

Post-Pandemic Epidemiological Dynamics of Human Metapneumovirus in Hospitalized Children with Acute Respiratory Infections: A Multi-Center Study in Fujian Province, China (2019–2025)

Lixia Zhuang

Shaowu Municipal Hospital

Huakang Yao

Yongtai County General Hospital

Xing'an Ye

Shaowu Municipal Hospital

Lin Cai

Fuzhou Children's Hospital Affiliated to Fujian Medical University

Xiaoman Gao

Fuzhou Children's Hospital Affiliated to Fujian Medical University

Fucun Zhu

Fuzhou Children's Hospital Affiliated to Fujian Medical University

Yanying Fan

Fuzhou Children's Hospital Affiliated to Fujian Medical University

Jie Lin

Fuzhou Children's Hospital Affiliated to Fujian Medical University

Juan Lin

Fuzhou Children's Hospital Affiliated to Fujian Medical University

Zijian Wang

Changle District Maternal and Child Health Hospital of Fuzhou

Tingyao Guo

Fuqing Hospital Affiliated to Fujian Medical University

Xiuhua Liu

Lianjiang County General Hospital, Lianjiang

Qingyan Chen

Luoyuan County General Hospital

Chu Zhuo

Minhou County General Hospital

Jing Qian

Fuzhou Economic and Technological Development Zone Hospital

Lijuan Lin

Jian'ou Municipal Hospital

Guanglin Zhang

Sanming Second Hospital

Xiaochen Zhang

Gutian County General Hospital

Xiaoping Lai

Tingzhou Hospital of Fujian Province

Shaoting Chen

Fuzhou University Affiliated Provincial Hospital

Pengju Cao

pengjucao528@126.com

Fuzhou University Affiliated Provincial Hospital

Article

Keywords: human metapneumovirus, acute respiratory tract infection, hospitalized children, Air Quality Index, coinfection, post-pandemic

Posted Date: October 7th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10541131/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

Additional Declarations: No competing interests reported.

Abstract

Human metapneumovirus (HMPV) is a leading cause of paediatric acute respiratory infections, yet its post-pandemic epidemiology and environmental drivers remain unclear. In a retrospective multi-centre surveillance of 108,701 hospitalized children across Fujian, China (June 2019 – December 2025), HMPV was detected in 6.06% (6,589/108,701). Following near-elimination during pandemic restrictions, an atypical spring surge emerged in 2025, peaking at 36.84% positivity in March. Children aged 3–6 years had the highest rate (8.43% overall; 15.35% at surge), and post-pandemic positivity was higher in females ($P < 0.001$). Co-infection (25.71%) was dominated by rhinovirus. Positivity correlated positively with Air Quality Index and PM_{2.5}, and negatively with temperature measures. LASSO regression identified minimum temperature (negative) and AQI (positive) as the most stable predictors. Lower temperatures and poorer air quality are thus major drivers of HMPV circulation, with a seasonal shift from winter to spring – calling for environment-tailored prevention strategies in paediatric populations.

Introduction

Human metapneumovirus (HMPV) is a single-stranded negative-sense RNA virus in the family Pneumoviridae. It was first identified in 2001 by van den Hoogen and colleagues in nasopharyngeal aspirates from children with unexplained respiratory illnesses[1]. Since then, HMPV has become recognized as a major cause of acute respiratory tract infections (ARTIs) across all ages, hitting young children, the elderly, and immunocompromised individuals hardest[2, 3]. In 2018 alone, an estimated 14.2 million ARTIs, 643,000 hospital admissions, and 16,100 deaths among children under five years of age were linked to HMPV globally[4]. Despite this heavy burden, HMPV remains underdiagnosed and underappreciated in many clinical and public health settings—largely because its symptoms overlap with those of respiratory syncytial virus (RSV) and influenza, and because access to multiplex molecular diagnostics is still limited[5, 6].

In temperate regions, HMPV typically peaks in late winter and early spring[7]. Temperature, humidity, and other weather factors clearly shape its transmission. A study from Scotland, for example, showed that HMPV, along with RSV and influenza, thrives at low temperatures[8]. Research from South Korea has linked HMPV activity to temperature, wind speed, diurnal temperature range, and sunshine duration[9]. However, the connection between air quality—especially fine particulate matter like PM_{2.5}—and HMPV transmission has received much less attention than it has for RSV or influenza, even though air pollutants are known to increase viral susceptibility and worsen respiratory outcomes[10, 11].

The COVID-19 pandemic turned the circulation of nearly all common respiratory viruses upside down. Non-pharmaceutical interventions (NPIs)—masks, social distancing, school closures—suppressed HMPV almost completely during 2020–2021[12, 13]. As NPIs were lifted, viruses returned in an asynchronous wave, and HMPV rebounded particularly dramatically. A global analysis of 92 surveillance sites found a clear sequence: HMPV reappeared later than rhinovirus but earlier than influenza B [14]. In Western Australia, HMPV incidence tripled in 2021 compared with pre-pandemic years, mainly because a large cohort of children aged 1–4 years had never been exposed[15]. More importantly, post-pandemic HMPV seasons have strayed from the usual winter peak, showing off-season surges and shifted age distributions that challenge long-standing assumptions[16, 17]. Recent surveillance from China adds to the concern: HMPV-related paediatric hospitalisations in early 2025 were 17% higher than the same period two years earlier[18].

Fujian Province, in subtropical southeastern China, has mild winters, humid summers, and marked seasonal swings in air quality. Yet long-term, comprehensive data on HMPV epidemiology among hospitalized children in this region—spanning the pre-pandemic, pandemic, and post-pandemic eras—are scarce. In particular, the combined effect of meteorological factors (e.g., minimum temperature) and air quality indicators (AQI, PM_{2.5}) on HMPV activity has never been systematically evaluated here.

To fill these gaps, we conducted a multi-center surveillance study across 11 paediatric tertiary hospitals in five regions of Fujian Province, covering 6.5 years from June 2019 to December 2025. Our aims were: (i) to describe how HMPV positivity changed before, during, and after the COVID-19 pandemic; (ii) to break down HMPV infections by age and sex; (iii) to examine co-infection patterns with other respiratory pathogens; and (iv) to identify the key environmental drivers—weather, temperature, and air quality indices—associated with HMPV detection rates. We hope these findings will help guide targeted prevention and resource allocation for paediatric HMPV infections in the post-pandemic era.

MATERIALS AND METHODS

Patients and specimens

This retrospective multicenter study included hospitalized children under 18 years old with acute respiratory tract infections (ARTIs) who had nucleic acid testing for 11 non-bacterial respiratory pathogens. The children were recruited from 12 hospitals across five regions of Fujian Province, spanning seven years from June 2019 to December 2025. All participating institutions were local pediatric medical centers: seven in Fuzhou (Lianjiang County General Hospital; Fuzhou Children's Hospital of Fujian Medical University; Changle District Maternal and Child Health Hospital; Luoyuan County General Hospital; Yongtai County General Hospital; Minhou County General Hospital; and Fuzhou Economic and Technological Development Zone Hospital), two in Nanping (Jian'ou Municipal Hospital and Shaowu Municipal Hospital), one in Sanming (Sanming Second Hospital), one in Ningde (Gutian County General Hospital), and one in Longyan (Tingzhou Hospital of Fujian Province). The study covered seven epidemic cycles, each running from March through February of the following year. All participating hospitals are regional pediatric referral centers.

ARTI diagnosis followed the 8th edition of Zhu Futang's Practical Pediatrics. Upper respiratory tract infection (URTI) required at least two of the following symptoms—fever, cough, nasal congestion, runny nose, sore throat, or sneezing—lasting no more than seven days. Lower respiratory tract infection (LRTI) required tachypnea, moist rales or wheezing, or chest retractions, plus radiological evidence of pneumonia or bronchitis. We excluded children with non-infectious respiratory conditions, including chronic lung disease, congenital heart disease, or iatrogenic infection.

