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Epidemiology and burden of acute respiratory infections associated with respiratory viruses: A multi-source integrated population-based surveillance study in Chongqing

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Epidemiology and burden of acute respiratory infections associated with respiratory viruses: A multi-source integrated population-based surveillance study in Chongqing

Running title: Epidemiology burden of respiratory virus

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Abstract:

Background: Acute respiratory infections (ARIs), particularly severe acute respiratory infections (SARIs), impose a huge disease burden globally. Respiratory viruses are key etiological agents of ARIs. Population-based data on respiratory virus disease burden in China are limited, with most studies focusing on single pathogens and lacking population-level incidence and hospitalization estimates.

Methods: We integrated data from national hospital-based surveillance, local health system electronic medical records (EMRs), and census records in Chongqing from October 2023 to April 2025. We also conducted a community-based healthcare utilization survey and a pilot survey. We analyzed the seasonality of six respiratory viruses and used Joinpoint software to characterize age-specific epidemiological trends. Furthermore, we identified risk factors for severe acute respiratory infection (SARI). A modified multiplier model was employed to estimate population-based incidence and hospitalization rates of ARI associated with these viruses.

Results: We included 16,363 respiratory infection patients (12,669 outpatients, 3,694 inpatients). Most viruses resumed pre-COVID-19 seasonal patterns. The detection rate of influenza virus (IFV) peaked in adolescents and adults; respiratory syncytial virus (RSV) and human parainfluenza virus (HPIV) mainly affected infants and the elderly; human adenovirus (HAdv), human rhinovirus (HRV), and human metapneumovirus (HMPV) were most prevalent in preschoolers. RSV infection was significantly associated with a higher risk of SARI compared with other respiratory viruses (RSV vs. IFV: adjusted odds ratio [aOR], 95% confidence interval [CI]: 7.88,

5.4–11.51; RSV vs. HRV: 1.52, 1.13–2.04; RSV vs. HAdv: 3.21, 2.14–4.81; RSV vs. HMPV: 1.76, 1.24–2.50; RSV vs. HPIV: 1.63, 1.14–2.33). Incidence and hospitalization rates (per 100,000 person-years) of HRV (30,183; 2,153), HMPV (22,774; 514), RSV (22,181; 2,065), IFV (13,086; 807), HPIV (7,824; 556), and HAdv (6,991; 1,487) were highest in children under 5 years of age. Hospitalization rates rose again in those aged ≥ 60 years: HRV (170), RSV (80), IFV (70), HMPV (54), HAdv (27), HPIV (23).

Conclusions: Distinct age distributions and the high SARI risk of specific viruses such as RSV support targeted prevention. Integrating multi-source surveillance with sentinel surveys and standardizing the ARI case definition can yield population-level, real-world estimates of incidence and hospitalization rates for these viruses.

Keywords: Respiratory viruses; incidence; hospitalization rate; clinical severity

Background

The 2024 Global Burden of Disease (GBD) data show that disability-adjusted life-years (DALYs) due to lower respiratory infections were among the top five global disease burdens in 2020 and 2021[1]. In 2021, the GBD study estimated that approximately 2.18 million deaths worldwide were attributed to lower respiratory infections caused by pathogens other than the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)[2]. The coronavirus disease 2019 (COVID-19)

pandemic altered the usual epidemiological patterns of several respiratory viruses, leading to off-season outbreaks in the post-pandemic period that may have increased the overall disease burden[3, 4]. Therefore, it is necessary to assess the epidemiology and disease burden of common respiratory viruses in the post-COVID-19 pandemic era.

Incidence and hospitalization rates are key for assessing respiratory virus disease burden, but prior studies mainly focused on estimating the population burden of influenza virus (IFV)[5]. In recent years, advances in vaccine development have increased focus on the disease burden of other respiratory viruses, especially respiratory syncytial virus (RSV) and human metapneumovirus (HMPV) in children and older adults[6, 7]. In China, there is a lack of population-based data on the incidence and hospitalization rates of respiratory virus-associated acute respiratory infections (ARIs), and no standardized methodological framework exists for generating such estimates. This gap hampers comprehensive disease burden assessments and the planning of preventive and immunization strategies.

On the other hand, severe clinical outcomes from pathogen infections significantly contribute to health and economic burdens. Studies show RSV-infected patients have a 41% longer hospital stay and 2.2 times higher need for mechanical ventilation compared to IFV patients[8]. Our prior research found that patients with single infections of RSV and enterovirus (EV) had a higher hospitalization risk than those

with other respiratory viruses[9]. This indicates that different respiratory viruses vary in their potential to cause severe clinical outcomes. Therefore, further analysis of risk factors for SARI associated with various respiratory viruses using data from multicenter studies is warranted as a supplement to disease burden assessment.

The enhancement of multi-pathogen surveillance in China provides an opportunity to further investigate the integration of diverse surveillance datasets. Such integration facilitates a comprehensive assessment of the epidemiology and disease burden of respiratory viruses. Therefore, we integrated data from a hospital-based multi-pathogen surveillance system, electronic medical records (EMRs), census records, a community-based healthcare utilization survey, and a pilot survey. The objectives were to analyze the epidemiology and SARI risk factors associated with six respiratory viruses in Chongqing and to estimate age-specific incidence and hospitalization rates of respiratory virus-associated ARI using a modified multiplier model.

