



Expanding the Diagnostic Horizon in COPD: Insights from GOLD 2025 on Early Detection and Comprehensive Assessment

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ABSTRACT

The 2025 update to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines redefines the chronic obstructive pulmonary disease (COPD) diagnostic framework by recognizing earlier-stage conditions like “pre-COPD” and “PRISm” (preserved ratio impaired spirometry). This new approach captures patients who display early symptoms or structural changes in the lungs but do not yet meet traditional COPD criteria, marking a shift toward early detection and personalized management. By broadening the diagnostic criteria and promoting advanced imaging and biomarker use, GOLD 2025 offers pulmonologists a more precise, individualized approach to assessing COPD. This article examines the implications of these diagnostic updates for clinical practice, emphasizing the importance of proactive intervention to improve outcomes, slow disease progression, and tailor treatment to the unique profiles of at-risk patients. By embracing diverse pathophysiological profiles, the new GOLD framework underscores the necessity for comprehensive diagnostic tools, including imaging and biomarker analyses, to redefine COPD as a preventable and manageable condition.

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) has traditionally been understood and diagnosed through a narrow focus on irreversible airflow limitation, assessed by spirometric measurements of the forced expiratory volume in 1 second (FEV₁)/forced vital capacity (FVC) ratio. However, this approach often delays diagnosis until significant lung damage has occurred, missing critical opportunities for early intervention. The 2025 update to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines represents a paradigm shift by expanding the diagnostic framework to recognize earlier stages of COPD, including the conditions termed “pre-COPD” and “PRISm” (preserved ratio impaired spirometry). These categories capture individuals who may show early symptoms or structural lung changes without meeting the full diagnostic criteria for COPD, thus addressing a broader spectrum of patients at various stages of disease risk.

This expanded framework acknowledges the heterogeneous nature of COPD, where factors like environmental exposures, genetic predispositions, and early lung abnormalities contribute to disease progression long before classic symptoms manifest. By integrating advanced imaging, biomarkers, and a refined understanding of the disease continuum, GOLD 2025 enables clinicians

to adopt a proactive approach to COPD management, focusing on early identification and personalized treatment strategies. This article explores the impact of these diagnostic advancements, detailing how they facilitate more effective screening, monitoring, and intervention in COPD care.

EXPANDED COPD DIAGNOSTIC FRAMEWORK

The 2025 update to the GOLD guidelines redefines the diagnostic framework for COPD by broadening the criteria to recognize earlier stages of the disease. This change addresses gaps in the previous understanding, which focused primarily on diagnosing COPD at more advanced stages, characterized by irreversible airflow limitation. In the past, COPD diagnosis was heavily reliant on the presence of airflow obstruction, measured through spirometry by a postbronchodilator FEV₁/FVC ratio <0.7. However, GOLD 2025 now introduces terms such as “pre-COPD” and “PRISm” to better capture a spectrum of patients who show signs of early disease or are at increased risk of progression but may not yet meet the traditional spirometric criteria for COPD.

Pre-COPD: Identifying Early Indicators

“Pre-COPD” is a new category for individuals who may present with respiratory symptoms

(e.g., cough, wheezing, or dyspnea) or structural lung changes (such as emphysema or small airway disease visible through imaging) despite having normal spirometry values. This term allows clinicians to identify patients in whom early structural and functional lung changes are occurring. Recognizing pre-COPD is particularly valuable as it opens the door to early therapeutic interventions that could potentially slow disease progression, reduce symptom burden, and improve overall outcomes.^{1,2}

PRISm: Preserved Ratio Impaired Spirometry

The GOLD 2025 also introduces the concept of “PRISm.” This category encompasses individuals with a normal FEV₁/FVC ratio (≥0.7) but a reduced FEV₁, indicating impaired lung function without full obstruction. Patients in the PRISm category may have various underlying lung changes that predispose them to developing COPD over time. Research has shown that PRISm patients are at an increased risk of future lung function decline and progression to COPD, particularly if they exhibit symptoms or comorbidities.^{3,4}

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Implications for Early Intervention and Prevention

By broadening the diagnostic framework, GOLD 2025 aims to address COPD as a disease with a progressive trajectory that may begin long before traditional diagnostic criteria are met. This expanded view recognizes that multiple factors, including environmental exposures, genetic predispositions, and early-life influences, contribute to COPD risk and progression. Consequently, this redefined approach promotes a shift toward proactive screening and management strategies, particularly for individuals with known risk factors, such as smokers or those with frequent environmental pollutant exposure. Early diagnosis in these cases allows for timely implementation of preventive and therapeutic measures, such as smoking cessation, environmental risk reduction, and, in some cases, pharmacologic intervention.

Incorporating Diverse Pathophysiological Profiles

The updated GOLD guidelines underscore the importance of acknowledging COPD as a heterogeneous disease with varying phenotypes and progression patterns. Patients categorized under pre-COPD and PRISm may exhibit diverse pathophysiological features, including emphysema, airway inflammation, or structural remodeling, that differ significantly from the classic COPD phenotype. This broader understanding encourages clinicians to use a more individualized approach in assessing, monitoring, and treating patients based on their specific disease profile, rather than relying solely on airflow limitation as the defining criterion for COPD.^{5,6}

Reinforcing the Need for New Diagnostic Tools and Biomarkers

The new diagnostic categories also highlight the need for more advanced diagnostic tools, such as imaging and biomarkers, to identify early structural changes in the lungs. GOLD 2025 advocates for the integration of such tools alongside traditional spirometry to gain a more comprehensive view of lung health and detect early changes indicative of potential COPD progression. Advanced imaging techniques, such as computed tomography (CT) scans, can reveal subclinical emphysema or small airway disease, while emerging biomarkers could offer insights into the inflammatory and genetic factors driving early disease.^{7,8}

Summary

The redefined diagnostic framework in GOLD 2025 acknowledges COPD as a disease continuum that includes early-stage

conditions, such as pre-COPD and PRISm, that are detectable before full obstruction develops. This shift toward recognizing at-risk and early-stage patients marks a significant evolution in COPD management. It underscores the importance of a proactive, personalized approach to COPD diagnosis and treatment, aiming to intervene earlier in the disease course to potentially improve long-term outcomes.

REVISED PHARMACOLOGICAL STRATEGIES

The 2025 GOLD report introduces updated pharmacological strategies for managing COPD, reflecting an increasing emphasis on personalized medicine and targeting specific inflammatory pathways. These updates incorporate new therapeutic agents, such as ensifentrine and dupilumab, which provide treatment options for patients with specific inflammatory profiles or those who do not respond adequately to traditional bronchodilators and anti-inflammatory agents. The addition of these agents signifies a shift toward understanding COPD not merely as a single disease but as a complex spectrum with varying pathophysiological drivers.