Based on COVID-19 control measures, we divided the study period into three phases: pre-pandemic (June 2019 to February 2020), pandemic control (March 2020 to February 2023), and post-pandemic (March 2023 to December 2025). Seasons were defined as spring (March–May), summer (June–August), autumn (September–November), and winter (December–February). The study was approved by the Medical Ethics Committee of Shaowu Municipal Hospital, Fujian Province [No. (2026)9].

Nasopharyngeal swabs were collected within 24 hours of admission using sterile flocked swabs (Copan Medical Devices, Shanghai, China), placed in inactivated RNA preservation medium, transported at 0–4°C on the same day, and tested the next morning at the Molecular Diagnostic Center of Fuzhou Children's Hospital of Fujian Medical University.

Pathogen detection

We extracted nucleic acids using the TANBead extraction kit (TANBead NanoTechnology Co., Ltd., Taiwan, China). Multiplex RT-PCR with capillary electrophoresis fragment analysis (Ningbo HEALTH Gene Technologies Co., Ltd., Ningbo, China; NMPA registration No. 20183400518) was used to detect the following pathogens according to the manufacturer's instructions: influenza A virus (FluA; including H3N2, 2009 H1N1, and untyped), influenza B virus (FluB), parainfluenza virus (PIV), respiratory syncytial virus (RSV), adenovirus (ADV), human rhinovirus (HRV), human bocavirus (HBoV), human coronavirus (HCoV), human metapneumovirus (HMPV), *Mycoplasma pneumoniae* (MP), and *Chlamydia* spp. (Ch).

Positive and negative controls supplied with the kit were included throughout extraction, amplification, and capillary electrophoresis. We used human DNA, human RNA, and an RT-PCR internal control to monitor specimen quality and assay performance. A result was considered valid only when all three internal control peaks were present and exceeded the corresponding reference peak height. Detection of a pathogen-specific peak was scored positive. Detection of a single pathogen was defined as a single infection; detection of two or more pathogens was defined as coinfection.

Data collection and statistical analysis

Demographic and clinical variables—sex, age, and sampling date—came from medical records. Weather, temperature, and air quality data were downloaded from <http://www.tianqi24.com>. Statistical analyses were performed with SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Categorical variables are presented as frequencies and percentages and were compared using the chi-square test, with pairwise comparisons adjusted by the Bonferroni correction.

For regularized regression, we used R software with the glmnet package for 10-fold cross-validated LASSO, the boot package for bootstrap-based LASSO internal validation, and the ggplot2 package for visualization (cross-validation error curves, coefficient paths, model performance plots). All tests were two-sided, and a P value < 0.05 was considered statistically significant.

RESULTS

Seasonal, Sex, and Age Distribution of hMPV Positivity

Between June 2019 and December 2025, we enrolled 108,701 hospitalized children with confirmed acute respiratory tract infection (ARTI). Of these, 63,821 (58.71%) were male and 44,880 (41.29%) female (male-to-female ratio 1.42:1). Ages ranged from 38 days to 18 years (median 3 years). The age breakdown was: <1 year, 16,580; 1–<3 years, 26,436; 3–<6 years, 36,228; and 6–<18 years, 29,457 (Table 1).

Table 1
Distribution of human metapneumovirus (HMPV) by sex and age group among hospitalized children with acute respiratory infections.

	Pre-pandemic	Pandemic control		Post-pandemic				Total
	Jun 2019-Feb 2020	Mar 2020-Feb 2021	Mar 2021-Feb 2022	Mar 2022-Feb 2023	Mar 2023-Feb 2024	Mar 2024-Feb 2025	Mar 2025-Dec 2025	Jun 2019-Dec 2025
	positive rate	positive rate	positive rate	positive rate	positive rate	positive rate	positive rate	positive rate
overall	86/3983 (2.16%)	585/6209 (9.42%)	72/13245 (0.54%)	949/13565 (7.00%)	2052/28286 (7.25%)	1146/26429 (4.34%)	1699/16984 (10.00%)	6589/108701 (6.06%)
Gender								
male	53/2345 (2.26%)	339/3727 (9.10%)	41/8112 (0.51%)	554/8139 (6.81%)	1150/16281 (7.06%)	599/15312 (3.91%)	942/9905 (9.51%)	3678/63821 (5.76%)
female	33/1638 (2.01%)	246/2482 (9.91%)	31/5133 (0.60%)	395/5426 (7.28%)	902/12005 (7.51%)	547/11117 (4.92%)	757/7079 (10.69%)	2911/44880 (6.49%)
χ ²	0.280	1.154	0.443	1.127	2.126	14.938	6.757	23.111
P	0.597	0.283	0.506	0.288	0.145	<0.001	0.009	<0.001
Age (years)								
Age ≤ 1	17/780 (2.18%)	25/609 (4.11%)	18/2004 (0.90%)	168/2691 (6.24%)	258/3678 (7.01%)	152/3905 (3.89%)	210/2913 (7.21%)	848/16580 (5.11%)
1 < age ≤ 3	28/1149 (2.44%)	172/1875 (9.17%)	20/3924 (0.51%)	295/3559 (8.29%)	501/5965 (8.40%)	304/5614 (5.42%)	349/4350 (8.02%)	1669/26436 (6.31%)
3 < age ≤ 6	32/1372 (2.33%)	300/2342 (12.81%)	26/4586 (0.57%)	428/4570 (9.37%)	937/8990 (10.42%)	488/8881 (5.49%)	842/5487 (15.35%)	3053/36228 (8.43%)
6 < age ≤ 18	9/682 (1.32%)	88/1383 (6.36%)	8/2731 (0.29%)	58/2745 (2.11%)	356/9653 (3.69%)	202/8029 (2.52%)	298/4234 (7.04%)	1019/29457 (3.46%)
χ ²	4.398	38.307	10.999	158.556	316.598	134.782	231.547	829.356
P	0.222	<0.001	0.012	<0.001	<0.001	<0.001	<0.001	<0.001

Overall, females had a significantly higher HMPV detection rate than males: 6.49% (2,911/44,880) vs. 5.76% (3,678/63,821); $\chi^2=23.111$, $P < 0.001$. During the pre-pandemic and pandemic control phases (June 2019 to February 2023), detection rates did not differ by sex (all $P > 0.05$). This pattern changed in the post-pandemic period. From March 2024 to February 2025, the positivity rate was again higher in females than in males [4.92% (547/11,117) vs. 3.91% (599/15,312); $P < 0.001$], and the same held true for March–December 2025 [10.69% (757/7,079) vs. 9.51% (942/9,905); $P = 0.009$] (Table 1).

HMPV positivity varied strongly across age groups ($\chi^2 = 829.356$, $P < 0.001$). Over the full study period, the highest detection rate consistently fell in children aged 3 to < 6 years [8.43% (3,053/36,228)], followed by those aged 1 to < 3 years [6.31% (1,669/26,436)] and infants under 1 year [5.11% (848/16,580)]. The lowest rate was among children and adolescents aged 6 to < 18 years [3.46% (1,019/29,457)]. In the 3 to<6-year group, the detection rate rose to 12.81% (300/2,342) during the 2020–2021 epidemic cycle and reached 15.35% (842/5,487) at the 2025 peak (Table 1)(Fig. 1).

Before the pandemic, positivity rates rose markedly in winter. During the first pandemic phase, the peak remained in winter; in the second phase, it shifted to spring. In the post-pandemic period, the autumn-winter 2023 positivity rate was substantially higher than the spring-summer rate. In 2024, both spring and winter saw notable increases, and the overall highest positivity rate occurred in spring 2025 (Table 2).

Table 2

Distribution of human metapneumovirus (HMPV) by season among hospitalized children with acute respiratory infections.

