

Chronic Obstructive Pulmonary Disease

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Associate Physician

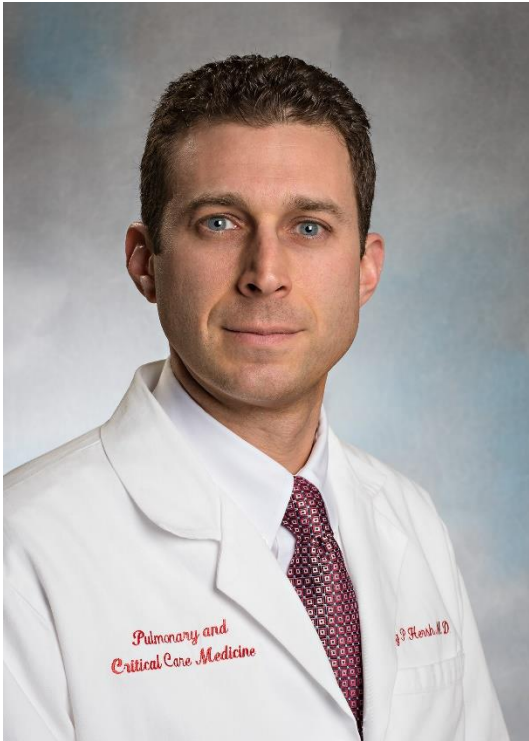
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- ▶ Medical School: Univ of Pennsylvania
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- ▶ Professor of Medicine at BWH
 - Clinical focus: COPD, Alpha-1 antitrypsin deficiency, severe asthma
 - Research focus: COPD epidemiology and genetics

Disclosures

- ▶ Consulting fees:
 - AstraZeneca, Chiesi, Genentech, Ono Pharma, Sanofi, Takeda

Objectives

- ▶ Review the diagnosis and assessment of the patient with COPD
 - ▶ Highlight current treatment strategies for stable COPD
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Outline

- ▶ COPD: Definition and pathophysiology
 - ▶ Assessment of COPD Patients
 - ▶ Treatment of stable COPD
 - ▶ Summary and Review Questions
- 

Outline

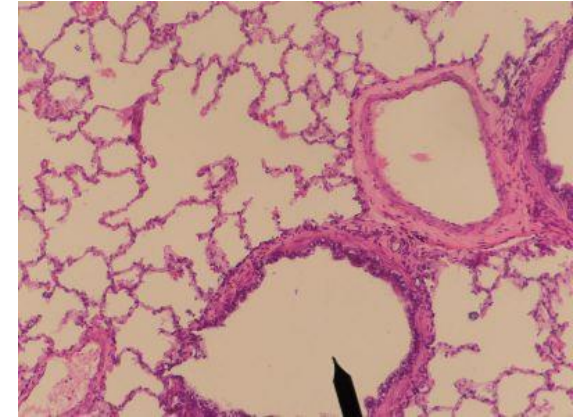
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Chronic obstructive pulmonary disease

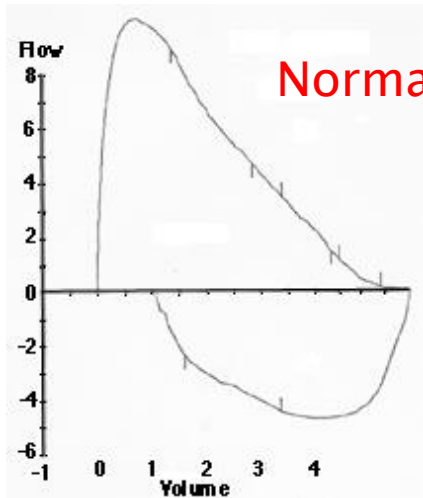
- ▶ Heterogeneous lung condition
- ▶ Chronic respiratory symptoms
- ▶ Abnormalities of the airways and/or alveoli
- ▶ Persistent, often progressive, airflow obstruction

Multiple pathologies of COPD

Normal

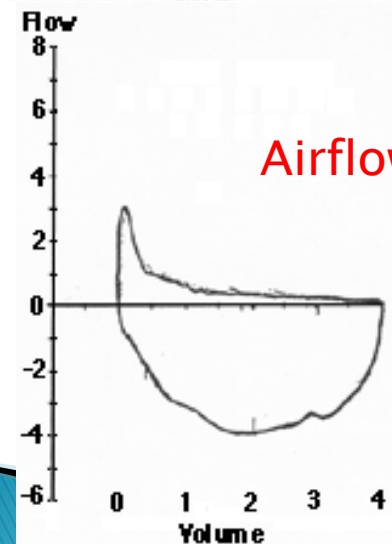
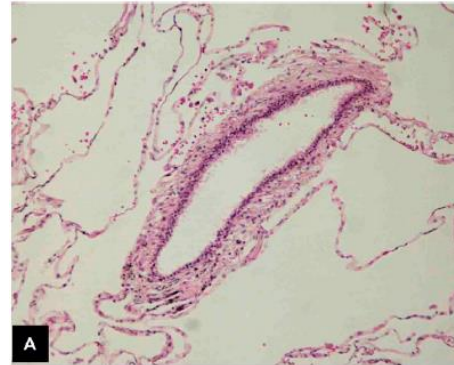


histology-world.com



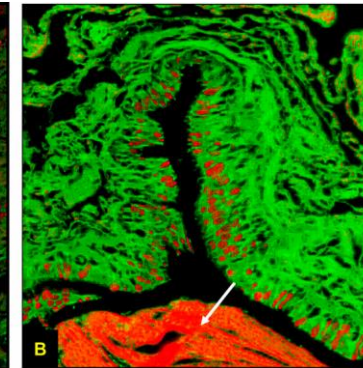
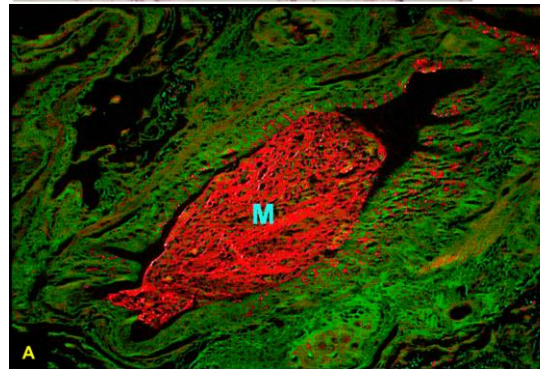
Normal spirometry

