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Review

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

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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 health care professional (HCP) perspectives. Coauthored 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, health care systems can better address the complex needs of patients with COPD and ultimately enhance their health outcomes.

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Abbreviations:

BI=brief intervention; **BIPI**=Boehringer Ingelheim Pharmaceuticals, Inc.; **CAPTURE**=COPD Assessment in Primary Care to Identify Undiagnosed Respiratory Disease and Exacerbation Risk; **CAT**=COPD Assessment Test™; **CDC**=Centers for Disease Control and Prevention; **CME**=continuing medical education; **COPD**=chronic obstructive pulmonary disease; **DPIs**=dry powder inhalers; **EMR**=electronic medical record; **EOS**=blood eosinophil count; **FEV_1**=forced expiratory volume in 1 second; **FVC**=forced vital capacity; **GAAPP**=Global Allergy & Airways Patient Platform; **GOLD**=Global initiative for chronic Obstructive Lung Disease; **HCP**=health care professional; **HRQoL**=health-related quality of life; **ICS**=inhaled corticosteroid; **INT$**=International Dollar; **IPCRG**=International Primary Care Respiratory Group; **LABA**=long-acting beta2-agonist; **LAMA**=long-acting muscarinic antagonist; **LMICs**=low- and middle-income countries; **MDIs**=metered-dose dose inhalers; **mMRC**=modified Medical Research Council, dyspnea questionnaire; **NRT**=nicotine replacement therapy; **PCP**=primary care physician; **PR**=pulmonary rehabilitation; **QoL**=quality of life; **SABA**=short-acting beta2-agonist; **SAMA**=short-acting muscarinic antagonist; **STAR**=STaging of Airflow Obstruction by Ratio; **TTG**=teach-to-goal; **WHO**=World Health Organization

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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 fourth leading cause of death and the eighth leading cause of poor health.[1] In 2020, 480 million (10.6%) people (age ≥25 years) worldwide suffered from COPD, and the global prevalence[3] is projected to reach approximately 600 million by 2050. The societal burden of COPD in the United States is also growing; in 2021, the prevalence of COPD was 6.5% (14.2 million cases).[4] Furthermore, the economic burden of COPD in the United States 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 3 decades.[5]

While tobacco smoking is the leading risk factor for COPD, other factors may include: (1) prolonged exposure to smoke from household biomass burning; (2) occupational exposure to gases, fumes, and other inhaled agents; and (3) poor air quality.[6,7] 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.[2]

Patients typically experience chronic dyspnea, wheezing, chest tightness, fatigue, and a productive or nonproductive cough, which are often present with comorbidities such as cardiovascular disease, musculoskeletal disorders, metabolic disorders, osteoporosis, anxiety, depression, and lung cancer.[2] 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.[2]

Patients with COPD face significant challenges in daily activities due to breathlessness and fatigue.[8] 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.[8,9] 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.[2] The goal of management strategies must include alleviating COPD symptoms, enhancing health status, and increasing the level of physical activity.[2]

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.[10] 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.[11] Patient-related barriers include low socioeconomic status, inadequate family and social support, and reluctance to participate in demanding interventions required to manage COPD.[11] Barriers related to the health care 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.[6,11] This review aims to explore the primary challenges and opportunities of managing COPD from both the patient and health care 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 patient-centered outcomes.

Methods

This article is coauthored 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. Supplementary Figure S1 in the online supplement 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.[6] 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.[2] The primary method for diagnosing COPD[2] is forced spirometry

(postbronchodilator forced expiratory volume in 1 second [FEV_1] to forced vital capacity [FVC] ratio of <0.7). Further assessments, including lung volume assessment, diffusion capacity, exercise testing, and/or lung imaging, should also be considered for an 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.[2]

Despite spirometry being the gold standard for diagnosing COPD, the percentage of diagnosed patients who underwent spirometry was low (range: 32%–36.7%) in 2 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 postbronchodilator 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.[6] 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.[6] About 80% of patients in the United States and 85% in the United Kingdom rely on primary care physicians (PCPs) for a COPD diagnosis.[22,23] 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 for early diagnosis.[22] 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.[24,25] Reasons for the misdiagnosis of COPD include poor access to diagnostic services and lack of expertise in performing and interpreting spirometry, which limits its use in primary care.[18] According to a recent meta-analysis, 14%–26% of symptomatic smokers visiting primary health care settings in the past 12 months had spirometry-confirmable COPD not documented by clinicians.[26] Additionally, 1 in 4 patients on inhaled therapies had irreversible airflow limitation consistent with COPD, unrecognized by both PCPs and patients.[26] In one study, only 22% of PCPs expressed the requirement for spirometry after initial presentation to confirm the diagnosis of COPD,[27] and in another study, only 34% of PCPs regularly used spirometry, despite 64% having access to spirometric tests.[28] 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.[2]

Appropriate Initial Assessment Needs to be Conducted for Multidimensional and Patient-Centric 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™ (CAT), exacerbation history, current smoking status, blood eosinophil level, alpha-1 antitrypsin level, and presence of comorbidities.[2] 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_1 was generally more accelerated during the early stages (GOLD 1 or 2) of COPD than during the later stages (GOLD 3 or 4).[29] 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_1/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.[30] 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.

Health Care Professionals 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: (1) handheld devices, such as a peak expiratory flow meter or microspirometer; (2) questionnaires (such as the COPD Assessment in Primary Care to Identify Undiagnosed Respiratory Disease and Exacerbation Risk [CAPTURE] screening tool, the COPD Population Screener, the COPD Diagnostic Questionnaire, and the PUMA COPD questionnaire); (3) a combination of handheld devices and questionnaires; or (4) prediction models for identifying undiagnosed COPD using routine electronic health record data.[6] In addition, app-based microspirometers have been reported to show favorable performance compared with other case-finding modalities.[6]

Nonconventional Risk Factors for COPD Should Not be Neglected

In addition to tobacco smoking and advanced age, risk factors such as biomass smoke (particulate matter 2.5 micrometers, particulate matter 10 micrometers, and nitrogen dioxide exposure), impaired lung growth, and lower peak lung function during early adulthood are associated with COPD.[6] Recurrent respiratory infections are common among patients with COPD and may indicate an underlying diagnosis of COPD.[31] Neglecting these factors could potentially lead to a delayed diagnosis of COPD.

