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# Effects of COVID-19-targeted nonpharmaceutical interventions on children's respiratory admissions in China: a national multicenter time series study

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## ABSTRACT

**Objectives:** To estimate the impact of nonpharmaceutical interventions (NPIs) targeted at the COVID-19 pandemic on the admission number of respiratory diseases, including pneumonia, acute bronchitis & bronchiolitis, and acute upper respiratory infections (AURIs) for children in China.

**Methods:** Continuous hospitalization records aged 0-18 years from January 1, 2016, to December 31, 2020, were collected from 26 tertiary children's hospitals. Interrupted time series analysis with a quasi-Poisson model was conducted with the start time of the COVID-19 pandemic as the interrupted timepoint and the weekly admission numbers of all-cause respiratory disease, pneumonia, acute bronchitis & bronchiolitis, and AURI as the outcome measures. Hospitalizations of childhood neoplasms were analyzed as the reference group.

**Results:** The reduction in admission numbers following NPIs was -55.0% (-57.9 to -51.9%) for all-cause respiratory diseases, -62.7% (-65.7 to -59.5%) for pneumonia, -48.1% (-53.3 to -42.3%) for bronchitis & bronchiolitis, and -24.3% (-28.6 to -19.8%) for AURI. The effect estimates of NPIs on childhood neoplasms was -29.1% (-33.6 to -24.4%). Stratification analysis showed the reduction was most drastic for children at 4-6 and 7-12 years.

**Conclusion:** The admission number for respiratory diseases among children in China decreased drastically after the implementation of NPIs. NPIs with low socio-economic burdens should be suggested even outside the COVID-19 pandemic.

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## Introduction

COVID-19 has exerted a profound influence on everyday life and the healthcare system worldwide. Since the outburst of COVID-19 in Wuhan city, China, in January 2020, a series of nonpharmaceutical interventions (NPIs) have been conducted nationwide. The NPIs refer to the combination of mask-wearing, handwashing, and social distancing, such as closing schools and public places, quaran-

ting infected patients and close contacts, and travel restrictions (Fricke et al., 2021; Zhang et al., 2021a). These measures have effectively curbed the large-scale spread of the epidemic, keeping the number of people infected with COVID-19 in China under control (Tang and Abbasi, 2021).

Since the COVID-19 pandemic, many countries have witnessed a sharp fall in non-COVID-19-related emergency visits, outpatients, and inpatients for children (Angoulvant et al., 2021; Dopfer et al., 2020; Hu et al., 2022; Isba et al., 2020; Keyes et al., 2021; Zhang et al., 2020). The reduction in hospital admission numbers could be explained in two ways, one being the change in healthcare-seeking behaviors. The public awareness of the pandemic has brought parents the fear of attending hospitals with

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**Figure 1.** The distribution of the 26 tertiary children's hospitals included in this study.

their sick children, and they may choose to postpone the visit or seek medical help online (Lim et al., 2020). In addition, the regional lockdown from time to time and the restriction of patient flow since the start of the pandemic also caused the inaccessibility of health care (Angoulvant et al., 2021). The other explanation is about the secondary benefit of COVID-19-targeted NPIs since these measures are not specific to COVID-19 and could reduce the transmission of other viruses as well (Kadambari et al., 2022).

The NPIs have been reported to have the strongest effect on children's respiratory systems. Respiratory diseases, especially pneumonia, are major causes of hospitalization and death among children younger than 5 years. Recently, a dramatic decrease in pediatric respiratory infections, such as pneumonia, bronchiolitis, and influenza, has been observed worldwide and deemed as the result of the interruption of person-to-person viral or bacterial transmission attributed mainly to mask-wearing, social distancing, and school closure (Cheng et al., 2020; Rybak et al., 2021; Sakamoto et al., 2020; Van Brusselen et al., 2021).

