Engineering 21 (2023) 195–202

Contents lists available at ScienceDirect

Engineering

journal homepage: www.elsevier.com/locate/eng

Research
Public Health—Article

Influenza's Plummeting During the COVID-19 Pandemic: The Roles of Mask-Wearing, Mobility Change, and SARS-CoV-2 Interference

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ARTICLE INFO

Article history:
Received 9 November 2021
Revised 13 December 2021
Accepted 26 December 2021
Available online 2 February 2022

Keywords:
Influenza
Mask-wearing
Mobility mitigation
SARS-CoV-2 interference
Non-pharmaceutical interventions

ABSTRACT

Seasonal influenza activity typically peaks in the winter months but plummeted globally during the current coronavirus disease 2019 (COVID-19) pandemic. Unraveling lessons from influenza's unprecedented low profile is critical in informing preparedness for incoming influenza seasons. Here, we explored a country-specific inference model to estimate the effects of mask-wearing, mobility changes (international and domestic), and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) interference in China, England, and the United States. We found that a one-week increase in mask-wearing intervention had a percent reduction of 11.3%–35.2% in influenza activity in these areas. The one-week mobility mitigation had smaller effects for the international (1.7%–6.5%) and the domestic community (1.6%–2.8%). In 2020–2021, the mask-wearing intervention alone could decline percent positivity by 13.3–19.8. The mobility change alone could reduce percent positivity by 5.2–14.0, of which 79.8%–98.2% were attributed to the deflected international travel. Only in 2019–2020, SARS-CoV-2 interference had statistically significant effects. There was a reduction in percent positivity of 7.6 (2.4–14.4) and 10.2 (7.2–13.6) in northern China and England, respectively. Our results have implications for understanding how influenza evolves under non-pharmaceutical interventions and other respiratory diseases and will inform health policy and the design of tailored public health measures.

1. Introduction

Seasonal influenza viruses circulate year-round throughout the world, typically peaking in the winter in each hemisphere. However, since the first report of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and non-pharmaceutical interventions (NPIs) to mitigate the virus, influenza activity has remained low, with laboratory-confirmed outbreaks globally nonexistent during the influenza seasons [1–3]. In Northern Hemisphere countries, data from respiratory surveillance systems in China, England, and the United States indicated a 92.4%–99.9% decrease in the past five years on average in the 2020–2021 season [4–6]. In the Southern Hemisphere, where cold seasons are opposite to those in the Northern Hemisphere, influenza has also remained scarce for two consecutive influenza seasons [7,8].

Influenza's global plummeting adds great uncertainty on preparedness for the incoming influenza circulations through a targeted vaccination program [1–3], calling for thorough investigation of the causes. Although the coronavirus disease 2019 (COVID-19) pandemic and interventions have been associated with this decline [7,9], how each individual NPI and SARS-CoV-2 interference contributes to long-term influenza decline remains elusive. Face-masking in public spaces, mobility change

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https://doi.org/10.1016/j.eng.2021.12.011
2095-8099/

(e.g., international travel and domestic movement mitigations), and physical distancing have been found to be highly effective in reducing respiratory infections in laboratory and clinical contexts [10,11] and by simulation models [12]. Furthermore, data have shown that the transmission of the influenza virus was interrupted by a seasonal rhinovirus epidemic [13], but one virus's circulation may also be boosted by that of another virus [14,15], leading to the mechanism of SARS-CoV-2 interference being largely unclear.

However, in the context of seasonal influenza, unraveling the roles of highly correlated NPIs is challenging even without considering SARS-CoV-2 interference. Cross-country modeling, which is widely used for assessing the individual effects of NPIs on SARS-CoV-2 transmission, is not applicable to seasonal influenza [16] owing to the high variation in viral antigenic evolutions, climate conditions, sociodemographic features, influenza circulation strains and subtypes, as well as influenza vaccination coverage across countries [17,18]. Here, we developed a country-specific inference model to estimate the individual effects of NPIs and SARS-CoV-2 interference. Our approach relies on long-term influenza surveillance data and mobility change and identifies the individual effects through a contrast of potential influenza activities under alternative hypothetical scenarios [19]. We assessed the short-term effects of a one-week increase in NPIs (denoted by percent reduction in percent positivity), as well as the long-term effects of NPIs and SARS-CoV-2 interference in influenza seasons (denoted by absolute reduction in percent positivity).

