

## Perspectives

## Experts' Consensus on the Management of Respiratory Disease Syndemic

Weizhong Yang<sup>1,2,3,#</sup>; Zhongjie Li<sup>1,2,3</sup>; Ting Yang<sup>4</sup>; Yanming Li<sup>5</sup>; Zhengde Xie<sup>6</sup>; Luzhao Feng<sup>1,2,3</sup>; Zhibin Peng<sup>7</sup>; Jue Liu<sup>8,#</sup>

The global burden of respiratory diseases is a significant and increasing threat to individuals worldwide. In 2017, there were 544.9 million cases of chronic respiratory diseases, a 39.8% increase since 1990 (1). These diseases were the third leading cause of global mortality in 2017, accounting for 7.0% of all deaths, an 18.0% increase compared to 1990. In addition to chronic respiratory diseases, acute infectious respiratory diseases, including influenza, coronavirus diseases 2019 (COVID-19), and respiratory syncytial virus, pose significant public health concerns and cause both short-term and long-term health damages (2–3). The presence of complex coexisting diseases in the respiratory system further complicates treatment and increases the burden of disease. To effectively address these challenges, it is crucial to implement a comprehensive and robust management approach.

A syndemic refers to the co-occurrence of multiple diseases or health conditions within a population, where biological or behavioral factors worsen the negative health impacts of these conditions (4). Syndemic theory suggests that the combined presence of diseases, along with social and environmental factors, synergistically affects population health. This theory provides a valuable framework for understanding and addressing respiratory disease syndemics. Managing respiratory diseases from a syndemic perspective necessitates a deep understanding of the intricate interplay between biological, social, and environmental factors that contribute to the occurrence and progression of these diseases. By adopting a syndemic approach, the focus shifts from managing individual diseases to a collaborative model that prioritizes population-level interventions, including proactive diagnosis, comprehensive assessment of disease severity, and integrated management of conditions associated with respiratory diseases. The expert consensus on managing respiratory disease syndemics aims to support research and practical interventions in addressing these complex respiratory health challenges.

### The Process of Consensus Formulation

The research team utilized evidence-based medicine methodology to focus on studies pertaining to the management of respiratory diseases. A comprehensive literature search was conducted, encompassing both domestic and international sources, resulting in the collection of 7,085 relevant articles in the database up to December 2023. Through meticulous examination of these articles, relevant information pertaining to the research objectives was extracted. Rigorous criteria were applied to select representative studies, ensuring the robustness and comprehensiveness of the analysis. Expert input was integrated from various fields such as public health, disease prevention and control, and clinical respiratory science. This involved consolidating guidelines, consensus statements, and recommendations related to respiratory disease management. The consensus was developed through three rounds of expert discussions, incorporating advancements in research and practices for the prevention and treatment of respiratory disease syndemic. The consensus primarily consists of fundamental principles that facilitate practical application by healthcare professionals involved in the management of respiratory disease syndemic. Regular revisions will be made based on feedback from prevention and treatment practices in the future. The consensus was initiated and developed by the Chinese Academy of Medical Sciences and Peking University and has been registered on the international Practice Guideline Registration for Transparency platform (PREPARE, <http://www.guidelines-registry.org>) in collaboration with the World Health Organization Guidelines Implementation and Knowledge Translation Center. The registration code for this consensus is PREPARE-2024CN181.

## RESULTS

### Concept and Impact

Recommendation 1: A respiratory disease syndemic

is characterized by the concurrent presence and interconnectedness of multiple respiratory diseases within a population.

At the individual level, the concept of respiratory disease syndemic refers to the occurrence of one or more acute or chronic respiratory diseases within a specific time period in conjunction with pre-existing chronic respiratory disease. This includes chronic non-communicable respiratory diseases such as chronic bronchitis, chronic obstructive pulmonary disease (COPD), asthma, interstitial lung diseases, pneumoconiosis, sleep-disordered breathing, pulmonary arterial hypertension, as well as acute and chronic communicable respiratory diseases like influenza, tuberculosis (TB), and others. The interaction between these conditions is complex and can have implications beyond respiratory health, extending to organ diseases, mental health issues, geriatric syndromes, and other related problems that can significantly impact overall well-being. Clinical evidence has demonstrated bidirectional relationships between certain respiratory diseases; for example, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection may increase the risk of TB, while latent TB can worsen COVID-19 outcomes (5). Depression has also been associated with an increased risk of TB, with a complex biopsychosocial mechanism (6). In COPD, patients often have additional clinically relevant chronic diseases, particularly cardiovascular diseases and cancer, which significantly contribute to mortality (7). These interactions emphasize the importance of a comprehensive and integrated approach to the diagnosis, management, and overall care of patients with respiratory diseases.

