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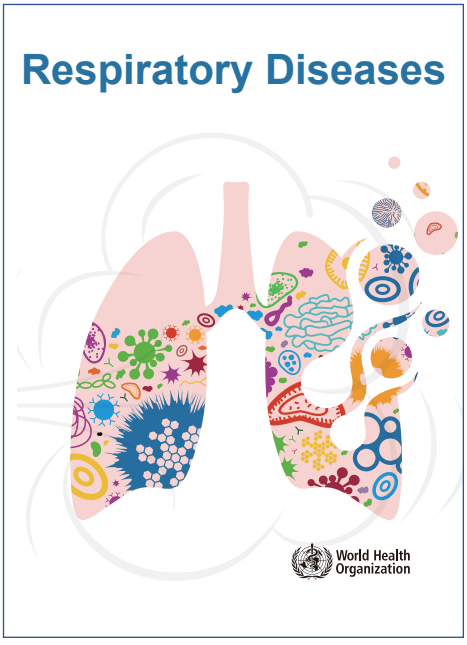

RESPIRATORY DISEASES ISSUE

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Cover Image: adapted from the World Health Organization, https://www.who.int/publications/i/item/clinical-care-of-severe-acute-respiratory-infections-tool-kit.

Perspectives

Experts' Consensus on the Management of Respiratory Disease Syndemic

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

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; Jue Liu, jueliu@bjmu.edu.cn.

[1] School of Population Medicine and Public Health, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [2] State Key Laboratory of Respiratory Health and Multimorbidity, Beijing, China; [3] Key Laboratory of Pathogen Infection Prevention and Control, Peking Union Medical College, Ministry of Education, Beijing, China; [4] 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; [5] Department of Pulmonary and Critical Care Medicine, National Center of Gerontology, Beijing Hospital, Institute of Geriatric Medicine, Chinese Academy of Medical Sciences, Beijing, China; [6] 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; [7] Chinese Center for Disease Control and Prevention, Beijing, China; [8] 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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Preplanned Studies

Respiratory Viruses and *Mycoplasma Pneumoniae* Surveillance Among Hospitalized Children with Acute Respiratory Infections — Wuhan City, Hubei Province, China, September–November 2023

Ying Li[1,2,3,4,&]; Yi Yan[5,&]; Jiaming Huang[1,4,5]; Yue Shi[1,5]; Hui Du[2,3]; Chao Xiong[6]; Kai Chen[6]; Di Liu[1,4,5,#]; Xiaoxia Lu[2,3,#]

Summary

What is already known about this topic?

Acute respiratory infections (ARIs) are a significant contributor to illness and death in children. There has been a notable rise in the occurrence of ARIs and the associated pathogens in China, which has garnered worldwide attention.

What is added by this report?

This study conducted a retrospective analysis of the clinical characteristics of children with ARIs in Wuhan City from September to November 2023. The study evaluated the epidemiological patterns of common respiratory viruses and *Mycoplasma pneumoniae* (MP), revealing a continued prevalence of MP and a growing trend of influenza. Our findings emphasize that the circulation of respiratory viruses and MP has not returned to pre-pandemic levels, underscoring the importance of enhancing surveillance for respiratory pathogens.

What are the implications for public health practice?

The epidemiology of ARIs and the pathogens involved need to be emphasized. This highlights the importance of developing policies to protect children from respiratory pathogens such as MP, influenza, and respiratory syncytial virus.

Acute respiratory infections (ARIs) are a major cause of illness and death in children under the age of five, particularly in developing countries, contributing significantly to the global burden of disease (*1*). The coronavirus disease 2019 (COVID-19) pandemic has changed the epidemiology of respiratory viruses and *Mycoplasma pneumoniae* (MP) (*2–3*). In response to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) outbreak in Wuhan, China implemented a comprehensive and evolving zero-COVID policy to control the pandemic, which continued until December 2022. Since the relaxation of pandemic control measures, there has been a noticeable shift in the prevalence of respiratory viruses and MP. On November 22, 2023, the World Health Organization (WHO) reported clusters of undiagnosed pneumonia in children in China based on media and ProMED reports (*4*), which was later attributed to known pathogens such as the influenza virus and MP. However, the increase in ARIs and associated pathogens in Chinese children has garnered global attention (*5*). Therefore, this study aimed to determine the prevalence patterns of respiratory viruses and MP among children with ARIs in the Wuhan region from September 1 to November 30, 2023. Our findings demonstrate a persistent prevalence of MP and a growing trend of influenza.

We conducted a retrospective study at Wuhan Children's Hospital, enrolling children with ARIs between September 1, 2023, and November 30, 2023. Specimens collected included nasopharyngeal aspirates/throat swabs or peripheral blood samples. These samples were analyzed using various methods such as real-time polymerase chain reaction (RT-PCR), targeted next-generation sequencing (tNGS), colloidal gold immunochromatographic tests, or direct immunofluorescence to detect microorganisms such as MP, respiratory syncytial virus (RSV), adenovirus (ADV), influenza A virus (IAV), influenza B virus (IBV), and parainfluenza virus (PIV). Demographic and clinical data were extracted from electronic medical records. Statistical analyses were performed using R (version 4.0.3, R Foundation for Statistical Computing, Minnesota, US) in RStudio (version 1.4.1103, RStudio, Inc., Minnesota, US) and GraphPad Prism (version 9.1.1.1, San Diego, CA). It is important to note that this study relied solely on the retrospective analysis of deidentified data. Ethical approval for this study was obtained from the Ethics Committee of Wuhan Children's Hospital (No.

2023R016-E02).

From September 1, 2023, to November 30, 2023, a total of 70,016 patients sought consultation at Wuhan Children's Hospital for ARIs, with 10,012 individuals requiring hospitalization. In the outpatient setting, 51,700 (73.8%) children provided peripheral blood samples for colloidal gold immunochromatographic tests to detect RSV, MP, and ADV. Nasopharyngeal aspirates from 8,977 (12.8%) children were tested for IAV and IBV. The average age of the children was 4.86 (3.27, 7.31) years, with the highest proportion belonging to the preschool age group (3–6 years) at 40.8%. The majority of the participants were male (56.2%). Out of the 51,700 outpatients included, 19,085 (36.9%) were infected with a single pathogen and 220 (0.4%) had co-infections. MP (36.2%) was the most commonly detected pathogen, followed by IAV (16.8%). Among the hospitalized patients, 7,568 (75.6%) children were included in the study for the simultaneous detection of MP, RSV, ADV, IAV, IBV, and PIV. Of the hospitalized children, 4,298 (56.7%) were male and 8,280 (38%) were school-age children (>6 years old), with an average age of 5.01 (3.12, 8.03) years. Across all tested settings, a total of 4,302 (56.8%) patients were infected with a single pathogen, while 373 (4.9%) were infected with multiple pathogens. Consistent with the findings in outpatients, MP (46.6%) showed the highest pathogen detection rate, followed by RSV (7.6%), PIV (5.9%), ADV (3.8%), and IAV (2.4%) (Table 1). During the study period, the enrollment of outpatients peaked during the second half of October, coinciding with an increase in MP detection. Additionally, the detection rate of MP remained consistently high throughout the study period. IAV continued to be detected, with a detection rate of approximately 10%, and peaked at the end of November (with a detection rate exceeding 30%). Furthermore, IBV started to be detected in late October but remained at low levels (Figure 1).

