Broad impacts of COVID-19 pandemic on acute respiratory infections in China: an observational study

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Brief summary

Test positive rates of eight respiratory viruses decreased during COVID-19 pandemic, compared to the average levels during 2012−2019. IFV and HMPV were consistently suppressed. RSV, HPIV, HCoV, HRV and HBoV resurged after NPIs were largely relaxed and schools reopened.

Abstract

Background To combat the COVID-19 pandemic, nonpharmaceutical interventions (NPI) were implemented worldwide, which impacted a broad spectrum of acute respiratory infections (ARI).

Methods Etiologically diagnostic data from 142 559 cases with ARIs, who were tested for eight viral pathogens (influenza virus, IFV; respiratory syncytial virus, RSV; human parainfluenza virus, HPIV; human adenovirus; human metapneumovirus; human coronavirus, HCoV; human bocavirus, HBoV, and human rhinovirus, HRV) between 2012 and 2021, were analyzed to assess the changes of respiratory infections in China during the first COVID-19 pandemic year compared to pre-pandemic years.

Results Test positive rates of all respiratory viruses decreased during 2020, compared to the average levels during 2012–2019, with changes ranging from -17·2% for RSV to -87·6% for IFV. Sharp decreases mostly occurred between February and August when massive NPIs remained active, although HRV rebounded to the historical level during the summer. While IFV and HMPV were consistently suppressed year round, RSV, HPIV, HCoV, HRV HBov resurged and went beyond historical levels during September, 2020–January, 2021, after NPIs were largely relaxed and schools reopened. Resurgence was more prominent among children younger than 18 years and in Northern China. These observations remain valid after accounting for seasonality and long-term trend of each virus.

Conclusions Activities of respiratory viral infections were reduced substantially in the early phases of the COVID-19 pandemic, and massive NPIs were likely the main driver. Lifting of NPIs can lead to resurgence of viral infections, particularly in children.

Keywords: COVID-19; Acute respiratory infection; Nonpharmaceutical interventions; China

Introduction

In response to the ongoing pandemic of the 2019 novel coronavirus disease (COVID-19), each country has implemented its own portfolio of public health interventions to mitigate the impact of the pandemic. During the first pandemic year, preventive interventions were mostly nonpharmaceutical (social distancing, mask-wearing, shelter-in-place, travel restrictions, school closure, etc.) while vaccines targeting SARS-CoV-2, the etiological pathogen for COVID-19, were being developed [1]. Nonpharmaceutical measures are known to act on a broad spectrum of respiratory pathogens [2-5], and studies have explored the impact of the COVID-19 related nonpharmaceutical interventions (NPIs) on respiratory infections [6-9], with most studies not including the time following the lifting of NPIs. Several studies for long-term impact of NPI in late 2020 have been done on the circulation level of influenza and other viral respiratory infections in North America [10, 11], tropical Asia [12], Europe [13], Japan [14, 15] and South Korea [16], where a common finding was that influenza decreased. However, in China, where COVID-19 was first reported and quickly controlled, the trends of common ARIs spectrum during and after the first epidemic wave remain largely uninvestigated.

In China, a nationwide Surveillance for Etiology of Respiratory Infections (SERI) program has been implemented by the Chinese Center for Disease Control and Prevention (China CDC) since 2009, testing a spectrum of common contagious pathogens causing acute respiratory infections (ARI) year round in 31 provinces [17]. A previous study based on SERI found that virus positive rates varied greatly across age groups and geographical regions [17]. While NPIs were more or less uniform in mainland China during the first wave, their effects might differ by age group and region. For example, closure and reopening of schools mainly affected children, and differences in seasonality of respiratory viruses, culture and contact behavior might lead to differential responses to the NPIs between southern and northern provinces [18]. Using the unique data collected by SERI, we characterize the circulation patterns of the ARI viruses before, during and after the first wave of COVID-19 in the mainland of China as a whole as well as by age group and region. Dynamic changes of these patterns are informative about the broad impact of the NPIs on respiratory infections that share similar transmission modes.

Methods

Data collection and epidemiological description

A total of 314 sentinel hospitals covering all 31 provinces across the mainland of China participated in the SERI project. During Jan 2012−Jan 2021, nasopharyngeal specimens from a random sample of inpatients and outpatients presenting ARIs at these hospitals were collected prior to any treatment. These samples were tested for the presence of eight viral pathogens including influenza virus (IFV), respiratory syncytial virus (RSV), human parainfluenza virus (HPIV), human adenovirus (HAdV), human metapneumovirus (HMPV), human coronavirus (HCoV), human bocavirus (HBoV) and human rhinovirus (HRV) [19]. IFV, RSV, HPIV, HMPV, HCoV, and HRV were tested by RT-PCR, and HAdV and HBoV were tested by PCR according to the standard operating protocol (SOP) of surveillance developed by China CDC. The SERI program included SARS-CoV-2 test from January 2020 and the test results were documented separately. SARS-CoV-2 positive patients were excluded from the current analysis. Details about the SERI program are given in the supplementary materials.