2. Methods

2.1. Study data

We collected data on influenza, mobility (international and domestic), and mask-wearing interventions from public sources in China, England, and the United States. All data were obtained from public sources and are summarized in Table S1 in Appendix A. We note that changes in domestic mobility during the COVID-19 period may reflect several highly correlated mobility-related NPIs, including movement restriction and physical distancing (Supplementary methods and Table S2 in Appendix A). As clinical influenza visits may be affected by NPIs [18], we used the percent positivity tests reported from laboratory surveillance data as a measure of influenza activity. We considered northern China and southern China separately because of the sharp differences in their patterns of seasonal influenza [9]. In northern China, England, and the United States, the influenza season lasts for 16–20 weeks (northern China, Weeks 49–14; England, Weeks 50–13; the United States, Weeks 48–15), whereas in southern China, the influenza season is much longer (23 weeks, Weeks 45–15).

2.2. Influenza surveillance data

The virological data from 2011 to 2021 were obtained from the corresponding government websites, Chinese National Influenza Center [4], Public Health England [6], and US Centers for Disease Control and Prevention (CDC) [5]. The Chinese National Influenza Surveillance Network monitors influenza viruses circulating in China and consists of 554 sentinel hospitals and 407 network laboratories located in over 300 cities in the mainland of China. The Respiratory DataMart System in Public Health England serves to systematically monitor influenza and other respiratory viruses circulating in England, with weekly viral test results reported by 14 laboratories representing all nine regions of England. Surveillance of the influenza virus in the United States is monitored through the United States influenza surveillance system and collated by the CDC and over 400 public health and clinical laboratories located throughout all 50 states, Puerto Rico, Guam, and the District of Columbia. Weekly virological data, including the percentage of respiratory specimens that tested positive for influenza, were released on the respective government influenza surveillance website. The weekly percent positivity is shown in Fig. S1 in Appendix A.

As in the literature [9], the start of an influenza epidemic period is defined as the first week starting from which the percent positivity stays above 10 for at least two weeks, and the end is defined as the last week after which the percent positivity drops below 10 for at least three consecutive weeks. Influenza activity typically peaks in the winter season for northern China, England, and the United States, while in southern China, it may also be active in summer. The influenza season represents the common period of the nine influenza epidemics from 2011 to 2020. The start and end of the influenza season were defined as the medians of the start and end of the nine influenza epidemics, respectively.

2.3. Mobility data

We used normalized international inbound travel volume to measure international mobility in the four areas. Inbound travel in the United Kingdom was obtained from the Department for Transport [41] in 2011–2021 and is used to represent inbound travel in England. Inbound travel in northern and southern China during 2011–2021 is represented by the monthly inbound travel in Shanghai released by the Shanghai Bureau of Statistics [42]. Data on inbound travel in the United States were collected from the US Department of Transportation [43,44] in 2011–2021. Weekly mobility was estimated using the moving average over the past M weeks to account for the delay between mobility changes and laboratory testing and reporting [45]. At baseline, we assume that $M = 2$ in England and the United States and $M = 4$ in northern and southern China to account for a longer delay in China. We conducted an extensive sensitivity analysis on the delay M. In normalization, since mobility increases with a steady yearly trend while influenza activity evolves with a highly irregular interannual pattern due to differences in circulating strains [46], we scaled down the weekly mobility using the average value in the first month for each year separately.

