

DEFINITION and DIAGNOSIS OF COPD

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Global Initiative for
Chronic Obstructive
Lung Disease

2025
REPORT



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

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Definition



Pre-COPD and PRISm: Early Abnormalities Without Obstruction



Who are these patients?

Some individuals may exhibit:

- **Structural lung changes** (e.g., emphysema)
 - **Physiological impairments:**
 - ↓ FEV1
 - Gas trapping
 - Hyperinflation
 - ↓ Diffusing capacity (DLCO)
 - Rapid FEV1 decline
- = BUT: FEV1/FVC $\geq$ 0.7 post-bronchodilator** → *No airflow obstruction*



Terminology

• **Pre-COPD:** Individuals with structural or physiological lung abnormalities without airflow obstruction.

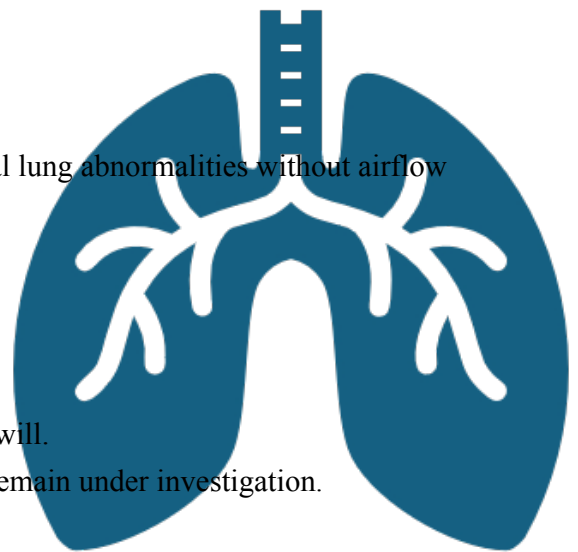
• **PRISm** (Preserved Ratio Impaired Spirometry):

- Normal FEV1/FVC ratio (≥ 0.7)
- But **reduced FEV1 and/or FVC**

Risk and Uncertainty

• These individuals may **progress to COPD**, but not all will.

• **Management strategies** (besides smoking cessation) remain under investigation.



Term	Definition / Description	Criteria	Prevalence / Notes
Early COPD	The very first “biological” steps of disease pathogenesis, identifiable only in research settings. Distinct from clinical or symptomatic onset.	N/A (experimental markers under investigation)	Should be used only in experimental contexts to study initial mechanisms leading to COPD.
Mild COPD	Describes the severity of airflow obstruction, not the timing of disease onset. A spirometric category that can occur at any age and may or may not progress.	Post-bronchodilator FEV₁ ≥ 80 % predicted (GOLD 1)	Do not equate with “early”—patients may have had low maximal lung function from youth and never experience a “mild” stage.
Young COPD	COPD in younger individuals, reflecting disease manifesting before the usual age of diagnosis. May include those who never achieved peak lung function or had early decline.	Age 20–50 years; post-bronchodilator FEV₁/FVC < 0.7	Often undiagnosed; frequently report family history or early-life events (e.g., hospitalization < 5 yrs) supporting early-life origins. Not necessarily “mild” in severity.
Pre-COPD	Individuals of any age with respiratory symptoms and/or imaging or physiological abnormalities without spirometric obstruction . At risk of progressing to COPD but not all will.	Post-bronchodilator FEV₁/FVC ≥ 0.7 and symptoms or structural/functional lung abnormalities	Treatment beyond smoking cessation is under study; RCTs are needed to guide management.
PRISm	“Preserved Ratio Impaired Spirometry”—normal ratio but reduced volumes on spirometry. Associated with increased morbidity and risk of later airflow obstruction but phenotype can revert to normal or progress to COPD.	Post-bronchodilator FEV₁/FVC ≥ 0.7 and FEV₁ < 80 % predicted	Prevalence 7–11 % in general populations; 10–11 % in smokers/former smokers. Higher in women, those with extremes of BMI, multimorbidity. 20–30 % progress to obstruction over time; predictors include lower baseline FEV ₁ , older age, current smoking.

Environmental Risk Factors for COPD



1. Cigarette Smoking

- **Primary risk factor** globally.

- Associated with:

- ↑ Respiratory symptoms

- ↑ Annual FEV₁ decline

- ↑ COPD mortality

- **>10 pack-years** exposure is common in studies, but even **<10 pack-years** increases risk.
- **<50%** of heavy smokers develop COPD → points to role of **non-smoking factors**.

- ◆ **Other tobacco forms:**

- Pipe, cigar, water pipe, marijuana

- **Environmental tobacco smoke (ETS)** = second-hand smoke → contributes to COPD

- ◆ **Smoking in pregnancy:**

- Affects **fetal lung development**
- Alters **immune response**



2. Biomass and Household Air Pollution (HAP)

- Common in **low- and middle-income countries (LMICs)**
- Includes wood, animal dung, and coal
- Leads to **indoor air pollution**, especially with poor ventilation
- **>3 billion** people at risk

- ◆ **Features of biomass-related COPD:**

- More common in **younger females**
- Similar or milder symptoms
- Less emphysema; more **small airway disease**
- ↑ **Eosinophils**, ↓ **neutrophils** in sputum



image credit: istockphoto.com/tchana

3. Occupational Exposures

- Includes **organic/inorganic dusts, chemical fumes, pesticides**
- ↑ Risk of:
 - Respiratory symptoms
 - Airflow obstruction
 - Emphysema and gas trapping (seen on CT)
- Estimated **10–20%** of COPD cases overall due to occupational exposures (ATS)

4. Ambient Air Pollution



- Major contributor, especially in LMICs
- **Components:** PM2.5, ozone, NOx, SOx, heavy metals
- **Responsible for approximately 50% of the attributable risk for COPD in low- and middle-income countries**
- **In never smokers, air pollution is the leading known risk factor for COPD**

