#### Review

# Challenges and Opportunities for the Management of COPD: A Narrative Review of Patient and Health Care Professional Perspectives

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Abbreviations: BI= brief intervention; CAPTURE= COPD Assessment in Primary Care to Identify Undiagnosed Respiratory Disease and Exacerbation Risk; CAT=COPD Assessment Test<sup>TM</sup>; CDC=Centers for Disease Control and Prevention; CI=confidence interval; CME= Continuing Medical Education; COPD=chronic obstructive pulmonary disease; CT=computed tomography; EMR=electronic medical record; FEV1=forced expiratory volume in one second; FVC=forced vital capacity; GAAPP= The Global Allergy & Airways Patient Platform; GOLD=Global Initiative for Chronic Obstructive Lung Disease; HCP=healthcare professional; HRQoL=health-related quality of life; ICS=inhaled corticosteroid; INT\$=International Dollar; IPCRG=The International Primary Care Respiratory Group; LABA=long-acting β-2 agonist; LAMA=long-acting muscarinic antagonist; LMICs=low- and middle-income countries; MDI= metered-dose dose inhalers; mMRC=modified Medical Research Council; NICE=National Institute for Health and Care Excellence; NO<sub>2</sub>=nitrogen dioxide; PM10=particulate matter 10 micrometers; NRT=Nicotine Replacement Therapy; PM2.5=particulate matter 2.5 micrometers; PCP=primary care physician; QoL=quality of life; RSV=respiratory syncytial virus; SABA=short-acting β-2 agonist; SAMA=short-acting muscarinic antagonist; SERPINA1=serpin peptidase inhibitor, clade A (alpha-1 antitrypsin); SGRQ=St. George Respiratory Questionnaire; STAR=STaging of Airflow Obstruction by Ratio; Tdap=tetanus, diphtheria, and pertussis vaccine; TTG= teach-to-goal; U.S.=United States; WHO=World Health Organization.

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#### **Abstract**

This review addresses the multifaceted challenges and opportunities in managing chronic obstructive pulmonary disease (COPD), from both the patient and healthcare professional (HCP) perspectives. Co-authored by a patient organization advocate, a pulmonologist, and a nurse practitioner, this article synthesizes insights gained through collaborative discussions and a comprehensive literature review. It highlights the critical importance of early diagnosis of COPD, emphasizing that delayed diagnosis can lead to significant underdiagnosis and mismanagement of the disease. Lung function declines more rapidly in the early stages of COPD. Therefore, delayed or underdiagnosed COPD results in a lost opportunity to improve or maintain lung function, prevent exacerbations, and enhance the quality of life. The typical patient journey is also outlined in this article, underscoring the necessity of encouraging patients to actively engage in their care. Patients and HCPs collectively call for improvements in COPD management, emphasizing the importance of maintenance therapy; a deeper understanding of COPD exacerbations, focusing on their prevention; and fostering a partnership between patients and their HCPs in care management. The role of HCPs is crucial in promoting the self-management and awareness of COPD among patients. By integrating patient perspectives into clinical practice, healthcare systems can better address the complex needs of patients with COPD and ultimately enhance their health outcomes.

#### INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common, chronic, heterogeneous lung condition, characterized by respiratory symptoms attributable to persistent airway and/or alveoli abnormalities that may result in progressive airflow limitation. 1,2 Globally, COPD is a major health concern as it is the third leading cause of death and the seventh leading cause of poor health. In 2020, 480 million (10.6%) people (age  $\geq$  25 years) worldwide suffered from COPD, and the global prevalence is projected to reach approximately 600 million by 2050.<sup>3</sup> The societal burden of COPD in the United States (US) is also growing; in 2021, the prevalence of COPD was 6.5% (14.2 million cases). Furthermore, the economic burden of COPD in the US is projected to be INT\$1.037 trillion (The INT\$ represents International Dollar, a hypothetical unit of currency that has the same purchasing power as the U.S. Dollar in a given year), or around 0.19% of its gross domestic product, over the next three decades.<sup>5</sup> While tobacco smoking is the leading risk factor for COPD, other factors may include prolonged exposure to smoke from household biomass burning; occupational exposure to gases, fumes, and other inhaled agents; and poor air quality. <sup>6,7</sup> Genetic factors such as SERPINA1 gene mutation leading to  $\alpha$ -1 antitrypsin deficiency, which elevates the expression of serine proteases, can also increase the predisposition for COPD.<sup>2</sup>

Patients typically experience chronic dyspnea, wheezing, chest tightness, fatigue, and productive or nonproductive cough, which are often present with comorbidities such as cardiovascular disease, musculoskeletal disorders, metabolic disorders, osteoporosis, anxiety, depression, and lung cancer.<sup>2</sup> In addition, acute episodes of worsened respiratory symptoms, termed "exacerbations," negatively affect the prognosis and health status of patients and require specific preventive and therapeutic interventions.<sup>2</sup>

Patients with COPD face significant challenges in daily activities due to breathlessness and fatigue. These challenges can affect their ability to perform routine tasks, which may necessitate external support or assistance. Furthermore, patients' inability to participate in social activities may often result in social isolation and emotional challenges.<sup>8,9</sup> Thus, international guidelines emphasize including COPD symptoms and history of exposure to risk factors in the initial assessment of COPD to determine patient-centric preventive and management strategies.<sup>2</sup> The goal of management strategies must include alleviating COPD symptoms, enhancing health status, and increasing the level of physical activities.<sup>2</sup> Appropriately administered maintenance pharmacotherapy can significantly reduce symptoms and prevent exacerbations in patients with COPD. However, recent real-world evidence has shown that most patients are not prescribed maintenance pharmacological therapy at initial diagnosis. <sup>10</sup> This represents a lost opportunity to improve or maintain lung function, prevent exacerbations, and enhance patients' quality of life (QoL). Several barriers to optimal COPD care have been previously identified.<sup>11</sup> Patient-related barriers include low socioeconomic status, inadequate family and social support, and reluctance to participate in demanding interventions required to manage COPD.<sup>11</sup> Barriers related to the healthcare system include delays in diagnosing COPD and initiating or intensifying treatment, limited provider awareness about treatment guidelines, lack of a positive doctor-patient relationship and an integrated disease management infrastructure, insurance coverage issues, and underdiagnosis. <sup>6,11</sup> This review aims to explore the primary challenges and opportunities of managing COPD from both the patient and healthcare professional (HCP) perspectives. Understanding the perspective of patients with COPD is a critical, yet often overlooked, insight. Thus, this review will also describe the typical journey of patients with COPD and offer insights into how patients can become more actively involved in their care and work

toward partnering more closely with their HCPs to ultimately enhance clinical and patientcentered outcomes.