In hospitalized patients, the detection rate of MP remains consistently high throughout the year, ranging from 30% to 60%, with the highest rates observed in October. IAV reached its peak in late November, while intermittent detections of IBV occur during this period. RSV and PIV were detected in September and October, but their numbers declined in November. ADV was consistently detected at levels below 10%. Interestingly, influenza typically peaked in late fall and winter, but the seasonal trends observed for MP and RSV in hospitalized patients differ from the expected patterns seen prior to the COVID-19 pandemic in this study (*6*–*7*) (Figure 2).

TABLE 1. Demographic and clinical data of patients enrolled.

Variable	Inpatients (*n*=7,568)	Outpatients (*n*=51,700)
Sex (male)	4,298 (56.7)	29,070 (56.2)
Age (years)	5.01 (3.12, 8.03)	4.86 (3.27, 7.31)
≤1	669 (8.8)	2,958 (5.7)
1–3	1,546 (20.4)	7630 (14.8)
3–6	2,485 (32.8)	2,1087 (40.8)
>6	2,868 (37.9)	20,025 (38.7)
Virus detection rate	4,675 (61.8)	19,085 (36.9)
Single virus	4,302 (56.8)	18,865 (36.5)
Multiple viruses	373 (4.9)	220 (0.4)
MP	3,532 (46.6)	18,755 (36.2)
ADV	294 (3.8)	234 (0.4)
IAV	182 (2.4)	1,510/8,977* (16.8)
IBV	36 (0.4)	114/8,977* (1.2)
RSV	576 (7.6)	324 (0.6)
PIV	451 (5.9)	-

Note: Data are presented as mean and variance or numbers (%).
'-' in the last line means that in outpatient settings, PIV was not tested in detection methods.
Abbreviation: MP=*Mycoplasma pneumoniae*; ADV=adenovirus; IAV=influenza virus A; IBV=influenza virus B; RSV=respiratory syncytial virus; PIV=parainfluenza virus.
* In outpatient settings, 8,977 children were tested for IAV and IBV.

DISCUSSION

During the period of September to November 2023, we retrospectively enrolled 51,700 outpatients and 7,568 inpatients with ARIs in our study. Children aged over 3 years accounted for more than 70% of the enrolled population, with those over 6 years comprising more than one-third of the hospitalized group. Notably, the age distribution differed from our previous study (*8*), which may be attributed to variations in the pathogens. For instance, MP tends to infect school-age children and was the most frequently detected pathogen across all settings, with a consistently high detection rate. This finding contradicts the seasonal prevalence trends observed prior to the COVID-19 pandemic. In contrast, the circulation of IAV aligns with previous patterns, starting in late autumn and early winter.

After the COVID-19 pandemic outbreak, several respiratory viruses experienced a significant decrease in transmission. However, unlike these other viruses, MP showed a different pattern. Initially, MP incidence decreased along with other respiratory pathogens in the

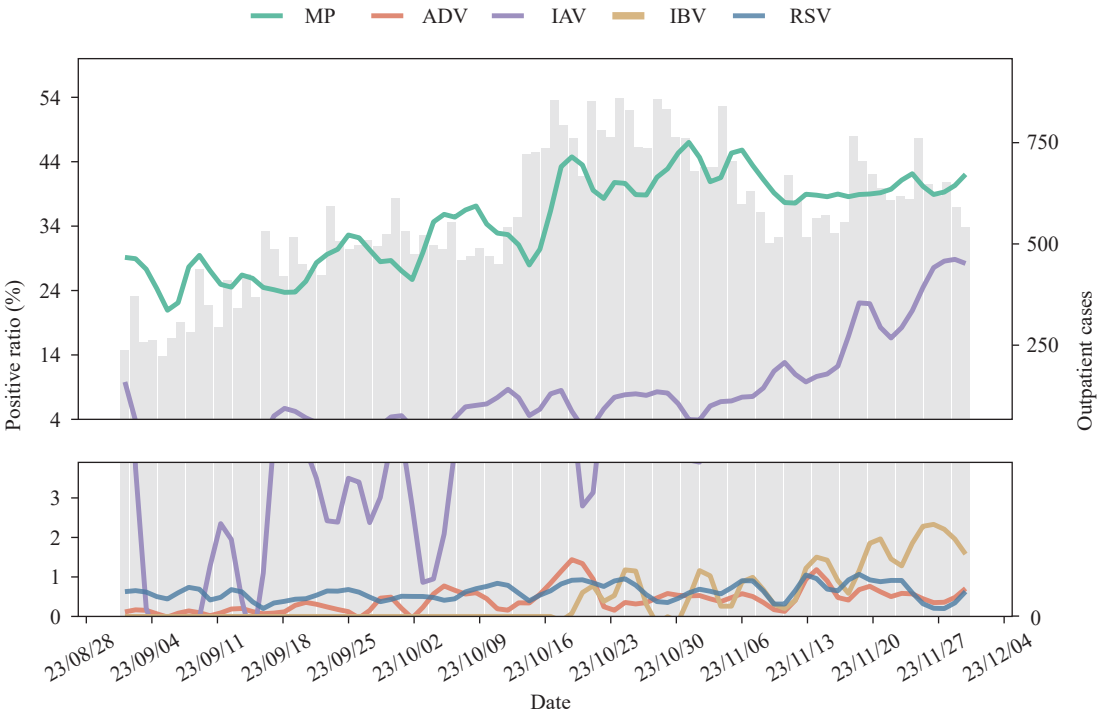

FIGURE 1. Respiratory virus detections among enrolled children in outpatient settings. Colored lines represent the positive rate of MP and viruses over time, and the gray bar represents the number of enrolled children.
Note: Smoothed curves were generated using loess regression to enhance the visualization of trends (span=0.1).
Abbreviation: MP=*Mycoplasma pneumoniae*; ADV=adenovirus; IAV=influenza virus A; IBV=influenza virus B; RSV=respiratory syncytial virus.