To demonstrate the impact of NPIs on the circulation patterns of the pathogens, we define three periods according to the timeline of major intervention events for containing the COVID-19 epidemic in China: Jan 23rd to Apr 7th 2020 (Phase I) when Wuhan city was placed under lockdown, Apr 8th to Aug 31st 2020 (Phase II) when nationwide NPIs were relaxed while schools remained closed, Sep 1st 2020 to Jan 22nd 2021 (Phase III) when schools were re-opened in most provinces. The details of NPIs implemented during the three phases were included in Supplementary Materials. To attain a controlled comparison with historical levels, the same periods were also defined based on corresponding calendar intervals for pre-pandemic years, starting from Jan 23rd, 2012 to Jan 22nd 2020.

Positive rates were then compared between average of pre-pandemic years and the pandemic year for each period, using the percent change calculated as:

$$[(PR_{t1}(k) - PR_{t0}(k)]/PR_{t0}(k) \times 100\%$$

where $PR_{t1}(k)$ is the positive rate during phase *k* of the pandemic year, Jan 23rd 2020 to Jan 22nd 2021, and $PR_{t0}(k)$ is the average positive rate during phase *k* of the pre-pandemic years, Jan 23rd 2012 to Jan 22nd 2020.

Both $PR_{t1}(k)$ and $PR_{t0}(k)$ were age-standardized positive rates based on population proportions of three age groups: children 0–17 years old, adults 18–59 years old, and senior adults ≥60 years old. Specifically,

$$PR_{t1}(k) = PR_{t1}^{cr}(k) \times Prop_{0-17} + PR_{t1}^{cr}(k) \times Prop_{18-59} + PR_{t1}^{cr}(k) \times Prop_{\geq 60}$$

$$PR_{t0}(k) = PR_{t0}^{cr}(k) \times Prop_{0-17} + PR_{t0}^{cr}(k) \times Prop_{18-59} + PR_{t0}^{cr}(k) \times Prop_{\geq 60}$$

where $PR_{t1}^{cr}(k)$ and $PR_{t0}^{cr}(k)$ are the crude positive rate (number of positive samples divided by the total number of samples tested) during phase *k* of the pandemic year and the pre-pandemic years, respectively. The $Prop_{0-17}$, $Prop_{18-59}$ and $Prop_{\geq 60}$ indicate the overall proportion of patients aged from 0 to 17, 18 to 59 and over 60 years old respectively during the whole pre-pandemic and pandemic years. The comparison was also conducted by age group, sex, geographic region and clinical type (pneumonia and non-pneumonia cases).

Statistical analysis

Time series of monthly positive rates were plotted and fitted with generalized linear models (GLM) to quantify the impact of the COVID-19 related NPIs in different periods for each virus, stratified by age groups (0–17 years old and ≥18 years old) and geographic regions (south and north of China, Supplementary Figure 1A). The periods were redefined for the monthly data, with phases I−III corresponding to February−March, April−August and September-January respectively. We assumed the number of positive cases in each month followed a beta-binomial distribution. This assumption accounts for overdispersion and also considers the limited numbers of tested specimens when the data are stratified by region and age group [20, 21]. The effect of NPIs was coded by three dummy indicators for four phases, with phases I−IV corresponding to Jan 2012–Jan 2020, Feb 2020–Mar 2020, Apr 2020–Aug 2020, and Sep 2020–Jan 2021, respectively. Seasonality was accounted for using sinusoidal functions with both annual and semiannual cycles [22]. Calendar year was included as a covariate to capture the long-term trend, and its functional format could be linear, quadratic or discrete, depending on the AIC. When the discrete year effect was chosen, i.e., each year had its own intercept, we assumed the years 2019 and 2020 share the same intercept, so that the effect of NPIs is estimable. We reported exponentiated regression coefficients as seasonality-adjusted odds ratios (OR). Statistical significance was evaluated with two-sided p-values at the level of $\alpha = 5\%$. All statistical analyses were conducted in the R software (version 4.0.3, R Development Core Team 2020).

Results

Overall change of recruited patients

We extracted diagnostic results and epidemiological data of 104 652 cases with ARI who were tested for the eight respiratory viruses over the period Jan 23, 2012–Jan 31, 2021. The annual number of tested ARI cases decreased from an average of 12 108 during the pre-pandemic years to 7 783 during the pandemic year (Supplementary Figure 1B). The baseline characteristics of the patients were compared between the two periods in Supplementary Table 1. Median age increased from 11 (IQR:2–45) years before to 25 (IQR:3–53) years during the COVID-19 pandemic. This age difference indicates the need for age-standardized test positive rates. Compared with the pre-pandemic years, ARI patients enrolled during the pandemic year were slightly more likely to be enrolled in the early phases, e.g., 26.1% during Phase I in 2020 vs. 21.2% before. No qualitative difference was found between the North and the South or between the two sexes.

Overall change pattern of positive rates

The overall activity of the eight tested viruses, measured by the percent of specimens positive for any virus, decreased from pre-pandemic years to the pandemic year by 58.8% (from 37.9% to 15.6%) in Phase I, 55.1% (from 30.6% to 13.7%) in Phase II, and by 10.3% (from 30.1% to 27.0%) in Phase III.