Underrepresentation of Women During COPD Diagnosis

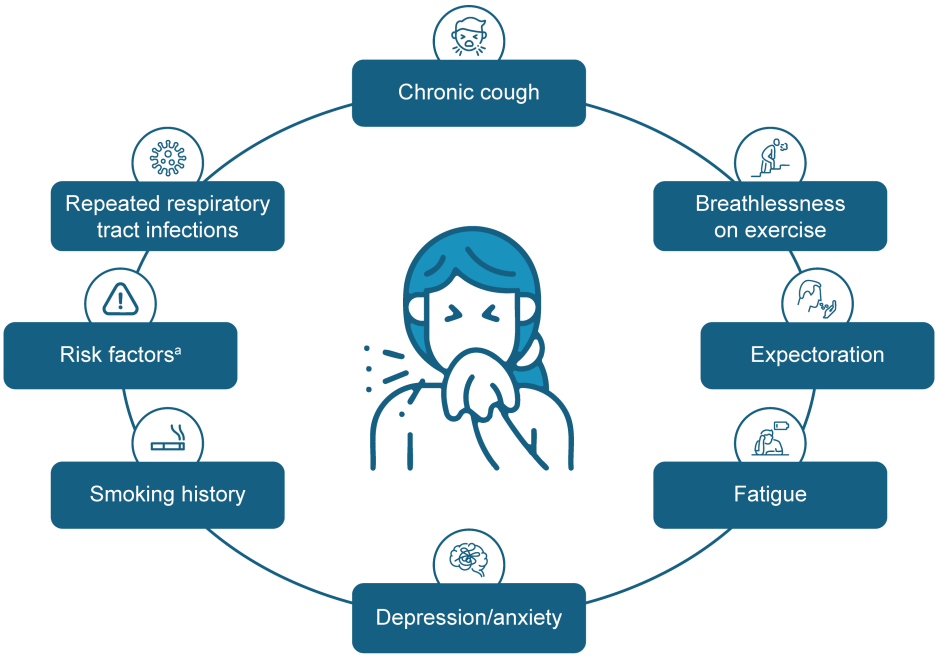
A common misperception that COPD primarily affects men may have led to previous underdiagnosis in women.[32] A diagnostic bias has been observed in PCPs, as illustrated by a hypothetical case description of cough and dyspnea in smokers.[22] This case was diagnosed as COPD more often in males than in females, despite no other differences in clinical presentation ($P<0.0001$).[22] 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.[33] 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 scans.[33]

Understanding 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 1-on-1 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 in the morning were reported in 22% of patients, at night in 19%, and at both times of the day in 10%, while no change was reported[8] in 29%. 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.[28] 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.[28] 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 health care settings.[37] These experiences may contribute to poorer patient–provider communication, reduced engagement with health care 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 health care 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.[41] Individuals with lower socioeconomic status and those living with smoking-related illnesses may be especially vulnerable to biased care and stigma.[42] 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

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



[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.

COPD=chronic obstructive pulmonary disease

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 compared with 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. Table 1 and Table 2 provide a list of suggested questions for patients that may help them 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.
- 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 (Health Care Professionals' Perspective):

- Prompt and effective management during the early stages of COPD can preserve lung function and prevent exacerbations.
- Understanding patients' perspectives is a critical but is often an 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.
- *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.

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?

COPD=chronic obstructive pulmonary disease

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)?

COPD=chronic obstructive pulmonary disease

Table 3. Resources for Patients to Seek Support

Organization Name/Contact	Description
The COPD Foundation www.copdfoundation.org **Helpline: 1-866-731-2673**	The COPD Foundation's mission is to help millions of people live longer and healthier lives by advancing research, advocacy, and awareness to stop COPD, bronchiectasis, and nontuberculous mycobacterial lung disease.
COPD360Social https://copdf.co/COPD360Social **Helpline: 1-866-316-2673**	The COPD Foundation's COPD360social is an interactive social community in which individuals can join and receive support, ask questions, learn about events, participate in research, chat with experts, download education materials, and learn how to take action.
RIGHT2BREATHE https://right2breathe.org	Right2Breathe's mission is to provide education, awareness, free screenings, and resources for people who are currently diagnosed or at higher risk of being diagnosed with respiratory disease.
American Lung Association www.lung.org **Helpline: 1-800-586-4872**	The American Lung Association's mission is to save lives by improving lung health and preventing lung disease. They do this through education, advocacy, and research.
GOLD Guidelines[2] www.goldcopd.org	The GOLD Guidelines provide up-to-date, evidence-based strategies for the diagnosis, management, and prevention of COPD. Developed by leading experts in respiratory medicine, the guidelines are used globally by health care professionals to improve patient outcomes and support personalized COPD care through recommendations based on the latest research.
IPCRG www.ipcrg.org/rightcare/copd-right-care **COPD Right Care**	IPCRG is a clnically-led, charitable organization. Its scope is research and education to improve prevention, diagnosis, and care of respiratory diseases in global community and primary care practices.
GAAPP www.gaapp.org/diseases/copd	GAAPP's mission is to globally support and empower patients with allergies, airways, and atopic diseases by protecting their rights and insisting on the duties of governments, health care professionals, and the general public.

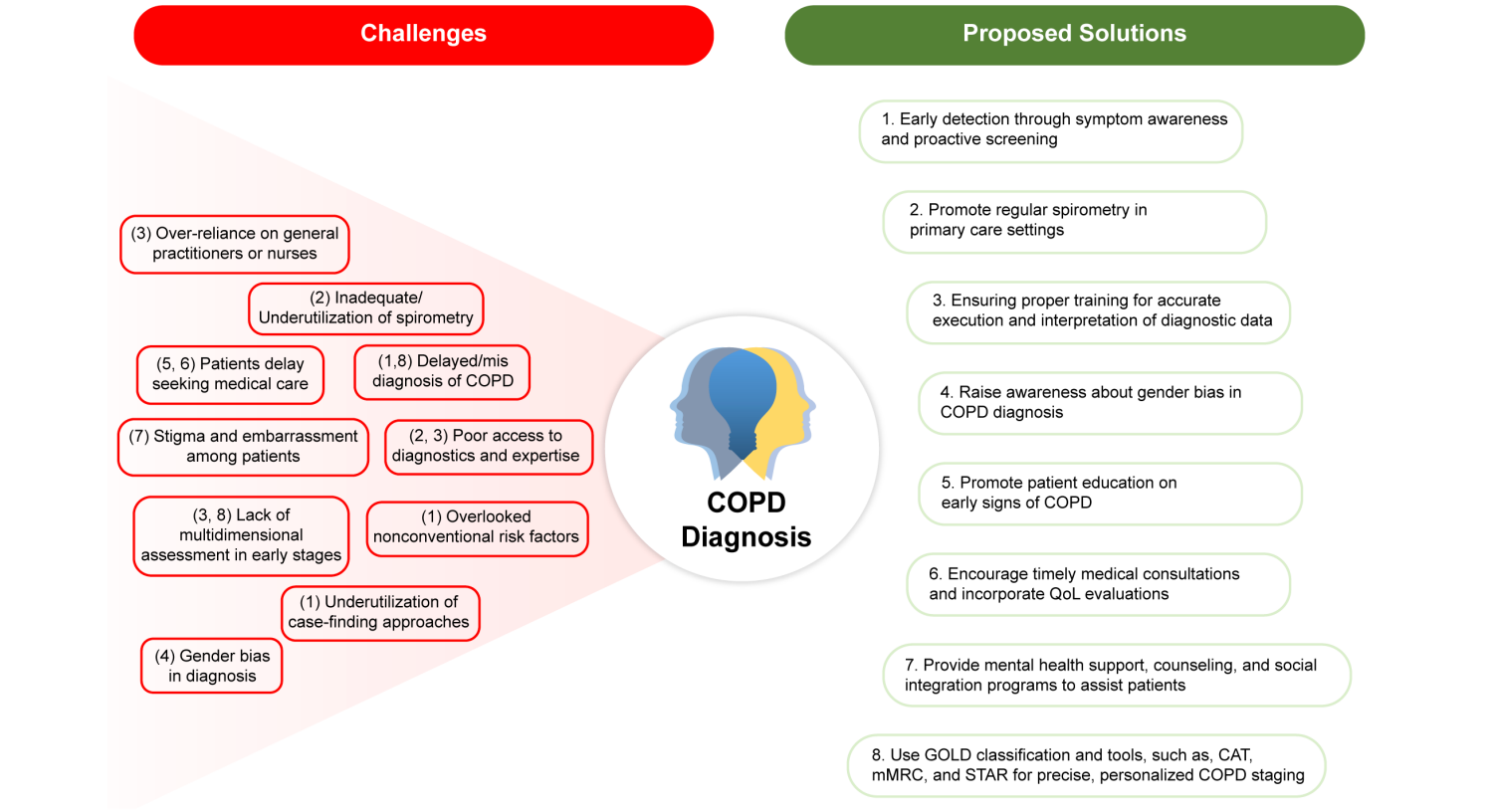
COPD=chronic obstructive pulmonary disease; GOLD=Global initiative for chronic Obstructive Lung Disease; IPCRG=International Primary Care Respiratory Group; GAAPP=Global Allergy & Airways Patient Platform