Since the NPIs are continuing in China, this study aimed to investigate how much the admission numbers of respiratory diseases, including pneumonia, bronchitis/bronchiolitis, and acute upper respiratory infections (AURI), have decreased in Chinese children since the implementation of NPIs. We utilized data from 26 tertiary children's hospitals in China from January 2016 to December 2020 and conducted an interrupted time series analysis with weekly data. In addition, we roughly estimated the effect of healthcare-seeking behavior change caused either by virus panic or by restriction of patient flow, using weekly admission numbers of childhood neoplasms. The rationale for choosing childhood neoplasms as the reference group was based on the hypothesis that the reduction in their admission number, if there is any, would be

mainly caused by the city or school lockdown, travel restrictions, and healthcare-seeking behavior change. We could therefore approximate the extent to which the reduction in respiratory admissions can be attributed to NPIs such as mask-wearing, handwashing, and social distancing.

## Methods

### Data source

The data was collected from The FUTang Updating medical REcords (FUTURE) Database. The database was set up by the Futang Research Center of Pediatric Development (FRCPD), which was founded in 2013 and was the first research-based organization of children's hospitals in China. Until June 2022, FRCPD has included 47 members who are all tertiary children's hospitals and distributed mostly in the capital cities of the provinces in China. This children's hospital alliance represents the best quality of health care for the diagnosis and treatment of children's diseases in China. Among the FRCPD members, 26 hospitals have agreed and uploaded the summary reports of discharged patients to the FUTURE database annually. The distribution of the 26 hospitals is shown in Figure 1. Up to the time that the research was conducted, the database had over 6 million hospitalization records from 2016 to 2020. The data recorded the demographic characteristics of each patient (age, gender, personal identification, etc.) and clinical information (diagnosis, comorbidity, surgery, etc.). Until now, FUTURE is still the largest and most representative database for hospitalized children in China and can reflect the situation and change in the composition of children's illnesses. More details about the database have been presented in a previous publication (Wang et al., 2021).

### Case selection and study outcome

Based on the International Classification of Diseases and Related Health Problems (10th-revision, ICD-10), we extracted hospital admissions with the following codes: J00–J06 for AURI; J12–J18 for pneumonia; J20 and J21 for bronchitis & bronchiolitis; J00–J99 for all-cause respiratory diseases; and C00–D48 for childhood neoplasms as the reference group.

The outcome variables were the weekly admission numbers of all-cause respiratory diseases, pneumonia, bronchitis & bronchiolitis, and AURI over time. The second outcome variables were the weekly admission numbers of the aforementioned diseases stratified by age. According to the physical development and education stages, children were grouped into five periods: less than 1 year old; 1–3 years old; 4–6 years old (kindergarten period); 7–12 years old (primary school period); and 13–18 years old (middle school period).

### Statistical analysis

We adopted the interrupted time series design in this study. Outcome variables were analyzed by quasi-Poisson regression, accounting for secular trends before and after the implementation of NPIs, seasonality, and overdispersion of data. The time unit of outcome variables was determined to be 1 week to achieve optimal model precision. We take the lockdown time of Wuhan city, which was January 23, 2020, as the beginning of the nationwide implementation of NPIs. The intervention was included in the model as a dummy variable estimating the immediate post-intervention change. We hypothesized that the implementation of NPIs would have an impact on the outcome variables of the next unit time. Therefore, the pre-NPIs period was from January 4, 2016, to January 26, 2020 (212 weeks), and the post-NPIs period was from January 27, 2020, to December 27, 2020 (48 weeks). There were strong seasonal fluctuations for respiratory diseases, with a higher number recorded in winter than in summer. We accounted for the seasonality by including harmonic terms (sines and cosines) with 52-week periods. Using data from the pre-NPIs period to generate a quasi-Poisson model that fits the observed values of weekly admission numbers for respiratory diseases, we can predict the “counterfactual” values if there had been no COVID-19 and NPIs. The discrepancy between the fitted values and the counterfactual values reveals the impact of NPIs on the admission number of respiratory diseases. The crude weekly numbers rather than the number per 1000 admissions were analyzed because the NPIs, including the lockdown, had an impact on all kinds of diseases. The model validation was conducted by visual inspection of the correlograms (autocorrelation and partial autocorrelation functions) and the residuals analysis. Statistical tests with  $p < 0.05$  were considered significant. All statistical analyses were performed by R v4.1.2 (<http://www.R-project.org>).