#### **METHODS**

This article is co-authored by a patient advocacy organization representative who is also living with COPD, a pulmonologist, and a nurse practitioner with expertise in COPD care. The authors collaborated through virtual meetings, via email, and by written feedback to develop the content of this article. Literature searches were conducted on PubMed using different combinations of the key terms to identify the content for this narrative review. Fig S1 illustrates the distribution and overlap of search terms used in conducting the literature searches. No timeline restrictions were applied. Articles obtained from the searches were evaluated for relevance to determine inclusion. Additional articles were identified from the reference lists of the pertinent articles that were retrieved. Authors also suggested articles for inclusion based on their detailed knowledge of the subject. All relevant articles were incorporated into the current narrative review.

# DIAGNOSIS OF COPD AND INITIAL ASSESSMENT

The early diagnosis of COPD is crucial to prevent increased rates of exacerbation, comorbidities, and cost burden.<sup>6</sup> A diagnosis of COPD should be suspected in patients with dyspnea, chronic cough or sputum production, prior recurrent lower respiratory tract infections, and/or past exposure to risk factors, particularly smoking.<sup>2</sup> The primary method for diagnosing COPD is forced spirometry (post-bronchodilator forced expiratory volume in 1 second [FEV<sub>1</sub>]/forced vital capacity [FVC] ratio of <0.7).<sup>2</sup> Further assessments, including lung volume assessment, diffusion capacity, exercise testing, and/or lung imaging, should also be considered for accurate diagnosis and differentiation from other conditions, such as

asthma,  $\alpha$ -1 antitrypsin deficiency, interstitial lung disease, pulmonary fibrosis, lung cancer, congestive heart failure, respiratory infections, and obstructive sleep apnea.<sup>2</sup>

Despite spirometry being the gold standard for diagnosing COPD, the percentage of diagnosed patients who underwent spirometry was low (range: 32%-36.7%) in two large, U.S.-based studies. 12,13 In a European study, only 67.6% of patients with physician-diagnosed COPD had undergone spirometry at any point in the past. 14 The inadequate/improper use of spirometry continues to play a major role in the misdiagnosis of COPD. 15 This can result from several factors, including inappropriate timing of spirometry (e.g., during acute illness), failure to use post-bronchodilator values as recommended, and reliance on outdated or misrepresentative reference equations. 16-18 Notably, the use of race-based reference values still embedded in many spirometers—can skew interpretation, potentially underestimating disease severity in certain populations. 19,20 Globally, 10%-95% of patients with COPD remain undiagnosed, whereas 5%-60% are overdiagnosed, consequently increasing the risk of delay in treatment and suboptimal disease management. Overdiagnosis occurs when a patient is identified as having COPD when their respiratory symptoms are attributable to a different etiology. 15 This overdiagnosis can occur due to misinterpretation of symptoms, inadequate use of spirometry in making diagnostic decisions, or failure to adhere to established diagnostic criteria, such as spirometry standards. 15 Factors associated with not undergoing diagnostic spirometry are advanced age, current smoking, low educational level, and management in primary care. 12,21

Evidence suggests that undiagnosed patients may have milder symptoms, less severe airway obstruction, and hence, lower disease burden, significantly delaying diagnosis due to underreported symptoms or physicians overlooking subtle early signs.<sup>6</sup> About 80% of patients in the U.S. and 85% in the United Kingdom (UK) rely on primary care physicians (PCPs) for COPD diagnosis.<sup>22,23</sup> Patients who eventually received a diagnosis of COPD had

consulted primary care for early symptoms within the previous 5 years, suggesting a significant missed opportunity of early diagnosis.<sup>22</sup> Thus, it is important to increase awareness and knowledge about COPD among all HCPs to avoid delays in diagnoses and progression/referral to secondary care. The following criteria must be considered:

Patients suspected of having COPD should be primarily diagnosed using spirometry

Misdiagnosis tends to be more common when the diagnosis is made by a general practitioner or a nurse in primary care compared with a specialist in a secondary care setting. <sup>24,25</sup> Reasons for the misdiagnosis of COPD include poor access to diagnostic services and lack of expertise in performing and interpreting spirometry, which limit its use in primary care. <sup>18</sup> According to a recent meta-analysis, 14%-26% of symptomatic smokers visiting primary healthcare settings in the past 12 months had spirometry-confirmable COPD not documented by clinicians. <sup>26</sup> Additionally, one in four patients on inhaled therapies had irreversible airflow limitation consistent with COPD, unrecognized by both PCPs and patients. <sup>26</sup> In one study, only 22% of PCPs expressed the requirement for spirometry after initial presentation to confirm the diagnosis of COPD, <sup>27</sup> and in another study, only 34% of PCPs regularly used spirometry, despite 64% having access to spirometric tests. <sup>28</sup> Consequently, it is important that PCPs incorporate the use of spirometry into their daily clinical practice. Appropriate training is crucial to facilitate accurate and reproducible spirometric measurements based on evidence-based guidelines. <sup>2</sup>

Appropriate initial assessment needs to be conducted for multidimensional and patientcentric diagnosis

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) recommends categorizing patients diagnosed with COPD based on the following criteria: disease severity (GOLD grades 1-4), nature and magnitude of symptoms (GOLD groups A, B, E) according

to the modified Medical Research Council (mMRC) dyspnea questionnaire or COPD Assessment Test<sup>TM</sup> (CAT), exacerbation history, current smoking status, blood eosinophil level, α1 antitrypsin level, and presence of comorbidities.<sup>2</sup> This integrated approach assists in guiding personalized management strategies in patients with COPD. Furthermore, a review of 11 longitudinal studies with a follow-up period of >3 years revealed that the rate of annual loss of lung function measured according to FEV<sub>1</sub> was generally more accelerated during the early stages (GOLD I or 2) of COPD than during the later stages (GOLD 3 or 4).<sup>29</sup> While the GOLD criteria remain widely used and foundational for the diagnosis and staging of COPD, recent studies have explored alternative approaches that may offer complementary insights into disease severity. One such method is the STaging of Airflow Obstruction by Ratio (STAR) method proposed by Bhatt et al., which uses the FEV<sub>1</sub>/FVC ratio alone—without requiring predictive equations based on age, sex, height, or ethnicity. STAR has shown promising results in distinguishing patients with mild COPD from healthy individuals and in predicting outcomes such as mortality and hyperinflation.<sup>30</sup> STAR may provide advantages in certain clinical contexts, although GOLD continues to perform well in assessing functional status, including changes in 6-minute walk distance and symptom scores such as the mMRC. Thus, prompt and effective management during the early stages of COPD can preserve lung function and prevent exacerbations.