- *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.[2] 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 A, B, and E classification (symptom severity/exacerbation history) and COPD endotypes (underlying biologic differences, such as bacterial colonization or eosinophilic inflammation).[2,47] Furthermore, the concept of *treatable traits* has been introduced.[48] This approach identifies all pulmonary and extrapulmonary aspects of COPD to manage each patient in an individualized manner.[49] However, the current level of understanding of 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.[2] Different management strategies include smoking cessation,

Figure 2. Challenges and Proposed Solutions in Diagnosing COPD



COPD=chronic obstructive pulmonary disease; QoL=quality of life; GOLD=Global initiative for chronic Obstructive Lung Disease; CAT=COPD Assessment Test™; mMRC=modified Medical Research Council dyspnea questionnaire; STAR=STaging of Airflow Obstruction by Ratio

vaccination, pharmacotherapy, comorbidity management, pulmonary rehabilitation, and patient education on self-management.[2]

Smoking Cessation

Preventive measures are critical in vulnerable individuals (e.g., those with a family history of COPD, alpha-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.[2,50] 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.[50] 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.[28]

Vaccination for Stable COPD

Vaccinations are important preventive measures for patients with respiratory diseases, such as COPD.[51] Typically, antipneumococcal and anti-influenza vaccines are recommended for individuals with such conditions.[51] 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.[52] 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).[2] The CDC also recommends the new respiratory syncytial virus and tetanus, diphtheria, and pertussis–Tdap–vaccines in patients with COPD. Additionally, both the World Health Organization (WHO) and the CDC recommend the SARS-CoV-2 vaccine in patients vulnerable to COPD.[2]

Pharmacotherapies

The primary treatment modalities for COPD include inhaled bronchodilators and anti-inflammatory drugs.[2] Predominantly, bronchodilators are either beta2-agonists or muscarinic antagonists. Short-acting beta2-agonists (SABAs)

and short-acting muscarinic antagonists (SAMAs) are only active for up to 6 hours, whereas long-acting beta2-agonists (LABAs) and long-acting muscarinic antagonists (LAMAs) retain their activity for 12–24 hours.[53,54] Combination treatment with LABAs and LAMAs is more effective in reducing exacerbations than monotherapy.[55] The main anti-inflammatory drugs used in COPD are inhaled corticosteroids (ICSs); however, regular ICS treatment has been shown to increase the risk of pneumonia in patients with severe disease.[56] When combined with LABAs and LAMAs, ICSs show 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.[2]

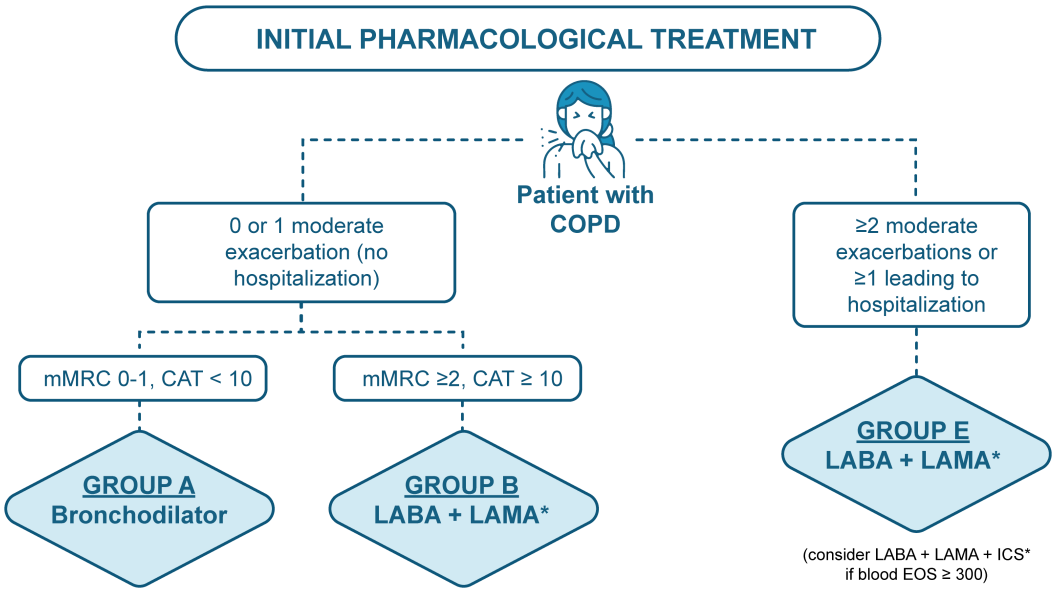
The GOLD recommendations[2] advocate considering the patient's specific group based on initial assessment when determining the initial pharmacotherapy for COPD (Figure 3):

- Group A (0–1 moderate exacerbation, no hospitalization, mMRC score 0–1, CAT score <10): A bronchodilator, preferably a long-acting one, except in patients with very occasional shortness of breath.
- Group B (0–1 moderate exacerbation, no hospitalization, mMRC score ≥ 2, CAT score ≥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+ICS is not encouraged for COPD.