Introduction of Ensifentrine: a Dual-mechanism Therapy

Ensifentrine is a novel phosphodiesterase 3 and 4 (PDE3 and PDE4) inhibitor that operates through a unique dual-action mechanism, combining bronchodilation with anti-inflammatory effects. The PDE3 inhibition primarily facilitates smooth muscle relaxation, resulting in bronchodilation, while PDE4 inhibition reduces inflammation in the airways. Ensifentrine's ability to simultaneously address two key aspects of COPD pathology—airway constriction and inflammation—makes it particularly valuable for patients who have had suboptimal responses to traditional therapies like long-acting beta-agonists (LABA), long-acting muscarinic antagonists (LAMA), and inhaled corticosteroids (ICS).⁹

This dual approach is especially relevant for COPD patients with chronic airway inflammation that persists despite standard treatment, as it provides a targeted anti-inflammatory effect without the potential corticosteroid-related side effects. Clinical trials have shown that ensifentrine can reduce exacerbation rates, improve lung function, and enhance symptom control, offering an effective option for individuals with frequent exacerbations or those who have difficulty achieving control with existing bronchodilators.¹⁰

Dupilumab: Targeting Type 2 Inflammation in COPD

Dupilumab is a monoclonal antibody that targets the interleukin-4 receptor alpha (IL-4Rα), effectively inhibiting the signaling pathways of IL-4 and IL-13, which are central to type 2 inflammation. Type 2 inflammation, characterized by elevated eosinophils and specific cytokine profiles, is increasingly recognized in a subset of COPD patients. This inflammatory phenotype often presents with overlapping asthma-like features, including airway hyper-responsiveness and mucus hypersecretion.

The GOLD 2025 incorporates dupilumab as an option for COPD patients with evidence of type 2 inflammation, particularly those with elevated blood eosinophil levels, who may derive limited benefit from conventional bronchodilators and ICS alone. By targeting the IL-4 and IL-13 pathways, dupilumab addresses the root cause of type 2 inflammation, leading to significant reductions in exacerbation rates and improvements in lung function and quality of life. Dupilumab's ability to reduce exacerbations makes it a valuable choice for patients with frequent hospitalizations or deteriorating lung function despite optimized treatment.¹¹

Refinement of Inhaled Therapy Recommendations

The GOLD 2025 also refines the recommendations for the use of inhaled therapies, including bronchodilators and corticosteroids, emphasizing a patient-centered approach. The report updates the guidelines for the combined use of LABA, LAMA, and ICS based on disease severity, symptom burden, and exacerbation history. For instance, patients with high symptom burden and frequent exacerbations are recommended to start or escalate to triple therapy (LABA + LAMA + ICS) to achieve optimal control. For others, ICS withdrawal may be advised, particularly in patients with lower blood eosinophil counts who have a higher risk of pneumonia when on ICS therapy. GOLD 2025 provides updated guidance on how to safely taper and discontinue ICS in these patients to minimize adverse effects.

Additionally, the guidelines outline the importance of adjusting treatment based on patient-reported outcomes and spirometric data, ensuring that therapy aligns with the patient's evolving needs. The updated pharmacological strategy encourages pulmonologists to continuously reassess the effectiveness of treatment and make adjustments to ensure optimal benefit and minimal adverse effects.

Incorporation of Biomarkers for Personalized Therapy

The GOLD 2025 report promotes the use of blood eosinophil counts as a biomarker to guide treatment choices, particularly regarding ICS and biologic therapies like dupilumab. Patients with elevated eosinophil counts are more likely to benefit from anti-inflammatory treatments targeting type 2 inflammation, as this biomarker reflects an underlying inflammatory process that corticosteroids or biologics can address. This biomarker-driven approach reduces the risk of overtreatment, aligning therapy with individual inflammatory profiles and making personalized treatment accessible and clinically relevant.¹²

Biomarkers are not only helpful for selecting appropriate therapies but also valuable for ongoing treatment monitoring. For instance, a rise in eosinophil levels may prompt the initiation of ICS or a biologic agent, while a decrease may indicate an opportunity to reduce or discontinue ICS, thereby reducing the potential for side effects.

Strengthening Nonpharmacological Support with Pharmacotherapy

The GOLD 2025 also emphasizes the role of pharmacotherapy in complementing nonpharmacological interventions, such as pulmonary rehabilitation (PR), smoking cessation, and lifestyle modifications. The integration of pharmacological and nonpharmacological approaches helps to improve patient outcomes by addressing both the physiological and lifestyle factors contributing to disease progression and exacerbation risk. For example, patients who successfully quit smoking or adhere to rehabilitation programs may require lower doses or fewer medications over time, underscoring the importance of a comprehensive COPD management strategy.¹³

Summary

The revised pharmacological strategies in GOLD 2025 reflect a more nuanced, patient-centered approach to COPD management. By incorporating innovative therapies like ensifentrine and dupilumab and by embracing biomarker-driven decisions, these guidelines empower clinicians to tailor treatment to each patient's specific inflammatory profile and symptom burden. This evolution in treatment strategy not only broadens the options available to manage COPD but also enhances the quality of care through more precise and individualized therapeutic interventions.

FOCUS ON MULTIMORBIDITY MANAGEMENT

The 2025 GOLD report places a heightened emphasis on the management of multimorbidity in COPD, recognizing the complex interplay between COPD and various comorbid conditions that significantly influence patient outcomes. Multimorbid conditions, particularly cardiovascular diseases (CVD), pulmonary hypertension (PH), metabolic disorders, and other systemic complications, contribute to the overall burden of COPD, impacting exacerbation frequency, hospitalizations, and mortality. The GOLD 2025 report introduces a comprehensive framework to help clinicians address these overlapping conditions effectively, moving toward a treatable-traits approach that encourages tailored, patient-specific management.^{14–16}

Cardiovascular Diseases and COPD

Cardiovascular diseases are among the most prevalent and impactful comorbidities in COPD, contributing to increased mortality and morbidity. COPD patients commonly experience heart failure, ischemic heart disease, arrhythmias, and hypertension, often due to shared risk factors like smoking and systemic inflammation. The GOLD 2025 report underscores the need for integrated management strategies that address both respiratory and cardiovascular health to mitigate the risk of cardiovascular events, such as heart attacks or strokes, which are particularly high in COPD patients with exacerbations.

