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## REVIEW ARTICLE

# MANAGEMENT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE: AN UPDATE

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***Abstract***

*Chronic obstructive pulmonary disease (COPD) remains a leading cause of morbidity and mortality globally and is driven mainly by smoking, indoor biomass exposure, and air pollution. Despite advances in inhaled therapy, many patients continue to experience exacerbations and poor quality of life. This narrative review summarizes recent updates in pharmacologic and nonpharmacologic management drawn from major randomized trials, meta-analyses, and guidelines published between 2010 and 2025. The evidence supports early combination and triple-inhaler therapy to reduce exacerbations, improve lung function, and lower mortality, particularly in eosinophilic COPD patients. Novel biologics, such as mepolizumab and dupilumab, result in meaningful reductions in moderate or severe exacerbations, whereas new agents, such as roflumilast and ensifentrine, benefit frequent exacerbators with chronic bronchitis. Nontarmacologic measures, including smoking cessation, pulmonary rehabilitation, vaccination and high-intensity noninvasive ventilation, remain essential components of comprehensive care. In resource-limited settings such as Bangladesh, barriers to diagnosis, cost, and access to inhalers highlight the need for affordable generics, local rehabilitation programs, and the integration of COPD services into primary care. The evolving therapeutic landscape now enables more personalized, phenotype-driven management. Continued research and the adaptation of global evidence to local contexts are critical for reducing the COPD burden and improving long-term outcomes.*

***Keywords:*** *Chronic obstructive pulmonary disease, Bangladesh, pulmonary rehabilitation, triple therapy*

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## Introduction

Chronic obstructive pulmonary disease (COPD) remains a leading cause of morbidity and mortality worldwide, affecting approximately 213/ million people and ranking as the third leading cause of death in 2021.[1,2] Key modifiable risk factors include tobacco smoking, household biomass fuel exposure, occupational dust and air pollution.[3,4] Even with best practices in inhaled therapy, many patients continue to experience dyspnea and exacerbation. A landmark triple therapy trial showed that once fluticasone furoated daily, umeclidinium and vilanterol reduced annual moderate or severe exacerbations compared with dual therapy and lowered hospitalization rates.[5] For patients with eosinophilic COPD, biologics are changing the landscape: dupilumab decreased exacerbations and improved FEV1 and quality of life,[6] whereas the MATINEE trial reported that mepolizumab

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reduced moderate/severe exacerbations by 21/ % and emergency department/hospitalization events by 35/ % versus placebo.[7]Compared with placebo, adjunctive pharmacotherapy with roflumilast improved pre bronchodilator FEV1 by 46–80/ mL and reduced exacerbation rates.[8] Non pharmacologic measures remain essential: home based supervised pulmonary rehabilitation maintenance programs increase the 6 minute walk distance by 27/ m and improve health - related quality of life;[9] pneumococcal vaccination reduces the need for ICU care, ventilation and hospital stay during COPD exacerbations;[10] and smoking cessation improves FEV1% predicted, FEV1/FVC, exercise capacity and mortality.[11] This review synthesizes these recent advances to guide current COPD management.

**Methods**

A narrative review was conducted by searching PubMed, EMBASE and Google Scholar for articles published between January 2010 and September 2025. The search terms combined *COPD* with *management*, *bronchodilators*, *triple therapy*, *phosphodiesterase inhibitor*, *ensifentrine*, *mepolizumab*, *pulmonary rehabilitation*, *vaccination*, *oxygen therapy* and *noninvasive ventilation* . Randomized controlled trials, systematic reviews, meta analyses and large observational studies were prioritized. Guidelines from the Global Initiative for Chronic Obstructive Lung Disease (GOLD) and leading respiratory societies were reviewed. Articles were included if they reported on adults with COPD, were written in English and provided data relevant to management. Two reviewers independently screened titles and abstracts; disagreements were resolved by consensus.