A short-acting bronchodilator should be prescribed to all patients as a rescue medication.[2] While LABAs provide longer-lasting relief, additional use of SABAs as needed can further improve FEV_1 and symptoms, particularly when combined with a SAMA.[2] 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).[2] Follow-up pharmacotherapy should focus on 2 key treatable traits: persistence of dyspnea and occurrence of exacerbations for escalating or de-escalating treatment.[2] 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.[57] 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.[58]

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.[59] 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 the use of spacers may be helpful in patients who may have difficulty in maintaining the hand-breath coordination required for MDIs.[2] 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 short-acting 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.[2,61] 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.[63] A study identified that over 70% of patients with COPD and asthma were using MDIs incorrectly, with common errors including failure to exhale prior to inhalation.[64] 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.[67] 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.[68] 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.[69] 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.[70,71] Spacers slow aerosol particle velocity, enhancing drug deposition in the lungs and

Figure 3. Initial Pharmacological Treatment of Stable COPD[a]



[a]Adapted from GOLD[2] 2024

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.

COPD=chronic obstructive pulmonary disease; GOLD=Global initiative for chronic Obstructive Lung Disease; mMRC=modified Medical Research Council dyspnea questionnaire; CAT=COPD Assessment Test™; LABA=long-acting beta2-agonist; LAMA=long-acting muscarinic antagonist; ICS=inhaled corticosteroid; EOS=blood eosinophil count

Figure 4. Nonpharmacological Measures for the Management of COPD

COPD=chronic obstructive pulmonary disease; PR=pulmonary rehabilitation; NRT=nicotine replacement therapy; CDC=Centers for Disease Control and Prevention; QoL=quality of life

addressing coordination issues with pressurized MDIs.[72] 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.[72]

Due to the substantial comorbidity burden that patients with COPD may have, annual health care costs may be prohibitively high, especially for patients having ≥3 comorbidities.[73] In low- and middle-income countries (LMICs), COPD medication costs can exceed >1 day's wage of the lowest paid government worker.[74] 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.[74] 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.[75] Such comorbidities are frequently associated with an increased risk of hospitalization, higher mortality rate, and polypharmacy.[76-78] 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.[49] These profiles suggest a multifactorial origin, emphasizing the importance of integrating clinical, genetic, environmental, and socioeconomic factors for comprehensive management.[49] It is necessary to implement preventive measures for any existing comorbidities.[49] For several comorbidities, such as short-term anxiety/depression, obesity, and cardiovascular disease, engaging patients in physical activity and regular exercise might be beneficial.[79-81] 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.[82,83]

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 well-being 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.[82] 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 health care costs, particularly unplanned hospital admissions.[84,85] Education in pulmonary rehabilitation can play a crucial role in promoting effective self-management of COPD.[86] 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 pulmonary rehabilitation programs are variable, and there is currently limited guidance for its optimal design and delivery.[87] 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.[88]

Self-Management and Quality of Life 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.[89] 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's Respiratory Questionnaire, 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.[90] Patients with COPD often require more support, including information about their condition, financial help, improved treatment options, and assistance with daily tasks.[8] Thus, the QoL of patients is also influenced by the type of health care 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.[91] The *chronic care model* of GOLD emphasizes that HCPs should promote self-management education and coaching among patients with COPD.[2] The National Institute for Health and Care Excellence in the United Kingdom also suggests promoting knowledge and awareness about COPD and its

management among patients.[92] 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.[93] 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.[94] 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.[95] 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.[96]

A longer duration of self-management intervention is associated with better outcomes.[97] In a 1-on-1 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.[8] 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.[8] Thus, continued HCP support is important for sustaining behavioral changes leading to QoL improvement.[98]

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, the 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 open-ended 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 (Health Care Professionals' 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 COPD 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.[2] Exacerbations may be caused by airway infection, pollution, or other stressors on the lungs.[2] 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.[2] 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.[2]

Oral therapies such as antibiotics should be prescribed for patients who exhibit dyspnea, increased sputum volume, and increased sputum purulence simultaneously.[2] 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.[99] For individuals with frequent exacerbations despite optimized inhaled maintenance therapy, long-term azithromycin treatment is suggested.[100] Roflumilast, a phosphodiesterase-4 inhibitor, is particularly beneficial for those with severe COPD and chronic bronchitis, as it reduces both inflammation and exacerbations.[101] 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.[102] Among treatments based on precision medicine, biologics target specific inflammatory pathways, offering improved lung function and reduced exacerbations.[103] The approval of dupilumab in the United States as the first biologic for COPD provides a new option for patients with eosinophilic phenotypes.[104] 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.[105,106] 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.[49] 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, a 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.[49] A meta-analysis of 10 randomized trials showed short-term benefits of pulmonary rehabilitation if initiated within a week of exacerbation.[107] 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.[108] To ensure high-quality pulmonary rehabilitation, these programs should undergo regular quality control audits and be delivered by well-trained staff.[109]

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 at-risk 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*: Continue to collaborate with patient advocacy organizations to codevelop 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 (Health Care Professionals' 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 health care 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 health care 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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References

1. World Health Organization (WHO). Chronic obstructive pulmonary disease (COPD).WHO website. Updated November 2024. Accessed September 09, 2024. https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd)

2. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for prevention, diagnosis and management of COPD, 2024 report. GOLD website. Published December 2023. Accessed September 09, 2024. https://goldcopd.org/2024-gold-report/

3. Boers E, Barrett M, Su JG, et al. Global burden of chronic obstructive pulmonary disease through 2050. *JAMA Netw Open*. 2023;6(12):e2346598. https://doi.org/10.1001/jamanetworkopen.2023.46598

4. Liu Y, Carlson SA, Watson KB, Xu F, Greenlund KJ. Trends in the prevalence of chronic obstructive pulmonary disease among adults aged ≥18 Years - United States, 2011-2021. *MMWR Morb Mortal Wkly Rep*. 2023;72(46):1250-1256. https://doi.org/10.15585/mmwr.mm7246a1

5. Chen S, Kuhn M, Prettner K, et al. The global economic burden of chronic obstructive pulmonary disease for 204 countries and territories in 2020-50: a health-augmented macroeconomic modelling study. *Lancet Glob Health*. 2023;11(8):e1183-e1193. https://doi.org/10.1016/S2214-109X(23)00217-6

6. Lin CH, Cheng SL, Chen CZ, Chen CH, Lin SH, Wang HC. Current progress of COPD early detection: key points and novel strategies. *Int J Chron Obstruct Pulmon Dis*. 2023;18:1511-1524. https://doi.org/10.2147/COPD.S413969

7. Murgia N, Gambelunghe A. Occupational COPD-the most under-recognized occupational lung disease? *Respirology*. 2022;27(6):399-410. https://doi.org/10.1111/resp.14272

