Apogee
CLINICAL IMMERSION

Overview of COPD

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Conflicts of Interest

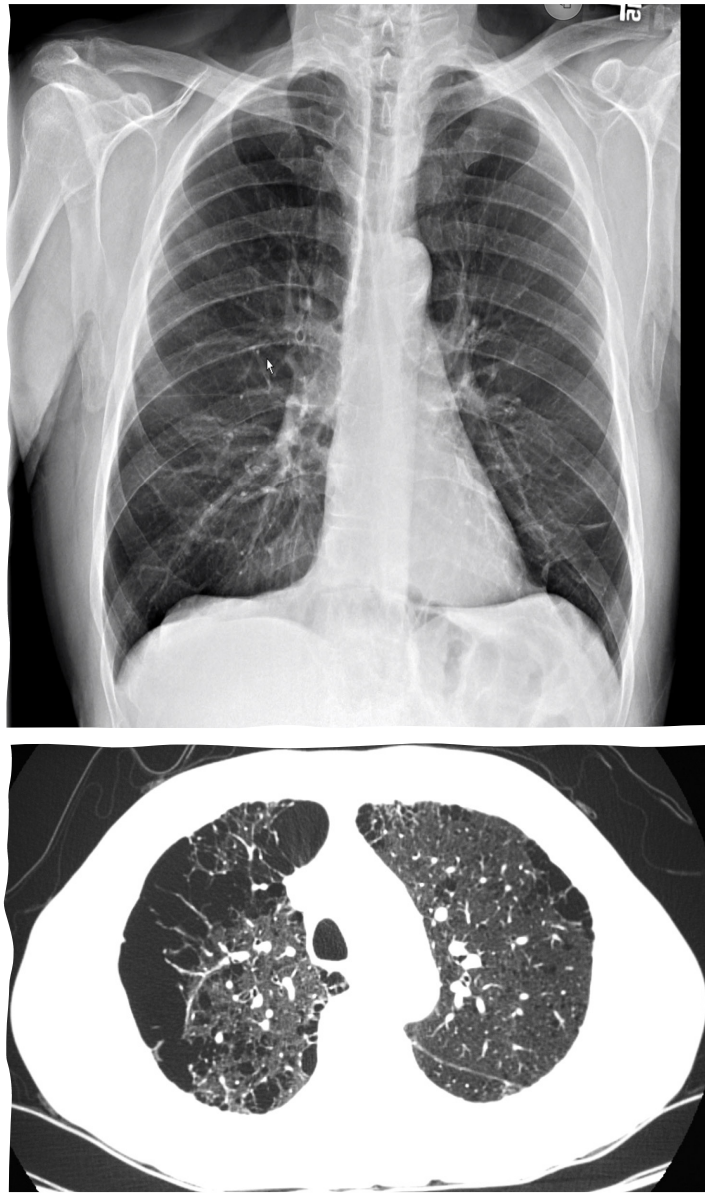
- Educational lecture for management of COPD for Verona Pharma 2023
- No other conflicts to declare

Overview

- Definition of COPD
- Global Prevalence
- Diagnostic Criteria
- Risk Factors
- Disease Burden
- Pathophysiology
- Clinical presentation
  - Symptoms
- Prognosis

Definition of COPD

- Heterogeneous pulmonary disease consisting of chronic respiratory symptoms (dyspnea, cough, sputum production), due to airway or alveoli abnormalities with evidence of persistent and often progressive airway obstruction. (GOLD COPD 2025)
- Diagnosis may be expanded to include other objective evidence of structural or physiologic pulmonary dysfunction



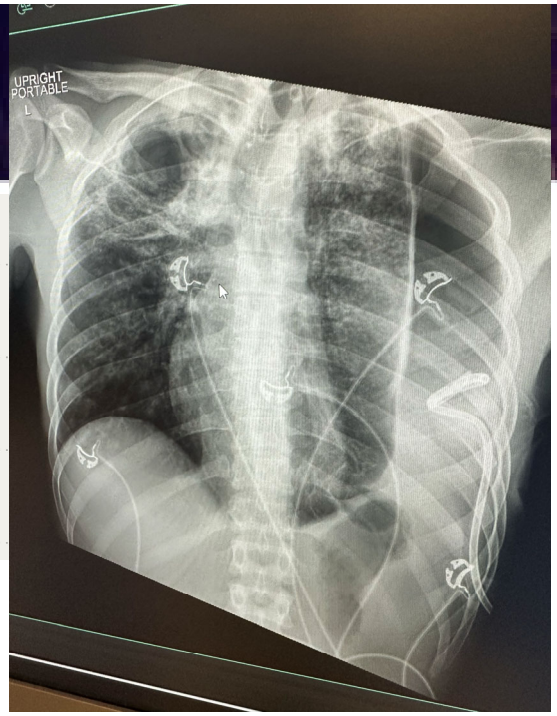
Etiology

- Gene/environment interactions over the lifetime of the individual leads to damage that alters the normal development/aging of the lung
- Historically required “significant” exposure to noxious particles or gases (primarily tobacco)
- Influenced by host factors including genetics and/or abnormal lung development
- Expanded causes of COPD may include biomass exposures, severe pulmonary infectious (TB), and asthma especially when considering global disease.
- Poverty link