HCPs should emphasize accurate and early diagnosis of COPD

Early detection of COPD can be facilitated using a case-finding approach, which includes actively screening a high-risk population for COPD using handheld devices, such as a peak expiratory flow meter or microspirometer; questionnaires (such as COPD Assessment in Primary Care to Identify Undiagnosed Respiratory Disease and Exacerbation Risk [CAPTURE], COPD Population Screener [COPD-PS], COPD Diagnostic Questionnaire [COPD-DQ], and PUMA); a combination of handheld devices and questionnaires; or

prediction models for identifying undiagnosed COPD using routine electronic health record data.<sup>6</sup> In addition, app-based microspirometers have been reported to show favorable performance compared with other case-finding modalities.<sup>6</sup>

Nonconventional risk factors for COPD should not be neglected

In addition to tobacco smoking and advanced age, risk factors such as biomass smoke; PM2.5, PM10, and NO<sub>2</sub> exposure; impaired lung growth, and lower peak lung function during early adulthood are associated with COPD.<sup>6</sup> Recurrent respiratory infections are common among patients with COPD and may indicate an underlying diagnosis of COPD.<sup>31</sup> Neglecting these factors could potentially lead to a delayed diagnosis of COPD.

Underrepresentation of women during COPD diagnosis

A common misperception that COPD primarily affects men may have led to previous underdiagnosis in women. A diagnostic bias has been observed in PCPs, as illustrated by a hypothetical case description of cough and dyspnea in smokers. This case was diagnosed as COPD more often in males than in females, despite no other differences in clinical presentation (P < 0.0001). Female smokers with symptoms are diagnosed with COPD less often and are less likely to undergo spirometry tests or receive specialist referrals than male smokers. Consequently, females with COPD may have a worse prognosis than males, showing higher hospitalization and death rates, faster lung function decline for the same exposure, and more rapid progression of lung density on computed tomographic (CT) scans.

Understanding the patients' perspective

The ability of individuals who may be susceptible to COPD to recognize symptoms during the early stages of the disease is one of the key criteria for successful early diagnosis of COPD. Figure 1 includes a list of key symptoms that could be used to encourage individuals who suspect that they may have COPD to seek medical advice. COPD can also negatively

impact patients' psychology, often leading to social isolation and withdrawal from social activities. 9,34 In a one-on-one remote interview (both in-person and via video call) with 62 patients, insights were gathered about their perspectives of living with COPD; 58% of patients responded that their diagnosis had a negative effect due to reduced physical activity, whereas 29% reported a positive impact of diagnosis on their health, as they either quit or cut down on smoking. Furthermore, worsening symptoms were reported in the morning in 22% of patients, at night in 19%, and at both times of the day in 10%, while no change was reported in 29%.8 However, instead of seeking medical intervention early, many patients adapt their lifestyle to compensate for their declining health, often delaying consulting their HCPs until irreversible loss of lung function has occurred. <sup>28</sup> This can be either due to a hesitation to discuss COPD symptoms with HCPs, considering breathlessness and reduced exercise capacity as consequences of normal aging, or attributing cough and sputum to their smoking habit.<sup>28</sup> Visible symptoms, such as cough and sputum production, and physical limitations, such as a slow pace of walking, were reported as embarrassing by patients. Reactions from strangers when patients experience shortness of breath or other symptoms in public were also a source of embarrassment. Having to explain themselves to avoid misinterpretation of their symptoms adds to the stigma burden of patients. 35,36 Many patients report feelings of guilt and shame associated with their condition, particularly when linked to smoking, which can lead to perceived or actual experiences of stigma in healthcare settings.<sup>37</sup> These experiences may contribute to poorer patient-provider communication, reduced engagement with healthcare services, and delays in seeking care. Quantitative studies reveal persistent gaps in the delivery of essential aspects of care for individuals with COPD, whereas qualitative studies suggest that patients' expectations are not always met. 38-40 Negative experiences may not only diminish trust in the healthcare system but can also exacerbate perceptions of inequality and lead to worse clinical outcomes. Care for COPD can be effectively managed in community settings, and the quality of patient experience in these contexts plays a key role in supporting self-management and preventing acute exacerbations. Individuals with lower socioeconomic status and those living with smoking-related illnesses may be especially vulnerable to biased care and stigma. As such, understanding and addressing these lived experiences is crucial for improving health equity and ensuring the delivery of person-centered, compassionate care.

Patients in the advanced stages of COPD often require long-term oxygen therapy, typically for the rest of their lives. 43 However, the use of supportive oxygen can significantly impact their daily lives, leading to feelings of self-consciousness and embarrassment. 44,45 Employment opportunities are also affected by COPD due to health insurance costs and increased loss of work days. 35 Worse health-related QoL (HRQoL) and more frequent hospital visits were also observed in patients with undiagnosed COPD than in those without the condition. 6 Thus, assessing patients with COPD should encompass not only pulmonary function tests but also QoL evaluations. 46 Early referral to a specialist, psychological assessments, and psychiatric consultations are crucial for alleviating COPD symptoms, enhancing QoL, and detecting and treating psychiatric symptoms that could exacerbate COPD and significantly impact QoL. Tables 1 and 2 provide a list of suggested questions for patients that may help them to initiate conversations with their HCPs about COPD and gain important insights about their condition. Table 3 provides a list of helpful patient resources for identifying support communities and gaining more information on living with COPD.