◆ Effects:

- ↓ Lung development in children
- Accelerated lung function decline in adults
- ↑ Risk of:
 - COPD
 - Exacerbations
 - Hospitalization
 - Mortality

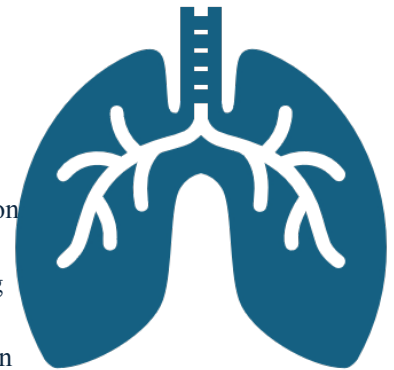
- **Genetic factors**

- **Hereditary deficiency of α -1 antitrypsin (AATD).**
- **AATD PiZZ genotypes in 0.12% of COPD patients**

Asthma and airway hyper-reactivity

Strong association with future COPD:

- Adults with asthma have up to a **12-fold increased risk** of developing COPD (Tucson study).
- **~20% of asthma patients** develop **irreversible airflow obstruction** and ↓ diffusing capacity.
- Childhood asthma may lead to **FEV₁ decline** and **COPD in early adulthood** (11% in one cohort).



. Airway Hyper-Responsiveness (AHR)

Independent risk factor for:

- **COPD development**
- **Accelerated FEV₁ decline**
- **Respiratory mortality**
- In the European Respiratory Health Survey:
 - AHR was responsible for **15% of COPD cases**
 - Second only to smoking (**39%**)

chronic bronchitis (CB) in COPD:

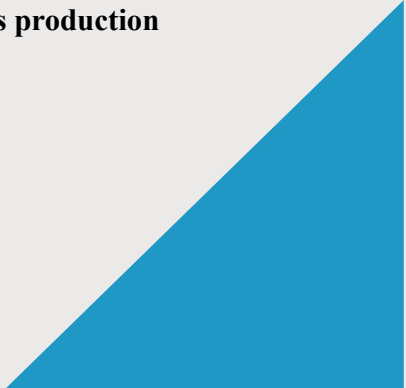
1. Definition and Prevalence

- **Classic definition:** Cough with sputum production ≥ 3 months/year for 2 consecutive years, excluding other causes.
- **Prevalence** in COPD varies (27–35%) depending on definition.
- CB is **common but heterogeneous** in COPD patients.

2. Epidemiologic and Risk Factors

- Associated with:
 - **Male sex**
 - **Younger age**
 - **Heavier smoking history**
 - **Rural residence**
 - **Occupational or environmental exposure**
 - **Gastroesophageal reflux**
- Not exclusive to smokers:

Impact on Lung Function and Disease Progression

- CB in **young adults** may predict future COPD, **independent of smoking**
 - In patients **<50 years**, CB (even without obstruction) may indicate increased COPD risk
 - Smoking cessation can **reverse mucus production**
 - Chronic mucus is associated with:
 - **FEV1 decline**
 - **Exacerbation frequency**
- 

- ***Pseudomonas aeruginosa***: with accelerated FEV1 decline.
- **Tuberculosis (TB)** is a risk factor for COPD.
- **HIV** patients are at increased risk of COPD.
- **IgG subclass deficiency** : observed in hospitalized patients with COPD.

(Etiotypes) for COPD

Figure 1.2

	Description
Alpha-1 antitrypsin deficiency (AATD)	Alpha-1 antitrypsin deficiency (AATD) Other genetic variants with smaller effects acting in combination
Early life events	Early life events, including premature birth and low birthweight, among others
COPD-C)	• Exposure to tobacco smoke, including <i>in utero</i> or via passive smoking • Vaping or e-cigarette use • Cannabis
Exposure	Exposure to household pollution, ambient air pollution, wildfire smoke, occupational hazards
D-I)	Childhood infections, tuberculosis-associated COPD, HIV-associated COPD
PD-U)	Particularly childhood asthma

Polz et al. (2022)





DIAGNOSIS

✓ When to Suspect COPD:

You should **consider COPD** in any patient with:

- **Dyspnea** (especially progressive, persistent, and exertional)
- **Chronic cough** (may be intermittent or unproductive)
- **Chronic sputum production**
- **History of exposure to:**
 - Tobacco smoke
 - Occupational dusts and chemicals
 - Biomass fuel smoke (especially in low- and middle-income countries)

✍ How to Confirm the Diagnosis:

- The **mandatory test** is **spirometry**
- **Diagnostic criterion:**

Clinical Indicators for Considering a Diagnosis of COPD

Figure 2.1

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

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

Differential Diagnosis of COPD

Figure 2.3

Diagnosis	Suggestive Features
COPD	Symptoms slowly progressive History of tobacco smoking or other risk factors
Asthma	Variable airflow obstruction Symptoms vary widely from day to day Symptoms worse at night/early morning Allergy, rhinitis, and/or eczema also present Often occurs in children Family history of asthma
Congestive heart failure	Chest X-ray shows dilated heart, pulmonary edema Pulmonary function tests indicate volume restriction, not airflow obstruction
Bronchiectasis	Large volumes of purulent sputum Commonly associated with bacterial infection Chest X-ray/HRCT shows bronchial dilation