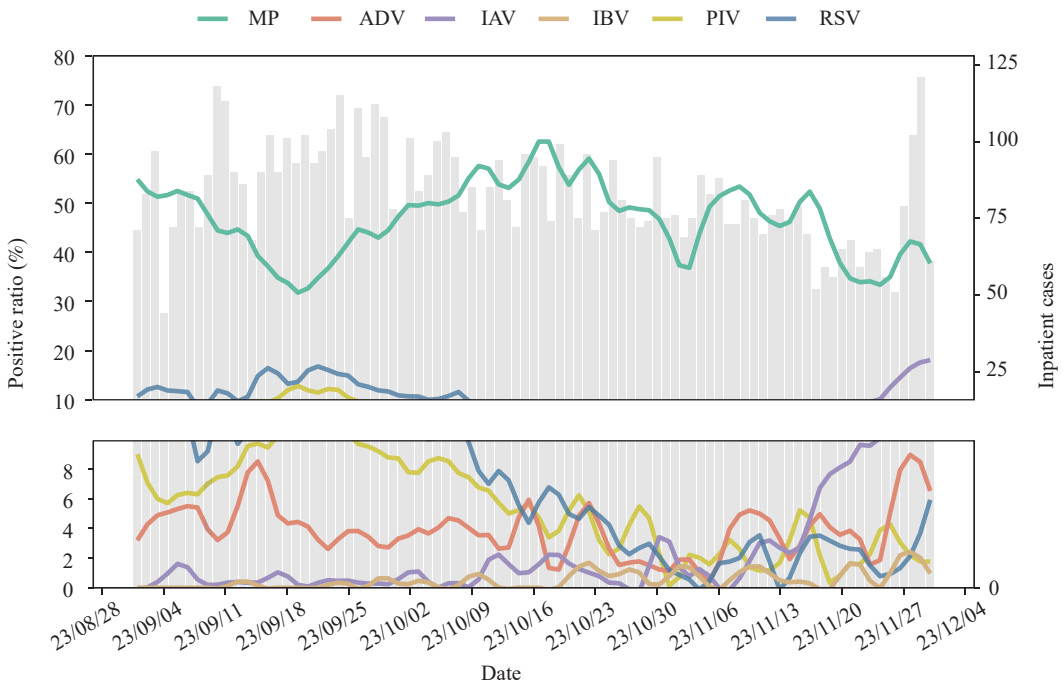

FIGURE 2. Respiratory virus detections among enrolled children in inpatient settings. Colored lines represent the positive rate of MP and viruses over time, and the gray bar represents the number of enrolled children.
Note: Smoothed curves were generated using loess regression to enhance the visualization of trends (span=0.1).
Abbreviation: MP=*Mycoplasma pneumoniae*; ADV=adenovirus; IAV=influenza virus A; IBV=influenza virus B; RSV=respiratory syncytial virus; PIV=parainfluenza virus.

first year, but in the second year, while other respiratory pathogens were resurging, the incidence of MP further decreased, indicating a decline in community transmission. Global surveillance data support this observation, showing the re-emergence of MP in Europe and Asia more than three years after the implementation of COVID-19 restrictions (*9*). Our findings demonstrate a notable increase in MP cases in Wuhan, which is unusual and distinct from the re-emergence pattern of other pathogens and warrants further attention.

We observed a significant decrease in the detection rate of IAV in Wuhan, with nearly 0 detection by April 2022 (*8*). This decline in cases resulted in the accumulation of immune debt (*10*). However, in the 2023–24 season, there was a rapid increase in influenza cases among outpatients, potentially indicating high activity and elevated hospitalization rates due to immune debt. Thus, it is crucial for children to receive seasonal influenza vaccinations as they are the most effective means of safeguarding against influenza and its related complications.

The findings in this report have several limitations. First, the data are restricted to individuals who underwent comprehensive pathogen testing, which may not be representative of all children seeking healthcare. Additionally, we only reported on a limited number of pathogens. While the prevalence of MP, RSV, and influenza is currently important, it would be beneficial to expand surveillance to include other respiratory pathogens. Lastly, the study was retrospective and conducted at a single center. Therefore, the establishment of a multicenter, prospective ARI surveillance system is needed.

Our study examined the epidemiological patterns of common respiratory viruses and MP, revealing the continuing prevalence of MP and a growing trend in influenza. This study emphasizes that the circulation of respiratory viruses and MP has not returned to pre-pandemic levels, highlighting the importance of enhancing surveillance for respiratory pathogens. These findings underscore the need for implementing policies to safeguard children from pathogens such as MP, influenza, and RSV.

Conflicts of interest: No conflicts of interest.

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[#] Corresponding authors: Di Liu, liud@wh.iov.cn; Xiaoxia Lu, lusi74@163.com.

[1] Computational Virology Group, Center for Bacteria and Viruses Resources and Bioinformation, Wuhan Institute of Virology, Chinese Academy of Sciences, Wuhan City, Hubei Province, China; [2] Department of Respiratory Medicine, Wuhan Children's Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan City, Hubei Province, China; [3] Pediatric Respiratory Disease Laboratory, Institute of Maternal and Child Health, Wuhan Children's Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan City, Hubei Province, China; [4] University of Chinese Academy of Sciences, Beijing, China; [5] CAS Key Laboratory of Special Pathogens and Biosafety, Wuhan Institute of Virology, Center for Biosafety Mega-Science, Chinese Academy of Sciences, Wuhan City, Hubei Province, China; [6] Data Center, Wuhan Children's Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan City, Hubei Province, China.

[&] Joint first authors.

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Preplanned Studies

Trends in Respiratory Infectious Pathogens in Children Under the Age of 14 — Xiamen City, Fujian Province, China, 2017–2023

Jiali Cao[1,&]; Jie Pan[2,&]; Xiaoqing Yang[3]; Jumei Liu[1]; Min Zhu[1]; Zeyu Zhao[2]; Ling Chen[1]; Tianmu Chen[2,#]; Huiming Ye[1,#]

Summary

What is already known about this topic?

Respiratory infections pose a significant burden on public health. Despite recent outbreaks occurring in various locations, there is limited information available on the prevalence trends of multiple common respiratory pathogens in China beyond 2022.

What is added by this report?

A retrospective analysis was conducted on respiratory pathogen infections in a Xiamen hospital over a seven-year period. The analysis revealed fluctuating trends, with the number of infections for certain viruses initially decreasing after 2019, only to rebound to previous or higher levels. Recently, there has been an observed collective increase in positive cases for certain pathogens.

What are the implications for public health practice?

The study improves understanding of respiratory pathogens, primarily in Xiamen, with potential implications for the improvement of strategies for the prevention and management of respiratory infectious diseases.

Respiratory tract infections (ICD-10/J00-J99) are infectious diseases caused by various microorganisms, including bacteria, viruses, mycoplasmas, fungi, and parasites. These infections are typically seasonal and have been extensively studied. The implementation of dynamic control measures in China from 2020 to 2023 may have helped reduce the spread of other respiratory pathogens. Certain regions have experienced a delayed outbreak of respiratory viruses due to these interventions (*1*–*5*). However, most existing studies have mainly focused on the period from 2020 to early 2022. Timely surveillance is crucial for understanding community health threats, especially when observed trends deviate from seasonal norms. This study aims to assess changes in the epidemiological trends of common respiratory pathogens among children in recent years. We conducted a retrospective analysis of the prevalence of various common respiratory pathogens among patients with respiratory infections admitted to the Women and Children's Hospital, School of Medicine, Xiamen University, in Fujian Province from 2017 to 2023.