- Key takeaways (patients' perspective):
  - COPD can lead to social isolation as the disease progresses and affects daily activities.

- Initial acceptance of the diagnosis is common, but resistance often follows as the disease impacts social life.
- O Patients receiving supplemental oxygen are particularly vulnerable to stigma, which can intensify feelings of self-consciousness.
- The stigma and self-consciousness associated with COPD often cause patients to withdraw from social activities.
- Implementation Suggestion: Integrate peer support groups into COPD care
  pathways (e.g., through pulmonary rehabilitation programs or telehealth
  platforms) to offer a structured forum for shared experiences and reducing
  social withdrawal.
- Implementation Suggestion: Include psychosocial counseling as part of a comprehensive approach to COPD care to address self-image and reduce isolation (Figure 2).
- Key takeaways (HCPs' perspective):
  - Prompt and effective management during the early stages of COPD can
     preserve lung function and prevent exacerbations.
  - O Understanding patients' perspectives is a critical but often overlooked insight that allows PCPs to devise a holistic management strategy for COPD.
  - PCPs should receive additional training in spirometry to increase their confidence in diagnosing COPD. PCPs also need to incorporate regular spirometric assessments into their daily clinical practice.
  - If a patient presents with respiratory infections on a regular basis, this should be indicative for the PCP to consider COPD as a possible diagnosis.

- o Implementation Suggestion: Offer Continuing Medical Education (CME) modules focused on spirometry—delivered through accessible platforms, such as local CME workshops, online courses endorsed by pulmonary societies, or embedded training during residency.
- Implementation Suggestion: In clinics without spirometry capabilities,
   establish referral protocols for nearby testing centers or specialist consultation,
   ensuring timely diagnosis while maintaining quality standards.
- Implementation Suggestion: Create clinical checklists integrated into electronic medical records (EMRs), which flag patterns indicative of COPD, prompting spirometry referral or further workup.

## MANAGEMENT OF COPD - PREVENTION AND MAINTENANCE THERAPY

The management strategy of COPD should be individualized based on symptom severity, exacerbation risk, side effects, comorbidities, drug availability and cost, patients' response and preference, and the ability to use drug delivery devices.<sup>2</sup> Precision medicine involves tailoring treatment strategies by utilizing information specific to each individual. To address the diverse and heterogeneous nature of COPD, there is significant interest in categorizing patients based on disease characteristics using different criteria, such as the GOLD ABE classification (symptom severity/exacerbation history) and COPD endotypes (underlying biologic differences, such as bacterial colonization or eosinophilic inflammation).<sup>2,47</sup> Furthermore, the concept of "treatable traits" has been introduced.<sup>48</sup> This approach identifies all pulmonary and extrapulmonary aspects of COPD to manage each patient in an individualized manner.<sup>49</sup> However, the current level of understanding for different concepts such as COPD endotypes or "treatable traits" is limited. Thus, it is crucial for HCPs to work

with the patients to identify the best strategies (including lifestyle changes) to manage their condition.<sup>2</sup> Different management strategies include smoking cessation, vaccination, pharmacotherapy, comorbidity management, pulmonary rehabilitation, and patient education on self-management.<sup>2</sup>

Smoking cessation

Preventive measures are critical in vulnerable individuals (e.g., those with a family history of COPD, α-1 antitrypsin deficiency, secondary smoke exposure, low birth weight, lung infections, and asthma). Smoking cessation is the key to managing or preventing COPD, with abundant evidence indicating decreased disease progression, symptom improvement, and reduced mortality.<sup>2,50</sup> An estimated 30%-50% of patients exhibiting symptoms of moderate to very severe COPD continue smoking. Results from clinical trials of approved pharmacotherapy for smoking cessation show a low success rate of 14%-25% in sustaining smoking cessation after 6-12 months.<sup>50</sup> Physician support, including discussions and education to enhance the patient's understanding, assistance with smoking cessation, and prioritizing COPD treatment irrespective of smoking habits, may help reduce patients' tendency to avoid treatment due to guilt.<sup>28</sup>

Vaccination for stable COPD

Vaccinations are important preventive measures for patients with respiratory diseases, such as COPD.<sup>51</sup> Typically, anti-pneumococcal and anti-influenza vaccines are recommended for individuals with such conditions.<sup>51</sup> Patients with COPD should receive all recommended vaccinations according to the applicable local guidelines. Influenza vaccination has been shown to reduce disease severity, exacerbations, and death in COPD.<sup>52</sup> Pneumococcal vaccination reduces the occurrence of community-acquired pneumonia and prevents exacerbations in individuals with COPD and is recommended by the Centers for Disease

Control and Prevention (CDC).<sup>2</sup> The CDC also recommends the new respiratory syncytial virus (RSV) and tetanus, diphtheria, and pertussis (Tdap) vaccines in patients with COPD.

Additionally, both the World Health Organization (WHO) and CDC recommends the SARS-CoV-2 vaccine in patients vulnerable to COPD.<sup>2</sup>

## **Pharmacotherapies**

The primary treatment modalities for COPD include inhaled bronchodilators and anti-inflammatory drugs.<sup>2</sup> Predominantly bronchodilators are either β-2 agonists or muscarinic (M3) antagonists. Short-acting β-2 agonists (SABAs) and short-acting muscarinic antagonists (SAMAs) are only active for up to 6 hours, whereas long-acting β-2 agonists (LABAs) and long-acting muscarinic antagonists (LAMAs) retain their activity for 12-24 hours.<sup>53,54</sup> Combination treatment with LABAs and LAMAs is more effective in reducing exacerbations than monotherapy.<sup>55</sup> The main anti-inflammatory drugs used in COPD are inhaled corticosteroids (ICS); however, regular ICS treatment has been shown to increase the risk of pneumonia in patients with severe disease.<sup>56</sup> When combined with LABAs and LAMAs, ICS shows superior effectiveness in improving lung function and health status and decreasing exacerbations but only in a small set of patients who have an inflammatory profile, as indicated by their blood eosinophil count.<sup>2</sup>

The GOLD recommendations advocate considering the patient's specific group based on initial assessment when determining the initial pharmacotherapy for COPD (Figure 3)<sup>2</sup>:

- Group A (0-1 moderate exacerbations, no hospitalization, mMRC 0-1, CAT < 10): A
  bronchodilator, preferably a long-acting one, except in patients with very occasional
  shortness of breath.</li>
- Group B (0-1 moderate exacerbations, no hospitalization, mMRC ≥ 2, CAT ≥ 10):
   LABA + LAMA.