Date	Pre-pandemic	Pandemic Phase I	Pandemic Phase II	Post-pandemic	Post-pandemic	Post-pandemic	Total
	(2019)	2020–2021	2022	(2023)	(2024)	(2025)	
Season	n = 3983	n = 19454	n = 13565	n = 28286	n = 26429	n = 16984	
Spring	-	20/4005 (0.50%)	598/3460 (17.28%)	43/6061 (0.71%)	632/9790 (6.46%)	1606/6332 (25.36%)	2899/29648 (9.78%)
Summer	5/549 (0.91%)	6/4488 (0.13%)	303/4677 (6.48%)	264/6678 (3.95%)	79/6918 (1.14%)	71/4059 (1.75%)	728/27369 (2.66%)
Autumn	8/1313 (0.61%)	123/4910 (2.51%)	38/3121 (1.22%)	1056/8114 (13.01%)	42/4773 (0.88%)	21/4907 (0.43%)	1288/27138 (4.75%)
Winter	73/2121 (3.44%)	508/6051 (8.40%)	10/2307 (0.43%)	689/7433 (9.27%)	393/4948 (7.94%)	1/1686 (0.06%)	1674/24546 (6.82%)
F Value	35.497	724.735	877.554	939.036	568.766	2651.455	1382.593
P Value	$P < 0.001$	$P < 0.001$	$P < 0.001$	$P < 0.001$	$P < 0.001$	$P < 0.001$	$P < 0.001$

Time Series Distribution of HMPV Positivity and Patterns of Single and Co-infections

The overall HMPV positivity rate across the entire study was 6.06% (6,589/108,701) (Table 1). In the pre-pandemic era (June 2019 to February 2020), HMPV detection was largely restricted to winter months (December-January; Fig. 1A). During the first pandemic year (March 2020 to February 2021), the rate initially rose to 9.42% (585/6,209) (Table 1), with winter still the peak season (Fig. 2A). It then dropped sharply to only 0.54% (72/13,245) in the following year (March 2021 to February 2022). From March 2022 to February 2023, HMPV rebounded quickly to 7.00% (949/13,565) (Table 1), though the seasonal peak moved to spring and summer (Fig. 2A).

The post-pandemic period was marked by continued fluctuations. Between March 2023 and February 2024, the detection rate climbed to 7.25% (2,052/28,286) (Table 1), with an atypical autumn-winter peak (Fig. 2A). It then fell to 4.34% (1,146/26,429) from March 2024 to February 2025, as the peak returned to spring (Fig. 2A). Finally, during the partial year from March to December

2025, HMPV positivity surged to the highest level of the entire study—10.00% (1,699/16,984) (Table 1)—characterized by a pronounced spring-dominant circulation (Fig. 2A).

Longitudinal analysis identified five distinct waves of increased HMPV activity, each differing in duration and intensity. The first wave appeared in January-February 2020, peaking at 4.97%. After eight months of low activity, a second wave began in October 2020, lasted five months, and peaked at 22.02% in December 2020. The third wave started in February 2022, persisted for six months, and reached 23.99% in April 2022. The fourth wave was the longest, spanning June 2023 to May 2024, with two secondary peaks—15.74% in October 2023 and 11.22% in March 2024. The fifth and final wave began in December 2024, continued for seven months, and attained the study’s highest monthly detection rate in March 2025 (36.84%), then gradually subsided (Fig. 2A).

Among the 6,589 HMPV-positive children, 25.71% (1,694/6,589) carried at least one additional respiratory pathogen. Dual infections were the most common pattern, accounting for 23.19% (1,528/6,589) of all HMPV-positive cases (Fig. 2B). Within dual infections, HMPV with human rhinovirus (HRV) ranked first (11.22%), followed by HMPV with *Mycoplasma pneumoniae* (MP; 2.76%), HMPV with adenovirus (ADV; 2.19%), and HMPV with parainfluenza virus (PIV; 1.61%) (Fig. 2C). Triple infections occurred in 2.40% (158/6,589) of cases; the most frequent triple combination was HMPV + HRV+MP (0.47%), followed by HMPV + HRV+ADV (0.42%) (Fig. 2D). Quadruple infections were rare—only eight cases in total. The most common four-pathogen combination was HMPV + HRV+PIV+Boca, accounting for 0.03% (2/6,589) of HMPV-positive cases (Fig. 2E).

The distribution of coinfecting pathogens changed over time. In the pre-pandemic era, HRV (10.47%), MP (4.65%), and respiratory syncytial virus (RSV; 3.49%) were the leading copathogens. During pandemic control, HRV remained the most common (8.16%), followed by ADV (1.74%) and PIV (1.49%). Coinfection was most frequent in the post-pandemic period, where HRV (14.83%), MP (4.68%), and ADV (3.17%) emerged as the top three (Fig. 3).

Associations of Weather, Temperature, Air Quality, and Related Parameters with HMPV Detection

HMPV spread is influenced by the source of infection, routes of transmission, and host susceptibility. Weather, temperature, and air quality are key factors affecting transmission and host vulnerability. To examine their role in HMPV positivity among hospitalized children, we collected corresponding environmental data over the same period. Pearson correlation analysis showed that the HMPV positivity rate was moderately positively correlated with the number of sunny days, the Air Quality Index (AQI), and PM2.5 levels, and weakly positively correlated with overcast and hazy days. In contrast, the positivity rate was moderately negatively correlated with average high temperature, average low temperature, and monthly minimum temperature, and weakly negatively correlated with cloudy days, rainy days, monthly maximum temperature, average wind speed, visibility, and rainfall(Fig. 4A). The forest plot displays the magnitude and direction of each correlation with its 95% confidence interval. Consistent with the heatmap, temperature-related variables showed negative associations, while poor air quality (AQI, PM2.5) and sunny days showed positive associations with HMPV detection (Fig. 4B).

Monthly Minimum Temperature and Poor AQI as Major Drivers of HMPV Circulation

Given the collinearity among weather, temperature, and air quality parameters(Table 3), along with the limited sample size, we employed both Bootstrap-based LASSO and 10-fold cross-validated LASSO for internal validation to identify the main determinants of hMPV positivity. The independent variables included sunny days, average high temperature, average low temperature, maximum temperature, minimum temperature, AQI, and average PM2.5.

Table 3
Collinearity analysis of weather, temperature, and air quality parameters.

Variable	VIF	Tolerance	Collinearity
Average low temperature(°C)	97.06	0.01	Severe
Average high temperature(°C)	82.21	0.01	Severe
Minimum temperature(°C)	26.88	0.04	Severe
Average PM2.5 value	20.52	0.05	Severe
AQI	19.17	0.05	Severe
Maximum temperature(°C)	10.69	0.09	Severe
Rainy(d)	10.30	0.10	Severe
Cloudy(d)	4.21	0.24	None/Low
sunny(d)	3.81	0.26	None/Low
Overcast(d)	2.69	0.37	None/Low
Average wind speed(km/h)	2.30	0.43	None/Low
Rainfall(mm)	1.78	0.56	None/Low
Average visibility(km)	1.66	0.60	None/Low
Sand, fog and haze(d)	1.40	0.71	None/Low

Bootstrap-based LASSO selected an optimal model at $\lambda = 0.0008$ (Fig. 5B), retaining minimum temperature, AQI, maximum temperature, and sunny days as the final predictors (Fig. 5A). Variable selection frequency analysis identified minimum temperature and AQI as the most stable predictors, with selection frequencies exceeding 96% (Fig. 5D). Minimum temperature showed a negative association with hMPV positivity, whereas AQI showed a positive association (Fig. 5C). The 10-fold cross-validated LASSO selected an optimal model at $\lambda = 0.0011$ (Figure S1B), retaining minimum temperature and AQI as the final predictors (Figure S1A). Minimum temperature exhibited a negative effect (i.e., lower temperatures were associated with higher positivity), and AQI exhibited a positive effect (Figure S1C). In model comparison, linear regression achieved the highest R^2 (0.4177) and the lowest RMSE (0.0533) and MAE (0.0394), followed closely by LASSO ($R^2 = 0.3946$, RMSE = 0.0543, MAE = 0.0401). Both models substantially outperformed the mean baseline ($R^2 = 0.0000$, RMSE = 0.0698, MAE = 0.0504) (Figure S1D). Given their comparable predictive performance, LASSO was preferred due to its ability to select a parsimonious set of predictors while handling collinearity. The final model explained approximately 39.5% of the variance, with a prediction curve slope of 0.354 (Figure S1D), suggesting that other factors also contribute to hMPV positivity.

