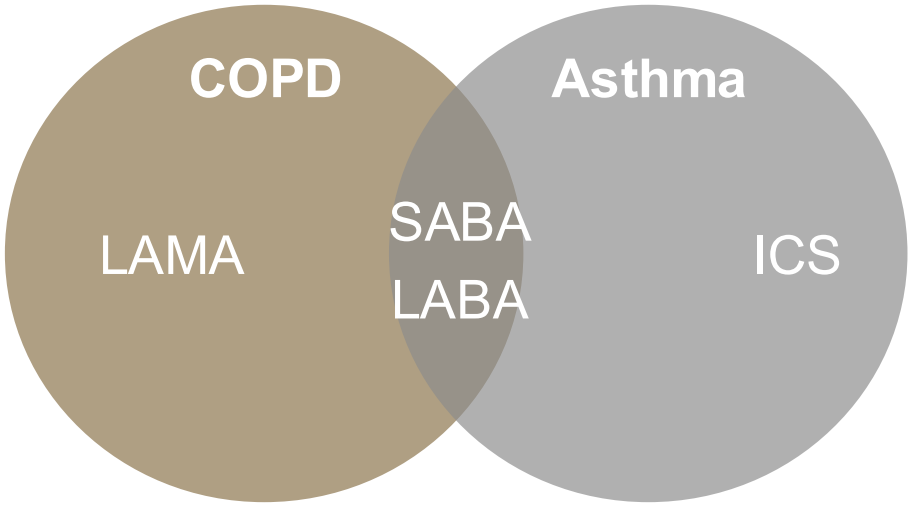
1. Integrate findings of obstruction on PFTs with clinical history to accurately diagnose obstructive disease processes

2. Outline an approach to both asthma and COPD based on contemporary evidence and guidelines

3. Appreciate the importance of distinguishing between asthma and COPD when recommending treatments

4. Understand how newly approved therapies fit into maintenance regimens for COPD





This Session

Outline

PFT Review (Obstruction)

Diagnosing asthma and COPD

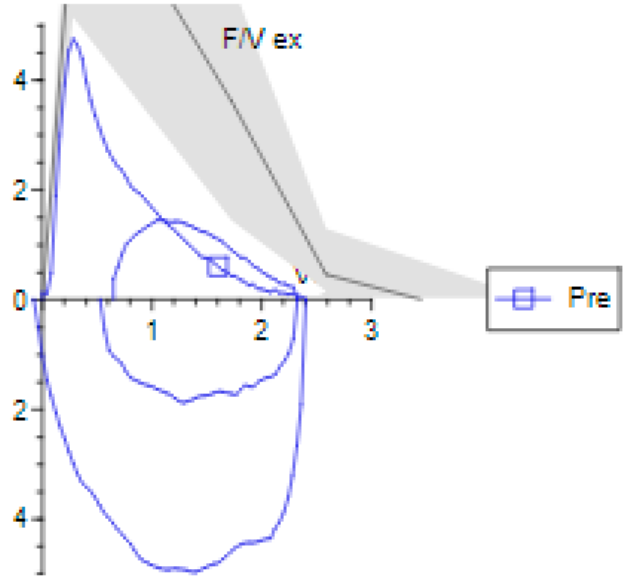
Contemporary management of asthma and COPD

New therapies and when to consider

Case 1

79-year-old former tobacco smoker (40 pk/yr) with progressive dyspnea on exertion and productive cough. Auscultated lung sounds are diminished without crackles.

Parameter	Ref	LLN	Pre	Z-Score
FVC (liters)	3.45	2.49	2.41	-1.77
FEV_1 (liters)	2.58	1.79	1.56	-2.08
FEV_1/FVC	75	60	65	
TLC (liters)	6.42	5.27	5.77	-0.93
DL_{CO} (ml/min/mmHg)	21.90	15.86	15.2	-1.70



Interpretation:

Spirometry reveals reduced airflow rates without airflow obstruction, suggesting possible restrictive disease. Diffusing capacity is mildly reduced.

What is the most likely diagnosis?

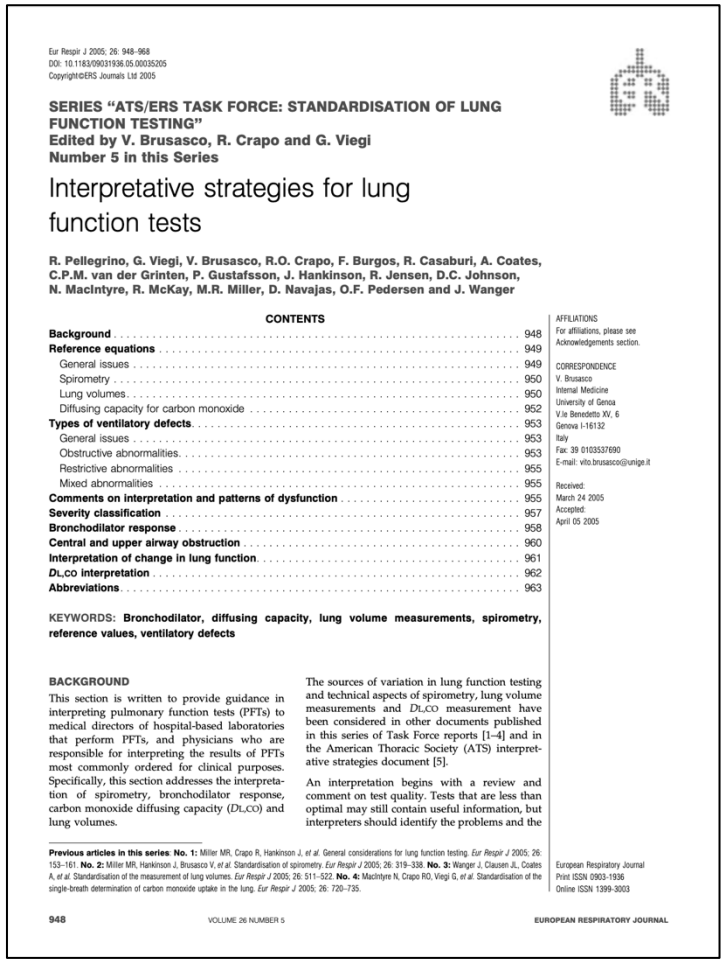
A. COPD
B. Idiopathic Pulmonary Fibrosis
C. Asthma
D. Chronic Bronchitis
E. Obesity

What is the most likely diagnosis?

A. **COPD**
B. Idiopathic Pulmonary Fibrosis
C. Asthma
D. Chronic Bronchitis
E. Obesity

Many standards in use

ATS/ERS (2005)



Eur Respir J 2005; 26: 948–968
DOI: 10.1183/09031936.05.00035205

SERIES "ATS/ERS TASK FORCE: STANDARDISATION OF LUNG FUNCTION TESTING"
Edited by V. Brusasco, R. Crapo and G. Viegi
Number 5 in this Series

Interpretative strategies for lung function tests

R. Pellegrino, G. Viegi, V. Brusasco, R.O. Crapo, F. Burgos, R. Casaburi, A. Coates, C.P.M. van der Grinten, P. Gustafsson, J. Hankinson, R. Jensen, D.C. Johnson, N. MacIntyre, R. McKay, M.R. Miller, D. Navajas, O.F. Pedersen and J. Wanger

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Received:
March 24 2005
Accepted:
April 05 2005

KEYWORDS: **Bronchodilator, diffusing capacity, lung volume measurements, spirometry, reference values, ventilatory defects**

BACKGROUND

This section is written to provide guidance in interpreting pulmonary function tests (PFTs) to medical directors of hospital-based laboratories that perform PFTs, and physicians who are responsible for interpreting the results of PFTs most commonly ordered for clinical purposes. Specifically, this section addresses the interpretation of spirometry, bronchodilator response, carbon monoxide diffusing capacity (*D*L,CO) and lung volumes.

The sources of variation in lung function testing and technical aspects of spirometry, lung volume measurements and *D*L,CO measurement have been considered in other documents published in this series of Task Force reports [1–4] and in the American Thoracic Society (ATS) interpretative strategies document [5].

An interpretation begins with a review and comment on test quality. Tests that are less than optimal may still contain useful information, but interpreters should identify the problems and the

Previous articles in this series: **No. 1:** Miller MR, Crapo R, Hankinson J, *et al*. General considerations for lung function testing. *Eur Respir J* 2005; 26: 153–161. **No. 2:** Miller MR, Hankinson J, Brusasco V, *et al*. Standardisation of spirometry. *Eur Respir J* 2005; 26: 319–338. **No. 3:** Wanger J, Clausen JL, Coates A, *et al*. Standardisation of the measurement of lung volumes. *Eur Respir J* 2005; 26: 511–522. **No. 4:** MacIntyre N, Crapo RO, Viegi G, *et al*. Standardisation of the single-breath determination of carbon monoxide uptake in the lung. *Eur Respir J* 2005; 26: 720–735.

European Respiratory Journal
Print ISSN 0903-1936
Online ISSN 1399-3003

ATS/ERS (2022)

EUROPEAN RESPIRATORY JOURNAL
ERS OFFICIAL DOCUMENTS
S. STANOJEVIC ET AL.