Emphysema

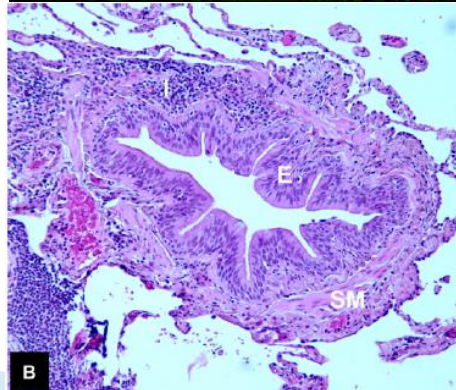


Airflow obstruction

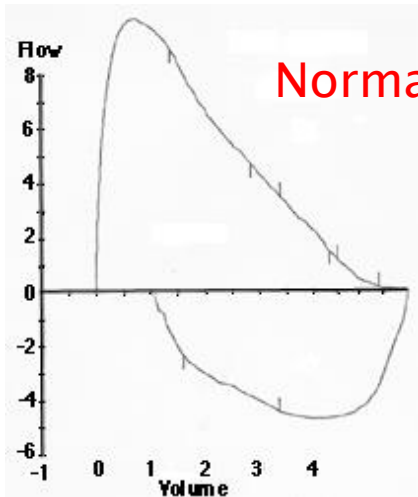
Mucus metaplasia



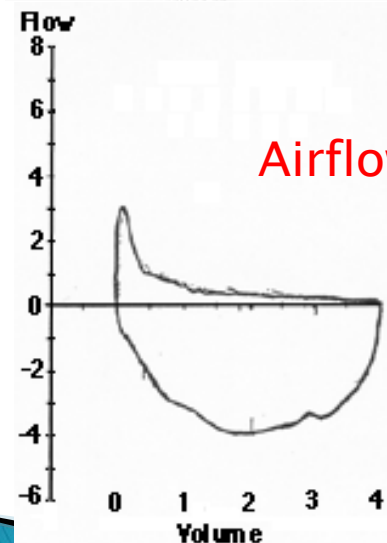
Small airway disease



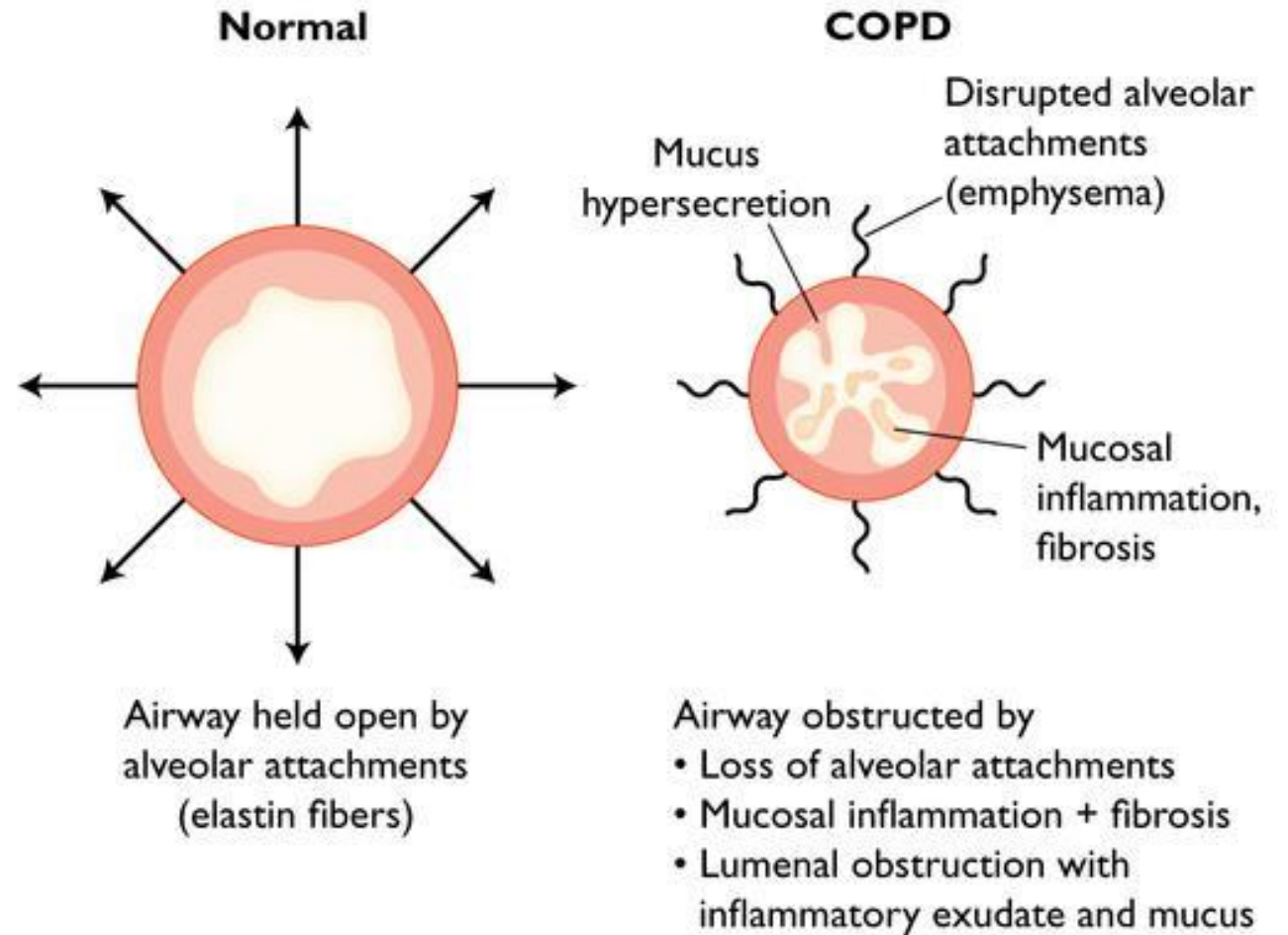
Mechanisms of airflow limitation



Normal spirometry



Airflow obstruction



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Outline

- ▶ COPD: Definition and pathophysiology
 - ▶ **Assessment of COPD Patients**
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- 

Symptoms and Signs of COPD

Symptoms

Cough

Sputum

Dyspnea

Wheeze

Chest tightness

Weight loss

Muscle weakness

Edema

Depression

Physical Exam

Tripod posture

Skin: cyanosis

Breathing: tachypnea, pursed lip breathing, prolonged expiration, accessory muscle use

Barrel Chest

Breath Sounds: distant, wheezes

Cardiac: distant, increased P2, JVD, edema

Cachexia

COPD Assessment Test (CAT)

I never cough	0 1 2 3 4 5	I cough all the time
I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5	My chest is completely full of phlegm (mucus)
My chest does not feel tight at all	0 1 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 1 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	0 1 2 3 4 5	I am very limited doing activities at home
I am confident leaving my home despite my lung condition	0 1 2 3 4 5	I am not at all confident leaving my home because of my lung condition
I sleep soundly	0 1 2 3 4 5	I don't sleep soundly because of my lung condition
I have lots of energy	0 1 2 3 4 5	I have no energy at all

Modified MRC Dyspnea scale

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.