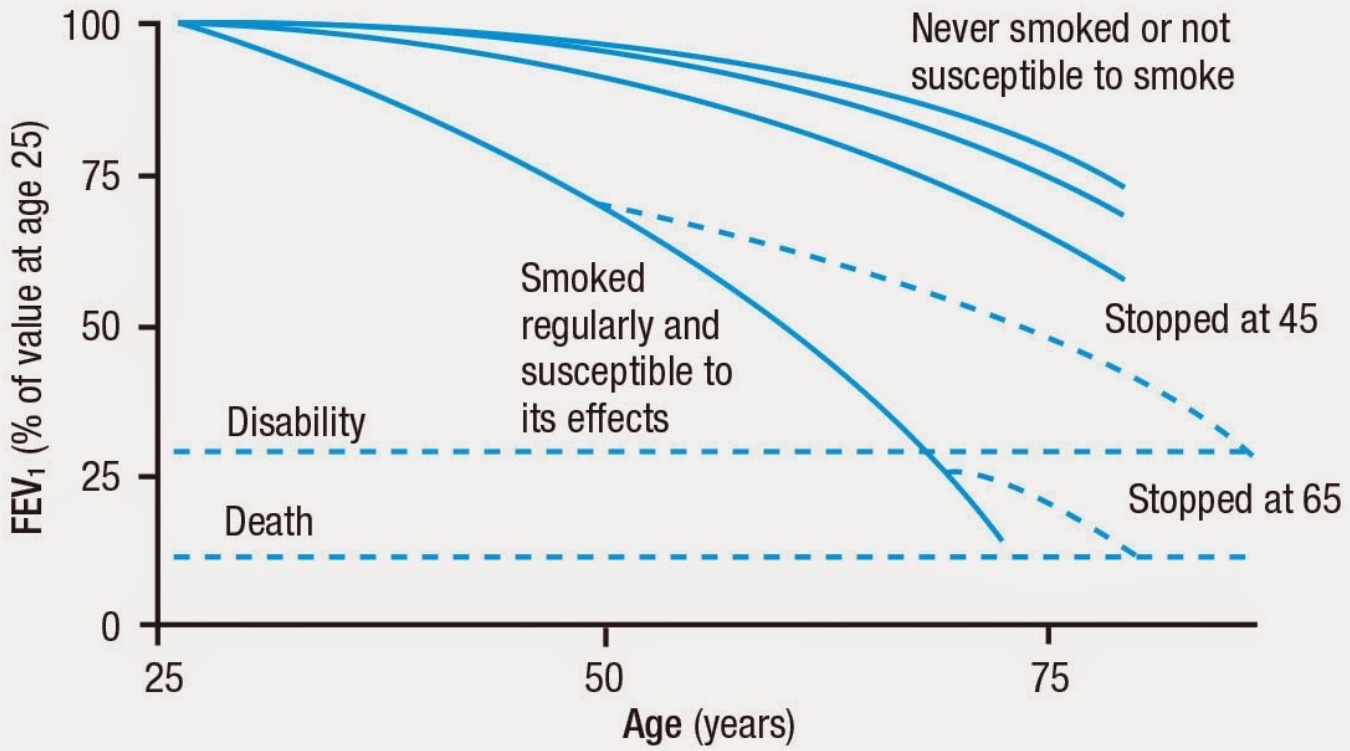
Risk Factors

Nine substantial risk factors for COPD have been identified

- ***Male sex***
- ***Advanced age***
- ***Smoking*** — *current smokers, ex-smokers, and ever smokers*
- ***Being underweight*** — *BMI <18·5 kg/m²*
- ***History of tuberculosis***
- ***Exposure to biomass***
- ***Family history of obstructive lung disease***
- ***Childhood hospital admission for severe respiratory disease***
- ***Occupational exposure to dust or smoke***



Effects of tobacco smoke on lung function

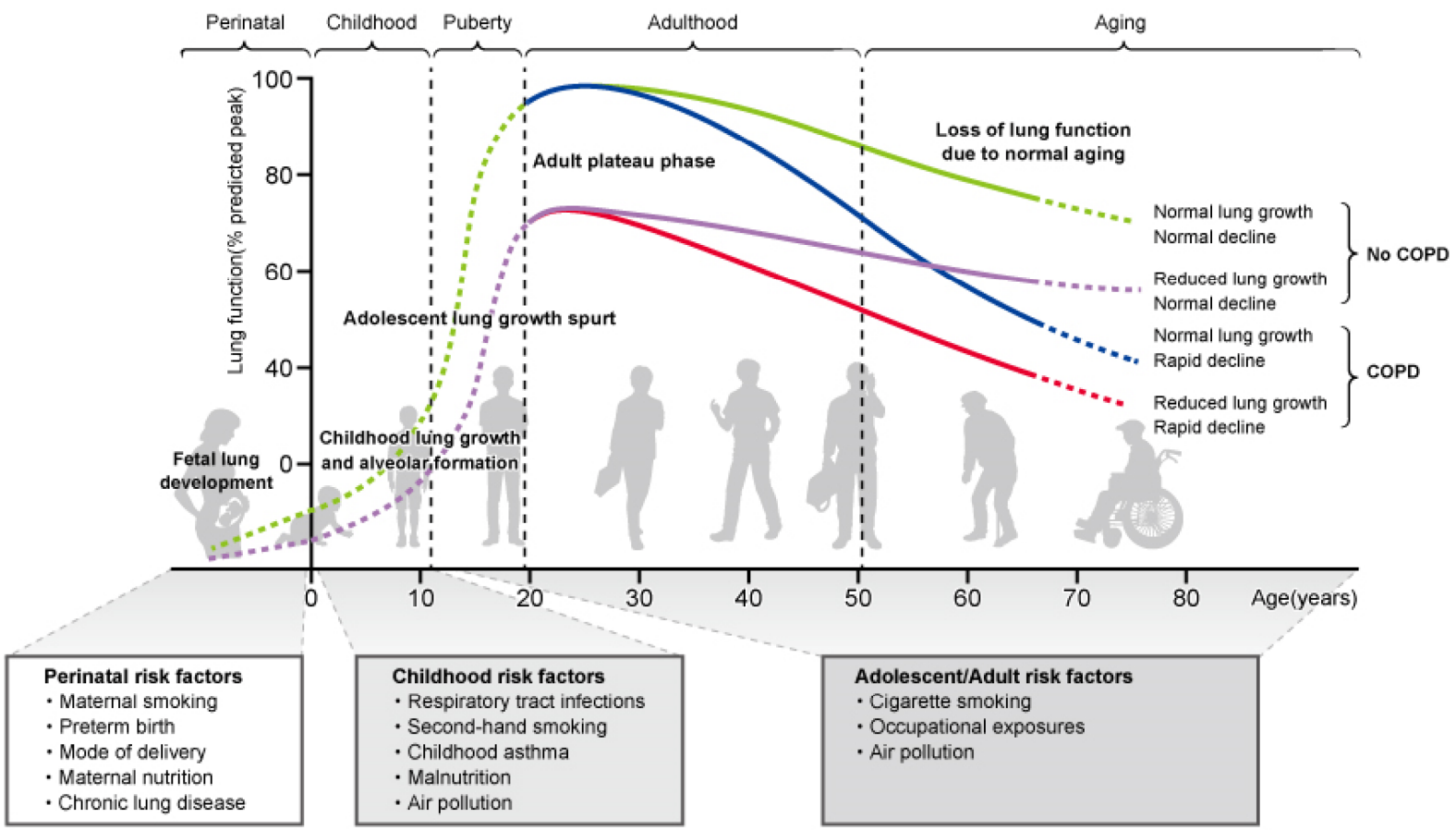


Fletcher C, Peto R. *Br Med J* 1977; 1: 1645-8.

COPD Risk Factors

- Additional risk factors beyond smoking influence the risk for development of COPD beyond smoking
- Genetic, developmental, environmental exposures
- Increased COPD risk with asthma (up to 20% will develop fixed obstruction)