### Results

From 2016 to 2020, there were a total of 5,660,475 admissions in the 26 participating centers, of which 1,566,284 met the ICD-10 code for all-cause respiratory diseases. As is presented in Table 1, before the implementation of NPIs, the weekly admission number for all-cause respiratory diseases was 6611.4 for all children, and it was reduced to 3430.4 after the NPIs. The percentage of change is estimated to be -55.0% (95% CI: -57.9%, -51.9%) by the interrupted time series analysis with a quasi-Poisson regression model (Figure 2). The stratification analyses showed that NPIs had the greatest impact on children aged 4–6 years (-61.9% 95% CI: -65.7%, -59.5%), followed by children aged 7–12 years (-61.4% 95% CI: -65.6%, -56.7%), and had the least impact on children aged 13–18

years (-24.0% 95% CI: -32.7%, -14.2%) (Figure 3). For hospitalizations due to childhood neoplasms, which served as the reference group in this study, the effect of NPIs is estimated to be -29.1% (95% CI: -33.6%, -24.4%), much lower than that on respiratory diseases.

Admissions with pneumonia accounted for most of the respiratory diseases, and the reduction in admission number is estimated to be -62.7% (95% CI: -65.7%, -59.5%), with the weekly admission number of 4038.5 before and 1857.5 after the implementation of NPIs (Table 1 and Figure 2). The impact of NPIs was found greatest among children aged 7–12 years (-80.1% 95% CI: -83.8%, -75.4%), followed by children aged 4–6 years (-74.0% 95% CI: -77.6%, -69.9%) (Figure 3).

For bronchitis and bronchiolitis, the weekly admission number was much lower than for pneumonia, which was 692 before the NPIs and 417.2 thereafter. The reduction caused by NPIs was estimated to be -48.1% (95% CI: -53.3%, -42.3%) (Table 1 and Figure 2). The two age groups most affected by NPIs were still 7–12 years (-60.0% 95% CI: -67.1%, -51.4%) and 4–6 years (-59.3% 95% CI: -66.2%, -51.0%) (Figure 3).

As to the AURI, the effect of NPIs was estimated to be -24.3% (95% CI: -28.6%, -19.8%) (Table 1 and Figure 2). The effect was greatest for children aged 4–6 years (-48.2% 95% CI: -53.4%, -42.3%), followed by children 7–12 years (-44.0% 95% CI: -49.1%, -38.3%). For children less than 1 year, the impact of NPIs was not statistically significant. It is worth noting that the impact of NPIs on the admission number of AURI for children aged 13–18 years was significantly upward, with an estimated increase of 36.6% (95% CI: 15.5%, 61.5%) (Figure 3).