Discussion

This 6.5-year study, based on data from 11 hospitals across five regions of Fujian Province, provides a comprehensive picture of how HMPV infection epidemiology evolved among hospitalized children from the pre- to post-pandemic period. Several key observations are worth highlighting: an unprecedented post-pandemic resurgence; a seasonal peak shifting from winter to spring; the highest positivity rate observed in children aged 3–6 years; persistently higher positivity in females after the pandemic; a 25.71% co-infection rate, with HRV as the leading copathogen; and the identification of minimum temperature (negative association) and AQI (positive association) as the most stable environmental drivers. Each of these findings is discussed in turn below.

1. Immunity debt-driven post-pandemic resurgence: from lull to explosion

The most striking finding is the strength and speed of the HMPV resurgence following the pandemic. During the late control phase (March 2021 to February 2022), the positivity rate reached a nadir of 0.54% – nearly undetectable. After the lifting of

restrictions, however, HMPV positivity rose sharply, peaking at a monthly rate of 36.84% in March 2025 (the fifth wave's peak). This pattern of "suppression followed by rebound" has been documented worldwide [19]. A recent global analysis using WHO FluNet data from 2016 to 2025, comprising approximately 145,000 HMPV tests across 54 countries, clearly showed that many countries experienced delayed or shifted seasonal peaks after the pandemic[20]. Another review noted that in the post-pandemic era, HMPV exhibited unusual seasonal patterns, higher rates of co-infection, and an altered age distribution[17].

The primary driver appears to be what has been termed "immunity debt"[21]. Years of mask-wearing, social distancing, and school closures reduced population exposure to common respiratory viruses, leading to a decline in herd immunity. A 2026 review articulated this concept as follows: immunity debt refers to the reduced immune protection resulting from prolonged low exposure to circulating pathogens, leaving children and adults who missed recent immune boosts more vulnerable[17]. The surge of HMPV in northern Chinese provinces in early 2025 provided a clear illustration of this phenomenon[21].

In the post-pandemic period, HMPV has transformed from a locally under-recognized virus into a growing global threat[17]. Data from the Chinese CDC for 2024 indicate that HMPV accounted for 6.2% of respiratory infections and 5.4% of hospitalizations nationally, and several regions (Hong Kong SAR, Kazakhstan, Malaysia) saw sharp increases in cases in early January 2025[21]. This rebound is not a transient fluctuation; rather, it reflects a profound reshaping of the viral landscape[19, 20].

2. Age-related immunity gap: why children aged 3–6 years are particularly affected

The age-specific pattern observed in this study warrants attention. Children aged 3–6 years had the highest overall positivity rate (8.43%), which rose to 15.35% at the spring 2025 peak. Conventional understanding holds that infants under two years of age are most vulnerable to HMPV[4]. The present findings, however, point to an immunity gap. Children born during the pandemic missed their initial opportunity for HMPV exposure. Surveillance data from Ningxia, China (2023–2024) on severe acute respiratory infection (SARI) showed the highest HMPV positivity (10.92%) in 4-year-olds[22]. Earlier studies have demonstrated that HMPV infection rates peak in children under five years, and nearly all children have been infected by age five[4]. HMPV seroprevalence increases rapidly during the first two years of life and plateaus after age five; consequently, the 3–6 year age range represents a window during which primary infections accumulate[4]. This immunity gap model aligns well with the data from Fuzhou[22]. An upward age shift has also been documented for RSV during its global post-pandemic rebound[19]. Taken together, these observations suggest that the epidemiology of respiratory viruses is undergoing fundamental changes in the post-pandemic era.

3. Viral interference between RSV and HMPV: insights from the pandemic

Beyond immunity debt and age-related susceptibility, viral interference with RSV appears to have shaped the post-pandemic evolution of HMPV waves. In the present data, the fourth HMPV wave was the longest and exhibited two secondary peaks, coinciding with a strong RSV resurgence from late 2023 to mid-2024. RSV and HMPV are known to interfere with each other, displaying out-of-phase biennial dynamics – high circulation of one virus reduces the susceptible pool for the other[23]. This phenomenon, referred to as viral interference, offers a plausible explanation for the complex waveform observed. A modelling study across ten US regions found that climate variables alone could not accurately predict HMPV timing, but adding RSV activity substantially improved model fit, suggesting that HMPV transmission slows during RSV epidemics[23]. That study also leveraged the COVID-19 disruption as a "natural experiment" to measure the asymmetric interference between RSV and HMPV[23]. In essence, RSV suppresses HMPV, whereas the reverse effect is weaker. During the pandemic, RSV was suppressed, yet HMPV did not rebound immediately; it only began to increase after RSV returned, and then followed a more complex two-peak pattern. This temporal lag suggests that RSV constrains the ecological niche available to HMPV[23]. To design effective seasonal prevention strategies, therefore, RSV and HMPV should be considered together as components of a single ecological system [19, 23].

4. Temperature and air quality: independent environmental predictors of HMPV positivity

A key contribution of this study is the use of LASSO regression with bootstrap validation to identify, from a set of potentially collinear environmental variables, minimum temperature (negative association) and AQI (positive association) as the most stable and critical predictors of HMPV positivity – both with selection frequencies exceeding 96%. Several lines of evidence support these associations. First, low temperature favors viral stability. Laboratory studies have shown that HMPV remains stable at 4°C and at room temperature but degrades rapidly at 37°C[24], indicating that lower temperatures prolong viral survival in the environment. At the population level, a French study of 4,300 hospitalized patients with acute respiratory infection found

that HMPV detection was negatively correlated with temperature; low temperature affected both HMPV and RSV, whereas humidity affected only RSV[25]. Research from subtropical southern China also linked low temperature and low absolute humidity to the timing of HMPV peaks[26]. A meta-analysis provided a quantitative estimate: each 1°C increase in ambient temperature was associated with an approximately 52% reduction in HMPV infection risk[24] – a magnitude similar to that observed for influenza.

The relationship with air pollution is more nuanced. Short-term exposure to PM_{2.5} has been shown to increase the risk of severe acute respiratory infection in children by 11% and the risk of ICU admission by 6% [27]. A large US cohort study covering major cities confirmed that PM_{2.5} exposure is associated with worse outcomes in respiratory infections[27]. Mechanistically, inhalation of PM_{2.5} induces airway inflammation, oxidative stress, and immune suppression, thereby increasing host susceptibility and impairing host defenses[28]. Air pollution has also been linked to reduced expression of AXIN1 protein, a key regulator of the Wnt/ β -catenin pathway; lower AXIN1 levels in turn elevate infection risk [28]. During the winter-spring transition, Fujian Province often experiences both low temperatures and high pollution levels – a concurrent exposure that aligns with our regression results, in which minimum temperature (negative) and AQI (positive) both remained in the model, indicating independent and additive effects[26, 27].

5. Co-infection patterns: pathogens circulating alongside HMPV

In this study, 25.71% of HMPV-positive children carried at least one additional respiratory pathogen. Dual infections were the most common (23.19%), with human rhinovirus (HRV) being the most frequent copathogen. This finding is consistent with global reports[29]. A paediatric surveillance study from Mexico (2021–2024) reported an HMPV positivity rate of 7.2%; co-infections occurred predominantly in moderate cases (20.0%) and were marginally associated with a higher risk of hospitalisation (odds ratio [OR] = 1.53)[29].

