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RESPIRATORY COMPLICATIONS BEYOND COVID-19: A FOCUS ON CHRONIC PULMONARY DISEASES

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Abstract
The COVID-19 pandemic has significantly impacted individuals with chronic pulmonary diseases (CPDs), including chronic obstructive pulmonary disease (COPD), asthma, and pulmonary fibrosis. As the focus shifts from the acute phase of COVID-19 to its long-term respiratory consequencespost-COVID-19 survivors with pre-existing lung conditions face an elevated risk of disease progression of fibrosis, and persistent pulmonary complications. This review highlights recent innovative approaches that are reshaping the management of CPDs in the post-pandemic era. These include the use of artificial intelligence (AI) for personalized disease risk prediction, the development of targeted biological therapies, advances in stem cell-based regenerative medicine, cutting-edge imaging technologies for early detection, and the repurposing of antiviral and antifibrotic agents. Together, these innovations present new opportunities for improving the long-term respiratory health of individuals with CPDs, paving the way for more personalized and effective treatment strategies.

Keywords: Chronic pulmonary diseases, asthma, pulmonary fibrosis, COVID-19, artificial intelligence, stem cell therapy, predictive modeling, regenerative medicine, advanced imaging.

The COVID-19 pandemic has profound implications for respiratory health, particularly among individuals with chronic pulmonary diseases (CPDs), such as chronic obstructive pulmonary disease (COPD), asthma, interstitial lung disease (ILD), and pulmonary fibrosis. While much attention has focused on the immediate impacts of the virus, it is now clear that COVID-19's longer-term consequences are reshaping the landscape of chronic pulmonary care (1).

Emerging data indicates that survivors of COVID-19, especially those with pre-existing lung conditions, may face prolonged respiratory impairment. A significant concern is the increased frequency of exacerbations in patients with conditions like COPD and asthma, as well as progressive scarring in diseases like pulmonary fibrosis (2). Moreover, viral-triggered hyper inflammation exacerbates airway remodeling, lung fibrosis, and bronchial hyper responsiveness, leading to more severe disease phenotypes in these populations(3).

The integration of artificial intelligence (AI) with genomic profiling is showing immense promise in the management of post-COVID-19 pulmonary complications (4). AI algorithms can analyze large datasets, including genetic predispositions, immune profiles, and environmental factors, to predict which patients are at risk for long-term sequelae. These predictive models are crucial for identifying individuals who may require more aggressive monitoring or early therapeutic interventions to prevent disease exacerbations(5).

As inflammation remains a key driver of chronic respiratory complications post-COVID, targeted biologics, such as monoclonal antibodies, are emerging as novel therapeutic options (6). Recent clinical trials have explored IL-5 and IL-13 inhibitors for managing asthma exacerbations post-viral infection. Additionally, antifibrotic agents, including nintedanib and pirfenidone, originally developed for idiopathic pulmonary fibrosis are being repurposed for post-COVID patients with fibrotic lung disease (7)(8).

Another ground-breaking approach is the exploration of mesenchymal stem cell (MSC) therapies to mitigate COVID-19-induced lung damage in patients with CPDs. MSCs have demonstrated the ability to reduce inflammation and promote tissue repair. Early phase trials are showing promise in reducing the severity of lung fibrosis and improving lung function in patients with persistent symptoms post-COVID-19 (9).

Chronic respiratory impairment is caused by various respiratory disorders like pulmonary hypertension, fibrosis, asthma, and cystic fibrosis. Chronic Obstructive Pulmonary Disease (COPD) and alpha-1 antitrypsin deficiency also compromise pulmonary function. Non-small cell lung cancer complicates diagnosis and treatment. The COVID-19 pandemic has intensified the clinical burden on pre-existing pulmonary conditions, exacerbating inflammation and respiratory failure. Understanding these interrelated conditions is crucial for developing targeted therapeutic strategies(10) (Figure 1).

Vaccination continues to play a vital role in preventing exacerbations of CPDs. beyond COVID-19 vaccines, new efforts are underway to develop vaccines targeting respiratory syncytial virus (RSV) and other viral pathogens that can trigger exacerbations in COPD and asthma. These vaccines aim to reduce the viral load in patients with chronic lung diseases, thereby preventing severe inflammatory responses that could worsen their condition (11).

The link between COPD and COVID-19 is significant, as COPD patients are more susceptible to severe respiratory infections. They have upregulated ACE2 receptors, which facilitate SARS-CoV-2 entry. Smoking also compromises innate antiviral defenses, leading to lung alterations and heightened inflammation (12). These factors contribute to severe acute disease and poorer clinical outcomes in COPD patients infected with COVID-19. Understanding these mechanisms is crucial for risk stratification and developing targeted therapeutic interventions (13) (Figure 2).