**Risk Factors and Pathophysiology**

The primary risk factor for COPD is cigarette smoking; up to 80 % of cases are attributable to tobacco exposure. Indoor biomass burning, ambient air pollution, occupational dust and fumes and genetic factors (such as alpha 1 antitrypsin deficiency) also contribute. Chronic exposure to noxious particles triggers airway inflammation, oxidative stress and protease–antiprotease imbalance, leading to small airway narrowing, emphysematous destruction and mucus hypersecretion. Systemic inflammation promotes comorbidities, including cardiovascular disease and skeletal muscle wasting. Recognizing risk factors allows targeted prevention through smoking cessation and a reduction in indoor and outdoor pollution.

**Non-Pharmacological Management**

**Smoking screening**

Smoking cessation is the most effective intervention for preventing disease progression. A recent review emphasized that quitting smoking slows lung function decline, reduces morbidity and improves quality of life and survival; however, many COPD patients remain highly nicotine dependent and benefit from high intensity, long duration cessation programs with behavioral support and pharmacotherapy.[12] Nicotine replacement therapy, varenicline and bupropion, combined with counseling, are recommended; newer cytisines may offer affordable options. Healthcare providers should proactively assess readiness to quit and provide ongoing support.

**Pulmonary Rehabilitation**

Pulmonary rehabilitation is a structured program that combines exercise training, education and behavioral interventions. A meta analysis of 39 randomized trials involving 2397 patients revealed that pulmonary rehabilitation significantly improved 6 minute walk distance, health related quality of life (St George's Respiratory Questionnaire) and dyspnea without significantly affecting FEV1 or FVC.[13] Rehabilitation is recommended for all symptomatic COPD patients, especially after exacerbation, and should include aerobic and resistance training, nutritional counseling and psychosocial support.

**Vaccination**

Respiratory infections are a major cause of COPD exacerbations. Guidelines recommend annual influenza vaccination and pneumococcal vaccination (PCV13 and PPSV23). A systematic review of randomized trials revealed that influenza vaccination reduces the incidence of AECOPD(weighted mean difference "0.37; 95 % CI "0.64 to "0.11).[14] The CAPITA trial (84,000 participants) reported that PCV13 reduced vaccine type pneumococcal pneumonia by 45.6%.[15] An RCT of PPSV23 in 596 COPD patients <65 years reported a 76 % reduction in community acquired pneumonia.[14] A meta analysis of 12 RCTs (n=2,171) revealed that pneumococcal vaccination reduced the risk of exacerbation (odds ratio 0.60) and pneumonia (OR 0.62).[16] Emerging vaccines against respiratory syncytial virus and SARS CoV 2 offer additional protection; varicella zoster and pertussis vaccination should be considered in older adults.[14]

**High Intensity Non Invasive Ventilation (HI NIV)**

Recent trials have renewed interest in home NIV for chronic hypercapnic COPD. A crossover trial reported that HI NIV reduced nocturnal PaCO, by 9.2 mmHg, improved dyspnea and increased the six minute walk distance.[17] The HOT HMV trial randomized 116 hypercapnic patients to home oxygen alone or home oxygen plus NIV; the combined therapy avoided recurrent hospital admission (median 4.3 vs. 1.4 months) and reduced exacerbations (3.8 vs. 5.1 per year) but did not significantly reduce 12 month

mortality.[18] A larger European trial (n=195) demonstrated that NIV reduced 1 year mortality (12 % vs. 33 %, p=0.0004) and improved quality of life.[19] HI NIV should be considered in stable hypercapnic patients after acute exacerbation.