We collected domestic mobility data in northern and southern China through the Gaode Map [47] in 2019–2021, which provides daily relative inflow of smartphone users for each city covered by the Chinese National Influenza Surveillance Network. The daily inflow was aggregated into the week level using the moving average method, as described above. The inflow in 2019–2020 is directly projected into 2011–2018 without adjustment because the yearly trend is removed in the analysis. Domestic mobility in England and the United States was estimated by relying on transportation data in the United Kingdom and the United States, respectively. We collected the monthly released domestic transportation data in the United Kingdom from the Office for National Statistics [48] and in the United States from the US Department of Transportation [43,49]. If monthly data were not available, we estimated the monthly mobility flow by equally allocating quarterly flow data to each month. In England, since monthly pedal data were only available for 2020, we estimated domestic mobility in 2020 as the average of vehicle and pedal flows. We estimated weekly domestic mobility in England and the United States using the same moving average and normalization methods. The mobility data are summarized in Table S3 in Appendix A. International and domestic mobility are presented in Fig. S2 in Appendix A.

2.4. Mask-wearing index data

We collected data on mask-wearing interventions from the start of SARS-CoV-2 transmission until Week 28, 2021. In China, the mask-wearing order was imposed starting from Week 4 of 2020 (January 23, obtained from Ref. [50]) until the end week, Week 28 of 2021. For England, the mask-wearing regulation was made from Week 30 of 2020 (July 23) until Week 28 of 2021 (July 19) [51]. We denoted the mask-wearing index as 1 during the implementation period and 0 otherwise. The US CDC imposed the mask-wearing order from Week 14 of 2020 until the end week, with a short-term lift during Week 22 of 2021 to Week 29 of 2021 for fully COVID-19 vaccinated people in non-healthcare settings [52]. We estimated the degree of mask-wearing as the proportion of the number of states that imposed the mask-wearing order during the period of CDC mask-wearing recommendations because state governments did not simultaneously comply with the order imposed by the CDC. We referred to the data here as the mask index, which is adjusted by the vaccination data (Fig. S3 in Appendix A) to estimate the time-varying mask-wearing intervention. The mask-wearing indices are displayed in Fig. S4 in Appendix A.

2.5. Method summary

The model consists of two self-correcting regularized multiple regression models, both of which are dynamically trained and regularized using the least absolute shrinkage and selection operator (LASSO) method and are fitted for each of the four areas separately. Modeling parameters capture the short-term effects of one-week interventions. We estimated the effects in influenza seasons due to an intervention through a contrast of the imputed influenza activities under the scenario without NPIs and under that intervention alone. We estimated the effect of SARS-CoV-2 interference by comparing influenza activity using data from 2011 to the first report of SARS-CoV-2 and that using data from 2011 to the start of NPIs. The delay between the start of NPIs and the first report of SARS-CoV-2 enables the identification of the effect of SARS-CoV-2 interference. We assumed that there was no substantial difference in climate conditions, sociodemographic features, influenza transmissibility, and influenza vaccination coverage between 2020 and 2021 compared with those in previous years. We also assumed that the impacts of these external factors on influenza are consistent and can be captured by past influenza activity.

2.6. Multiple regression models

We explored two self-correcting regularized multiple regression models to forecast the weekly influenza activity. Both regression models are dynamically trained and regularized using the LASSO method; unlike autoregressive integrated moving average models [53,54], they allow the self-selection of multiple lags (up to 52) of influenza activities as model inputs. The regression models are described as follows:

First, we use a multiple regression model with a linear combination of N lags of influenza activity as well as the current domestic mobility (denoted by V_t, t represents for week t) and international mobility (denoted as W_t) to fit the percent positivity under the mobility change only (denoted as Y_t^{mob}). International mobility was included during the influenza season only; a sensitivity analysis considering international mobility throughout the year was conducted and compared to the baseline analysis. S_t indicates the influenza season.

The model is represented by

$$Y_t^{\mathrm{mob}} = \alpha + \sum_{n=1}^{N} \beta_n Y_{t-n}^{\mathrm{mob}} + \gamma \cdot V_t + \theta \cdot W_t S_t + \varepsilon_t \tag{1}$$

where α, β_n, γ, and θ are the parameters, and ε_t represents the error term, with $\varepsilon_t \sim \mathbb{N}(0, \sigma^2)$, a normal distribution with variance σ^2. Parameters α and β_n capture the association between influenza activity and domestic and international mobility during the influenza season, respectively. Model (1) was used to predict influenza activity under various scenarios with different assumptions on mobility mitigation as well as SARS-CoV-2 transmission. Influenza activity in the scenario with no SARS-CoV-2 transmission is predicted from the first week when the first few COVID-19 cases are reported worldwide (i.e., Week 1 of 2020) [55].