Group E (≥2 moderate exacerbations or ≥1 leading to hospitalization; formerly GOLD
 C and D): LABA + LAMA, with added ICS (triple therapy) only if blood eosinophil
 count is ≥300 cells/µL. LABA plus ICS is not encouraged for COPD.

A short-acting bronchodilator should be prescribed to all patients as rescue medication.<sup>2</sup>
While LABAs provide longer-lasting relief, additional use of SABAs as needed can further improve FEV<sub>1</sub> and symptoms, particularly when combined with a SAMA.<sup>2</sup> After the initiation of therapy, further management should follow the principle of review (symptoms and exacerbations), assess (inhaler technique, adherence, and nonpharmacological strategies [Figure 4]), and adjust (escalate, switch, and de-escalate).<sup>2</sup> Follow-up pharmacotherapy should focus on two key treatable traits: persistence of dyspnea and occurrence of exacerbations for escalating or de-escalating treatment.<sup>2</sup> Although the majority of patients in routine clinical practice have mild/moderate COPD, where a long-acting bronchodilator is indicated, up to 37.6% of patients receive a prescription of triple therapy (LAMA + LABA + ICS) as first-line maintenance therapy, in contrast to GOLD recommendations.<sup>57</sup> Prescribing COPD pharmacological treatment according to guideline-recommended use ensures better symptom control, lower exacerbation risk, preserved lung function, and improved patient outcomes and is associated with fewer drug-related adverse events.<sup>58</sup>

It is also important to prioritize patient preferences when prescribing an inhalational drug and selecting an inhaler for COPD management. All prescribed inhalers should be of the same type (e.g., dry-powder inhalers [DPIs] or metered-dose inhalers [MDIs]); combining different types of devices should be avoided. DPIs are more suitable for patients who are capable of deep, forceful inhalation.<sup>59</sup> The coordination between actuation and inhalation required in an MDI is critical for the effectiveness of the drug, and DPIs/MDIs should be given to patients who are able to accurately follow the technique. Soft mist inhalers or use of spacers may be helpful in patients who may have difficulty in maintaining the hand-breath coordination

required for MDIs.<sup>2</sup> Patient satisfaction and preference studies conducted using the Respimat® soft mist inhaler have consistently shown higher levels of satisfaction and preference over other device types. 60 Soft mist inhalers also address drawbacks typically associated with MDIs and DPIs, such as nontargeted deposition of medication in the lungs. 61 Nebulized therapies can be a viable alternative for patients who struggle with using handheld inhaler devices due to physical limitations or severe symptoms. Several nebulized shortacting and long-acting bronchodilators are available for the treatment of COPD. 62 Shared decision-making is the most appropriate strategy when choosing an inhalation device, taking patient capabilities and preferences into account.<sup>2,61</sup> Apart from that, educating patients with COPD on proper inhaler techniques can influence treatment adherence and health outcomes. Usmani et al. revealed a strong correlation between inhaler errors and worsening health outcomes, reinforcing the critical importance of optimal inhaler technique education.<sup>63</sup> A study identified that over 70% of patients with COPD and asthma were using metered-dose inhalers (MDIs) incorrectly, with common errors including failure to exhale prior to inhalation.<sup>64</sup> Methods such as brief intervention (BI) and teach-to-goal (TTG) are commonly employed to educate patients on inhalation techniques. 65,66 BI involves verbal instructions, whereas TTG includes multiple sessions to ensure patients achieve self-care learning goals. Recent systematic reviews and meta-analyses indicate that educational interventions can effectively reduce critical errors across all inhaler types.<sup>67</sup> For MDIs specifically, the success of interventions is influenced by factors such as clinical setting, poor initial technique, and time elapsed since the intervention, with outpatient clinics showing the best outcomes.<sup>68</sup> Axtell et al. compared various inhaler teaching methods and showed that face-to-face direct instructions from pharmacists were statistically superior to methods such as reading package inserts or watching video demonstrations.<sup>69</sup> Evidence also supports pharmacist-led education to be effective in improving adherence and asthma control. Spacer/valved holding chamber

usage is another vital aspect of inhaler pharmacotherapy.<sup>70,71</sup> Spacers slow aerosol particle velocity, enhancing drug deposition in the lungs and addressing coordination issues with pressurized MDIs.<sup>72</sup> All patients using pressurized MDIs should be advised to use spacers, especially children (those < 3 years should use pressurized MDIs with a face mask), the elderly, and those with compromised manual dexterity or comprehension, for improving medication delivery and patient outcomes.<sup>72</sup>

Due to the substantial comorbidity burden that patients with COPD may have, annual healthcare costs may be prohibitively high, especially for patients having ≥3 comorbidities.<sup>73</sup> In low- and middle-income countries (LMICs), COPD medication costs can exceed >1 day's wage of the lowest paid government worker.<sup>74</sup> Thus, treatment choices should be individualized. Significant issues in the availability and affordability of COPD medications have been identified in LMICs, with most medicines not meeting the WHO global action plan target of >80% availability.<sup>74</sup> Treatment decisions should hence be personalized according to drug availability and financial capability of the patient to ensure adherence.