Mahler DA, Chest 1988;93:580
Jones P, ERJ 2009;34:648



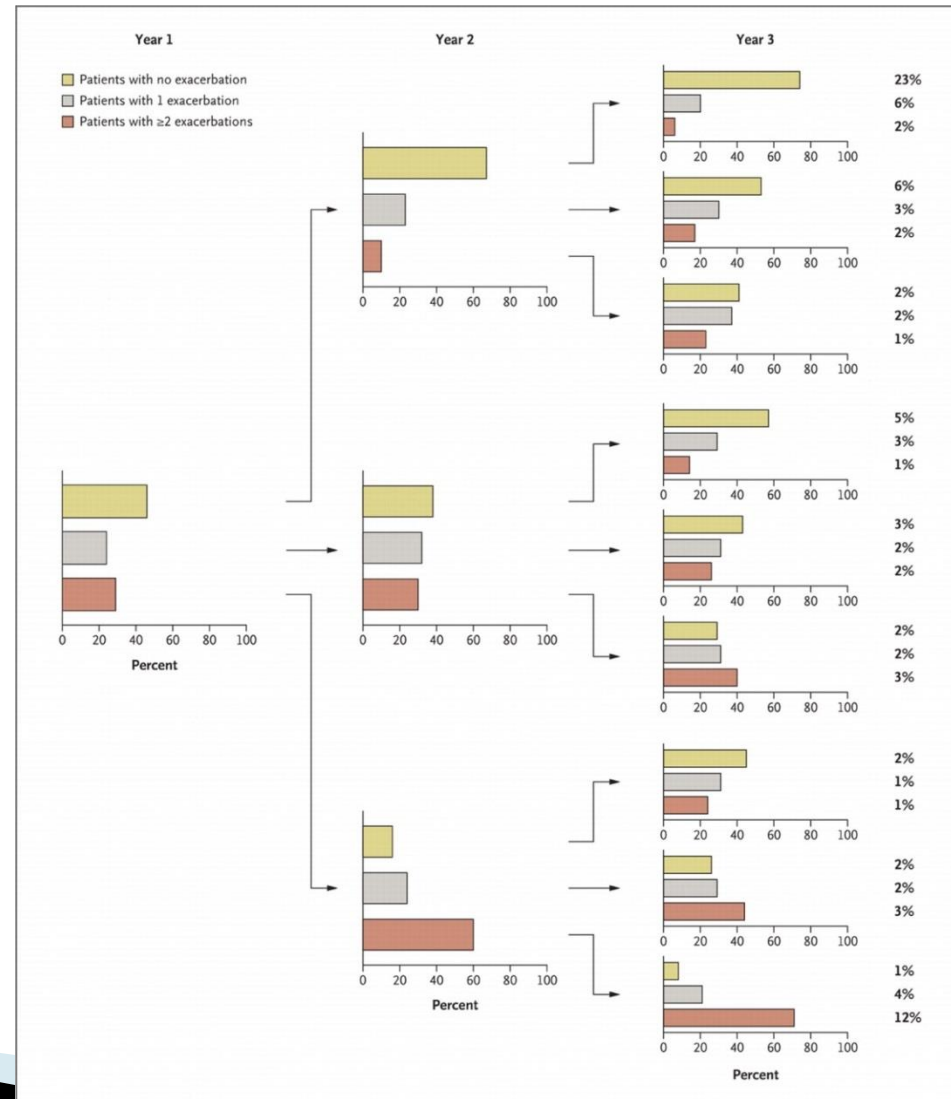
Classification of Severity of Airflow Limitation in COPD*

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

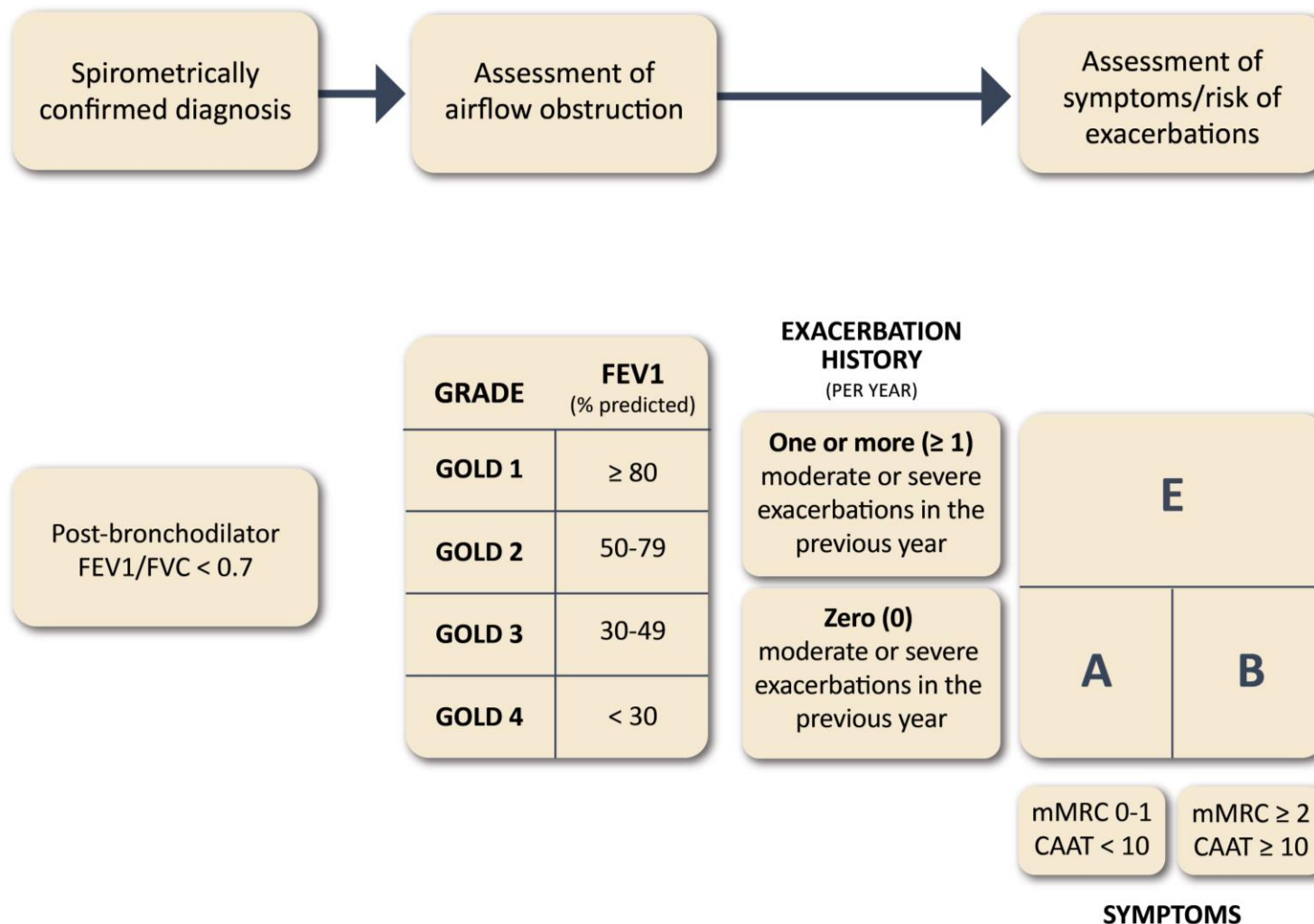
**Based on Post-Bronchodilator FEV_1*

Exacerbation Risk: Past exacerbations are the best predictor of future exacerbations