8. Scichilone N, Whittamore A, White C, Nudo E, Savella M, Lombardini M. The patient journey in chronic obstructive pulmonary disease (COPD): a human factors qualitative international study to understand the needs of people living with COPD. *BMC Pulm Med*. 2023;23(1):506. https://doi.org/10.1186/s12890-023-02796-8

9. Johansson H, Bertero C, Berg K, Jonasson LL. To live a life with COPD - the consequences of symptom burden. *Int J Chron Obstruct Pulmon Dis*. 2019;14:905-909. https://doi.org/10.2147/COPD.S192280

10. Anzueto A, Rogers S, Donato B, et al. Treatment patterns in patients with newly diagnosed COPD in the USA. *BMC Pulm Med*. 2024;24(1):395. https://doi.org/10.1186/s12890-024-03194-4

11. Siu DCH, Gafni-Lachter L. Addressing barriers to chronic obstructive pulmonary disease (COPD) care: three innovative evidence-based approaches: a review. *Int J Chron Obstruct Pulmon Dis*. 2024;19:331-341. https://doi.org/10.2147/COPD.S426050

12. Joo MJ, Lee TA, Weiss KB. Geographic variation of spirometry use in newly diagnosed COPD. *Chest*. 2008;134(1):38-45. https://doi.org/10.1378/chest.08-0013

13. Han MK, Kim MG, Mardon R, et al. Spirometry utilization for COPD: how do we measure up? *Chest*. 2007;132(2):403-409. https://doi.org/10.1378/chest.06-2846

14. Lamprecht B, Mahringer A, Soriano JB, Kaiser B, Buist AS, Studnicka M. Is spirometry properly used to diagnose COPD? Results from the BOLD study in Salzburg, Austria: a population-based analytical study. *Prim Care Respir J*. 2013;22(2):195-200. https://doi.org/10.4104/pcrj.2013.00032

15. Diab N, Gershon AS, Sin DD, et al. Underdiagnosis and overdiagnosis of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2018;198(9):1130-1139. https://doi.org/10.1164/rccm.201804-0621CI

16. Aggarwal AN, Gupta D, Agarwal R, Jindal SK. Comparison of the lower confidence limit to the fixed-percentage method for assessing airway obstruction in routine clinical practice. *Respir Care*. 2011;56(11):1778-1784. https://doi.org/10.4187/respcare.01160

17. Chaiwong W, Uthaikhup S, Liwsrisakun C, Pothirat C. Effect of changing reference equations for spirometry interpretation in Thai people. *J Thorac Dis*. 2019;11(1):113-122. https://doi.org/10.21037/jtd.2018.11.06

18. Hangaard S, Helle T, Nielsen C, Hejlesen OK. Causes of misdiagnosis of chronic obstructive pulmonary disease: a systematic scoping review. *Respir Med*. 2017;129:63-84. https://doi.org/10.1016/j.rmed.2017.05.015

19. Brems JH, Balasubramanian A, Raju S, et al. Changes in spirometry interpretative strategies: implications for classifying COPD and predicting exacerbations. *Chest*. 2024;166(2):294-303. https://doi.org/10.1016/j.chest.2024.03.034

20. Schiavi E, Ryu MH, Martini L, et al. Application of the European Respiratory Society/American Thoracic Society spirometry standards and race-neutral equations in the COPDGene study. *Am J Respir Crit Care Med*. 2024;210(11):1317-1328. https://doi.org/10.1164/rccm.202311-2145OC

21. Athlin Å, Lisspers K, Hasselgren M, et al. Diagnostic spirometry in COPD is increasing, a comparison of two Swedish cohorts. *NPJ Prim Care Respir Med*. 2023;33(1):23. https://doi.org/10.1038/s41533-023-00345-8

22. Jones RC, Price D, Ryan D, et al. Opportunities to diagnose chronic obstructive pulmonary disease in routine care in the UK: a retrospective study of a clinical cohort. *Lancet Respir Med*. 2014;2(4):267-276. https://doi.org/10.1016/S2213-2600(14)70008-6

23. Perez X, Wisnivesky JP, Lurslurchachai L, Kleinman LC, Kronish IM. Barriers to adherence to COPD guidelines among primary care providers. *Respir Med*. 2012;106(3):374-381. https://doi.org/10.1016/j.rmed.2011.09.010

24. Akhtar R, Wilson A. A comparison of spirometry in general practice and a pulmonary function laboratory. *Prim Care Respir J*. 2005;14(4):215-220. https://doi.org/10.1016/j.pcrj.2004.12.005

25. Starren ES, Roberts NJ, Tahir M, et al. A centralised respiratory diagnostic service for primary care: a 4-year audit. *Prim Care Respir J.* 2012;21(2):180-186. https://doi.org/10.4104/pcrj.2012.00013

26. Perret J, Yip SWS, Idrose NS, et al. Undiagnosed and 'overdiagnosed' COPD using postbronchodilator spirometry in primary healthcare settings: a systematic review and meta-analysis. *BMJ Open Respir Res.* 2023;10(1):e001478. https://doi.org/10.1136/bmjresp-2022-001478

27. Chapman KR, Tashkin DP, Pye DJ. Gender bias in the diagnosis of COPD. *Chest.* 2001;119(6):1691-1695. https://doi.org/10.1378/chest.119.6.1691

28. Fromer L. Diagnosing and treating COPD: understanding the challenges and finding solutions. *Int J Gen Med.* 2011;4:729-739. https://doi.org/10.2147/IJGM.S21387

29. Tantucci C, Modina D. Lung function decline in COPD. *Int J Chron Obstruct Pulmon Dis.* 2012;7:95-99. https://doi.org/10.2147/COPD.S27480

30. Bhatt SP, Nakhmani A, Fortis S, et al. STAR has better discrimination for mortality than ERS/ATS chronic obstructive pulmonary disease severity classification. *Am J Respir Crit Care Med.* 2024;210(11):1376-1379. https://doi.org/10.1164/rccm.202311-2172LE

31. Miravitlles M, Anzueto A. Chronic respiratory infection in patients with chronic obstructive pulmonary disease: what is the role of antibiotics? *Int J Mol Sci.* 2017;18(7):1344. https://doi.org/10.3390/ijms18071344

32. Zysman M, Raherison-Semjen C. Women's COPD. *Front Med (Lausanne).* 2021;8:600107. https://doi.org/10.3389/fmed.2021.600107

33. Somayaji R, Chalmers JD. Just breathe: a review of sex and gender in chronic lung disease. *Eur Respir Rev.* 2022;31(163):210111. https://doi.org/10.1183/16000617.0111-2021

34. Miravitlles M, Ribera A. Understanding the impact of symptoms on the burden of COPD. *Respir Res.* 2017;18(1):67. https://doi.org/10.1186/s12931-017-0548-3

35. Berger BE, Kapella MC, Larson JL. The experience of stigma in chronic obstructive pulmonary disease. *West J Nurs Res.* 2011;33(7):916-932. https://doi.org/10.1177/0193945910384602