Second, we consider a time-varying mask-wearing intervention, denoted by D_t^{mas}, the mask-wearing intervention at time t. Mask-wearing interventions and NPIs related to mobility change are the focus of this study and are referred to as two major NPIs; other NPIs that may affect influenza activity are referred to as minor NPIs. We used Y_t^{npi} to represent the percent influenza positivity for all NPIs. Since Y_t^{mob} is capable of accounting for the NPIs associated with mobility change, the difference between Y_t^{npi} and Y_t^{mob} is attributed to the effect of the mask-wearing intervention and minor NPIs. Note that the effects of mask-wearing interventions can be isolated if they vary over time. We include L lags of mask-wearing intervention to account for the lingering effect of mask use as well as the delay in the compliance [11]. The best value of L is selected according to R^2 criteria and reflects the accumulated intervention time required to achieve the maximal weekly reduction.

The influenza activity under all NPIs is modeled as

$$Y_t^{\mathrm{npi}} = Y_t^{\mathrm{mob}} \cdot e^{\mu \cdot I + \tau \left(\sum_{l=0}^{L} D_{t-l}^{\mathrm{mas}}\right) + \xi_t}, l = 1, \ldots L \tag{2}$$

where ξ_t represents the normally distributed error term with mean 0 and variance ϵ^2, $\xi_t \sim \mathbb{N}(0, \epsilon^2)$, and I is an indicator, with $I = 1$ if there exists at least one minor NPI during the week and 0 otherwise. Parameter τ represents the effect of a one-week increase in mask-wearing intervention. Parameter μ captures the effects of minor NPIs. Here, Y_t^{mob} is obtained from the forecast values from the first regression Model (1) under mitigated mobility, as observed. Under the mobility mitigation measure alone, that is, there exist no minor NPIs ($I = 0$) or mask interventions ($\sum_{l=0}^{L} D_{t-l}^{\mathrm{mas}} = 0$), Y_t^{npi} is equivalent to Y_t^{mob}. Finally, we explore Model (2) to forecast influenza activity under the mask-wearing intervention alone, where the values of Y_t^{mob} are estimated based on normal mobility under a hypothetical scenario without mobility mitigation measures. The model was implemented in scikit-learn 0.24.2 with Python (version 3.6.13; Python Software Foundation, USA). The code is openly available [56]. Parameter selection for baseline and sensitivity analyses was detailed in Supplementary methods.

3. Results

3.1. Effect of mask-wearing

A one-week increase in mask-wearing intervention, under the realistic contexts of mask-wearing intervention, was capable of dramatically reducing the percent positivity tests in all four areas, with the mean percent reduction varying from 11.3% to 35.2% (Table S4 in Appendix A). The accumulated intervention time needed to achieve the maximal weekly reduction (i.e., estimated lags of mask-wearing included) was 13 and 11 weeks in northern China and southern China, respectively, whereas in England and the United States, they were much longer, 24 and 35 weeks, respectively (Table S4). Considering the long-term impact of mask-wearing intervention, we estimated that, during the 2020–2021 season, the mask-wearing order alone could lead to reduction in percent positivity of 19.8 (95% confidence interval (95%CI), 15.8–24.8) in northern China, 16.6 (95%CI, 13.1–21.5) in southern China, 13.3 (95%CI, 9.7–16.6) in England, and 15.2 (95%CI, 11.9–18.5) in the United States (Table 1 and Fig. 1), compared with the scenario without NPIs. A larger variation was identified when the timing of the mask-wearing orders differed. For example, in northern China, the mask-wearing order started before the end of the 2019–2020 season, and the influenza positivity was estimated to decline by 12.3 (95%CI, 8.1–17.0) in the order alone. In the United States, the order started at the end of the 2019–2020 season, and no significant effect was found (Figs. 1(a) and (d) and Table 1).