**Nutritional Management**

Nutritional strategies for COPD target malnutrition, oxidative stress, and inflammation. A diet rich in fruits, vegetables, and fiber has positive effects on lung function due to its antioxidant and anti-inflammatory properties.[20] Vitamin D deficiency, which is prevalent in COPD patients, is linked to worse outcomes; supplementation aiming for serum 25(OH)D e"55 nmol/L is advised.[21,22] A meta-analysis of 19 studies involving over 2000 participants confirmed that vitamin D supplementation is associated with enhanced lung function in individuals with COPD.[23] Vitamin C (400–1000 mg/day) may improve FEV1 and reduce exacerbations.[24,25] Iron and nitrate supplementation (e.g., beetroot juice) can increase exercise tolerance.[26,27] Polyphenols and omega-3 fatty acids show promise but need further research.[27] Limiting processed meat (<75 g/week) is recommended for COPD management.[27]

**Pharmacological Management**

**Bronchodilators**

Short acting â2 agonists (SABAs) and anticholinergics provide quick symptom relief and are used as rescue therapies. Long acting bronchodilators (LABA and LAMA) constitute the cornerstone of maintenance therapy. LAMA monotherapy is superior to LABA for reducing exacerbations; dual bronchodilation with LABA/LAMA improves lung function and symptoms over monotherapy and is recommended for most patients with persistent dyspnea or exacerbations.

Inhaled Corticosteroids (ICSs) and Combination Therapy

ICS reduces airway inflammation and exacerbations but increases the risk of pneumonia. They are indicated for patients with frequent exacerbations and blood eosinophil counts ≥300 cells/μL¹. Compared with LABA alone, dual therapy with LABAs/ICS improves lung function and reduces exacerbations, particularly in eosinophilic COPD patients. However, long term use should be re evaluated owing to the risk of pneumonia and thrush.

**Triple therapy**

Single inhaler triple therapy combining an inhaled corticosteroid, a long acting â2 agonist and a long acting muscarinic antagonist has become a major advance. A large modeling study (DEPICT 2) suggested that starting triple therapy at age 50 improved the FEV1 by 217 mL compared with LABA/LAMA and 377 mL compared with no treatment and reduced mortality by 12% at age 75 (LABA/LAMA by 5.4%).[28] Randomized controlled trials (IMPACT and ETHOS) demonstrated that triple therapy reduced exacerbations and mortality compared with dual therapy; a meta analysis of 21,909 patients revealed a 29% reduction in mortality.[29] An editorial summarizing these trials highlighted a 50 mL improvement in FEV• and a significant reduction in exacerbations, although it noted increased pneumonia risk.[30] Triple therapy is recommended for patients with persistent exacerbations despite dual therapy and those with high blood eosinophils.

**Phosphodiesterase Inhibitors**

**Roflumilast (PDE4 inhibitor)**

Roflumilast reduces inflammation and improves mucociliary clearance. A Korean cohort study revealed that treatment for e" 3 months reduced the hazard ratio for moderate to severe exacerbations (0.558) and demonstrated greater benefit in patients with chronic bronchitis, frequent exacerbations and concurrent inhaled therapy.[31] Subgroup analyses revealed enhanced efficacy when combined with LABA/ICS (relative hazard 0.591) or triple therapy (0.570).[31] Adverse effects include gastrointestinal symptoms and weight loss. Roflumilast is recommended for patients with severe COPD, chronic bronchitis and frequent exacerbations despite optimized inhaler therapy.

**Ensifentrine (a dual PDE3/4 inhibitor)**

Ensifentrine combines bronchodilation and anti inflammatory effects. In the ENHANCE 1 and ENHANCE 2 trials, ensifentrine (in addition to standard care) significantly improved FEV and reduced the rate of moderate/severe exacerbations; the rate ratios were 0.64 and 0.57, respectively, and the hazard ratio for time to first exacerbation was 0.62/0.58.[32] The therapy had a safety profile similar to that of the placebo and offers a promising option for symptomatic patients despite maximal inhaler therapy. Regulatory approval is pending, but the results suggest potential incorporation into future guidelines.