36. Mathioudakis AG, Ananth S, Vestbo J. Stigma: an unmet public health priority in COPD. *Lancet Respir Med.* 2021;9(9):955-956. https://doi.org/10.1016/S2213-2600(21)00316-7

37. Madawala S, Osadnik CR, Warren N, Kasiviswanathan K, Barton C. Healthcare experiences of adults with COPD across community care settings: a meta-ethnography. *ERJ Open Res.* 2023;9(1):00581-02022. https://doi.org/10.1183/23120541.00581-2022

38. Boland VC, Mattick RP, McRobbie H, Siahpush M, Courtney RJ. "I'm not strong enough; I'm not good enough. I can't do this, I'm failing"- A qualitative study of low-socioeconomic status smokers' experiences with accessing cessation support and the role for alternative technology-based support. *Int J Equity Health.* 2017;16(1):196. https://doi.org/10.1186/s12939-017-0689-5

39. Chang YY, Dai YT, Chien NH, Chan HY. The lived experiences of people with chronic obstructive pulmonary disease: a phenomenological study. *J Nurs Scholarsh.* 2016;48(5):466-471. https://doi.org/10.1111/jnu.12230

40. Philip K, Gaduzo S, Rogers J, Laffan M, Hopkinson NS. Patient experience of COPD care: outcomes from the British Lung Foundation Patient Passport. *BMJ Open Respir Res.* 2019;6(1):e000478. https://doi.org/10.1136/bmjresp-2019-000478

41. Higginson R, Parry A. Managing chronic obstructive pulmonary disease in the community setting. *Br J Community Nurs.* 2018;23(1):6-12. https://doi.org/10.12968/bjcn.2018.23.1.6

42. Madawala S, Enticott J, Sturgiss E, Selamoglu M, Barton C. The impact of smoking status on anticipated stigma and experience of care among smokers and ex-smokers with chronic illness in general practice. *Chronic Illn.* 2023;19(3):557-570. https://doi.org/10.1177/17423953221101337

43. Jacobs SS, Krishnan JA, Lederer DJ, et al. Home oxygen therapy for adults with chronic lung disease. An official American Thoracic Society clinical practice guideline. *Am J Respir Crit Care Med.* 2020;202(10):e121-e141. https://doi.org/10.1164/rccm.202009-3608ST

44. Bueno GH, Campos CJG, Turato ER, et al. Experiences in elderly people with chronic obstructive pulmonary disease in relation to the use of long-term home oxygen therapy: a qualitative study about feelings attributed to therapy. *BMC Pulm Med.* 2022;22(1):96. https://doi.org/10.1186/s12890-022-01891-6

45. Arnold E, Bruton A, Donovan-Hall M, Fenwick A, Dibb B, Walker E. Ambulatory oxygen: why do COPD patients not use their portable systems as prescribed? A qualitative study. *BMC Pulm Med.* 2011;11:9. https://doi.org/10.1186/1471-2466-11-9

46. Zamzam MA, Azab NY, El Wahsh RA, Ragab AZ, Allam EM. Quality of life in COPD patients. *Egypt J Chest Dis Tuberc.* 2012;61(4):281-289. https://doi.org/10.1016/j.ejcdt.2012.08.012

47. Garudadri S, Woodruff PG. Targeting chronic obstructive pulmonary disease phenotypes, endotypes, and biomarkers. *Ann Am Thorac Soc.* 2018;15(Suppl 4):S234-S238. https://doi.org/10.1513/AnnalsATS.201808-533MG

48. Agusti A, Bel E, Thomas M, et al. Treatable traits: toward precision medicine of chronic airway diseases. *Eur Respir J.* 2016;47(2):410-419. https://doi.org/10.1183/13993003.01359-2015

49. Franssen FM, Alter P, Bar N, et al. Personalized medicine for patients with COPD: where are we? *Int J Chron Obstruct Pulmon Dis.* 2019;14:1465-1484. https://doi.org/10.2147/COPD.S175706

50. Tashkin DP. Smoking cessation in COPD: confronting the challenge. *Intern Emerg Med.* 2021;16(3):545-547. https://doi.org/10.1007/s11739-021-02710-2

51. Ji Z, Jareño-Esteban JJ, de Miguel-Díez J. Role of vaccines in COPD patients. *Open Respir Arch.* 2022;4(3):100191. https://doi.org/10.1016/j.opresp.2022.100191

52. Simon S, Joean O, Welte T, Rademacher J. The role of vaccination in COPD: influenza, SARS-CoV-2, pneumococcus, pertussis, RSV and varicella zoster virus. *Eur Respir Rev.* 2023;32(169):230034. https://doi.org/10.1183/16000617.0034-2023

53. American Lung Association (ALA). Understanding your COPD medications. ALA website. Updated April 2025. Accessed October 28, 2024. https://www.lung.org/lung-health-diseases/lung-disease-lookup/copd/treating/copd-medications#:~:text=Short%2Dacting%20beta%2Dagonists%20(,to%20be%20taken%20every%20day

54. Ridolo E, Montagni M, Olivieri E, Riario-Sforza GG, Incorvaia C. Role of indacaterol and the newer very long-acting β2-agonists in patients with stable COPD: a review. *Int J Chron Obstruct Pulmon Dis.* 2013;8:425-432. https://doi.org/10.2147/COPD.S49179

55. Mammen MJ, Pai V, Aaron SD, Nici L, Alhazzani W, Alexander PE. Dual LABA/LAMA therapy versus LABA or LAMA monotherapy for chronic obstructive pulmonary disease. A systematic review and meta-analysis in support of the American Thoracic Society clinical practice guideline. *Ann Am Thorac Soc.* 2020;17(9):1133-1143. https://doi.org/10.1513/AnnalsATS.201912-915OC

56. Suissa S, Patenaude V, Lapi F, Ernst P. Inhaled corticosteroids in COPD and the risk of serious pneumonia. *Thorax.* 2013;68(11):1029-1036. https://doi.org/10.1136/thoraxjnl-2012-202872

57. Bhatt SP, Blauer-Peterson C, Buysman EK, Bengtson LGS, Palli SR. Trends and characteristics of global initiative for chronic obstructive lung disease guidelines-discordant prescribing of triple therapy among patients with COPD. *Chronic Obstr Pulm Dis.* 2022;9(2):135-153. https://doi.org/10.15326/jcopdf.2021.0256

58. Brunton SA, Hogarth DK. Overuse of long-acting beta(2)-agonist/inhaled corticosteroids in patients with chronic obstructive pulmonary disease: time to rethink prescribing patterns. *Postgrad Med.* 2023;135(8):784-802. https://doi.org/10.1080/00325481.2023.2284650

59. Levy ML, Carroll W, Izquierdo Alonso JL, Keller C, Lavorini F, Lehtimäki L. Understanding dry powder inhalers: key technical and patient preference attributes. *Adv Ther.* 2019;36(10):2547-2557. https://doi.org/10.1007/s12325-019-01066-6

