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Letter to the Editor

Resurgence of influenza virus activity during COVID-19 pandemic in Shanghai, China*Dear editor,*

Recent study by Han et al., reported the dramatic impact of nonpharmaceutical interventions (NPIs) introduced during the coronavirus disease 2019 (COVID-19) pandemic on influenza and other common respiratory virus detections among children in Hangzhou, China.¹ Their results demonstrated that the influenza virus activity had apparent seasonality before COVID-19 pandemic, while it was suppressed and the seasonality was not fully highlighted during COVID-19 pandemic (From February 2020 to October 2021). Besides, a study conducted in Singapore also reported that although rhinoviruses, parainfluenza, respiratory syncytial viruses and other common respiratory viruses have returned, the activity of influenza remains absent in circulation during COVID-19 pandemic.² Herein, we presented a resurgence of influenza virus activity among children during COVID-19 pandemic in Shanghai, China.

In this cross-sectional study, pediatric patients with respiratory disease symptoms (fever, cough, rhinitis, sore throat or myalgia) in the outpatient clinic at Children's Hospital of Fudan University from Jan 1, 2014 to Aug 31, 2022 were enrolled. Nasopharyngeal swabs were collected from all enrolled outpatients and tested by chromatographic immunoassay for influenza A/B virus (Standard Diagnostics, Yongin, Republic of Korea). Time series models of seasonal autoregressive integrated moving average (SARIMA) were trained using data from Jan 2014 to Jan 2020 (pre-COVID-19) to forecast the monthly positive rates of influenza A/B virus from February 2020 to August 2022 (COVID-19 pandemic). Goodness-of-fit tests of models were performed by comparing Akaike's information criterion (AIC) and Schwarz Bayesian Criterion (SBC). Smaller AIC and SBC indicate the better fitting model.³ For comparisons between different periods, Chi-squared test was used for categorical data and Mann-Whitney U test for numeric data.

A total of 452,552 patients were enrolled in the study, including 328,220 (72.5%) patients in the pre-COVID-19 period and 124,332 (27.5%) patients in the COVID-19 pandemic period. The median age of patients in the pandemic period (6 years) was older than in the pre-pandemic period (4 years), and no qualitative difference was found between the two sexes (Table 1). A significant decline in influenza A/B activity was observed in the pandemic period compared to the pre-COVID-19 period from a positive rate of 20.3 to 6.8% (Table 1). The usual bimodal peaks of influenza A activity, in summer (June to August) and winter (December to February) were present in the pre-COVID-19 period. However, the seasonality of influenza A was interrupted after the introduction of tight nation-

wide NPIs in February 2020. The peaks disappeared completely in the year of 2020 and 2021. Whereas, a resurgence of influenza A activity was observed in the summer of 2022, and the actual activity significantly exceeded model-projected levels in the hypothetical scenario without COVID-19 related NPIs (Fig. 1A).

The annual peak of influenza B activity occurred in winter or early spring (January to March) in the pre-COVID-19 period and it was also flattened or suppressed after the implementation of NPIs. However, the resurgence of influenza B was earlier than influenza A. The activity increased from July 2021 and peaked in January 2022, which was almost in agreement with the model-projected seasonality (Fig. 1B).

Early studies conducted in both Southern Hemisphere and Northern Hemisphere reported that influenza seasons were entirely suppressed during the COVID-19 pandemic.⁴⁻⁶ Likewise, the activity of influenza declined sharply and was reduced to near zero during the early stage of pandemic in our study. Influenza virus can be transmitted by contact, droplet, or aerosol.⁷ Leung et al. reported that surgical face masks significantly reduced the detection of influenza virus RNA in respiratory droplets, indicating that surgical face masks could prevent the transmission of influenza viruses from symptomatic individuals.⁸ These results demonstrated that the current NPIs, including international mobility restriction and mask-wearing, social distancing, increased hand hygiene, could be highly effective against influenza activity. This positive effect in the short term is welcome. However, the lack of immune stimulation due to the reduced circulation of influenza and the related reduced vaccine uptake may induce an "immunity debt" which could have negative consequences and may render the population more vulnerable in the following season.⁹ Unsurprisingly, after a relative absence during the pandemic period, a large resurgence of influenza activity was observed in July 2021 for influenza B and June 2022 for influenza A in Shanghai, China. These findings raise concerns for influenza control. The eventual cancellation of COVID-19 related NPIs may herald a more significant rise in influenza activity. Vaccination is one of the most effective measures in influenza control. Identifying and developing universal vaccines, as well as increasing the vaccination coverage are of primary importance after influenza's long-term absence. Additionally, further studies are still needed to better understand the circulation patterns change of influenza viruses during COVID-19 pandemic in the different stages and regions.