The report highlights evidence showing that managing cardiovascular risk factors—including blood pressure control, lipid management, and anticoagulation where indicated—can reduce exacerbation frequency and improve survival in COPD patients. Additionally, the use of beta-blockers, previously controversial in COPD, is now encouraged in patients with coexisting cardiovascular conditions, as studies have shown they can be safely used without worsening respiratory function.¹⁷

Pulmonary Hypertension and the PH-COPD Phenotype

Pulmonary hypertension is a recognized complication of COPD, particularly in advanced cases, where chronic hypoxemia and vascular remodeling contribute to increased pulmonary artery pressures. GOLD 2025 identifies PH-COPD as a specific phenotype, emphasizing that this group of patients has distinct management needs and often poorer prognosis. For these patients,

targeted management strategies—such as long-term oxygen therapy (LTOT) and careful monitoring of right heart function—are essential to prevent further deterioration.¹⁸

The GOLD report introduces “treatable traits” specific to PH-COPD, guiding clinicians in selecting appropriate interventions based on individual patient characteristics. This may include therapies that improve oxygenation, reduce pulmonary pressures, and support right ventricular function. By addressing PH directly, these tailored treatments can alleviate symptoms, reduce hospitalizations, and improve quality of life in patients with this complex comorbidity.

Dysbiosis and Its Role in COPD Progression

The 2025 report introduces a new section on dysbiosis, the disruption of the normal microbial balance within the body, particularly within the lungs and gut. Emerging evidence suggests that dysbiosis may exacerbate systemic inflammation, contributing to disease progression and worsening outcomes in COPD. The GOLD 2025 framework advocates for further exploration of microbiome-targeted interventions, such as probiotics, prebiotics, and possibly microbiome-based therapies, which could help restore a healthier microbial environment and reduce inflammation.

Understanding and addressing dysbiosis in COPD management is a step toward a more holistic approach to treatment, recognizing that the microbial ecosystem within the body can significantly impact respiratory health. By acknowledging dysbiosis as a modifiable trait, GOLD 2025 opens new avenues for research and potential therapeutic interventions aimed at stabilizing the COPD disease course through microbiome modulation.¹⁹

Impact of Climate Change on COPD

The GOLD 2025 takes a pioneering approach by incorporating climate change and environmental factors into the COPD management framework, acknowledging that rising air pollution and extreme weather events pose significant health risks for COPD patients. Poor air quality, particularly high levels of particulate matter (PM), is strongly associated with an increase in COPD exacerbations, while temperature extremes can exacerbate symptoms and increase mortality rates. The report encourages pulmonologists to incorporate environmental considerations into patient care, advising patients on strategies to minimize exposure to pollutants and manage symptoms during extreme weather conditions.

This section reflects a forward-thinking approach to COPD care, recognizing that environmental health is closely tied to respiratory health. By addressing climate-related impacts on COPD, GOLD 2025 encourages preventive strategies, such as advising patients on indoor air quality improvement and reinforcing the importance of vaccinations to protect against respiratory infections that may be more prevalent during extreme weather events.²⁰

Metabolic and Systemic Comorbidities

Metabolic disorders, including diabetes, obesity, and osteoporosis, are also recognized as significant comorbidities in COPD, affecting disease progression and patient outcomes. These conditions can lead to increased inflammation, reduced physical activity, and impaired lung function. GOLD 2025 recommends an integrative approach to managing metabolic conditions alongside COPD, encouraging weight management, dietary modifications, and exercise to improve overall health and reduce the systemic burden of the disease.

Additionally, osteoporosis is particularly prevalent in COPD patients, especially those on long-term corticosteroids, due to their increased risk of bone density loss. GOLD 2025 advises routine screening for osteoporosis in COPD patients and recommends preventive measures, such as calcium and vitamin D supplementation, along with consideration of pharmacologic treatment when needed.²¹

Treatable Traits Approach in Multimorbidity Management

A central theme in GOLD 2025's approach to multimorbidity is the "treatable traits" concept, which advocates identifying and targeting specific modifiable traits in each patient. For example, a COPD patient with both CVD and PH may have traits related to systemic inflammation, right heart strain, and reduced physical endurance. Addressing these traits individually allows for a more holistic, tailored approach that aligns with each patient's unique needs, improving both respiratory and systemic outcomes.

This treatable traits model enables clinicians to move away from a one-size-fits-all approach and instead design integrative treatment plans based on the totality of each patient's health profile. This framework not only allows for more effective COPD management but also promotes collaboration between pulmonologists, cardiologists, and other specialists, ensuring a coordinated

approach to complex cases with multiple comorbidities.^{22,23}

Summary

The GOLD 2025 report's focus on multimorbidity management represents a paradigm shift in COPD care. By recognizing the intricate links between COPD and various comorbid conditions and encouraging a treatable traits approach, GOLD 2025 promotes a holistic, patient-centered management strategy. This comprehensive framework equips clinicians to address COPD as part of a broader health context, targeting the unique needs of patients and ultimately improving quality of life and long-term outcomes in this complex population.

ADVANCED NONPHARMACOLOGICAL INTERVENTIONS

The 2025 GOLD report highlights the critical role of advanced nonpharmacological interventions in COPD management, especially in light of pandemic-related challenges and the growing need for accessible, flexible care models. Recognizing that effective COPD treatment requires a comprehensive approach beyond pharmacotherapy, the GOLD 2025 guidelines expand on the importance of PR, self-management education, and telehealth to enhance patient outcomes, improve adherence, and increase access to care.

Pulmonary Rehabilitation as a Cornerstone of Nonpharmacological COPD Management

Pulmonary rehabilitation remains a cornerstone of COPD management due to its well-documented benefits, which include reduced symptoms, improved exercise tolerance, and enhanced quality of life. PR programs typically involve a multidisciplinary approach with components such as exercise training, education, nutritional support, and psychosocial care. GOLD 2025 continues to emphasize that all COPD patients with moderate to severe disease, particularly those with a history of exacerbations, should be encouraged to participate in PR.

The guidelines note that PR not only improves physical function but also decreases the risk of future exacerbations and hospitalizations. By enhancing the patient's ability to perform daily activities and cope with breathlessness, PR serves as a nonpharmacological strategy that has a lasting impact on COPD progression and patient well-being. GOLD 2025 also highlights the importance of individualized PR programs

that can be tailored to meet each patient's specific needs, maximizing engagement and benefit.²⁴

Telehealth and Virtual Rehabilitation: Expanding Access and Adaptability

One of the significant advancements in GOLD 2025 is its endorsement of telehealth and virtual rehabilitation as viable and effective alternatives to in-person care. The pandemic underscored the importance of remote care models, which ensure continuity of care even during times of restricted access to healthcare facilities. Virtual rehabilitation includes remote delivery of exercise training, education, and self-management support through online platforms, video conferencing, and wearable technology.