Several factors may explain the predominance of HRV in co-infections. As a non-enveloped virus, HRV is more stable in the environment and more resistant to disinfectants[30]. Consequently, during the pandemic, HRV was one of the few viruses that were not completely suppressed; it rebounded more rapidly than enveloped viruses and became the first to re-enter circulation, thereby creating a favourable “window of opportunity” for subsequent HMPV co-infection[30]. A comparative study of HMPV single infection versus HRV single infection found that HMPV alone caused more fever, cough, and rales in most age groups, whereas bacterial co-infection exacerbated the severity of HRV cases[30]. In patients with HRV, bacterial co-infection significantly increased cough frequency, pneumonia rate, paediatric intensive care unit (PICU) admissions, and length of hospital stay, whereas no clear difference in disease severity was observed between HMPV single infection and HMPV co-infection[30]. Therefore, the clinical burden of HMPV co-infection cannot be generalised; it depends on the specific viral or bacterial copathogen involved. The post-pandemic synchronous rebound of HRV and *Mycoplasma pneumoniae*, together with their frequent co-detection with HMPV, underscores the need to reconsider the use of multiplex PCR panels in clinical practice [29].

6. Public health implications and future directions

The findings of this study carry several practical implications. First, the post-pandemic spring peak of HMPV indicates that the conventional “winter-only” surveillance window for respiratory viruses is no longer adequate [19]. Global data have shown that many countries experienced delayed or shifted HMPV peaks after the pandemic [20]; accordingly, surveillance strategies need to be seasonally adaptive and tailored to local epidemiological rhythms. Second, the positive associations between AQI/PM_{2.5} and HMPV positivity suggest that air quality improvement is not only an environmental objective but also a primary measure for preventing respiratory infections [27, 28]. Third, the high burden of HMPV in the 3–6 years age group – the “immunity gap” population – clearly identifies a priority target for vaccine development [4, 22]. Although no HMPV vaccine is currently licensed, an RSV-HMPV combination subunit vaccine is in phase IIa trials and has shown safety and immunogenicity in adults over 60 years of age [19]. The present data provide strong epidemiological grounds for including children aged 3–6 years in future vaccine trials [4, 19]. Finally, post-pandemic HMPV has emerged as a growing global health threat [17]. Future research should focus on surveillance of co-circulating genotypes, improved modelling of environment-pathogen interactions, clinical development of vaccines and monoclonal antibodies, and an ecology-based framework that integrates HMPV with other respiratory viruses [19, 23].

7. Limitations

Several limitations of this study should be acknowledged. First, the analysis was restricted to hospitalised children, which may not fully capture the spectrum of mild or asymptomatic community infections; thus, selection bias cannot be ruled out. Second, the environmental data are observational in nature, precluding causal inference. Although LASSO regression with bootstrap validation helped address collinearity and overfitting, the possibility of unmeasured confounding remains. Third, HMPV genotyping was not performed. Different genotypes may exhibit differential responses to temperature and air pollution, and the temporal evolution of genotype distribution in the study area is unknown. Fourth, non-pharmaceutical interventions varied in timing and stringency across regions, and these policy differences were not modelled. Fifth, the co-infection analysis did not explore clinical outcomes in depth; consequently, the independent effect of HMPV co-infection on length of hospital stay, disease severity, or mortality could not be systematically assessed.

Conclusions

This 6.5-year study, based on data from 11 hospitals across five regions of Fujian Province, provides a comprehensive picture of how HMPV epidemiology among hospitalized children evolved from the pre-pandemic to the post-pandemic period. Key findings include an intense post-pandemic resurgence of HMPV; a seasonal peak shifting from winter to spring; the highest susceptibility in children aged 3–6 years; persistently higher positivity in females after the pandemic; and the identification of minimum temperature (negative association) and AQI (positive association) as the most stable environmental drivers. These observations indicate that HMPV has long been underestimated as a pediatric respiratory pathogen. The findings underscore the need for seasonally adaptive surveillance, integration of air quality management into infection prevention strategies, and accelerated development of pediatric HMPV vaccines.

Declarations

Ethics approval and consent to participate

This study adhered to the tenets of the Declaration of Helsinki and was approved by the Shaowu Municipal Hospital [No. (2026)9]. Informed consent was obtained from guardians of all participants.

Consent for publication

Not Applicable

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due to the sensitive nature of patient privacy, but are available from the corresponding author on reasonable request.

Competing interests

The authors declare no competing interests.

Funding

This study were supported by Startup Fund for Scientific Research, Fujian Medical University (2019QH1165) and the Joint Fund Project for Science and Technology Innovation in the Medical and Health Field of Nanping City, China (Nanping City) (No. N2024LH031) and Fuzhou Municipal Clinical Specialty Strengthening Program Research Project for Clinical Specialty Development (2024-YJ-ZK14)

Authors' contributions

Pengju Cao and Shaoting Chen wrote the original draft. Pengju Cao and Shaoting Chen revised the manuscript. Pengju Cao, Shaoting Chen, Lixia Zhuang, Huakang Yao and Lin Cai participated in data collation and writing. All authors participated in

sample testing and data collection.

Acknowledgment

Thank you for Fujian Health Young Talent Overseas Training Program

References

1. van den Hoogen, B.G., et al., *A newly discovered human pneumovirus isolated from young children with respiratory tract disease*. Nat Med, 2001. **7**(6): p. 719–24.
2. Williams, J.V., et al., *Human metapneumovirus and lower respiratory tract disease in otherwise healthy infants and children*. N Engl J Med, 2004. **350**(5): p. 443–50.
3. Falsey, A.R., et al., *Human metapneumovirus infections in young and elderly adults*. J Infect Dis, 2003. **187**(5): p. 785–90.
4. Wang, X., et al., *Global burden of acute lower respiratory infection associated with human metapneumovirus in children under 5 years in 2018: a systematic review and modelling study*. Lancet Glob Health, 2021. **9**(1): p. e33–e43.
5. Mohamed, M.G. and S.H. Elsalous, *Forging a global shield against HMPV: Uniting healthcare systems and community action to counter a silent respiratory epidemic*. AIMS Public Health, 2026. **13**(1): p. 158–177.
6. Feng, Y., et al., *Epidemiology and diagnosis technologies of human metapneumovirus in China: a mini review*. Virol J, 2024. **21**(1): p. 59.
7. Jobe, N.B., et al., *Human Metapneumovirus Seasonality and Co-Circulation with Respiratory Syncytial Virus - United States, 2014-2024*. MMWR Morb Mortal Wkly Rep, 2025. **74**(11): p. 182–187.
8. Price, R.H.M., C. Graham, and S. Ramalingam, *Association between viral seasonality and meteorological factors*. Sci Rep, 2019. **9**(1): p. 929.
9. Lim, Y.K., et al., *Clinical Features, Epidemiology, and Climatic Impact of Genotype-specific Human Metapneumovirus Infections: Long-term Surveillance of Hospitalized Patients in South Korea*. Clin Infect Dis, 2020. **70**(12): p. 2683–2694.
10. Poniedzialek, B., et al., *Viral respiratory infections and air pollution: A review focused on research in Poland*. Chemosphere, 2024. **359**: p. 142256.
11. Lee, M.H., et al., *Air quality, meteorological variability and pediatric respiratory syncytial virus infections in Singapore*. Sci Rep, 2023. **13**(1): p. 1001.
12. Chow, E.J., T.M. Uyeki, and H.Y. Chu, *The effects of the COVID-19 pandemic on community respiratory virus activity*. Nat Rev Microbiol, 2023. **21**(3): p. 195–210.
13. Olsen, S.J., et al., *Changes in influenza and other respiratory virus activity during the COVID-19 pandemic-United States, 2020-2021*. Am J Transplant, 2021. **21**(10): p. 3481–3486.
14. Zhao, C., et al., *Characterising the asynchronous resurgence of common respiratory viruses following the COVID-19 pandemic*. Nat Commun, 2025. **16**(1): p. 1610.
15. Foley, D.A., et al., *An Unusual Resurgence of Human Metapneumovirus in Western Australia Following the Reduction of Non-Pharmaceutical Interventions to Prevent SARS-CoV-2 Transmission*. Viruses, 2022. **14**(10).
16. Garcia-Garcia, M.L., et al., *Clinical and epidemiological changes in severe viral respiratory infections in pediatric patients after the COVID-19 pandemic in Spain*. Sci Rep, 2026.
17. Ching, L.Y. and A.P. Kunnath, *The resurgent threat: human metapneumovirus in a post-pandemic landscape*. Diagn Microbiol Infect Dis, 2026. **116**(1): p. 117445.
18. Adepoju, V.A., et al., *Global Burden of Human Metapneumovirus: Bridging Gaps in Prevention, Diagnostics and Treatment*. Public Health Chall, 2025. **4**(3): p. e70094.
19. Billard, M.N., et al., *Post-Pandemic Dynamics of the Global Circulation of Human Metapneumovirus and Respiratory Syncytial Virus*. J Infect Dis, 2025. **232**(Supplement_1): p. S10–S18.
20. Castellana, E., et al., *Human Metapneumovirus Circulation and Seasonality on a Global Scale, 2016-2025: Changes in Patterns and Epidemic Timing in the Pre- Versus Post-COVID-19 Era*. Influenza Other Respir Viruses, 2025. **19**(12): p. e70200.