### Discussion

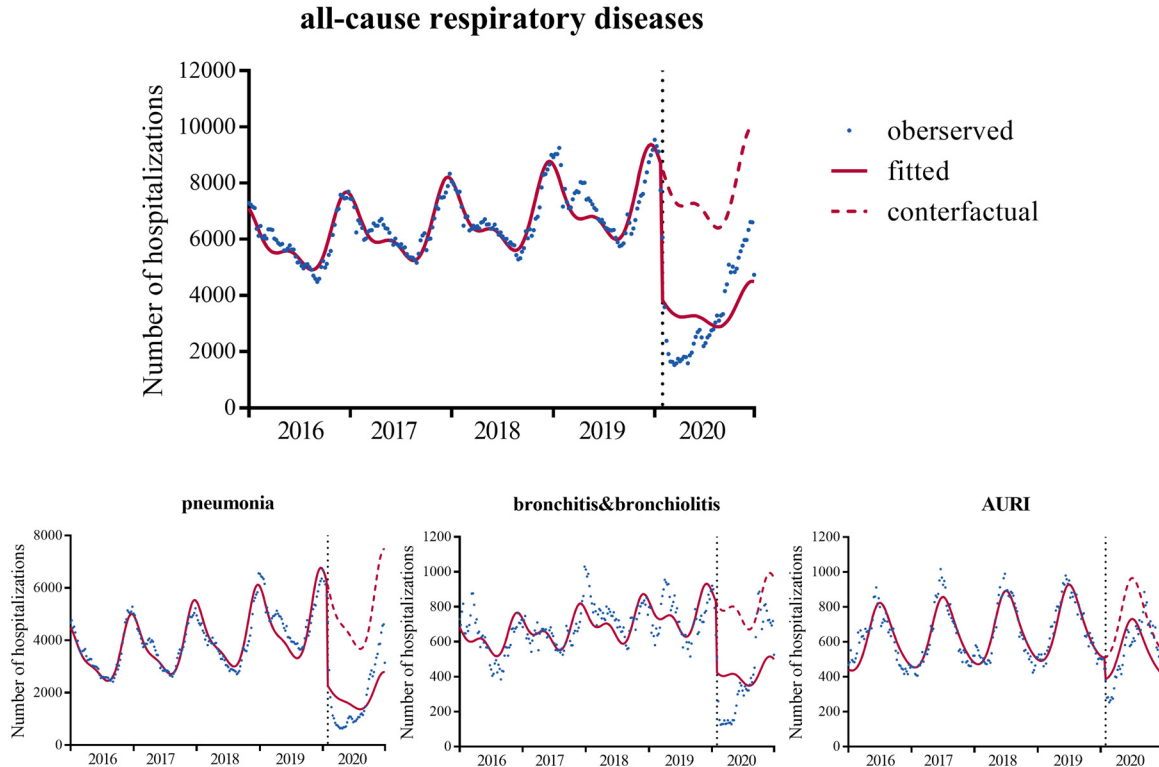
In this interrupted time series analysis with 1,566,284 respiratory hospitalization records among Chinese children, the numbers of admission following NPIs decreased by -55%, -62.7%, -48.1%, and -24.3% for all-cause respiratory diseases, pneumonia, bronchitis/bronchiolitis, and AURI, respectively. This is the first time in China to assess the impact of COVID-19-targeted NPIs on the admission numbers for children with data from 26 tertiary children's hospitals across 5 years. The unprecedented data volume and study period make the conclusions of this study representative and reliable and can provide scientific evidence for the following control and prevention policy of the pandemic.

Compared to the effect of NPIs on childhood neoplasms, which was estimated to be -29.1%, NPIs were found to have an additional effect of -25.9% on all-cause respiratory admissions, -33.6% on pneumonia admissions, and -19% on bronchitis/bronchiolitis admissions. The additional effect might be mostly attributed to the effects of mask-wearing, handwashing, and social distancing on the interruption of person-to-person viral or bacterial transmission. Mask-wearing has been strongly recommended in the world since the COVID-19 pandemic. Up till now, it is still a mandatory health policy in China and people wearing no masks are not allowed in transportation, entertainment venues, or other public places. Masks play a vital role in controlling the transmission of infectious agents by preventing both droplets and aerosols (Jones and Podolsky, 2021; Long et al., 2020; Radonovich et al., 2019). As aerosol and droplets are also the route of transmission for viral respiratory diseases but not for nonrespiratory diseases, the additional decrease in pediatric respiratory admissions in the present study might be attributed to mask-wearing to a large extent. In addition, hand hygiene and hand cleansing awareness, which have been emphasized since the COVID-19 pandemic, could also help reduce pediatric respiratory diseases. It is reported that proper hand hygiene could decrease a proportion of the spread of transmissible disease and a meta-analysis quantitatively demonstrated that improvements