Tsuge, M *Children* **2022**



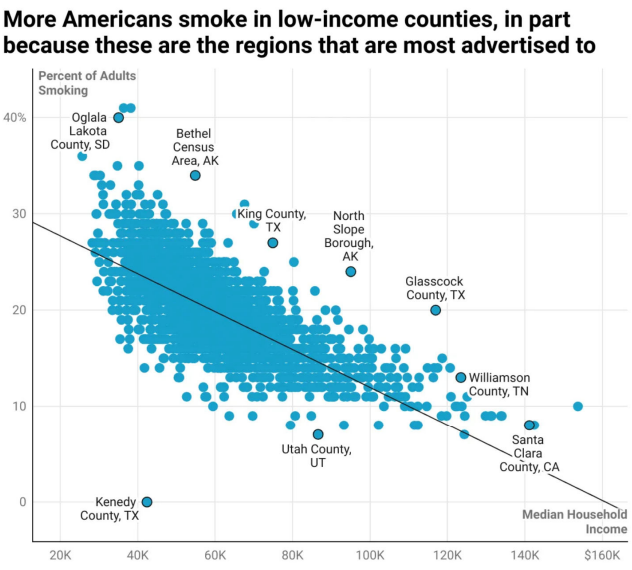
Proposed Taxonomy (Etiotypes) for COPD

Figure 1.2

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

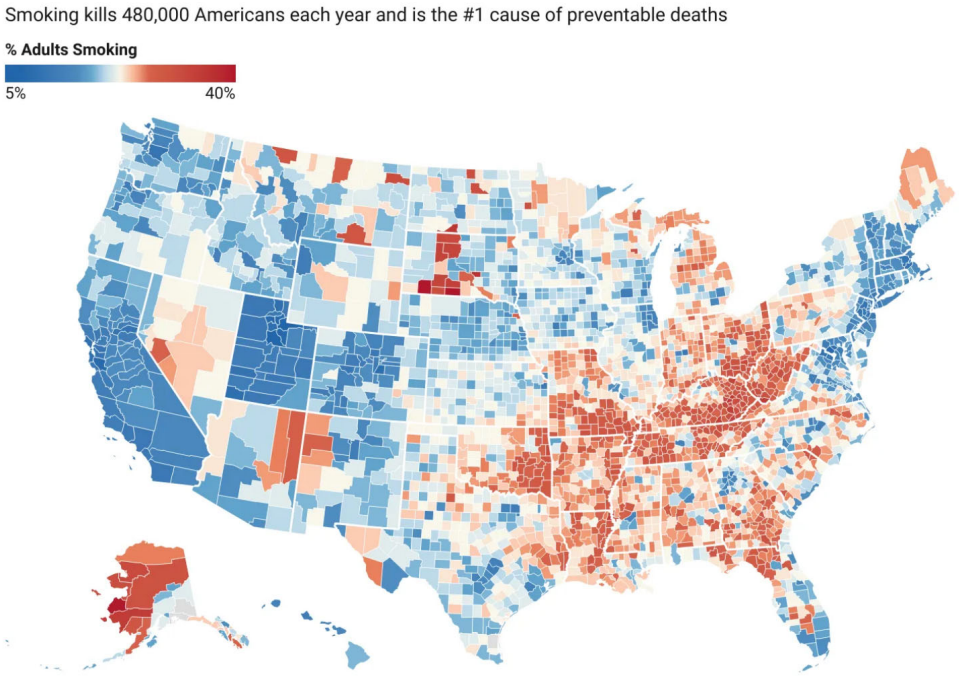
*Adapted from Celli et al. (2022) and Stolz et al. (2022)

Smoking in US



2023

Chart: Jeremy Ney @AMERICANINEQAULITY • Source: Behavioral Risk Factor Surveillance System • Created with Datawrapper

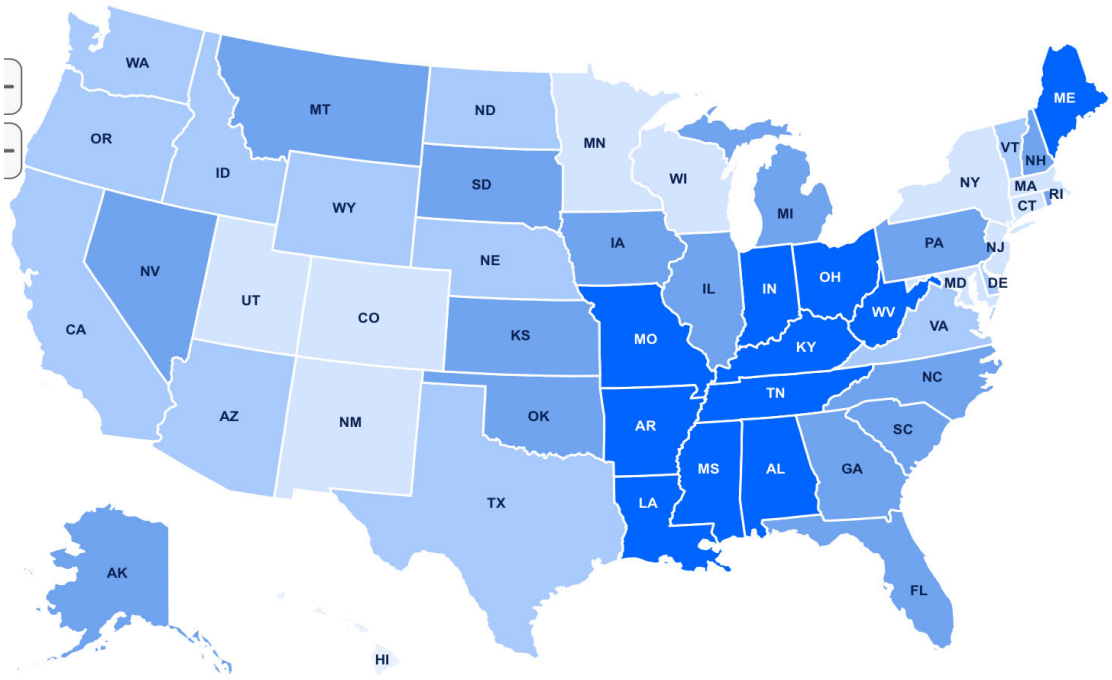


2023

Map: Jeremy Ney @AMERICANINEQUALITY • Source: Behavioral Risk Factor Surveillance System • Created with Datawrapper

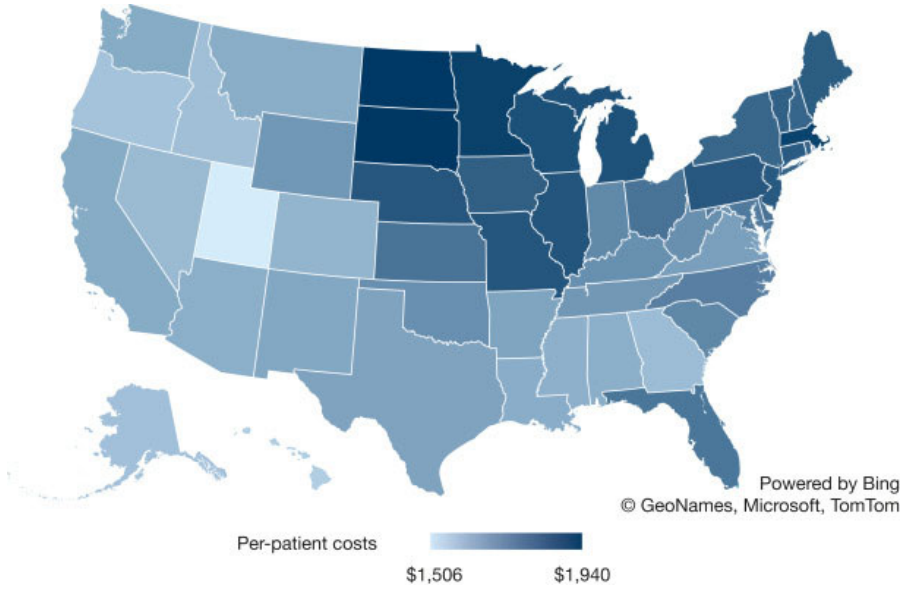
National Burden of Disease

- State prevalence ranges from 3.7% in Hawaii to 13.6% in West Virginia
- Prevalence higher in rural areas (8.2%) vs urban (4.7%)
- Prevalence corresponds with higher rates of smoking in rural vs urban areas (19.2% vs 14.4 in 2020)



Cost of COPD

- Nation wide estimate in 2019 of $31.3 billion for medical costs
- Varies widely by state
  - $44.8 million in Alaska vs $3.1 billion in Florida
- Costs expected to increase to $60.5 billion in 2029
- Cost may include effect of comorbidities including CVD