21. Ngwoke, I., et al., *Molecular characteristics, epidemiological trends, and public health implications of human metapneumovirus (hMPV): a review*. *Virology*, 2026. **619**: p. 110897.
22. Mu, T., et al., *Epidemiology and Genetic Diversity of Human Metapneumovirus in Patients with Severe Acute Respiratory Infection from 2023 to 2024 in Ningxia, China*. *Diseases*, 2025. **13**(8).
23. Howerton, E., et al., *Using COVID-19 pandemic perturbation to model RSV-hMPV interactions and potential implications under RSV interventions*. *Nat Commun*, 2025. **16**(1): p. 7261.
24. Shang, X., et al., *Global meta-analysis of short-term associations between ambient temperature and pathogen-specific respiratory infections, 2004 to 2023*. *Euro Surveill*, 2025. **30**(11).
25. Darniot, M., et al., *Different meteorological parameters influence metapneumovirus and respiratory syncytial virus activity*. *J Clin Virol*, 2018. **104**: p. 77–82.
26. Liu, W.K., et al., *Paramyxoviruses respiratory syncytial virus, parainfluenza virus, and human metapneumovirus infection in pediatric hospitalized patients and climate correlation in a subtropical region of southern China: a 7-year survey*. *Eur J Clin Microbiol Infect Dis*, 2019. **38**(12): p. 2355–2364.
27. Foo, D., et al., *Association Between Fine Particulate Matter (PM_{2.5}) and Severity of Acute Respiratory Infections Among Young US Children in the Major Cities in the United States: A Claims-based Cohort Study*. *Open Forum Infect Dis*, 2025. **12**(10): p. ofaf442.
28. Esposito, S., et al., *How air pollution fuels respiratory infections in children: current insights*. *Front Public Health*, 2025. **13**: p. 1567206.
29. Aleman-Garcia, Y.P., et al., *Seasonal trends, clinical outcomes, and viral coinfections of human metapneumovirus infections in Mexican children from 2021 to 2024*. *Eur J Clin Microbiol Infect Dis*, 2026. **45**(2): p. 419–427.
30. Zhang, G., et al., *Dynamic changes in the circulation of respiratory pathogens in children during and after the containment of the 2019 coronavirus disease pandemic in Kunming, China*. *Eur J Clin Microbiol Infect Dis*, 2024. **43**(12): p. 2259–2268.

Figures

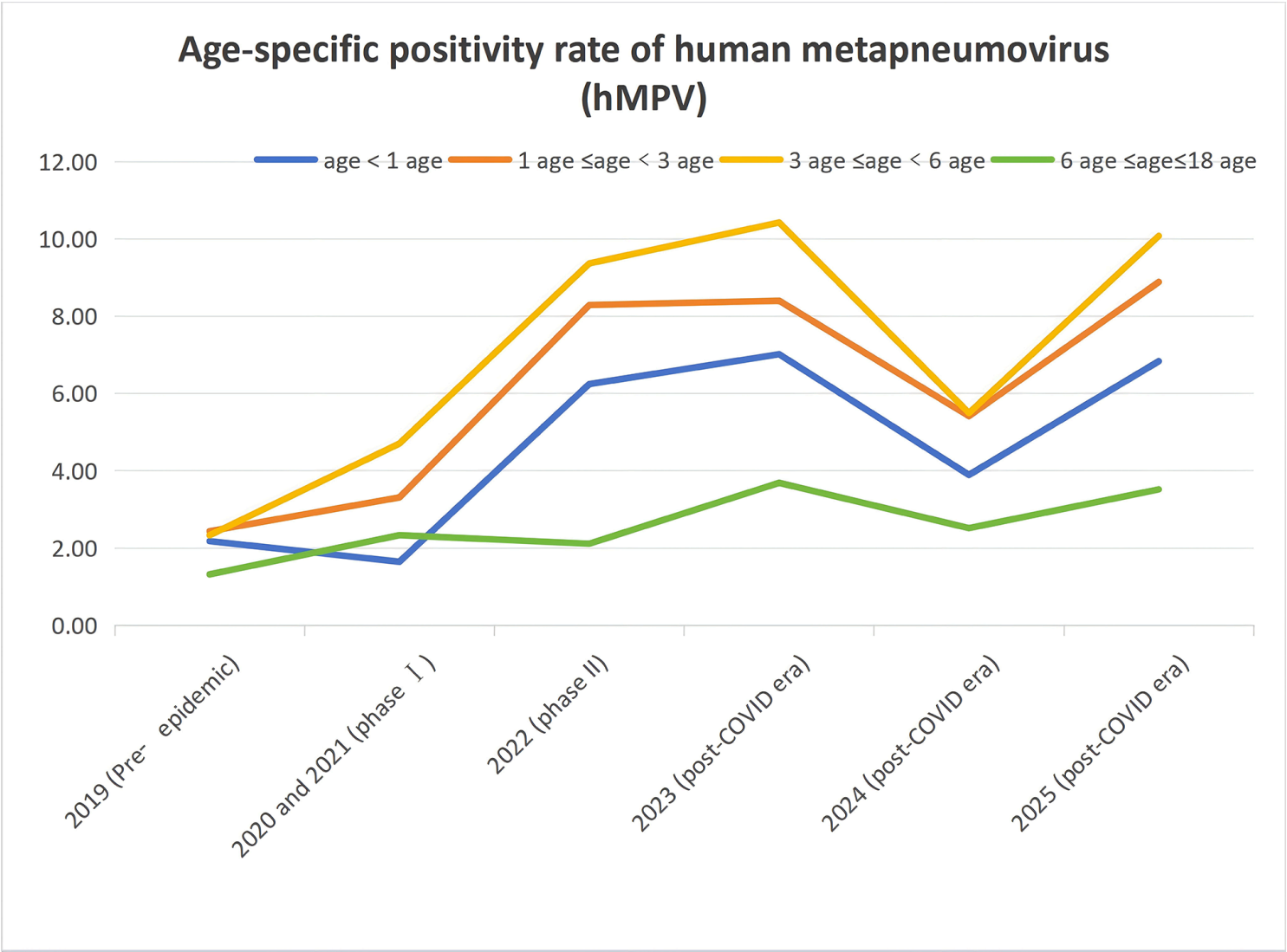
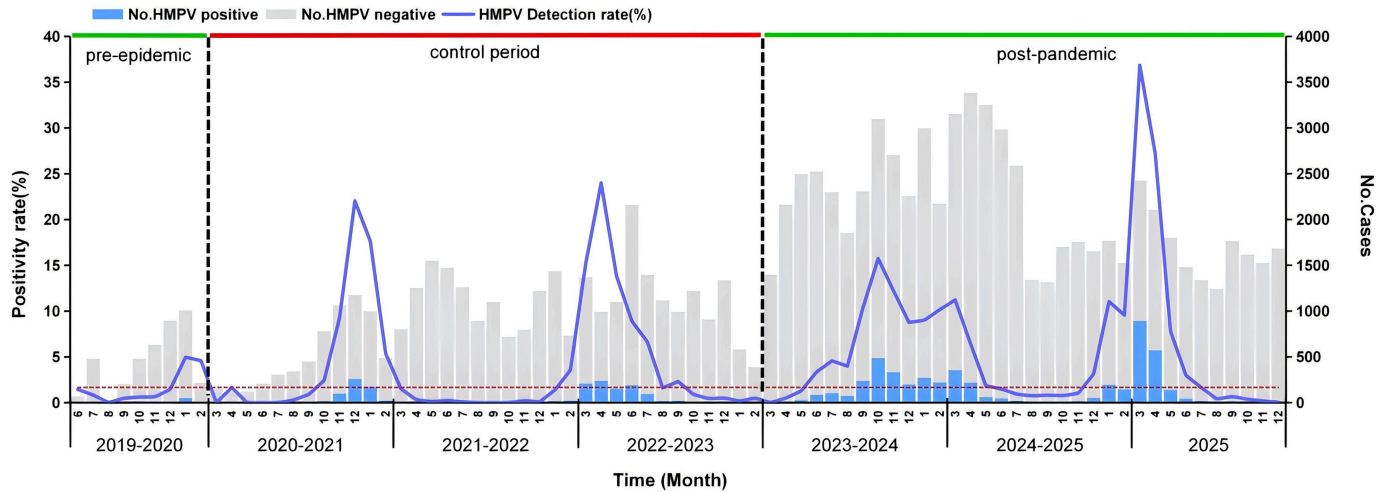