Significant reductions of test-positive rate from pre-pandemic years to the pandemic year were noted for all tested virus (Table 1, Supplementary Table 2 and Supplementary Figure 2). The largest drop of annual cumulative positive rate was observed for IFV, a reduction of 87.6% (from 9.94% to 1.23%), followed by 70.6% (1.63% to 0.48%) for HMPV, 47% (3.98% to 2.11%) for HAdV, and 32.3% (5.11% to 3.46%) for HPIV.

The change patterns differed across the three phases (Table 1, Supplementary Table 2 and Supplementary Figure 1). Dramatic reductions in positive rates were seen for most pathogens in both Phase I and Phase II. Percent changes above 70% were seen for HMPV (86.5%), IFV (76.8%), HRV (70.3%) and HPIV (70.1%) during Phase I and for IFV (92.6%), HPIV (81.3%), HMPV (78%) and HBoV (77.1%) during Phase II. Reductions of IFV, HPIV, HAdV and HBoV were more substantial in Phase II compared to Phase I, despite partial relaxation of the mass NPIs in Phase II. IFV and HMPV are the only two with persistent decreases throughout all phases. Positive rates of RSV, HPIV, HCoV and HBoV, however, rose significantly above historical levels during Phase III, when NPIs were largely lifted, including reopening of schools. HAdV returned to the pre-pandemic level (Table 1).

IFV-A and HPIV-3 remained as the dominant types in their genera during both pre-pandemic years and the pandemic year. RSV-A and RSV-B exhibit a clear alternating pattern over the years (Supplementary Figure 3). In addition, coinfections with 2 or more viruses decreased during the pandemic (Supplementary Results, Supplementary Figure 4 and Supplementary Table 3).

Change pattern of positive rates by demographic and clinical subgroups

Positive rates of IFV, HPIV and HMPV decreased significantly from pre-pandemic years to the pandemic year in all three age groups (Figure 1 A−C). For HRV, RSV and HBoV, positive rates were significantly reduced in adults (≥18 years) but not in children (<18 years). The declines of positive rates during the first two phases were similar in all three age groups, except for the increased activity of HRV among children during Phase II. During Phase III, the activities of RSV, HPIV, HCoV and HBoV among children resurged to be substantially above historical levels, and the circulation of HRV, HAdV and HMPV also nearly reached historical levels. In particular, the higher than historical levels of RSV, HPIV, HCoV and HBoV in Phase III observed for the whole population (Supplementary Figure 2) were mostly attributed to their resurgence in children (Figure 1A). Among adults ≥18 years, activities of HPIV, HAdV and HCoV also returned to their historical levels during period III (Figure 1B, Figure 1C).

The change patterns were largely consistent between the two sexes (Figure 2A); however, they did differ to some extent between Northern China and Southern China, especially during Phase III. Positive rates of HRV and HAdV increased significantly in the North but decreased significantly in the South during the Phase III (Figure 2B). In addition, more increases of RSV, HPIV, HCoV and HBoV were seen in the North than in the South during Phase III. No regional difference was seen for IFV and HMPV. The resurgence of HPIV and HCoV was more associated with patients without pneumonia, whereas the resurgence of HBoV was more associated with pneumonia patients, during Phase III (Figure 2C).

Effects of NPIs on seasonality and activity of respiratory viruses

We fitted generalized linear models (GLM) to temporal trajectories of monthly positive rates of the viruses by age group (Figure 3) and by region, South vs. North (Supplementary Figure 5). As the change patterns of virus positive rate were similar between adults (18–59 years) and older adults (≥60 years) in all phases (Figure 1B, Figure 1C). We therefore combined the two adult age groups to model the specific impact of NPIs during the COVID-19 pandemic on a finer time scale (monthly data), which also helps to ensure adequate sample sizes. For viruses peaking in late winter, spring or early summer, their expected peaks in the first half of 2020 were either suppressed or delayed, consistent with the massive strict NPIs during Phase I. The peaks of IFV, HAdV, HMPV and RSV were suppressed or flattened. The peaks of HPIV and HBoV were delayed to Phase III among children. The only exception is HRV, for which the actual activity during the summer and autumn of 2020 exceeded model-projected levels among children for the hypothetical scenario. During the second half of 2020, most viruses went back to or beyond historical levels except for IFV. Resurgence of most viruses in later 2020 was more notable in Northern China than in Southern China (Supplementary Figure 5).

The pattern of the phase-specific ORs (Table 2) was further revealed largely consistent with that of the percentage changes in Figure 1 and Figure 2, with some subtle differences. During Phase I or Phase II, the ORs of NPIs on most viruses were observed <1. Only HRV showed strong early resurgence in Phase II, especially in the South, OR=1.40 (95% CI:1.02–1.94), and among children, OR=1.91 (95% CI: 1.39–2.62). During Phase III, most viruses renewed their activities, especially in the North, with the odds of positive samples more than doubled for HBoV (OR=3.74), HCoV (OR=3.62), HPIV (OR=2.73) and HRV (OR=2.48). RSV significantly increased its activity in both the South and the North, but age-standardized percent changes in Figure 2B failed to capture the increase in the South. During Phase III, HCoV resurged sharply in both age groups, and children additionally experienced substantial resurgence of HBoV, HPIV and RSV. IFV was consistently suppressed in all periods, regardless of region or age, and suppression of HAdV also persisted in the South and among children.