## Comorbidity management

A wide range of comorbidities can present with COPD, including cardiovascular disease, metabolic disorders, gastroesophageal reflux disease, osteoporosis, rheumatoid diseases, cachexia, and mental health conditions including anxiety and depression. Such comorbidities are frequently associated with an increased risk of hospitalization, higher mortality rate, and polypharmacy. Although screening for all comorbidities in every patient is not feasible, guidance in identifying high-risk subgroups is needed. Five distinct patient clusters with unique comorbidity profiles—metabolic, cardiovascular, cachectic, psychological, and less comorbidity—have been identified in COPD, showing variations in lung function, body weight, fat-free mass, and health status, despite comparable airflow

limitation.<sup>49</sup> These profiles suggest a multifactorial origin, emphasizing the importance of integrating clinical, genetic, environmental, and socioeconomic factors for comprehensive management.<sup>49</sup> It is necessary to implement preventive measures for any existing comorbidities.<sup>49</sup> For several comorbidities such as short-term anxiety/depression, obesity, and cardiovascular disease, engaging patients in physical activity and regular exercise might be beneficial.<sup>79-81</sup> The management of COPD in patients with comorbidities requires a holistic approach that targets shared risk factors and leverages evidence-based treatments across conditions. For example, pulmonary rehabilitation programs have shown benefits not only for respiratory symptoms but also for comorbid anxiety, depression, and cardiovascular risk.<sup>82,83</sup>

# Pulmonary rehabilitation

Pulmonary rehabilitation, a nonpharmacological intervention, should begin with a detailed patient assessment and proceed with customized therapies to enhance the physical and psychological wellbeing of those with chronic respiratory diseases. Essential to every rehabilitation program is providing individualized, comprehensive care that addresses complex needs and encourages lasting health-enhancing behavior. Part in addition to comprehensive care, pulmonary rehabilitation may provide patients with an opportunity to network with fellow patients and find creative solutions to their difficulties through peer-to-peer interaction. Pulmonary rehabilitation improves exercise tolerance and overall HRQoL, thereby resulting in lower healthcare costs, particularly unplanned hospital admissions. Education in pulmonary rehabilitation can play a crucial role in promoting effective self-management of COPD. By promoting behavioral change through informed and appropriate self-management strategies, the educational component of pulmonary rehabilitation can contribute to health improvement and disease control. However, data on the delivery of education in PR programs are variable, and there is currently limited guidance for its optimal design and delivery. Mendes et al. suggested that educational sessions in

pulmonary rehabilitation are designed to enhance knowledge, develop skills, and build confidence, enabling individuals to become active and autonomous participants in managing their condition.<sup>88</sup>

Self-management and QoL improvement

An ideal goal for any management strategy for COPD is to improve the overall QoL by reducing functional impairments, optimizing physical health, improving social and emotional wellbeing, and enhancing effective alliances with HCPs, family, friends, and the community. A significant correlation has been observed between QoL and survival outcomes in patients living with COPD. A study of 543 patients revealed that a preserved HRQoL score, according to the St. George Respiratory Questionnaire (SGRQ), was correlated with improved survival, while a reduction of >4 points in any domain of the questionnaire over a 1-year period was linked to an increased risk of death and hospitalization. Patients with COPD often require more support, including information about their condition, financial help, improved treatment options, and assistance with daily tasks. Thus, the QoL of patients is also influenced by the type of healthcare support they receive. Conversely, successful COPD management also requires patients to be proactive in disease management.

A post hoc analysis indicated that increased awareness of COPD among patients is associated with improved clinical outcomes and better disease management. The "chronic care model" of GOLD emphasizes that HCPs should promote self-management education and coaching among patients with COPD. The National Institute for Health and Care Excellence (NICE) in the UK also suggests promoting knowledge and awareness about COPD and its management among patients. A multicentric, randomized controlled trial reported that a self-management program in patients with COPD, including different forms of exercises such

as stretching, walking, running, cycling, and climbing stairs for 30-45 minutes at least thrice weekly, led to a 41.0% (P = 0.02) reduction in hospitalizations. <sup>93</sup> A systematic review reported that strategies involving planned exercises or enhanced professional care (such as proactive telephone calls from HCPs) were associated with an improvement in HRQoL. <sup>94</sup> Another systematic review and meta-analysis reported that self-management, whether through education or as part of pulmonary rehabilitation, significantly enhances HRQoL in patients with COPD. <sup>95</sup> Engaging in peer-to-peer interactions allows patients with COPD to share their experiences with others who genuinely understand their condition. Social support has a strong positive impact on mental health, QoL, and self-efficacy in patients with COPD. <sup>96</sup>

A longer duration of self-management intervention is associated with better outcomes.<sup>97</sup> In a one-on-one remote interview (both in-person and via video call) (N = 62), patients' feelings about their currently prescribed COPD therapy were positive in 52%, neutral in 31%, and negative in 17%. Six (12%) of the 52 respondents confirmed using digital or analogic reminders to take their scheduled doses. Most patients (69%) had received training for their ongoing treatment; however, the remainder did not but would have preferred to.<sup>8</sup> Patients generally refrained from looking up instructions on inhaler usage or information about their condition on the internet because they lacked trust in the source and feared becoming depressed from excessive reading about their disease.<sup>8</sup> Thus, continued HCP support is important for sustaining behavioral changes leading to QoL improvement.<sup>98</sup>

- Key takeaways (patients' perspective):
  - Engaging in peer-to-peer interactions provides patients with a chance to discuss their experiences with others who truly understand their condition.

- There is a need to remove restrictions on the number of pulmonary rehabilitation sessions that a patient can attend.
- Pulmonary rehabilitation should be treated like other prescriptions, continuing until cancelled by the physician or patient.
- Investing in pulmonary rehabilitation could potentially reduce costs associated with treating depression and other mood disorders.
- Mobile health apps such as MyCOPD, COPD Foundation's Pocket Consultant
   Guide, and m-PAC are promising tools for improving treatment adherence and
   enabling more personalized care.
- Implementation Suggestion: Advocate for insurance reform to allow openended pulmonary rehabilitation prescriptions, similar to physical therapy.
   Develop modular, accredited pulmonary rehabilitation programs that can be delivered both in person and virtually, expanding patient accessibility.
- Key takeaways (HCPs' perspective):
  - Annual assessments must be conducted to determine the impact of prevention and management strategies on COPD symptoms and HRQoL.
  - Developing and personalizing effective management strategies based on assessment results are crucial.
  - Ensuring that management strategies are tailored to the individual needs of each patient is essential for optimal care.
  - Implementation Suggestion: Develop EMR templates that prompt annual COPD-specific evaluations, incorporating symptom scales (e.g., CAT, mMRC), exacerbation history, and HRQoL measures.

#### MANAGEMENT OF EXACERBATIONS

Exacerbations of COPDs are acute respiratory events during which patients exhibit increased respiratory symptoms (dyspnea, cough, and/or sputum) that worsen over <14 days.

