Global Initiative For Chronic Obstructive Lung Disease: GOLD 2023

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I- Introduction

In 2001, the GOLD initiative was firmly launched in collaboration with NHLBI and WHO.

The goals of GOLD are to increase awareness of COPD and decrease morbidity and mortality from this disease.

GOLD aims to improve prevention and management of COPD through a concerted worldwide effort of people involved in all facets of healthcare and healthcare policy, and to encourage a renewed research interest in this extremely prevalent disease.

Pauwels, R. (2001) “Global initiative for chronic obstructive lung diseases (gold): Time to act,” European Respiratory Journal, 18(6), pp. 901–902. Available at: https://doi.org/10.1183/09031936.01.00274001.

Every year, a new report is generated based on an analysis of published studies which attempts to improve the way physicians handle COPD.

GOLD reports are considered to be essential evidence-based reference tools for the implementation of effective management plans, and represent the current best practices for the care of patients with COPD.

The 2017 report greatly revised the guidelines and added a few components that changed the system of COPD diagnosis and treatment.

Patel A R, Patel A R, Singh S, et al. (June 24, 2019) Global Initiative for Chronic Obstructive Lung Disease: The Changes Made. Cureus 11(6): e4985. DOI 10.7759/cureus.4985

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II- What is new in the definition?

Definition 2022

Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases. The most common respiratory symptoms include dyspnea, cough and/or sputum production. These symptoms may be under reported by patients.

Definition 2023

Chronic Obstructive Pulmonary Disease (COPD) is a heterogeneous lung condition characterized by chronic respiratory symptoms (dyspnea, cough, sputum production and/or exacerbations) due to abnormalities of the airways (bronchitis, bronchiolitis) and/or alveoli (emphysema) that cause persistent, often progressive, airflow obstruction.

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Proposed Taxonomy (Etiotypes) for COPD

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)

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III- What is new in the diagnostic criteria?

Clinical Indicators for Considering a Diagnosis of COPD

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 unproductive
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.)

In the appropriate clinical context, the presence of non-fully reversible airflow limitation (i.e., FEV1/FVC < 0.7 post-bronchodilation) measured by spirometry confirms the diagnosis of COPD.

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

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

Pre - COPD

The section on diagnostic criteria added a proposed category “PRISm” denoting “preserved ratio impaired spirometry”, encompassing individuals who present with structural lung lesions (for example, emphysema) and /or other physiological abnormalities such as low-normal forced expiratory volume in 1 second (FEV_1), gas trapping, hyperinflation, reduced lung diffusing capacity and/or rapid FEV_1 decline, but without airflow obstruction ($FEV_1/FEV \geq 0.7$ post bronchodilation).

Some of theses “pre-COPD” (chronic obstructive pulmonary disease) individuals, who have a normal ratio but abnormal spirometry, are at risk of developing airflow obstruction over time. The best treatment for them, beyond smoking cessation, needs to be determined through research, the report states.