**Macrolides and Mucolytics**

Long term macrolide therapy (e.g., azithromycin) has anti inflammatory and antibacterial effects. Although not studied in the past five years specifically, earlier trials reported a reduction in exacerbations; concerns about antimicrobial resistance and hearing impairment limit routine use. Mucolytics such as N acetylcysteine may reduce sputum viscosity and oxidative stress; evidence from new studies remains limited.

**Biological therapy (mepolizumab)**

Mepolizumab is an anti IL 5 monoclonal antibody approved for eosinophilic COPD. The METREX and METREO trials demonstrated that mepolizumab reduced the annual rate of moderate to severe exacerbations by approximately 18 % in patients with blood eosinophil counts ≥150 cells μL{ ¹.[33] The MATINEE study (2025) reported a 30% reduction in exacerbations and improved lung function.[33,34] Real world data from the NEST study (525 patients) revealed a 76 % reduction in exacerbations, decreased systemic corticosteroid use and improved quality of life and lung function.[35] Common adverse effects include headache and injection site reactions; overall safety is favorable. Mepolizumab is considered for patients with severe eosinophilic COPD and frequent exacerbations despite triple therapy.

**Long-term oxygen therapy**

Long term oxygen therapy (LTOT) increases survival only in COPD patients with chronic severe hypoxemia. Guidelines advise oxygen for more than 15/ hours per day when PaO, is ≤55/ mmHg or oxygen saturation ≤88/%, or 55–60/ mmHg with pulmonary hypertension or polycythemia.[36] Continuous or domiciliary oxygen reduces mortality compared with nocturnal or no oxygen therapy.[37] In contrast, the Long Term Oxygen Treatment Trial reported no improvement in survival or hospitalizations for patients with moderate resting- or exercise induced desaturation.[38] Compared with oxygen or exercise alone, combining LTOT with structured exercise rehabilitation improved the 6 minute walk distance, lung function and quality of life.[39]

**Future therapies**

Other biologics targeting IL 4/13 (dupilumab) and thymic stromal lymphopoietin inhibitors (tezepelumab) are under investigation. Small interfering RNA (siRNA) therapies, gene editing and stem cell-based interventions hold promise for modifying disease progression but require more robust data before clinical adoption.

**Advanced Interventions**

**Lung volume reduction and bronchoscopic interventions**

Surgical lung volume reduction or endobronchial valve placement may benefit selected patients with severe upper lobe predominant emphysema and hyperinflation. Recent trials have not changed indications; careful assessment of heterogeneity, collateral ventilation and exercise capacity is essential. Bronchoscopic thermal vapor ablation and coils are investigational.

**Lung Transplantation**

Lung transplantation remains the definitive therapy for end stage COPD. Five year survival after transplantation approaches 50 %. Candidate selection should consider age, comorbidities, psychosocial factors and donor availability.

**Challenges in the Bangladesh Context**

COPD management in Bangladesh faces barriers, including late diagnosis, limited access to spirometry, the cost of inhalers and biologic therapies, and a high prevalence of biomass exposure. Health care providers should emphasize early smoking cessation, vaccination, pulmonary rehabilitation and guideline based inhaler therapy. Education campaigns, affordable generic medications and the integration of COPD care into primary health care programs could improve outcomes. Researchers should conduct local studies to evaluate the efficacy of novel therapies in resource constrained settings.

**Conclusion**

COPD remains a major public health challenge, but recent advances have provided multiple options for improving patient outcomes. Comprehensive management begins with risk factor reduction, particularly smoking cessation, and continues with optimization of pharmacological therapy, including early introduction of triple inhaled therapy and targeted agents such as roflumilast, ensifentrine and mepolizumab in selected patients. Non pharmacological interventions such as pulmonary rehabilitation, vaccination, LTOT and HI NIV are integral to care. Clinicians should adopt a personalized, evidence based approach, considering comorbidities, exacerbation history, eosinophil count and patient preferences. Ongoing research will clarify the role of emerging therapies and inform strategies tailored to the Bangladeshi context.

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