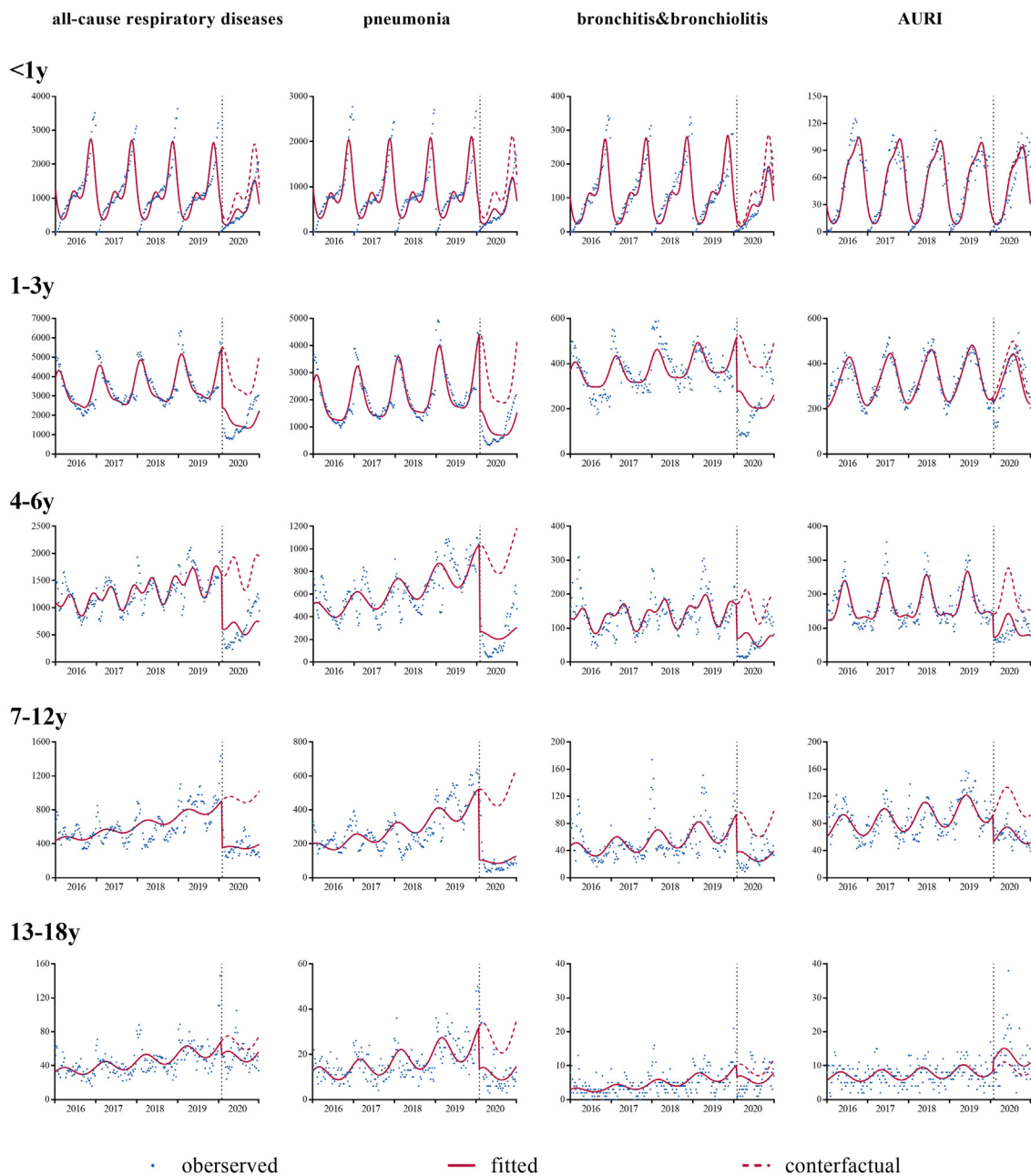
**Table 1**  
The mean weekly admissions before and after the implementation of NPIs and the estimated changes.

