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Editorial

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Changing epidemiology of respiratory pathogens since 2020: Shenzhen case study and global perspectives

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SUMMARY: The coronavirus disease 2019 (COVID-19) pandemic fundamentally disrupted global respiratory virus epidemiology through widespread non-pharmaceutical interventions. Analysis of a tertiary hospital in Shenzhen (2021-2024) reveals profound alterations in seasonal patterns. Influenza A exhibited multiple atypical peaks including summer circulation, while influenza B showed delayed resurgence with sustained winter activity. Respiratory syncytial virus demonstrated altered seasonality with substantial warm-season transmission replacing traditional winter patterns. World Health Organization (WHO) global surveillance confirmed parallel worldwide trends. Influenza activity collapsed dramatically in 2021 before resurging with irregular timing and unprecedented intensity through 2025. Respiratory syncytial virus exhibited off-season epidemics across multiple regions before gradually re-establishing modified seasonal patterns at elevated baseline levels. These epidemiological shifts resulted from immunity gaps created by reduced viral exposure, staggered lifting of pandemic restrictions across regions, and viral competition dynamics. Emerging technologies including AI-driven prediction models, expanded wastewater surveillance systems, and universal vaccine development offer promising approaches for managing future respiratory disease dynamics in this evolving post-pandemic landscape.

Keywords: respiratory viruses, epidemiological shift, seasonality

1. Introduction

The COVID-19 pandemic represents an unprecedented natural experiment in respiratory virus epidemiology. Widespread implementation of non-pharmaceutical interventions during 2020-2021 drastically suppressed seasonal respiratory viruses globally, creating historical circulation nadirs. However, subsequent relaxation of restrictions triggered atypical resurgences characterized by altered seasonality, irregular peak timing, and amplified disease burden. Understanding these epidemiological shifts holds critical implications for future surveillance strategies, vaccine development, and public health preparedness. This study analyzes local hospital surveillance data from Shenzhen (2021-2024) alongside global World Health Organization (WHO) monitoring systems to characterize post-pandemic respiratory virus dynamics, elucidate underlying mechanistic drivers, and identify emerging technologies for enhanced epidemic forecasting and control.

2. Local epidemiological patterns: Shenzhen hospital surveillance data (2021-2024)

A retrospective observational analysis was conducted on laboratory testing data from 101,151 patients with influenza-like illness (ILI) or severe acute respiratory infection (SARI) at Shenzhen Third People's Hospital (January 2021–December 2024). The study evaluated temporal detection patterns of seven respiratory viral pathogens: Influenza A virus (IAV) and influenza B virus (IBV), respiratory syncytial virus (RSV), adenovirus, rhinovirus (RV), and parainfluenza virus type I (PIV-I) and parainfluenza virus type III (PIV-III). The study primarily evaluated changes in the detection counts of six viral respiratory pathogens. Data from Shenzhen Third People's Hospital (2021–2024) reveal substantial year-to-year changes in respiratory virus activity (Figure 1). IAV was virtually undetected in 2021 but rebounded in subsequent years. Mid-2022 saw an atypical summer outbreak with elevated case counts peaking in June. IAV

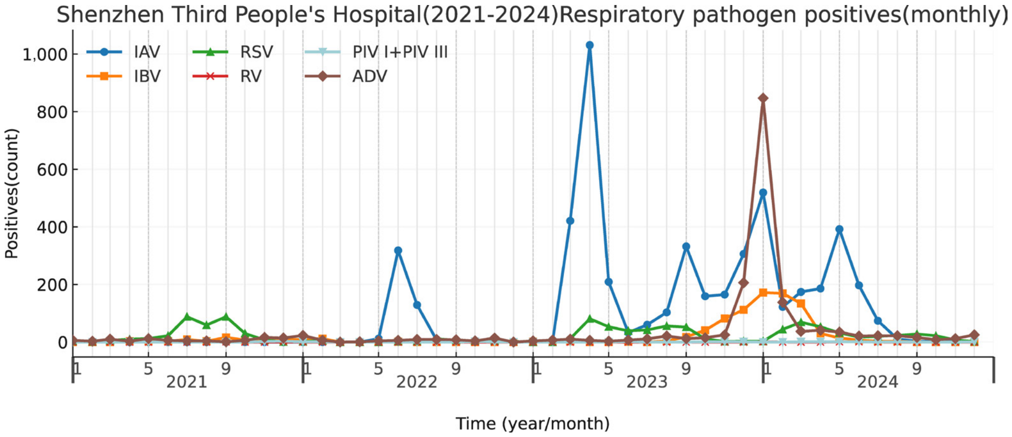

Figure 1. Monthly test-positivity rates for IAV, IBV, RSV, PIV I+III and ADV at Shenzhen Third People's Hospital, 2021–2024.