Discussion

Understanding how the transmission dynamics of other respiratory viral infections coevolve with that of SARS-CoV-2 is an integral part of the assessment of the broad impact of the COVID-19 pandemic and associated interventions on global health. The current study explored impact using the national surveillance data of ARI related to eight common respiratory pathogens in China during the past decade. We found that the spread and seasonality of most of these pathogens were interrupted during 2020, particularly during weeks 5−15 (phases I−II) when massive stringent NPIs were active. Transmission activities of HMPV, IFV and HPIV were more suppressed than other tested respiratory viruses. However, during Phase III when most NPIs were lifted and schools were reopened, HRV, RSV, HPIV, HCoV and HBoV resurged quickly, especially in children. The buildup of susceptibility during the control periods might have contributed to the resurgence [23]. These observations verified the critical role of school-aged children in spreading respiratory infections. Notably, the rebound of many viruses was more drastic in Northern China than in

Southern China, suggesting the possibility of heterogeneity in the level of maintaining NPIs for preventing COVID-19 resurgence.

In contrast to most other respiratory pathogens, the activity of influenza viruses remained lower than historical levels consistently throughout the pandemic year, regardless of region and age group. Similar situations were found in other countries on both Northern and Southern Hemispheres [4, 11]. A possible reason is the greatly reduced regional and international travel during the pandemic. It has long been recognized that domestic and international air travels likely play an important role in the spread of IFV from the tropical zones towards subtropical and temperate zones in winters [24-26]. Towards the end of 2020, international travel was far from recovered. Although domestic travel essentially returned to normal in many countries, but some NPIs such as mask wearing and social distancing were still in place in transportation hubs, which could be highly effective against influenza which was mainly transmitted via droplets and fomites. For example, a study found that wearing masks could effectively block the transmission of IFV and HCoV but might be less effective in blocking HRV [27]. In addition to travel restrictions and NPIs, interactions among respiratory viruses might have also played a role. For example, infection with HRV was shown to reduce the risk of infection with IFV [28, 29]. On the other hand, influenza vaccine was unlikely a plausible reason for the reduced IFV transmission, as the vaccine coverage rate had been significantly reduced in China during the COVID-19 pandemic [30].

Despite the reduced overall circulation of most viruses, the dominant types of these viruses remained largely unchanged during the pandemic. For example, IFV-A and HPIV-3 still constituted the majority of their genera. The alternation between RSV-A and RSV-B over the years also seemed unaffected by the pandemic. These compositions are more likely driven by virus-specific dynamics of population-level immunity profiles. These results may shed light on future immunization campaigns in the post-COVID-19 era.

This study has several limitations. Firstly, causality between viral activity and NPI measures cannot be inferred from the surveillance data. Secondly, the COVID-19 pandemic might have substantially changed healthcare-seeking behavior of patients with ARIs. While the inclusion/exclusion criteria for the testing stayed the same during the pandemic, the total number of tests did decrease, likely a result of reduced healthcare seeking behavior during the pandemic [31]. Our analyses were based on test-positive rate which should be less sensitive to healthcare-seeking behavior, but it cannot be ruled out that the pandemic has shifted the profile of people who seek medical assistance for ARIs.

In future public health emergencies, interruptive NPIs may serve as a frontline control before efficacious vaccines become ready. When it is possible or necessary to lift the NPIs, strategies need to be developed to protect children from both the emerging pathogen and the common respiratory viruses. In the COVID-19 pandemic, this age group is the last to have access to novel vaccines. Other respiratory viral infections such as influenza may subject them to severe health consequences, and they should be prioritized for vaccination and other preventions targeting these viral diseases. Our findings might not be unique to China, and similar studies should be encouraged worldwide for more effective control of respiratory infections in the post-pandemic era.

Notes

Contributors

WZY, GFG, ZJL, LPW, YY, WL and LQF conceived and designed the study. LJY, HYZ, CXS, XR, CHZ, YFW, SHL, XAZ, QX, BGJ, TJ, CLL, JJC, ZJL and LPW collected, cleaned, and analyzed the data. Statistical analyses were supervised by LQF and YY. LJY, HYZ, CXS, YY, LQF and WL wrote the first drafts of the manuscript. YY, LQF and WL refined the manuscript to its final version. All authors read and approved the final version.

Acknowledgments

The authors would like thank all the subjects, their families, and collaborating clinicians for their participation. We thank staff members of the Department of Science and Education of the National Health Commission, and the ARIs surveillance network laboratories and sentinel hospitals in the participating 31 provinces of China for assistance with field investigation, administration, and data collection.

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Funding

This work was supported financially by grants from the China Mega-Project on Infectious Disease Prevention [grant numbers 2018ZX10713002, 2018ZX10713001 and 2017ZX10103004], the National Natural Science Funds [grant numbers 81825019 and 91846302], Capital's Funds for Health Improvement and Research [grant numbers 2021-1G-4271], and the US NIH grants [grant numbers R56 AI148284 and R01 AI139761].

Potential conflicts of interest.

The No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

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Table 1. Comparison of age-standardized test positive rate (%) of eight respiratory viruses between pre-pandemic years (2012–2019) and the COVID-19 pandemic year (2020) in the mainland of China.