DIFFERENTIAL DIAGNOSIS OF COPD

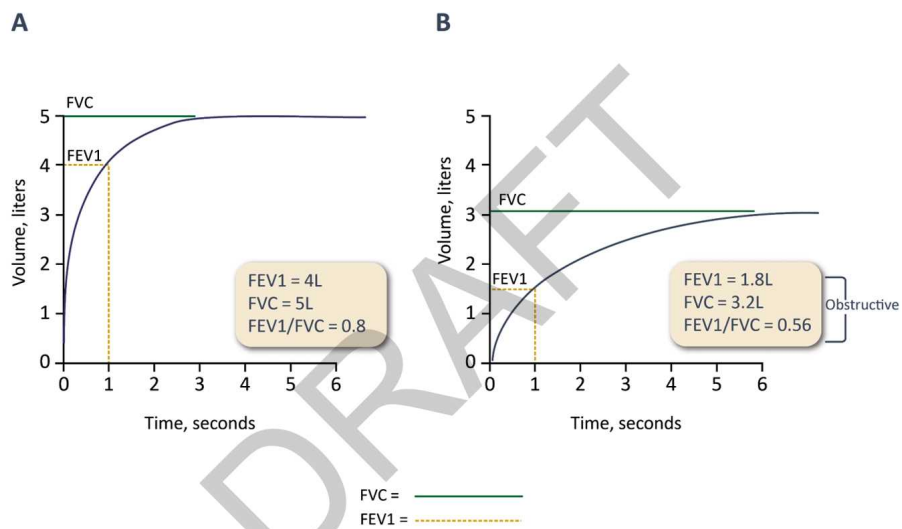
Tuberculosis	Onset at all ages Chest X-ray shows lung infiltrate Microbiological confirmation High local prevalence of tuberculosis
Obliterative bronchiolitis	Can occur in children Seen after lung or bone marrow transplantation HRCT on expiration shows hypodense areas
Diffuse panbronchiolitis	Predominantly seen in patients of Asian descent Most patients are male and nonsmokers Almost all have chronic sinusitis Chest X-ray & HRCT show diffuse small centrilobular nodular opacities & hyperinflation

spirometry



A. Spirometry - Normal Trace B. Spirometry - Airflow Obstruction

Figure 2.5

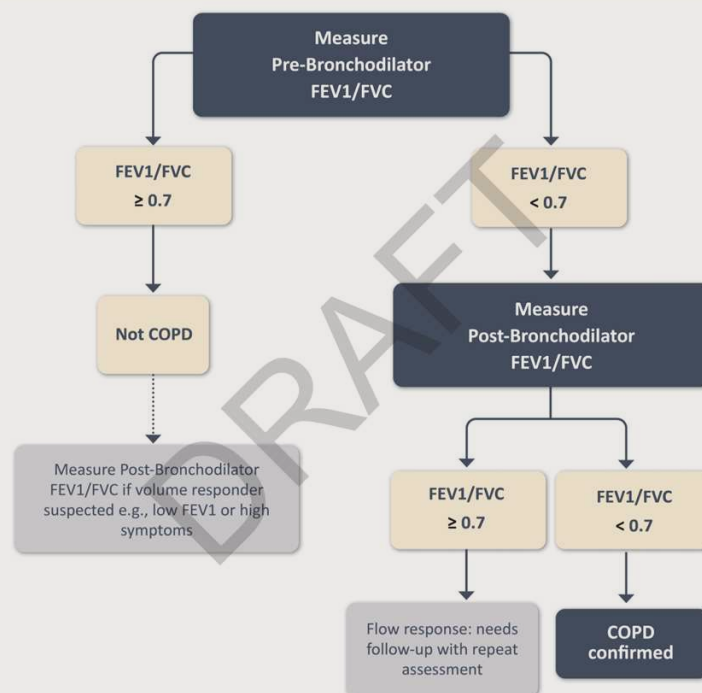


Pre- vs Post-Bronchodilator Spirometry in COPD Evaluation

Step	Action
1	Start with pre-bronchodilator spirometry
2	If no obstruction and low suspicion → no further testing needed
3	If no obstruction but high suspicion → consider post-BD spirometry & follow-up
4	If obstruction present → confirm with post-BD spirometry
5	If pre-BD abnormal, post-BD normal → observe for future COPD development

Pre- and Post- Bronchodilator Spirometry

Figure 2.6



Point!

- **Post-bronchodilator (post-BD) spirometry** is:
- **Required** to confirm diagnosis of COPD
- Also used for **severity assessment**
- it is also **unnecessary to stop inhaled medications** (e.g., LABA, LAMA, ICS) **before follow-up spirometry**, as it's no longer considered critical for clinical decision-making
- **Focus is on:**
 - Confirming **persistent obstruction** via post-BD spirometry
 - Guiding **treatment** based on **symptoms, exacerbation history, and treatable traits**, **not** on reversibility response

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



Spirometric Criteria for Airflow Obstruction in COPD

Primary GOLD Criterion (Preferred Standard):

- **Post-bronchodilator $FEV_1/FVC < 0.70$**
- Simple and reproducible
- Independent of reference values
- Consistent with major **clinical trials and GOLD treatment evidence base**

Limitations of the Fixed Ratio (<0.7):

- **Overdiagnosis in elderly:**
- FEV_1/FVC naturally declines with age $\rightarrow$ false positives
- **Underdiagnosis in young adults (esp. <50 years):**
- Some with true airflow limitation may be missed if fixed ratio > 0.7

Lower Limit of Normal (LLN):

- Based on the **bottom 5th percentile** of a healthy population
- More age-adjusted but **requires reference equations**
- Still not clearly shown to improve **clinical outcomes**

2. Z-Scores:

- Express deviation from predicted mean as **standard deviations**
- **$Z = -1.645 \approx$ 5th percentile (LLN)**
- GLI recommends this, but:
- Clinical significance in COPD diagnosis still **uncertain**
- Dependent on high-quality reference data

FEV ₁ /FVC Result	Action
< 0.6	Highly likely COPD; rarely reverses spontaneously
0.6 – 0.8	Borderline; repeat spirometry recommended
> 0.7	Likely normal—but assess clinical context (esp. in younger patients)