Methods

Hospital-based surveillance

We conducted a prospective hospital-based surveillance in 22 sentinel hospitals across 13 administrative districts in Chongqing, China (the municipality with the largest permanent resident population in China), from October 15, 2023, to April 30, 2025. Consecutive patients with influenza-like illness (ILI) or SARI were enrolled via

random sampling from outpatient departments or inpatient wards. Patients who had received antiviral therapy within 48 hours prior to presentation or declined written informed consent were excluded. Upper respiratory tract specimens were collected from all enrolled ILI and SARI cases and tested for IFV, human rhinovirus (HRv), human adenovirus (HAdv), HMPV, RSV, human parainfluenza virus (HPIV) using real-time reverse-transcription polymerase chain reaction (RT-PCR) following standardized protocols.

De-identified EMRs for all ILI and SARI patients during the time period from October 15, 2023, to April 30, 2025, were extracted from the Chongqing Intelligent Disease Control Cloud Platform, which covers 84.11% of medical institutions in Chongqing. Using standard World Health Organization (WHO) case definitions for ILI and SARI[10], we derived municipal-level case totals for each syndrome throughout the surveillance period.

Community-based healthcare utilization survey

Healthcare-seeking behavior among individuals with ARI was assessed through a retrospective, population-based healthcare utilization survey conducted between May and June 2024. The full methodological details of the pilot study have been reported previously[11]; the present analysis extends the survey to cover the entire municipality of Chongqing (**appendix p3**). We estimated age-specific healthcare-seeking rates among community-dwelling ARI patients and subsequently performed post-stratification weight estimation[12], conditioning on age and sex, to calibrate these rates.

Case definition and variables collected

ILI was defined as an acute respiratory infection with measured fever (≥ 38 ℃) and either cough or sore throat, with symptom onset within the preceding 10 days. SARI was defined as an ILI episode that required hospitalization[10]. ARI was defined as the sudden onset of illness accompanied by at least one of the following respiratory symptoms: cough, sore throat, shortness of breath, or nasal congestion[13]. Demographic variables included age, sex, occupation, and hospital level. Disease severity was classified based on to hospitalization status (SARI vs. non-SARI). Age-stratified population denominators were obtained from Chongqing Health Bureau.

Pilot survey in Wanzhou District

The case definitions for ILI and SARI both require a body temperature >38 °C as an essential inclusion criterion, which may exclude respiratory viral infections without fever and thus underestimate incidence and hospitalization rates. To address this limitation, a pilot hospital-based survey was conducted in Wanzhou District to obtain pathogen-specific detection rates among ARI patients from 20 October 2021 to 31 July 2024[13]. The weighting adjustment parameter (W) was computed according to Equation (3). Details of the pilot survey are presented in **appendix p4**, and the parameters are provided in **Table. S1**.

Statistical analysis

Categorical variables are presented as frequencies (n) and percentages (%). Continuous variables are expressed as means ± standard errors (SE) or medians with

interquartile ranges (IQRs), as appropriate. The association between respiratory virus infection and SARI was assessed using multivariable logistic regression, adjusting for season, age group, region, sex, occupation, and hospital level. All analyses were conducted in R software (version 4.4.2). To characterize age-related trends that were non-linear or exhibited inflection points, Joinpoint regression (JPR) analyses was performed using the Joinpoint Regression Program (Version 5.2.0.0). Two-sided *P* values < 0.05 were considered statistically significant.

We adopted the methodological framework outlined in the *Handbook for Estimating the Disease Burden of Seasonal Influenza* recommended by the World Health Organization (WHO)[14]. The incidence and hospitalization rates of respiratory viral-associated ARIs were estimated using a modified multiplier model. The data sources of each parameter are illustrated in **Figure. 1**. The calculation for the incidence of respiratory viral-associated ARIs is shown below as an example.

$$P = \frac{\text{viral-positive cases identified among enrolled outpatients with ILI}}{\text{Enrolled outpatients with ILI}} \quad (1)$$

$$uN = \frac{P \times \text{Total number of outpatients with ILI}}{\text{PCR sensitivity for viral detection}} \quad (2)$$

$$W = \frac{\text{Annual detection rate of viral-associated ARI outpatients}}{\text{Annual detection rate of viral-associated ILI outpatients}} \quad (3)$$

$$wN = uN \times W \quad (4)$$

$$uI = \frac{wN}{\text{Person-years}} \quad (5)$$

$$aI = \frac{uI}{\text{Proportion of outpatients with ARI in the community}} \quad (6)$$

P represents the viral detection rate among outpatients with ILI; uN, the unweighted total number of viral-associated outpatients with ILI; W, the weighted adjustment parameter; wN, the total number of viral-associated outpatients with ARI; uI, the

crude incidence rate of viral-associated ARI in outpatients; and aI, the adjusted incidence rate of viral-associated ARI in outpatients. The sensitivity of RT-PCR testing, estimated at 95–100%, was incorporated into the model. The person year was calculated by multiplying the permanent resident population of the catchment area by the number of years the study was conducted[15]. We accounted for uncertainty in model parameters by using a probabilistic (Monte Carlo) approach with 10,000 independent simulation trails. A parallel approach was employed to estimate the hospitalization rate of viral-associated ARIs without adjustment for healthcare-seeking behavior.