ERS/ATS technical standard on interpretive strategies for routine lung function tests

Sanja Stanojevic[1], David A. Kaminsky[2], Martin R. Miller[3], Bruce Thompson[4], Andrea Aliverti[5], Igor Barjaktarevic[6], Brendan G. Cooper[7], Bruce Culver[8], Eric Derom[9], Graham L. Hall[10], Teal S. Hallstrand[8], Joerg D. Leuppi[11,12], Neil MacIntyre[13], Meredith McCormack[14], Margaret Rosenfeld[15] and Erik R. Swenson[8,16]

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Shareable abstract (@ERSpublications)
Data from pulmonary function tests must be complemented with clinical expertise and consideration of the inherent biological variability and uncertainty of the test result to ensure appropriate interpretation of an individual's lung function measurements https://bit.ly/3ecluFc

Cite this article as: Stanojevic S, Kaminsky DA, Miller MR, *et al*. ERS/ATS technical standard on interpretive strategies for routine lung function tests. *Eur Respir J* 2022; 60: 2101499 [DOI: 10.1183/13993003.01499-2021].

This article has an editorial commentary: https://doi.org/10.1183/13993003.00317-2022

Received: 26 May 2021
Accepted: 18 Nov 2021

Abstract

Background Appropriate interpretation of pulmonary function tests (PFTs) involves the classification of observed values as within/outside the normal range based on a reference population of healthy individuals, integrating knowledge of physiological determinants of test results into functional classifications and integrating patterns with other clinical data to estimate prognosis. In 2005, the American Thoracic Society (ATS) and European Respiratory Society (ERS) jointly adopted technical standards for the interpretation of PFTs. We aimed to update the 2005 recommendations and incorporate evidence from recent literature to establish new standards for PFT interpretation.

Methods This technical standards document was developed by an international joint Task Force, appointed by the ERS/ATS with multidisciplinary expertise in conducting and interpreting PFTs and developing international standards. A comprehensive literature review was conducted and published evidence was reviewed.

Results Recommendations for the choice of reference equations and limits of normal of the healthy population to identify individuals with unusually low or high results are discussed. Interpretation strategies for bronchodilator responsiveness testing, limits of natural changes over time and severity are also updated. Interpretation of measurements made by spirometry, lung volumes and gas transfer are described as they relate to underlying pathophysiology with updated classification protocols of common impairments.

Conclusions Interpretation of PFTs must be complemented with clinical expertise and consideration of the inherent biological variability of the test and the uncertainty of the test result to ensure appropriate interpretation of an individual's lung function measurements.

Introduction

Pulmonary function tests (PFTs)/respiratory function tests reflect the physiological properties of the lungs (*e.g.* airflow mechanics, volumes and gas transfer). These tests have been used for decades to help

GOLD

Global Initiative for Chronic Obstructive Lung Disease

REPORT

GLOBAL INITIATIVE FOR CHRONIC OBSTRUCTIVE LUNG DISEASE™

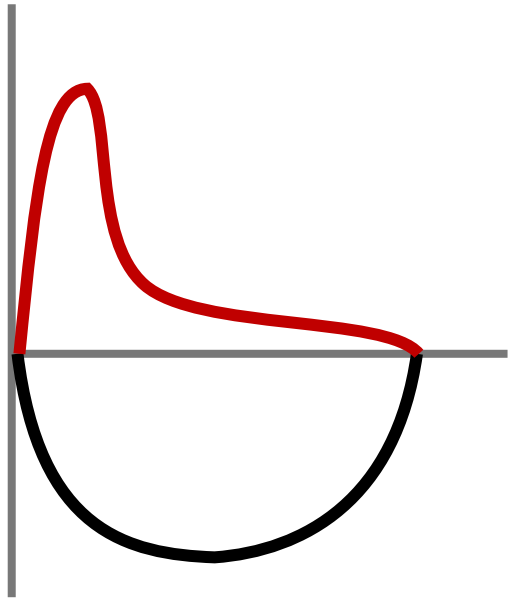
Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease

Obstruction

Definition

Reduced FEV1/FVC

- < LLN (ATS/ERS)
- < 0.7 (GOLD)



Clues to underlying disease process

Bronchodilator response

Doesn't distinguish between asthma and COPD
Higher values (≥15%) are more convincing for asthma

Reversible obstruction (i.e. no obstruction on post-BD testing)

Rules out COPD in favor of asthma

Obstruction with normal DLCO

Think mostly airways disease (chronic bronchitis or asthma)

Obstruction with reduced DLCO

Think airways plus parenchymal disease (emphysema)

! In most cases, PFTs alone do not distinguish between asthma and COPD. Clinical history is required.

Reconciling different definitions

For the majority of PFTs, I apply ATS 2022 guidelines

- Obstruction = FEV1/FVC < LLN
  - Severity based on FEV1 Z-Score

For patients with suspected COPD:

- Use fixed ratio of FEV1/FVC < 0.7*
  - Severity based on FEV1* %Pred

Young pt + high suspicion for COPD, consider both

*GOLD definition specifies post-BD value for FEV1/FVC and FEV1 %pred. OK to use pre-BD value in most cases unless diagnosis uncertain

Outline

PFT Review (Obstruction)

Diagnosing asthma and COPD

Contemporary management of asthma and COPD

New therapies for advanced COPD

GOLD 2026 definition of COPD

A heterogenous lung condition characterized by chronic respiratory symptoms due to abnormalities of the airways and/or alveoli that cause persistent, often progressive, airflow obstruction

Causes

- Gene/environment interactions over a lifetime
- Lung development/aging
- Main exposures: inhalation of toxic particles/gases

Diagnostic Criteria

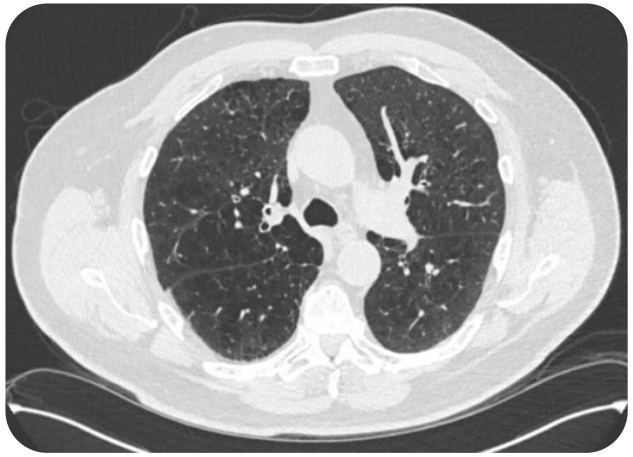
Appropriate clinical context

+

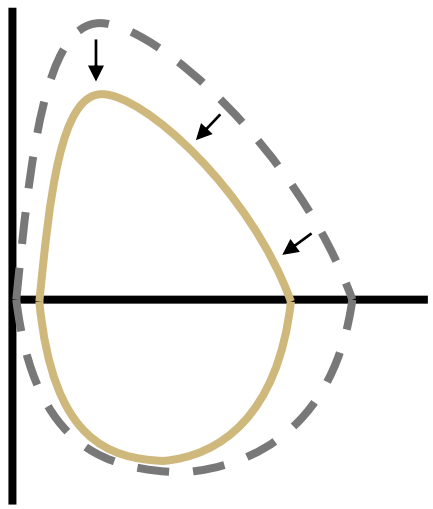
Post-bronchodilator FEV1/FVC <0.7

Pre-COPD

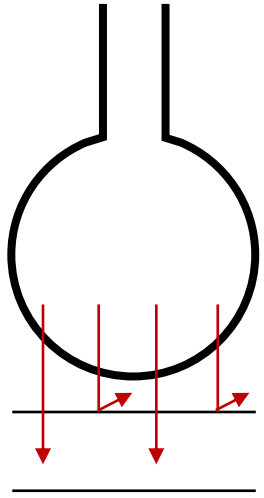
Respiratory symptom plus any of:



Emphysema

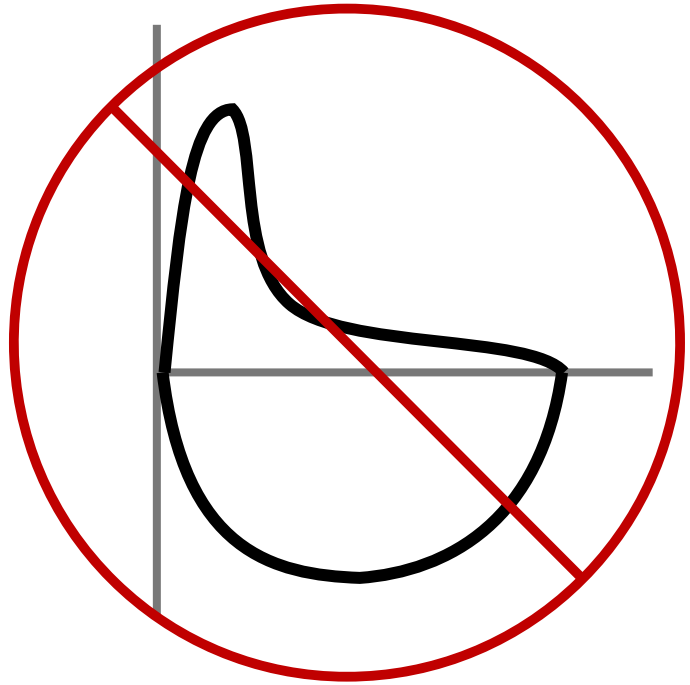


PRISm



Reduced D_LCO

No airflow obstruction



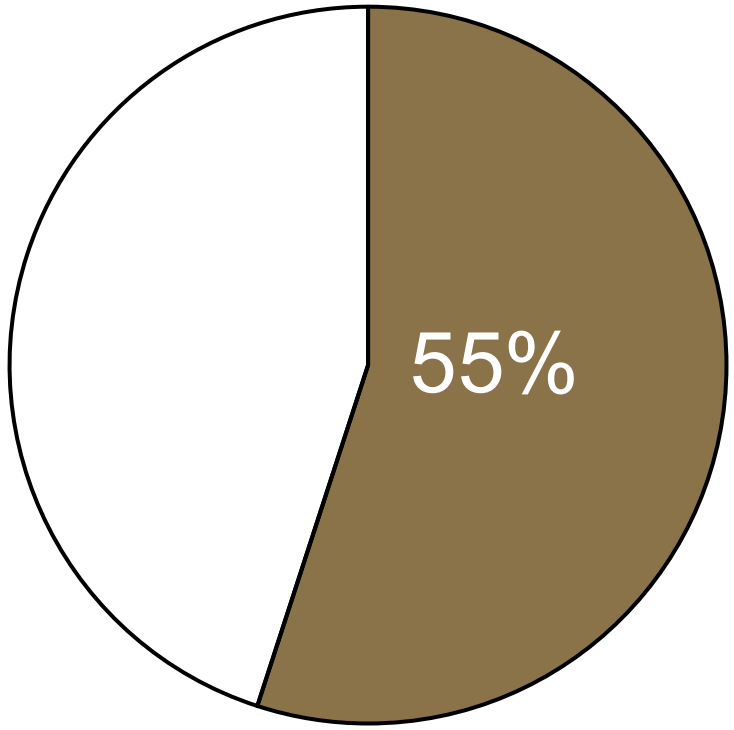
FEV1/FVC > 0.7

AJRCCM 2022;206(11):1317-1325
GOLD 2025

PRISm = Preserved ratio impaired spirometry

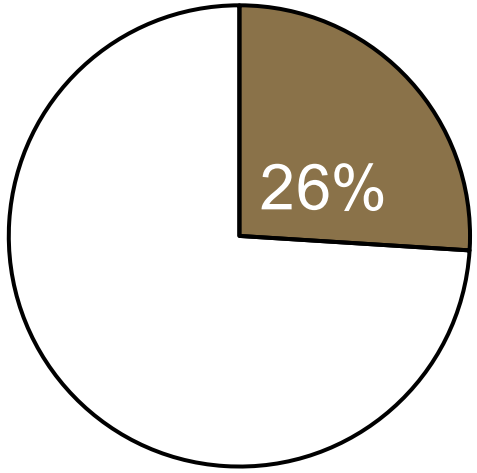
COPD in never smokers

Global

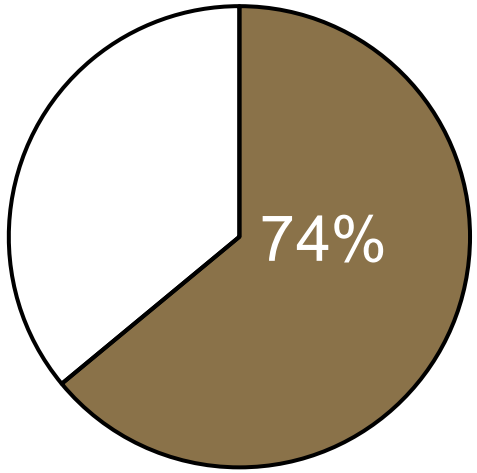


Proportion of COPD* in never smokers

*post-BD FEV1/FVC < 0.7



High income



Low income

Risk factors

- Air pollution (indoor and outdoor)
- Asthma
- Occupational exposures
- Infections
- Low lung development
- Low SES
- 2nd hand tobacco
- Diet
- Age
- Genetics

Lancet Respir Med 2022;10:497–511

GINA 2025 Definition of Asthma

A heterogenous disease, usually characterized by chronic airway inflammation. It is defined by a history of respiratory symptoms (wheezing, dyspnea, cough, chest tightness) that vary over time, together with variable expiratory flow limitation.

Symptoms

Wheeze, dyspnea, chest tightness, and/or cough

- Varies in time and intensity
- Often worse at night or on waking
- Common triggers: exercise, laughter, allergens, cold air
- Worse at end-exercise
- Worse with viral infections

Variable Expiratory Airflow

Excessive variability in lung function:

- Positive bronchodilator response on PFT (≥12% in adults)
- Increase PEF after bronchodilator (≥20% in adults)
- Excessive variability in PEF over ~2 weeks (>10% variability)
- high variability, high confidence in dx

Features of asthma vs COPD

Both are heterogenous diseases that produce respiratory symptoms like dyspnea, cough, wheezing and chest tightness

	Asthma	COPD
Age at diagnosis	• Childhood or young adulthood (more likely allergic) • Second peak in middle age (more likely non-allergic)	Incidence increases with age
Pathology	Airways only	• Airways (chronic bronchitis) • Parenchyma (emphysema)
Symptoms	**Varies** over time	**Persistent**, often progressive
Airflow limitation	• **Varies** over time • May be fully reversible	• **Fixed** • May respond to BD, but is not reversible
Diagnostic criteria	Airflow obstruction helpful, but not required	Airflow **obstruction required**

Asthma-COPD Overlap

Back to case 1

79-year-old former tobacco smoker (40 pk/yr) with progressive dyspnea on exertion and productive cough. Auscultated lung sounds are diminished without crackles.

Parameter	Ref	LLN	Pre	Z-Score
FVC (liters)	3.45	2.49	2.41	-1.77
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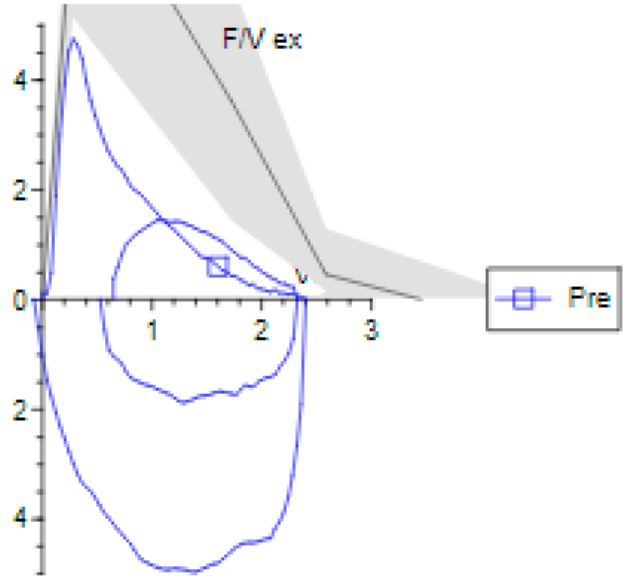


No obstruction by ATS criteria (FEV1/FVC is > LLN), but is <70, which is consistent with obstruction using GOLD criteria in this patient with suspected COPD based on history.

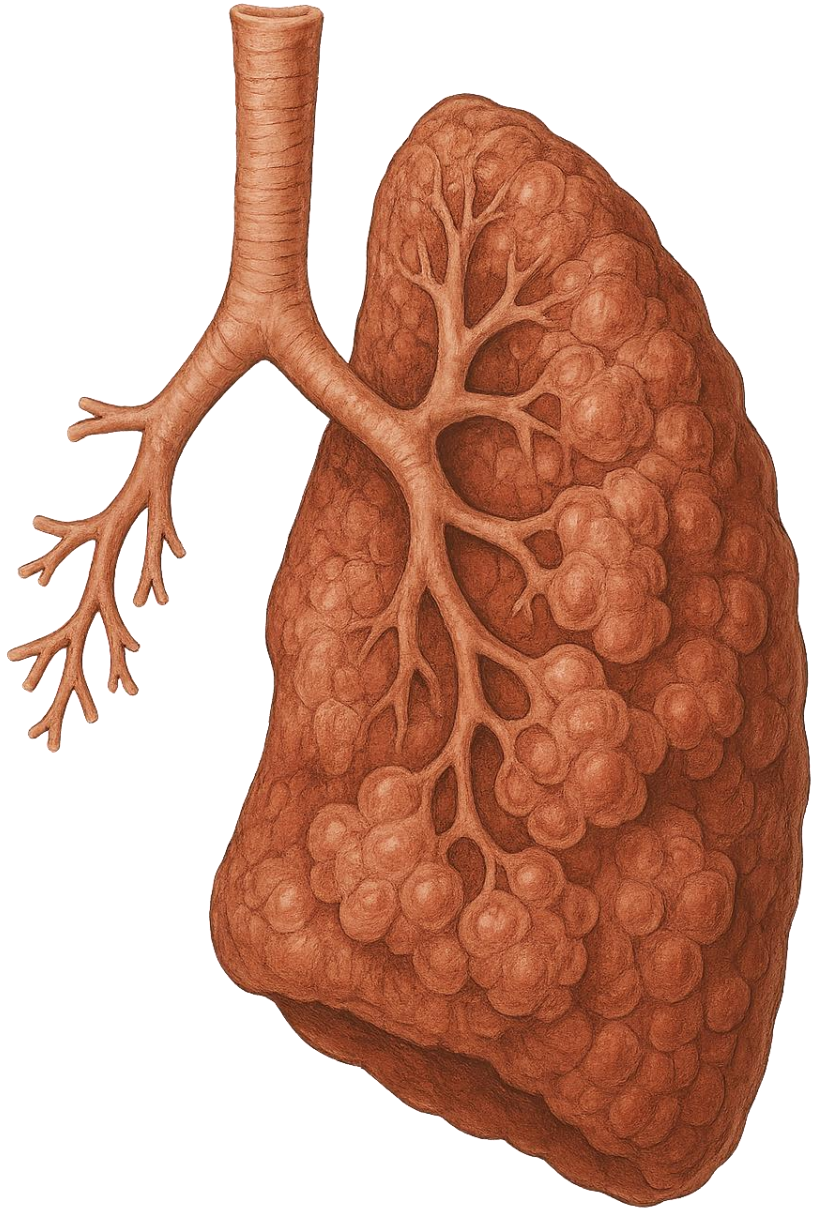
Outline

PFT Review (Obstruction)

Diagnosing asthma and COPD

Contemporary management of asthma and COPD

New therapies for advanced COPD



COPD Management Principles

Case 2

A 68-year-old woman with confirmed COPD is establishing with you for primary care. She quit smoking 10 years ago when diagnosed with COPD. She reports dyspnea that limits her when shopping and during regular walks with her friends where she stops after several minutes to catch her breath. She has never had an exacerbation. Her current medication regimen includes fluticasone/salmeterol 100/50 mcg and albuterol as needed.