Telehealth allows healthcare providers to monitor patients' symptoms, progress, and adherence to exercise programs from a distance. Virtual PR has been shown to offer comparable benefits to traditional in-person programs, improving exercise capacity, reducing symptom severity, and maintaining quality of life. This model also offers additional advantages by eliminating geographical barriers, reducing the burden of travel, and making care accessible to patients who may face mobility or transportation challenges. Virtual PR programs are particularly valuable for rural populations and underserved communities, where access to PR facilities may be limited.

Self-management Education: Empowering Patients in COPD Care

Self-management education is another essential component of nonpharmacological COPD interventions, equipping patients with the knowledge and skills to manage their condition effectively. GOLD 2025 underscores the value of patient education in promoting adherence to treatment, recognizing exacerbation symptoms, and implementing appropriate self-care practices, such as breathing exercises and energy conservation techniques.

Self-management programs are designed to improve patients' ability to make informed decisions, manage symptoms, and avoid triggers. Such programs have been shown to decrease hospital admissions, improve health-related quality of life, and enhance patient confidence in managing their condition. Telehealth platforms can enhance self-management education by providing access to educational resources, symptom trackers, and communication tools that enable patients to engage with their healthcare providers as needed.

Incorporating Digital Health Tools and Remote Monitoring

The GOLD 2025 highlights the potential of digital health tools and wearable technology in the remote management of COPD. Remote monitoring devices can track key health metrics, such as oxygen saturation, heart rate, and physical activity levels, allowing for continuous, real-time monitoring. By analyzing this data, clinicians can detect early signs of exacerbation, monitor adherence to exercise regimens, and adjust care plans based on the patient's current health status.

Digital tools, including mobile apps and online platforms, enable patients to log symptoms, receive automated reminders for medication adherence, and access health education materials. GOLD 2025 supports the integration of these tools to enhance patient engagement and adherence while providing healthcare professionals with valuable insights into the patient's day-to-day experience with COPD.²⁵

Physical Activity and Exercise Training: Essential Components of Rehabilitation

Physical activity and structured exercise training are crucial components of PR and are strongly encouraged in the GOLD 2025 guidelines. Regular physical activity is linked to improved cardiorespiratory fitness, reduced symptoms, and a lower risk of exacerbations. GOLD 2025 advocates for integrating exercise training into both in-person and virtual PR programs, encouraging patients to maintain an active lifestyle despite the limitations posed by COPD.

Exercise training can be tailored to each patient's capability and gradually increased as they build endurance and strength. For remote or virtual settings, telehealth platforms provide exercise videos, tutorials, and support from healthcare providers to ensure patients can perform exercises safely at home. Physical activity is not only a treatment modality but also a preventive strategy, helping to slow disease progression and improve resilience against COPD exacerbations.

Psychosocial Support in Pulmonary Rehabilitation

The psychosocial aspect of COPD care, including mental health support, is a growing focus in GOLD 2025. Patients with COPD frequently experience anxiety and depression, which can worsen symptoms, reduce quality of life, and affect treatment adherence. GOLD 2025 encourages the integration of mental health support within PR programs, whether

through counseling, peer support groups, or telecounseling sessions.

Providing access to psychosocial resources as part of nonpharmacological care is particularly valuable in a virtual format, where patients may feel more comfortable engaging in counseling from home. By addressing the psychological impact of COPD, clinicians can support overall well-being and help patients manage the emotional burden of their disease.

Summary

The GOLD 2025's advanced nonpharmacological interventions reflect an expanded, patient-centered approach to COPD care. By emphasizing PR, telehealth, self-management education, and the use of digital health tools, GOLD 2025 promotes accessible, flexible, and effective treatment options that enhance patient engagement and adherence. The integration of virtual rehabilitation models and remote monitoring technologies offers innovative pathways for delivering high-quality COPD care, particularly for patients who face barriers to in-person services. Through these comprehensive, multidisciplinary strategies, GOLD 2025 provides a robust framework for improving outcomes, quality of life, and overall health in COPD patients.

UPDATED VACCINATION

The GOLD 2025 report places a renewed emphasis on vaccination as a preventive measure in COPD management, recognizing the heightened susceptibility of COPD patients to respiratory infections, which can lead to exacerbations, hospitalizations, and even mortality. By aligning with the latest CDC guidelines, GOLD 2025 aims to improve protection against common respiratory pathogens, specifically through updated recommendations for influenza, pneumococcal, and respiratory syncytial virus (RSV) vaccines. These revised guidelines underscore the importance of vaccinations in reducing the disease burden and stabilizing patient health by preventing acute respiratory infections that often worsen COPD symptoms.²⁶

Influenza Vaccination: Annual Immunization as a Critical Preventive Measure

Influenza poses a significant threat to COPD patients, who are more likely to experience severe illness, complications, and exacerbations if infected. GOLD 2025 reaffirms the importance of annual influenza vaccination for all individuals with COPD,

emphasizing that vaccination reduces the risk of influenza-related morbidity and mortality.

Influenza vaccines are typically updated yearly to match circulating virus strains, making annual vaccination necessary for effective protection. GOLD 2025 advises healthcare providers to encourage their COPD patients to receive the vaccine each year before the flu season starts, usually in the fall. Notably, patients should be informed of the availability of high-dose or adjuvanted influenza vaccines, which may provide enhanced protection for older adults and those with weakened immune systems, who are at higher risk of complications.²⁷

Pneumococcal Vaccination: Preventing Bacterial Pneumonia and Associated Complications

Pneumococcal infections are a common cause of bacterial pneumonia, which can be particularly severe in individuals with COPD. GOLD 2025 emphasizes the critical role of pneumococcal vaccination in preventing these infections, recommending both pneumococcal conjugate and polysaccharide vaccines to maximize protection.

The CDC currently recommends two types of pneumococcal vaccines for adults with COPD:

- PCV20 (20-valent pneumococcal conjugate vaccine): This vaccine provides broad coverage against pneumococcal strains and is recommended as a single dose.
- PPSV23 (23-valent pneumococcal polysaccharide vaccine): This vaccine offers extended protection against additional pneumococcal strains not covered by the conjugate vaccine.

The GOLD 2025 recommends that COPD patients who have not previously received any pneumococcal vaccine should receive the PCV20 vaccine alone or as a series with the PPSV23 if indicated, following CDC's age- and risk-specific guidelines. For patients with a history of pneumococcal vaccination, providers should assess the timing and type of previous doses to determine the need for additional doses. These recommendations are particularly important for patients with severe COPD and older adults, who are at an increased risk of pneumococcal infections.^{28,29}

Respiratory Syncytial Virus Vaccination: New Recommendations for COPD Patients

For the first time, GOLD 2025 includes recommendations for the RSV vaccine, reflecting the availability of new vaccines for adults and the recognition of RSV as a

significant respiratory pathogen in older adults and those with chronic lung disease. RSV can cause severe lower respiratory tract infections in COPD patients, leading to exacerbations and complications.