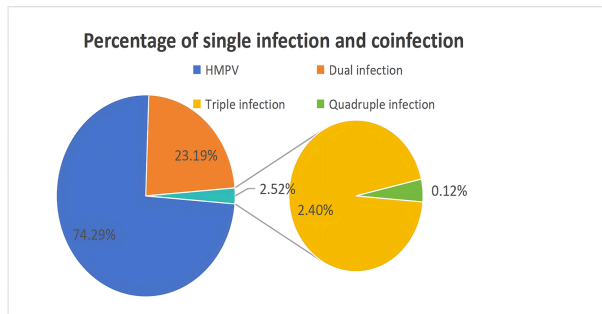
Figure 1

Age-stratified HMPV positivity rates from 2019–2025. The 3–6 year group exhibited the highest positivity, while the 6–18 year group the lowest. Rates declined in 2020–2021, followed by a post-pandemic resurgence.

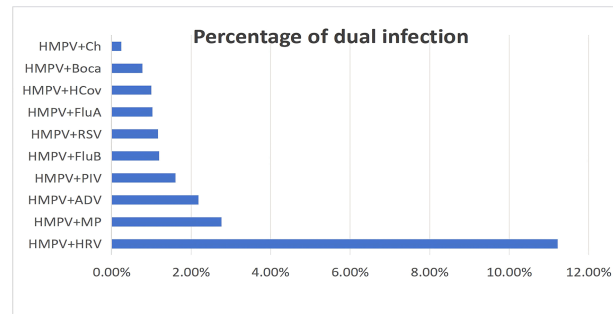
A



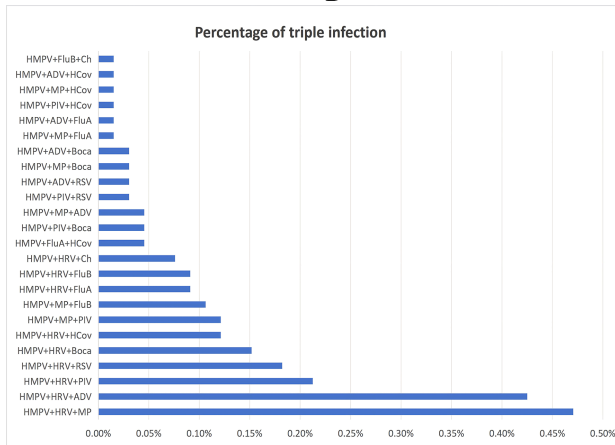
B



C



D



E

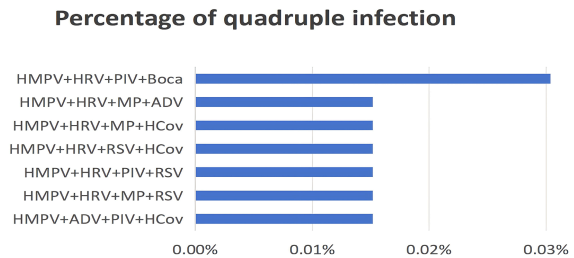


Figure 2

Epidemiological dynamics and pathogen co-infection profiles of human metapneumovirus (HMPV) over a six-year period spanning pre-pandemic, control, and post-pandemic eras. (A) Temporal trends: blue bars (HMPV-positive cases), gray bars (negative cases), blue line (positivity rate). Seasonal peaks emerged prominently post-pandemic. (B) Infection status: single infection (75.20%), dual (23.12%), triple (2.57%), quadruple (0.12%). (C) Dual co-infections: HRV most frequent (>11%), followed by MP, ADV, and CMV. (D) Triple co-infections: HMPV+HRV+MP triad dominated (<0.5%). (E) Quadruple co-infections: extreme rarity (<0.03%), with HMPV+HRV+PIV+Boca being most common.

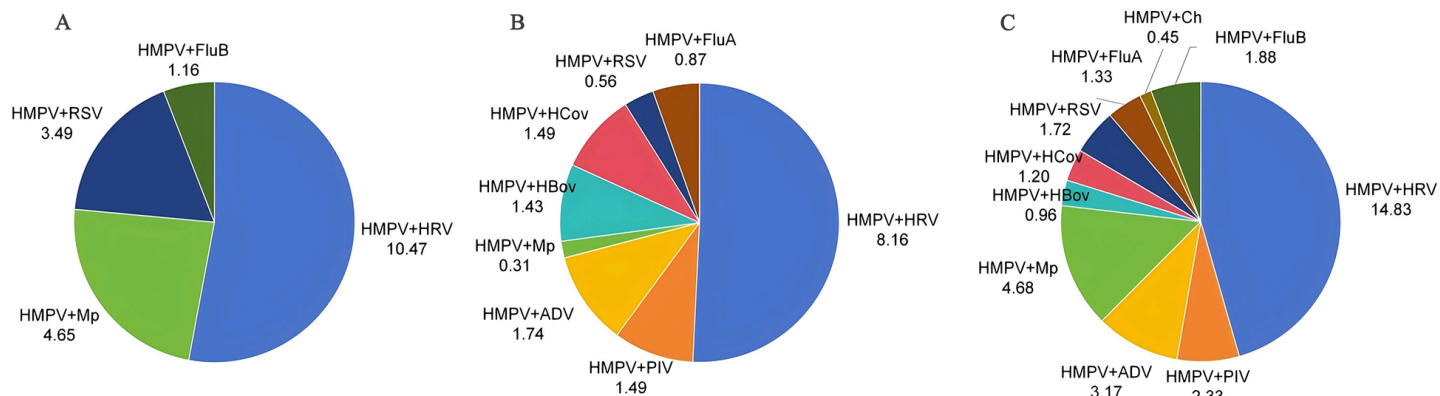


Figure 3

Proportional distribution of hMPV dual co-infections. (A–C) Pie charts display the relative frequencies of hMPV co-infected with a second pathogen. Across all panels, hMPV+HRV was the most frequent combination (10.47%, 8.16%, and 14.83%, respectively). hMPV+Mp and hMPV+RSV remained major contributors in A and C. hMPV+ADV and hMPV+PIV showed higher proportions in B and C. Numbers represent co-infection rates.