What changes to her inhaler regimen do you recommend?

A. Add LAMA to her current regimen
B. Stop current ICS/LABA and start LABA/LAMA
C. Increase the dose of the ICS component of her current inhaler
D. Change as-needed albuterol to albuterol/budesonide
E. No change to her current regimen

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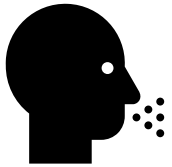
Assess symptoms and history

Evaluating confirmed COPD

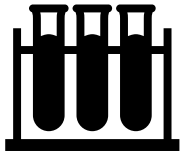


Symptoms

Dyspnea
Cough
Sputum
Energy

Exacerbations

Number
Frequency
Severity



Labs

Serum Eos
A1AT

FEV1

Mild
Moderate
Severe
Very severe

Tobacco use history

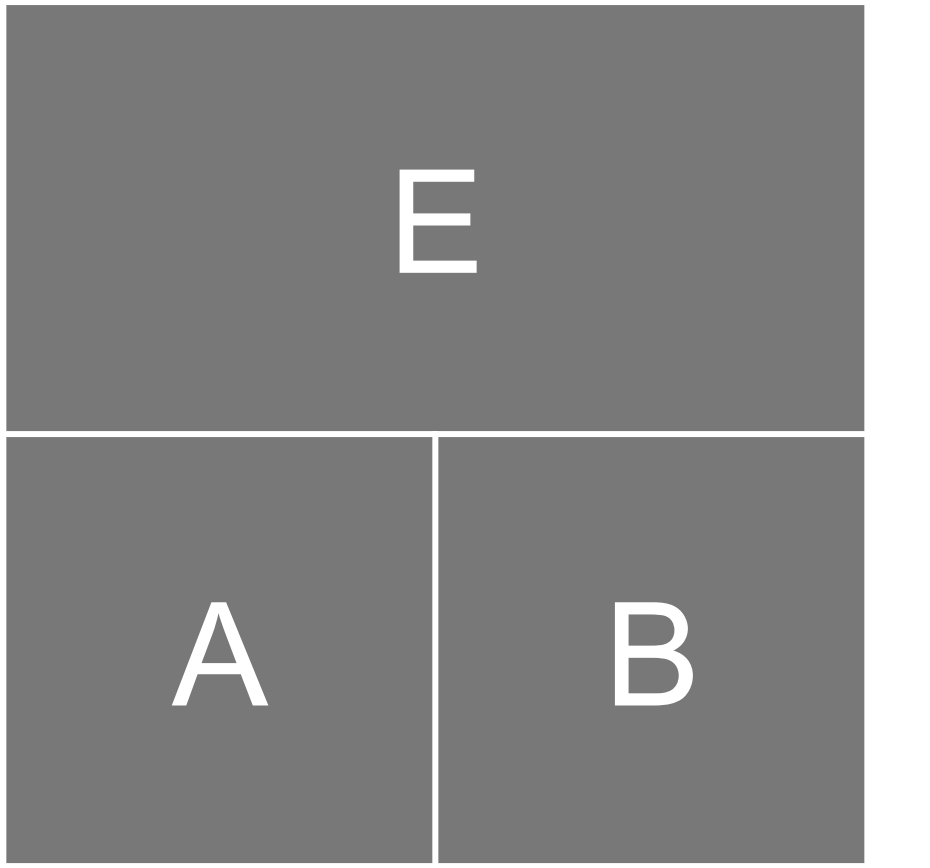
Overall treatment goals in COPD

- Improve survival
- Minimize symptoms and improve QOL
- Decrease exacerbation risk
- Slow lung function decline

GOLD Classification

≥1 moderate or severe exacerbation

Exacerbations



mMRC ≥2 / CAT ≥10

Symptoms

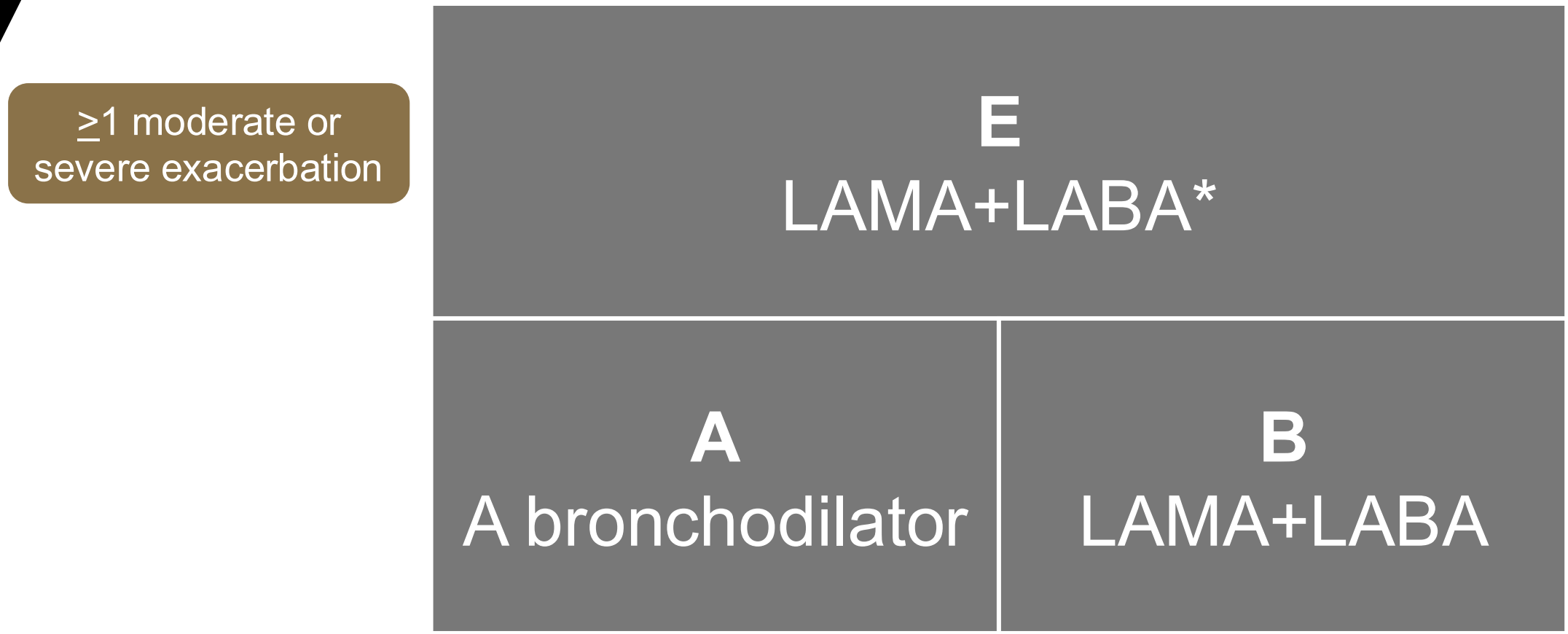
Change for 2026!