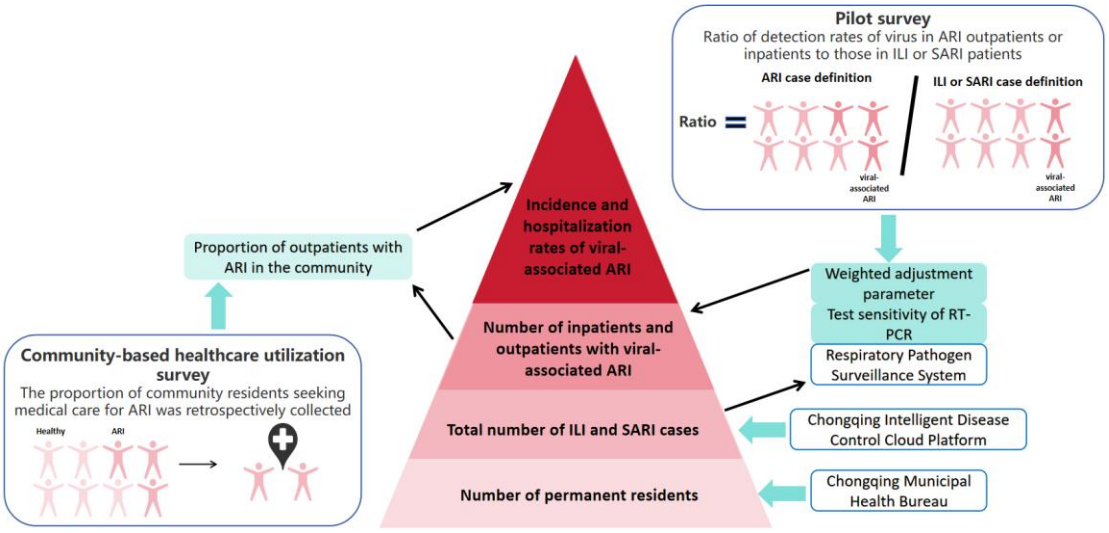


Figure 1. Flow chart

Note: Influenza-like illness (ILI), severe acute respiratory infection (SARI), acute respiratory illness (ARI).

Ethical Approval

Our study was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all human participants. Additionally, the study was approved by the Ethics Review Committee of Peking Union Medical College (No.

CAMS&PUMC-IEC-2025-013).

Results

Social demographic and clinical characteristics of ILI and SARI patients.

A total of 16,363 patients with respiratory infections were included in the analysis, comprising 12,669 (77.4%) outpatients with ILI and 3,694 (22.6%) inpatients with SARI. Among the patients, 68.9% resided in suburban areas, 31.8% in urban areas, with a median age of 17 years old and a male-to-female ratio of approximately 1:1. Of these, 51.2% were unemployed, and 77.1% sought care at tertiary hospitals. The detection rates of the six viral pathogens—IFV, RSV, HRv, HAdv, HMPV, and HPIV—were 11.7%, 7.6%, 3.9%, 3.1%, 2.9%, and 2.8%, respectively (**Table. 1**). The RSV detection rate was higher among SARI patients than ILI outpatients (3.2% vs. 2.8%), while detection rates of other viruses were lower in SARI patients (IFV: 4.3% vs. 13.9%; HRV: 6.0% vs. 8.0%; HAdv: 1.5% vs. 4.6%; HMPV: 2.3% vs. 3.4%; HPIV: 2.1% vs. 3.0%) (**Table. 1**).

Table 1. Social demographic and clinical characteristics of ILI and SARI patients

Characteristic, n (n/N)	Overall	ILI outpatients	SARI inpatients
Total	**16363**	**12669**	**3694**
Regions			
Urban	5086 (31.8%)	4021 (31.7%)	1065 (28.8%)

Suburban	11277 (68.9%)	8648 (68.3%)	2629 (71.2%)
Age group, years old [M (IQR)]	**17 [4, 52]**	**14 [3, 35]**	**58 [4, 74]**
＜ 1	2054 (12.6%)	1555 (12.3%)	499 (13.5%)
1	919 (5.6%)	766 (6.0%)	153 (4.1%)
2	1006 (6.1%)	857 (6.8%)	149 (4.0%)
3	837 (5.1%)	713 (5.6%)	124 (3.4%)
4	661 (4.0%)	588 (4.6%)	73 (2.0%)
5~14	2303 (14.1%)	2087 (16.5%)	216 (5.8%)
15~49	4351 (26.6%)	4004 (31.6%)	347 (9.4%)
50~59	1108 (6.8%)	708 (5.6%)	400 (10.8%)
60~64	416 (2.5%)	216 (1.7%)	200 (5.4%)
65~74	1385 (8.5%)	643 (5.1%)	742 (20.1%)
75~79	604 (3.7%)	249 (2.0%)	355 (9.6%)
≥80	719 (4.4%)	283 (2.2%)	436 (11.8%)
Sex			
Male	8896 (54.4%)	6539 (51.6%)	2357 (63.8%)
Female	7467 (45.6%)	6130 (48.4%)	1337 (36.2%)
Occupation			
Employed	3407 (20.8%)	2311 (18.2%)	1096 (29.7%)
Student	2933 (17.9%)	2706 (21.4%)	227 (6.1%)
Unemployed[†]	8371 (51.2%)	6314 (49.8%)	2057 (55.7%)
Unknown	1652 (10.1%)	1338 (10.6%)	314 (8.5%)