The study was conducted at the Women and Children's Hospital, School of Medicine, Xiamen University, which serves as a regional medical center for maternal and child healthcare in southwestern Fujian. The study retrospectively analyzed pediatric patients with respiratory tract infections who visited the hospital between January 1, 2017, and November 30, 2023. The inclusion criteria included children tested for pathogens (bacteria, virus, or mycoplasma) and excluded those above 14 years old or who didn't undergo pathogen testing. The study focused on detecting five viruses [Respiratory syncytial virus (RSV), adenovirus, influenza A (Flu A), influenza B (Flu B), parainfluenza], five bacteria (*H. influenzae*, *M. catarrhalis*, *S. pneumoniae*, *S. aureus*, *K. pneumoniae*) and *Mycoplasma pneumoniae*. The five viruses were detected by polymerase chain reaction (PCR) capillary electrophoresis fragment analysis (multiple detection kits for 13 types of respiratory pathogens, Ningbo Health Gene Technologies Co., Ltd, Ningbo, China), probe-based PCR (Respiratory virus nucleic acid six-fold test kit, Beijing Zhuo Cheng Hui Sheng Biotechnology Co., Ltd., Beijing, China) or immunofluorescence (D$^{®3}$ Ultra DFA Respiratory Virus Screening and ID Kit, Diagnostic Hybrids Inc., Athens, USA) with nasal swabs. *Mycoplasma pneumoniae* was detected by Probe-based PCR (*Mycoplasma pneumoniae* nucleic acid test kit, Daan Gene Co., Ltd, Guangzhou, China). Sputum was tested for typical bacteria using conventional culture

method. A total of 25,506 virus detection samples, 21,640 bacterial detection samples, and 23,579 pneumonia detection samples were collected. Trend analysis was conducted using GraphPad Prism and ArcGIS.

According to the current addresses of the patients included in the study, the majority (77.71%) were from Xiamen, while 18.38% were from other cities in Fujian Province, and 3.91% were from other provinces (Figure 1A). The annual distribution of these samples is shown in Figure 1C. The number of outpatient visits for respiratory infections exceeded one hundred thousand from 2017 to 2019, decreased in 2020 and 2021, and then increased again in 2022 and 2023 (Figure 1B). The prevalence of various viruses declined between 2019 and 2023. However, cases of some pathogen infections have returned to previous levels, and in some cases, have even exceeded previous levels. Of particular note is the unprecedented surge in cases of *Mycoplasma pneumoniae* in recent months.

As previously described, there have been changes in the epidemiology of respiratory infections in recent years. Our study observed a significant reduction in circulating respiratory pathogens, including major viruses, bacteria, and mycoplasma, in early 2020. Subsequently, several viruses demonstrated a "peak" pattern over the following three years, while bacteria did not exhibit such a pattern. Respiratory syncytial virus (RSV) emerged as the predominant virus in pediatric respiratory infections, with a surge in infections occurring after 2020, resulting in an infection peak higher than usual in July 2021 (Figure 2A). Adenovirus did not display a distinct seasonal pattern. Although a relatively large number of infected patients and increase in positive rates were seen in the summer of 2019, the number of infections has remained low in subsequent years. However, in recent months, there has been a steady increase in the number of adenovirus infections and positive rates, surpassing the previous years' levels (Figure 2C). Before 2020, influenza A and influenza B traditionally alternated in dominance. In 2020 and 2021, the number of influenza A and influenza B infections was low. However, in the 2022–2023 period, influenza B re-emerged, while influenza A experienced two peaks, with a higher number of infections than the pre-March 2020 timeframe. Notably, both the number of influenza A and B infections and positivity rates rose simultaneously last month (Figure 2E, 2G). Since the winter of 2020, there has been a significant increase in parainfluenza infections and positive rates (Figure 2I). Among the five bacteria of interest (*H. influenzae*, *M. catarrhalis*, *S. pneumoniae*, *S. aureus*, *K. pneumoniae*), there was no observable trend of post-decline

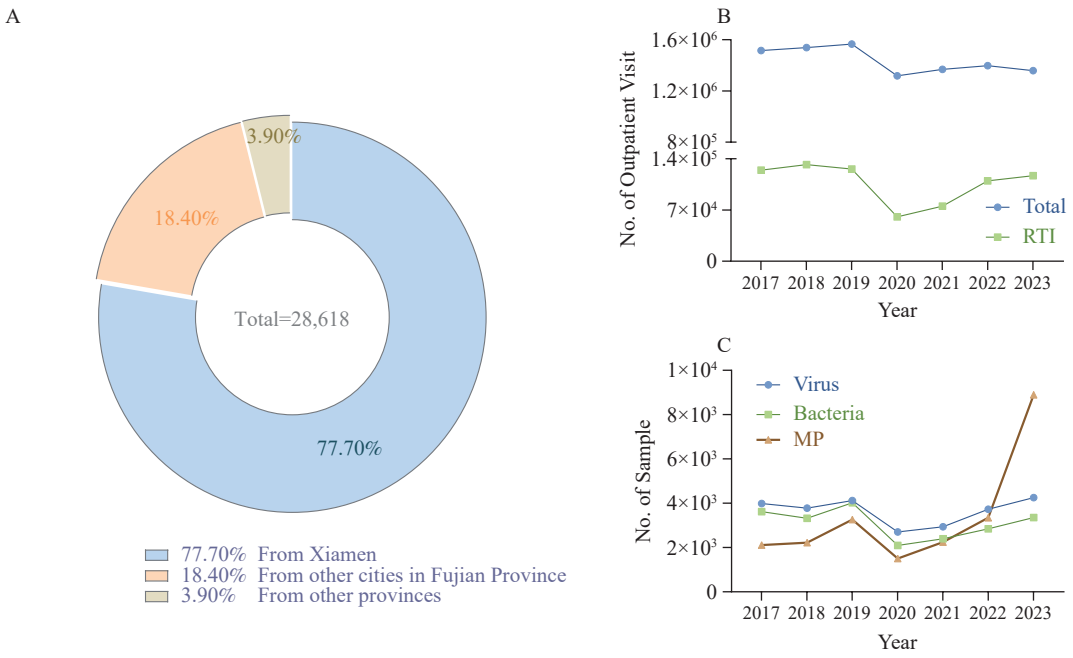

FIGURE 1. Information on the population and tested samples included in this study. (A) Distribution of patient sources included in this study; (B) total outpatient visits and visits for respiratory symptoms in the hospital over the past 7 years; (C) Number of samples tested for viruses, bacteria, and *Mycoplasma pneumoniae* in the last seven years.
Abbreviation: RTI=respiratory tract infection, MP=*Mycoplasma pneumoniae*.