3.2. Effect of mobility change

Compared with the mask-wearing intervention, the effect of mobility change was smaller. We estimated that for a one-week restriction of international mobility during the influenza season, the influenza activity in the current week had an immediate percent reduction of 4.5% in northern China. The effects in southern China, England, and the United States were similar, varying from

Table 1
Estimated effects of mask-wearing and mobility mitigation and SARS-CoV-2 interference in the influenza seasons.

Non-pharmaceutical interventions	Percent positivity							
	Northern China		Southern China		England		The United States	
	Mean	95%CI	Mean	95%CI	Mean	95%CI	Mean	95%CI
In 2019–2020								
Relative to no NPIs								
Mask-wearing alone	12.3	(8.1, 17.0)	11.7	(6.8, 16.8)	–[a]	–[a]	0	(0, 0)
Mobility change alone	5.6	(2.0, 9.9)	3.1	(−0.2, 7.5)	0.2	(0.1, 0.6)	0.7	(0.2, 1.5)
Observed NPIs	11.2	(6.4, 16.4)	10.2	(5.0, 15.6)	1.4	(0.9, 1.9)	1.3	(0.8, 1.9)
Relative to no SARS-CoV-2								
SARS-CoV-2	7.6	(2.4, 14.4)	4.3	(−1.4, 12.1)	10.2	(7.2, 13.6)	2.9	(−1.1, 8.3)
In 2020–2021								
Relative to no NPIs								
Mask-wearing alone	19.8	(15.8, 24.8)	16.6	(13.1, 21.5)	13.3	(9.7, 16.6)	15.2	(11.9, 18.5)
Mobility change alone	14.0	(8.0, 18.9)	5.2	(1.4, 9.0)	10.4	(3.9, 16.6)	9.5	(2.8, 18.0)
Observed NPIs	21.2	(16.7, 26.8)	16.0	(12.2, 21.1)	14.6	(10.6, 18.2)	16.2	(12.8, 19.8)
Relative to no SARS-CoV-2								
SARS-CoV-2	2.1	(−1.5, 8.9)	0.7	(−1.6, 4.8)	1.5	(−2.0, 5.4)	1.2	(−2.2, 6.1)

[a] In England, the mask-wearing order started after the end of the 2019–2020 influenza season.