Recent advances have led to the development of effective RSV vaccines specifically targeting adults aged 60 and older, a population that includes many COPD patients. GOLD 2025 recommends that COPD patients within this age-group receive the RSV vaccine to reduce the risk of severe RSV infection and associated respiratory complications. As RSV vaccines are a new addition to adult vaccination schedules, healthcare providers are encouraged to discuss the benefits and availability of the RSV vaccine with their COPD patients, particularly those with advanced disease or frequent exacerbations.³⁰

Integrated Vaccination Strategy for COPD Patients

The GOLD 2025 promotes a coordinated approach to vaccinations, advising healthcare providers to use routine visits as opportunities to assess patients' vaccination status and ensure they are up to date with all recommended immunizations. The report underscores that vaccinations are a key component of COPD preventive care, helping to reduce the frequency and severity of respiratory infections, which in turn minimizes exacerbation risk, hospital admissions, and overall healthcare costs.

By incorporating a proactive, integrated vaccination strategy, healthcare providers can help maintain stability in COPD patients and improve their quality of life. This preventive approach is particularly relevant for COPD patients with comorbidities or those at high risk of severe infection, as even minor respiratory infections can have substantial impacts on disease progression and long-term outcomes.

Future Directions: Continuous Monitoring and Updates in Vaccination Recommendations

The GOLD 2025 acknowledges that the landscape of infectious diseases and vaccines is continually evolving, and vaccination recommendations may be updated as new data and vaccines become available. The report encourages ongoing research and surveillance of vaccine efficacy and safety, particularly among COPD patients, who may have unique immune responses to vaccines. This commitment to evidence-based updates ensures that vaccination strategies remain aligned with

the latest scientific developments, offering the most effective protection for COPD patients against emerging respiratory threats.

Summary

The updated vaccination recommendations in GOLD 2025 emphasize a proactive stance on infection prevention in COPD through influenza, pneumococcal, and RSV vaccinations. These guidelines aim to provide comprehensive protection against common respiratory infections, thereby reducing exacerbations and supporting better long-term disease management. By aligning with CDC guidelines and introducing RSV vaccination, GOLD 2025 strengthens the role of immunization in COPD care, equipping healthcare providers to better safeguard their patients against infection-related complications.

IMPACT OF CLIMATE CHANGE

The 2025 GOLD report marks a significant step forward by addressing the impact of climate change on COPD for the first time. This new focus reflects an evolving understanding of COPD as not only a disease of the airways but also one profoundly affected by environmental factors beyond traditional risk factors like smoking. Climate change, with its influence on air quality, temperature extremes, and pollutant exposure, poses direct and indirect threats to respiratory health, particularly for COPD patients who are more vulnerable to fluctuations in environmental conditions. By recognizing the links between climate change and COPD, GOLD 2025 encourages pulmonologists and healthcare providers to adopt a broader perspective on COPD management, integrating awareness of environmental determinants into patient care.

Air Pollution: A Major Driver of COPD Exacerbations

One of the most pressing environmental risks associated with climate change is air pollution, which has been extensively linked to increased COPD exacerbations and accelerated lung function decline. Air pollutants such as PM_{2.5}, PM₁₀, nitrogen dioxide (NO₂), sulfur dioxide (SO₂), and ozone (O₃) can penetrate the respiratory tract, leading to inflammation, oxidative stress, and exacerbation of respiratory symptoms. COPD patients are especially susceptible to air pollution because of their already compromised lung function and heightened inflammatory response.

The GOLD 2025 emphasizes that COPD patients should minimize exposure to high

levels of air pollution, which are increasingly common in urban areas and during specific times of the year when climate conditions exacerbate pollution levels. The report encourages healthcare providers to educate patients about air quality indices (AQI) and suggest practical strategies, such as avoiding outdoor activities during peak pollution times, using air purifiers indoors, and wearing protective masks on high-pollution days to reduce exposure.³¹

Temperature Extremes and Respiratory Health in COPD

Climate change has led to more frequent and severe temperature extremes, including both heatwaves and cold spells. These extremes pose significant health risks for COPD patients, as both high and low temperatures can exacerbate respiratory symptoms and increase the risk of hospitalization. Hot weather can cause dehydration and exacerbate breathlessness, while cold weather can lead to bronchoconstriction, airway inflammation, and a heightened risk of respiratory infections.

The GOLD 2025 underscores the importance of temperature management for COPD patients, especially during extreme weather events. Recommendations include staying hydrated, maintaining indoor air quality, using humidifiers in winter, and ensuring that patients have access to air conditioning or heating as needed. The guidelines also advise patients to monitor local weather forecasts and take preventive measures to avoid unnecessary exposure to extreme temperatures, which can help prevent symptom exacerbation and maintain stability in COPD management.

Wildfires and Other Climate-related Disasters: A Growing Concern for COPD Patients

Wildfires, increasingly common due to climate change, pose severe health risks, especially for COPD patients who are sensitive to smoke and PM. Smoke from wildfires can travel long distances, impacting air quality in areas far from the actual fire location. Exposure to wildfire smoke can cause a sharp increase in respiratory symptoms, trigger exacerbations, and lead to acute respiratory distress in vulnerable populations, including those with COPD.

The GOLD 2025 recommends that COPD patients in wildfire-prone regions stay informed about air quality alerts and take measures to protect themselves during fire events. This may include staying indoors, using HEPA filters, and keeping windows closed. For healthcare providers, the guidelines suggest

incorporating preparedness for climate-related events into patient education, helping COPD patients plan for emergencies and minimize smoke exposure during wildfire events.³²

Environmental and Social Inequalities in COPD Care

Climate change disproportionately impacts individuals in lower socioeconomic brackets who may have limited access to healthcare, live in high-pollution areas, or lack resources for air conditioning or heating during temperature extremes. GOLD 2025 highlights the role of environmental and social inequalities in COPD care, acknowledging that some patients may face greater challenges in protecting themselves from environmental triggers due to financial or geographic constraints.

The report encourages healthcare providers to consider these disparities when developing COPD management plans, offering guidance on low-cost strategies to reduce environmental exposure and improve respiratory health. This could include education on monitoring AQI, using simple household interventions to improve air quality, and providing resources for patients with limited means to manage their environment.