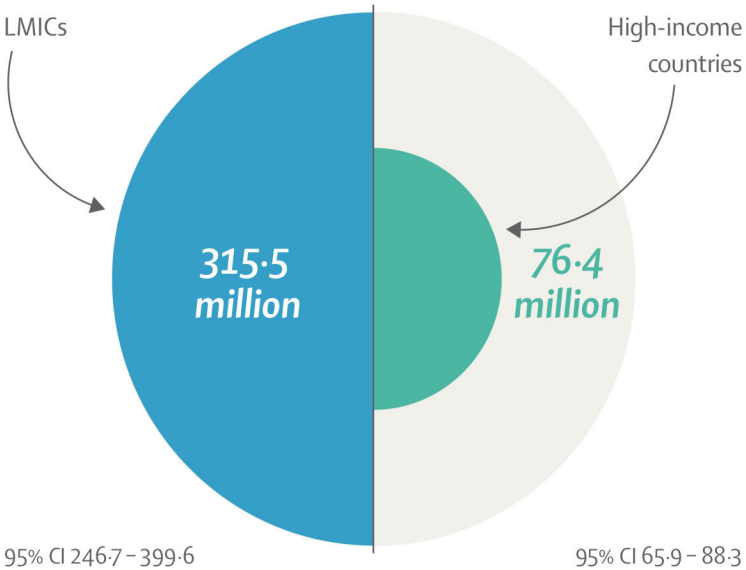
Mannino, *CHEST* 2024

Global Burden of COPD

Chronic obstructive pulmonary disease (COPD) affects up to 392 million people worldwide

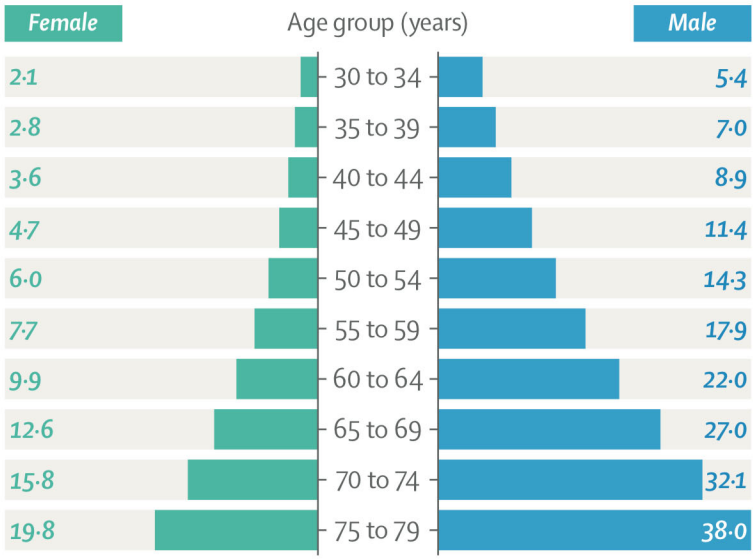
Four in every five cases of COPD are found in low-income and middle-income countries (LMICs)

Estimated worldwide COPD cases,[1] by socioeconomic region



Globally, the disease is more prevalent in men than in women at all ages

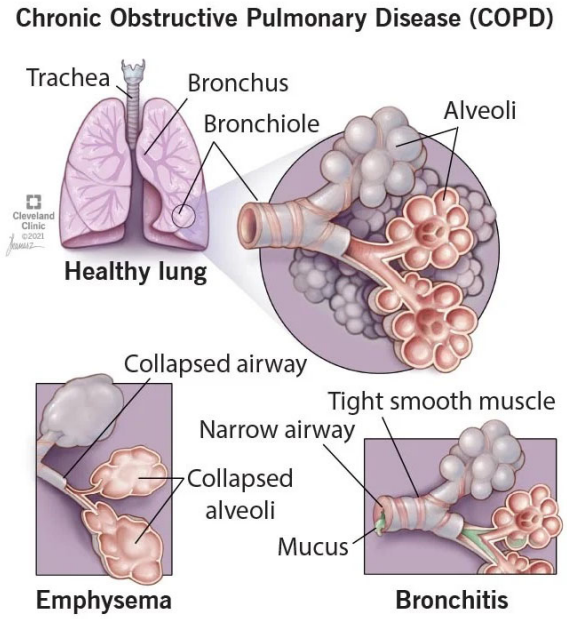
Estimated worldwide prevalence of COPD (%),[1] by sex and age group



Read the full paper: Adeloye D, Song P, Zhu Y, Campbell H, Sheikh A, Rudan I. Global, regional, and national prevalence of, and risk factors for, chronic obstructive pulmonary disease (COPD) in 2019: a systematic review and modelling analysis. *Lancet Respiratory Medicine* 2022. Published online March 10

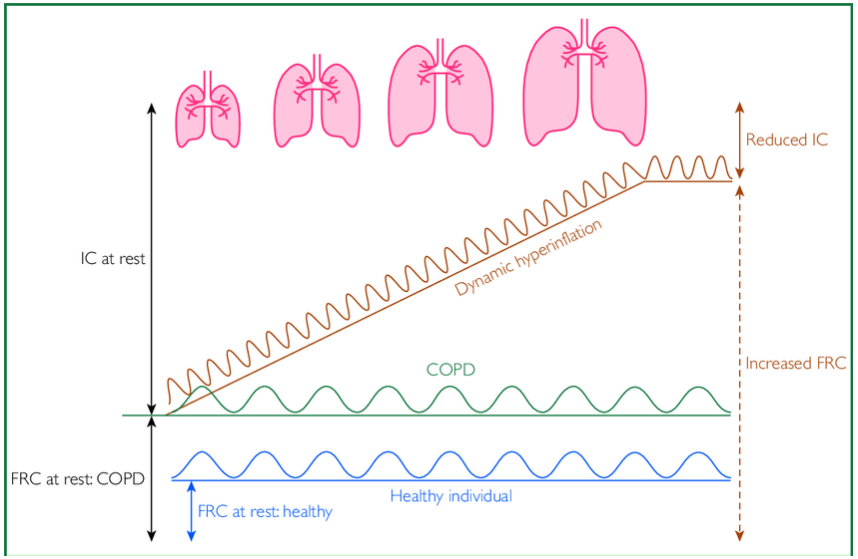
Pathophysiology:Airflow obstruction and gas trapping

- Caused by a mixture of small airways disease (increased airway resistance) and parenchymal destruction (emphysema)
- Chronic inflammation causes narrowing of small airways, luminal exudates, and destruction of parenchyma
  - Leads to loss of alveolar attachments to small airways
  - Decreases lung elastic recoil
- Decreases ability of small airways to remain open during expiration
- Mucociliary dysfunction
- Limit ability of lung to empty normally during exhalation

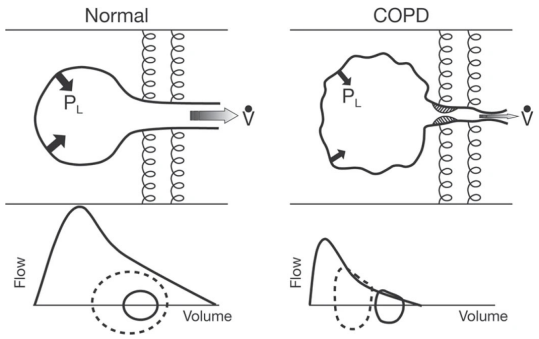


Hyperinflation

- Gas volume in lungs is increased compared with normal at end of expiration
- Clinically relevant because this impacts dyspnea
- Dynamic hyperinflation impairs exercise tolerance
- Increased risk for respiratory failure (hypercarbia)
- Increased hospitalizations
- Increased mortality