Practical Interpretation

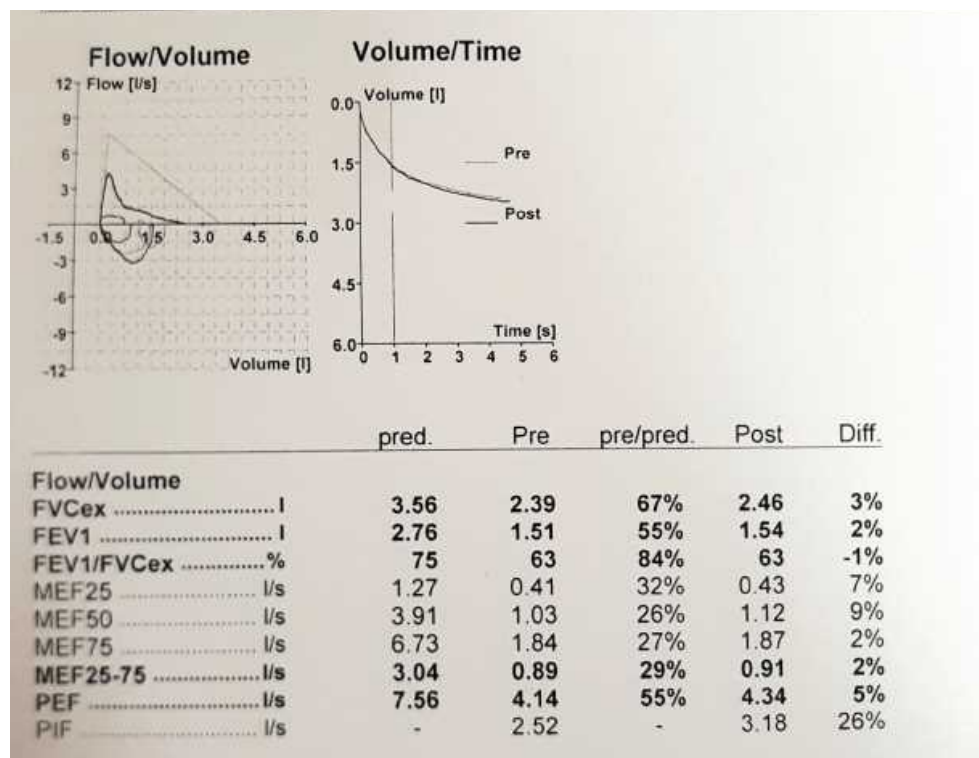
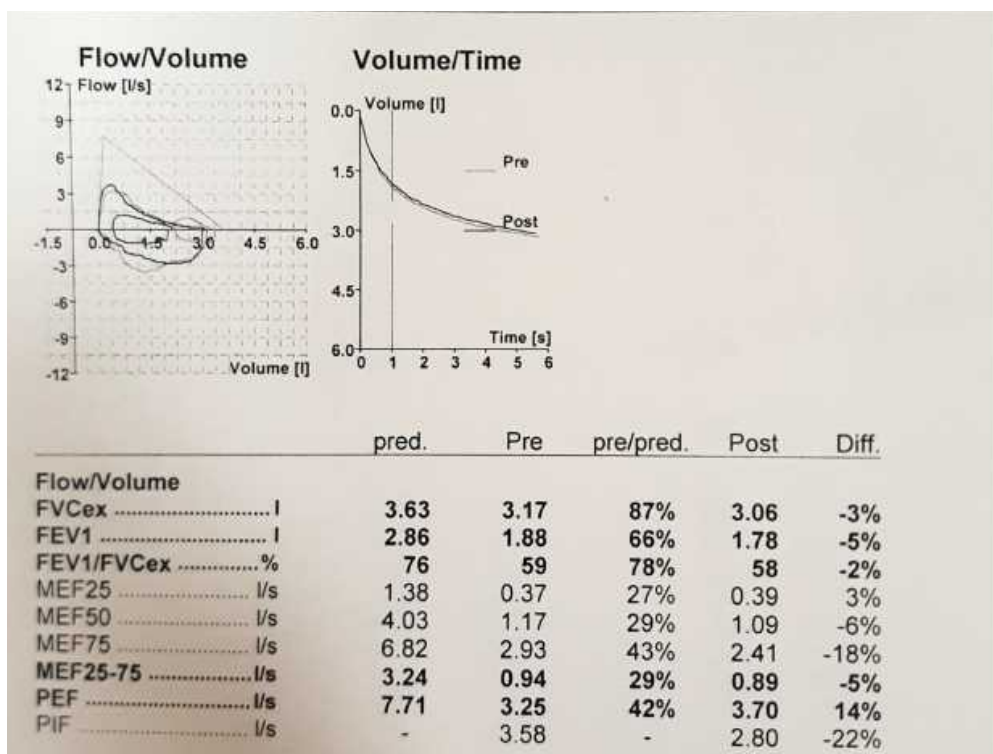


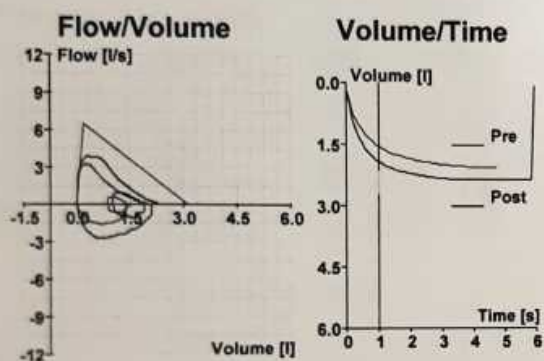
Key Clinical Messages:

- **Irreversible airflow obstruction $\neq$ COPD diagnosis**
by itself
→ Always consider **clinical context + risk factors**
- Spirometry is **one component** of diagnosis
→ Combine with **history, symptoms, exposures**

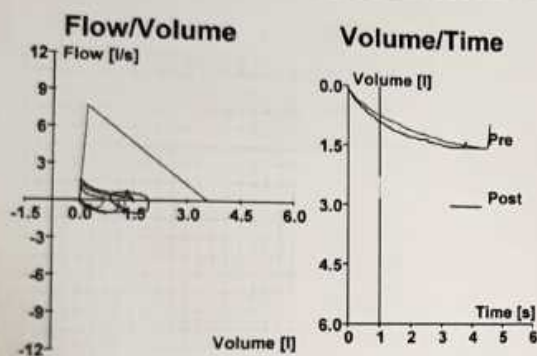
Why GOLD Still Recommends the Fixed Ratio:

- **Simplicity and consistency** are critical for busy clinical settings
- Using **FEV₁/FVC < 0.7** does **not result in**





	Pred.	Pre	Pre/pred.	Post	Diff.
Flow/Volume					
FVCex l	3.14	2.04	65%	2.34	15%
FEV1 l	2.72	1.51	56%	1.88	24%
FEV1/FVCex %	82	74	91%	80	8%
MEF25 l/s	1.84	0.50	27%	0.77	55%
MEF50 l/s	4.10	1.40	34%	2.04	46%
MEF75 l/s	5.76	2.79	48%	3.83	37%
MEF25-75 l/s	3.64	1.17	32%	1.79	53%
PEF l/s	6.49	3.26	50%	3.89	19%
PIF l/s	-	1.58	-	2.75	74%



	Pred.	Pre	Pre/pred.	Post	Diff.
Flow/Volume					
FVCex l	3.57	1.49	42%	1.51	1%
FEV1 l	2.84	0.71	25%	0.86	21%
FEV1/FVCex %	76	48	62%	57	20%
MEF25 l/s	1.38	0.26	19%	0.33	29%
MEF50 l/s	4.02	0.41	10%	0.61	47%
MEF75 l/s	6.77	0.73	11%	0.93	27%
MEF25-75 l/s	3.28	0.41	12%	0.57	40%
PEF l/s	7.67	1.21	16%	1.67	38%
PIF l/s	-	1.11	-	1.07	-4%



Staging the Severity of Airflow Limitation in COPD

GOLD Grade	FEV ₁ (% predicted)
GOLD 1	≥ 80%
GOLD 2	50–79%
GOLD 3	30–49%
GOLD 4	< 30%

 GOLD Recommendation (Still Preferred by GOLD):

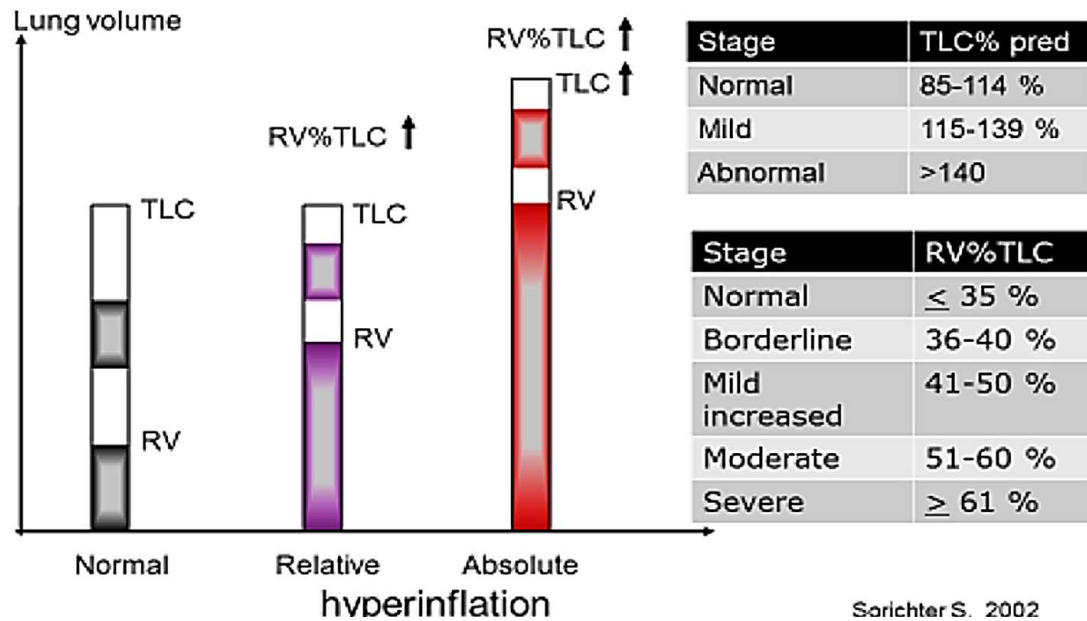
- Uses **FEV₁ % predicted** based on:
 - **GLI-Global reference equations (2022)**
- GOLD’s spirometric classification (post-bronchodilator FEV₁ % predicted):

Severity	FEV ₁ z-score
Normal	> −1.65
Mild	−1.65 to −2.5
Moderate	−2.51 to −4
Severe	< −4.1

 ERS/ATS Recommendation (Alternative):

- Proposes using **FEV₁ z-scores** instead of % predicted
 - Based on deviation from the population mean (adjusted for age, sex, height)
 - **Severity classification by z-score:**
-

Relative and absolute hyperinflation



SCREENING AND CASE-FINDING

Screening vs Case-Finding for COPD

◆ 1. Population-Based Screening Spirometry:

- Not recommended in asymptomatic individuals without significant exposures

Active Case-Finding (**GOLD Recommendation**):

- Perform **spirometry** in individuals with:
 - **Respiratory symptoms**
 - **Significant risk factors:**
 - **≥20 pack-years smoking**
 - **Recurrent chest infections**
 - **Adverse early life events**
- Recommends **against** routine **screening spirometry** for COPD in **asymptomatic adults**