**Recommendation 2:** It is essential to assess the impact of respiratory disease syndemics at both the individual and population levels.

Medical evaluation, which includes physical examinations and specialized tests such as pulmonary function tests and chest imaging, plays a crucial role in assessing the health of the respiratory system. These tests provide a comprehensive understanding of both respiratory and non-respiratory disorders, helping in the diagnosis of conditions like cardiac or neuromuscular diseases (8). However, it is important to note that pulmonary function tests, despite their effectiveness, carry a risk of generating aerosols that can lead to infection (9). Therefore, it is essential to prioritize the safety of all individuals involved and take measures to minimize infection risks when conducting these tests. In addition to pulmonary function tests,

quality of life questionnaires like the St. George's Respiratory Questionnaire (SGRQ) for COPD (10), the Asthma Quality of Life Questionnaire (AQLQ) for asthma (11), the Chronic Respiratory Questionnaire (CRQ) for chronic respiratory diseases (12), the Leicester Cough Questionnaire (LCQ) for cough symptoms (13), and the Short Form Health Survey (SF-36) (14) can provide valuable insights into the impact of respiratory disease syndemics on individuals. However, there is currently a lack of standardized scales to quantitatively measure this impact on patients' health and lives. Therefore, further research and development of relevant scales and diagnostic tools are necessary to comprehensively assess and quantify the impact of respiratory disease syndemics on populations. This may involve creating new scales or adopting comprehensive assessment approaches that combine existing scales to measure different aspects of the impact.

**Recommendation 3:** The presence of respiratory disease syndemics adds complexity to diagnostic and treatment procedures, which can lead to increased demands for healthcare services and complicated medication regimens. This poses long-term challenges for communities.

The simultaneous presence of multiple chronic health conditions necessitates a coordinated treatment approach, which adds complexity to medical decision-making. There are ongoing uncertainties regarding the mechanisms underlying the association between different respiratory diseases (15). Clinical interventions for one respiratory disease may have varying effects on coexisting comorbidities (16). It is crucial for individuals with respiratory disease syndemics to receive regular management, including consultations and adherence to healthcare professionals' recommendations, in order to reduce the risk of disease progression and complications. Additionally, respiratory disease syndemics lead to increased healthcare expenditures, as the presence of intertwined co-infections reduces treatment efficacies and drives up costs (17). Due to the chronic nature of these diseases, regular medical assessments are necessary, leading to elevated expenses, especially during acute exacerbations. This increased spending creates financial pressure, thereby calling for the exploration of health insurance coverage, government assistance programs, patient support organizations, and prescription assistance programs (18). Developing a comprehensive financial plan with the assistance of advisors can provide effective strategies for managing

healthcare expenses. Integrating regular management, education, and financial strategies into the treatment plan can help individuals and families better navigate the challenges, thus mitigating the overall impact of additional healthcare costs.

### Management Targets

Recommendation 4: The main goal of managing respiratory disease syndemics is to proactively reduce the incidence of new respiratory diseases.

Respiratory comorbidities have a significant impact on both the respiratory and immune systems, making patients more susceptible to various irritants such as smoke, smog, viruses, bacteria, and mycoplasma. This susceptibility can worsen symptoms, lead to the development of new respiratory diseases, and increase the overall disease burden, thereby affecting patients' quality of life and contributing to the transmission of respiratory infectious diseases (19). To mitigate these risks, it is essential to implement comprehensive medical assessments and personalized management plans that include rehabilitation services and the creation of a conducive environment. Furthermore, patients should adopt personal protective measures such as wearing masks and getting vaccinated to protect themselves against emerging respiratory infections (20). To effectively reduce the incidence of new respiratory diseases, mitigate the spread of infectious diseases, and safeguard overall health, it is imperative to enhance health education, implement preventive strategies, and provide timely medical interventions. This requires collaborative efforts to address the challenges posed by respiratory disease syndemics and to foster a healthier and more sustainable living environment.

Recommendation 5: Enhancing the overall health status and quality of life of populations with respiratory comorbidities is also a crucial objective in managing the syndemic of respiratory diseases.