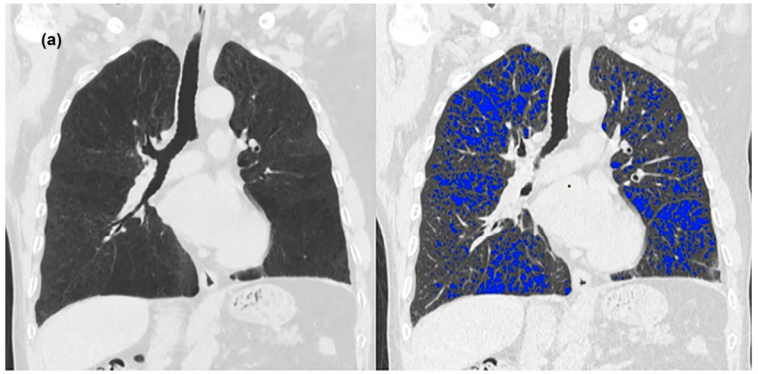


Lavorini, Mayo Clinic Procedings 2021

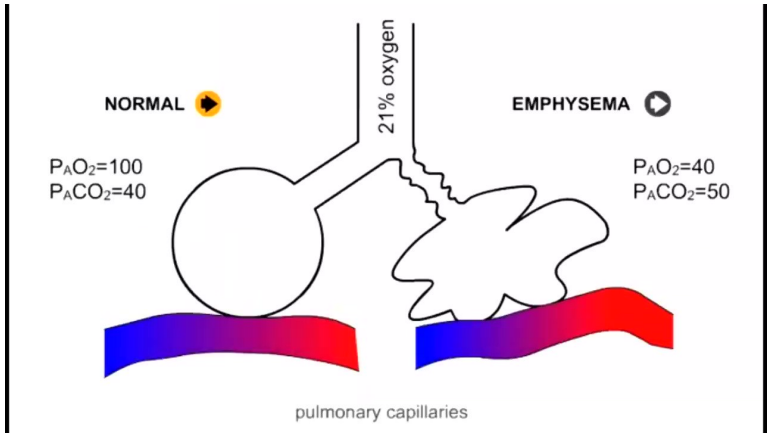


Primary Care Respiratory Journal (*Prim Care Respir J*)

Pulmonary gas exchange abnormalities



- Ventilation and perfusion do not match equally due to heterogeneous damage in the lungs
- Areas without airflow (emphysema) with retained perfusion



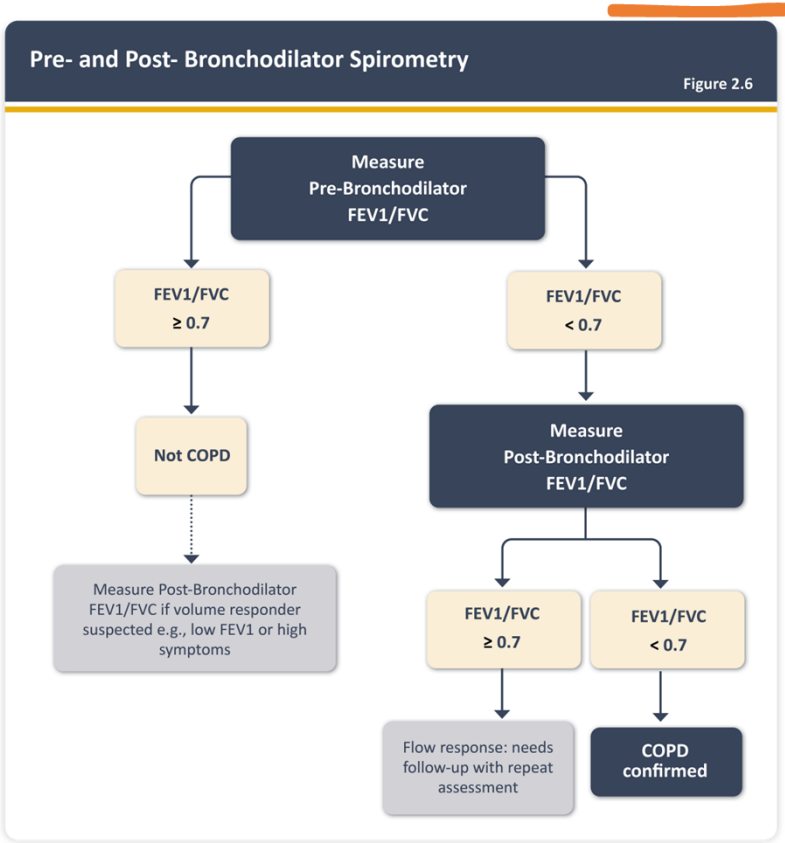
Diagnosing COPD: Patient example

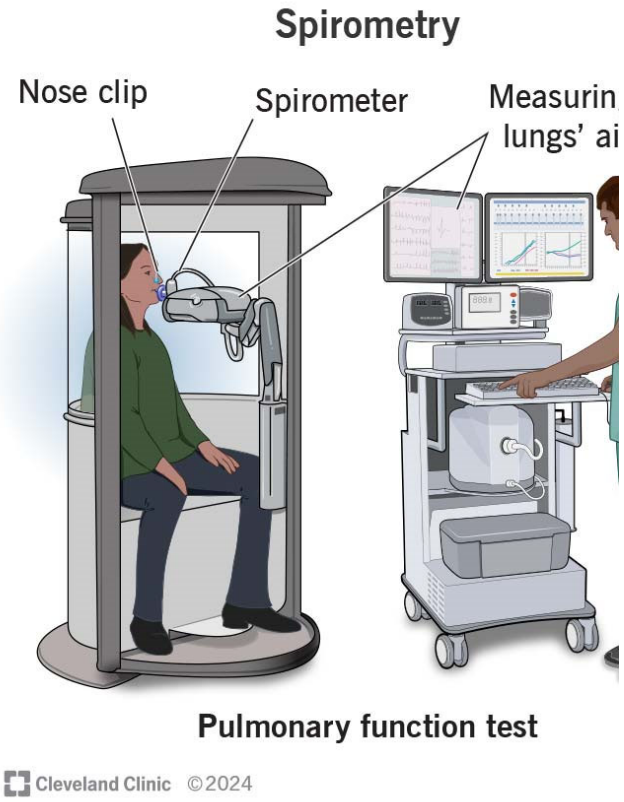
- 73 year old man, 25-30 pack year history (quit 2023)
- Presents for second opinion regarding “new diagnosis of COPD”
- Hospitalized twice in 2024 for AECOPD
- Feels breathing has “gone downhill” in the past year.
  - Previously reported no limitation in breathing and no exacerbations.
  - Started on ICS/LABA/LAMA therapy in past year
- Spirometry 2024 showed post bronchodilator FEV1 of 34%
- Review of prior records show FEV1 of 55% in 2013 and FEV1 of 51% in 2021
  - Previously declined inhalers, due to no perceived need

Clinical Presentation of COPD

- Patient often presents with history of dyspnea, cough (productive or non), frequent respiratory illnesses, decreased exercise capacity
- Diagnosis often made after hospitalization or AECOPD diagnosis
- Further history may reveal symptoms present for longer than patient initially reports
  - Patients often modify their own activity in response to symptoms of dyspnea, fatigue (slowly becoming less able to do the activities of past)
- Can give false sensation that the diagnosis is “sudden” rather than slow progressive decline