	Before NPIs	After NPIs	Percentage of change (95% CI)	P-value
Childhood neoplasms				
	738.8	644.8	-29.1 (-33.6; -24.4)	<0.001
Respiratory diseases				
Total	6611.4	3430.4	-55.0(-57.9; -51.9)	<0.001
<1 year	1197.6	699.4	-41.0(-51.9; -27.6)	<0.001
1-3 years	3455.3	1680.7	-56.4(-60.4; -51.9)	<0.001
4-6 years	1293.4	639.9	-61.9(-65.7; -57.7)	<0.001
7-12 years	620.3	359.5	-61.4(-65.6; -56.7)	<0.001
13-18 years	44.9	50.9	-24.0(-32.7; -14.2)	<0.001
Pneumonia				
Total	4038.5	1857.5	-62.7(-65.7; -59.5)	<0.001
<1 year	906.0	537.9	-43.3(-54.0; -30.2)	<0.001
1-3 years	2197.4	969.3	-63.6(-67.6; -59.2)	<0.001
4-6 years	629.9	240.8	-74.0(-77.6; -69.9)	<0.001
7-12 years	288.4	98.1	-80.1(-83.8; -75.4)	<0.001
13-18 years	16.8	11.4	-58.0(-64.8; -49.9)	<0.001
Bronchitis & bronchiolitis				
Total	692.0	417.2	-48.1(-53.3; -42.3)	<0.001
<1 year	116.5	83.3	-33.0(-45.0; -18.4)	<0.001
1-3 years	375.3	228.8	-47.0(-53.1; -40.1)	<0.001
4-6 years	140.9	68.1	-59.3(-66.2; -51.0)	<0.001
7-12 years	54.6	31.0	-60.0(-67.1; -51.4)	<0.001
13-18 years	4.7	5.9	-33.5(-48.0; -14.8)	<0.001
Acute upper respiratory infections				
Total	646.2	554.6	-24.3(-28.6; -19.8)	<0.001
<1 year	52.1	50.9	-3.5(-16.9; 12.0)	0.638
1-3 years	329.5	331.2	-11.4(-16.7; -5.6)	<0.001
4-6 years	169.8	98.3	-48.2(-53.4; -42.3)	<0.001
7-12 years	87.3	61.9	-44.0(-49.1; -38.3)	<0.001
13-18 years	7.5	12.4	36.6(15.5; 61.5)	<0.001

Abbreviation: NPIs, nonpharmaceutical interventions.



**Figure 2.** Impact of NPIs on weekly admission numbers for all-cause respiratory diseases, pneumonia, bronchitis and bronchiolitis, and AURI, from January 1, 2016, to December 31, 2020. The blue dots show the observed data. The red line shows the model estimates based on observed data using quasi-Poisson regression modeling. The dotted red line shows the expected values without COVID-19 and the following NPIs in the post-intervention period. The start of the NPIs is indicated by the vertical dotted black line. Abbreviations: AURI, acute upper respiratory infections; NPIs, nonpharmaceutical interventions.



**Figure 3.** Impact of NPIs on weekly admission numbers for all-cause respiratory diseases, pneumonia, bronchitis & bronchiolitis, and AURI for different age groups, from January 1, 2016, to December 31, 2020.

The blue dots show the observed data. The red line shows the model estimates based on observed data using quasi-Poisson regression modeling. The dotted red line shows the expected values without COVID-19 and the following NPIs in the post-intervention period. The start of the NPIs is indicated by the vertical dotted black line. Abbreviations: AURI, acute upper respiratory infections; NPIs, nonpharmaceutical interventions.

in hand hygiene resulted in reductions in 21% of respiratory illnesses (Aiello et al., 2008).

The present study found that NPIs had the most significant impact of -62.7% on pneumonia admissions, which is in line with the results of another related study in France that reported the monthly number of hospitalized community-acquired pneumonia decreased by -63.0% after NPI implementation (Rybak et al., 2022). The reduction may be related to the drastic change in the distribution of causative pathogens of respiratory tract infections (Dähne et al., 2021; Mutnal et al., 2020; Tang et al., 2022). It is reported that among children infected with community-acquired pneumonia in Shanghai, China, the detection rate of eight of

the most common respiratory viruses, which ranged from 16.9–26.9% from 2011 to 2019, dramatically decreased to 10.5% in 2020 (Li et al., 2022). Another microbiological study in Poland discovered a 99% drop in the respiratory syncytial virus among pediatric infections during the pandemic season until April 2021 compared to the pre-pandemic years (Grochowska et al., 2022). In addition, many studies also noticed the change in the incidence of bacterial pneumonia during the COVID-19 pandemic (Amin-Chowdhury et al., 2021; Brueggemann et al., 2021; Chan et al., 2021; Chao and Lai, 2022; Danino et al., 2022; Fujita, 2021; Zhang et al., 2021b). For example, *Streptococcus pneumoniae* is the most common pathogen of community-acquired pneumonia, but

the incidence of invasive pneumococcal disease significantly declined during this pandemic (Chan et al., 2021; Huh et al., 2021; Juan et al., 2021; Lim et al., 2020).