mMRC 2 =
Unable to keep up with peers due to dyspnea

OR

Has to stop to catch breath walking at own pace

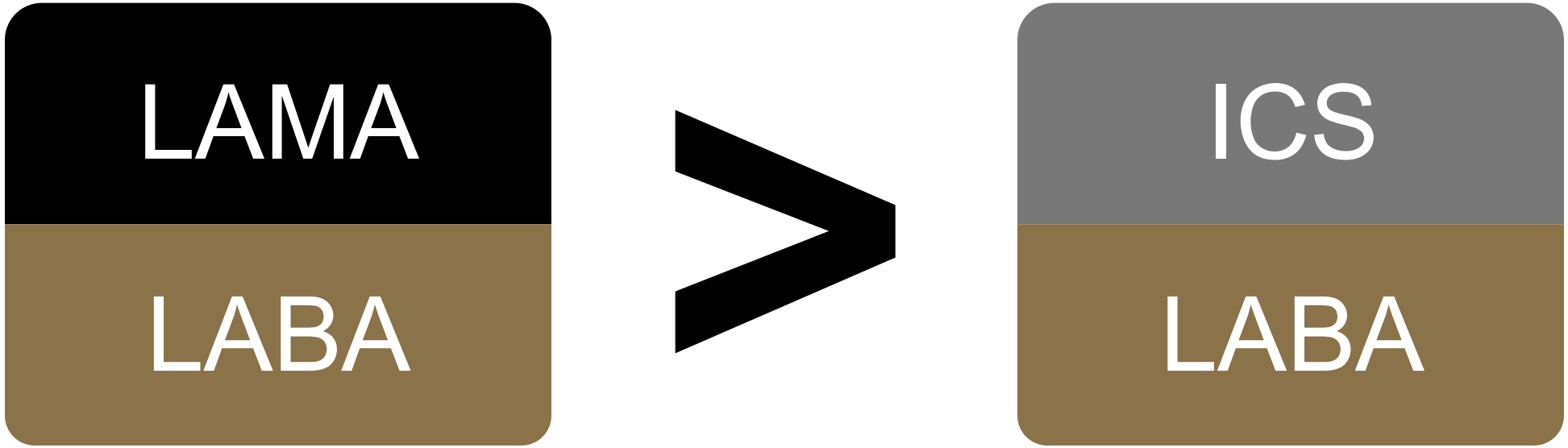
Initial treatment based on GOLD class



*Consider LAMA+LABA+ICS if serum eos >300

LAMA: Long-acting muscarinic antagonist
LABA: Long-acting beta agonist
ICS: Inhaled corticosteroid

Bronchodilators first in COPD!



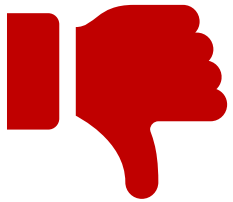
- ✓ Exacerbation prevention
- ✓ Symptoms
- ✓ Pneumonia risk

NEJM. 2016 Jun 9;374(23):2222-34
Chest. 2008 Aug;134(2):255-262
Cochrane Database Syst Rev. 2018 Dec 3;12

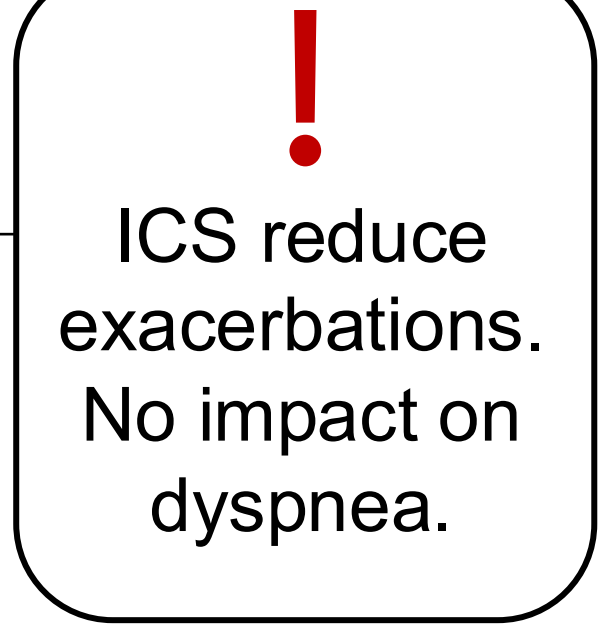
Inhaled corticosteroids in COPD

In COPD, use of ICS should be in conjunction with LABA-LAMA (ICS-LABA should be avoided, never ICS alone)

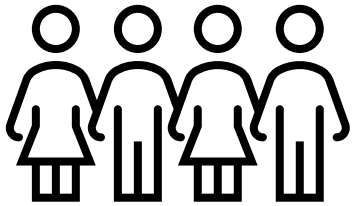
- Continued **exacerbations** despite LABA-LAMA
  - ≥2 per year OR
  - ≥1 hospitalization
- Asthma-COPD overlap



- As initial therapy for COPD
- No history of exacerbations
- Consistently low serum eos (<100)
- History of pneumonia while on ICS
- History of mycobacterial infection



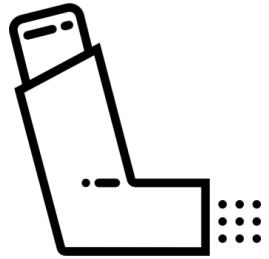
”Triple therapy” (i.e. LABA-LAMA-ICS)



Patients with history of recent exacerbations (GOLD E)

- Reduced frequency of moderate/severe exacerbations
- Improved health status
- **Reduced mortality**

- Increased risk of pneumonia
- **Lack of benefit if eos <100**

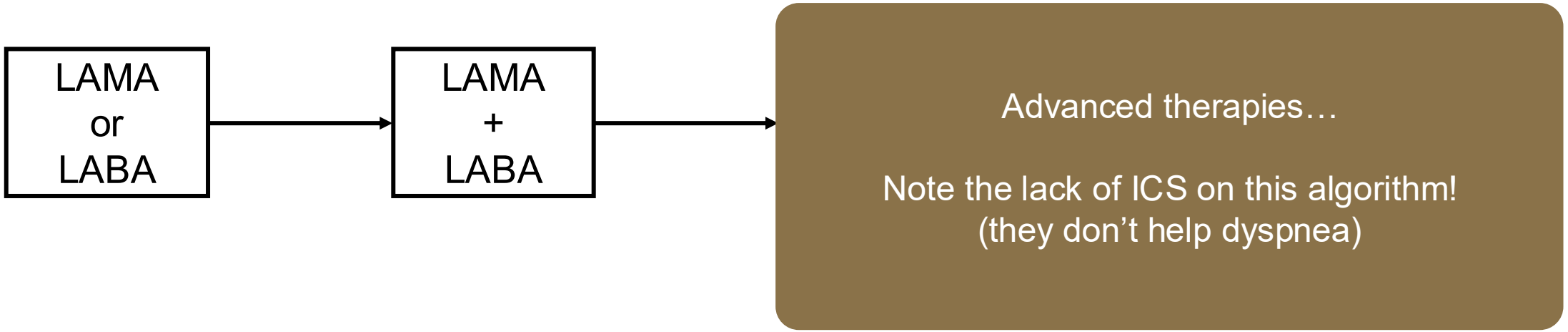


Single inhaler if possible

N Engl J Med 2018;378:1671-80
N Engl J Med 2020; 383:35-48

Lancet. 2018 17;391(10125):1076-1084
AJRCCM 2020 Jun 15;201(12):1508-1516

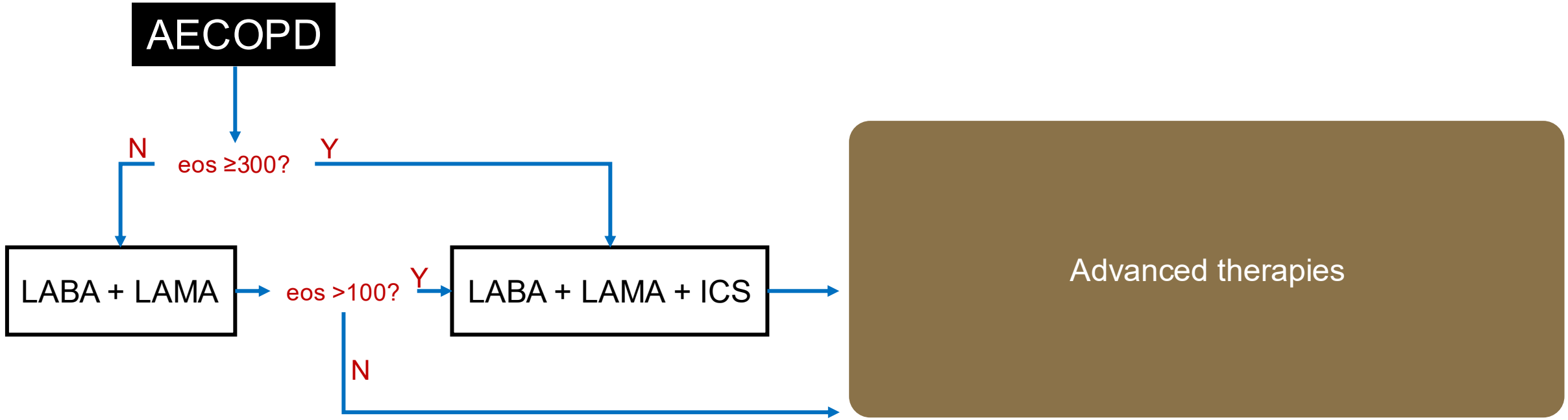
Managing dyspnea in COPD



- Smoking Cessation
- Pulmonary Rehab
- Supplemental O_2 and NIV if indicated
- Regular Aerobic Exercise
- Investigate other causes, treat comorbidities*

*OSA, CHF, CAD, arrhythmias, pulm HTN, anemia, VTE, anxiety/depression, thyroid disease, iron deficiency, etc

Preventing exacerbations in COPD



→ Indicates ongoing AECOPD despite current therapy

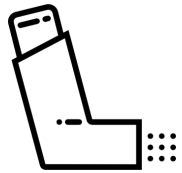
Key non-pharmacologic interventions at every phase

- Smoking cessation
- Pulmonary rehab
- Noninvasive ventilation (if $P_aCO_2 \geq 52$)
- Regular exercise
- Vaccinations (COVID, Flu, RSV)
- Manage comorbidities

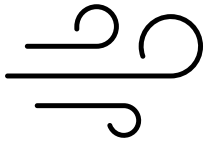
Critical non-pharmacologic interventions

Smoking cessation

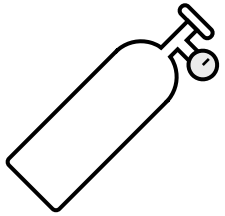
Pulmonary rehab



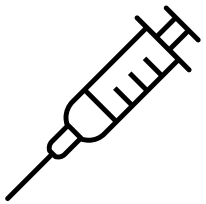
Inhaler teaching



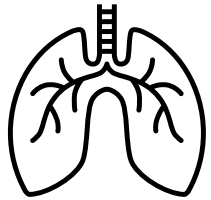
Nocturnal NIV (if chronic hypercapnia)



Supplemental O_2 (if severe resting hypoxemia)



Vaccinations (Influenza, Pneumococcus, RSV, SARS-CoV-2)



Lung cancer screening (if qualifies)

Bold = Possible mortality benefit

Back to case 2

A 68-year-old woman with confirmed COPD, GOLD category B. Currently on LABA/ICS with persistent dyspnea on exertion.