activity surged dramatically in 2023, with a spring peak in April recording 1,031 positive cases. Following this spring maximum, sustained autumn activity continued through November, culminating in a winter wave from December 2023 through February 2024 that peaked in January (519 cases). A subsequent spring to early summer increase occurred in 2024, reaching its highest point in May (392 cases), before declining rapidly by August and remaining at minimal levels throughout autumn (fewer than 15 cases monthly from August through December). Annual IAV case totals rose from near-zero in 2021 to higher levels in 2022, then surged in 2023 and remained elevated in 2024, demonstrating multiple seasonal peaks within individual years. IBV exhibited delayed resurgence. IBV remained at negligible levels through 2022. A substantial wave emerged in late 2023, with November 2023 recording increased cases. This wave peaked in January 2024 with 172 positive cases and persisted through February 2024 (169 cases), representing the first major IBV activity in the city since the pandemic onset. Following this sustained winter peak, IBV declined to very low levels by mid-2024 but remained at moderately higher baseline levels compared to the 2021–2022 period.

RSV exhibited altered seasonality throughout the observation period. In July 2021, RSV case counts surged to elevated summer levels (88 cases). RSV detections remained subdued throughout 2022. In 2023, activity continued to show atypical seasonal distribution, with April recording 81 positive cases and late summer showing additional increases. In 2024, RSV cases increased during spring, peaking in March (69 cases). These patterns indicate that RSV demonstrated altered seasonal characteristics in Shenzhen during 2021–2024, with substantial activity persisting in warmer months. Adenovirus (ADV) remained at low levels during 2021–2022 but experienced a concentrated outbreak from December 2023 through early 2024. This winter surge began in December 2023 (206 cases), peaked in January 2024 (847 cases), remained elevated in February 2024 (138 cases), and declined by March–April (37-41 cases). This outbreak represents a substantial increase in ADV circulation compared to earlier pandemic years, likely reflecting accumulated susceptibility during China's prolonged COVID-19 control measures through December 2022. RV, PIV-I, and PIV-III maintained relatively low case counts throughout the observation period without substantial surges comparable to other pathogens.

Overall findings demonstrate altered seasonal patterns from the pandemic period (2021–2022) to post-pandemic years (2023–2024). IAV exhibited multiple peaks within individual years, with major spring 2023 activity, sustained autumn circulation, and winter 2023 increases. IBV showed delayed resurgence with a sustained winter 2023 peak. RSV peaked during summer and spring periods rather than winter. Multiple pathogens co-circulated at significant levels during 2023–2024. Although these data offer valuable insights into local respiratory virus dynamics, this analysis was conducted at a single tertiary care center and predominantly included patients seeking care for acute respiratory symptoms. As such, hospital-based case counts may not fully capture the broader patterns of community transmission.

3. Global surveillance evidence: WHO data analysis (2020-2025)

Globally, influenza activity experienced unprecedented disruption during the COVID-19 pandemic, followed by atypical recovery patterns that fundamentally altered traditional seasonal rhythms. Global influenza and respiratory syncytial virus surveillance data from January 2020 to August 2025 were obtained from the Global Influenza Surveillance and Response System (GISRS) (Figure 2). During January and February 2020, global influenza positivity rates exceeded 40%, with positive specimens exceeding 180,000 monthly. Following widespread non-pharmaceutical interventions, activity collapsed from March 2020 onward, declining to 18.6% positivity. Throughout 2021, influenza remained at