Hospital			
Secondary hospital	3742 (22.9%)	2900 (22.9%)	842 (22.8%)
Tertiary hospital	12621 (77.1%)	9769 (77.1%)	2852 (77.2%)
Pathogen detection results			
IFV	1921 (11.7%)	1764 (13.9%)	157 (4.3%)
HRv	1236 (7.6%)	1015 (8.0%)	221 (6.0%)
HAdv	638 (3.9%)	581 (4.6%)	57 (1.5%)
HMPV	512 (3.1%)	427 (3.4%)	85 (2.3%)
RSV	474 (2.9%)	357 (2.8%)	117 (3.2%)
HPIV	460 (2.8%)	382 (3.0%)	78 (2.1%)

Note: Medium (M), interquartile range (IQR), influenza-like illness (ILI), severe acute respiratory infection (SARI), influenza virus (IFV), human rhinovirus (HRv), human adenovirus (HAdv), human metapneumovirus (HMPV), respiratory syncytial virus (RSV), human parainfluenza virus (HPIV). †Unemployed refers to preschool children or retirees.

Patients aged 15-50 years had the highest proportion of IFV and HRV positives. Those aged 5-15 years had the highest proportion of HAdv and HMPV positives. Patients aged 0-1 year had the highest proportion of RSV and HPIV positives (**Table. S2**). JPR analysis revealed age-specific patterns. IFV detection peaked at 16.7% in the 15-50 age group (APC = 2.33, $P<0.05$), then declined (APC = -2.03, $P<0.05$). RSV detection reached 8.9% in the 2-3 age group, decreased with age (APC = -16.35, $P<0.05$), and rose again to 1.1% in the ≥80 age group (APC = 10.43, $P>0.05$). HPIV detection peaked at 6.8% in the 3-4 age group, declined with age (APC = -15.48,

223 P<0.05), and increased to 1.0% in the 75-80 age group (APC = 2.42, P>0.05). HAdv
224 detection was highest at 10.1% in the 4-5 age group and decreased thereafter (APC =
225 -2.93, P<0.05). HRV detection peaked at 13.5% in the 0-1 age group and declined
226 (APC = -3.94, P<0.05). HMPV detection reached 9.6% in the 2-3 age group and
227 decreased (APC = -12.64, P<0.05) (**Figure. 2 and Figure. S1**).

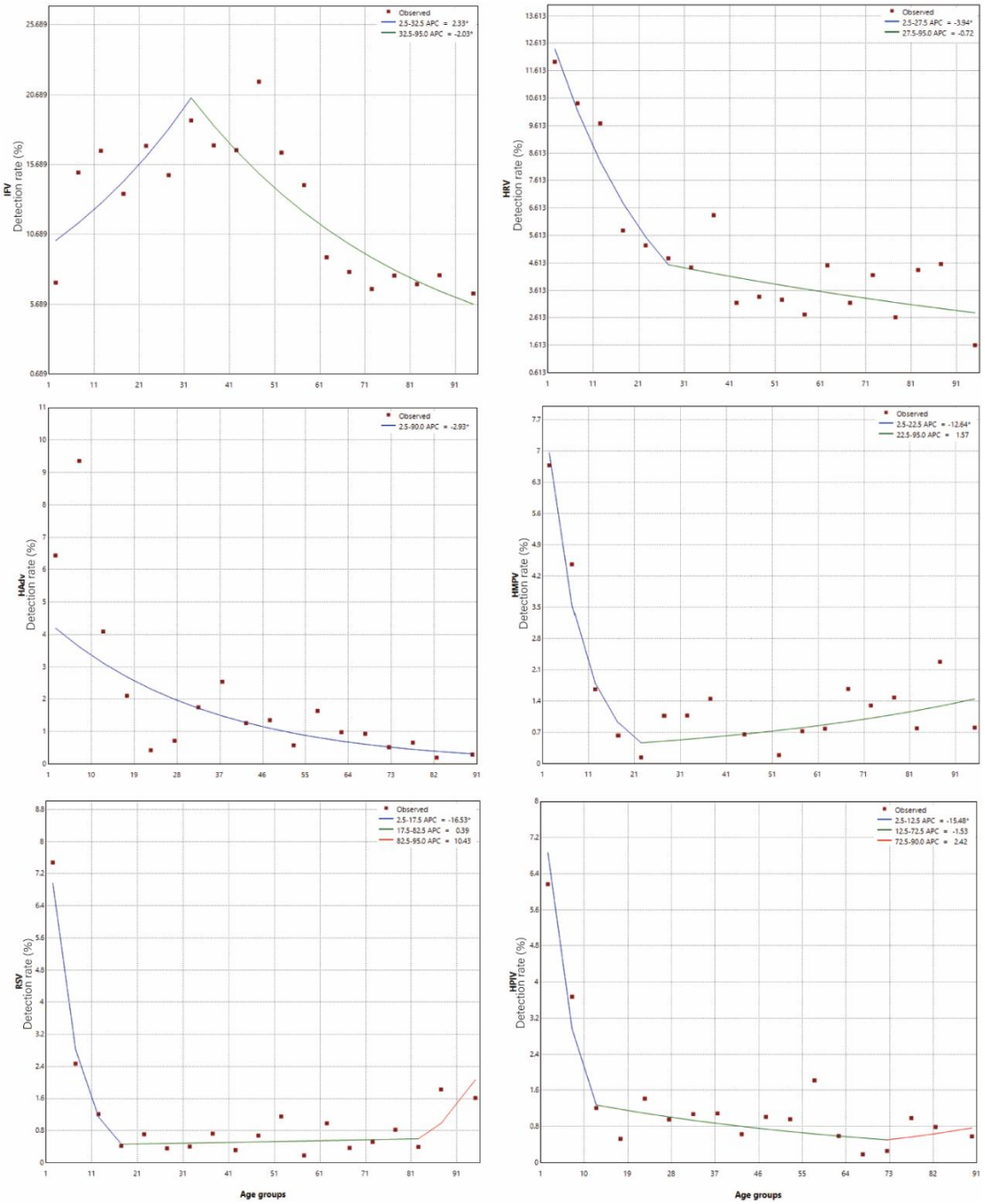


Figure 2. Detection rate of PCR-confirmed viral infections among patients by age group