GOLD ABE Assessment Tool

Figure 2.13

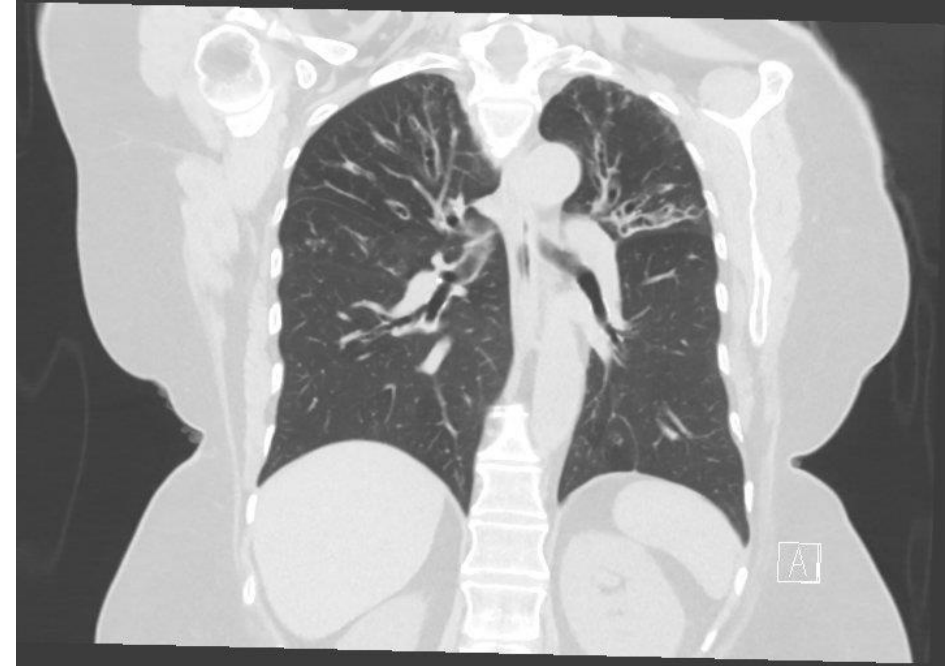


Differential Diagnosis

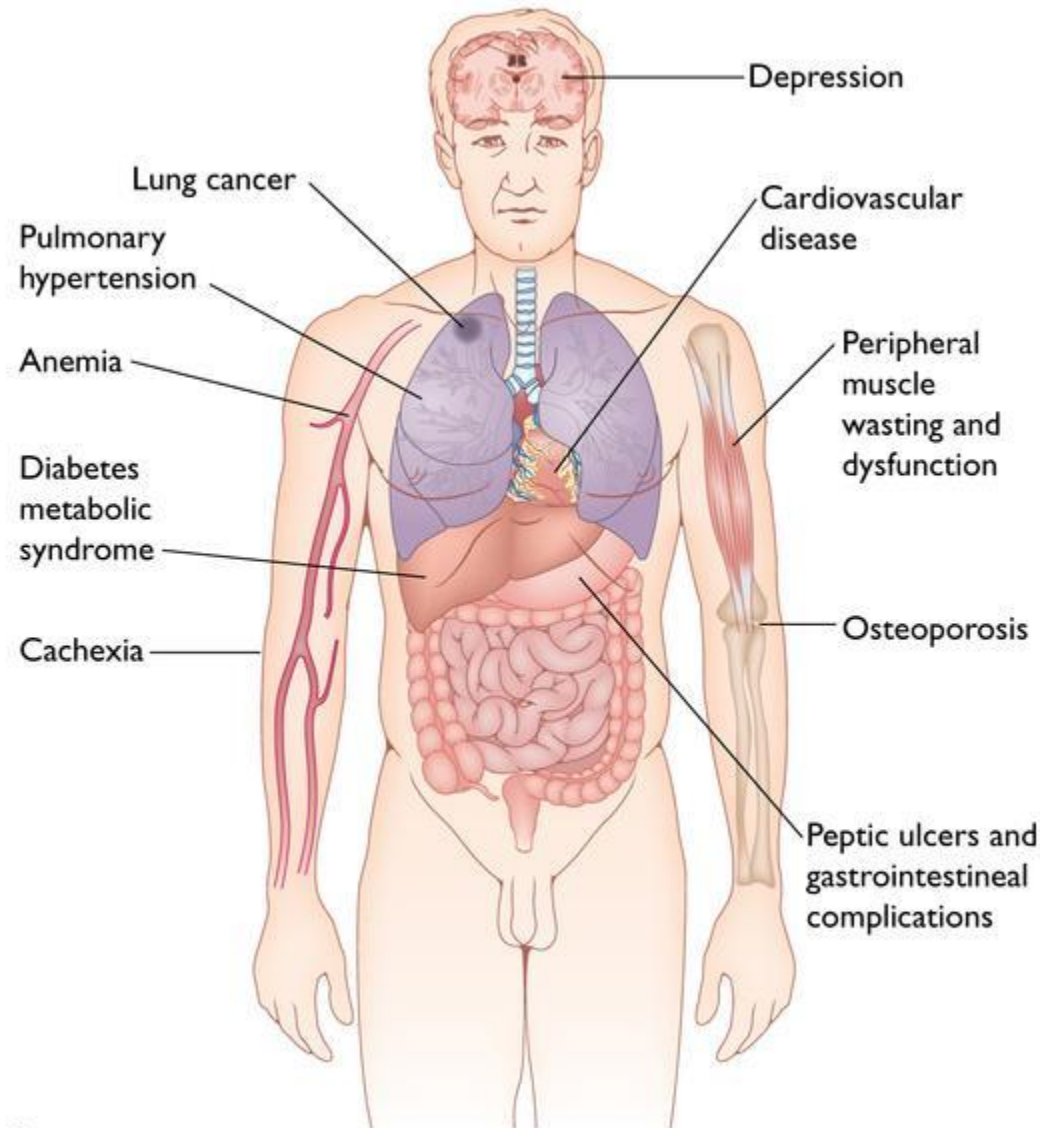
- ▶ Asthma
 - ▶ Bronchiectasis
 - ▶ Interstitial Lung Disease
 - ▶ Congestive Heart Failure
 - ▶ Tuberculosis
 - ▶ Obliterative Bronchiolitis
 - ▶ Diffuse Panbronchiolitis
- 

Other assessments

- ▶ Chest CT scan
 - Differential diagnosis
 - Bronchiectasis
 - “symptoms out of proportion”
 - Lung cancer screening
 - Lung volume reduction
- ▶ CBC with differential
- ▶ Alpha-1 antitrypsin deficiency
 - 1–2% of COPD in USA
 - AAT level +/- genotype or protein phenotype



Comorbidities: COPD is a systemic disease



A

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Crapo J, ed.,
Atlas of COPD, 2009

Outline

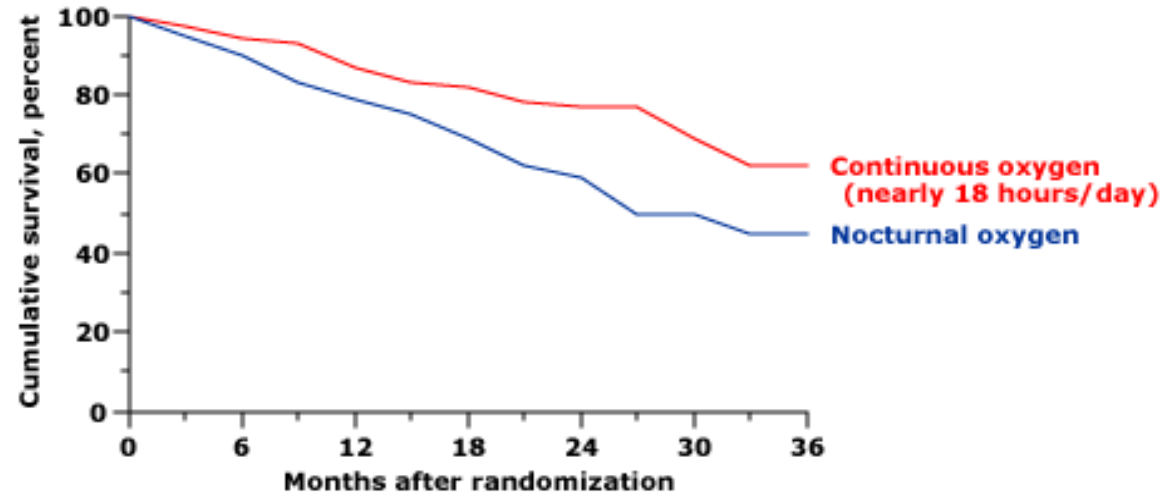
- ▶ COPD: Definition and pathophysiology
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COPD treatment: overview