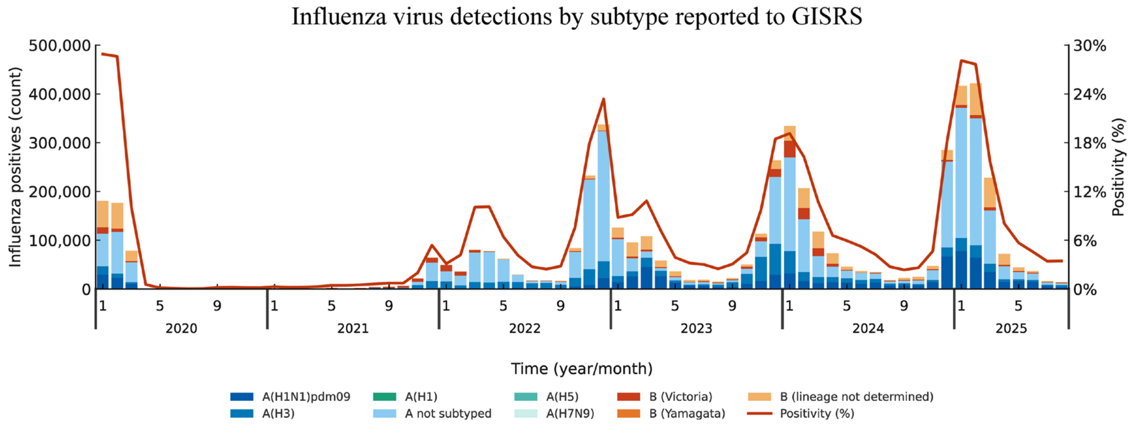

Figure 2. Influenza virus detections by subtype reported to GISRS, January 2020–August 2025.

historically low levels with an annual positivity rate of only 1.70% and total annual detections of 114,863 specimens. December 2021 exhibited a modest rebound with 64,776 cases, indicating initial stirring of circulation. March 2022 showed a secondary transitional peak before the true resurgence began in October 2022. November and December 2022 recorded sharp peaks with 232,910 and 337,079 positive specimens respectively, occurring one to two months earlier than traditional patterns. Activity declined through early 2023 but extended into April 2023, forming a secondary spring elevation. The 2023/24 season exhibited more conventional winter rhythms, peaking during December 2023 and January 2024 with 263,948 and 334,173 specimens respectively. However, the 2024/25 season demonstrated the highest recorded peaks in the entire surveillance period. December 2024 recorded 285,394 cases, followed by January and February 2025 reaching unprecedented levels with 417,206 and 421,509 positive specimens respectively. The five highest monthly case counts all occurred from December 2022 onward, demonstrating exceptional intensity of post-pandemic resurgence and ongoing instability in seasonal timing.

As pandemic restrictions were relaxed, atypical resurgences of these viruses were observed. Many regions saw off-season or earlier-than-usual outbreaks. In the United States and Europe, the influenza season of 2021–2022 was delayed and relatively mild, but the 2022–2023 season was early and intense, with influenza and RSV cases peaking roughly one to two months earlier than pre-pandemic norms (*1*). In some areas, multiple waves occurred within a single year. Australia and parts of East Asia noted significant influenza circulation during their summer months, a phenomenon virtually unheard of prior to COVID-19 (*2*). One study from India documented an unusual influenza surge in June through September 2022 instead of the usual winter peak. RSV peaked in autumn 2022 instead of spring (*3*). Similarly, Latin America reported altered timing of influenza. Chile saw early influenza outbreaks beginning in January 2022 ahead of the typical winter schedule. Brazil experienced unusual influenza activity in the off-season period of August through October 2022 (*4,5*). These observations underscore a shift in seasonality on a global scale.

Influenza type and subtype composition underwent significant reorganization. Influenza A maintained stable dominance, increasing from 65.4% in 2020 to 93.4 percent in 2022, then consistently representing 78% to 82% during 2023 through 2025. Influenza B remained suppressed at 6.6% in 2022 and generally below 22% subsequently. A critical progressive shift in influenza A subtype dominance occurred from 2021 through 2025, though interpretation is constrained by high proportions of A not subtyped specimens ranging from 63% to 76% annually. Among subtyped specimens, A(H3N2) clearly predominated during 2021 and 2022. A transitional phase emerged in 2023 when the relative proportions of A(H3N2) and A(H1N1)pdm09 converged closely, signaling an emerging shift in subtype dominance. This transition solidified in 2024 and strengthened further through 2025, with A(H1N1)pdm09 establishing clear dominance over A(H3N2) during this later period. Within influenza B detections, B/Yamagata effectively disappeared with 0% detection from 2022 onward, while B/Victoria persisted as the sole circulating lineage at reduced levels. These patterns demonstrate the complex interplay between pandemic control measures, immunity gaps, and viral competitive dynamics reshaping global influenza epidemiology.