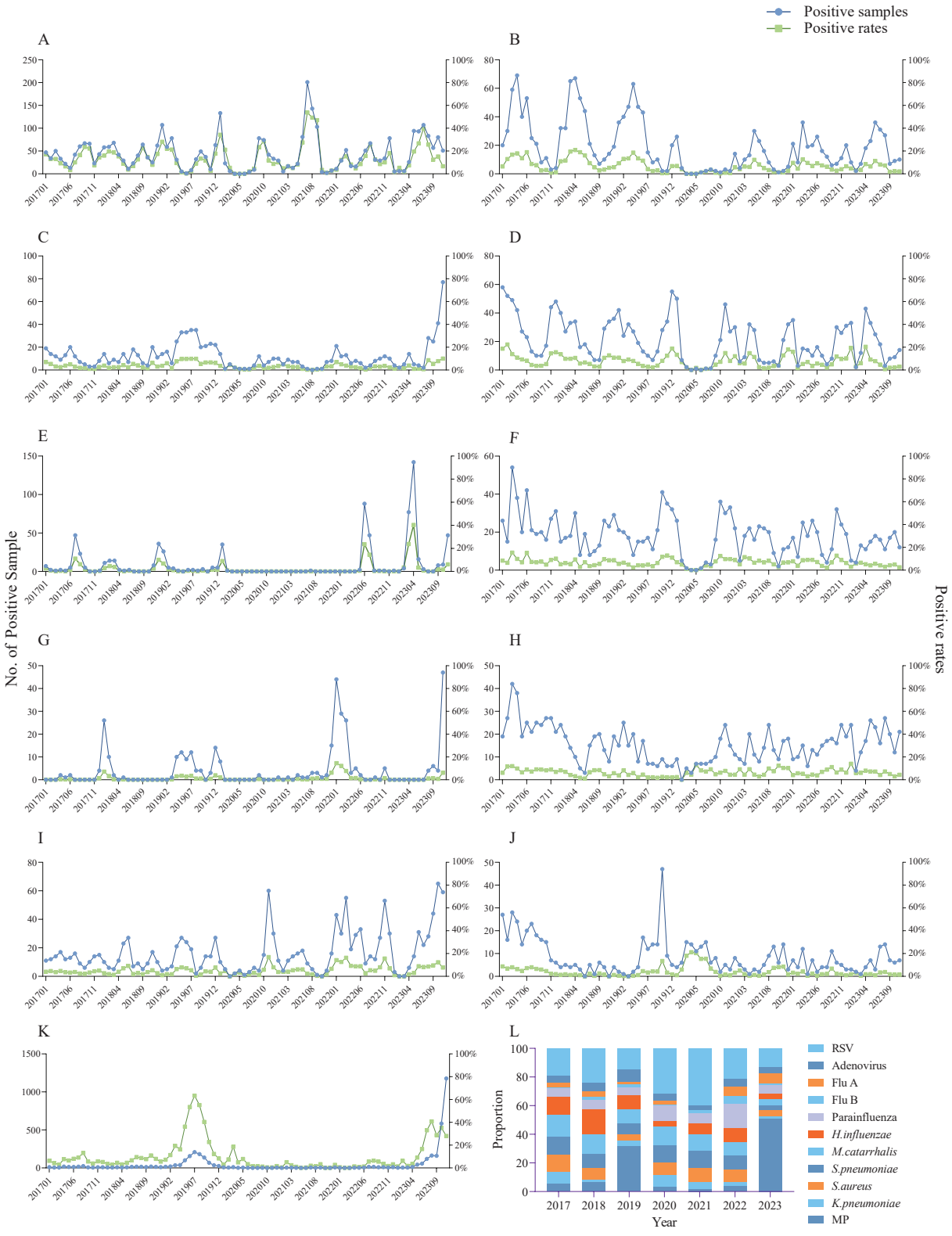

FIGURE 2. Changes in positive samples for different pathogens in the last seven years. (A) RSV; (B) *H. influenzae*; (C) Adenovirus; (D) *M. catarrhalis*; (E) influenza A; (F) *S. pneumoniae*; (G) Influenza B; (H) *S. aureus*; (I) Parainfluenza; (J) *K. pneumoniae*; (K) *Mycoplasma pneumoniae*; (L) Percentage of positive samples infected with different respiratory pathogens in different years (Number of positive samples for different pathogens divided by the sum of positive samples for all pathogens).
Abbreviation: RSV=respiratory syncytial virus.

"upsurge" (Figure 2B, 2D, 2F, 2H, 2J). The last significant outbreak of *Mycoplasma pneumoniae* occurred in 2019. After 2020, *Mycoplasma pneumoniae* infections remained at low levels until the second half of 2023. However, in the past two months, there has been a remarkable surge in *Mycoplasma pneumoniae* infections and positive rates, making it the primary pathogen in respiratory infections in 2023 (Figure 2K, 2L). It is important to note that cases where pathogenic microorganisms were not detected or could not be identified among patients were not included in Figure 2L.

DISCUSSION

The implementation of non-pharmaceutical interventions (NPIs) has played a significant role in reducing hospital utilization for respiratory tract infections (*4*,*6*–*7*). In this study, we conducted an analysis of major respiratory pathogens detected in our laboratory over a seven-year period. RSV, adenovirus, influenza A and B, parainfluenza, and *Mycoplasma pneumoniae* all exhibited "off-season" periods followed by surges, consistent with previous findings (*1*–*6*). Recent global surveillance data have indicated a resurgence of *Mycoplasma pneumoniae* infections in Europe and Asia (*8*). *Mycoplasma pneumoniae* infections occur year-round in various climates worldwide, with periodic epidemics every few years. Our study observed an outbreak of *Mycoplasma pneumoniae* in 2019, which took place from May to October, with the highest number of infections occurring in July. Additionally, Xiamen has experienced a recent re-emergence of *Mycoplasma pneumoniae*, with significantly more positive detections compared to 2019.

It is important to highlight that the findings of this study demonstrate an increase in the prevalence of *Mycoplasma pneumoniae* cases, as well as infections caused by various viruses in recent months. For instance, there was a surge in adenovirus infections starting from August 2023, surpassing previous levels. In addition, Influenza A reached peaks above previous levels in June 2022 and April 2023, respectively. Notably, there was a significant rise in positive cases of Influenza B in November and a substantial increase in parainfluenza viruses since the winter of 2020. These findings emphasize the need for monitoring and surveillance of these pathogens.