The management of respiratory disease syndemics should go beyond focusing on individual diseases and avoiding integrated care to reduce costs and enhance patient safety. It is important to pay attention to patients and consider the impact of respiratory disease syndemics on their health needs (21). Patients with respiratory comorbidities often experience severe symptoms that significantly affect their quality of life (22). In cases of COVID-19, patients with comorbidities have been found to have worse clinical outcomes compared to those without comorbidities (23). Therefore, it is crucial to adopt patient-centered,

integrated approach that includes personalized treatment plans and symptom-oriented rehabilitation services to improve the health status and overall well-being of patients (7). This approach should involve comprehensive medical evaluation, timely intervention, and continuous rehabilitation services. By prioritizing the patient in the management process and providing comprehensive care, we can empower patients to better cope with the challenges of respiratory disease syndemics, leading to a healthier and more fulfilling life.

Recommendation 6: Another crucial objective is to prevent deaths resulting from the syndemic of respiratory diseases.

Chronic respiratory diseases and respiratory infectious diseases contribute significantly to the global disease burden (24). The presence of multiple respiratory conditions, known as respiratory disease syndemics, has a profound impact on patients, increasing their risk of exacerbated symptoms and mortality (25). Early diagnosis, prompt medical intervention, and effective treatment strategies are pivotal in reducing mortality associated with respiratory disease syndemics. The BODE Index (Body mass index, airflow Obstruction, Dyspnoea, and Exercise capacity), which has been validated for assessing all-cause or respiratory mortality (26), holds promise in evaluating the prognosis of patients with respiratory comorbidities (25). Our commitment lies in providing active medical care and health management to reduce mortality, mitigate threats to life, and establish a safer and more sustainable healthcare environment for individuals affected by respiratory disease syndemics.

### Management Principles

Recommendation 7: It is essential to consistently evaluate the health status and efficacy of treatment methods among populations affected by respiratory disease syndemics. This is important for early detection, optimizing treatment strategies, and effectively managing concurrent chronic non-communicable and communicable respiratory diseases.

Implementing routine health assessments within healthcare institutions is crucial for managing respiratory diseases at a population level (27). Clinical follow-up, systematic symptom assessments, and early detection of issues such as additional pulmonary diseases or heart failure necessitate adjustments in overall management strategies (28). The positive outcomes, including improved patient well-being and

quality of life, underscore the efficacy of systematic health assessments. Integrating these principles into medical education emphasizes the indispensable role of regular health assessments in delivering comprehensive and patient-centered care. Additionally, considering the seasonality and climate sensitivity of respiratory diseases, particularly before peak seasons, conducting assessments for climate-sensitive respiratory diseases is essential. The escalating burden of chronic respiratory diseases emphasizes the need for innovative treatment approaches (29). Adapting treatment strategies in response to ongoing advancements ensures patients benefit from the latest medical knowledge (30). Given the complexity of patients contending with multiple chronic conditions, vigilant adjustments to treatment strategies accommodate the interaction and changes in these ailments over time (31). Periodic assessments address patient heterogeneity, leading to personalized medical services. Regular adjustments to treatment plans mitigate potential drug interactions, especially in cases of concurrent medication use. Close communication with patients, including feedback on experiences, symptoms, and quality of life, facilitates timely adjustments to treatment strategies, aligning with patient needs and expectations.

**Recommendation 8:** Surveillance plays a crucial role in the management of respiratory disease syndemics as it facilitates early detection and intervention.

Surveillance is essential for early detection, personalized intervention, and timely adjustments to treatment plans in the context of respiratory disease syndemics. It provides real-time prevalence data, contributing to better patient outcomes and overall public health (32). Genomic surveillance, such as the global INFORM-RSV study on Respiratory Syncytial Virus (RSV), is crucial for understanding RSV strain prevalence and genetic diversity across different countries (33). These genetic insights are important for early detection, understanding transmission dynamics, and evaluating vaccine and treatment effectiveness. Previous studies have underscored the often-overlooked aggregated impact of respiratory viruses, underlining the ongoing diversification of influenza variants as well as the critical need for surveillance of various respiratory viruses, at regional and international levels (34). Therefore, surveillance is fundamental in the management of respiratory disease syndemics as it facilitates early detection, tailored interventions, and prompt modifications to therapeutic strategies. This process is essential for gaining a critical understanding of the incidence and genetic variability of respiratory

viruses.

**Recommendation 9:** Minimizing medication is a fundamental principle in the management of respiratory disease syndemics.

Optimizing patient care in respiratory disease syndemics requires a streamlined approach to medication management, considering the complexity of multi-morbidity and potential drug interactions (35). Inaccurate prescribing may occur due to the presence of comorbidities (36). As multi-morbidity becomes more prevalent with age, especially in the elderly population, simplifying medication regimens becomes crucial (37). Treatment burden, including multiple medication administration, negatively impacts health-related quality of life (38). Minimizing medication not only reduces treatment burden but also improves patient compliance, decreases the risk of adverse drug interactions, and enables a comprehensive and personalized approach to care. Emphasizing non-pharmacological interventions further contributes to better patient outcomes and quality of life. It is essential to regularly review medications to align with the current health status and optimize treatment strategies. Overall, a thoughtful and streamlined approach to medication management is pivotal in addressing the unique challenges posed by respiratory disease syndemics.