Note: influenza virus (IFV), human rhinovirus (HRv), human adenovirus (HAdv), human metapneumovirus (HMPV), respiratory syncytial virus (RSV), human parainfluenza virus (HPIV).

228

229 ***Trends in detection rates of the six respiratory viruses.***

230 IFV and RSV showed distinct epidemic peaks, with detection rates rising from
231 October and falling by March. IFV peaked in December 2024 (40.4%) and January
232 2025 (26.2%), while RSV peaked in February 2024 (5.2%) and March 2025 (6.2%).
233 HRV had biannual peaks in spring and autumn, reaching 13.7% in April 2024, 15.58%
234 in October 2024, and 11.37% in April 2025. HPIV and HAdv had flat curves with
235 minor summer peaks: HPIV at 8.12% in June 2024, and HAdv at 7.39% in June 2024.
236 HMPV showed no clear peak but had a modest winter increase, with rates of 7.14% in
237 October 2023 and 7.86% in January 2025 (**Figure. S2**).

238

239 ***Association between respiratory virus detection and SARI.***

240 Multivariable analysis showed that risk factors for SARI among ARI patients included
241 illness onset during autumn (aOR: 1.91, 95% CI: 1.11–3.29) and winter (aOR: 1.74,
242 95% CI: 1.18–2.58), and age ≥60 years (aOR: 5.89, 95% CI: 3.74–9.29) (**Table. 2**). In
243 pairwise comparisons among patients with single-pathogen detection, after adjustment,
244 RSV was associated with a significantly higher risk of SARI compared to other
245 respiratory viruses (RSV vs. IFV: aOR=7.88, 95% CI=5.4–11.51; RSV vs. HRV: 1.52,
246 1.13–2.04; RSV vs. HAdv: 3.21, 2.14–4.81; RSV vs. HMPV: 1.76, 1.24–2.5; RSV vs.
247 HPIV: 1.63, 1.14–2.33). Similarly, HPIV, HMPV, and HRV were associated with a

higher SARI risk compared to IFV and HAdv (HPIV vs. IFV: 4.85, 3.3–7.1; HPIV vs. HAdv: 1.97, 1.3–2.99; HMPV vs. IFV: 5.56, 3.81–8.13; HMPV vs. HAdv: 1.75, 1.14–2.69; HRV vs. IFV: 3.13, 2.45–4.00; HRV vs. HAdv: 2.14, 1.50–3.07). Additionally, HAdv was associated with a higher SARI risk compared to IFV (HAdv vs. IFV: 2.75, 1.83–4.14) (**Table. 2**).

Table 2. Risk factors for progression to SARI

Variables[†]	OR[‡]	*P*-value	aOR[§]
Season			
Spring	Ref		Ref
Summer	1.71 (1.53–1.91)	<0.001	1.41 (0.75–2.66)
Autumn	1.27 (1.14–1.41)	<0.001	1.91 (1.11–3.29)
Winter	0.99 (0.90–1.09)	0.825	1.74 (1.18–2.58)
Regions			
Urban	Ref		Ref
Rural	1.15 (1.06–1.24)	0.001	1.02 (0.76–1.38)
Age group, years old			
0~4	Ref		Ref
5~14	0.46 (0.40–0.54)	<0.001	0.40 (0.16–1.00)
15~59	0.71 (0.64–0.79)	<0.001	0.64 (0.36–1.11)
≥60	5.59 (5.07–6.17)	<0.001	5.89 (3.74–9.29)
Sex			

Male	Ref		Ref
Female	0.61 (0.56–0.65)	<0.001	0.56 (0.42–0.75)
Occupation			
Employed	Ref		Ref
Student	0.18 (0.15–0.21)	<0.001	0.20 (0.09–0.49)
Unemployed¶	0.69 (0.63–0.75)	<0.001	0.41 (0.26–0.65)
Unknown	0.49 (0.43–0.57)	<0.001	0.16 (0.07–0.33)
Hospital			
Secondary general hospital	Ref		Ref
Tertiary general hospital	1.13 (0.91–1.39)	0.265	——
Pairwise comparisons			
RSV vs IFV	3.64 (2.75–4.83)	<0.001	7.88 (5.40–11.51)
RSV vs HRv	1.46 (1.10–1.92)	0.008	1.52 (1.13–2.04)
RSV vs HAdv	3.24 (2.21–4.75)	<0.001	3.21 (2.14–4.81)
RSV vs HMPV	1.60 (1.14–2.24)	0.006	1.76 (1.24–2.50)
RSV vs HPIV	1.60 (1.13–2.27)	0.009	1.63 (1.14–2.33)
HPIV vs IFV	2.28 (1.66,3.12)	<0.001	4.85 (3.30–7.10)
HPIV vs HRv	0.91 (0.67–1.24)	0.545	0.94 (0.68–1.29)
HPIV vs HAdv	2.03 (1.35–3.04)	0.001	1.97 (1.30–2.99)
HPIV vs HMPV	1.00 (0.69–1.44)	0.995	1.09 (0.74–1.61)
HMPV vs IFV	2.28 (1.69–3.08)	<0.001	5.56 (3.81–8.13)
HMPV vs HRv	0.91 (0.68–1.22)	0.531	0.96 (0.71–1.32)

