

SENTARA HEALTH PLANS CLINICAL PRACTICE GUIDELINE:

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

Guideline History

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Guideline Change Summary

Date	Description
9/2025	Review and Recommendations provided by Dr. Charles Lovell for presentation to Committee 11/2025. Recommended updates include adoption of the Gold 2025 Report (Global Initiative for Chronic Obstructive Lung Disease)

For the full 2025 GOLD Report, please visit: https://goldcopd.org/2025-gold-report/



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2025 GOLD Report: What is New and What is Noteworthy for the Practicing Clinician

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The Global initiative for chronic Obstructive Lung Disease (GOLD) report is revised annually and released each November in parallel with World COPD Day. The 2025 GOLD report has incorporated multiple changes with clinical relevance, including the diagnostic approach with spirometry and other tests, the management of patients with cardiovascular comorbidities and pulmonary hypertension, novel treatments and the refinement of the use of older ones, and the proactive management to minimize future risk of COPD patients [1].

Diagnostic approach and modalities

The role of *pre*-bronchodilator spirometry as a diagnostic test for COPD is now highlighted in the GOLD 2025 document, as a simpler option that requires less time and may reduce barriers to testing. Bronchodilator reversibility is not absolutely necessary for the diagnosis of COPD, especially since this process is time-consuming and sometimes difficult to implement in clinical practice. An initial testing with a *pre*-bronchodilator FEV_1/FVC ratio ≥0.7 likely rules out COPD; however, in this case bronchodilator reversibility is useful in high-risk individuals, as it may reveal those (relatively few) patients who are volume responders (i.e. will have a *post*-bronchodilator increase in FVC). A *pre*-bronchodilator FEV_1/FVC ratio <0.7 is highly indicative of COPD and does not necessarily need to be followed by bronchodilator reversibility. Importantly, if the *post*-bronchodilator ratio is ≥0.7 in patients with pre-bronchodilator value <0.7, the flow response to salbutamol identifies individuals at need for close follow-up, as they have increased risk for COPD development in the future [2]. However, these findings cannot be applied to individual subjects, because variable obstruction was defined as any change from *pre*-bronchodilator FEV_1/FVC <0.70 to *post*-bronchodilator values ⩾0.70, without considering short-term interindividual variability.

GOLD further stresses the importance of the use of the lower limit of normal (LLN) or z-scores of FEV_1/FVC as an individualized approach for each patient, not only in (the relatively many) older individuals in whom the fixed ratio may over-diagnose COPD, but also in (the relatively few) younger ones in whom the fixed ratio may under-diagnose high-risk COPD patients [3]. A recent study in the Tasmanian Longitudinal Health Study cohort using z-scores showed that individuals without COPD and with pre-bronchodilator FEV_1/FVC in the lower 10^{th} percentile at the age of 45 had increased risk of developing COPD in the following 8 years [4]. Although more complex for daily clinical practice, the use of z-scores may allow for the identification of patients in a "grey zone" where follow-up or additional investigations are required [5]. The ERS/ATS classification of severity based on z-scores and the use of race-neutral equations is also discussed, but not recommended by GOLD so far. The use of z-scores for severity will likely shift older individuals into milder categories and younger individuals into more severe categories, whereas the use of race-neutral equations may re-classify some non-white individuals as "more severe" and some white individuals as "less severe" with potential treatment implications and unknown clinical significance in the future [6]. In all these considerations we always need to remember that most clinical trials that have evaluated treatments implementing spirometric criteria so far have evaluated severity using % predicted values. Spirometry is also discussed as a marker of global health, with individuals with lung function above or below the "normal" trajectory being more likely to have healthier or more accelerated aging, respectively, with the latter often suffering from cardiopulmonary comorbidities [7].

The role of CT scans is further highlighted, with focus on the phenotyping and identification of potential high-risk patients, by the quantification of emphysema and complex airways disease, including bronchiectasis and mucous plugging [8]. In the clinic we should always take advantage of synergies, including the incidental diagnosis of lung nodules, interstitial lung abnormalities (ILA) or coronary artery disease in CT scans performed for COPD, and the presence of emphysema or airways disease in low-dose CT scans for lung cancer screening. Although these are useful recommendations for areas with wide access to CT scans, they are not applicable in many parts of the world.

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Multimorbidity and cardiovascular risk

The presence of multiple comorbidities is common in the aging COPD patients. GOLD 2025 makes a specific mention to cardiovascular disease, including pulmonary hypertension, coronary artery disease, arrhythmias and heart failure, that increase the risk of adverse outcomes in COPD, and yet remain underrecognized and often undertreated [9]. The document stresses the need for the differential diagnosis of events with common presentation (e.g. dyspnea in decompensated COPD and heart failure), the use of biomarkers (e.g. troponin and brain-natriuretic peptides) and meticulous treatment of both conditions. The association between COPD exacerbations and increased cardiovascular risk around and shortly after these events is also highlighted [10], and provides an additional reason for aggressive prevention of these events.

Mild pulmonary hypertension (PH) is common in patients with COPD, with the majority of patients classified as PH associated with lung disease and/or hypoxia (group 3) or left heart disease (group 2). However, some patients with PH-COPD may present with severe/disproportionate PH, whereas others may have treatable traits, including pulmonary arterial hypertension (PAH, group 1 PH) or chronic thromboembolic PH (CTEPH, group 4). Such patients should be referred to specialized centers and treated according to the ESC/ERS guidelines with a multi-disciplinary approach [11], as earlier and recent studies have not shown universal benefit of currently available medication for PAH in COPD patients [12].