This study provides crucial epidemiological information on respiratory infections, including the seasonal and annual trends of various pathogens. First, this information can assist relevant authorities in enhancing their surveillance systems, increasing alertness, and disseminating early warning information to healthcare organizations and the public in a timely manner. By doing so, necessary measures can be implemented to control and prevent the spread of respiratory infections. Second, it can aid in optimizing the allocation and management of medical resources, ensuring timely diagnosis and accessible treatment. Lastly, identifying epidemiological trends in pathogens can guide clinicians in implementing targeted preventive measures, reducing the overuse of antibiotics, shortening the duration of medical care, and improving efficiency. The escalation in the number of infections has placed a significant burden on healthcare institutions, thus highlighting the urgent need for rapid pathogen diagnostics.

There are several limitations to this study. First, due to constraints in the laboratory testing projects, this study only analyzed the historical changes of 11 respiratory pathogens. Other common respiratory pathogens such as rhinovirus, human metapneumovirus, and bocavirus were not included. Additionally, some patients were not tested for all eleven pathogens, making it impossible to analyze co-infection scenarios. A positive test result does not necessarily indicate infection with the respective pathogen; it could be indicative of colonization. This study solely reported positive test results without distinguishing between colonization and infection. Second, this study did not differentiate between inpatients and outpatients or analyze patient symptoms. Therefore, it cannot determine if the observed increase in viral infections since 2020 has resulted in more severe disease outcomes. Lastly, the use of different pathogen detection methods in the laboratory over the course of this study's long time span limits the comparability of data. The viral epidemic trend observed can only be considered as a reference.

In conclusion, this study conducted a retrospective analysis to determine the prevalence of major respiratory pathogens over a seven-year period. The study focused on patients primarily from Xiamen, with some patients from other cities in Fujian Province and a few from other provinces. The findings provide important data on trends in respiratory pathogen prevalence. It was observed that there has been a concurrent increase in infections caused by different

viruses in recent months, highlighting the need for heightened attention.

Conflicts of interest: No conflicts of interest.

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[#] Corresponding authors: Tianmu Chen, 13698665@qq.com; Huiming Ye, yehuiming@xmu.edu.cn.

[1] Department of Laboratory Medicine, Fujian Key Clinical Specialty of Laboratory Medicine, Women and Children's Hospital, School of Medicine, Xiamen University, Xiamen City, Fujian Province, China; [2] State Key Laboratory of Vaccines for Infectious Diseases, Xiang An Biomedicine Laboratory, School of Public Health, Xiamen University, Xiamen City, Fujian Province, China; [3] Department of Pediatrics, Women and Children's Hospital, School of Medicine, Xiamen University, Xiamen City, Fujian Province, China.
[&] Joint first authors.

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Notes from the Field

A Case of an 86-Year-Old Male Survivor with Human Respiratory Syncytial Virus and SARS-CoV-2 Virus Coinfection

Lan Wang[1,&]; Jinren Pan[2,&]; Yajie Fu[3]; Haiyan Lou[4]; Yin Chen[5,#]; Yunmei Yang[1,#]; Shelan Liu[2,#]

As coronavirus disease 2019 (COVID-19) public health restrictions are relaxed, the circulation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) alongside other respiratory viruses may lead to an increased likelihood of coinfection (*1*). Older patients face a higher risk of severe outcomes, when infected with multiple respiratory viruses (*2*). This study highlights the successful recovery of the oldest older adult (≥80 years) from pneumonia caused by the dual infection of human respiratory syncytial virus (HRSV) and SARS-CoV-2.

On May 18, 2023, an 86-year-old male patient with a medical history of hypertension, prostate cancer, and prior SARS-CoV-2 vaccination was admitted to the single ward of the Department of Geriatrics, First Affiliated Hospital, Zhejiang University School of Medicine. The patient presented with symptoms of cough and shortness of breath that started three days prior to admission. On May 19, a chest computed tomography (CT) scan revealed acute inflammation in both lungs (Supplementary Figure S1A, available at https://weekly.chinacdc.cn/). On May 20 (Admission day 2), the patient developed a fever. Real-time polymerase chain reaction (RT-PCR) and metagenomic next-generation sequencing (mNGS) confirmed the patient's positive status for the HRSV-B subtype and SARS-CoV-2 (reinfection). The patient received treatment including high-flow nasal cannula oxygen therapy, aerosol inhalation of ipratropium bromide, budesonide, acetylcysteine, and other symptomatic care and excellent nursing service. His respiratory symptoms significantly improved, and a positron emission tomography/CT (PET/CT) scan on May 24 a showed notable reduction in lung inflammation (Supplementary Figure S1B). The patient fully recovered after a 13-day hospital stay. Table 1 displays all the clinical symptoms and signs.

The patient's sputum was collected on May 20 at the hospital and a respiratory viral panel using RT-PCR confirmed the presence of HRSV, while influenza A and B viruses were not detected. Several swab samples and sputum were collected from May 20 to May 30, and sent to Zhejiang Provincial Center for Disease Control and Prevention. The median duration of HRSV shedding was found to be 11 days (Supplementary Figure S2, available at https://weekly.chinacdc.cn/). The HRSV strain identified in this patient was identified as HRSV-B. Sputum collected on May 24 tested negative for SARS-CoV-2, while samples collected on May 26, 28, and 29 tested positive (Supplementary Figure S2). A follow-up RT-PCR test for COVID-19 conducted on June 10 yielded a negative result. A sputum sample collected on May 29 was subjected to mNGS analysis. The results revealed the presence of 85 reads for HRSV, 13,471 reads for SARS-CoV-2, and 60 reads for *Aspergillus fumigatus* (Table 1).

To further investigate the transmission of HRSV in this elderly case, we collected throat swabs from two medical workers, one bedside caregiver, and 40 inpatients on the same floor. All 43 samples tested negative for HRSV using RT-PCR, except for the sample from the bedside caregiver. The caregiver, a 23-year-old woman without symptoms and no personal protective equipment (PPE), tested positive for HRSV-B on May 24 (Ct value =32.0) (Supplementary Figure S3, available at https://weekly.chinacdc.cn/). She had received a SARS-CoV-2 vaccination and tested negative for SARS-CoV-2.

We also took five swabs from the ward environment on May 20, and one swab collected from the bathroom tested positive for HRSV (Ct value =36.8) (Supplementary Figure S3).

We obtained the second hypervariable region (HVR2) sequences of the HRSV G gene from the elderly patient, the bedside caregiver, and one positive environmental sample. Phylogenetic analysis revealed that all three sequences belonged to the HRSV B/BA9 genotype, with 99.68% amino acid sequence similarity.

Previous studies have shown that older patients with multiple respiratory pathogens are at a higher risk of experiencing worse outcomes (*2–4*). However, this case report describes a rare coinfection of HRSV-B/BA9 and SARS-CoV-2 in the oldest known patient, which

TABLE 1. Symptoms and results of pathogenic testing in the case of an elderly man with dual infection of HRSV and SARS-CoV-2 virus in Hangzhou, Zhejiang Province in May 2023.

