

Proposed Taxonomy (Etiotypes) for COPD

Table 1.1

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)	<ul style="list-style-type: none"> • Exposure to tobacco smoke, including <i>in utero</i> 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)

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

Table 2.6

In COPD patients (FEV₁/FVC < 0.7):

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

Modified MRC Dyspnea Scale

Table 2.7

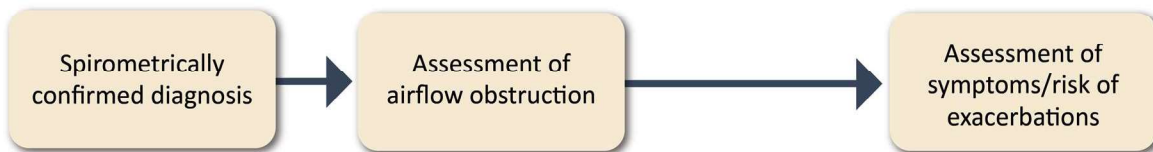
PLEASE TICK IN THE BOX THAT APPLIES TO YOU | ONE BOX ONLY | Grades 0 - 4

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
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

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

GOLD ABE Assessment Tool

Figure 2.3



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

SYMPTOMS

- mMRC 0-1
CAT < 10
- mMRC ≥ 2
CAT ≥ 10

Use of CT in Stable COPD

Table 2.8

Differential Diagnosis

- Frequent exacerbations with excessive cough with sputum production, raising concern for bronchiectasis or atypical infection
- Symptoms out of proportion to disease severity based on lung function testing

Lung Volume Reduction

- Endobronchial valve therapy may be a therapeutic option for patients if they demonstrate postbronchodilator FEV1 between 15-45% and evidence of hyperinflation
- Lung volume reduction surgery may be a therapeutic option for patients with hyperinflation, severe upper lobe predominant emphysema and low exercise capacity after pulmonary rehabilitation

Lung Cancer Screening

- Annual low-dose CT scan is recommended for lung cancer screening in patients with COPD due to smoking according to recommendations for the general population

Factors to Consider when Initiating ICS Treatment

Figure 3.1

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.

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Vaccination for Stable COPD

Table 3.2

- Influenza vaccination is recommended in people with COPD (**Evidence B**)
- The WHO and CDC recommends SARS-CoV-2 (COVID-19) vaccination for people with COPD (**Evidence B**)
- The CDC recommends one dose of 20-valent pneumococcal conjugate vaccine (PCV20); or one dose of 15-valent pneumococcal conjugate vaccine (PCV15) followed by 23-valent pneumococcal polysaccharide vaccine (PPSV23) in people with COPD (**Evidence B**)
- Pneumococcal vaccination has been shown to reduce the incidence of community-acquired pneumonia and exacerbations in people with COPD (**Evidence B**)
- The CDC recommends Tdap (dTaP/dTPa) vaccination to protect against pertussis (whooping cough) for people with COPD that were not vaccinated in adolescence (**Evidence B**), and Zoster vaccine to protect against shingles for people with COPD over 50 years (**Evidence B**)

Differential Diagnosis of COPD

Table 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
Tuberculosis	Onset 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

These features tend to be characteristic of the respective diseases, but are not mandatory. For example, a person who has never smoked may develop COPD (especially in LMICs where other risk factors may be more important than cigarette smoking).

Initial Pharmacological Treatment

Figure 4.2



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

Commonly Used Maintenance Medications in COPD*

Table 3.3

Generic Drug Name	Inhaler Type	DELIVERY OPTIONS			Duration of Action
		Nebulizer	Oral	Injection	
BETA₂-Agonists					
Short-acting (SABA)					
Fenoterol	MDI	✓	pill, syrup		4-6 hours
Levalbuterol	MDI	✓			6-8 hours
Salbutamol (albuterol)	MDI & DPI	✓	pill, syrup, extended release tablet	✓	4-6 hours 12 hours (ext. release)
Terbutaline	DPI		pill	✓	4-6 hours
Long-acting (LABA)					
Arformoterol		✓			12 hours
Formoterol	DPI	✓			12 hours
Indacaterol	DPI				24 hours
Olodaterol	SMI				24 hours
Salmeterol	MDI & DPI				12 hours
Anticholinergics					
Short-acting (SAMA)					
Ipratropium bromide	MDI	✓			6-8 hours
Oxitropium bromide	MDI				7-9 hours
Long-acting (LAMA)					
Acclidinium bromide	DPI,				MDI 12 hours
Glycopyrronium bromide	DPI		solution	✓	12-24 hours
Tiotropium	DPI, SMI, MDI				24 hours
Umeclidinium	DPI				24 hours
Glycopyrrolate		✓			12 hours
Revefenacin		✓			24 hours
Combination Short-Acting Beta₂-Agonist Plus Anticholinergic in One Device (SABA+SAMA)					
Fenoterol/ipratropium	SMI	✓			6-8 hours
Salbutamol/ipratropium	SMI, MDI	✓			6-8 hours
Combination Long-Acting Beta₂-Agonist Plus Anticholinergic in One Device (LABA+LAMA)					
Formoterol/aclidinium	DPI				12 hours
Formoterol/glycopyrronium	MDI				12 hours
Indacaterol/glycopyrronium	DPI				12-24 hours
Vilanterol/umeclidinium	DPI				24 hours
Olodaterol/tiotropium	SMI				24 hours
Methylxanthines					
Aminophylline			solution	✓	Variable, up to 24 hours
Theophylline (SR)			pill	✓	Variable, up to 24 hours
Combination of Long-Acting Beta₂-Agonist Plus Corticosteroid in One Device (LABA+ICS)					
Formoterol/beclometasone	MDI, DPI				12 hours
Formoterol/budesonide	MDI, DPI				12 hours
Formoterol/mometasone	MDI				12 hours
Salmeterol/fluticasone propionate	MDI, DPI				12 hours
Vilanterol/fluticasone furoate	DPI				24 hours
Triple Combination in One Device (LABA+LAMA+ICS)					
Fluticasone/umeclidinium/vilanterol	DPI				24 hours
Beclometasone/formoterol/glycopyrronium	MDI, DPI				12 hours
Budesonide/formoterol/glycopyrrolate	MDI				12 hours
Phosphodiesterase-4 Inhibitors					
Roflumilast			pill		24 hours
Mucolytic Agents					
Erdosteine			pill		12 hours
Carbocysteine [†]			pill		
N-acetylcysteine [†]			pill		

*Not all formulations are available in all countries. In some countries other formulations and dosages may be available. †Dosing regimens are under discussion. MDI = metered dose inhaler; DPI = dry powder inhaler; SMI = soft mist inhaler. Note that glycopyrrolate & glycopyrronium are the same compound.