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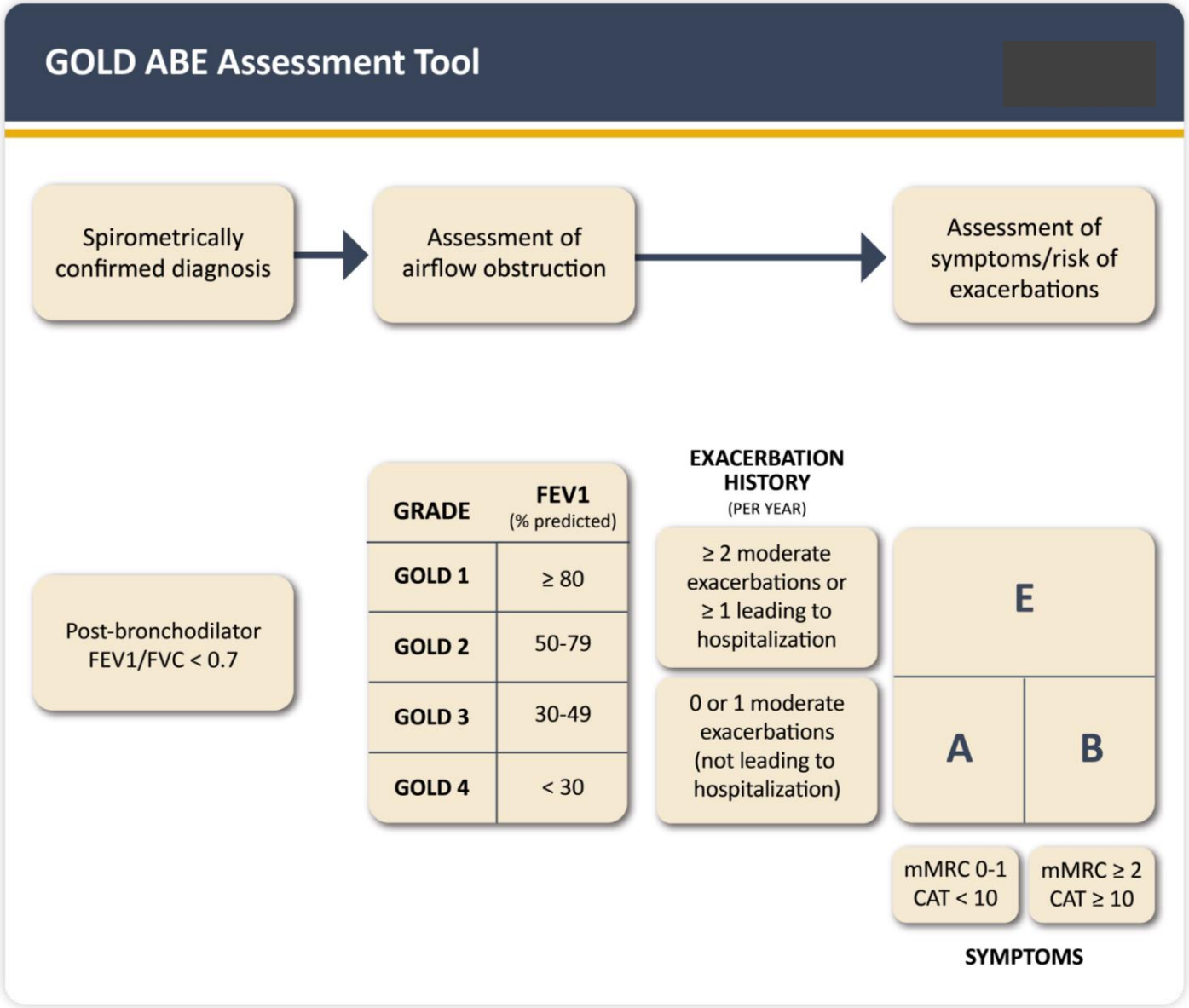
IV- What is new in the assessment tool?


GOLD ABE Assessment Tool
Spirometrically confirmed diagnosis
Assessment of airflow obstruction
Assessment of symptoms/risk of exacerbations
Post-bronchodilator FEV1/FVC < 0.7
GRADE
FEV1 (% predicted)
GOLD 1
≥ 80
GOLD 2
50-79
GOLD 3
30-49
GOLD 4
< 30
EXACERBATION HISTORY (PER YEAR)
≥ 2 moderate exacerbations or ≥ 1 leading to hospitalization
0 or 1 moderate exacerbations (not leading to hospitalization)
E
A
B
mMRC 0-1 CAT < 10
mMRC ≥ 2 CAT ≥ 10
SYMPTOMS

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V- What is new in the management of stable COPD?

Initial Pharmacological Treatment

≥ 2 moderate exacerbations or ≥ 1 leading to hospitalization

GROUP E

LABA + LAMA*

consider LABA+LAMA+ICS if blood eos ≥ 300*

0 or 1 moderate exacerbations (not leading to hospital admission)

GROUP A

A bronchodilator

mMRC 0-1, CAT < 10

GROUP B

LABA + LAMA*

mMRC ≥ 2, CAT ≥ 10

*single inhaler therapy may be more convenient and effective than multiple inhalers
Exacerbations refers to the number of exacerbations per year

Key Points for the Use of Bronchodilators

- LABAs and LAMAs are preferred over short-acting agents except for patients with only occasional dyspnea **(Evidence A)**, and for immediate relief of symptoms in patients already on long-acting bronchodilators for maintenance therapy
- When initiating treatment with long acting bronchodilators the preferred choice is a combination of a long-acting muscarinic antagonist and a long acting ß2-agonist. In patients with persistent dyspnea on a single long acting bronchodilator treatment should be escalated to two **(Evidence A)**. The combination can be given as single inhaler or multiple inhaler treatment
- Inhaled bronchodilators are recommended over oral bronchodilators **(Evidence A)**
- Theophylline is not recommended unless other long-term treatment bronchodilators are unavailable or unaffordable **(Evidence B)**

Key Points for the Use of Anti-Inflammatory Agents

- Long-term monotherapy with ICS is not recommended **(Evidence A)**
- We do not encourage the use of a LABA+ICS combination in COPD. If there is an indication for an ICS the combination LABA+LAMA+ICS has been shown to be superior to LABA+ICS and is therefore the preferred choice. This combination can be given as single or multiple inhaler therapy.
- If patients with COPD have features of asthma, treatment should always contain an ICS