HMPV vs HAdv	2.03 (1.36–3.01)	<0.001	1.75 (1.14–2.69)
HRv vs IFV	2.50 (1.99–3.15)	<0.001	3.13 (2.45–4.00)
HRv vs HAdv	2.23 (1.58–3.15)	<0.001	2.14 (1.50–3.07)
HAdv vs IFV	1.12 (0.79–1.59)	0.512	2.75 (1.83–4.14)

Note: Adjusted odds ratio (aOR), reference (Ref), influenza-like illness (ILI), severe acute respiratory infection (SARI), influenza virus (IFV), human rhinovirus (HRv), human adenovirus (HAdv), human metapneumovirus (HMPV), respiratory syncytial virus (RSV), human parainfluenza virus (HPIV). †When conducting pairwise comparisons among viral-detected patients, we included only those with single pathogen detection. ‡The odds ratio (OR) was derived from the chi-square test for univariate analysis. §We adjusted for season, region, age group, sex, occupation, and hospital level in the multivariate logistic regression model to obtain the adjusted odds ratio; ¶Unemployed refers to preschool children or retirees.

Estimated incidence and hospitalization rate of virus-associated ARI.

Among the total population, the incidence rates of the six viruses (per 100,000 person-years) were: IFV (4,704), HRV (2,294), HMPV (1,900), RSV (1,012), HAdv (489), and HPIV (483). Hospitalization rates (per 100,000 person-years) were: HRV (138), IFV (133), RSV (66), HPIV (42), HMPV (41), and HAdv (36). In children aged 0–4 years, incidence rates (per 100,000 person-years) were: HRV (30,183), HMPV (22,774), RSV (22,181), IFV (13,086), HPIV (7,824), and HAdv (6,991). Hospitalization rates (per 100,000 person-years) were: HRV (2,153), RSV (2,065), HAdv (1,487), IFV (807), HPIV (556), and HMPV (514). In children and adolescents aged 5–14 years, incidence rates (per 100,000 person-years) were: IFV (10,379), HRV (6,992), HMPV (4,727), HAdv (1,863), RSV (1,824), and HPIV (759).

Hospitalization rates (per 100,000 person-years) were: IFV (505), HPIV (202), HMPV (161), RSV (89), HRV (72), and HAdv (67). In individuals aged 15–59 years, incidence rates (per 100,000 person-years) were: IFV (2,211), HRV (678), HMPV (316), RSV (158), HPIV (123), and HAdv (102). Hospitalization rates (per 100,000 person-years) were: IFV (53), HRV (31), RSV (14), HPIV (9), HMPV (7), and HAdv (6). In individuals aged 60 years and older, incidence rates (per 100,000 person-years) were: IFV (852), HRV (583), HMPV (492), HPIV (287), RSV (135), and HAdv (60). Hospitalization rates (per 100,000 person-years) were: HRV (170), RSV (80), IFV (70), HMPV (54), HAdv (27), and HPIV (23) (**Figure. 3**).