- ▶ Goals of treatment
 1. Reduce symptoms
 2. Reduce risk
- ▶ Smoking Cessation
- ▶ Supplemental oxygen
- ▶ Pulmonary Rehabilitation
- ▶ Vaccinations
 - Influenza, Pneumococcal, COVID-19, RSV

Supplemental oxygen reduces mortality in hypoxemic COPD patients

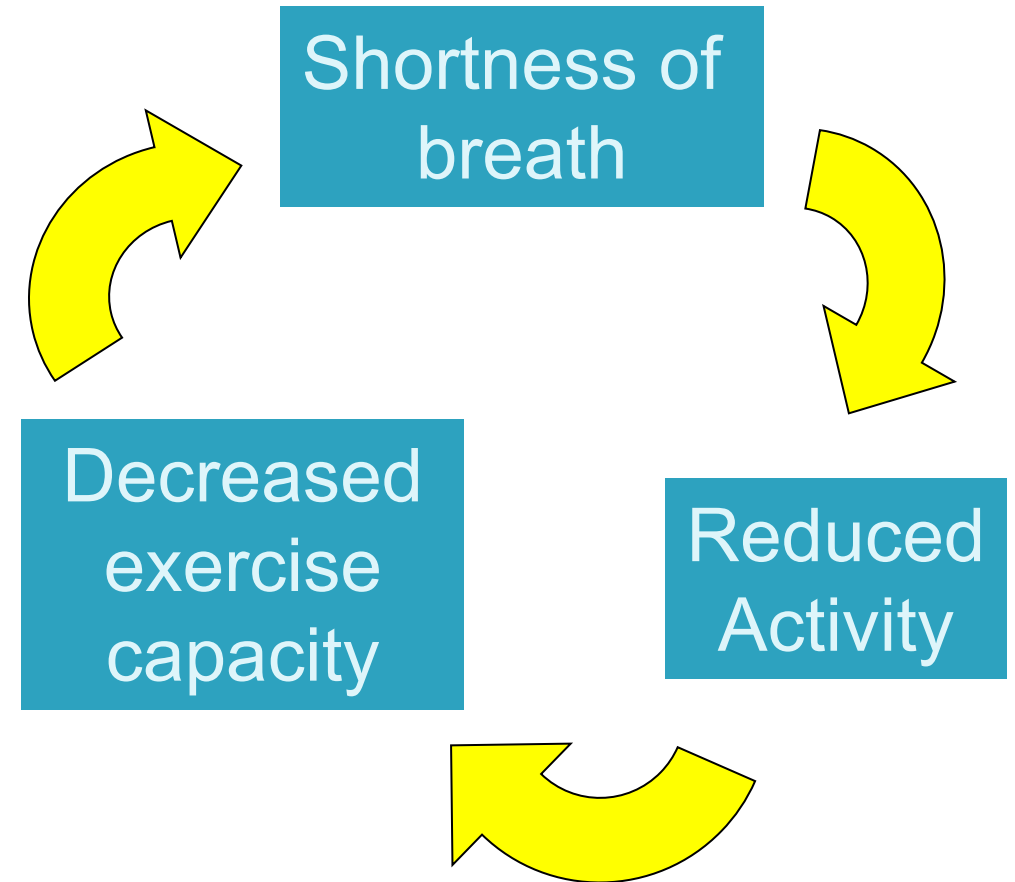
NOTT trial, Ann Intern Med 1980;93:391



- ▶ $\text{PaO}_2 \leq 55\text{mmHg}$ or $\text{SaO}_2 \leq 88\%$, or
- ▶ $\text{PaO}_2 \leq 60\text{mmHg}$ or $\text{SaO}_2 \leq 89\%$,
 - with cor pulmonale, right heart failure or polycythemia
- ▶ Benefit for exercise-induced desaturation?

Pulmonary Rehabilitation

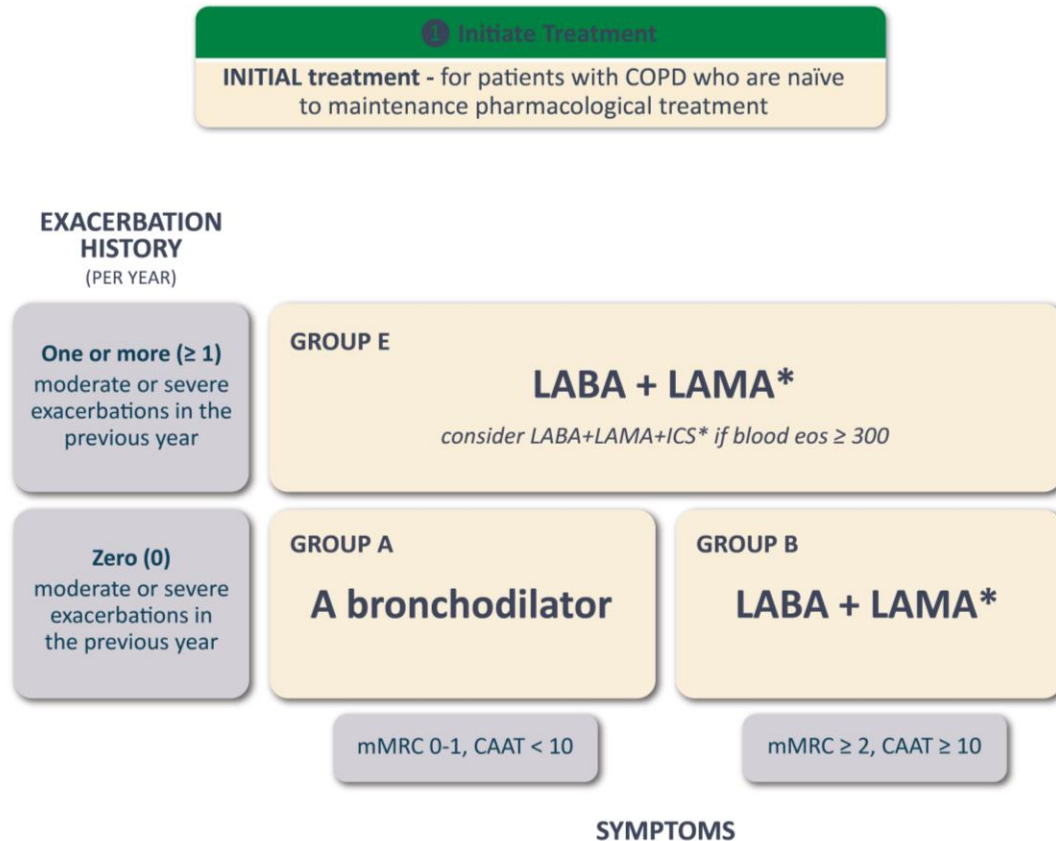
- ▶ Multidisciplinary
- ▶ 6–12 weeks
 - 2–3 times/week
- ▶ Exercise
 - Lower body
 - Upper body
 - Respiratory Muscle Training
- ▶ Education
- ▶ Psychosocial Support