Exacerbations are associated with elevated inflammation (local and/or systemic) and need specific preventive and therapeutic measures.<sup>2</sup> Exacerbations may be caused by airway infection, pollution, or other stressors on the lungs.<sup>2</sup> A SABA with or without a SAMA is recommended for the initial management of COPD exacerbation, followed by maintenance therapy with LABA and/or LAMA.<sup>2</sup> Initiation of ICS, as part of triple therapy, can be considered in patients who frequently experience exacerbations and have an increased blood eosinophil level (≥300 cells/µL). Systemic corticosteroids are also known to improve lung function in severe exacerbations.<sup>2</sup>

Oral therapies such as antibiotics should be prescribed for patients who exhibit dyspnea, increased sputum volume, and increased sputum purulence simultaneously.<sup>2</sup> When indicated, having access to broad-spectrum antibiotics and corticosteroids may also help patients manage their exacerbations more effectively at home. Macrolide antibiotics, such as azithromycin, exhibit immunomodulatory and anti-inflammatory properties, contributing to reduced exacerbation rates in patients with COPD.<sup>99</sup> For individuals with frequent exacerbations despite optimized inhaled maintenance therapy, long-term azithromycin treatment is suggested.<sup>100</sup> Roflumilast, a phosphodiesterase-4 inhibitor, is particularly beneficial for those with severe COPD and chronic bronchitis, as it reduces both inflammation and exacerbations.<sup>101</sup> The recent approval of ensifentrine offers a novel dual-action mechanism combining bronchodilation and anti-inflammatory effects, improving lung function and reducing the exacerbation rate.<sup>102</sup> Among treatments based on precision medicine, biologics target specific inflammatory pathways, offering improved lung function and reduced exacerbations.<sup>103</sup> The approval of dupilumab in the U.S. as the first biologic for

COPD provides a new option for patients with eosinophilic phenotypes. <sup>104</sup> Oral biologic therapies have gained popularity for managing frequent exacerbations in patients with COPD. However, their adoption is influenced by varied perceptions among both patients and HCPs. Patients reported concerns about side effects, such as gastrointestinal discomfort with roflumilast or antibiotic resistance with azithromycin, which can hinder adherence to long-term therapies. <sup>105,106</sup> Shared decision-making emerges as a crucial facilitator, allowing patients to actively participate in treatment choices based on their preferences and capabilities.

History of exacerbations and poor health status should be collectively considered to inform therapeutic decisions and predict future occurrences of COPD. <sup>49</sup> Exacerbations can be grouped into clusters according to sputum biomarkers to discriminate against those associated with bacteria, viruses, or eosinophilic airway inflammation. Other events such as acute cardiovascular diseases, pulmonary embolism, and acute physiological distress may mimic the symptoms of exacerbation, which need to be differentiated to enable precision management of a flare-up of respiratory symptoms. <sup>49</sup> A meta-analysis of 10 randomized trials showed short-term benefits of pulmonary rehabilitation if initiated within a week of exacerbation. <sup>107</sup> Another systematic review of 18 studies supported the effectiveness of pulmonary rehabilitation in patients with acute exacerbations, irrespective of the setting; however, heterogeneity was observed among different rehabilitation programs. <sup>108</sup> To ensure high-quality pulmonary rehabilitation, these programs should undergo regular quality control audits and be delivered by well-trained staff. <sup>109</sup>

• Key takeaways (patients' perspective):

- Acute exacerbations can significantly impair QoL and emotional well-being,
   highlighting the need for mental health support and preventive strategies in atrisk individuals.
- Equip patients with individualized, easy-to-follow action plans to recognize early signs of exacerbation and respond appropriately, including when to seek medical help.
- Pulmonary rehabilitation programs should be accredited by a regulatory body to ensure that they meet quality standards and are delivered by qualified professionals.
- Provide culturally and linguistically appropriate educational resources from trusted sources, such as patient organizations, on recognizing exacerbations.
- Implementation Suggestion: Collaborate with patient advocacy organizations
  to co-develop standardized, multilingual materials covering topics such as
  recognizing exacerbations and managing COPD on a day-to-day basis.
  Incorporate visual aids and multimedia formats, such as videos, to ensure
  accessibility and understanding.
- Key takeaways (HCPs' perspective):
  - SABA/SAMA is recommended for the initial management of COPD exacerbations.
  - LABA and/or LAMA are recommended for ongoing treatment following initial exacerbation management.
  - ICS initiation can be considered in patients with frequent exacerbations and increased blood eosinophil count (≥ 300 cells/μL).

 Implementation Suggestion: Embed evidence-based COPD treatment algorithms into clinical decision support tools within EMRs to streamline pharmacologic escalation and align with the guidelines.

## **CONCLUSIONS**

COPD symptoms can significantly impact patient QoL, restricting daily activities, reducing physical fitness, and leading to social isolation and emotional distress. Thus, early diagnosis and appropriate management of COPD are critical. Given the complexities and heterogeneity of COPD, transforming the patient-HCP relationship into a collaborative partnership is crucial to develop tangible and realistic healthcare goals. This involves understanding and contextualizing patients' ideas, concerns, and expectations, along with their physical, social, and psychological circumstances. PCPs often serve as the first point of contact within the healthcare system and continue to manage patients with chronic diseases, such as COPD, over many years. Therefore, PCPs should be aware of evidence-based guidelines for diagnosing and managing COPD and participate in encouraging behavioral changes among patients. Personalized evidence-based strategies tailored to each patient are essential to improve and optimize treatment. Thus, a collaborative approach, patient-centered care, and continuous education are key to enhancing COPD management and improving patient outcomes.

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All authors contributed to the conceptualization, review, and editing of the manuscript. All authors have approved the final manuscript for submission.

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Antonio Anzueto reports speaking and consulting fees from AstraZeneca, GlaxoSmithKline, Sanofi/Regeneron, and Viatrix. Caroline Gainer is a member of the COPD360 Community Engagement Committee (COPD360CEnCo) and the committee for Oxygen Strategies. Haley Hoy reports consulting fees from BIPI and Pulmonx Corporation.

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### **Tables**

### Table 1. Questions to be asked by the patient to the care provider upon diagnosis

What lifestyle changes should I make to manage my COPD effectively?

How can I recognize the signs of a COPD flare-up, and what should I do if it happens?

What medications will I need to take, and how should I use them correctly?

Are there any specific exercises or pulmonary rehabilitation programs that can help improve my breathing?