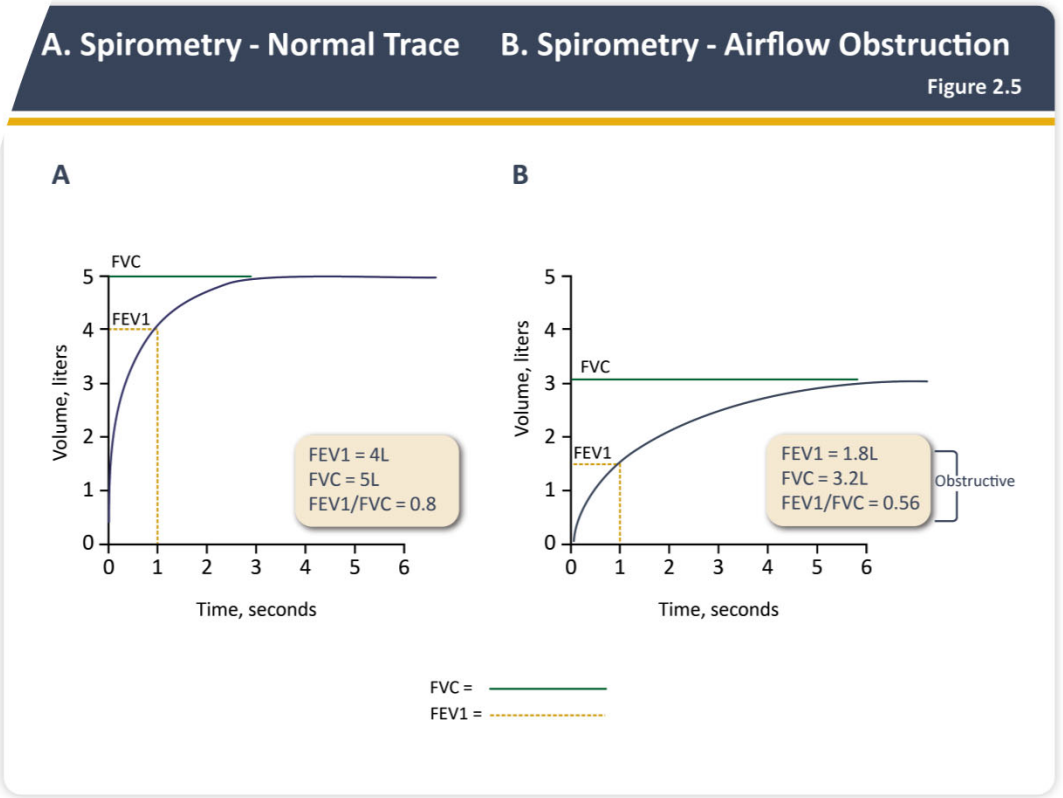
Diagnosis of COPD





Diagnostic Criteria

- Most widely accepted: The presence of non-fully reversible airflow obstruction FEV1/FVC < 0.70 post-bronchodilation



Beyond a Diagnosis

Role of Spirometry in COPD

Figure 2.7

- **Diagnosis**
- **Assessment of severity of airflow obstruction (for prognosis)**
- **Follow-up assessment**
  - Therapeutic decisions
    - Pharmacological in selected circumstances (e.g., discrepancy between spirometry and level of symptoms)
    - Consider alternative diagnoses when symptoms are disproportionate to degree of airflow obstruction
    - Non-pharmacological (e.g., interventional procedures)
  - Identification of rapid decline

Classifying severity of COPD

GOLD Grades and Severity of Airflow Obstruction in COPD (based on post-bronchodilator FEV1)

Figure 2.8

In COPD patients (FEV1/FVC < 0.7):

GOLD 1:	Mild	FEV1 ≥ 80% predicted
GOLD 2:	Moderate	50% ≤ FEV1 < 80% predicted
GOLD 3:	Severe	30% ≤ FEV1 < 50% predicted
GOLD 4:	Very Severe	FEV1 < 30% predicted

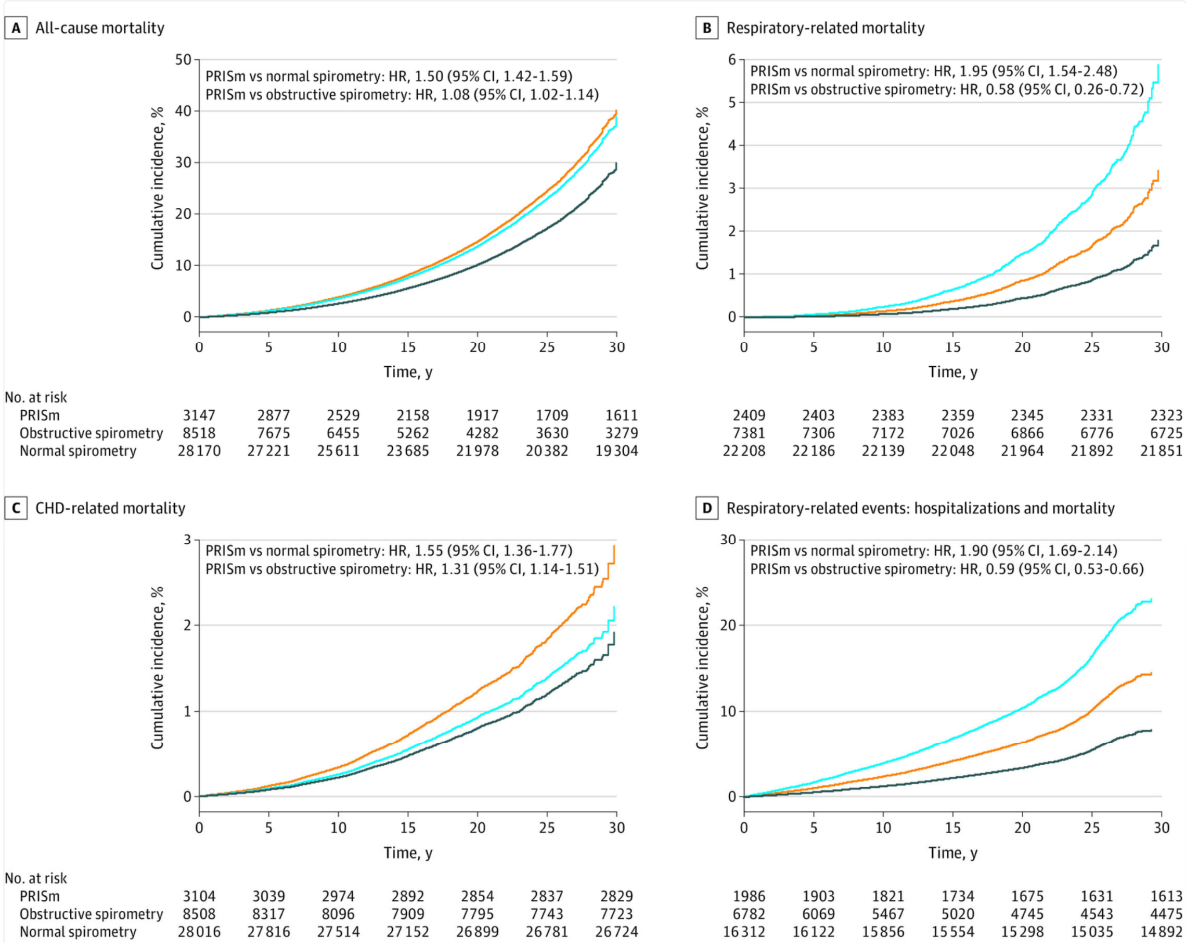
Limitation of Current Spirometry Diagnosis:PRISm

- Fails to capture those with early disease or structural lung disease with preserved lung function
- Patients with emphysema, or other physiologic abnormalities (air trapping, hyperinflation, decline in FEV1, decreased DLCO) BUT normal FEV1/FVC ratio
- Proposed diagnosis of PRISm (preserved ratio/impaired spirometry) or Pre-COPD
- Some PRISm or pre-COPD patients progress to COPD, some don’t
- Prevalence of PRISm estimated to be 7.1% to 11% of population

PRISm

- Associated with obesity, female sex and current smoking
- Associated with increased all cause mortality and respiratory mortality

Figure 1. Associations Between Lung Function Category, Mortality, and Hospitalizations.



