REVIEW ARTICLE

Pathophysiology and Risk Factors for Chronic Respiratory Diseases



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Abstract: Chronic respiratory diseases are a significant and growing global health burden, contributing substantially to morbidity and mortality worldwide. These heterogeneous disorders affect the airways, lung parenchyma, and pulmonary vasculature, leading to progressive physiological impairment. The pathophysiology is complex, often driven by chronic inflammation, structural remodeling, and tissue damage initiated by a variety of etiological factors. The main contributing factors include tobacco smoke, household and ambient air pollution, occupational exposures, and genetic predispositions. Moreover, emerging risk factors, such as the use of electronic cigarettes, present new challenges to respiratory health. A prominent feature of chronic lung disease is its frequent coexistence with other non-communicable diseases, a phenomenon known as multimorbidity, which complicates diagnosis, management, and patient outcomes. This pathophysiology is often mediated by shared risk factors and systemic inflammatory pathways. Addressing the global impact of these conditions necessitates a multifaceted approach. Critical imperatives include advancing diagnostic capabilities, particularly in low-resource settings, ensuring equitable access to effective treatments and pulmonary rehabilitation, and integrating palliative care for advanced stages of disease. More investment in implementation programs and targeted research is crucial for translating existing knowledge into effective public health strategies and clinical practices to alleviate the burden of chronic lung disease on a global scale.

Keywords: Chronic Obstructive Pulmonary Disease (COPD); Asthma; Interstitial Lung Disease; Pulmonary Hypertension; Air Pollution

1. Introduction

Chronic respiratory diseases constitute a major global health challenge, ranking among the leading causes of death and disability across all regions [1]. In 2017, it was estimated that these conditions were the third leading cause of mortality worldwide, with their prevalence having increased by nearly 40% since 1990 [2]. This escalating burden is driven by a complex interplay of demographic shifts, environmental exposures, and lifestyle factors. These diseases encompass a diverse group of disorders that impair the structure and function of the lungs, including conditions that obstruct the airways, damage the lung tissue, or affect the pulmonary circulation.

The etiology of chronic lung disease is multifactorial. Tobacco smoking remains the most significant and preventable risk factor for many of these conditions, particularly Chronic Obstructive Pulmonary Disease (COPD) [3]. However, a substantial proportion of the disease burden, especially in low- and middle-income countries (LMICs), is attributable to other exposures. Household air pollution from the burning of biomass fuels for cooking and heating, ambient air pollution from industrial and traffic sources, and occupational exposure to dusts, chemicals, and fumes are major contributors [4, 5].

In recent years, the landscape of inhalational exposures has evolved with the rise of electronic cigarettes (e-cigarettes). Initially marketed as a less harmful alternative to conventional smoking, their long-term health effects remain largely unknown, and acute lung injuries associated with their use have raised significant public health concerns [6].

Concurrently, the clinical management of chronic lung disease is increasingly complicated by the presence of multimorbidity, where patients suffer from one or more additional chronic conditions. Cardiovascular disease, osteoporosis, and mental health disorders frequently coexist with respiratory ailments, often linked by shared risk factors and common pathophysiological mechanisms such as persistent systemic inflammation [7]. This review provides the current literature of the major categories of chronic lung disease, their underlying risk factors, and the critical global health imperatives required to mitigate their impact.

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Table 1. Major Etiological Risk Factors for Chronic Respiratory Diseases

Risk Factor	Specific Examples	Primary Associated Diseases	
Category			
Tobacco Smoke	- Cigarette smoking (active) - Secondhand smoke exposure	e COPD, Emphysema, Chronic Bronchitis,	
		Lung Cancer	
Environmental	- Household air pollution (biomass fuel) - Ambient air	COPD, Asthma, Interstitial Lung Diseases,	
Pollutants	pollution (particulate matter, ozone) - Climate factors (dust	Acute Exacerbations	
	storms, wildfire smoke)		
Occupational	- Mineral dusts (silica, asbestos) - Organic dusts (molds,	Silicosis, Asbestosis, Hypersensitivity	
Exposures	agricultural dusts) - Chemical fumes and vapors	Pneumonitis, Occupational Asthma	
Genetic	- Alpha-1 antitrypsin deficiency - Familial genetic variants	Early-onset Emphysema (COPD), Familial	
Predisposition	. , , ,	Pulmonary Fibrosis, Pulmonary	
•		Hypertension	
Infections & Early	- Severe childhood respiratory infections - Low birth	COPD, Bronchiectasis, Asthma	
Life Events	weight, premature birth		

2. Classification and Pathophysiology of Major Lung Diseases

Lung diseases can be broadly categorized based on the primary site of pathology and the resulting physiological impairment. The three principal categories are obstructive lung diseases, which affect the airways; restrictive lung diseases, which involve the lung parenchyma; and pulmonary vascular diseases, which impact the lung circulation.