Management of stable COPD

The vaccination scheme for COPD patients is updated in the GOLD 2025 document to reflect the guidance of the US Centers for Disease Control (CDC), including yearly influenza, updated SARS-CoV-2, pneumococcal conjugate vaccines (single dose of PCV20 or PCV21), respiratory syncytial virus (RSV) for patients ≥60 years or with cardiopulmonary comorbidities, and protection against pertussis and shingles. The recommendation to follow local/national vaccination schemes remains.

The list of maintenance medications for stable COPD has also been revised and now includes 10 categories with 40 different substances and combinations of treatment options. The newly added medicines for 2025 include two treatment options with novel mechanisms of actions for COPD:

1. *Ensifentrine*, a nebulized phosphodiesterase (PDE) 3 & 4 inhibitor that improves lung function and breathlessness [13], is currently available only in the US. In the newly revised algorithms for the follow-up pharmacological treatment, ensifentrine is proposed as potential add-on therapy in patients with dyspnea on dual bronchodilation with LABA+LAMA.
2. *Dupilumab*, a monoclonal antibody that targets the interleukin 4 receptor alpha, reduced exacerbations and improved lung function and health status in two clinical trials of patients with chronic bronchitis, exacerbations despite triple therapy (LABA+LAMA+ICS) and type 2 inflammation, as documented by blood eosinophil count (BEC) of ≥300 cells/μL [14, 15]. In the revised algorithm for follow-up treatment, dupilumab is proposed on top of triple therapy, in exacerbating patients with BEC ≥300 cells/μL and a chronic bronchitis phenotype. Dupilumab has also been added in the list of interventions that reduce the frequency of COPD exacerbations.

It is important to highlight that, although GOLD recommendations are designed to be applicable worldwide, some of the treatment options mentioned in the document, and especially these two novel treatments are not licensed and/or available in many parts of the world.

Since the 2023 document, GOLD has advocated against the use of LABA+ICS combinations in patients who need ICS and suggests adding ICS only on top of optimal bronchodilation with LABA+LAMA, given the superiority of triple therapy in multiple clinical trials. However, there was no specific guidance on how to handle patients who are on LABA+ICS, and this gap is covered by the 2025 document, that provides recommendations based on prior exacerbation history and/or beneficial response with LABA+ICS:

- In patients exacerbating on LABA+ICS, if their BEC is <100 cells/μL we may consider switch to LABA+LAMA, whereas if BEC is ≥100 cells/μL escalation to triple therapy is preferable.
- In patients on LABA+ICS with no history of exacerbations, we may consider changing to LABA+LAMA.
- In patients with no recent exacerbations but with previous exacerbation reduction benefit with LABA+ICS, we may continue this treatment if the patient is not symptomatic, whereas if the patient is dyspneic, we may consider escalation to triple therapy.

GOLD 2025 has also revised the recommendations for ICS withdrawal, stating clearly that it should be avoided in patients with BEC >300 cells/μL due to the increased risk of exacerbations. This recommendation has now been removed from the follow-up pharmacological treatment algorithm for exacerbating patients. The document also refers to other biologics that are currently tested in phase 3 trials in patients with COPD, some of which are now licensed for severe asthma, and further developments are expected in this area. As in previous versions, GOLD 2025 does not have a section on asthma-COPD overlap, however it recommends that such patients should be treated as asthma, as covered in recent Global Initiative for Asthma (GINA) documents [16].

Following the COVID-19 pandemic that mandated the use of telehealth solutions, GOLD 2025 stresses the importance and benefits of tele-rehabilitation [17], tele-education and self-management programs, mentioning also their limitations and the importance of avoiding misuse of the appealing technology that is becoming available. As an optimistic sign, the section on COVID-19 has now been removed.

Finally, GOLD 2025 has a specific session on climate change and COPD. Extreme (both high and low) temperatures and air

pollution have significant consequences on COPD patients' health, with cold bringing patients at the highest risk of death [18]. The ideal bedroom conditions proposed by GOLD for these patients are >18 °C during the cold periods and <24 °C during heatwaves, as recommended by WHO [19]. The detrimental effects of indoor and outdoor pollution are also highlighted, as well as the need for preventative behavioral measures, including avoiding going out, proper ventilation and air-conditioning.

As stated by Claus Vogelmeier, the Chair of the GOLD Science Committee, the 2025 document "is an important step from a reactive to a proactive type of medicine." [20]. As per the quote of Hippocrates of Kos (460–370 BC), the father of modern medicine, *"Το δε προνοείν και προλαμβάνειν κρείττον εστί του θεραπεύειν"* (or *"looking ahead and preventing is preferable than curing"*), this update focuses on proper (and hopefully earlier) diagnosis, vaccination and exercise, management of multimorbidity including cardiovascular risk, and proper personalized management to prevent adverse outcomes of COPD patients. Although in the right direction, many of the recommendations are not applicable worldwide due to differences in access to diagnostic modalities, in approvals and reimbursement of medication and vaccines, and rehabilitation and interventional techniques. This is challenging for practicing clinicians, especially in primary care, and renders important the critical evaluation and the potential adaptation of the GOLD document to local/national recommendations.

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