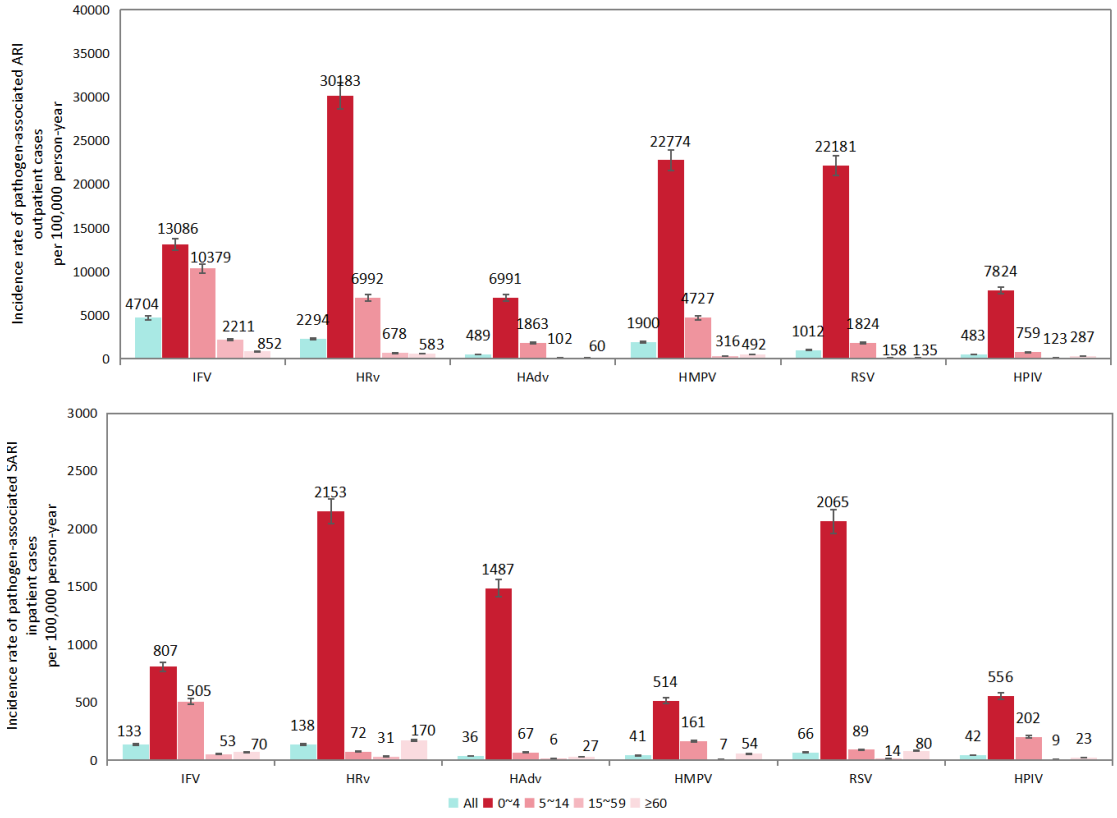


Figure 3. Estimated incidence and hospitalization rate of viral-associated ARI, Chongqing, China, October 2023 - April 2025.

Note: Influenza-like illness (ILI), severe acute respiratory infection (SARI), influenza virus (IFV),

human rhinovirus (HRv), human adenovirus (HAdv), human metapneumovirus (HMPV), respiratory syncytial virus (RSV), human parainfluenza virus (HPIV).

Discussion

Chongqing, China's most populous city with 31.9143 million residents as of 2024, established a multi-pathogen respiratory surveillance system in October 2023, expanding on existing ILI and SARI surveillance system. An EMR collection system covering 84.11% of medical institutions across the city was also implemented. Using data from these multi-source systems, we examined the epidemiology and risk factors for SARI associated with six respiratory viruses (IFV, HRV, HAdv, HMPV, RSV, and HPIV). Additionally, after integrating multi-source data, we supplemented on-site assessments at pilot medical institutions and a retrospective community-based healthcare utilization survey to develop a methodology for estimating the incidence and hospitalization rates of respiratory virus-associated ARI at the population level. This framework provides foundational data and analytical support for future disease burden assessments.

During the COVID-19 pandemic, many studies reported disruptions in the seasonal patterns of non-SARS-CoV-2 respiratory viruses, with some pathogens suppressed and others emerging out of season in the post-pandemic period[3, 4, 16]. Our study in Chongqing, China, starting six months after COVID-19 was no longer a Public Health Emergency of International Concern (PHEIC)[17], found that most respiratory viruses

(IFV, RSV, HPIV, HAdv) had reverted to pre-pandemic trends. RSV and IFV peaked in winter with significant overlay[18], though RSV had a lower detection rate and peaked 1–2 months later. HPIV and HAdv showed relatively flat trends with minor summer peaks. However, HRV exhibited distinct biannual peaks in spring and autumn, differing from its usual year-round circulation with modest summer peaks[19]. HMPV, which typically peaks in March-April in China[19], showed low activity during those months and a minor peak in January 2025. Ongoing multi-pathogen surveillance is crucial for elucidating the evolving seasonality of these pathogens and for guiding the development of prevention and control measures, as well as informing immunization strategies.

From 2009 to 2019, active ARI surveillance in mainland China showed that IFV and HAdV had higher positivity rates in school-age children and adults than in the elderly or younger children[19]. These findings align with our current post-COVID-10 results. Previous studies indicated that RSV, HRV, and HPIV exhibited a child−elderly bimodal age distribution before the pandemic[19]. In post-pandemic Chongqing, RSV and HPIV showed a U-shaped distribution with peaks in infants and older adults, while HRV did not significantly increase in older adults. Infants and young children remain key targets for respiratory virus prevention and control. For pathogens like RSV and HPIV, which follow a child−elderly pattern, intra-household transmission is a critical concern. Data from the U.S. CDC show that RSV has a household transmission rate of 35%–40%, with 58% of events involving children under five

infecting older adults and 22% involving older adults infecting children, highlighting the increased hospitalization risk for child contacts and underscoring the detrimental cycle of intergenerational transmission[20].

Multivariable analysis revealed that seasonal factors, age, and viral etiology are potential risk factors for SARI. Older adults often have poorer health conditions and greater comorbidity burden[21], which may exacerbate the severity of ARIs and increase SARI risk. The peak incidence of most viruses occurs during the colder and drier months of autumn and winter[22], likely contributing to the higher SARI burden during these seasons. In terms of viral etiology, patients with single RSV detection had a significantly higher risk of SARI compared to those with any of the other five viruses, whereas patients with single IFV detection had a significantly lower risk. These findings align with prior research. A meta-analysis summarizing the results of 539 studies on pediatric RSV infection between 1992 and 2025 showed that RSV infection was significantly associated with the risk of SARI (OR: 14.9, 95% CI: 8.2–27.0)[23]. A study analyzing clinical symptoms across 13 respiratory viruses found that RSV infection was associated with a significantly higher clinical severity score (CSS) (mean CSS: 2.74) compared to other viruses[24]. Data further indicate that the average length of hospital stay for adult RSV patients is 63% longer than that for influenza patients, and the proportion hospitalized for over one week is nearly twice as high[25]. Research in China also showed that among older adult inpatients with RSV and IFV-A infections, the 30-day mortality rate was significantly higher in the

RSV group compared to influenza virus-infected patients[8]. These data suggest that despite its relatively low detection rate in outpatient and inpatient settings, RSV infections are associated with more severe clinical manifestations and poorer outcomes[26].