The circulation hiatus created by pandemic measures left populations with varying levels of protective antibodies against H3N2, H1N1, and influenza B viruses. Viral strains encountering cohorts with reduced immunity gained competitive fitness advantages, resulting in strain-specific outbreak patterns (*6*). Such patterns were reported in 30 EU/EEA countries during the 2022/23 influenza season, where an atypical bi-phasic epidemic pattern emerged with co-circulation of A(H1N1)pdm09 (36%), A(H3N2) (64%), and B/Victoria lineage viruses, characterized by an initial influenza A-dominated peak followed by an influenza B-dominated peak, while B/Yamagata lineage remained absent for the third consecutive season (*7*).

RSV has also shown globally altered behavior. WHO weekly RSV surveillance data aggregated globally (January 2020–August 2025) revealed that overall activity was markedly suppressed in 2020, followed by an off-season resurgence in 2021 peaking in November, indicating pronounced seasonal displacement (Figure 3). From 2022 through 2024, seasonality progressively re-established with winter peaks occurring in December each year, and epidemic intensity exceeded the suppressed 2020 baseline. In 2025, activity peaked in January before declining to moderate–low levels through August, yet background transmission remained elevated compared to the 2020 baseline, consistent with re-balanced seasonality on a moderately elevated baseline. Numerous countries experienced out-of-season RSV epidemics in 2021 or 2022. For example, an off-season summer RSV wave occurred in Western Europe and the United States in mid-2021 when restrictions were briefly loosened. Post-2020, RSV seasons have often started earlier and been more intense compared to pre-pandemic years. Intensified circulation of RSV and associated hospital burden in the EU/EEA (*8*). Data from a study in Mexico indicated that RSV outbreaks post-pandemic began weeks earlier than usual and with higher case counts, consistent with the notion of an accumulating cohort of RSV-naive infants born during lockdown periods (*9*). By 2023–2024, there are signs that RSV seasonality is gradually realigning with its previous schedule in some regions, but the overall trend has been erratic timing and larger susceptible populations (*10,11*).

Other respiratory viruses experienced similar disruptions, including parainfluenza, seasonal coronaviruses, adenovirus, human metapneumovirus, and rhinovirus. Recovery patterns varied considerably across different pathogens. Non-COVID coronaviruses and rhinoviruses were among the first to return to near-normal circulation, frequently causing summer colds as early as 2021 (*12*). In contrast, certain viruses have not fully returned to their prior patterns. Reports suggest some seasonal viruses are still finding a new equilibrium. For example, one analysis noted that some respiratory pathogens "failed to return to pre-pandemic seasonality" even by 2023. Adenoviruses have been increasingly reported worldwide, including outbreaks of adenoviral respiratory illness in children after 2021, possibly due to lowered immunity and more frequent testing (*13*). Globally, respiratory virus epidemiology has undergone an uneven resetting process, with surge patterns shaped by regional variations in COVID-19 control measures and their subsequent relaxation.

4. Drivers of epidemiological shifts since 2020

Multiple factors underlie these epidemiological shifts. The foremost driver was the implementation of non-pharmacological interventions (NPIs) during the COVID-19 pandemic, which drastically reduced transmission opportunities for other respiratory viruses (*14*). Measures such as mask wearing, school and daycare closures, travel limitations, improved hand hygiene, and crowd avoidance broke the typical chains of infection for flu, RSV, and others. This resulted in historically low incidences in 2020–2021. A positive outcome was fewer respiratory infections during that period, but a side effect was the creation of an "immune debt" in the population (*15*). Because people were not exposed to these common viruses for one or two seasons, a larger susceptible pool accumulated. Once restrictions lifted, those viruses could spread more easily among immunologically naïve groups, leading to larger outbreaks than normal.

The staggered lifting of COVID-19 measures across different regions and times also contributed to out-of-