2.1. Obstructive Lung Diseases

Obstructive lung diseases are characterized by a limitation of expiratory airflow, making it difficult to exhale air from the lungs. This obstruction can result from inflammation and narrowing of the airways or from a loss of elastic recoil in the lung tissue.

2.1.1. Chronic Obstructive Pulmonary Disease (COPD)

COPD is a progressive and largely irreversible obstructive lung disease defined by persistent respiratory symptoms and airflow limitation [3]. It is an umbrella term that primarily encompasses two overlapping conditions: chronic bronchitis and emphysema.

Chronic Bronchitis is clinically defined by the presence of a chronic productive cough. Pathologically, it involves inflammation of the bronchial tubes, leading to mucosal thickening, goblet cell hyperplasia, and excessive mucus production, which narrows the airway lumen [8].

Emphysema is characterized by the permanent enlargement of airspaces distal to the terminal bronchioles, accompanied by the destruction of their walls. This loss of alveolar septa reduces the surface area available for gas exchange and diminishes the lung's elastic recoil, leading to air trapping and dynamic hyperinflation [9].

The predominant cause of COPD is long-term exposure to inhaled irritants, most notably cigarette smoke. However, exposure to biomass fuel smoke and other environmental pollutants are also recognized as significant risk factors [4].

Table 2. Classification of Major Chronic Lung Diseases

Category	Primary Pathology	Examples	Physiological Impact
Obstructive Lung Diseases	Airway inflammation, narrowing, and/or loss of elastic recoil	Chronic Obstructive Pulmonary Disease (COPD) Asthma Bronchiectasis	Limitation of expiratory airflow (difficulty exhaling)
Restrictive Lung Diseases	Inflammation and fibrosis (scarring) of the lung parenchyma/interstitium	Idiopathic Pulmonary Fibrosis (IPF) Sarcoidosis Asbestosis	Reduced lung volumes and compliance (difficulty inhaling fully)
Pulmonary Vascular Diseases	Remodeling, obstruction, or damage to the blood vessels of the lungs	Pulmonary Hypertension (PH) Chronic Thromboembolic Pulmonary Hypertension (CTEPH)	Impaired gas exchange and increased workload on the right side of the heart

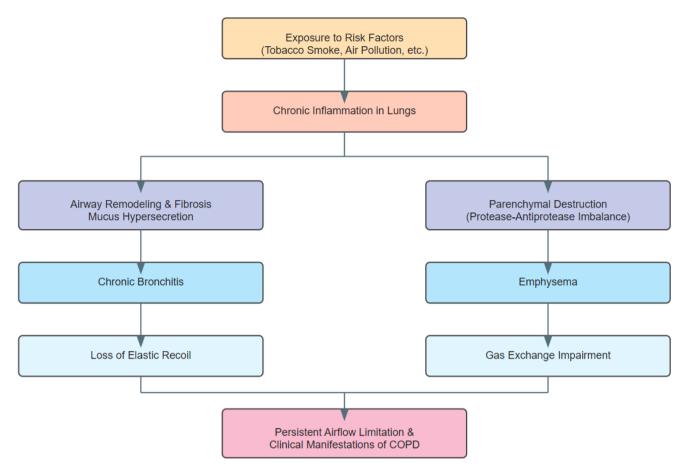


Figure 1. Pathophysiological Pathways in Chronic Obstructive Pulmonary Disease (COPD)

2.1.2. Asthma

Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by a history of respiratory symptoms such as wheeze, shortness of breath, chest tightness, and cough that vary over time and in intensity, together with variable expiratory airflow limitation [10]. Unlike COPD, the airflow obstruction in asthma is typically reversible, either spontaneously or with treatment. The underlying pathophysiology involves airway hyperresponsiveness to various stimuli, inflammation mediated by immune cells such as eosinophils and mast cells, and structural changes in the airway known as remodeling [11]. The etiology is a complex interaction between genetic susceptibility and environmental triggers, including allergens, viruses, and pollutants.