Future research should focus on refining AI-driven predictive models, expanding the use of biologics and regenerative therapies, and enhancing remote pulmonary rehabilitation strategies. By harnessing these innovations, we can significantly improve the quality of life and long-term outcomes for those affected by chronic pulmonary diseases beyond COVID-19.Continued multidisciplinary research efforts are essential to fully understand the long-term impacts of COVID-19 on pulmonary health. This will enable us to establish more effective, personalized treatment approaches for individuals with CPDs, ultimately reducing morbidity and improving patient outcomes.

Figure 1 The diagram illustrates the key risk factors contributing to chronic obstructive pulmonary disease (COPD), with genetics at the core. Surrounding factors include premature birth, early respiratory infections, asthma, altered lung development, and maternal, pre-natal, and childhood exposures. Additional risks involve ageing and comorbidities, socioeconomic disadvantage, limited access to healthcare, exposure to pollution and biomass combustion, and tobacco smoke. These factors interact across different life stages and environments, collectively influencing the onset and progression of COPD.

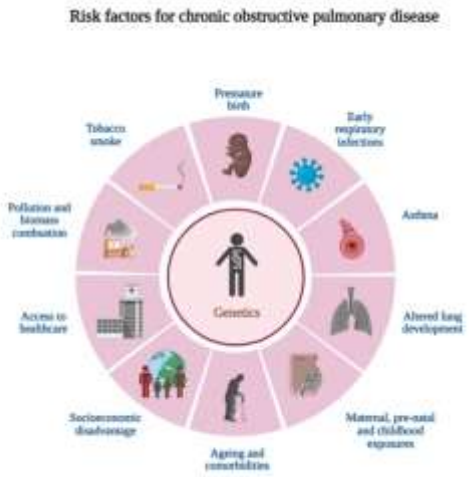

Figure 2 The diagram depicts the progression of chronic obstructive pulmonary disease (COPD) due to exposure to toxic particles and pathogens like cigarette smoke, industrial pollutants, and biomass combustion. These exposures trigger immune responses, exacerbate inflammation, and upregulate ACE2 expression in the airway, leading to symptoms like small airways disease and chronic bronchitis

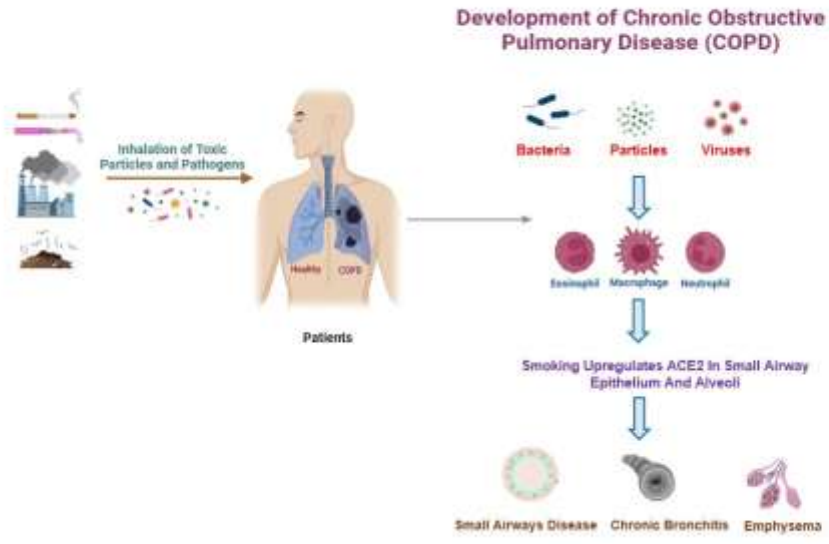

Table 1 The table presents key emerging approaches and therapeutic strategies for the management of chronic pulmonary diseases in the post-COVID-19 era. It highlights innovations across advanced technologies, targeted biologic therapies, regenerative medicine, and preventive strategies such as vaccination. These interventions aim to enhance early diagnosis, improve disease monitoring, and support better long-term respiratory health outcomes for individuals with chronic pulmonary conditions.

Therapeutic Technological Approach	Description	Potential Benefit	References
Artificial Intelligence (AI)	AI models integrate genomic, immune, and environmental data	Personalized risk prediction, early detection of complications	(4), (5)
Targeted Biologics	Monoclonal antibodies such as IL-5 and IL-13 inhibitors	Reduces inflammation and manages post-viral asthma/COPD	(6), (7)
Antifibrotic Therapies	Repurposed drugs like nintedanib and pirfenidone	Mitigates lung fibrosis progression post-COVID	(7), (8)
Mesenchymal Stem Cell (MSC) Therapy	MSCs reduce inflammation and promote lung repair	Regenerative potential in fibrotic CPDs	(9)
Vaccination Strategies	Beyond COVID-19, targeting RSV, influenza, etc.	Prevents exacerbations triggered by respiratory pathogens	(11)
ACE2 Pathway Research	Focus on ACE2 receptor regulation and smoking-related vulnerability	Improved risk stratification and treatment design	(12), (13)

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