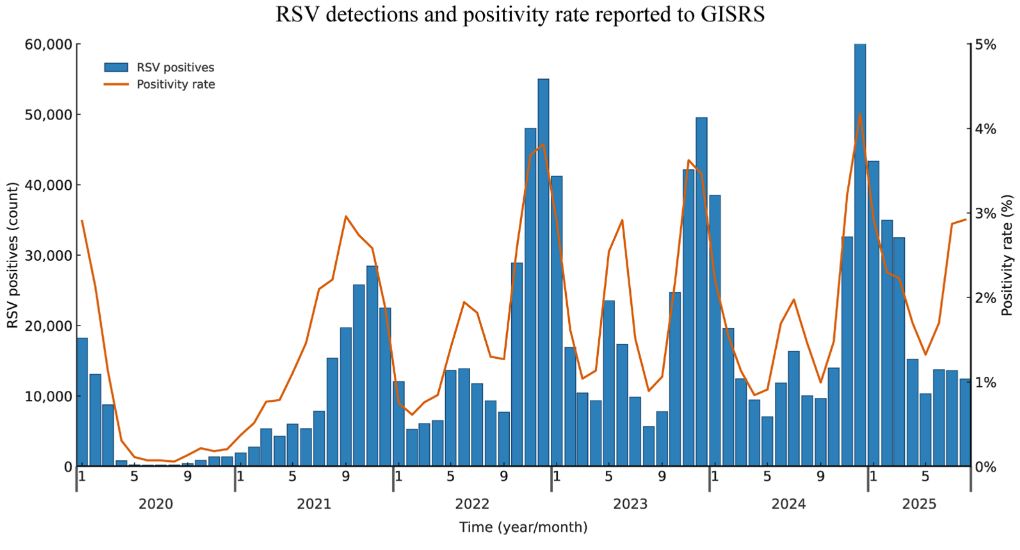

Figure 3. RSV detections and positivity rate reported to GISRS, January 2020–August 2025.

phase outbreaks. When one country or region relaxed interventions earlier than others, it often experienced an off-season resurgence of viruses. For example, Japan's early relaxation in mid-2021 coincided with a summer influenza outbreak there, and similarly, parts of China that eased measures in 2022 saw unseasonal flu waves. Each region's trajectory depended on when and how rapidly normal social mixing resumed, which explains why the timing of post-pandemic surges varied globally (*16,17*).

Viral interference and competition may have also played a role. During the pandemic, SARS-CoV-2 was the dominant circulating respiratory virus, and its high prevalence might have competitively suppressed other viruses to some extent (*via* viral interference mechanisms or simply by occupying ecological niches). As the prevalence of COVID-19 oscillated, other viruses found opportunities to resurge when COVID-19 waves subsided. There is some evidence that influenza and RSV did not significantly co-circulate with large COVID surges, but when COVID incidence dropped, flu and RSV filled the void (*18*). In late 2022, a "tripledemic" of COVID-19, influenza, and RSV was noted in some countries, suggesting that eventually co-circulation can occur, but the initial re-emergence dynamics were likely influenced by such interactions(*19*).

Changes in healthcare-seeking and testing during the pandemic also affected reported epidemiology. Routine surveillance was disrupted in many places, and people avoided hospitals except for severe illness. This led to under-detection of mild cases early in the pandemic. Later, increased testing (through multiplex PCR panels) meant that some viruses (like adenovirus or metapneumovirus) were detected more than before, which could partly contribute to higher case counts post-2020. However, the consensus is that true circulation changes (not just detection artifacts) occurred for major pathogens, given consistent signals from multiple locations.

In summary, the shifts since 2020 have been driven by a combination of behavioral, immunological, and virological factors. NPIs created a lull and subsequent rebound. Immunity gaps made populations more vulnerable when viruses returned. The synchronization of seasonal cycles was lost and is still readjusting. These drivers emphasize the interconnected nature of respiratory pathogen dynamics and how large-scale interventions can reset endemic disease patterns.

5. Emerging technologies for enhanced surveillance and prevention

AI-driven viral prediction technologies are fundamentally transforming influenza vaccine development paradigms. MIT's VaxSeer system, the Beth-1 model, and the University of Missouri's MAIVeSS framework represent three distinct yet complementary technical approaches. VaxSeer's core advantage lies in using large protein language models to learn combinatorial mutation effects (*20*). Traditional methods analyze single amino acid mutations independently. VaxSeer captures synergistic interactions between multiple mutation sites. This approach better reflects the reality of viral evolution. In 10-year retrospective evaluations, vaccine strains selected by VaxSeer consistently showed superior genetic matching compared to WHO-recommended strains. More importantly, VaxSeer can predict dominant influenza strains months in advance. This provides valuable lead time for vaccine production. Beth-1 employs site-specific mutation fitness modeling (*21*). The model can calibrate mutation transition times and project fitness landscapes into the future. MAIVeSS compresses vaccine strain selection time from months to days (*22*). It also predicts yield potential of candidate viruses.