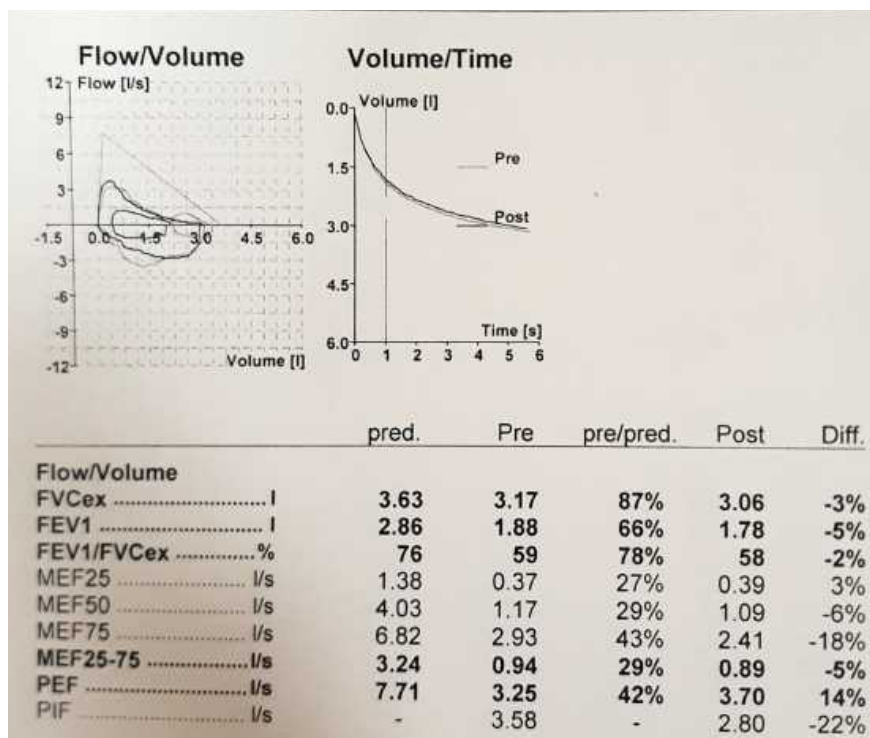
Leveraging Lung Cancer Imaging for COPD Screening

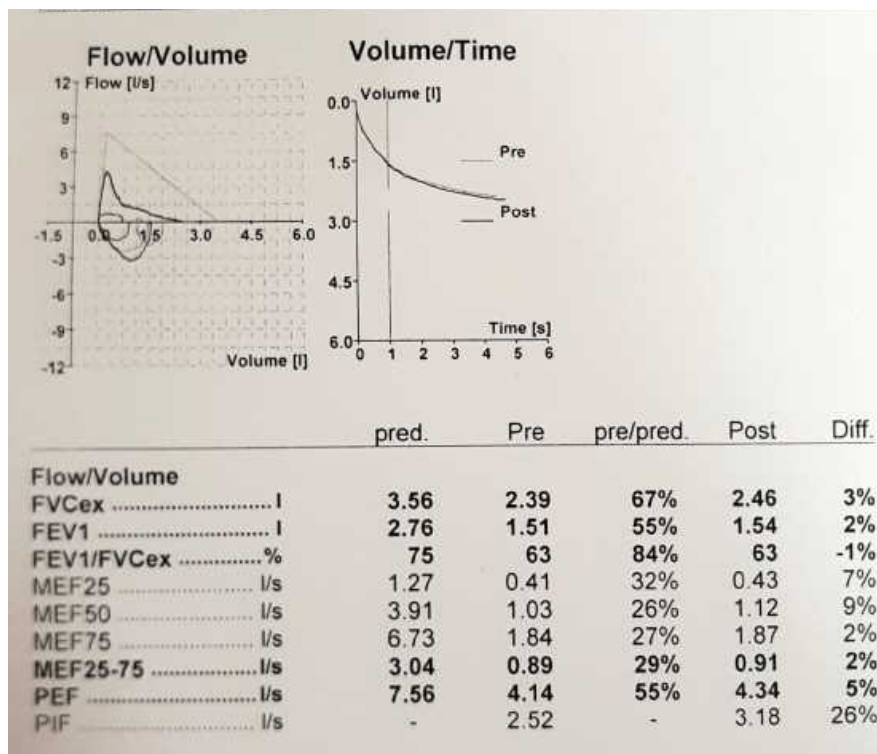
Annual low-dose chest CT (LDCT) is recommended by the **USPSTF** for **lung cancer screening** in:

- Adults aged **50–80**
- With a **≥20 pack-year smoking history**
- **Performing spirometry** in individuals undergoing LDCT for lung cancer screening to **simultaneously screen** for symptoms of COPD.
- **Prevalence of the underdiagnosis of COPD** in those undergoing lung cancer screening can approach **90%** in some reports

INITIAL ASSESSMENT

- Once **COPD is confirmed** (post-bronchodilator $FEV_1/FVC < 0.7$), assess the following five components:
 - **1. Severity of Airflow Obstruction**
 - Measured by FEV_1 % predicted (GOLD grades 1–4)
 - Important for **prognosis**, but **not the sole factor** in treatment decisions





2. Current Symptoms

- Quantified using validated tools:
 - **mMRC dyspnea scale**
 - **CAT (COPD Assessment Test)**
- Helps guide **initial pharmacologic therapy**

Dyspnea questionnaire: the modified Medical Research Council (mMRC)



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
☐	☐	☐	☐	☐

COPD Assessment Test

امتیاز			
هرگز سرفه نمیکنم	5 4 3 2 1 0	تمام مدت سرفه می کنم	
اصلاً خلط سینه ندارم	5 4 3 2 1 0	سینه ام کاملاً پر از خلط است	
اصلاً احساس سنگینی قفسه سینه ندارم	5 4 3 2 1 0	احساس سنگینی قفسه سینه خیلی شدید دارم	
هنگام بالا رفتن از پله ها نفس نفسم نمی زنم	5 4 3 2 1 0	هنگام بالا رفتن از پله ها به شدت نفس نفسم می زنم	
در انجام فعالیت ها و امور معمول محدودیت ندارم.	5 4 3 2 1 0	در انجام فعالیت ها و امور معمول محدودیت زیادی دارم.	
علیرغم وضعیت ریه خود با خیال راحت منزل را ترک می کنم	5 4 3 2 1 0	هیچ عنوان هنگام خروج از منزل خیالم راحت نیست و نگران هستم.	
خواب خوبی دارم	5 4 3 2 1 0	به علت وضعیت ریه خود خوب نمی خوابم	
انرژی زیادی دارم	5 4 3 2 1 0	اصلاً انرژی ندارم	
امتیاز کل			