COPD and the Role of Climate-related Respiratory Infections

Climate change is also associated with the spread of respiratory infections, such as influenza and RSV, which can be particularly harmful to COPD patients. Warmer temperatures and humidity changes influence the distribution and seasonality of pathogens, potentially leading to more frequent or severe outbreaks. GOLD 2025 emphasizes the need for vaccinations and preventive measures to protect COPD patients from infections that could exacerbate their condition during climate-related changes in infectious disease patterns.

Vaccinations against influenza, pneumococcus, and RSV are highlighted as essential preventive steps, and healthcare providers are encouraged to stay vigilant about emerging infectious risks linked to climate change. By aligning infection prevention strategies with environmental health considerations, GOLD 2025 seeks to protect COPD patients from the dual threat of infection and climate-related respiratory challenges.

Integrating Climate Awareness into COPD Management

The GOLD 2025 promotes the integration of climate awareness into routine COPD

care, encouraging pulmonologists and healthcare providers to proactively consider environmental triggers in patient assessments. This approach includes discussing the impacts of air quality, temperature extremes, and other climate-related factors during patient visits, helping individuals with COPD make informed choices to reduce environmental risks. For instance, providers can recommend digital tools or apps that offer real-time air quality and weather updates, enabling patients to make lifestyle adjustments that minimize exposure to environmental stressors.

Additionally, the guidelines advocate for a collaborative approach that involves public health initiatives and policy measures to reduce air pollution and mitigate the health impacts of climate change. The involvement of policymakers, public health agencies, and community organizations is essential to create a supportive infrastructure that safeguards vulnerable populations, including COPD patients, from environmental risks associated with climate change.³³

Summary

The inclusion of climate change in the GOLD 2025 report marks a forward-thinking approach to COPD management, recognizing that environmental factors play a crucial role in disease progression and symptom exacerbation. By addressing air pollution, temperature extremes, wildfires, and infectious disease risks, GOLD 2025 offers comprehensive guidance for managing COPD in an increasingly unpredictable climate. This expanded framework empowers healthcare providers to incorporate climate-related considerations into patient care, enhancing protection against environmental threats and promoting resilience in COPD patients. Through proactive strategies and patient education, GOLD 2025 seeks to improve long-term outcomes for individuals with COPD in the face of climate challenges.

ENHANCED SPIROMETRIC CRITERIA AND IMAGING UTILIZATION

The GOLD 2025 report introduces important updates to spirometry standards and imaging guidelines aimed at enhancing the precision and reliability of COPD diagnosis, monitoring, and treatment. These enhancements reflect a commitment to providing pulmonologists with detailed, evidence-based tools that support a more nuanced understanding of disease severity, progression, and structural changes in the lungs over time. The updated guidelines on spirometry and imaging align with GOLD's overarching goal of refining

COPD management through early diagnosis and individualized care.

Refined Spirometric Standards: Pre- and Postbronchodilator Testing

Spirometry remains a fundamental tool for diagnosing and assessing the severity of COPD, primarily by measuring the FEV₁ and the FVC. GOLD 2025 elaborates on spirometric criteria with updated pre- and postbronchodilator testing standards, particularly in Table 1, which provides guidance on measuring and interpreting changes in lung function after bronchodilator administration. This distinction between pre- and postbronchodilator measurements helps in distinguishing COPD from other respiratory conditions, such as asthma, by assessing the reversibility of airway obstruction.

The revised spirometry criteria emphasize the importance of accurately measuring the FEV₁/FVC ratio to confirm nonreversible airflow limitation, which is the hallmark of COPD. The postbronchodilator FEV₁/FVC ratio remains the gold standard diagnostic criterion, with a value <0.7 confirming COPD. However, the guidelines now provide additional context for identifying patients at risk who may not yet meet this threshold but still exhibit symptoms or structural changes associated with COPD. This shift allows for more inclusive monitoring of individuals who may be in early stages or at risk of progression to full COPD.³⁴

Introduction of "Lower Limit of Normal" and Z-scores

The GOLD 2025 encourages the use of the "lower limit of normal" (LLN) and z-scores alongside the fixed FEV₁/FVC ratio for interpreting spirometric results. While the fixed ratio of 0.7 is widely used, it can sometimes lead to misclassification, especially in older adults who may have reduced lung elasticity, resulting in lower FEV₁/FVC ratios even without COPD. Conversely, younger individuals with COPD may have ratios >0.7 due to the natural variability in lung function across ages and body sizes.

The LLN and z-scores address these issues by accounting for individual variations, providing a more precise reference for diagnosing airflow limitation based on age, sex, height, and ethnicity. The LLN represents the fifth percentile of a healthy population, meaning that values below this threshold suggest abnormal lung function. Incorporating these additional metrics helps pulmonologists avoid both under- and overdiagnosis, improving the accuracy of COPD diagnosis and the ability to track disease progression across different patient populations.³⁵

Table 1: Key updates in spirometry standards and imaging utilization in GOLD 2025

Aspect	GOLD 2025 update	Clinical implication
Spirometry standards	Emphasizes both pre- and postbronchodilator testing to assess reversibility of airflow obstruction	Helps distinguish COPD from asthma and identify COPD patients with nonreversible airflow limitation
FEV ₁ /FVC ratio	Reaffirms postbronchodilator FEV ₁ /FVC <0.7 as the primary diagnostic criterion for COPD	Standardizes COPD diagnosis based on irreversible airflow limitation
LLN	Encourages use of LLN and z-scores to adjust for individual variations in age, sex, height, and ethnicity	Reduces misclassification, especially in older adults and younger individuals with atypical lung function
Imaging utilization	Expands use of CT imaging for assessing lung structure, including emphysema and small airway disease	Complements spirometry by detecting structural changes, especially in early or atypical cases of COPD
Quantitative imaging	Supports adoption of quantitative imaging (e.g., lung density, airway wall thickness) and AI-based analysis	Provides standardized, objective measurements that enhance accuracy and enable early detection of structural changes
Disease severity and progression	Stratifies COPD severity based on imaging findings such as emphysema extent and air trapping	Assists in tailored treatment planning and timely adjustments to management based on progression risk
Combined assessment approach	Advocates for integrated use of spirometry and imaging for comprehensive COPD assessment	Facilitates a holistic view of COPD, supporting early diagnosis, accurate staging, and a personalized treatment plan

Expanded Role of Imaging in COPD Management

The GOLD 2025 places an increased emphasis on imaging, particularly chest CT scans, as a complementary tool to spirometry for assessing lung structure and diagnosing COPD-related abnormalities, such as emphysema and small airway disease. While spirometry remains the primary diagnostic tool, imaging provides valuable insights into structural changes that spirometry alone cannot capture, enabling a more comprehensive assessment of the disease.