	Overall				**Phase I**				**Phase II**				**Phase III**			
	2012–2019	2020	Relative change	Absolute change#	2012–2019	2020	Relative change	Absolute change#	2012–2019	2020	Relative change	Absolute change#	2012–2019	2020	Relative change	Absolute change#
IFV	9.94	1.23	-87.60%*	-8.71*	15.23	3.54	-76.80%*	-11.69*	7.17	0.53	-92.60%*	-6.64*	9.72	0.95	-90.20%*	-8.77*
HRV	6.54	5.39	-17.60%*	-1.15*	6.17	1.83	-70.30%*	-4.34*	6.86	7.88	14.90%	1.02	6.41	4.56	-28.90%*	-1.85. *
RSV	5.57	4.61	-17.20%*	-0.96*	8.03	3.05	-62.00%*	-4.98*	3.69	1.84	-50.10%*	-1.85*	6.1	7.44	22.00%*	1.34*
HPIV	5.11	3.46	-32.30%*	-1.65%*	4.48	1.34	-70.10%*	-3.14*	6.69	1.25	-81.30%*	-5.44*	3.94	6.06	53.80%*	2.12*
HAdV	3.98	2.11	-47.00%*	-1.87*	3.67	1.49	-59.40%*	-2.18*	4.55	1.44	-68.40%*	-3.11*	3.61	3.17	-12.20%	-0.44
HCoV	2.31	1.9	-17.70%*	-0.41*	2.13	1.02	-52.10%*	-1.11*	3	1.76	-41.30%*	-1.24*	1.77	2.48	40.10%*	0.71*
HBoV	1.75	1.5	-14.30%*	-0.25*	1.05	0.84	-20.00%*	-0.21*	2.23	0.51	-77.10%*	-1.72*	1.63	2.46	50.90%*	0.83*
HMPV	1.63	0.48	-70.60%*	-1.15*	3.11	0.42	-86.50%*	-2.69*	1.32	0.29	-78.00%*	-1.03*	1.16	0.64	-44.80%*	-0.52*

* Statistically significant changes were found (p-value<0.05 based on chi-square test).

#The absolute change was calculated as positive rate in 2012–2019 minus that in 2020.

†Period I: 23rd Jan to 7th Apr; Period II: 8th Apr to 31st Aug; Period III: 1st Sep to 22nd Jan of the following year. The p-values were based on chi-square test. Blue (red) color indicates statistically significant decrease (increase) of test positive rate during the first pandemic year compared to pre-pandemic year

Table 2. GLM-estimated odds ratios (OR) for the odds of a positive test between the pandemic year 2020 and pre-pandemic years 2012–2019 within each of the three period and for each of the eight respiratory viruses. Statistically significant increases (decreases) were colored in red (blue).

Virus		Phase I[†]		Phase II[†]		Phase III[†]	
		OR (95%CI)	*P* value	OR (95%CI)	*P* value	OR (95%CI)	*P* value
Region							
South	HAdV	0.05 (0.01–0.34)	0.002	0.23 (0.14–0.37)	<0.001	0.51 (0.34–0.76)	<0.001
	HBoV	1.73 (0.61–4.87)	0.302	0.21 (0.09–0.48)	<0.001	0.94 (0.54–1.63)	0.828
	HCoV	0.22 (0.05–0.92)	0.038	0.49 (0.26–0.92)	0.027	1.48 (0.89–2.48)	0.134
	HMPV	0[‡]		0.4 (0.17–0.94)	0.036	0.91 (0.42–1.98)	0.820
	IFV	0.09 (0.03–0.23)	<0.001	0.19 (0.10–0.36)	<0.001	0.23 (0.12–0.44)	<0.001
	HPIV	0.38 (0.16–0.93)	0.035	0.28 (0.17–0.47)	<0.001	1.14 (0.77–1.69)	0.517
	HRV	0.46 (0.22–0.98)	0.043	1.40 (1.02–1.94)	0.040	0.59 (0.39–0.89)	0.012
	RSV	0.50 (0.22–1.11)	0.089	0.66 (0.38–1.15)	0.14	1.54 (1.04–2.28)	0.031
North	HAdV	0.58 (0.26–1.30)	0.187	0.21 (0.09–0.50)	<0.001	1.09 (0.61–1.96)	0.763
	HBoV	0.49 (0.06–3.65)	0.482	0.77 (0.29–2.03)	0.593	3.74 (1.95–7.19)	<0.001
	HCoV	1.26 (0.54–2.90)	0.594	1.46 (0.82–2.58)	0.199	3.62 (1.97–6.64)	<0.001
	HMPV	0.17 (0.04–0.70)	0.014	0.16 (0.04–0.68)	0.013	0.52 (0.16–1.63)	0.259
	IFV	0.28 (0.12–0.68)	0.004	0.10 (0.02–0.42)	0.002	0.08 (0.02–0.32)	<0.001
	HPIV	0.69 (0.28–1.70)	0.420	0.10 (0.03–0.32)	<0.001	2.73 (1.67–4.48)	<0.001
	HRV	0.14 (0.02–0.99)	0.049	1.11 (0.65–1.91)	0.707	2.48 (1.49–4.12)	<0.001
	RSV	0.26 (0.08–0.84)	0.024	0.11 (0.01–0.79)	0.029	1.71 (1.04–2.81)	0.033
Age groups							
0–17 years	HAdV	0.31 (0.11–0.87)	0.027	0.22 (0.12–0.40)	<0.001	0.64 (0.41–0.99)	0.046
	HBoV	1.56 (0.55–4.46)	0.407	0.26 (0.13–0.52)	<0.001	1.66 (1.08–2.55)	0.021
	HCoV	0.71 (0.22–2.34)	0.578	0.93 (0.53–1.64)	0.805	2.09 (1.26–3.46)	0.004
	HMPV	0.10 (0.01–0.75)	0.025	0.23 (0.08–0.62)	0.004	0.75 (0.39–1.47)	0.405
	IFV	0.17 (0.05–0.54)	0.003	0.14 (0.05–0.38)	<0.001	0.17 (0.08–0.39)	<0.001
	HPIV	0.27 (0.08–0.85)	0.026	0.12 (0.05–0.27)	<0.001	2.08 (1.49–2.90)	<0.001
	HRV	0.62 (0.25–1.57)	0.316	1.91 (1.39–2.62)	<0.001	1.38 (0.96–1.97)	0.078
	RSV	0.37 (0.15–0.91)	0.030	0.64 (0.34–1.20)	0.168	1.93 (1.34–2.78)	<0.001
≥ 18 years	HAdV	0.21 (0.07–0.63)	0.005	0.29 (0.14–0.62)	0.001	0.77 (0.37–1.58)	0.469