What changes to her inhaler regimen do you recommend?

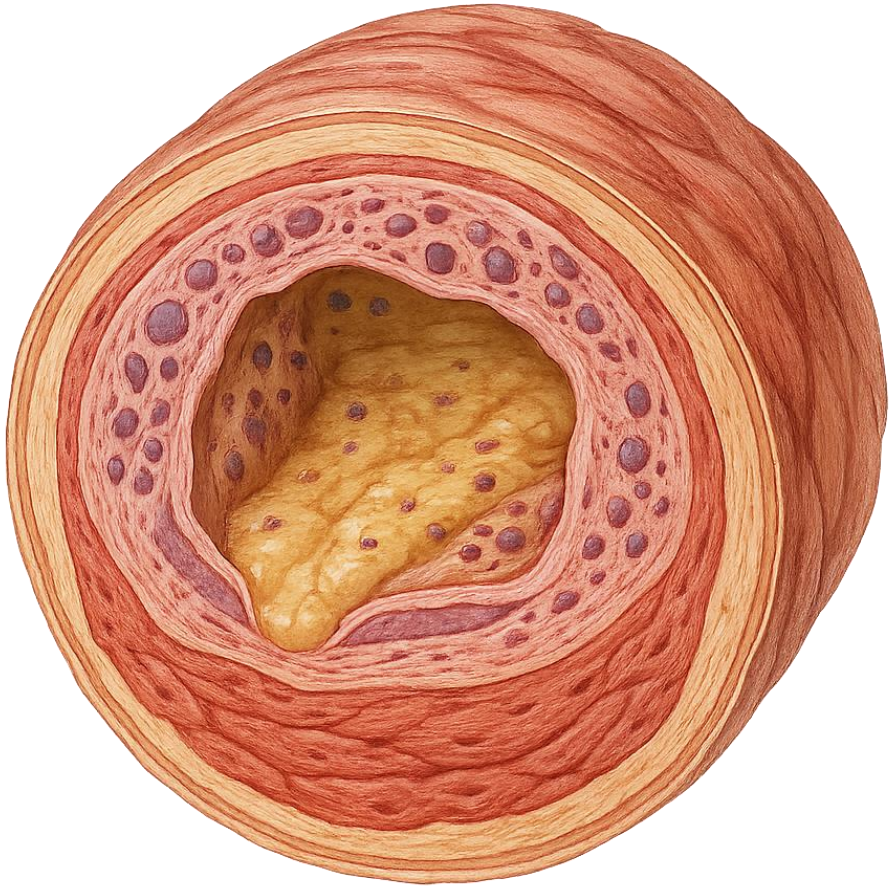
A. Add LAMA to her current regimen
   ✕ Triple therapy not indicated in her case given no exacerbations

B. Stop current ICS/LABA and start LABA/LAMA
   ☑ LABA/LAMA is more effective in COPD and appropriate for her GOLD category

C. Increase the dose of the ICS component of her current inhaler
   ✕ ICS has no impact on symptoms in COPD and should only be added if exacerbations despite LABA/LAMA and serum eos >100

D. Change as-needed albuterol to albuterol/budesonide
   ✕ Albuterol/budesonide should NOT be used in COPD

E. No change to her current regimen
   ✕ ICS/LABA is not appropriate for her GOLD category



Asthma Management Principles

Case 3

A 29-year-old otherwise healthy man presents for a visit to discuss his asthma. He has experienced 2 exacerbations in the last 12 months treated with oral prednisone at home triggered by viral infections. In between these exacerbations he rarely requires his as-needed albuterol inhaler and is not on maintenance therapy. Spirometry is normal today but has revealed mild obstruction in the past when more symptomatic. He is currently asymptomatic.

What changes to his inhaler regimen do you recommend?

A. Start daily low-dose ICS and continue albuterol as needed
B. Start daily low-dose ICS/LABA and continue albuterol as needed
C. Change as-needed albuterol to as-needed formoterol/budesonide
D. No change to current regimen

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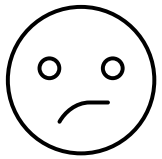
Assessing asthma

Symptom Control

In the past 4 weeks, has the patient had (y/n):

- Daytime asthma symptoms >2x per week?
- Any nighttime awakening due to asthma?
- SABA use as reliever >2x per week (excluding before exercise)?
- Any activity limitation due to asthma?

None	1 – 2	3 – 4
		
Well controlled	Partly controlled	Not controlled

Risks for poor outcome

- Asthma not controlled
- SABA overuse
- Inadequate ICS
- Exposures (e.g. smoking, vaping, allergens, pollution, occupational etc)
- Psychosocial comorbidities
- Low FEV1
- Exacerbation history
- Presence of type II biomarkers
- Frequent or persistent oral steroid use
- Need for high dose ICS
- Poor inhaler technique

Must-know terminology in 2026

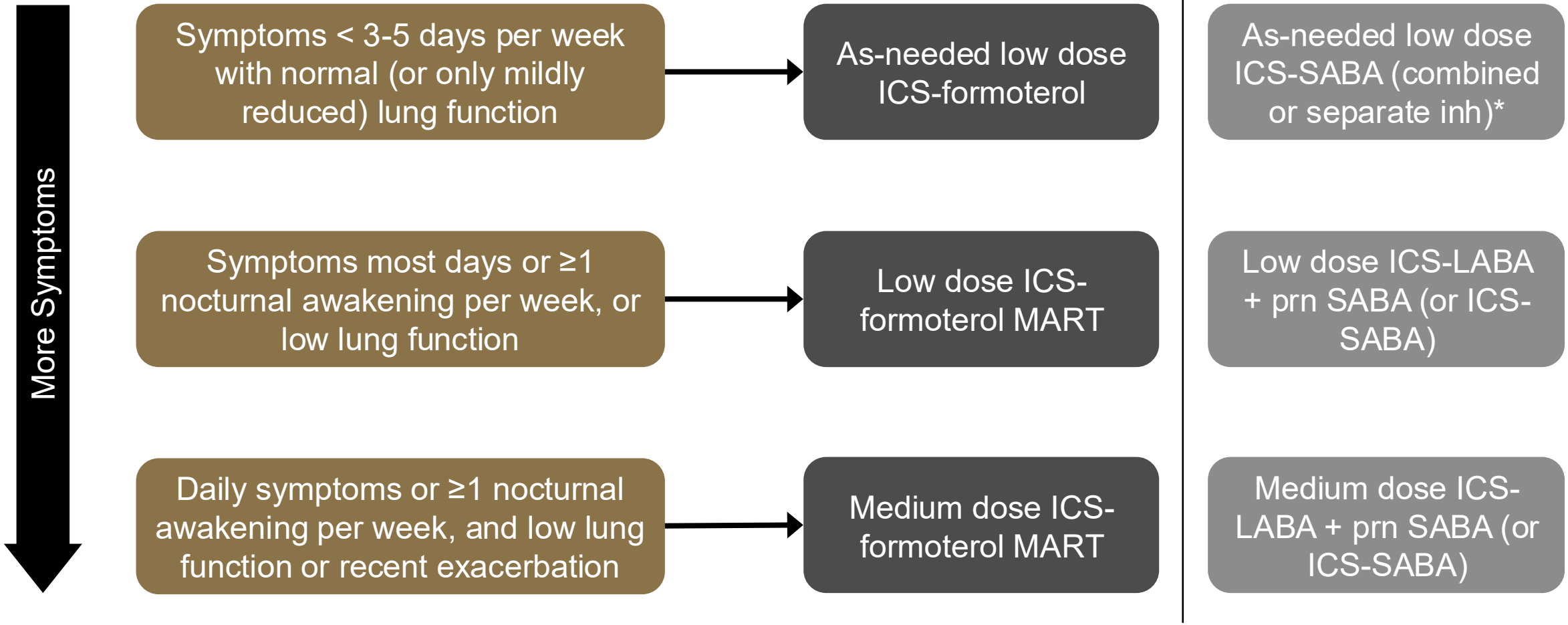
AIR = “Anti-Inflammatory Reliever”

- As-needed SABA-ICS
- As-needed Formoterol-ICS
- As-needed SABA with separate as-needed ICS inhaler

SMART/MART = “(Single) Maintenance and Reliever Therapy”

- *Can only be with **formoterol** containing inhalers*
  - Formoterol onset of action is equivalent to albuterol. Not true for other LABAs (e.g. salmeterol and vilanterol)

Initial treatment selection



Adapted from GINA 2025 Report

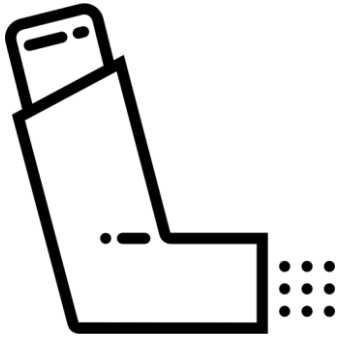
*Alternative for mild symptoms: daily low dose ICS + prn SABA or ICS-SABA

Notes on combination inhaler dosing

Formoterol containing inhalers

Budesonide-formoterol (Symbicort® or Breyna®)

- Low dose: 80mcg-4.5mcg, 2 puffs twice daily
- Medium dose: 160mcg-4.5mcg, 2 puffs twice daily



Mometasone-formoterol (Dulera®)

- Medium dose: 100mcg-5mcg, 2 puffs twice daily
- High dose: 200mcg-5mcg, 2 puffs twice daily

SABA-ICS combination inhaler

Albuterol-budesonide (AirSupra®) 90mcg-80mcg, 1-2 puffs as needed

Alternative approach: instruct patient to take puff of low dose ICS whenever they feel need for rescue albuterol

And don’t forget a spacer chamber!