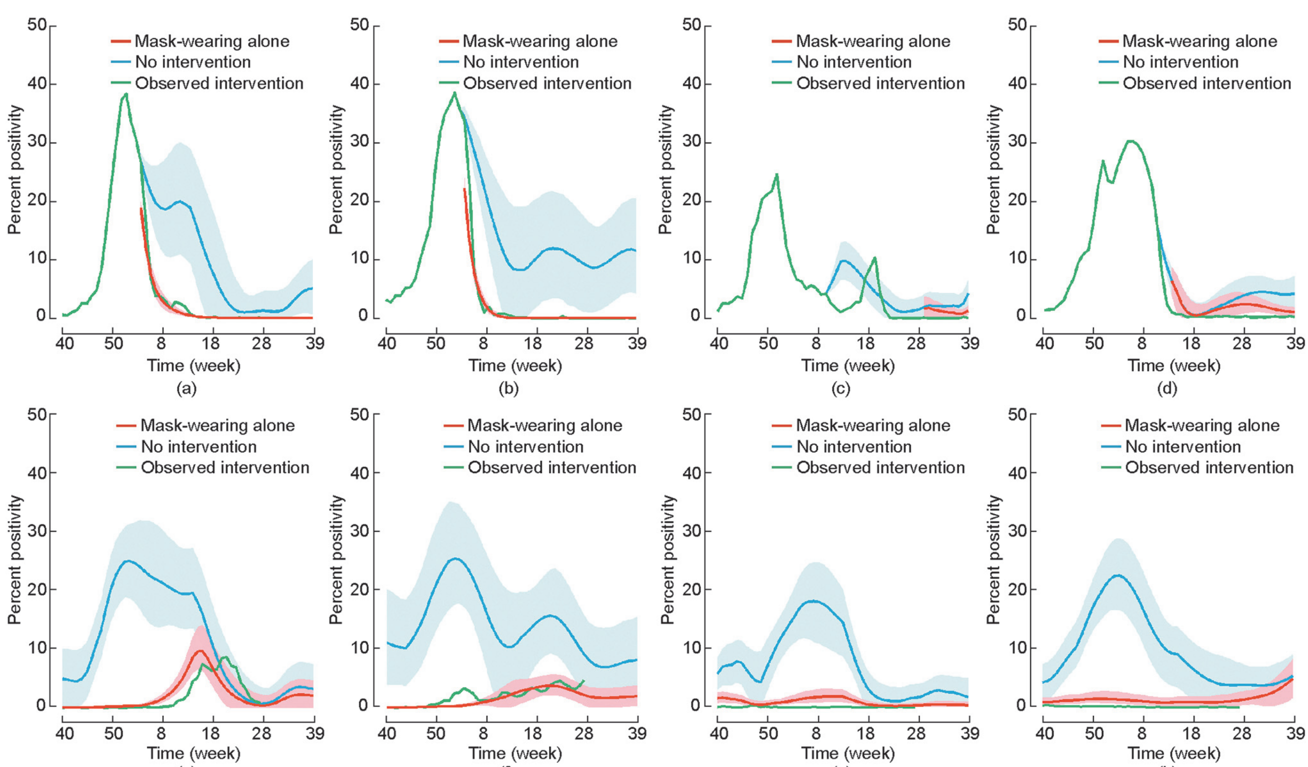

Fig. 1. Estimated influenza activities under the mask-wearing order alone and no intervention as well as the observed activity. (a–d) Weekly percent positivity in 2019–2020 season for (a) northern China, (b) southern China, (c) England, and (d) the United States. (e–h) Weekly percent positivity in 2020–2021 seasons for (e) northern China, (f) southern China, (g) England, and (h) the United States. Shaded area refers to 95%CI.

1.7% to 6.5%. Domestic mobility mitigation measures had closer effects, varying slightly from 1.6% to 2.8% (Table S4). Further, despite the differentiation in the timing and magnitude of mobility mitigation measures across areas (Fig. S2), the international travel mitigation had a larger effect than the domestic movement mitigation (Fig. S5 in Appendix A). In the 2020–2021 season, the mobility mitigation measures reduced 14.0 (95%CI, 8.0–18.9) percent positivity in northern China, 5.2 (95%CI, 1.4–9.0) in southern China, 10.4 (95%CI, 3.9–16.6) in England, and 9.5 (95%CI, 2.8–18.0) in the United States (Table 1 and Fig. 2); 79.8%–98.2% of the reductions were attributable to the international mobility mitigation measures (Table S4). In the 2019–2020 season, only China implemented a short period of mobility mitigation, and we estimated that the reductions due to the mobility mitigation measures were 5.6 (95%CI, 2.0–9.9) in northern China and 3.1 (95%CI, −0.2–7.5) in southern China (Figs. 2(a) and (b) and Table 1).

3.3. Effect of SARS-CoV-2 interference

SARS-CoV-2 has an observable effect when it spreads throughout the influenza season. During the 2019–2020 season, we estimated that SARS-CoV-2 interference reduced percent positivity by 7.6 (95%CI, 2.4–14.4) and 10.2 (95%CI, 7.2–13.6) in northern China and England, respectively, and 4.3 (95%CI, −1.4–12.1) and 2.9 (95%CI, −1.1–8.3) in southern China and the United States, respectively (Table 1 and Fig. 3). The reductions were only significant in northern China and England, where SARS-CoV-2 virus spread starting at the peak of the influenza season and was followed by small rebounds (Figs. 3(a) and (c)). A large effect (12.0 (95%CI, 4.3–25.3)) of SARS-CoV-2 interference was also identified in Hubei Province, China during the 2019–2020 season (Fig. S6 in Appendix A). However, in all four areas, no significant effects of SARS-CoV-2 interference were found during 2020–2021.

In the sensitivity analysis, we found that the smoothing method and training window had little impact on the estimated effects, but the exclusion of seasonal indicators may result in small negative effects on mobility change (Figs. S7–S9 in Appendix A). We also conducted a state-level analysis for the United States, and the results were consistent with those for the United States (Figs. S10–S13 in Appendix A).