Computed tomography imaging can reveal areas of emphysema, airway wall thickening, air trapping, and other structural lung changes associated with COPD. These structural findings are particularly valuable for identifying patients with “pre-COPD” or “PRISm” phenotypes, where early lung changes occur before traditional spirometric criteria indicate COPD. GOLD 2025 recommends using imaging to assess the extent of emphysema and monitor disease progression, especially in patients with persistent symptoms or at high risk of progression. These insights allow for tailored treatment planning, including early intervention strategies that may slow or prevent disease progression.³⁶

Assessing Disease Severity and Progression through Imaging

Imaging plays a crucial role in assessing disease severity and progression, particularly in advanced cases of COPD. GOLD 2025 provides guidance on how to utilize imaging findings to

stratify disease severity based on the extent of emphysema, air trapping, and other structural abnormalities. This stratification can help clinicians determine the most appropriate interventions, from pharmacological treatments to nonpharmacological options like PR.

By monitoring changes in lung structure over time, imaging enables clinicians to assess the effectiveness of treatments and identify rapid disease progression, allowing for timely adjustments to the management plan. For instance, a significant increase in emphysema detected through CT imaging may indicate the need for more aggressive treatment, while stable imaging results could support a conservative approach focused on maintenance and preventive care.

Advancements in Quantitative Imaging and Artificial Intelligence Integration

The GOLD 2025 guidelines acknowledge the growing role of quantitative imaging techniques, such as automated CT analysis and artificial intelligence (AI) tools, in COPD assessment. Quantitative imaging uses software algorithms to measure lung density, airway wall thickness, and emphysema extent, providing standardized, objective data that enhances the accuracy of disease assessment. AI-driven tools can assist in analyzing complex imaging data, identifying subtle structural changes that may not be easily visible to the human eye.

These advancements in imaging technology support more precise and consistent measurements, enabling clinicians to detect early structural changes and evaluate treatment effects with greater objectivity. GOLD 2025 encourages the adoption of these technologies, particularly in research and specialist settings, as they become more widely available and accessible. By incorporating quantitative imaging and AI analysis, clinicians can gain deeper insights into each patient’s unique COPD profile, facilitating a more personalized approach to care.

Combining Spirometry and Imaging for a Comprehensive COPD Assessment

The GOLD 2025 emphasizes the complementary roles of spirometry and imaging, advocating for an integrated approach that uses both tools to provide a full picture of lung function and structure. While spirometry is effective for diagnosing airflow limitation and monitoring functional decline, imaging offers critical insights into structural abnormalities and can reveal early changes that spirometry might miss.

For example, a patient with mild airflow limitation on spirometry but significant emphysema visible on imaging may benefit from closer monitoring and targeted interventions to address disease progression. Conversely, patients with normal imaging but abnormal spirometry results may represent different COPD phenotypes, potentially guiding different therapeutic approaches. This combined approach enables a more comprehensive assessment, supporting early diagnosis, accurate staging, and tailored management strategies based on both functional and structural data.³⁷

Table 1 captures the essence of the updated spirometry and imaging standards in GOLD 2025, emphasizing how these refinements aim to improve diagnostic precision and enable a more personalized approach to COPD management.

Summary

The enhanced spirometric criteria and imaging guidelines in GOLD 2025 offer pulmonologists refined tools to accurately diagnose, stage, and monitor COPD. By incorporating LLN and z-scores, emphasizing pre- and postbronchodilator testing, and expanding imaging utilization, these updates provide a more nuanced framework for understanding COPD as a heterogeneous and progressive disease. The integration of quantitative imaging and AI further supports a personalized approach, enabling clinicians

to identify early structural changes, tailor interventions, and optimize long-term outcomes for COPD patients.

CONCLUSION

The GOLD 2025 update introduces a transformative approach to COPD diagnosis, moving beyond the traditional criteria of irreversible airflow limitation to encompass early disease stages like pre-COPD and PRISm. This broadened framework, supported by advanced diagnostic tools such as imaging and biomarkers, equips clinicians with enhanced capabilities for detecting early lung changes and assessing disease risk before significant damage occurs. By emphasizing early intervention, personalized management, and the diversity of COPD phenotypes, GOLD 2025 sets the foundation for a more effective and individualized COPD care model. As pulmonologists integrate these new guidelines into clinical practice, the potential to slow disease progression, reduce symptom burden, and improve long-term patient outcomes becomes increasingly achievable. This proactive stance redefines COPD not as an inevitable consequence of aging and exposure but as a manageable and potentially preventable condition, marking a critical advancement in the field of pulmonary medicine.

Take-home messages from GOLD 2025 COPD guidelines updates:

- Expanded diagnostic scope: GOLD 2025 introduces earlier-stage diagnostic categories, “pre-COPD” and “PRISm,” allowing clinicians to identify and manage patients at risk of COPD progression before significant airflow limitation occurs.
- Proactive intervention: Recognizing early symptoms and structural lung changes enables timely intervention, which can potentially slow disease progression, reduce exacerbations, and improve long-term outcomes.
- Personalized management: GOLD 2025 emphasizes individualized care by tailoring interventions based on each patient’s unique COPD phenotype and pathophysiological profile, rather than relying solely on airflow limitation as the defining criterion.
- Role of imaging and biomarkers: Advanced diagnostic tools, such as CT imaging and biomarkers, are integrated into COPD assessment, providing detailed insights into lung structure and inflammatory profiles that support early diagnosis and monitoring.

- Spirometric innovations: The updated spirometry standards in GOLD 2025 encourage the use of the LLN and z-scores alongside traditional FEV₁/FVC ratios, enhancing diagnostic accuracy and reducing misclassification.
- Importance of treatable traits: The guidelines promote a treatable-traits approach, targeting modifiable risk factors and comorbid conditions for a holistic management strategy that addresses both respiratory and systemic health in COPD.
- New pharmacological options: New therapeutic agents, such as ensifentrine and dupilumab, offer targeted treatment for COPD patients with specific inflammatory profiles, broadening options for those unresponsive to conventional therapies.
- Nonpharmacological interventions: GOLD 2025 supports telehealth and virtual rehabilitation, ensuring continued access to PR, self-management education, and remote monitoring for patients facing barriers to in-person care.
- Climate change and environmental awareness: GOLD 2025 recognizes the impact of environmental factors, such as air pollution and temperature extremes, on COPD severity, urging providers to incorporate environmental risk-reduction strategies into patient education.
- Prevention focused on vaccination: Updated vaccination recommendations for influenza, pneumococcus, and RSV protect COPD patients from infections that exacerbate symptoms, highlighting the importance of preventive care in disease management.