Feature Chronic Obstructive Pulmonary Disease (COPD) Asthma Often in childhood, but can occur at any age Age of Onset Typically > 40 years Etiology Primarily smoking; environmental/occupational Complex interplay of genetics and environmental exposures triggers (allergens, viruses) Airflow Variable and largely reversible (spontaneously or Persistent and progressive; largely irreversible Limitation with treatment) sputum Episodic wheeze, breathlessness, chest tightness, **Key Symptoms** Persistent dyspnea, chronic cough, production cough (often nocturnal) Eosinophilic and/or neutrophilic Primary Neutrophilic Inflammation Pathological Alveolar destruction (emphysema), Bronchial hyperresponsiveness, airway airway Changes inflammation (chronic bronchitis) inflammation, airway remodeling

Table 3. Comparative Features of COPD and Asthma

2.2. Restrictive Lung Diseases

Restrictive lung diseases, often referred to as interstitial lung diseases (ILDs), are a large group of disorders characterized by damage to the lung parenchyma. This damage leads to inflammation and fibrosis (scarring) of the interstitium—the delicate network of

tissue that supports the alveoli. The resulting stiffness of the lung tissue reduces lung compliance and decreases total lung capacity, which restricts the ability of the lungs to expand fully [12].

2.2.1. Pulmonary Fibrosis

Pulmonary fibrosis is the archetypal restrictive lung disease, marked by the progressive scarring of lung tissue. This fibrotic process thickens the alveolar walls, impairing the diffusion of oxygen from the air into the bloodstream. While it can be secondary to autoimmune diseases, certain medications, or environmental exposures, the most common form is idiopathic pulmonary fibrosis (IPF), for which the cause is unknown [13]. The prognosis for IPF is generally poor, with a median survival of 3 to 5 years after diagnosis, as the condition relentlessly progresses, leading to severe dyspnea and eventual respiratory failure [14].

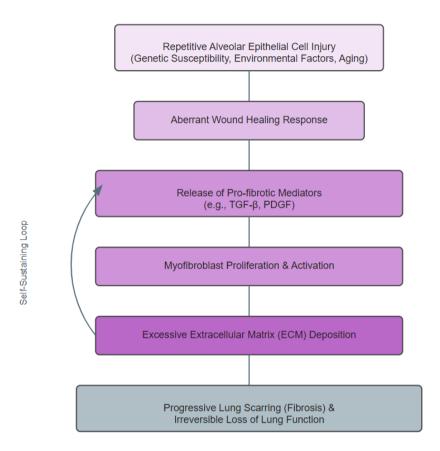


Figure 2. Pathogenesis in Idiopathic Pulmonary Fibrosis (IPF)

2.2.2. Sarcoidosis

Sarcoidosis is a multisystem inflammatory disease of unknown etiology characterized by the formation of non-caseating granulomas in various organs. The lungs are the most frequently affected site, with over 90% of patients exhibiting pulmonary involvement [15]. The clinical course of pulmonary sarcoidosis is highly variable. Many patients experience spontaneous remission, while others develop chronic disease. In a subset of patients, the persistent granulomatous inflammation can progress to advanced pulmonary fibrosis, resulting in significant respiratory impairment. Sarcoidosis can also lead to the development of pulmonary hypertension, a serious complication that increases morbidity and mortality [16].

2.3. Pulmonary Vascular Diseases

This category of diseases primarily affects the blood vessels of the lungs, disrupting the intricate process of pulmonary circulation. The pulmonary circulation is a low-pressure system designed to carry deoxygenated blood from the right ventricle to the lungs and return oxygenated blood to the left atrium. Diseases affecting these vessels can lead to impaired gas exchange and significant strain on the heart.

2.3.1. Pulmonary Hypertension

Pulmonary hypertension (PH) is a hemodynamic and pathophysiological condition defined by an increase in mean pulmonary arterial pressure [17]. It results from the narrowing, remodeling, or obstruction of the small pulmonary arteries, which increases the

resistance to blood flow through the lungs. This increased afterload forces the right ventricle of the heart to work harder to pump blood, which can lead to right ventricular hypertrophy and, eventually, right-sided heart failure (cor pulmonale). PH can be an isolated condition (idiopathic) or can occur in association with a wide range of other conditions, including connective tissue diseases, congenital heart disease, and chronic lung diseases like COPD and pulmonary fibrosis [18].