Medication algorithms

Initial Pharmacological Treatment

Figure 3.8

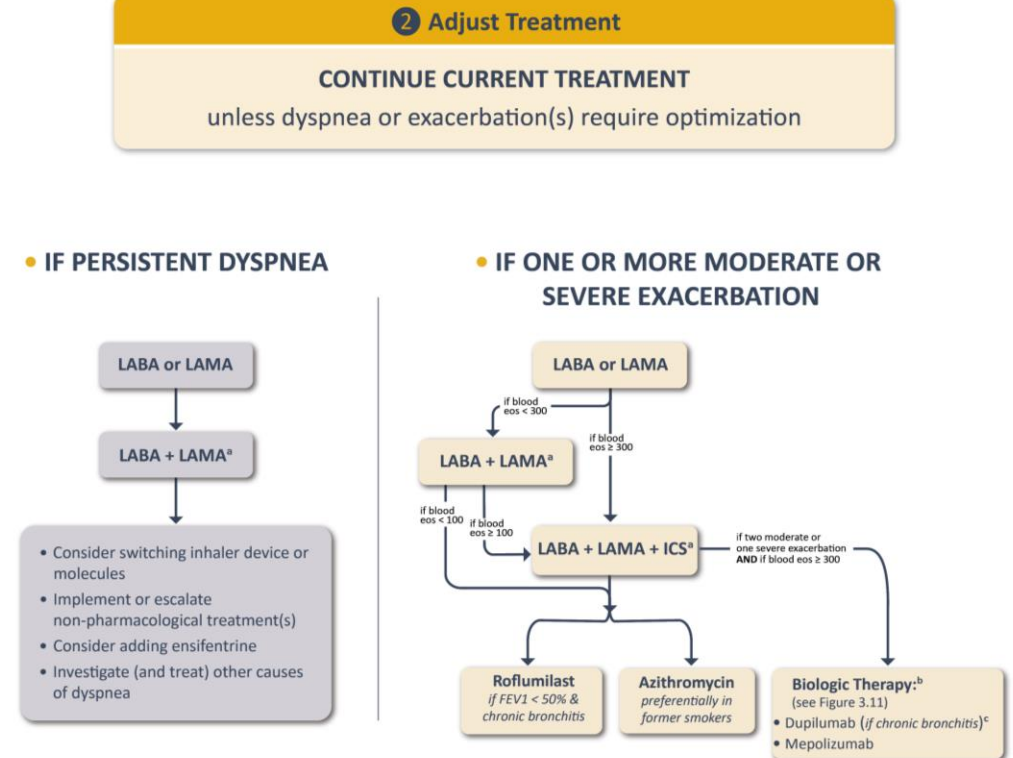


*Single inhaler therapy may be more convenient and effective than multiple inhalers; single inhalers improve adherence to treatment

Exacerbations refers to the number of exacerbations per year; eos: blood eosinophil count in cells per microliter; mMRC: modified Medical Research Council dyspnea questionnaire; CAAT™: Chronic Airways Assessment Test™.

Follow-up Pharmacological Treatment

Figure 3.9



*Single inhaler therapy may be more convenient and effective than multiple inhalers; single inhalers improve adherence to treatment.

^bListed in order of approval in the US.

^cPatient-reported history of chronic bronchitis (chronic productive cough) for 3 months in the year up to screening, absent other known causes.

Consider de-escalation of ICS if pneumonia or other considerable side-effects. In case of blood eosinophils ≥ 300 cells/ μ l de-escalation is more likely to be associated with the development of exacerbations.

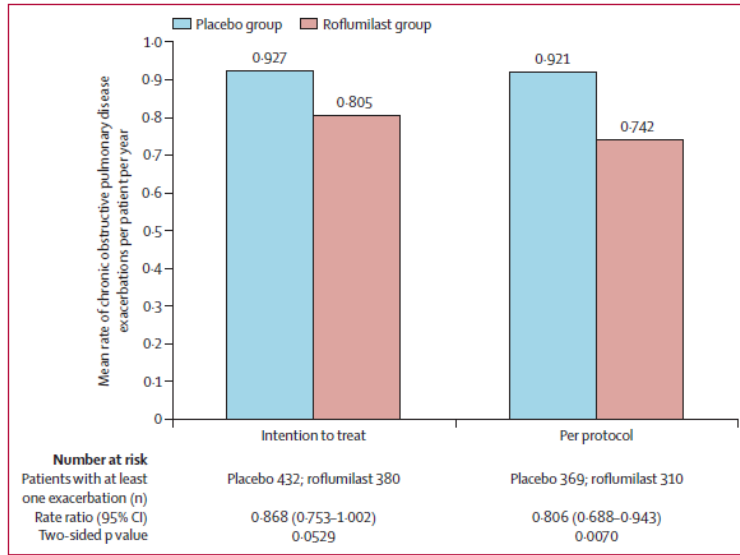
COPD pharmacotherapy: general principles

- ▶ Bronchodilators are first-line
- ▶ Long-acting: LABA or LAMA
- ▶ Dual bronchodilators: LAMA+LABA
- ▶ Short-acting bronchodilators in all patients

- ▶ Targeted use of inhaled corticosteroids
 - blood eosinophil count
- ▶ Triple therapy: LABA+LAMA+ICS
- ▶ Risk of pneumonia

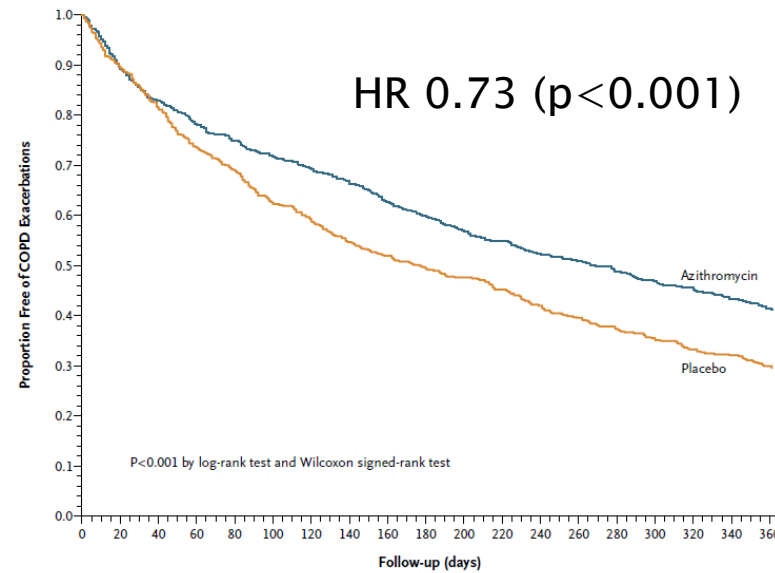
Oral therapies to decrease exacerbation risk

Roflumilast



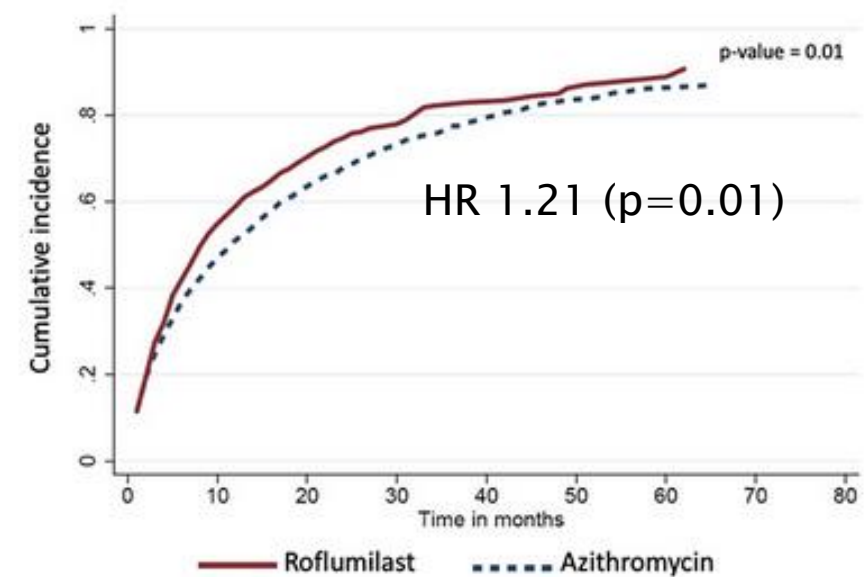
Severe COPD ($FEV_1 < 50\%$)
chronic bronchitis
exacerbation history
GI side effects