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REFERENCES

- Wouters EFM. Pre-chronic obstructive pulmonary disease: toward the limits of the spirometric funnel. *Am J Respir Crit Care Med* 2021;204(1):112.
- Lee BY, Han MK. Understanding early COPD. *Respir Care* 2023;68(7):881–888.
- Miura S, Iwamoto H, Omori K, et al. Preserved ratio impaired spirometry with or without restrictive spirometric abnormality. *Sci Rep* 2023;13(1):2988.
- Huang J, Li W, Sun Y, et al. Preserved ratio impaired spirometry (PRISm): a global epidemiological overview, radiographic characteristics, comorbid associations, and differentiation from chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis* 2024;19:753–764.
- Leap J, Arshad O, Cheema T, et al. Pathophysiology of COPD. *Crit Care Nurs Q* 2021;44(1):2–8.
- Walters EH, Shukla SD, Mahmood MQ, et al. Fully integrating pathophysiological insights in COPD:

- an updated working disease model to broaden therapeutic vision. *Eur Respir Rev* 2021;30(160):200364.
- Vegas-Sánchez-Ferrero G, José RSE. A CT scan harmonization technique to detect emphysema and small airway diseases. *Image Anal Mov Organ Breast Thorac Images* 2018;11040:180–190.
- Lynch DA, Austin JHM, Hogg JC, et al. CT-definable subtypes of chronic obstructive pulmonary disease: a statement of the Fleischner Society. *Radiology* 2015;277(1):192–205.
- 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.
- Donohue JF, Rheault T, MacDonald-Berko M, et al. Ensifentrine as a novel, inhaled treatment for patients with COPD. *Int J Chron Obstruct Pulmon Dis* 2023;18:1611–1622.
- Tan RV, Aung HWW, Flynn C, et al. Dupilumab in type 2 airway inflammation—a step forward in targeted therapy for COPD. *J Allergy Clin Immunol* 2024;153(2):404–406.
- Sivapalan P, Bikov A, Jensen JU. Using blood eosinophil count as a biomarker to guide corticosteroid treatment for chronic obstructive pulmonary disease. *Diagnostics (Basel)* 2021;11(2):236.
- Samajdar SS, Chatterjee R, Mukherjee S. Empowering the next generation: strategies and importance of smoking cessation. *J Modern Med* 2024;2:62–76.
- Divo M, Celli BR. Multimorbidity in patients with chronic obstructive pulmonary disease. *Clin Chest Med* 2020;41(3):405–419.
- Carmona-Pirez J, Poblador-Plou B, Ioakeim-Skoufa I, et al. Multimorbidity clusters in patients with chronic obstructive airway diseases in the EpiChron Cohort. *Sci Rep* 2021;11(1):4784.
- Burke H, Wilkinson TMA. Unravelling the mechanisms driving multimorbidity in COPD to develop holistic approaches to patient-centred care. *Eur Respir Rev* 2021;30(160):210041.
- Polman R, Hurst JR, Uysal OF, et al. Cardiovascular disease and risk in COPD: a state of the art review. *Expert Rev Cardiovasc Ther* 2024;22(4–5):177–191.
- Weatherald J, Hemmes AR, Maron BA, et al. Phenotypes in pulmonary hypertension. *Eur Respir J* 2024;64(3):2301633.
- Liang W, Yang Y, Gong S, et al. Airway dysbiosis accelerates lung function decline in chronic obstructive pulmonary disease. *Cell Host Microbe* 2023;31(6):1054–1070.
- Tran HM, Chuang TW, Chuang HC, et al. Climate change and mortality rates of COPD and asthma: a global analysis from 2000 to 2018. *Environ Res* 2023;233:116448.
- Mariniello DF, D’Agnano V, Cennamo D, et al. Comorbidities in COPD: current and future treatment challenges. *J Clin Med* 2024;13(3):743.
- Cazzola M, Rogliani P, Blasi F. Can treatable traits be the approach to addressing the complexity and heterogeneity of COPD? *Int J Chron Obstruct Pulmon Dis* 2023;18:1959–1964.
- Thomas M, Beasley R. The treatable traits approach to adults with obstructive airways disease in primary and secondary care. *Respirology* 2023;28(12):1101–1116.
- Tonga KO, Oliver BG. Effectiveness of pulmonary rehabilitation for chronic obstructive pulmonary disease therapy: focusing on traditional medical practices. *J Clin Med* 2023;12(14):4815.
- Long H, Li S, Chen Y. Digital health in chronic obstructive pulmonary disease. *Chronic Dis Transl Med* 2023;9(2):90–103.
- Simon S, Joann O, Welte T, et al. The role of vaccination in COPD: influenza, SARS-CoV-2, pneumococcus, pertussis, RSV and varicella zoster virus. *Eur Respir Rev* 2023;32(169):230034.
- Al-Qerem W, Jarab A, Eberhardt J, et al. Evaluating influenza vaccination practices among COPD patients. *Vaccines (Basel)* 2023;12(1):14.

28. Walters JA, Tang JNQ, Poole P, et al. Pneumococcal vaccines for preventing pneumonia in chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2017;1(1):CD001390.
29. Paróczai D, Burian K, Bikov A. Bacterial vaccinations in patients with chronic obstructive pulmonary disease. *Vaccines (Basel)* 2024;12(2):213.
30. Topalidou X, Kalergis AM, Papazisis G. Respiratory syncytial virus vaccines: a review of the candidates and the approved vaccines. *Pathogens* 2023;12(10):1259.
31. Li J, Sun S, Tang R, et al. Major air pollutants and risk of COPD exacerbations: a systematic review and meta-analysis. *Int J Chron Obstruct Pulmon Dis* 2016;11:3079–3091.
32. Behinaein P, Hutchings H, Knapp T, et al. The growing impact of air quality on lung-related illness: a narrative review. *J Thorac Dis* 2023;15(9):5055–5063.
33. Souto-Miranda S, Gonçalves AC, Valente C, et al. Environmental awareness for patients with COPD undergoing pulmonary rehabilitation: is it of added value? *Int J Environ Res Public Health* 2020;17(21):7968.
34. Alexis A, Punjabi NM, Grealis K, et al. A comparative study of bronchodilator response: utilizing pre-bronchodilator versus predicted normal values. *BMC Pulm Med* 2024;24(1):54.
35. Lee HW, Lee JK, Hwang YI, et al. Spirometric interpretation and clinical relevance according to different reference equations. *J Korean Med Sci* 2024;39(4):e20.
36. Washko GR. The role and potential of imaging in COPD. *Med Clin North Am* 2012;96(4):729–743.
37. Wang JM, Han MK, Labaki WW. Chronic obstructive pulmonary disease risk assessment tools: is one better than the others? *Curr Opin Pulm Med* 2022;28(2):99–108.