2.3.2. Pulmonary Embolism

A pulmonary embolism (PE) is an acute obstruction of the pulmonary arteries, most commonly caused by a blood clot that has traveled from a deep vein, typically in the legs (deep vein thrombosis). This blockage prevents blood from reaching the lung tissue downstream, creating a mismatch between ventilation (air getting into the alveoli) and perfusion (blood flow to the alveoli). This mismatch severely impairs gas exchange. A large PE can cause a sudden increase in pulmonary artery pressure, leading to acute right ventricular failure, shock, and potentially sudden death [19].

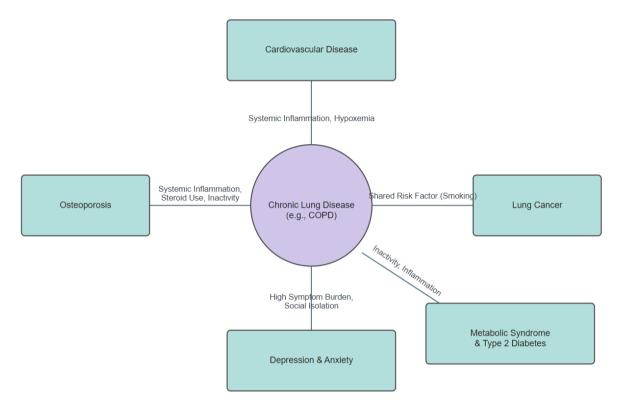


Figure 3. Chronic Lung Diseases and Major Comorbidities

3. Global Health Efforts and Imperatives

Addressing the substantial burden of chronic lung disease requires a coordinated global effort focused on several key strategic areas. These imperatives range from improving fundamental diagnostic and therapeutic access to leveraging innovation and ensuring ethical care delivery.

3.1. Improved Diagnostics

A foundational challenge in managing chronic respiratory diseases, particularly in LMICs, is profound underdiagnosis. Spirometry, the gold standard for diagnosing and assessing obstructive lung diseases, remains largely unavailable or underutilized in primary care settings across these regions due to costs, lack of equipment, and insufficient numbers of trained personnel [20]. This diagnostic gap means that a vast majority of individuals with conditions like COPD remain undiagnosed until their disease is advanced, limiting the effectiveness of interventions. There is an urgent need to validate and implement simpler, low-cost screening tools and to invest in training frontline health workers to better identify at-risk individuals [21].

3.2. Ensuring Equitable Access to Care

Significant disparities in access to evidence-based care for chronic lung disease exist both between and within countries. These inequities are often driven by social determinants of health, including poverty, education level, and geographic location [22]. Access to essential inhaled medications, smoking cessation programs, and preventative measures like vaccination is often limited for the

most vulnerable populations. Addressing this requires a multi-pronged approach: strengthening health systems, implementing policies that ensure the affordability of essential medicines, and enacting public health regulations to reduce exposure to tobacco smoke and air pollution [5].

Table 4. Global Health Imperatives for Chronic Lung Disease

Imperative	Identified Problem	Proposed Strategy /	Desired Outcome
		Intervention	
Advancing Diagnostics	Widespread underdiagnosis, especially in low-resource	Validate and scale low-cost screening tools	Early and accurate diagnosis, enabling timely intervention and
	settings, due to lack of access to tools like spirometry.	Train primary healthcare workers in case-finding	improved prognosis.
Ensuring Equitable Access	Disparities in access to essential medicines, preventative care, and smoking cessation support.	Strengthen health systems Implement policies for affordable medication Enact clean air regulations	Reduced health inequities and improved disease management across all populations.
Expanding Rehabilitation	Extremely limited global access to pulmonary rehabilitation despite proven benefits.	Develop low-cost, scalable community- or home-based models Invest in professional training	Improved quality of life, reduced symptoms, and lower hospitalization rates for patients.
Integrating Palliative Care	Underutilization of palliative care for patients with severe symptoms and advanced disease.	Integrate palliative principles early in the care pathway Increase awareness among clinicians and patients	Better symptom management, enhanced quality of life, and improved end-of-life care.
Leveraging Technology	The digital divide limits the potential of telehealth, remote monitoring, and mHealth applications.	Develop accessible and context- specific digital health tools Promote digital literacy	Improved self-management, treatment adherence, and access to care for remote populations.