Wastewater surveillance has evolved from a COVID-19 emergency measure into a normalized population-level early warning system. The US CDC's National Wastewater Surveillance System (NWSS) now covers approximately 1,500 monitoring sites (*23*). The system monitors influenza A/B, RSV, SARS-CoV-2, and H5 avian influenza weekly. The core advantage of wastewater surveillance lies in providing viral concentration data within 24 hours. It captures viral shedding from asymptomatic individuals and those not seeking medical care. Most critically, it detects signals of increased viral activity before clinical cases appear. China conducted RSV wastewater surveillance in four regions: Yingkou, Xi'an, Nanchang, and Nanning. The research team first detected RSV RNA in fecal samples from 300 patients. This established patterns of viral excretion and concentration characteristics in feces. They then developed wastewater models based on these data. The research filled gaps in clinical surveillance. It provided local evidence for RSV vaccination strategy formulation (*24*). Additionally, China has conducted SARS-CoV-2 wastewater surveillance research. Coverage includes multiple cities such as Beijing, Shanghai, and Shenzhen (*25*). These studies established multi-level monitoring networks from community to city levels. This provided technical support for early warning and precise epidemic control.

Machine learning prediction models have achieved significant progress in outbreak forecasting. Rodriguez *et al.* developed feature-based time series classification methods (*26*). The study developed 32 prediction algorithms for identifying disease outbreak and non-outbreak situations. These algorithms predict by learning characteristic patterns from historical epidemic data. Accuracy rates exceed 90% on real-world datasets. A universal disease risk prediction system demonstrates powerful cross-disease prediction capabilities (*27*). The system integrates outbreak data from 43 diseases across 206 countries. The research team employed five different machine learning algorithms to build prediction models.

By integrating predictions from these algorithms, system accuracy reaches 80-90%. The system can predict risks across countries and diseases based on economic, cultural, social, and epidemiological factors.

Universal influenza vaccine development is a key breakthrough that will transform long-term prevention landscapes. WHO set clear standards in 2024 (*28*). Vaccines must work in all age groups, provide protection for at least 3 years against current circulating subtypes, and offer better protection than currently approved seasonal influenza vaccines. Current universal influenza vaccine research focuses primarily on immune targets in conserved viral regions. The EU-funded FLUniversal consortium is developing an intranasal universal influenza vaccine (*29*). The vaccine employs a prime-boost strategy, using attenuated live vaccine strains combined with conserved antigen design to induce broadly protective immune responses. The vaccine is expected to enter clinical trials in 2025. Success of universal vaccines will fundamentally transform influenza prevention strategies. It will eliminate the need for annual vaccine strain updates. It will provide more reliable protection barriers for global influenza pandemic preparedness. This will not only reduce costs of vaccine research and production. It will also ensure more timely protection when novel influenza viruses emerge.

6. Strategic recommendations for global health security

WHO's expansion of GISRS into a comprehensive surveillance platform covering influenza, RSV, and SARS-CoV-2 marks a new era for global surveillance systems. However, significant gaps in surveillance capacity persist between different countries and regions. The international community needs to establish more equitable technology transfer mechanisms. Development of open-source platforms and tools can lower technical barriers and facilitate technology dissemination globally. Data sharing remains a main obstacle to global cooperation. More transparent data governance frameworks need establishment. Clearly defining data usage scope and benefit distribution.

Improving influenza vaccination coverage represents a critical yet underutilized public health intervention. Annual vaccination provides substantial protection, yet global uptake remains insufficient. China's influenza vaccination rate reached only 2.94% in the 2020-2021 flu season compared to 48.4% in the United States (*30,31*) .This disparity reflects broader global inequities. High-income countries reach 40-50% coverage among priority populations. In contrast, only 34% of low- and lower-middle-income countries have policies supporting influenza vaccination, and these countries consume less than 5% of global vaccine supply (*32*). Seasonal influenza causes an estimated 290,000-650,000 respiratory deaths annually worldwide (*33*).Scaling up vaccination programs could substantially reduce disease burden. It would simultaneously strengthen pandemic preparedness infrastructure.

Building a resilient global respiratory disease prevention and control system requires systems thinking. Multi-level surveillance networks form the foundation of resilient systems. Community-level surveillance can detect abnormal signals earliest. National-level surveillance provides a holistic perspective. Global-level surveillance identifies cross-border transmission risks. Platform-based construction can improve system scalability. New pathogens and new surveillance technologies should be rapidly integrated into existing platforms. Rapid response capability determines system effectiveness. AI prediction technologies can help identify risks in advance. Wastewater surveillance provides early warning signals. But these technical advantages only matter when converted into actual public health actions. Adaptability is the most important characteristic of resilient systems. Systems must be able to continuously learn and improve. Interdisciplinary collaboration can bring innovative solutions. Only in this way can the world be truly prepared. Effectively addressing potential respiratory disease pandemic threats that may emerge in the future.

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