4. Discussion

Although international travel has been found to play an important role in the spread of influenza A (H1N1) virus in the 2009 influenza pandemic [20], evidence on face masks from clinical trials, with limited sample size and low adherence, appears controversial in mechanistic studies [11,21–23]. Our results suggest that, in a large population study of the four areas, mask-wearing alone can substantially reduce influenza activity, comparable to combined NPIs. Mobility mitigation measures are mostly effective in flattening influenza activity in influenza seasons, with international mitigation making a larger contribution in areas where influenza profiles exhibit single winter-peak outbreaks (e.g., northern China, England, and the United States) and domestic mitigation in areas with a secondary summer-peak outbreak (e.g., southern China).

It is important to note that the high effectiveness of mask intervention is obtained based on the actual acceptance of mask-wearing measures during the COVID-19 period, with compliance to the order, the supply of mask, and the lingering habit of mask use being potentially higher than in previous years [11]. The estimated weeks of mask-wearing intervention needed to achieve

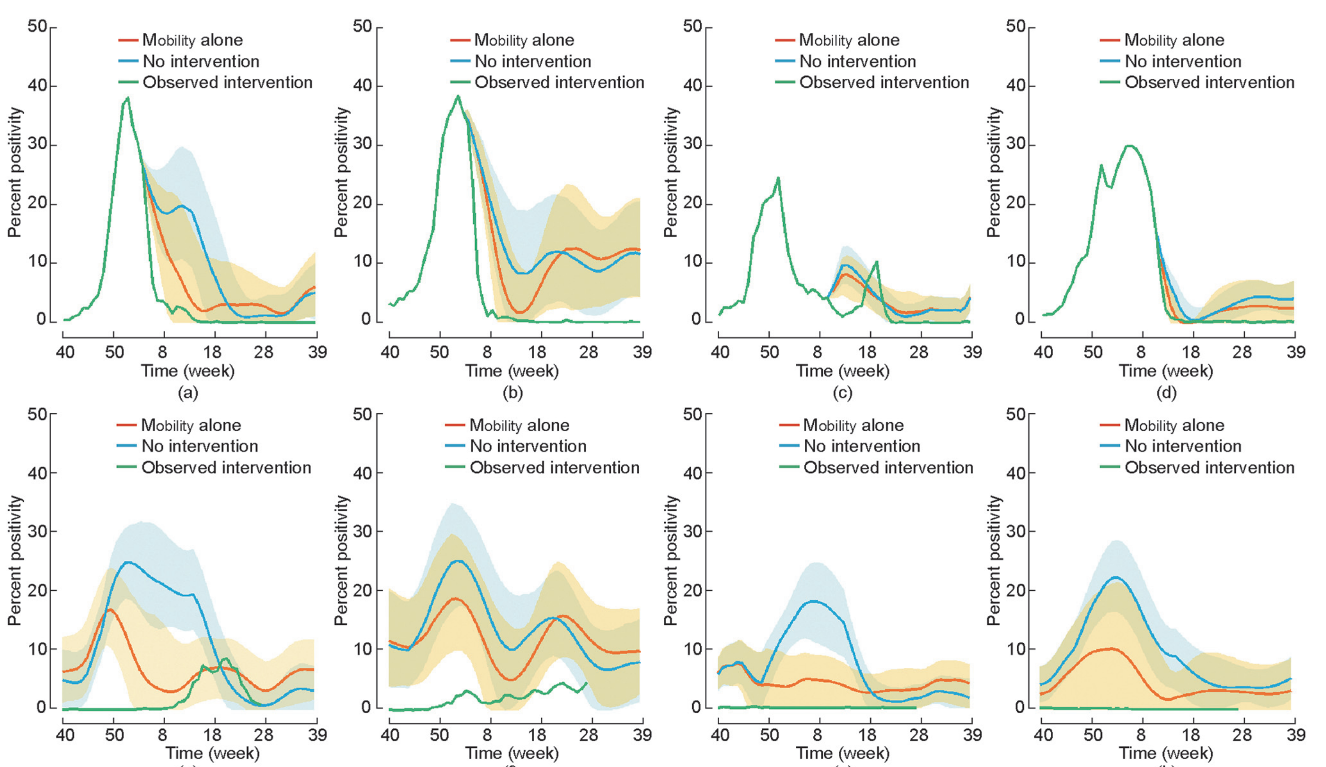

Fig. 2. Estimated influenza activities under the mobility change alone and no intervention as well as the observed activity. (a–d) Weekly percent positivity in 2019–2020 season for (a) northern China, (b) southern China, (c) England, and (d) the United States. (e–h) Weekly percent positivity in 2020–2021 seasons for (e) northern China, (f) southern China, (g) England, and (h) the United States. Shaded area refers to 95%CI.