3.3. Pulmonary Rehabilitation

Pulmonary rehabilitation is a comprehensive, evidence-based intervention that combines exercise training, education, and behavior change to improve the physical and psychological condition of people with chronic respiratory disease [23]. It is proven to reduce symptoms of dyspnea, improve quality of life, and decrease hospital admissions for patients with COPD and other chronic lung conditions. Despite its strong recommendation in international guidelines, global access is extremely limited, with estimates suggesting that fewer than 2% of eligible patients receive it [24]. Expanding access requires the development of low-cost, scalable models of rehabilitation that can be delivered in community or home-based settings, alongside dedicated training for healthcare professionals.

Table 5. Core Components of a Comprehensive Pulmonary Rehabilitation Program

Component	Description	Primary Goals
Exercise Training	Supervised aerobic exercises (e.g., walking, cycling)	Improve exercise tolerance and endurance
	and strength training for upper and lower limbs.	Reduce dynamic hyperinflation
		Increase muscle strength and reduce fatigue
Patient	Sessions on disease process, medication use (including	Enhance self-management skills
Education	inhaler technique), breathing strategies, nutrition, and	Improve treatment adherence
	energy conservation.	Empower patients to recognize and manage
		symptoms
Psychosocial	Counseling and support groups to address anxiety,	Improve coping mechanisms
Support	depression, and social isolation commonly associated	Reduce psychological symptom burden
	with chronic lung disease.	Provide peer support
Nutritional	Assessment and advice on maintaining a healthy	Optimize body composition and muscle mass
Counseling	weight, as both underweight and overweight can	Improve overall health status
	negatively impact respiratory function.	

3.4. Palliative Care

Patients with advanced chronic lung disease experience a significant symptom burden, including severe breathlessness, fatigue, and depression, which is often comparable to that of patients with advanced cancer. However, palliative care services remain profoundly underutilized in this population [25]. Referrals are often made very late in the disease course, if at all. Barriers include a lack of

awareness among both clinicians and patients, difficulties in prognostication, and limited availability of palliative care services, especially in LMICs. Integrating palliative care principles early in the management of severe respiratory disease is essential to improve symptom control, support patients and families in decision-making, and enhance overall quality of life.

3.5. Digital Transformation

The digital transformation of healthcare offers promising opportunities to improve the management of chronic lung diseases. Telehealth, remote monitoring, and mobile health (mHealth) applications can facilitate patient education, support self-management, improve treatment adherence, and provide clinical support, particularly for patients in remote areas [26]. While the COVID-19 pandemic accelerated the adoption of these technologies, the digital divide remains a significant barrier to equitable access. Future innovation must focus on developing and implementing digital health solutions that are accessible, affordable, and tailored to the specific needs of diverse populations and health systems.

4. Conclusion

Chronic respiratory diseases impose an immense and growing burden on individuals and health systems globally. Their diverse pathophysiology, driven by a convergence of genetic, environmental, and lifestyle factors, presents complex challenges for prevention and management. The frequent coexistence of these conditions with other chronic diseases further complicates patient care. Mitigating the global impact of respiratory illness is contingent upon a renewed and coordinated commitment to several key imperatives. Enhancing diagnostic capacity, eliminating inequities in access to care, expanding the availability of pulmonary rehabilitation, and integrating palliative care are fundamental components of a comprehensive response. Moreover, sustained investment in implementation science and targeted research is critical to translate scientific knowledge into effective, scalable interventions. Without a collaborated focus on lung health within the broader agenda of non-communicable diseases, the global community will fail to address one of the most significant health challenges of our time.