HBoV	0.47 (0.06–3.75)	0.478	0.85 (0.24–3.05)	0.802	0‡	
HCoV	0.61 (0.24–1.51)	0.283	0.76 (0.43–1.34)	0.338	2.23 (1.22–4.07)	0.009
HMPV	0.08 (0.01–0.58)	0.012	0.47 (0.16–1.37)	0.168	0.43 (0.06–2.92)	0.384
IFV	0.16 (0.06–0.42)	<0.001	0.20 (0.08–0.46)	<0.001	0.14 (0.05–0.40)	<0.001
HPIV	0.47 (0.18–1.20)	0.113	0.34 (0.17–0.68)	0.002	0.69 (0.34–1.39)	0.299
HRV	0.24 (0.09–0.68)	0.007	0.73 (0.45–1.19)	0.207	0.48 (0.26–0.87)	0.016
RSV	0.38 (0.14–1.05)	0.062	0.21 (0.05–0.88)	0.033	0.81 (0.35–1.87)	0.623

* Phase I: Feb–Mar, 2020; Phase II: Apr–Aug, 2020; Phase III: Sep, 2020 – Jan, 2021

† IFV, influenza virus; HRV, human rhinovirus; RSV, respiratory syncytial virus; HPIV, human parainfluenza virus; HAdV, human adenovirus; HCoV, human coronavirus; HBoV, human bocavirus; HMPV, human metapneumovirus.

‡ When OR=0, the 95% CI and p-value were not calculated.

Figure Legends

Figure 1. Percent change of test positive rate during the COVID-19 pandemic year 2020 compared to the average incidences during pre-pandemic years 2012–2019 for each of three predefined periods and stratified by age group. (A) Children <18 years old; (B) Younger adults 18-59 years old; (C) Older adults ≥60 years old. Eight respiratory pathogens were investigated: influenza virus (IFV), human rhinovirus (HRV), respiratory syncytial virus (RSV), human parainfluenza virus (HPIV), human adenovirus (HAdV), human coronavirus (HCoV), human bocavirus (HBoV), and human metapneumovirus (HMPV). Red and blue bars indicate positive and negative percent changes, respectively. Statistically significant changes were marked with asterisks.

Figure 2. Percent change of test positive rate during the COVID-19 pandemic year 2020 compared to the average incidences during pre-pandemic years 2012–2019 for each of three predefined periods and stratified by sex, region and clinical type. (A) Males (solid) vs. females (unfilled); (B) North (solid) vs. South (unfilled); (C) Pneumonia cases (solid) vs. Non-pneumonia cases (unfilled). Eight respiratory pathogens were investigated: influenza virus (IFV), human rhinovirus (HRV), respiratory syncytial virus (RSV), human parainfluenza virus (HPIV), human adenovirus (HAdV), human coronavirus (HCoV), human bocavirus (HBoV), and human metapneumovirus (HMPV). Red and blue bars indicate positive and negative percent changes, respectively. Statistically significant changes were marked with asterisks.