A more interesting discovery is that the reduction in admission numbers was most drastic in children aged 4–6 years, who are mostly in kindergarten, then in children aged 7–12 years, who are mostly in primary school. The phenomenon could be explained that: firstly, children in primary school and kindergarten experienced longer school closures than children aged 13–18 years, who had a heavier course load. Therefore, they were less likely to be infected by classmates. Secondly, children in these two age groups are supposed to have higher compliance with wearing masks than children aged 1–3 years and younger. Thirdly, mask-wearing may play a stronger protective effect on younger children who have immature lungs with smaller airways and immature immune systems but longer outdoor time or more chance of exposure to pathogens related to respiratory disease (Schraufnagel et al., 2019). Just as shown in Table 1, among all children with respiratory disease, the proportion was highest in the 1–3 years old group than the 4–6 years old group but lowest in the 13–18 years old group. Thus, the preventive effect of mask-wearing for respiratory disease was more apparent among children 4–6 years old. These findings highlight the great significance of mask-wearing to prevent pediatric respiratory disease, in view of mask “slackers” rejecting public health advice and refusing to wear them in some regions worldwide. Considering the cost-effective and sustainable characteristics of mask-wearing and handwashing, these two interventions should be strongly suggested even after the pandemic.

The most notable strength of this study relies on the multicenter design and long time duration. We included 26 tertiary children’s hospitals accounting for more than 40% of all national public tertiary children’s hospitals in this study. Among them, 20 were located in the capital of the province and had the most representative population of hospitalized children in that area. Therefore, the conclusions can reflect the national situation to a large extent regarding how much the NPIs affected children’s respiratory admission numbers. There are also several limitations of this study, so the interpretation of the results should be treated with caution. Firstly, the NPIs refer to the combination of several interventions, but part of NPIs, such as the closure of schools, entertainment venues, and public places, and travel restrictions, was not implemented continuously, so the impact of NPIs on the admission number might fluctuate depending on the severity of the pandemic. Secondly, we did not exclude noninfectious respiratory diseases from all-cause respiratory diseases. Therefore, the effect of mask-wearing, social distancing, and handwashing on infectious respiratory disease, which was supposed to be reflected by the disparity between the reduction of respiratory admissions and that of childhood neoplasms, might have been underestimated. Thirdly, some of the avoided infections during NPIs were reported to have shown an outbreak after the NPIs had been lifted, especially for children, and the concept of immune debt has been raised and further explored (Cohen et al., 2022). Since this study ended in 2020, it could not evaluate the long-term effect of NPIs in China. Further analysis would be imperative when the database is complete with data for 2021.

## Conclusion

In conclusion, the NPIs following the COVID-19 pandemic caused a drastic reduction in the admission number of pediatric respiratory diseases in China, and NPIs such as mask-wearing, handwashing, and social distancing played a significant role in preventing infectious respiratory disease. The reduction was most drastic for pneumonia and in children aged 4–6 and 7–12 years.

## Declaration of competing interest

The authors have no competing interests to declare.

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## Ethical approval

Ethical approval to hold and analyze the dataset was obtained from the Ethics Committee of Beijing Children’s Hospital, Capital Medical University (Approval number: 2020-k-10).

## Author contributions

Concept and design: **Xinyu Wang, Guoshuang Feng**. Acquisition, analysis, or interpretation of data: **Guoshuang Feng, Xinyu Wang, and Hui Xu**. Drafting of the manuscript: **Xinyu Wang**. Critical revision of the manuscript for important intellectual content: **Ping Chu, Yongli Guo, and Fei Song**. Obtained funding: **Guoshuang Feng**. Administrative, technical, or material support: **Xin Xu, Jian Tian, and Xin Ni**. The manuscript has been read and approved by all the authors.

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## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.ijid.2022.10.009](https://doi.org/10.1016/j.ijid.2022.10.009).

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