References

- [1] World Health Organization. The top 10 causes of death. Geneva: WHO; 2020.
- [2] GBD 2017 Chronic Respiratory Diseases Collaborators. Prevalence and attributable health burden of chronic respiratory diseases, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Respir Med. 2020;8(6):585-596.
- [3] Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease (2024 Report). [Internet]. 2024. Available from: https://goldcopd.org/2024-gold-report/
- [4] Gordon SB, Bruce NG, Grigg J, Hibberd PL, Kurmi OP, Lam KB, et al. Respiratory risks from household air pollution in low and middle income countries. Lancet Respir Med. 2014;2(10):823-60.
- [5] Williams S, Sheikh A, Campbell H, Fitch N, Griffiths C, Heyderman RS, et al. Respiratory research funding is inadequate, inequitable, and a missed opportunity. Lancet Respir Med. 2020;8(8):e67-e68.
- [6] Siegel DA, Jatlaoui TC, Koumans EH, et al. Update: Interim Guidance for Health Care Providers Evaluating and Caring for Patients with Suspected E-cigarette, or Vaping, Product Use–Associated Lung Injury — United States, October 2019. MMWR Morb Mortal Wkly Rep. 2019;68:919–927.
- [7] Smith SM, Soubhi H, Fortin M, Hudon C, O'Dowd T. Managing patients with multimorbidity: systematic review of interventions in primary care and community settings. BMJ. 2012;345:e5205.
- [8] Kim V, Criner GJ. Chronic bronchitis and chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2013;187(3):228-37.
- [9] Barnes PJ. Chronic obstructive pulmonary disease. N Engl J Med. 2000;343(4):269-80.
- [10] Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention, 2024. [Internet]. 2024. Available from: https://www.google.com/search?q=https://ginasthma.org/2024-gina-main-report/
- [11] Lambrecht BN, Hammad H. The immunology of asthma. Nat Immunol. 2015;16(1):45-56.
- [12] Travis WD, Costabel U, Hansell DM, King TE Jr, Lynch DA, Nicholson AG, et al. An official American Thoracic Society/European Respiratory Society statement: Update of the international multidisciplinary classification of the idiopathic interstitial pneumonias. Am J Respir Crit Care Med. 2013;188(6):733-48.
- [13] Raghu G, Collard HR, Egan JJ, et al. An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. Am J Respir Crit Care Med. 2011;183(6):788-824.

- [14] Ley B, Collard HR, King TE Jr. Clinical course of idiopathic pulmonary fibrosis: a systematic review. Am J Respir Crit Care Med. 2011;183(4):431-40.
- [15] Baughman RP, Teirstein AS, Judson MA, Rossman MD, Yeager H Jr, Bresnitz EA, et al. Clinical characteristics of patients in a case control study of sarcoidosis. Am J Respir Crit Care Med. 2001;164(10 Pt 1):1885-9.
- [16] Shorr AF, Helman DL, Davies DB, Nathan SD. Sarcoidosis, race, and pulmonary hypertension: a study of 445 patients. Chest. 2004;125(2):485-91.
- [17] Humbert M, Kovacs G, Hoeper MM, Badagliacca R, Berger RMF, Brida M, et al. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. Eur Heart J. 2022;43(38):3618-3731.
- [18] Simonneau G, Montani D, Celermajer DS, Denton CP, Gatzoulis MA, Krowka M, et al. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. Eur Respir J. 2019;53(1):1801913.
- [19] Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Heart J. 2020;41(4):543-603.
- [20] Stolz D, Mkorombindo T, Schumann DM, Agusti A, Ash SY, Bafadhel M, et al. Towards the elimination of chronic obstructive pulmonary disease: a Lancet Commission. Lancet. 2022;400(10361):921-972.
- [21] Mortimer K, Ndamala CB, Awomi EJ, Katundu C, Weston W, Havens D, et al. Lung health in rural Africa: a population-based study of adults and children in Malawi. Thorax. 2017;72(3):210-217.
- [22] Marmot M. Social determinants of health inequalities. Lancet. 2005;365(9464):1099-104.
- [23] Spruit MA, Singh SJ, Garvey C, ZuWallack R, Nici L, Rochester C, et al. An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation. Am J Respir Crit Care Med. 2013;188(8):e13-64.
- [24] Rochester CL, Vogiatzis I, Holland AE, Lareau SC, Marciniuk DD, Puhan MA, et al. An Official American Thoracic Society/European Respiratory Society Policy Statement: Enhancing Implementation, Use, and Delivery of Pulmonary Rehabilitation. Am J Respir Crit Care Med. 2015;192(11):1373-86.
- [25] Pinnock H, Kendall M, Murray SA, Worth A, Levack P, Sheikh A. Living and dying with severe COPD: multi-perspective longitudinal qualitative study. BMJ. 2011;342:d142.
- [26] Pinnock H, Hanley J, McCloughan L, Todd A, Krishan A, Lewis S, et al. Effectiveness of telemonitoring integrated into existing clinical services on hospital admission for people with chronic obstructive pulmonary disease: a pragmatic randomised controlled trial. BMJ. 2013;347:f6070.