**Recommendation 10:** It is essential to establish an interdisciplinary team consisting of experts in infectious diseases, respiratory medicine, immunology, public health, and related fields. This team will play a critical role in the prevention, diagnosis, control, treatment, and rehabilitation of respiratory disease syndemics.

Interdisciplinary care has shown success in managing diseases such as diabetes despite barriers like hierarchical structures and financial constraints (39). Healthcare policies now prioritize interconnected factors to optimize patient outcomes, improve effectiveness, and reduce costs through integrated care delivery (40). The World Health Organization (WHO) emphasizes the importance of interdisciplinary teamwork in primary care as a key element in healthcare reform (41). Effective interdisciplinary teamwork relies on clear policies, explicit expectations, regular team meetings, open communication, and a dedicated focus on patient care (42). Smooth teamwork within interdisciplinary management teams is facilitated by clear divisions of labor, trust, mutual respect, and regular communication, whether face-to-face or electronic (43). In the comprehensive



management of respiratory disease syndemics, establishing a thorough evaluation system is crucial for continuous improvement, adaptability, and improved patient outcomes.

Recommendation 11: Effective management of respiratory disease syndemics necessitates strong collaboration among hospitals, communities, families, and patients.

The collaboration between hospitals and the community has become increasingly important, particularly in light of the COVID-19 pandemic. Hospitals played crucial roles during the pandemic, conducting testing, monitoring, promoting workforce health, caring for the sick, and administering vaccines. This experience highlighted the vital connection between hospitals and community well-being. This connection extends beyond direct nursing care and is also an organizational characteristic. The strong ties between healthcare institutions at different levels and the community have positive effects on nursing personnel and patients within and beyond the hospital setting (44). Furthermore, involving families in decision-making for patients is considered crucial. Family members play significant roles in the decision-making process regarding patient care and other relevant matters (45). In summary, collaboration between hospitals, communities, families, and patients is crucial in managing respiratory disease syndemics.

### Management Strategies

Recommendation 12: In the management of respiratory disease syndemics, it is essential to implement classification management based on the types of syndemics.

The classification management of respiratory disease syndemics follows the health management concept of “promotion, prevention, diagnosis, control, treatment, and rehabilitation.” It divides respiratory disease syndemics into three categories: co-infection of multiple acute respiratory infectious diseases, comorbidity of multiple chronic respiratory diseases, and chronic respiratory disease patients experiencing acute respiratory infections. This approach aims to comprehensively assess patients, determine their health and disease status, and tailor treatment strategies for more effective management. By emphasizing disease prevention, targeted interventions can be implemented. This classification management enables the medical team to accurately address patient needs, providing personalized and comprehensive services to control disease progression, improve prognosis, and

promote overall health.

Recommendation 13: The management of co-infection of multiple acute respiratory infectious diseases should prioritize personalized treatment, disease transmission control, and disease prevention.

Patients require individualized treatment regimens that focus on medication and symptom management to control infection and support recovery. Disease control and prevention measures, such as essential quarantine, health monitoring, personal protection, and vaccination, are essential for minimizing transmission risks. Co-infection in respiratory infectious diseases, particularly during influenza pandemics, significantly burdens patients by worsening symptoms and impacting their quality of life (46). Managing co-infection should prioritize symptom improvement and individual preventive measures, taking into account the issue of antimicrobial resistance (47). It is crucial to practice rational drug use by avoiding unnecessary antibiotics and antivirals to prevent the development of antimicrobial resistance (48). Studies indicate that bacterial co-infection is rare among COVID-19 patients, reducing the need for empirical antibacterial treatment (49).

Improving symptoms requires a personalized medication regimen tailored to specific symptoms, taking into account the challenges posed by antimicrobial resistance and limited virus-targeting drugs (47). Disease surveillance and medical evaluation are essential for assessing disease prevalence and patient characteristics, which provide the foundation for implementing quarantine measures. Health monitoring, including regular testing, and epidemiological surveillance, play a pivotal role in controlling disease transmission (50). Adjusting treatment promptly based on monitoring conditions helps minimize the risk of transmission. For both individual patients and the population at large, personal protection measures such as wearing medical masks and N95 respirators, along with promoting vaccination, are critical for disease prevention (51). Vaccination is highly effective in preventing respiratory infectious diseases and their associated complications, including influenza and COVID-19 (52).