Wan, *JAMA* 2021 Dec 14;326

Further Assessment

- Nature and magnitude of current symptoms
- Previous history of moderate and severe exacerbations
- Blood eosinophil count
- Presence and type of other diseases (multimorbidity)

Evaluating symptoms

- Clinical symptom questionnaires can encourage patients to evaluate change in exercise/activities of daily living due to disease

Modified MRC Dyspnea Scale

Figure 2.9

PLEASE TICK IN THE BOX THAT APPLIES TO YOU | ONE BOX ONLY | Grades 0 - 4

mMRC Grade 0	mMRC Grade 1	mMRC Grade 2	mMRC Grade 3	mMRC Grade 4
I only get breathless with strenuous exercise	I get short of breath when hurrying on the level or walking up a slight hill	I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level	I stop for breath after walking about 100 meters or after a few minutes on the level	I am too breathless to leave the house or I am breathless when dressing or undressing
☐	☐	☐	☐	☐

Reference: ATS (1982) Am Rev Respir Dis. Nov;126(5):952-6.

CAT™ Assessment

Figure 2.10

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 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	

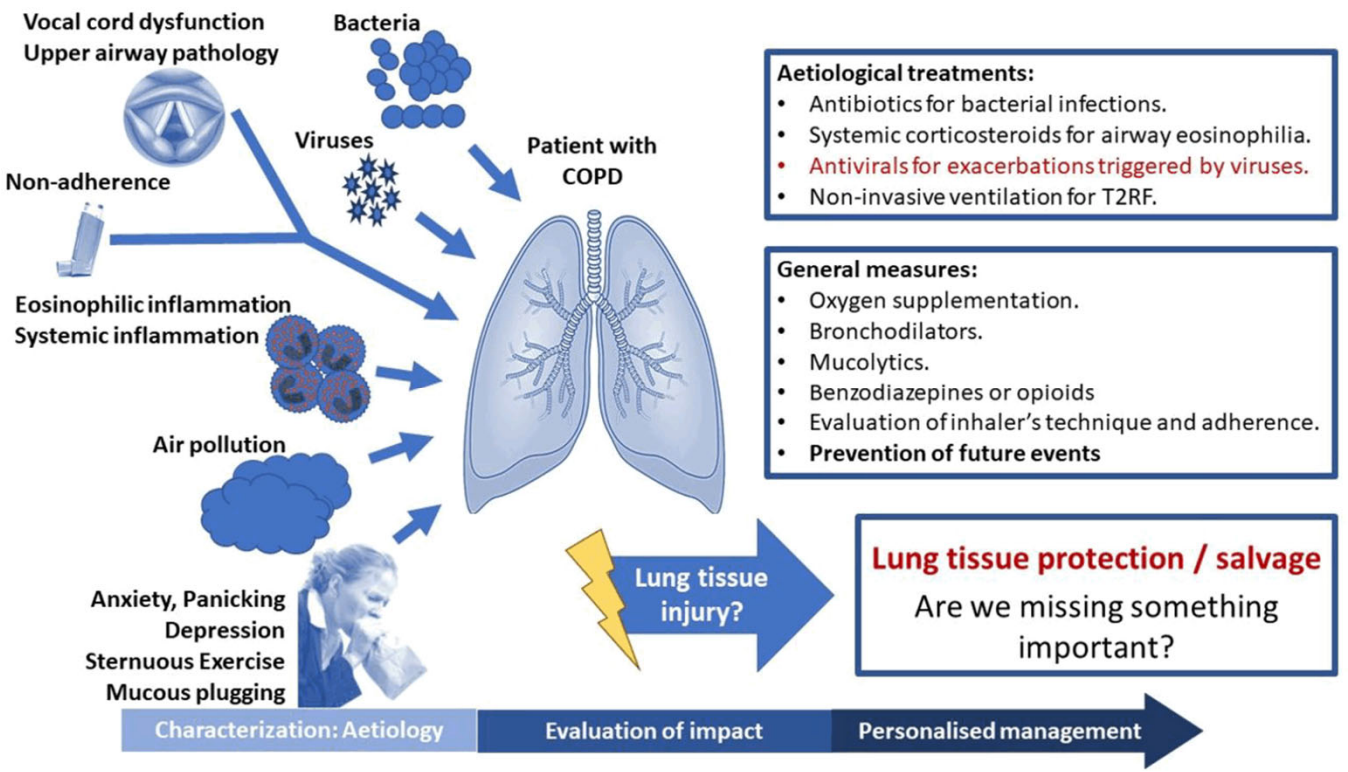
Reference: Jones et al. ERJ 2009; 34 (3); 648-54.

TOTAL SCORE: ☐

Exacerbations

- Acute respiratory symptom worsening often associated with increased local and systemic inflammation
- Significant impact on health of patient (often for prolonged time)
- Increased rate of lung function decline
  - especially in GOLD stage 1 disease where each exacerbation led to additional 23 ml/yr decline in FEV1 (Make *Am J Respir Crit Care Med* 2017)
- Worsening prognosis
- Associated with most of healthcare costs of COPD

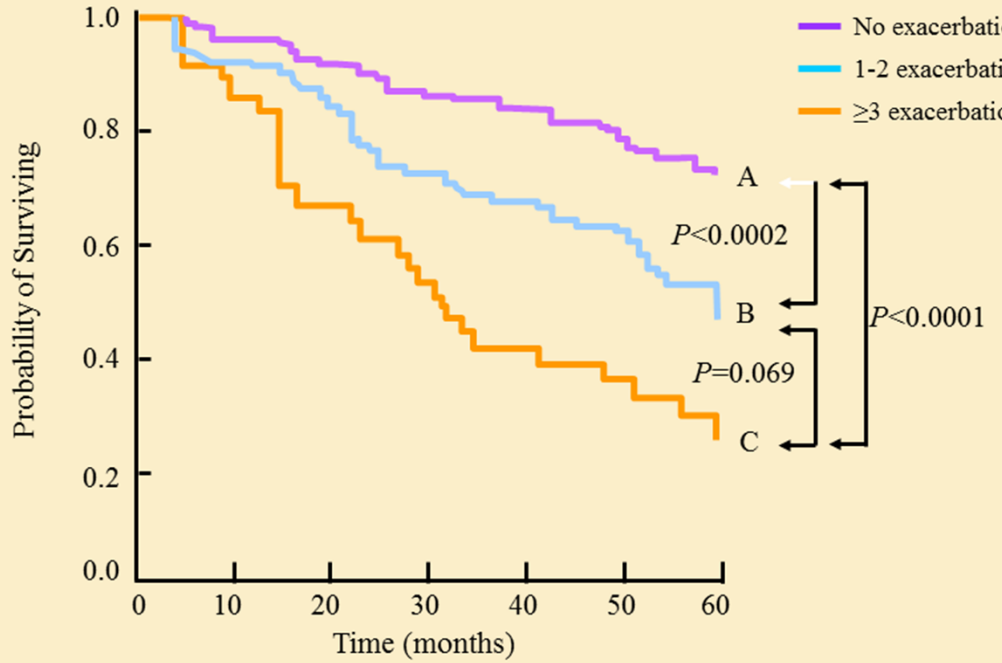
Pathophysiology: Identifying causes of exacerbations



Alexander Mathioudakis et al. Thorax 2020; 75:520-527

Impact of Exacerbations

COPD PATIENTS WITH A GREATER FREQUENCY OF SEVERE EXACERBATIONS* PER YEAR HAVE A HIGHER RISK OF ALL-CAUSE MORTALITY



*Severe exacerbations = exacerbation required emergency visits or hospital admissions.