Item		In community				In hospital													
		May 14	May 15	May 16	May 17	May 18	May 19	May 20	May 21	May 22	May 23	May 24	May 25	May 26	May 27	May 28	May 29	May 30	May 31
Symptoms	Fever							38 °C									37.3 °C		
	Fatigue							√	√	√	√								
	Rhinorrhea						√	√											
	Sore throat																		
	Cough		√	√	√	√	√	√	√	√	√	√	√	√	√	√			
	Productive cough							√ (Yellow)	√ (Yellow)	√ (Yellow)	√ (Yellow)	√ (White)	√ (White)	√ (White)	√ (White)				
	Wheeze																		
	Shortness of breath		√	√	√	√	√	√	√	√									
	Loss of appetite							√	√	√	√								
	Nausea																		
	Abdominal discomfort							√	√										
Signs	Throat congestion							√	√										
	Lung rales									√	√	√	√	√	√				
Pathogen findings																			
Influenza A and B (RT-PCR)								Sputum /-											
HRSV (RT-PCR)								Sputum /+			Throat swab/ Sputum /HRSV-B (+)	Sputum / HRSV-B (+)		Sputum / HRSV-B (+)		Sputum / HRSV-B (+)	Sputum / HRSV-B (+)	Sputum / HRSV-B (-)	
SARS-CoV-2 (RT-PCR)												Sputum /-		Sputum /+		Sputum /+	Sputum /+		
mNGS																	Sputum / HRSV + SARS-CoV-2 + Aspergillus fumigatus +		
Bacterial culture of sputum specimens								Sputum /-			Sputum /-			Sputum /-			Sputum /-		
Date		May 14	May 15	May 16	May 17	May 18	May 19	May 20	May 21	May 22	May 23	May 24	May 25	May 26	May 27	May 28	May 29	May 30	May 31

Note: +: Positive; -: Negative.

Abbreviation: HRSV=human respiratory syncytial virus; mNGS=metagenomic next-generation sequencing; RT-PCR=real-time polymerase chain reaction; SARS-CoV-2=severe acute respiratory syndrome coronavirus 2.

did not necessarily increase the clinical severity, but instead prolonged the hospital stay (13 days *vs*. 7 days) (*5*). This finding can be explained by several factors. First, the patient in this case was diagnosed with HRSV infection two days after admission, enabling early initiation of proper treatment and receiving excellent healthcare services from a highly skilled professional team. Second, infections with HRSV-B genotype typically have lower disease severity scores compared to HRSV-A infections (*6*–*7*). Lastly, the patient in this case experienced a reinfection with SARS-CoV-2 six months after the initial natural infection and vaccination against SARS-CoV-2, which can provide protection against severe SARS-CoV-2 infection and COVID-19-related death (*8*–*9*).

This study has important implications for public health policies. First, older patients should take precautions to reduce their risk of exposure to respiratory viruses and prevent the spread of respiratory infections. This includes measures such as isolation in a single room, adherence to hand hygiene and PPE by healthcare workers, and caregivers. Second, early and accurate multi-etiologic diagnosis, along with prompt antiviral and symptomatic treatment, should be prioritized in order to improve clinical outcomes in older patients. Lastly, our study highlights the need to increase vaccination coverage for preventable respiratory infections, including influenza, SARS-CoV-2, HRSV, etc., in order to reduce morbidity and mortality among the elderly population.

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[#] Corresponding authors: Yunmei Yang, 1194070@zju.edu.cn; Shelan Liu, liushelan@126.com; Yin Chen, yinch@cdc.zj.cn.

[1] Department of Geriatrics, First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou City, Zhejiang Province, China; [2] Department of Infectious Diseases, Zhejiang Provincial Center for Disease Control and Prevention, Hangzhou City, Zhejiang Province, China; [3] Department of Laboratory Medicine, First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou City, Zhejiang Province, China; [4] Department of Radiology, First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou City, Zhejiang Province, China; [5] Department of Microbiology, Zhejiang Provincial Center for Disease Control and Prevention, Hangzhou City, Zhejiang Province, China.

[&] Joint first authors.