Figure 3. Observed and model-fitted time series of monthly numbers of test positive samples in two age groups (A) 0–17 years old; (B) ≥18 years old. Eight respiratory pathogens were investigated: influenza virus (IFV), human rhinovirus (HRV), respiratory syncytial virus (RSV), human parainfluenza virus (HPIV), human adenovirus (HAdV), human coronavirus (HCoV), human bocavirus (HBoV), and human metapneumovirus (HMPV). GLM was fitted for Jan 2012–Jan 2020 (blue) and for Feb 2020–Jan 2021 (red) separately. Hypothetical numbers of positive samples during Feb, 2020–Jan, 2021 (blue) in the absence of NPIs was projected using the model based on Jan 2012–Jan 2020. The pandemic year (from Feb 2020 to Jan 2021) was shaded in blue. Confidence bands were shaded grey, and black dots indicated observed data. For each virus, the image during pandemic phases was separately magnified to improve readability. Phase I included most intense NPIs such as stay-at-home or shelter-in-place order, closure of nonessential businesses, restaurant, schools and hotels, prohibition of gatherings, etc. Phase II relaxed human movement restrictions in areas without cases and allows restaurants to operate with limited capacity. Schools remain closed and indoor gathering activities (such as cinema) are prohibited. Phase III included schools reopening and businesses and recreational activities resumed nationwide.

Figure 1

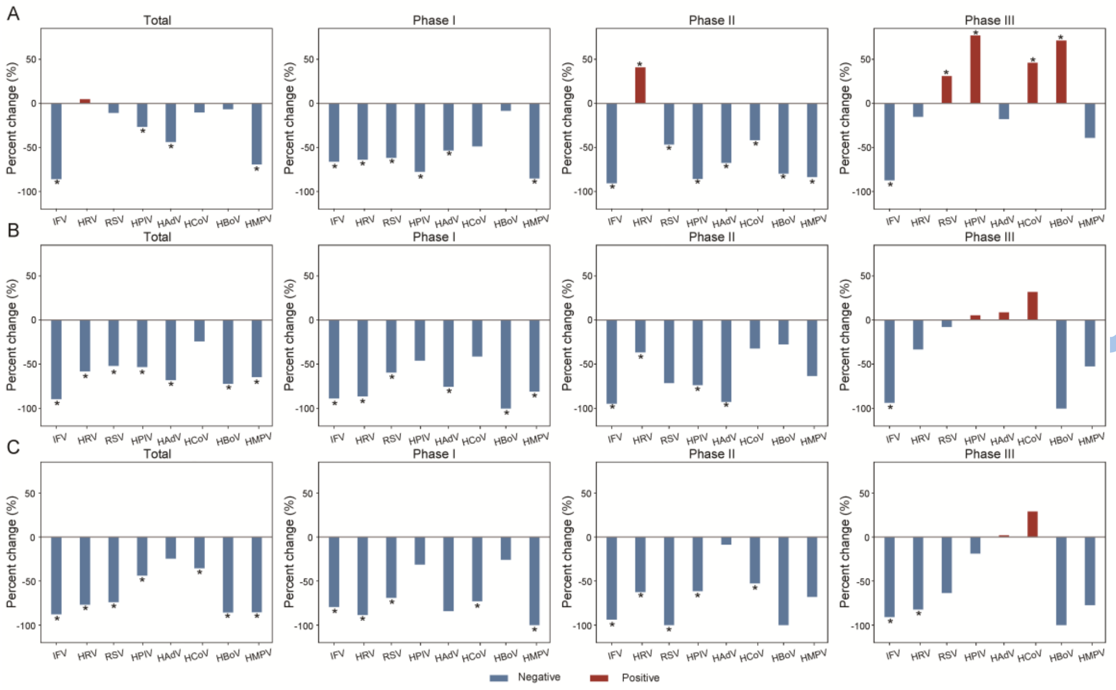

A
B
C
Total
Phase I
Phase II
Phase III
Percent change (%)
50
0
-50
-100
IFV
HRV
RSV
HPIV
HAdV
HCoV
HBoV
HMPV
Negative
Positive