Azithromycin 250mg daily



More effective: older, ex-smokers,
milder COPD
Adverse effect: hearing loss

Comparison

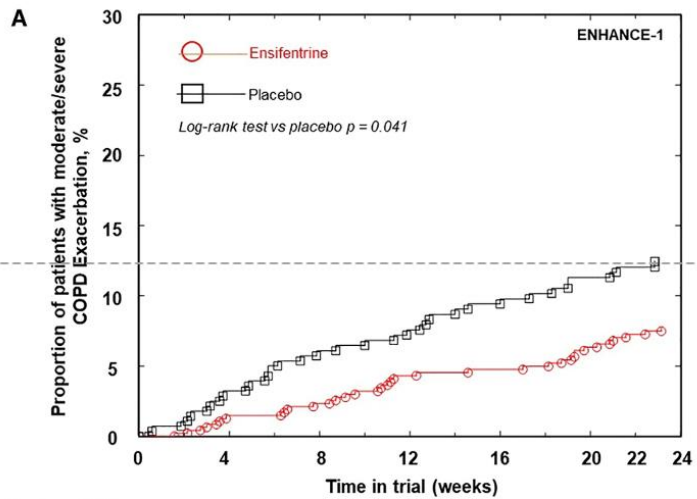


VA database study:
Prefers azithromycin

Martinez, Lancet 2015;385:857
Albert, NEJM 2011;365:689
Lam, JCOOPDF 2021;8:450

Recently approved COPD therapies

Ensifentrine:
nebulized PDE3/4 inhibitor

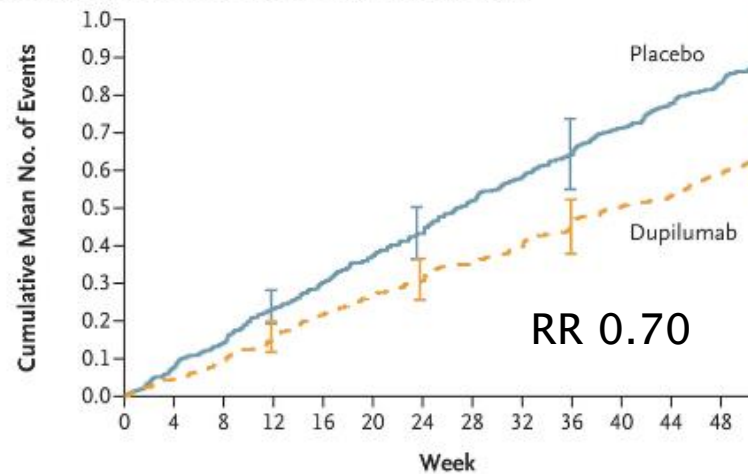


Number at Risk								
Ensifentrine	477	466	453	431	422	412	404	279
Placebo	283	270	258	250	243	235	232	155

Bronchodilator
Anti-inflammatory

Dupilumab: anti-IL4/13

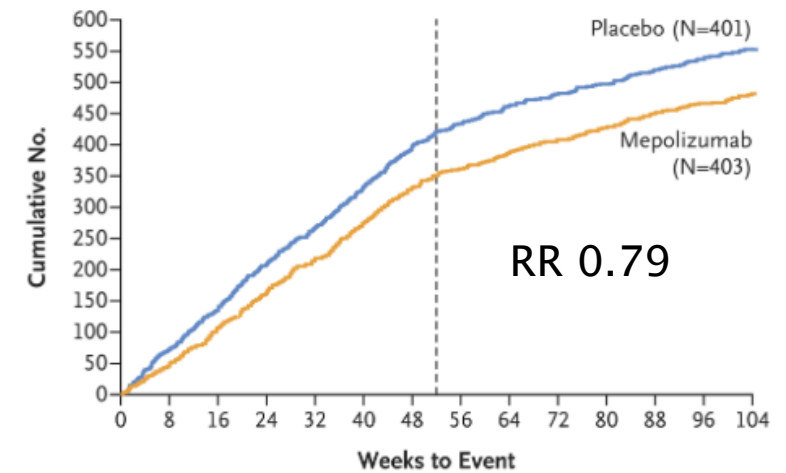
A Cumulative Moderate or Severe COPD Exacerbations



Blood eosinophils ≥ 300
Exacerbation history

Mepolizumab: anti-IL5

A Moderate or Severe Exacerbations



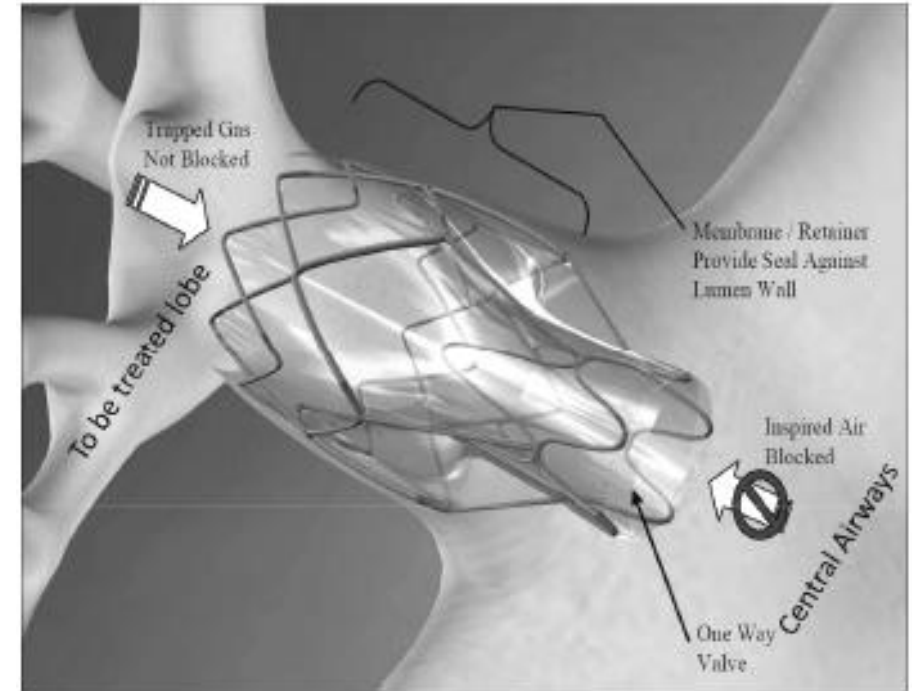
Blood eosinophils ≥ 150 (?)
Exacerbation history

Anzueto, AJRCCM 2023;208:406

Bhatt, NEJM 2023;389:205. Sciurba, NEJM 2025;392:1710

Surgical or interventional treatments

- ▶ Lung volume reduction surgery
 - Upper lobe predominant
 - Low exercise capacity
- ▶ Bronchoscopic lung volume reduction
- ▶ Lung transplantation