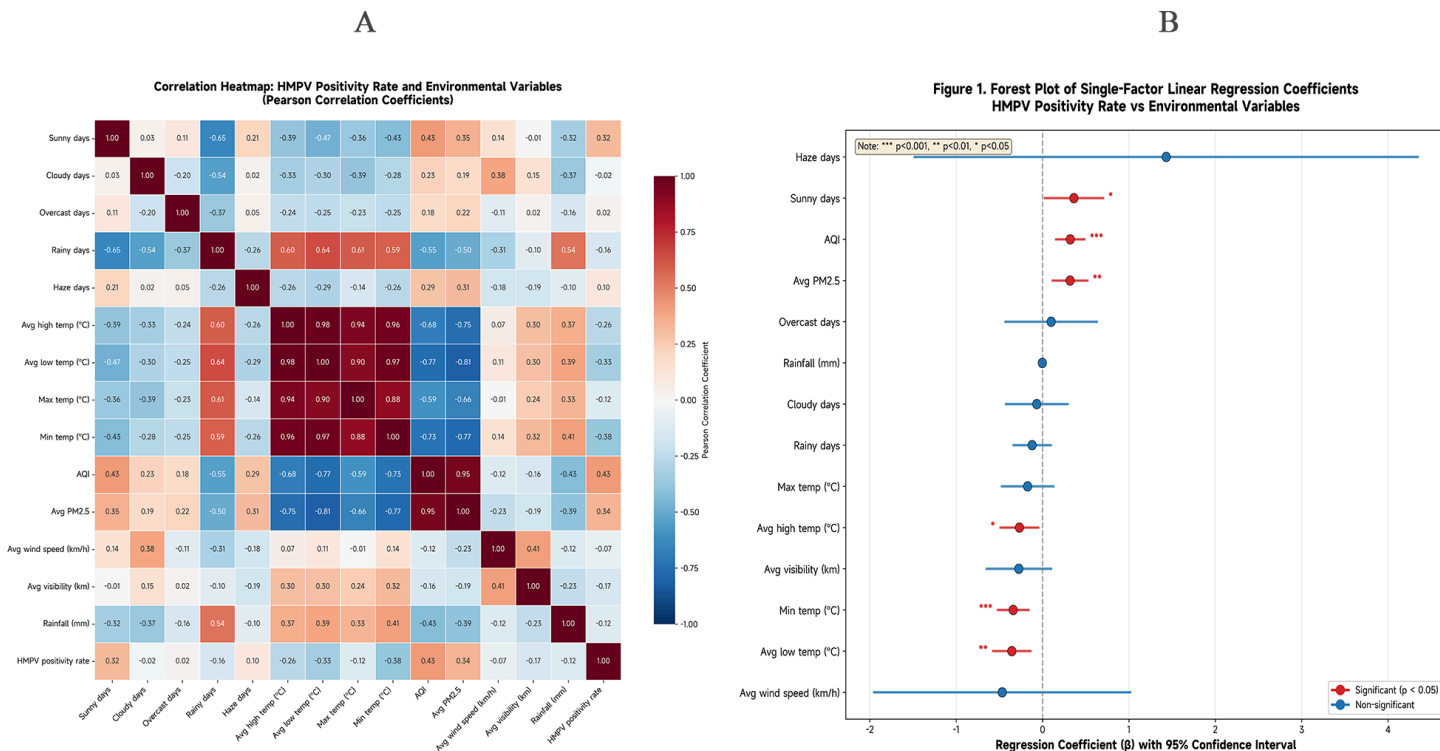


Figure 4

Associations between meteorological/environmental variables and hMPV positivity rate. (A) Correlation heatmap displaying Pearson correlation coefficients between hMPV positivity and selected environmental parameters. The color gradient (red to blue) indicates the direction of correlation: red for positive, blue for negative. hMPV positivity shows positive correlations with AQI and PM2.5, but negative correlations with temperature variables (e.g., avg low/min temp) and rainfall. (B) Forest plot summarizing single-factor linear regression coefficients (β) with 95% confidence intervals. Red dots represent statistically significant associations (p < 0.05) and blue dots indicate non-significant ones. Significant positive

predictors include AQI, PM2.5, and sunny days; significant negative predictors include low/min temperature, rainfall, and wind speed.

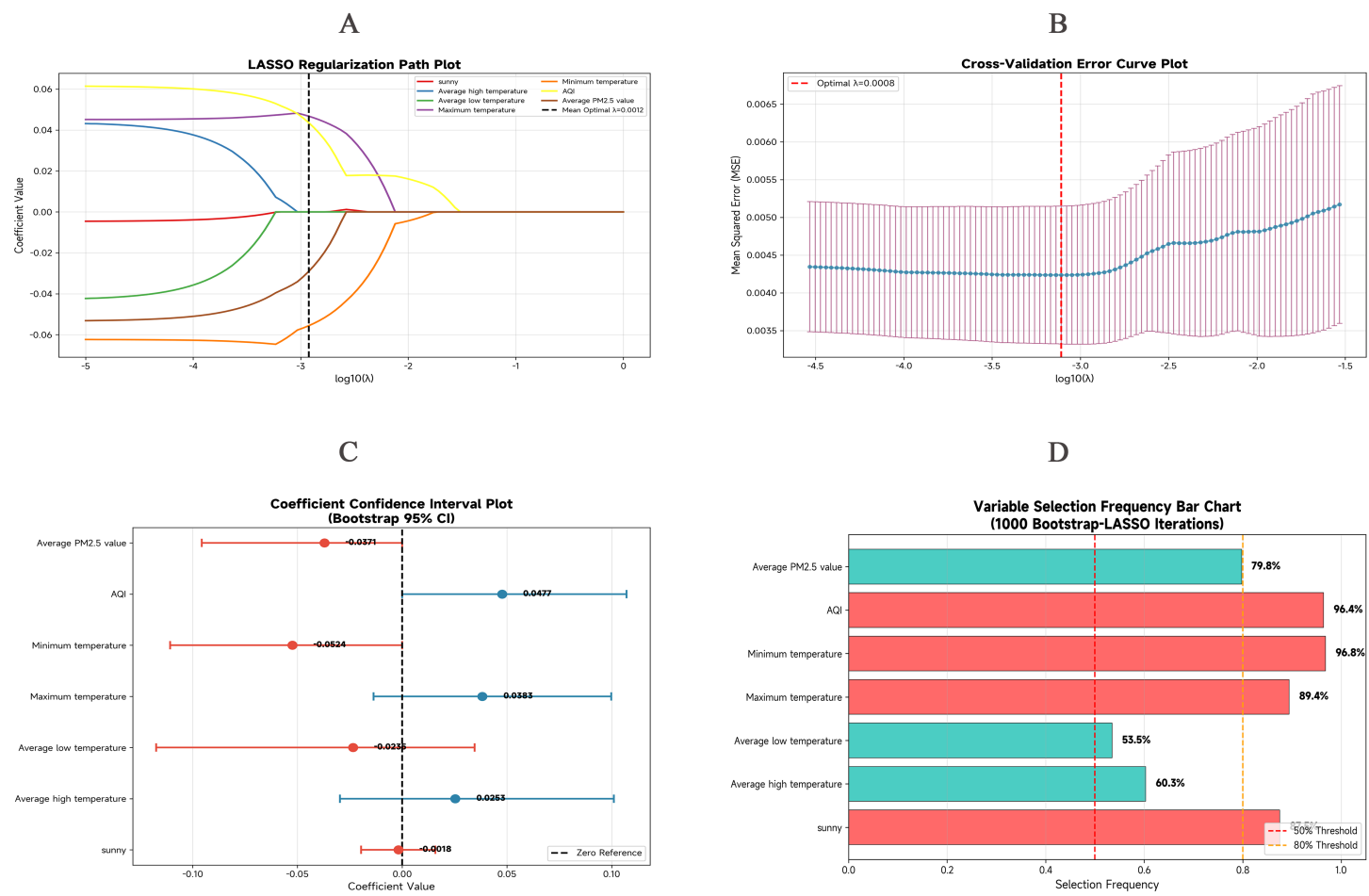


Figure 5

LASSO model selection for environmental predictors of hMPV.

(A) Coefficient paths for all variables as a function of $\log(\lambda)$.

(B) Cross-validation error curve. Mean squared error (MSE) with error bars is shown. The optimal $\lambda=0.0008$ is marked.

(C) Bootstrap coefficient estimates with 95% confidence intervals. Positive and negative associations are shown in blue and red, respectively.

(D) Variable selection frequency in 1000 bootstrap iterations. The dashed lines indicate 50% and 80% selection thresholds.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SupplementaryFigure1.png](#)