Using multi-source surveillance data from Chongqing, we estimated the incidence and hospitalization rates of ARI associated with six respiratory viruses. Both rates were highest in children under five, with hospitalization rates showing a U-shaped distribution. HRV, HMPV, and RSV had higher incidence, and HRV and RSV had higher hospitalization rates than the other viruses. These findings align with a study conducted in America showing higher incidence of RSV and HRV in children under two (RSV: 21.0 per 100 person-years; HRV: 20.5; HPIV: 14.2; HMPV: 9.2; IFV: 5.9; HAdv: 5.1)[27]. In adults, incidence rates decreased with age, while hospitalization rates were higher in those aged ≥60 years. This was aligned with a study conducted in America that found increasing hospitalization rates with age in adults ≥18 years[28]. Their rates for those ≥65 years were slightly higher than ours, possibly due to our SARI case definition requiring fever >38°C, which likely under-ascertained cases in older adults who often present with atypical or blunted febrile responses [9]. A systematic review that adjusted for variations in diagnostic methods, specimen types, and case definitions using a standard approach found that adjusted RSV-associated hospitalization rates in adults ≥60 years were 2.2 to 6.4 times higher than the unadjusted estimates[29]. Historically, the primary objective of respiratory pathogen

surveillance has been to monitor the epidemiological trends of pathogens. This focus has led to the adoption of more specific case definitions for the inclusion of patients. However, the implementation of future immunization policies will necessitate precise quantification of the disease burden associated with respiratory viruses, particularly age-specific incidence and hospitalization rates. Future multi-pathogen surveillance systems could adopt broader inclusion criteria, such as ARI definitions without fever requirements, and explore integration with other multi-source data to accurately generate these epidemiological indicators.

The primary limitation of our study was that the detection rates and visit counts were extracted from ILI and SARI systems, which require a body temperature >38 °C, thus introducing selection bias, particularly for pathogens like RSV that often cause afebrile illness in older adults. This bias can delay care-seeking and underestimate true infection rates. We addressed this by conducting a Wanzhou pilot using an ARI definition without body temperature criteria and applying a weighted adjustment, though statistical correction can only partially offset the underestimation. Second, the extraction of ILI and SARI cases from EMR strings via regular-expression matching may be influenced by the quality of documentation among healthcare workers, which may also lead to underestimation of incidence and hospitalization rates. Third, although we adjusted for age, gender, occupation, and medical institution level as covariates in the SARI risk analysis, some important confounding factors (e.g., comorbidities and vaccination status) could not be collected due to the use of routine

surveillance data. Further analyses based on more comprehensive medical data are warranted in future studies. Fourth, this study was conducted in Chongqing, and the estimated incidence and hospitalization rates only reflect the local situation during the study period. Future studies could extend the estimation to other regions and nationwide in China using our multi-source data fusion approach combined with field investigations, to better support disease burden assessment.

Conclusions

We provided a comprehensive analysis of the epidemiology and disease burden of respiratory viruses in a major southern Chinese city, using multi-source data. Seasonal patterns of HRV and HMPV remain altered compared to pre-COVID-19 pandemic trends. IFV detection showed an inverted U-shaped age distribution, while RSV and HPIV exhibited a U-shaped distribution with peaks in young children and older adults. HAdv, HRV, and HMPV were most prevalent in preschoolers. RSV infection was identified as risk factors for SARIs. Incidence and hospitalization rates were highest among children under five, with hospitalization rates showing a U-shaped age distribution. The findings offer foundational data for the development of future respiratory viruses' surveillance and the implementation of preventive and immunization measures.

List of abbreviations

ARI: Acute respiratory infection; SARI: Severe acute respiratory infection; IFV:

Influenza virus; RSV: Respiratory syncytial virus; HPIV: Human parainfluenza virus; HAdv: Human adenovirus; HRV: Human rhinovirus; HMPV: Human metapneumovirus; GBD: Global Burden of Disease; DALYs: Disability-adjusted life-years; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; COVID-19: Coronavirus disease 2019; EMRs: Electronic medical records; T-PCR: Real-time reverse-transcription polymerase chain reaction; WHO: World Health Organization; ILI: Influenza-like illness; SE: Standard errors; IQRs: Interquartile ranges; aOR: Adjusted odds ratio; CI: Confidence interval; PR: Joinpoint regression; APC: Annual percentage change; PHEIC: Public Health Emergency of International Concern; CDC: Centers for Disease Control and Prevention; CSS: Clinical severity score.

Declarations

Ethics approval and consent to participate

Our study was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all human participants. Additionally, the study was approved by the Ethics Review Committee of Peking Union Medical College (No. CAMS&PUMC-IEC-2025-013).

Consent for publication

Not applicable.

Availability of data and materials

The data that support the findings of this study are available from the Chongqing

Center for Disease Control and Prevention but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the Chongqing Center for Disease Control and Prevention.

Competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Authors' contributions

MJ and YD conceived the study, designed the methodology, and wrote the original draft of the manuscript. JW, BL, JY, and YY conducted the investigation and curated the data. MJ, YD, and QW performed the formal analysis and created the visualizations. LQ, LF, WY, and JQ provided resources, supervision, and acquired funding. All authors read and approved the final manuscript.

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