Benefits of AIR and (S)MART

AIR

Compared to traditional SABA only rescue

- Reduces severe exacerbations by 65% (ICS-Form)
- Reduces ED visits and hospitalizations by 65% (ICS-Form)
- Reduced severe exacerbations by 26-47% (ICS-albuterol)
- ICS-formoterol >> ICS-albuterol based on indirect comparisons

Compared to low-dose ICS + SABA rescue

- Similar exacerbation rates, lower hospitalizations and ED visits
- Patients prefer this

MART

Compared to traditional regimens with ICS or ICS/LABA and SABA rescue

- Reduce exacerbations compared to both higher and lower dose ICS-LABA regimens.
- Overall lower maintenance ICS dose
- Similar to improved symptom control
- *The most effective way to prevent exacerbations in mild to moderate asthma!*

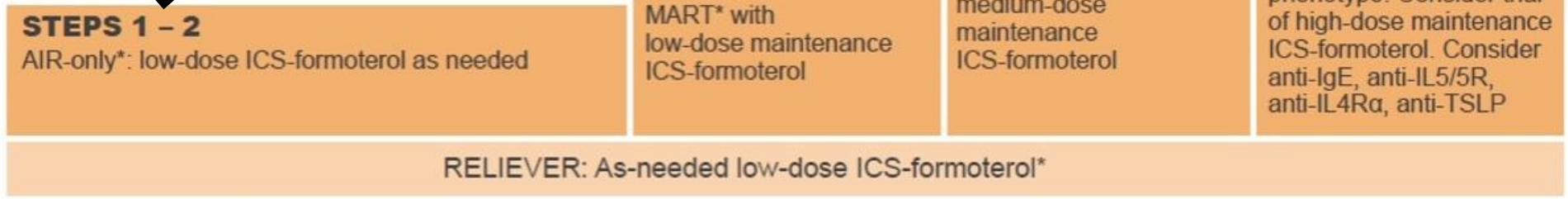
TL;DR These approaches decrease exacerbation risk with similar symptom control and are preferred by patients

From: GINA 2025 Report

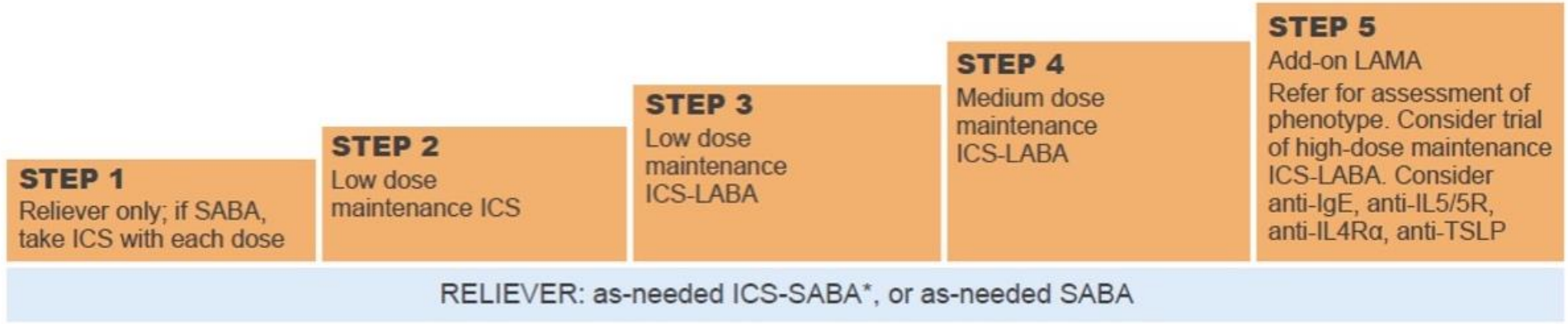
Escalating therapy in asthma

The major barrier to track 1 continues to be insurance formularies… 😫

Track 1 (Preferred) uses AIR and MART



Track 2 (Alternate) uses separate controller and reliever



From: GINA 2025 Report

Back to case 3

A 29-year-old man with mild asthma and 2 exacerbations requiring prednisone in the past year, asymptomatic between episodes.

What changes to his inhaler regimen do you recommend?

A. Start daily low-dose ICS and continue albuterol as needed
   ✗ reasonable and effective. Would decrease exacerbation risk but compliance with daily low-dose ICS is poor. C is better answer
B. Start daily low-dose ICS/LABA and continue albuterol as needed
   ✗ severity wouldn't warrant this, plus same problem as above with compliance concerns
C. Change as-needed albuterol to as-needed formoterol/budesonide
   ☑ preferred approach for mild asthma. Decreases exacerbation risk similar to daily ICS but less concerns with ICS compliance. Alternative would be ICS-albuterol
D. No change to current regimen
   ✗ SABA alone no longer preferred even in mild asthma.

Outline

PFT Review (Obstruction)

Diagnosing asthma and COPD

Contemporary management of asthma and COPD

New therapies for advanced COPD

Case 4

A 61-year-old man with confirmed, very severe COPD continues to struggle with severe dyspnea. He is on a LABA/LAMA with excellent inhaler technique. He has no history of exacerbations and quit smoking 15 years ago. He completed pulmonary rehabilitation with only transient benefit. He was referred for bronchoscopic lung volume reduction but deemed not a candidate. He uses supplemental oxygen at 4 L/min at rest, increasing to 6 L/min with exertion. He has no evidence of heart failure or other major medical issues. He is dissatisfied with his current quality of life due to his severe dyspnea.

What do you recommend to this patient?

A. Start azithromycin three times weekly
B. Start dupilumab 300mg subQ every 2 weeks
C. Change LABA/LAMA to LABA/LAMA/ICS
D. Start ensifentrine 3mg nebulized twice daily
E. Refer for consideration of lung transplantation

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New COPD agents

FDA Approved for COPD

June 2024: Ensifentrine (Ohtuvayre®)

- Completely new class
- PDE 3 & 4 inhibitor

September 2024: Dupilumab (Dupixent®)

- anti IL-4Rα mAb

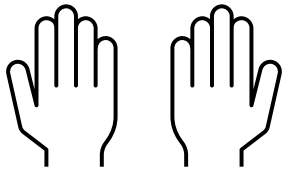
May 2025: Mepolizumab (Nucala®)

- Anti IL-5 mAb

Disease features guide selection

Medications

	Exacerbations	Symptoms
Azithromycin	✓	✗
Roflumilast	✓	✗
Biologic*	✓	✗
Ensifentrine	Probably	?



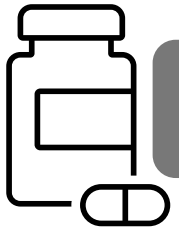
Procedures

BLVR	Maybe	✓
LVRS	?	✓
Lung Transplantation	✓	✓

LVRS: Lung volume reduction surgery
BLVR: Bronchoscopic lung volume reduction

*Dupilumab or mepolizumab

Azithromycin and Roflumilast

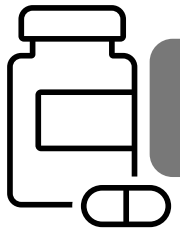


Azithromycin

27% reduction in exacerbations over 1 year

Less effective in active smokers
Avoid if concern for NTM

Side effects:
QTc, hearing loss, macrolide resistance



Roflumilast

13% reduction in exacerbations over 1 year

Only indicated if chronic bronchitis
FEV1 must be <50%

Side effects:
GI (nausea, vomiting, diarrhea), psychiatric, weight loss

NEJM. 2011 Aug 25;365(8):689-98
Lancet 385:857, 2015
Chong. Cochrane Database Syst Rev. 2017

Ensifentrine

3mg twice daily

Mechanism: Nebulized PDE3/4i (bronchodilator and anti-inflammatory)

ENHANCE 1 & 2: ~1500 patients with GOLD B COPD(FEV1 30-70%)

- Either not on maintenance or LAMA *or* LABA +/- ICS
- Ensifentrine vs placebo

Undertreated?
(not on LABA-LAMA)

Results:

- Improved FEV1 by ~80mL
- ~40% reduction in exacerbations
- No difference in QOL
- No adverse events or side effects

Unclear if benefits would extend to patients on LABA-LAMA or Triple Rx

Am J Respir Crit Care Med. 2023 Jun 26;208(4):406–416

Proven record of biologics for asthma

Agent	Indication(s)	Benefits				
		↓ Sx	↓ Exac	↑QOL	↓or OGs	↑FEV1
Omalizumab (anti-IgE)	Severe allergic asthma	✓	✓	✓		Small
Mepolizumab (anti-IL-5)	Severe eosinophilic asthma	✓	✓	✓	✓*	✓
Reslizumab (anti-IL-5)	Severe eosinophilic asthma	✓	✓	✓		✓
Benralizumab (anti-IL-5Rα)	Severe eosinophilic asthma	✓	✓	✓	✓*	✓
Dupilumab (anti IL-4Rα)	Severe eosinophilic asthma; OG-dependent asthma	✓	✓	✓	✓	✓
Tezepelumab (anti-TSLP)	Severe asthma	✓	✓	✓		✓

Adapted from: N Engl J Med 2022;386:157-71.