Recommendation 14: The management of comorbidity in patients with multiple chronic respiratory diseases should prioritize comprehensive pulmonary rehabilitation services and the prevention of infectious diseases.

Patients with multiple chronic respiratory diseases often experience severe symptoms that have a

significant impact on their health. To address this, comprehensive care is needed (53). Integrated pulmonary rehabilitation services are crucial in managing both pulmonary and extrapulmonary aspects of comorbidity, leading to significant improvements in patients' prognosis and quality of life (54). It is important to implement preventive measures such as personal protection and vaccination, considering the heightened vulnerability of these patients to respiratory pathogens (55). Pulmonary rehabilitation involves thorough assessments, personalized exercise programs, and education focused on self-management and health-promoting behavior change (54). This hospital-based approach, supported by an interdisciplinary team, ensures optimal outcomes for patients with multiple chronic respiratory diseases (56). The integration of pulmonary rehabilitation services with preventive measures is vital in effectively managing comorbidity and enhancing overall patient health.

**Recommendation 15:** The management of acute respiratory infections in patients with chronic respiratory diseases should prioritize infection control, prevention of disease worsening, mortality, and new infections. Additionally, comprehensive rehabilitation services should be provided to these patients.

Patients with chronic respiratory diseases are at a higher risk of developing acute respiratory infections, including bacterial and viral pathogens such as COVID-19. This increases the severity of their existing respiratory conditions (55). To address this vulnerability, it is crucial to prioritize infection control, prevention of exacerbations, and integrated rehabilitation services (57). Control measures should include rational drug use, health monitoring, personal protection, and vaccination. Symptom-oriented medication, including the use of antimicrobials when necessary, helps with timely infection control. Close health monitoring allows for prompt treatment adjustments. Personal protective measures, such as wearing masks, reduce the spread of infections and the susceptibility to new pathogens (58). Immunization plays a critical role in preventing new infections and associated complications, reducing the risks of severe illness and mortality. Additionally, timely integrated pulmonary rehabilitation services are recommended to improve the health status, quality of life, and mental well-being of patients. These comprehensive measures aim to alleviate symptoms, minimize disease severity and mortality risks, prevent new infections, and provide holistic health protection.

## CONCLUSION

In conclusion, research on the management of respiratory disease syndemics is still in its preliminary stages, encountering challenges in practical application and inadequate research efforts. The establishment of this consensus is anticipated to act as a catalyst, fostering wider advocacy and practical implementation of concepts and methods for managing respiratory disease syndemics.

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# Corresponding authors: Weizhong Yang, [yangweizhong@cams.cn](mailto:yangweizhong@cams.cn); Jue Liu, [jueliu@bjmu.edu.cn](mailto:jueliu@bjmu.edu.cn).

<sup>1</sup> School of Population Medicine and Public Health, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; <sup>2</sup> State Key Laboratory of Respiratory Health and Multimorbidity, Beijing, China; <sup>3</sup> Key Laboratory of Pathogen Infection Prevention and Control, Peking Union Medical College, Ministry of Education, Beijing, China; <sup>4</sup> National Center for Respiratory Diseases, State Key Laboratory of Respiratory Health and Multimorbidity, National Clinical Research Center for Respiratory Diseases, Institute of Respiratory Medicine, Chinese Academy of Medical Sciences, Department of Pulmonary and Critical Care Medicine, Center of Respiratory Medicine, China-Japan Friendship Hospital, Beijing, China; <sup>5</sup> Department of Pulmonary and Critical Care Medicine, National Center of Gerontology, Beijing Hospital, Institute of Geriatric Medicine, Chinese Academy of Medical Sciences, Beijing, China; <sup>6</sup> Beijing Key Laboratory of Pediatric Respiratory Infection Diseases, Key Laboratory of Major Diseases in Children, Ministry of Education, National Clinical Research Center for Respiratory Diseases, Research Unit of Critical Infection in Children, Chinese Academy of Medical Sciences, 2019RU016, National Key Discipline of Pediatrics (Capital Medical University), Beijing Pediatric Research Institute, Beijing Children's Hospital, Capital Medical University, National Center for Children's Health, Beijing, China; <sup>7</sup> Chinese Center for Disease Control and Prevention, Beijing, China; <sup>8</sup> Department of Epidemiology and Biostatistics, School of PublicHealth, Key Laboratory of Epidemiology of Major Diseases, Ministry of Education, Peking University Health Science Center-Weifang Joint Research Center for Maternal and Child Health, Peking University, Beijing, China.

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