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Table 1
Comparison of demographics and positive rates (%) of influenza viruses between pre-COVID-19 and COVID-19 pandemic.

	Whole study period*	pre-COVID-19*	COVID-19 pandemic*	P value [#]
Demographics				
Total patients	452,552	328,220	124,332	
Male sex, n (%)	244,946 (54.1)	177,467 (54.1)	67,479 (54.3)	0.221
Age, median	5y (16m-9y)	4y (7m-8y)	6y (3m-10y)	<0.001
Virus detections, n (%)				
Influenza A	42,293 (9.3)	39,950 (12.2)	2343 (1.9)	<0.001
Influenza B	32,634 (7.2)	26,519 (8.1)	6115 (5.9)	<0.001
Total	74,927 (16.6)	66,469 (20.3)	8458 (6.8)	<0.001

* Whole study period: Jan 1, 2014 to Aug 31, 2022; pre-COVID-19: Jan 1, 2014 to Jan 31, 2020; COVID-19 pandemic: Feb 1, 2020 to Aug 31, 2022.

[#] Comparison between pre-COVID-19 and COVID-19 pandemic; Abbreviations: y, years; m, months.

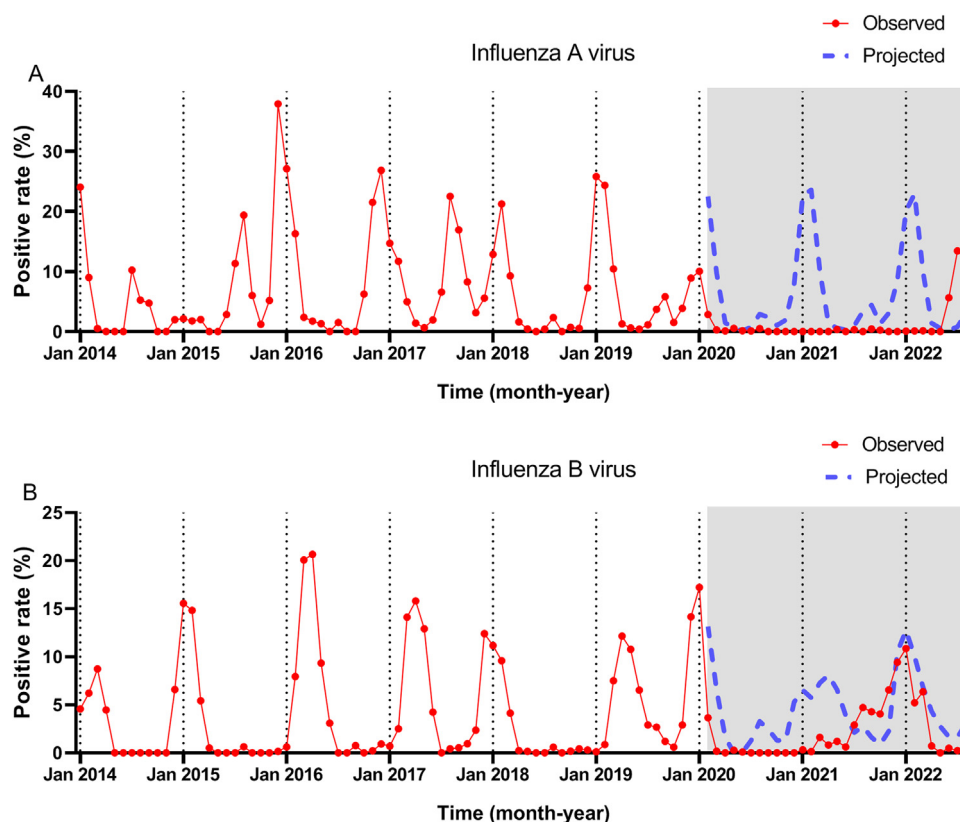


Fig. 1. Observed and model-fitted time series of monthly influenza activity between Jan, 2014 and Aug, 2022. (A) influenza A virus; (B) influenza B virus. Hypothetical positive rates during Feb, 2020–Agu, 2022 (blue) in the absence of NPIs was projected using the SARIMA model based on Jan 2014–Jan 2020. Gray block represents the period of the “COVID-19 pandemic” when NPIs were implemented. NPIs, nonpharmaceutical interventions; SARIMA, seasonal autoregressive integrated moving average.

Declaration of Competing Interest

All authors claim no conflict of interest.

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