*Only if blood eos ≥ 150

Biologics in COPD summary to date

Agent	Serum eosinophil threshold studied (cells/uL)	Benefits		
		↓ Exac	↓ Sx	↑FEV1
Dupilumab (anti IL-4Rα)	≥300 at screening	+	+/-	+
Mepolizumab (anti-IL-5)	≥300 at screening	+	-	-
Mepolizumab (anti-IL-5)	≥150 at screening or ≥300 in last year	-	-	-
Benralizumab (anti-IL-5Rα)	≥220 at enrollment	-	-	-

Dupilumab (Sept 2024) and Mepolizumab (May 2025) FDA approved for COPD as add on maintenance therapy with inadequately controlled COPD and eosinophilic phenotype (≥300/ul)

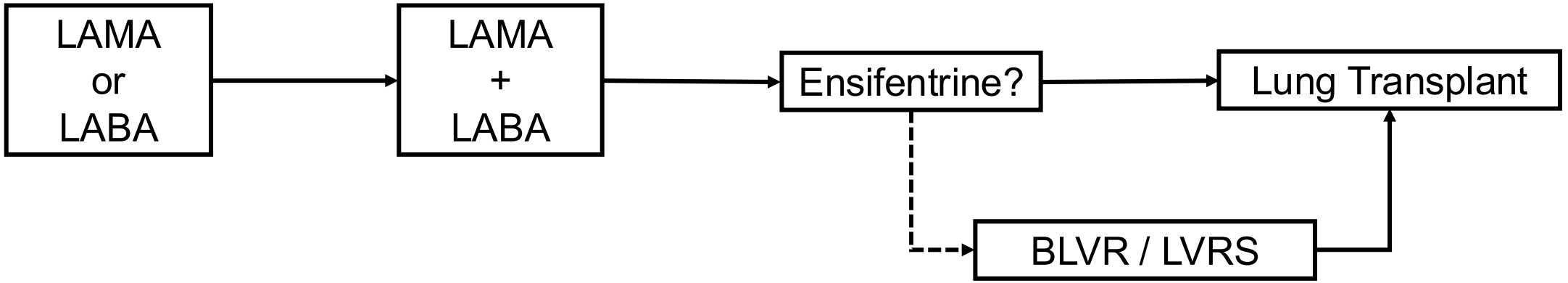
N Engl J Med 2023;389:205-14
N Engl J Med 2024;390:2274-2283
N Engl J Med 2017;377:1613-29
N Engl J Med 2025;392:1710-20
N Engl J Med 2019;381:1023-1034

Biologics in COPD

	Dupilumab	Mepolizumab
Exacerbations	30 – 34% reduction	21% Reduction
Lung Function	Improved by ~80mL	No change
Symptoms/QOL	Small improvement in 1 of 2 studies	No change

No major events for either drug

Managing dyspnea in COPD



Smoking Cessation

Pulmonary Rehab

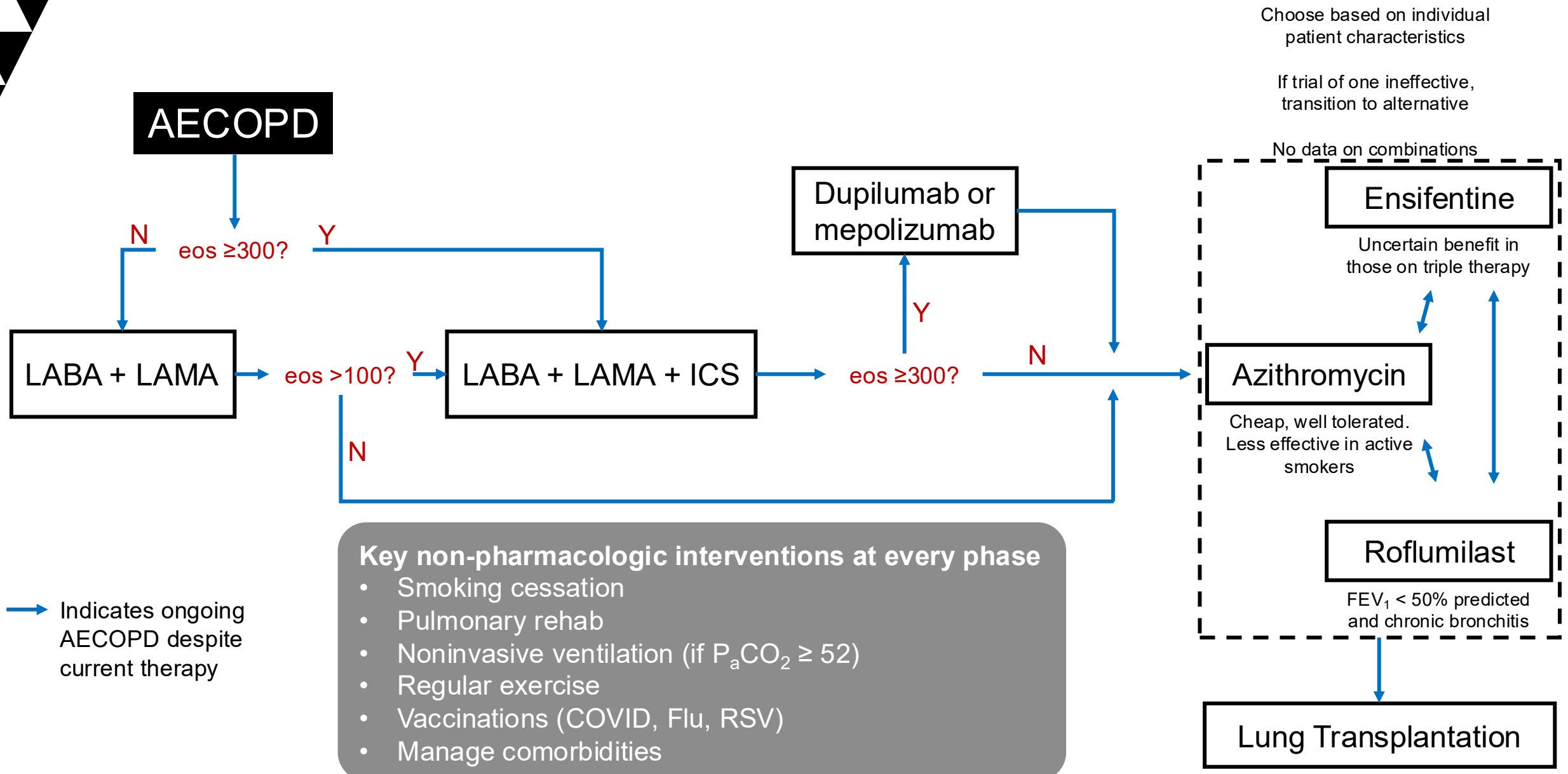
Supplemental O_2 and NIV if indicated

Regular Aerobic Exercise

Investigate other causes, treat comorbidities*

*OSA, CHF, CAD, arrhythmias, pulm HTN, anemia, VTE, anxiety/depression, thyroid disease, iron deficiency, etc

Preventing exacerbations in COPD



Back to case 4

A 61-year-old man with very severe COPD (GOLD B) and refractory dyspnea despite maximal therapy, pulmonary rehab, and supplemental O2. Not BLVR candidate. No other identifiable comorbidities.

What do you recommend to this patient?

A. Start azithromycin three times weekly
   ✕ Only reduces exacerbations
B. Start dupilumab 300mg subQ every 2 weeks
   ✕ Biologics only reduce exacerbations (in patients with serum eos ≥300)
C. Change LABA/LAMA to LABA/LAMA/ICS
   ✕ Not indicated given GOLD category, ICS don't help with symptoms and may increase risk of pneumonia
D. Start ensifentrine 3mg nebulized twice daily
   ✕ Could consider, but benefit is uncertain. Mainly reduced exacerbations in less severe COPD
E. Refer for consideration of lung transplantation
   ☑ Pt has refractory dyspnea without other pharmacologic or non-pharmacologic options

Conclusions

1. Accurate diagnosis of obstructive disease requires integrating clinical history with PFTs in addition to other data.

2. Asthma is a variable disease that doesn't always require the presence of obstruction, whereas COPD is usually persistent or progressive and requires the presence of obstruction.

3. Management of inhaled medications for asthma and COPD differ, specifically where ICS are initiated (first in asthma, last in COPD).

4. The pharmacologic toolbox for COPD is finally expanding into new classes of medications.

Questions?

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