3. History of Exacerbations

- Number and severity in the **previous 12 months**:
 - **Moderate** = requiring oral corticosteroids and/or antibiotics
 - **Severe** = requiring **hospitalization or ED visit**
- Predicts **future risk** and influences **treatment escalation**

4. Blood Eosinophil Count

- Assists in predicting **response to inhaled corticosteroids (ICS)**
- Thresholds:
 - **<100 cells/ μ L** → less likely to benefit from ICS
 - **≥ 300 cells/ μ L** → greater ICS benefit
 - **100–300 cells/ μ L** → intermediate likelihood

5. Multimorbidity

- Identify and address **comorbid conditions** that impact:
 - **Symptoms**
 - **Functional status**
 - **Exacerbation risk**
 - **Survival**

Examples:

- **Cardiovascular disease**
- **Osteoporosis**
- **Depression/anxiety**
- **Lung cancer**
- **Metabolic syndrome**

Combined Initial Assessment of COPD (GOLD Evolution)



Revisions Over Time:



Pre-2017: Included GOLD 1–4 in combined grouping (A, B, C, D)



This was **complex** and **less predictive** of individual outcomes.



Post-2017 (simplified ABCD tool):

- **Removed spirometric grade (GOLD 1–4)** from treatment classification
- Used only:
 - **Symptoms** (mMRC / CAT)
 - **Exacerbation history**

2023 GOLD Revision: The ABE Tool

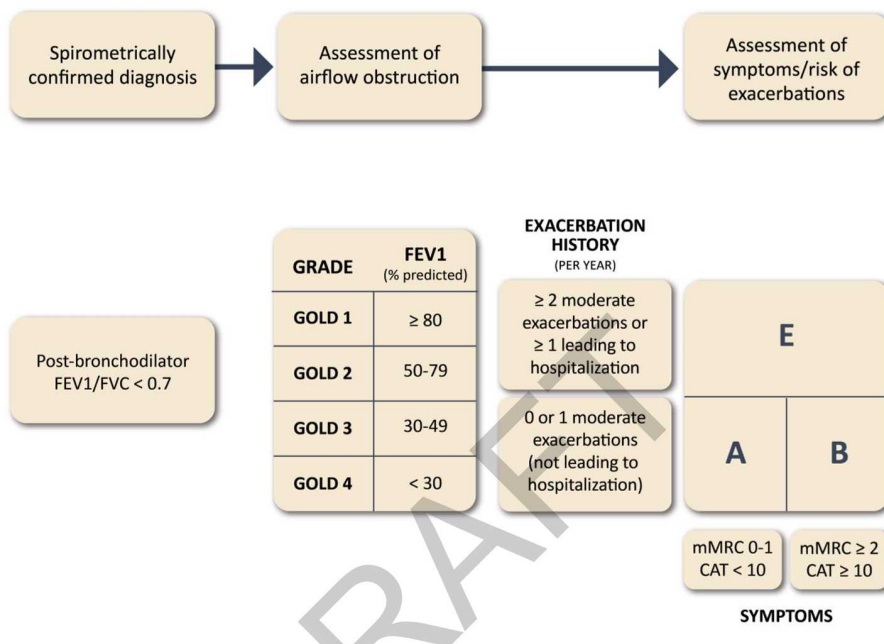
Group	Symptoms (mMRC/CAT)	Exacerbation History
A	Low symptoms	0 or 1 moderate (non-hospitalized)
B	High symptoms	0 or 1 moderate (non-hospitalized)
E	Any symptom level	≥ 2 moderate OR ≥ 1 severe (hospitalized)

C and D groups merged into a new group **E**

► Recognizes **exacerbation risk** as **independent and clinically dominant**

GOLD ABE Assessment Tool

Figure 2.11



CASE 1:

		Pred	Pre	% Pred	LLN	ULN	Z-Score
VC IN	[L]	4.41	3.57	81 %	3.49	5.33	-1.5
FVC	[L]	4.24	3.60	85 %	3.24	5.24	-1.1
FEV 1	[L]	3.32	2.29	69 %	2.49	4.16	-2.0
FEV1%VCin	[%]	76.05	64.06	84 %	64.29	87.81	-1.2
FEV1%FVC	[%]	76.05	63.57	84 %	64.29	87.81	-1.7
MEF 75	[L/s]	7.40	4.05	55 %	4.59	10.20	-2.0
MEF 50	[L/s]	4.44	1.53	35 %	2.27	6.60	-2.2
MEF 25	[L/s]	1.67	0.52	32 %	0.39	2.95	-1.5
MMEF	[L/s]	3.47	1.25	36 %	1.76	5.17	-2.1
PEF	[L/s]	8.35	4.55	54 %	6.37	10.34	-3.1