Factors to Consider when Initiating ICS Treatment

Factors to consider when adding ICS to long-acting bronchodilators:

(note the scenario is different when considering ICS withdrawal)

STRONGLY FAVORS USE	**History of hospitalization(s) for exacerbations of COPD[#]**
	≥ 2 moderate exacerbations of COPD per year[#]
	Blood eosinophils ≥ 300 cells/µL
	History of, or concomitant asthma
FAVORS USE	1 moderate exacerbation of COPD per year[#]
	Blood eosinophils 100 to < 300 cells/µL
AGAINST USE	**Repeated pneumonia events**
	Blood eosinophils < 100 cells/µL
	History of mycobacterial infection

[#]despite appropriate long-acting bronchodilator maintenance therapy (see Table 3.4 and Figure 4.3 for recommendations);
*note that blood eosinophils should be seen as a continuum; quoted values represent approximate cut-points; eosinophil counts are likely to fluctuate.

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

Therapy	RCT*	Treatment effect on mortality	Patient characteristics
Pharmacotherapy			
LABA+LAMA+ICS[1]	Yes	Single inhaler triple therapy compared to dual LABD therapy relative risk reduction: IMPACT: HR 0.72 (95% CI: 0.53, 0.99)[1a] ETHOS: HR 0.51 (95% CI: 0.33, 0.80)[1b]	Symptomatic people with a history of frequent and/or severe exacerbations
Non-pharmacological Therapy			
Smoking cessation[2]	Yes	HR for usual care group compared to intervention group (smoking cessation) HR 1.18 (95% CI: 1.02, 1.37)[2]	Asymptomatic or mildly symptomatic
Pulmonary rehabilitation[3#]	Yes	Old trials: RR 0.28 (95% CI 0.10, 0.84)[3a] New trials: RR 0.68 (95% CI 0.28, 1.67)[3b]	Hospitalized for exacerbations of COPD (during or ≤ 4 weeks after discharge)
Long-term oxygen therapy[4]	Yes	NOTT: ≥ 19 hours of continuous oxygen vs ≤ 13 hours: 50% reduction[4a] MRC: ≥ 15 hours vs no oxygen: 50% reduction[4b]	PaO_2 ≤ 55 mmHg or < 60 mmHg with *cor pulmonale* or secondary polycythemia
Noninvasive positive pressure ventilation[5]	Yes	12% in NPPV (high IPAP level) and 33% in control HR 0.24 (95% CI 0.11, 0.49)[5]	Stable COPD with marked hypercapnia
Lung volume reduction surgery[6]	Yes	0.07 deaths/person-year (LVRS) vs 0.15 deaths/person-year (UC) RR for death 0.47 (p = 0.005)[6]	Upper lobe emphysema and low exercise capacity

*RCT with pre-specified analysis of the mortality outcome (primary or secondary outcome); #Inconclusive results likely due to differences in pulmonary rehabilitation across a wide range of participants and settings.

1. a) IMPACT trial (Lipson et al. 2020) and b) ETHOS trials (Martinez et al. 2021); 2.Lung Health Study (Anthonisen et al. 2005); 3. a) Puhan et al. (2011) and b) Puhan et al. 2016; 4. a) NOTT (NOTT, 1980) and b) MRC (MRC, 1981); 5. Kohlein trial (Kohlein et al. 2014); 6. NETT trial (Fishman et al. 2003)

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

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VI- What is new in the definition of exacerbations?

Definition of exacerbations

2022:

An exacerbation of COPD is defined as an acute worsening of respiratory symptoms that results in additional therapy.

2023:

An exacerbation of COPD is defined as an event characterized by dyspnea and/or cough and sputum that worsen over < 14 days.

Exacerbations of COPD are often associated with increased local and systemic inflammation caused by airway infection, pollution, or other insults to the lungs.

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VII- What is new in the classification of exacerbations?