60. Hodder R, Price D. Patient preferences for inhaler devices in chronic obstructive pulmonary disease: experience with Respimat Soft Mist inhaler. *Int J Chron Obstruct Pulmon Dis.* 2009;4:381-390. https://doi.org/10.2147/COPD.S3391

61. Dekhuijzen PN, Lavorini F, Usmani OS. Patients' perspectives and preferences in the choice of inhalers: the case for Respimat(®) or HandiHaler(®). *Patient Prefer Adherence.* 2016;10:1561-1572. https://doi.org/10.2147/PPA.S82857

62. Barjaktarevic IZ, Milstone AP. Nebulized therapies in COPD: past, present, and the future. *Int J Chron Obstruct Pulmon Dis.* 2020;15:1665-1677. https://doi.org/10.2147/COPD.S252435

63. Usmani OS, Lavorini F, Marshall J, et al. Critical inhaler errors in asthma and COPD: a systematic review of impact on health outcomes. *Respir Res.* 2018;19(1):10. https://doi.org/10.1186/s12931-017-0710-y

64. Ocakli B, Ozmen I, Tunçay EA, et al. A comparative analysis of errors in inhaler technique among COPD versus asthma patients. *Int J Chron Obstruct Pulmon Dis.* 2018;13:2941-2947. https://doi.org/10.2147/COPD.S178951

65. Baker DW, DeWalt DA, Schillinger D, et al. Teach to goal: theory and design principles of an intervention to improve heart failure self-management skills of patients with low health literacy. *J Health Commun.* 2011;16(Suppl 3):73-88. https://doi.org/10.1080/10810730.2011.604379

66. Press VG, Arora VM, Trela KC, et al. Effectiveness of interventions to teach metered-dose and diskus inhaler techniques. A randomized trial. *Ann Am Thorac Soc.* 2016;13(6):816-824. https://doi.org/10.1513/AnnalsATS.201509-603OC

67. Marko M, Pawliczak R. Inhalation technique-related errors after education among asthma and COPD patients using different types of inhalers - systematic review and meta-analysis. *NPJ Prim Care Respir Med.* 2025;35(1):15. https://doi.org/10.1038/s41533-025-00422-0

68. Klijn SL, Hiligsmann M, Evers SMAA, Román-Rodríguez M, van der Molen T, van Boven JFM. Effectiveness and success factors of educational inhaler technique interventions in asthma and COPD patients: a systematic review. *NPJ Prim Care Respir Med.* 2017;27(1):24. https://doi.org/10.1038/s41533-017-0022-1

69. Axtell S, Haines S, Fairclough J. Effectiveness of various methods of teaching proper inhaler technique. *J Pharm Pract.* 2017;30(2):195-201. https://doi.org/10.1177/0897190016628961

70. Mayzel B, Muench S, Lauster C. Impact of pharmacist education on inhaler technique and adherence in an outpatient clinic. *Hosp Pharm.* 2022;57(3):402-407. https://doi.org/10.1177/00185787211046863

71. Paoletti G, Keber E, Heffler E, et al. Effect of an educational intervention delivered by pharmacists on adherence to treatment, disease control and lung function in patients with asthma. *Respir Med.* 2020;174:106199. https://doi.org/10.1016/j.rmed.2020.106199

72. Vincken W, Levy ML, Scullion J, Usmani OS, Dekhuijzen PNR, Corrigan CJ. Spacer devices for inhaled therapy: why use them, and how? *ERJ Open Res.* 2018;4(2):00065-02018. https://doi.org/10.1183/23120541.00065-2018

73. Larsen DL, Gandhi H, Pollack M, Feigler N, Patel S, Wise RA. The quality of care and economic burden of COPD in the United States: considerations for managing patients and improving outcomes. *Am Health Drug Benefits.* 2022;15(2):57-64.

74. Stolbrink M, Thomson H, Hadfield RM, et al. The availability, cost, and affordability of essential medicines for asthma and COPD in low-income and middle-income countries: a systematic review. *Lancet Glob Health.* 2022;10(10):e1423-e1442. https://doi.org/10.1016/S2214-109X(22)00330-8

75. Chetty U, McLean G, Morrison D, Agur K, Guthrie B, Mercer SW. Chronic obstructive pulmonary disease and comorbidities: a large cross-sectional study in primary care. *Br J Gen Pract.* 2017;67(658):e321-e328. https://doi.org/10.3399/bjgp17X690605

76. Schnell K, Weiss CO, Lee T, et al. The prevalence of clinically-relevant comorbid conditions in patients with physician-diagnosed COPD: a cross-sectional study using data from NHANES 1999-2008. *BMC Pulm Med.* 2012;12:26. https://doi.org/10.1186/1471-2466-12-26

77. Divo M, Cote C, de Torres JP, et al. Comorbidities and risk of mortality in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 2012;186(2):155-161. https://doi.org/10.1164/rccm.201201-0034OC

78. Putcha N, Drummond MB, Wise RA, Hansel NN. Comorbidities and chronic obstructive pulmonary disease: prevalence, influence on outcomes, and management. *Semin Respir Crit Care Med.* 2015;36(4):575-591. https://doi.org/10.1055/s-0035-1556063

79. Reis LF, Guimarães FS, Fernandes SJ, et al. A long-term pulmonary rehabilitation program progressively improves exercise tolerance, quality of life and cardiovascular risk factors in patients with COPD. *Eur J Phys Rehabil Med.* 2013;49(4):491-497.

80. Coventry PA, Hind D. Comprehensive pulmonary rehabilitation for anxiety and depression in adults with chronic obstructive pulmonary disease: systematic review and meta-analysis. *J Psychosom Res.* 2007;63(5):551-565. https://doi.org/10.1016/j.jpsychores.2007.08.002

81. McDonald VM, Gibson PG, Scott HA, et al. Should we treat obesity in COPD? The effects of diet and resistance exercise training. *Respirology.* 2016;21(5):875-882. https://doi.org/10.1111/resp.12746

82. Wouters EF, Posthuma R, Koopman M, et al. An update on pulmonary rehabilitation techniques for patients with chronic obstructive pulmonary disease. *Expert Rev Respir Med.* 2020;14(2):149-161. https://doi.org/10.1080/17476348.2020.1700796

83. Myers LC, Quint JK, Hawkins NM, et al. A research agenda to improve outcomes in patients with chronic obstructive pulmonary disease and cardiovascular disease: an official American Thoracic Society Research statement. *Am J Respir Crit Care Med.* 2024;210(6):715-729. https://doi.org/10.1164/rccm.202407-1320ST

84. Toubes-Navarro ME, Gude-Sampedro F, Álvarez-Dobaño JM, et al. A pulmonary rehabilitation program reduces hospitalizations in chronic obstructive pulmonary disease patients: a cost-effectiveness study. *Ann Thorac Med.* 2023;18(4):190-198. https://doi.org/10.4103/atm.atm_70_23