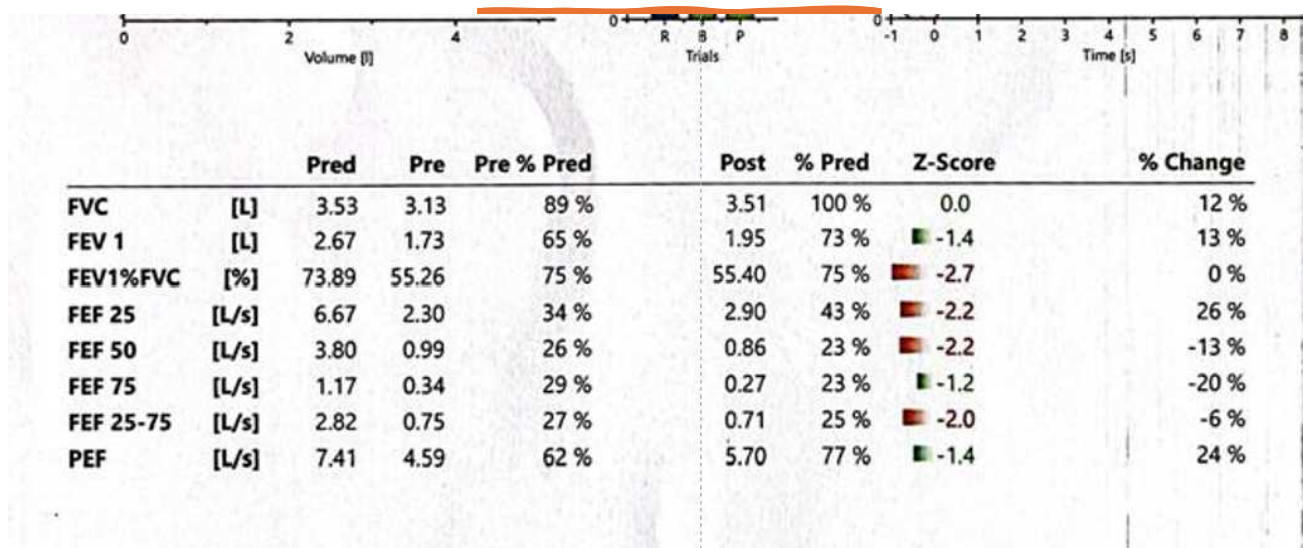
		Pred	Pre	Pre % Pred	Post	% Pred	LLN	ULN	Z-Score	% Change
VC IN	[L]	4.38	2.74	62 %	2.91	66 %	3.46	5.30	-2.6	6 %
FVC	[L]	4.22	2.94	70 %	2.93	69 %	3.22	5.22	-2.1	0 %
FEV 1	[L]	3.29	1.65	50 %	1.66	50 %	2.46	4.13	-3.2	1 %
FEV1%VCin	[%]	75.87	60.20	79 %	56.87	75 %	64.11	87.63	-2.6	-6 %
FEV1%FVC	[%]	75.87	56.02	74 %	56.56	75 %	64.11	87.63	-2.7	1 %
MEF 75	[L/s]	7.37	2.03	28 %	2.17	29 %	4.56	10.17	-3.0	7 %
MEF 50	[L/s]	4.40	0.99	22 %	1.06	24 %	2.24	6.57	-2.5	7 %
MEF 25	[L/s]	1.64	0.40	25 %	0.30	18 %	0.36	2.92	-1.7	-26 %
MMEF	[L/s]	3.42	0.86	25 %	0.83	24 %	1.72	5.13	-2.5	-4 %
PEF	[L/s]	8.31	2.96	36 %	2.63	32 %	6.32	10.29	-4.7	-11 %

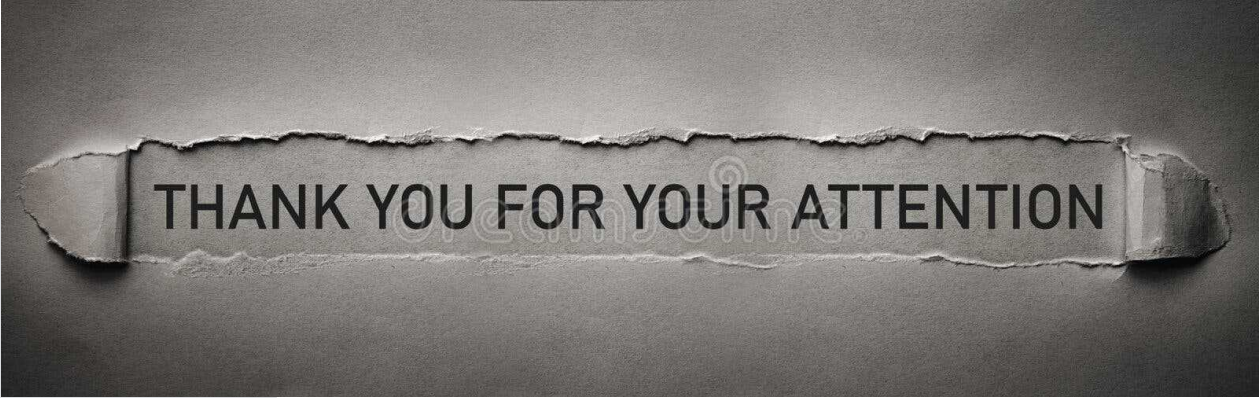
Case 2:

		Pred	Pre	% Pred	Z-Score
FVC	[L]	3.28	3.73	114 %	0.8
FEV 1	[L]	2.50	2.45	98 %	-0.1
FEV1%FVC	[%]	78.34	65.58	86 %	-1.3
FEF 25	[L/s]	6.23	7.62	122 %	0.8
FEF 50	[L/s]	3.50	1.45	42 %	-1.5
FEF 75	[L/s]	0.49	0.48	99 %	0.0
FEF 25-75	[L/s]	1.93	1.29	67 %	-0.8
PEF	[L/s]	6.91	8.46	122 %	1.3

		Pred	Pre	% Pred	Z-Score
DLCO	[mmol/min/kPa]	7.08	2.82	40 %	-3.0
KCO	[mmol/min/kPa/L]	1.21	0.54	45 %	-1.4
VA	[L]	5.71	5.22	91 %	
TLC	[L]	5.86	5.84	100 %	0.0
VC IN	[L]	3.16	3.22	102 %	0.1
RV	[L]	2.52	2.02	80 %	-1.2
FRC	[L]	3.37	3.95	117 %	1.0
RV%TLC	[%]	42.82	34.66	81 %	-1.5

Case3:





THANK YOU FOR YOUR ATTENTION