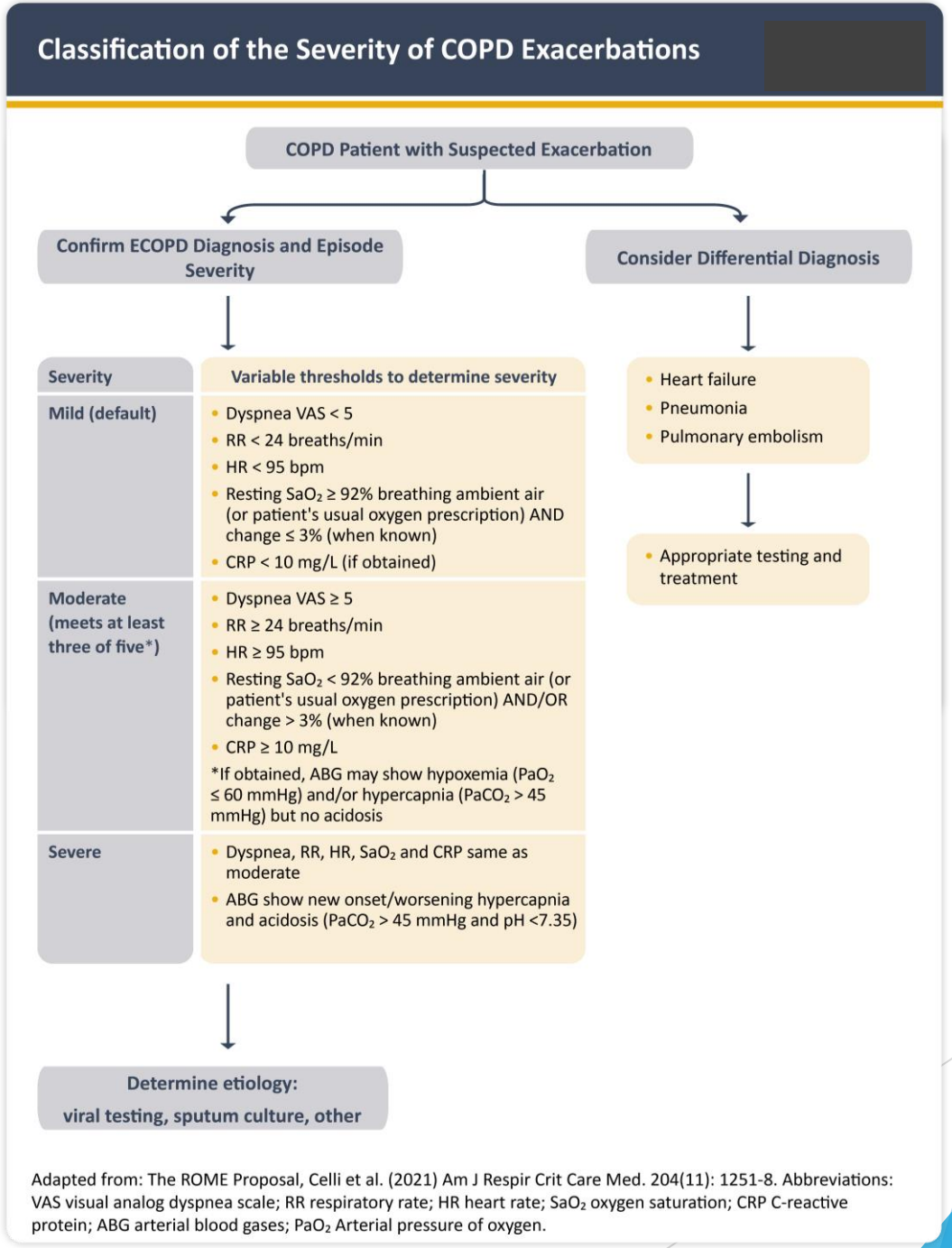
Diagnosis and Assessment

1.	Complete a thorough clinical assessment for evidence of COPD and potential respiratory and nonrespiratory concomitant diseases, including consideration of alternative causes for the patient's symptoms and signs: primarily pneumonia, heart failure, and pulmonary embolism.
2.	**Assess:** a. Symptoms, severity of dyspnea that can be determined by using a VAS, and documentation of the presence of cough. b. Signs (tachypnea, tachycardia), sputum volume and color, and respiratory distress (accessory muscle use).
3.	Evaluate severity by using appropriate additional investigations such as pulse oximetry, laboratory assessment, CRP, arterial blood gases.
4.	Establish the cause of the event (viral, bacterial, environmental, other).

Definition of abbreviations: COPD = chronic obstructive pulmonary disease; CRP = C-reactive protein; VAS = visual analog scale.

Currently, exacerbations are classified after the event has occurred as:

- Mild (treated with short acting bronchodilators only, SABDs)
- Moderate (treated with SABDs and oral corticosteroids ± antibiotics)
- Severe (patient requires hospitalization or visits the emergency room). Severe exacerbations may also be associated with acute respiratory failure.



Adapted from: The ROME Proposal, Celli et al. (2021) Am J Respir Crit Care Med. 204(11): 1251-8. Abbreviations: VAS visual analog dyspnea scale; RR respiratory rate; HR heart rate; SaO_2 oxygen saturation; CRP C-reactive protein; ABG arterial blood gases; PaO_2 Arterial pressure of oxygen.

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Thank you