NETT, NEJM 2003;348:2059

*Klooster K, NEJM 2015;373:2325

Davey C, Lancet 2015;386:1066

Yusen R, J Heart Lung Transplant 2015;34:1264

Outline

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Summary (1)

- ▶ COPD includes emphysema, large and small airway disease
 - ▶ Spirometry is essential for diagnosis
 - ▶ Multidimensional assessment
 - Symptoms
 - Airflow limitation
 - Exacerbation risk
 - Comorbidities
- 

Summary (2)

- ▶ Tried and true treatments
 - Smoking cessation
 - Supplemental oxygen
 - Pulmonary rehab
- ▶ Pharmacotherapy
 - Bronchodilators are first line
 - LAMA+LABA
 - ICS: add-on/combination, e.g. elevated BEC
 - Azithromycin or roflumilast for frequent exacerbations
 - Newer therapies: ensifentrine, dupilumab, mepolizumab

1) A 65 year old male current smoker with presents with cough and exertional dyspnea (MMRC 2). He had one exacerbation last year. $FEV1 = 55\%$ predicted, $FEV1 / FVC = 0.6$. Blood eos = 50/ul. Appropriate treatments include:

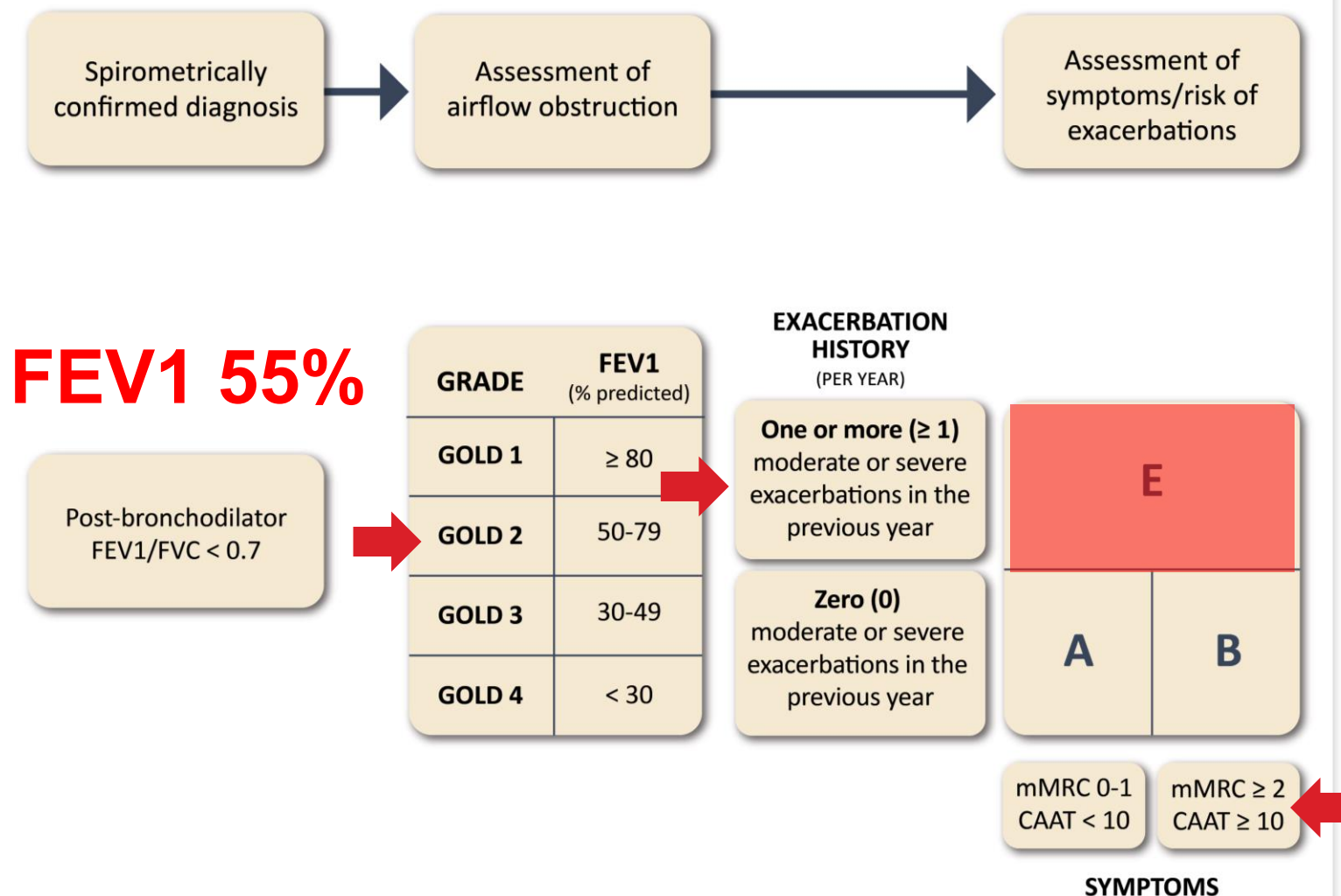
- a) LABA+LAMA
- b) Triple therapy (LABA+LAMA+ICS)
- c) Nicotine replacement therapy
- d) All of the above
- e) (a) and (c) only

1) A 65 year old male current smoker with presents with cough and exertional dyspnea (MMRC 2). He had one exacerbation last year. $FEV1 = 55\%$ predicted, $FEV1 / FVC = 0.6$. Blood eos = 50/ul. Appropriate treatments include:

- a) LABA+LAMA
- b) Triple therapy (LABA+LAMA+ICS)
- c) Nicotine replacement therapy
- d) All of the above
- e) (a) and (c) only

GOLD ABE Assessment Tool

Figure 2.13



Treatment: group E

- ▶ Bronchodilators first-line
 - LAMA+LABA combination preferred
 - ▶ ICS for high blood eosinophils
 - ▶ Smoking cessation for all current smokers
 - ▶ Assessment of comorbidities
- 

2) You see a 70 year-old woman in follow-up after hospital admission for a COPD exacerbation. She has daily cough and sputum. She has to stop walking after a few minutes on flat ground. She uses continuous supplemental oxygen at 2 lpm. She was treated with antibiotics for acute bronchitis 6 months ago. You order spirometry, and her FEV₁ is 45% predicted.

Which of the following is her strongest risk factor for a future COPD exacerbation?

- A. Chronic bronchitis symptoms
- B. FEV₁ < 50% predicted
- C. History of two or more COPD exacerbations in the past year
- D. Use of supplemental O₂
- E. MMRC dyspnea score ≥ 2

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COPD exacerbations

- ▶ Definition: treatment with antibiotics and/or systemic corticosteroids for a chest illness
- ▶ Risk factors:
 - severe airflow obstruction, current smoking, COPD symptoms, GERD, elevated WBC, elevated blood eosinophils
- ▶ High risk:
 - 2 or more exacerbations in previous year

References

- ▶ Global Initiative for Chronic Obstructive Lung Disease, Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease, available at www.goldcopd.org
 - ▶ COPD Foundation, www.copdfoundation.org
 - ▶ Wedzicha JA, et al. Prevention of COPD exacerbations: an ERS/ATS guideline. Eur Respir J 2017;50:1602265.
 - ▶ Nici L, et al., Pharmacologic Management of Chronic Obstructive Pulmonary Disease. An Official American Thoracic Society Clinical Practice Guideline. Am J Respir Crit Care Med 2020;201:e56–e69
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