Figure 2

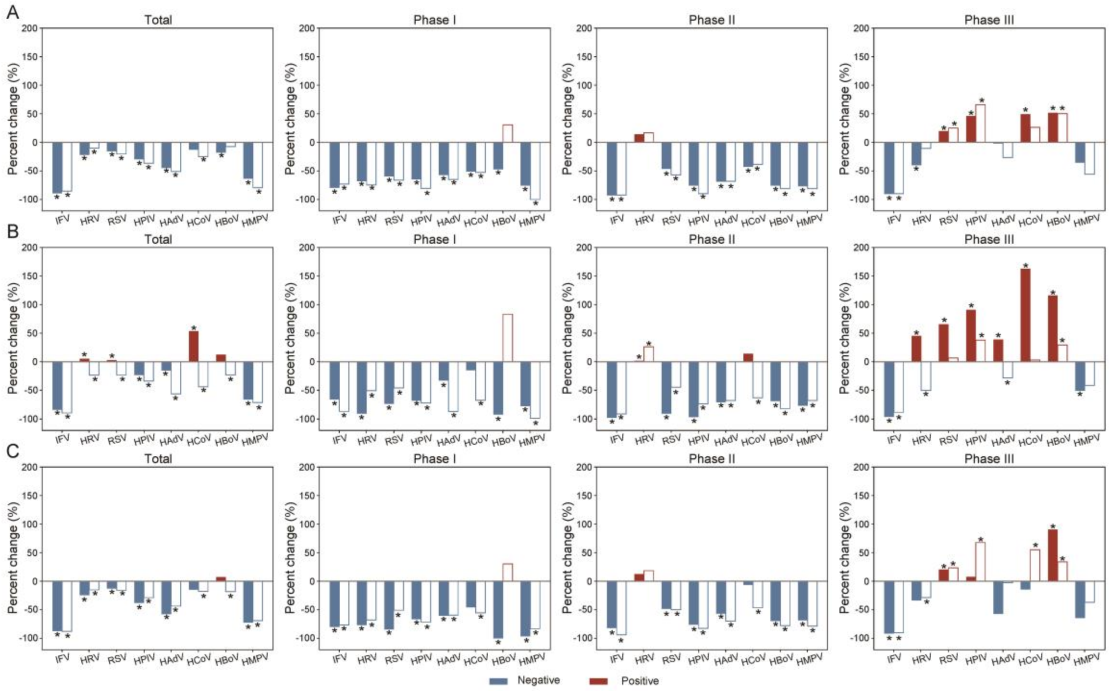
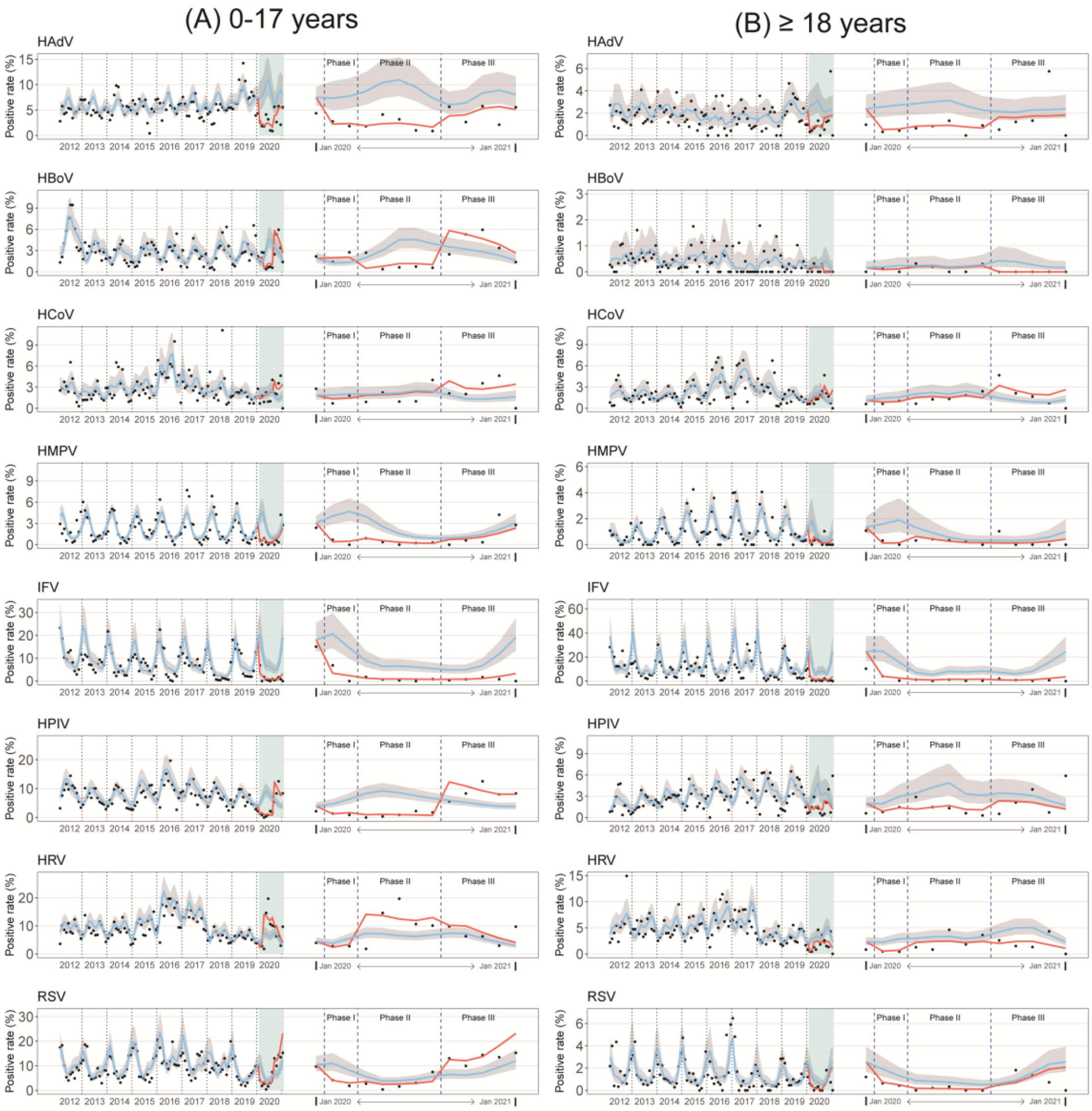

A
B
C
Total
Phase I
Phase II
Phase III
Percent change (%)
IFV HRV RSV HPIV HAdV HCoV HBoV HMPV
Negative
Positive

Figure 3



(A) 0-17 years
(B) ≥ 18 years
HAdV
HBoV
HCoV
HMPV
IFV
HPIV
HRV
RSV
Positive rate (%)
Phase I
Phase II
Phase III
2012 2013 2014 2015 2016 2017 2018 2019 2020
Jan 2020
Jan 2021