85. Mosher CL, Nanna MG, Jawitz OK, et al. Cost-effectiveness of pulmonary rehabilitation among US adults with chronic obstructive pulmonary disease. *JAMA Netw Open.* 2022;5(6):e2218189. https://doi.org/10.1001/jamanetworkopen.2022.18189

86. Blackstock FC, Lareau SC, Nici L, et al. Chronic obstructive pulmonary disease education in pulmonary rehabilitation. An official American Thoracic Society/Thoracic Society of Australia and New Zealand/Canadian Thoracic Society/British Thoracic Society workshop report. *Ann Am Thorac Soc.* 2018;15(7):769-784. https://doi.org/10.1513/AnnalsATS.201804-253WS

87. Roberts NJ, Kidd L, Kirkwood K, Cross J, Partridge MR. A systematic review of the content and delivery of education in pulmonary rehabilitation programmes. *Respir Med.* 2018;145:161-181. https://doi.org/10.1016/j.rmed.2018.11.002

88. Mendes MA, Rodrigues G, Janssen DJA, Spruit MA, Marques A. Understanding the determinants and outcomes of education in pulmonary rehabilitation moving toward person-centered care. *Chest.* 2025; 167(6):1615-1627. https://doi.org/10.1016/j.chest.2025.01.005

89. Effing TW, Vercoulen JH, Bourbeau J, et al. Definition of a COPD self-management intervention: international expert group consensus. *Eur Respir J.* 2016;48(1):46-54. https://doi.org/10.1183/13993003.00025-2016

90. Esteban C, Arostegui I, Aramburu A, et al. Changes in health-related quality of life as a marker in the prognosis in COPD patients. *ERJ Open Res.* 2022;8(1):00181-02021. https://doi.org/10.1183/23120541.00181-2021

91. Baiardini I, Contoli M, Corsico AG, et al. Exploring the relationship between disease awareness and outcomes in patients with chronic obstructive pulmonary disease. *Respiration.* 2021;100(4):291-297. https://doi.org/10.1159/000513953

92. National Institute for Health and Care Excellence (NICE). Overview: chronic obstructive pulmonary disease in over 16s: diagnosis and management guidance. NICE website. Published December 2018. Updated July 2019. Accessed October 28, 2024. https://www.nice.org.uk/guidance/ng115

93. Bourbeau J, Julien M, Maltais F, et al. Reduction of hospital utilization in patients with chronic obstructive pulmonary disease: a disease-specific self-management intervention. *Arch Intern Med.* 2003;163(5):585-591. https://doi.org/10.1001/archinte.163.5.585

94. Jordan RE, Majothi S, Heneghan NR, et al. Supported self-management for patients with moderate to severe chronic obstructive pulmonary disease (COPD): an evidence synthesis and economic analysis. *Health Technol Assess.* 2015;19(36):1-516 https://doi.org/10.3310/hta19360

95. Murphy LA, Harrington P, Taylor SJ, et al. Clinical-effectiveness of self-management interventions in chronic obstructive pulmonary disease: An overview of reviews. *Chron Respir Dis.* 2017;14(3):276-288. https://doi.org/10.1177/1479972316687208

96. Aravantinou-Karlatou A, Bouloukaki I, Christodoulakis A, Tsiligianni I. The influence of social support in PROMs of patients with COPD in primary care: a scoping review. *Healthcare (Basel).* 2023;11(24):3141. https://doi.org/10.3390/healthcare11243141

97. Jonkman NH, Westland H, Trappenburg JC, et al. Characteristics of effective self-management interventions in patients with COPD: individual patient data meta-analysis. ***Eur Respir J.*** 2016;48(1):55-68. https://doi.org/10.1183/13993003.01860-2015

98. Pinnock H, Steed L, Jordan R. Supported self-management for COPD: making progress, but there are still challenges. *Eur Respir J.* 2016;48(1):6-9. https://doi.org/10.1183/13993003.00576-2016

99. Qiu S, Zhong X. Macrolides: a promising pharmacologic therapy for chronic obstructive pulmonary disease. *Ther Adv Respir Dis.* 2017;11(3):147-155. https://doi.org/10.1177/1753465816682677

100. Naderi N, Assayag D, Mostafavi-Pour-Manshadi SM, et al. Long-term azithromycin therapy to reduce acute exacerbations in patients with severe chronic obstructive pulmonary disease. *Respir Med.* 2018;138:129-136. https://doi.org/10.1016/j.rmed.2018.03.035

101. Wedzicha JA, Calverley PM, Rabe KF. Roflumilast: a review of its use in the treatment of COPD. *Int J Chron Obstruct Pulmon Dis.* 2016;11:81-90. https://doi.org/10.2147/COPD.S89849

102. Anzueto A, Barjaktarevic IZ, Siler TM, et al. Ensifentrine, a novel phosphodiesterase 3 and 4 inhibitor for the treatment of chronic obstructive pulmonary disease: randomized, double-blind, placebo-controlled, multicenter phase III trials (the ENHANCE Trials). *Am J Respir Crit Care Med.* 2023;208(4):406-416. https://doi.org/10.1164/rccm.202306-0944OC

103. Kersul AL, Cosio BG. Biologics in COPD. *Open Respir Arch.* 2024;6(2):100306. https://doi.org/10.1016/j.opresp.2024.100306

104. Mullard A. FDA approves first monoclonal antibody for COPD. *Nat Rev Drug Discov.* 2024;23(11):805. https://doi.org/10.1038/d41573-024-00164-7

105. Li H, Liu DH, Chen LL, et al. Meta-analysis of the adverse effects of long-term azithromycin use in patients with chronic lung diseases. *Antimicrob Agents Chemother.* 2014;58(1):511-517. https://doi.org/10.1128/AAC.02067-13

106. Joo H, Han D, Lee JH, Rhee CK. Incidence of adverse effects and discontinuation rate between patients receiving 250 micrograms and 500 micrograms of roflumilast: a comparative study. *Tuberc Respir Dis (Seoul).* 2018;81(4):299-304. https://doi.org/10.4046/trd.2018.0015

107. Shibuya M, Yamamoto S, Kobayashi S, et al. Pulmonary rehabilitation for patients after COPD exacerbation. *Respir Care.* 2022;67(3):360-369. https://doi.org/10.4187/respcare.09066

108. Meneses-Echavez JF, Chavez Guapo N, Loaiza-Betancur AF, Machado A, Bidonde J. Pulmonary rehabilitation for acute exacerbations of COPD: a systematic review. *Respir Med.* 2023;219:107425. https://doi.org/10.1016/j.rmed.2023.107425

109. Holland AE, Cox NS, Houchen-Wolloff L, et al. Defining modern pulmonary rehabilitation. An official American Thoracic Society workshop report. *Ann Am Thorac Soc.* 2021;18(5):e12-e29. https://doi.org/10.1513/AnnalsATS.202102-146ST