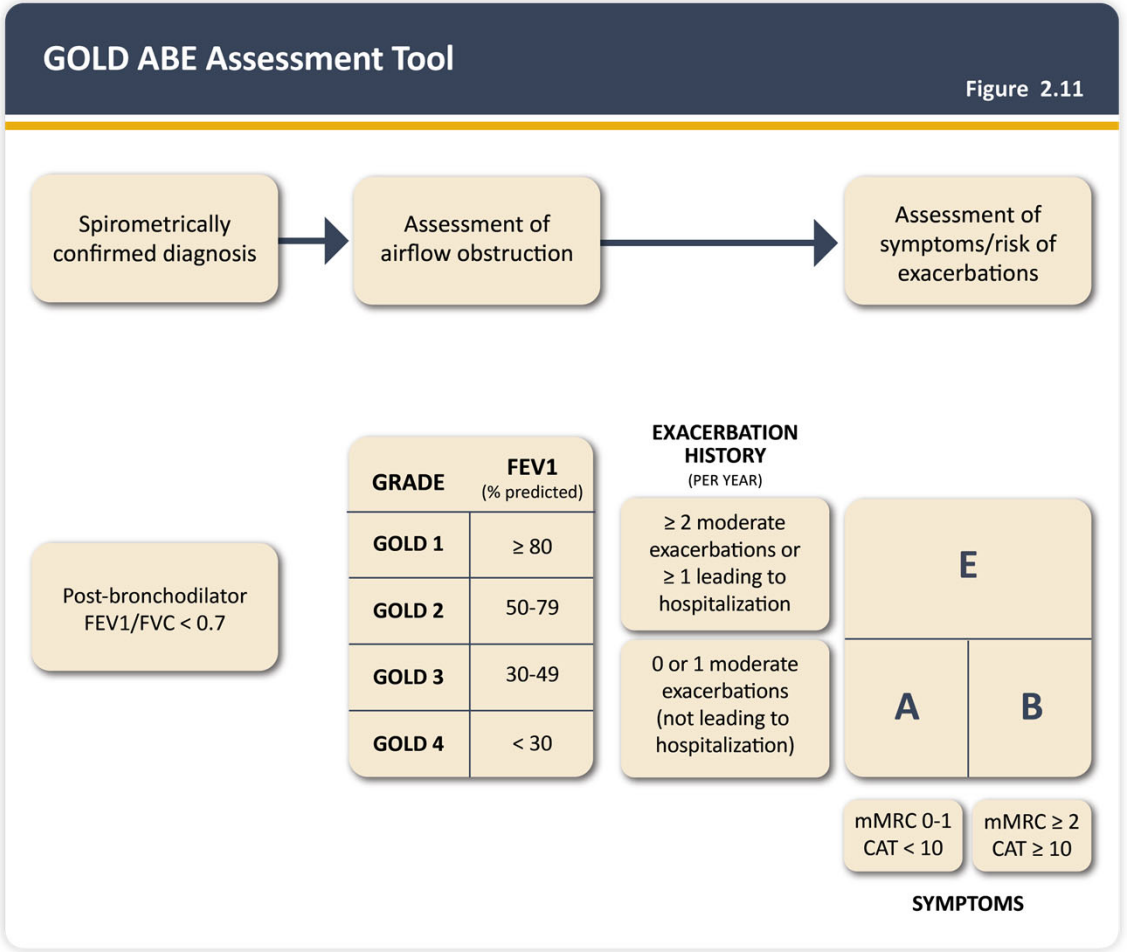
Soler-Cataluna JJ, et al. *Thorax*. 2005;60:925-931.

Blood eosinophil count

- Peripheral blood eosinophil count associated with increased lung eosinophil numbers
- Suggests increased type-2 inflammation in airways
- May or may not predict future exacerbations
- For younger individuals without COPD, higher counts associated with increased risk for developing COPD
- Suggest positive response to treatments
  - ICS
  - Biologic therapy

Comprehensive Assessment

- Combination of objective and subjective patient patient factors



Co-morbid conditions

- Multimorbidity (concomitant chronic disease) influences mortality and hospitalizations (independent of severity of airflow obstruction)
- Should screen for comorbid diseases
  - Cardiovascular disease
  - Pulmonary hypertension)
  - Metabolic syndrome
  - Osteoporosis
- CVD and COPD share risk factors
- COPD may be associated with increased systemic inflammation which can cause endothelial dysfunction, platelet activation, and increase CVD risk
- CVD risk increases during ECOPD episodes

Additional Testing

- Lung volume measurements
  - May have implications for interventions (EBV, LVRS)
- DLCO
  - Strong predictor of COPD hospitalizations, independent of obstruction
  - Implications for surgical intervention (may preclude surgical lung resection for lung cancer)
- Oximetry and arterial blood gas measurements
  - Screen for need for supplemental oxygen
- Exercise testing – evaluate symptoms of dyspnea which may be multifactorial
- CXR and CT
  - Lung cancer screening
  - Screening for emphysema/LVRS/EBV placement

Evaluating COPD Impact: HRQOL

- Health Related Quality of Life (HRQOL) can be estimated using the St George's Respiratory Questionnaire
- Attempts to capture impact of symptoms on patient QOL
  - Measures Symptoms (cough, dyspnea, exacerbations), Activity (limitations) and Impact (social functioning and psychological well being)
  - Generates 4 scores (symptoms, activity, impact and total score)
- Implications for predicting exacerbations, hospitalizations and mortality
- Used in clinical research, but not patient care

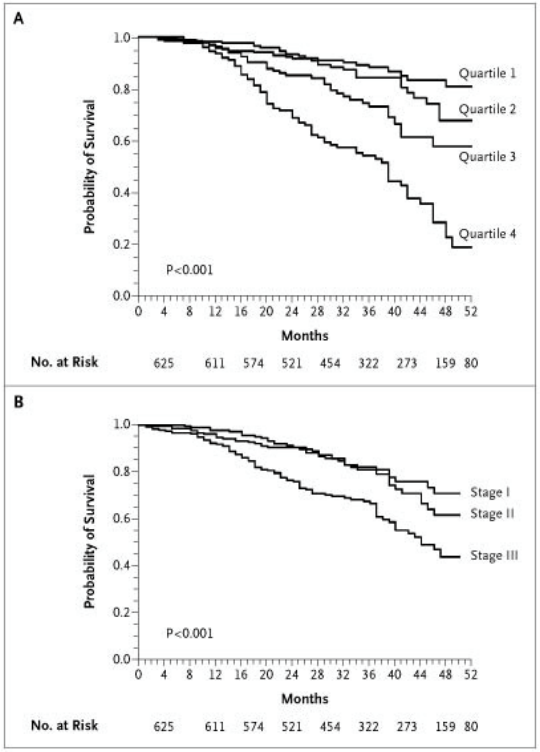
Prognosis: BODE index

- Depends on the severity of obstruction, symptoms, and exercise capacity
- BODE index developed for predicting disease mortality
- Better predictor than FEV1 alone

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

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

* The cutoff values for the assignment of points are shown for each variable. The total possible values range from 0 to 10. FEV_1 denotes forced expiratory volume in one second.
† The FEV_1 categories are based on stages identified by the American Thoracic Society.
‡ Scores on the modified Medical Research Council (MMRC) dyspnea scale can range from 0 to 4, with a score of 4 indicating that the patient is too breathless to leave the house or becomes breathless when dressing or undressing.
§ The values for body-mass index were 0 or 1 because of the inflection point in the inverse relation between survival and body-mass index at a value of 21.



Celli, *NEJM* 2004