# Table 2. Questions care providers can ask patients with COPD during their first visit

How long have you had your symptoms?

What symptoms do you have (coughing, wheezing, shortness of breath) and how are these affecting your days and nights?

Do you have a family history of breathing problems?

What medications are you taking?

Do you have a history of smoking (how many years, how much, and how often)?

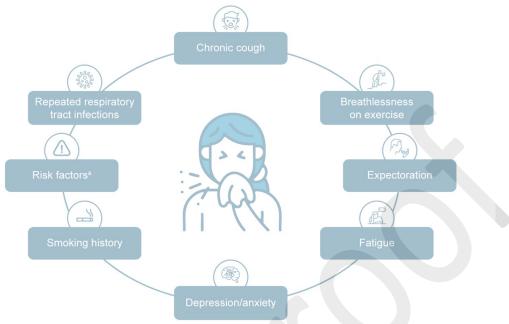
Table 3. Resources for patients to seek support

Organization	Description
Name/Contact	
The COPD Foundation	The COPD Foundation's mission is to help millions of
Link	people live longer and healthier lives by advancing
Helpline: 1-866-731-2673	research, advocacy, and awareness to stop COPD,
	bronchiectasis, and nontuberculous mycobacterial
	lung disease.
COPD360Social	COPD360social is a free online social community
Link	about everything COPD. Members can share
Helpline: 1-866-316-2673	thoughts and ideas, ask questions, give and receive
	support, discuss what matters to them, and learn how
	to take action.
RIGHT2BREATHE	RIGHT2BREATHE is a lung health education,
Link	awareness, and screening campaign hosted at public
	venues for patients with respiratory conditions.
American Lung	The American Lung Association is the leading
Association	organization working to save lives by improving lung
Link	health and preventing lung disease, through
Helpline: 1-800-586-4872	advocacy, education and research.

Global Initiative for Chronic	The GOLD Guidelines provide up-to-date,
Obstructive Lung Disease	evidence-based strategies for the diagnosis,
(GOLD) Guidelines	management, and prevention of COPD. Developed
Link	by leading experts in respiratory medicine, the
	guidelines are used globally by healthcare
	professionals to improve patient outcomes and
	support personalized COPD care through
	recommendations based on the latest research.
The International Primary	IPCRG improves respiratory health globally through
Care Respiratory Group	primary care. It supports initiatives such as COPD
(IPCRG)	Right Care for better COPD diagnosis and
Link	management and publishes resources such as
COPD Right Care	COPD Magazine to aid individuals in managing their
	condition effectively.
The Global Allergy &	GAAPP is an organization dedicated to empowering
Airways Patient Platform	patients with allergies, airway diseases, and atopic
(GAAPP)	conditions worldwide. GAAPP provides resources
Link	such as educational flyers, patient care maps, and
	advocacy tools to help manage COPD.

### FIGURE LEGENDS

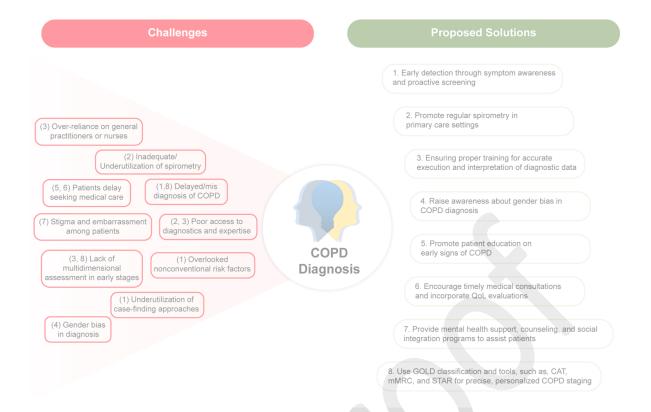
Figure 1. A Chart for Guiding Patients to Recognize Early Symptoms of COPD



<sup>a</sup>Risk factors include environmental exposure to tobacco smoke and smoke from biomass burning, occupational exposure to triggers, and genetic predisposition due to α-1 antitrypsin deficiency.

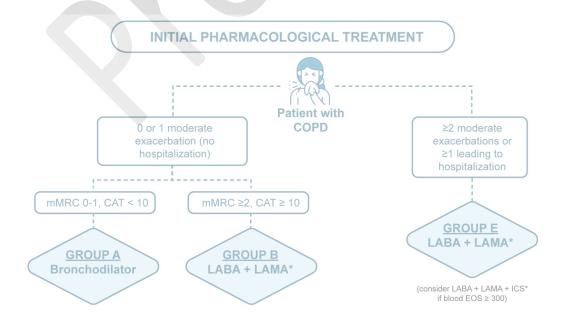
 $^{a}$ Risk factors include environmental exposure to tobacco smoke and smoke from biomass burning, occupational exposure to triggers, and genetic predisposition due to  $\alpha$ -1 antitrypsin deficiency.

Figure 2. Challenges and Proposed Solutions in Diagnosing COPD



Abbreviations: CAT=COPD Assessment Test<sup>TM</sup>; GOLD=Global Initiative for Chronic Obstructive Lung Disease; mMRC=modified Medical Research Council; QoL=quality of life; STAR=STaging of Airflow Obstruction by Ratio

Figure 3. Initial Pharmacological Treatment of Stable COPD (Adapted from GOLD 2024)<sup>2</sup>



Treatment decisions are guided by symptom severity (assessed using tools such as the mMRC and CAT) and the risk of exacerbations, which can be determined by factors such as EOS. \*Single inhaler therapy may be more convenient and effective than multiple inhaler therapy. Abbreviations: CAT=COPD Assessment Test<sup>TM</sup>; EOS=blood eosinophil count (cells/μL); GOLD=Global Initiative for Chronic Obstructive Lung Disease; ICS=inhaled corticosteroids; LABA=long-acting β-2 agonist; LAMA=long-acting muscarinic antagonist; mMRC=modified Medical Research Council.

Figure 4. Nonpharmacological Measures for the Management of COPD



Abbreviations: CDC=Centers for Disease Control and Prevention; NRT=nicotine replacement therapy; PR =pulmonary rehabilitation.

# Online Supplement

**Figure S1.** Venn diagram illustrating the distribution and overlap of key search terms used in conducting the literature searches.