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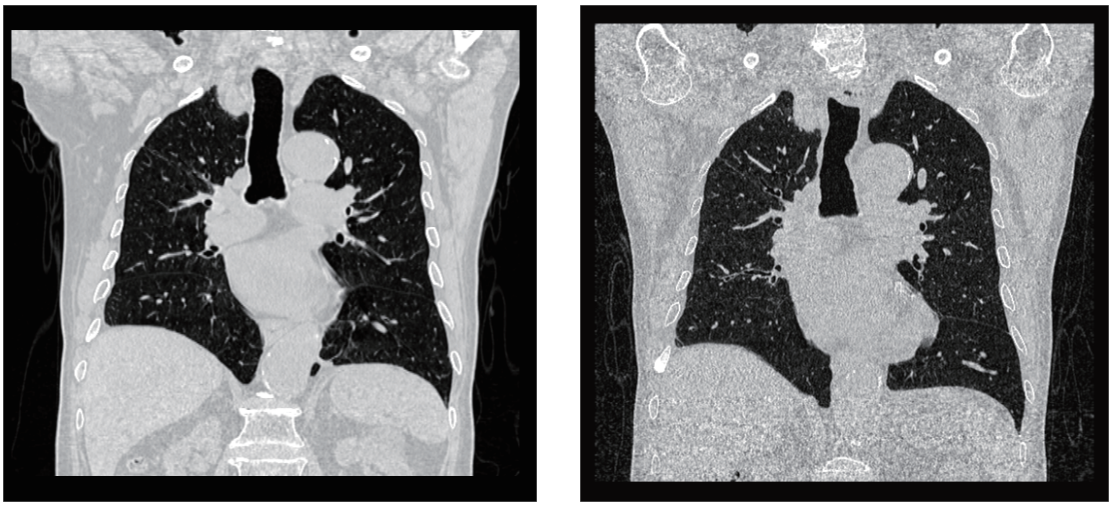
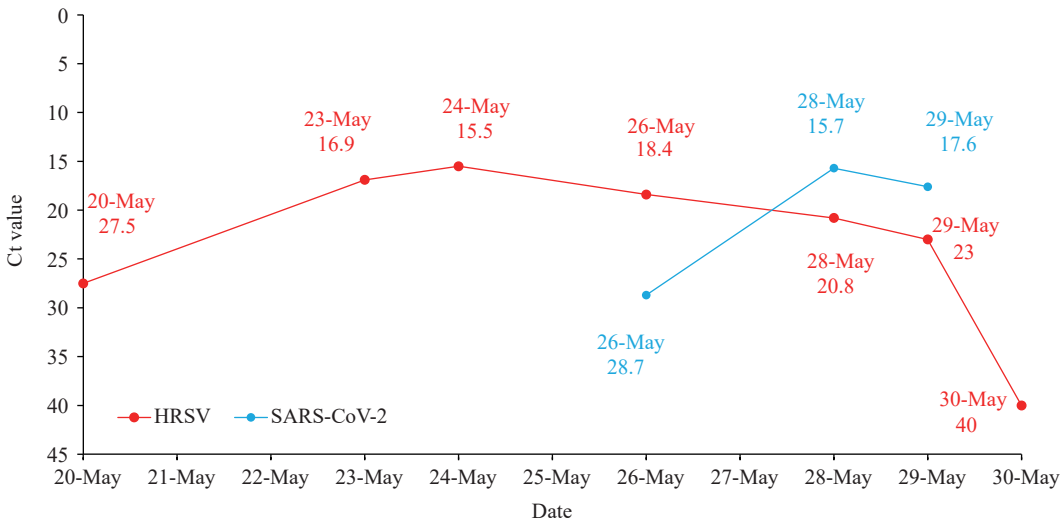
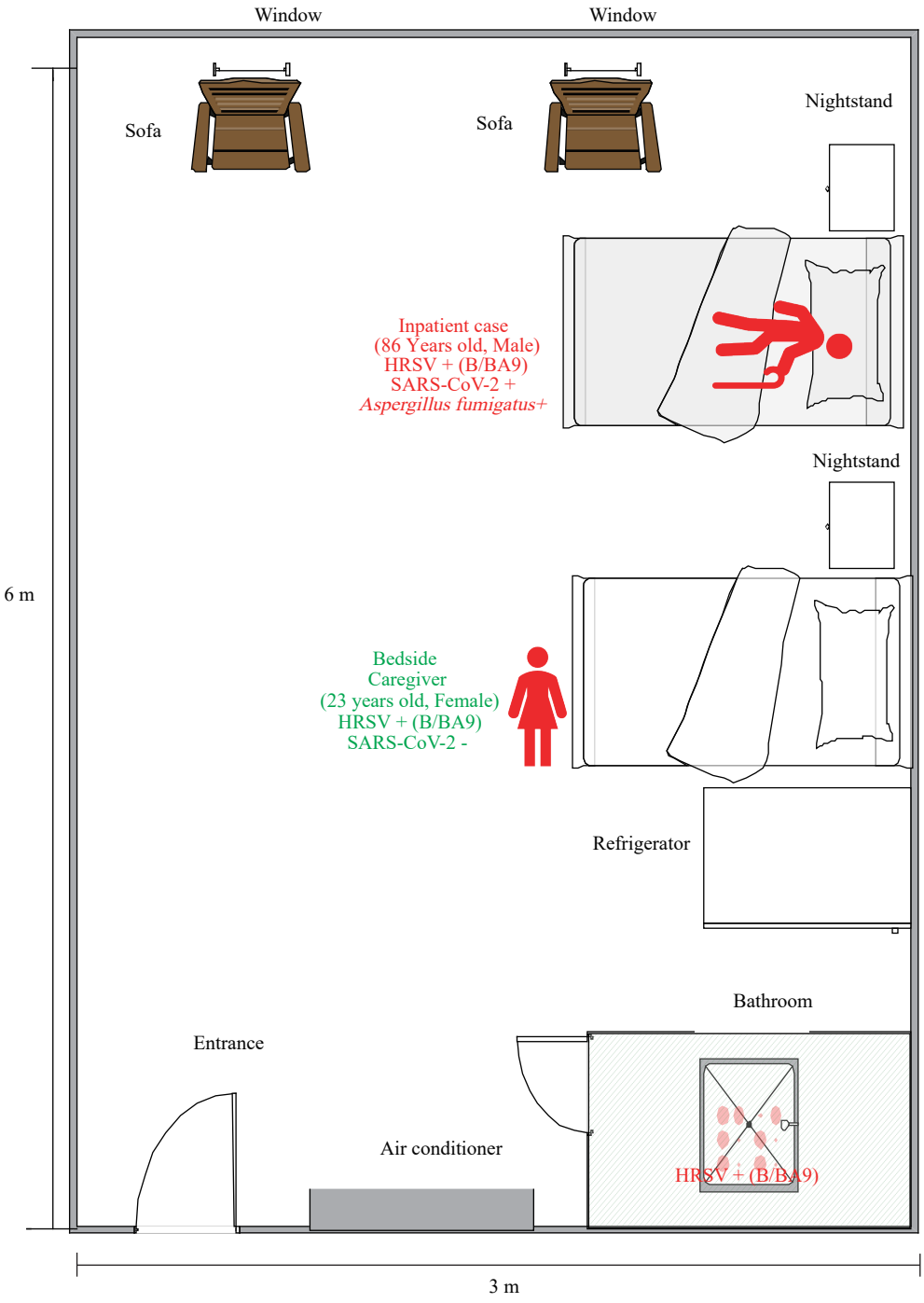
SUPPLEMENTARY MATERIAL



SUPPLEMENTARY FIGURE S1. Chest CT and PET/CT images of an elderly man coinfected with HRSV and SARS-CoV-2, obtained on May 19 and 24, 2023, respectively, in Zhejiang Province, China.
Note: Panel A shows a CT scan of the elderly patient's chest obtained on Day 1 (Day 1 = day of admission). The image indicates bronchiectasis in the upper lobe and middle lobe of the right lung and the lower lobe of both lungs, cystic bronchiectasis, and bullae formation under the pleura. Diffuse miliary nodules appear in both lungs, evenly distributed, involving the subpleural area. There is bilateral pleural thickening with nodules, calcifications, and interlobar pleural thickening with multiple subpleural nodules. In Panel B, a PET/CT scan of the elderly patient's chest obtained on Day 6 of admission shows that the pneumonic lesions in the right upper lobe and those previously present on the left side demonstrate pronounced absorption and improvement compared to before treatment.
Abbreviation: CT=computed tomography; PET/CT=positron emission tomography/CT; HRSV=human respiratory syncytial virus; SARS-CoV-2=severe acute respiratory syndrome coronavirus 2.



SUPPLEMENTARY FIGURE S2. Ct values for detection of HRSV and SARS-CoV-2 during the hospital stay of an elderly man coinfected with HRSV-B and SARS-CoV-2 from May 18 to May 31, 2023.
Note: Ct-values of RT-PCR >40 were considered negative for HRSV and SARS-CoV-2.
Abbreviation: HRSV=human respiratory syncytial virus; RT-PCR=real-time polymerase chain reaction; SARS-CoV-2=severe acute respiratory syndrome coronavirus 2.



SUPPLEMENTARY FIGURE S3. Diagram of the ward in which the elderly man coinfected with HRSV-B and SARS-CoV-2 shared HRSV-B with a bedside caregiver infected in the same room from May 18 to 31, 2023, in Zhejiang Province, China.
Note: +: Positive; -: Negative. Red dots mean HRSV positive.
Abbreviation: HRSV B=human respiratory syncytial Virus B genotype; SARS-CoV-2=severe acute respiratory syndrome coronavirus 2

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