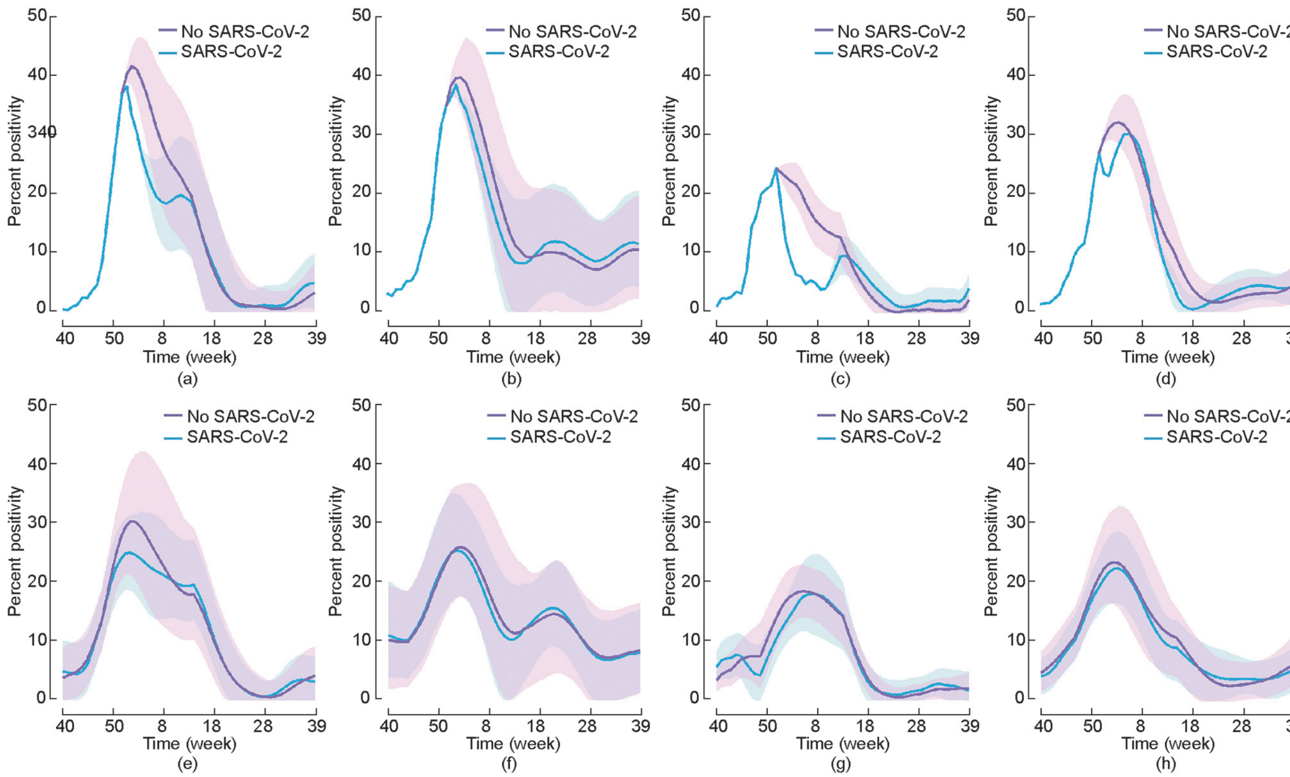

Fig. 3. Estimated influenza activities under the scenarios with no SARS-CoV-2 transmission and with SARS-CoV-2 transmission, both without COVID-19 NPIs. (a–d) Weekly percent positivity in 2019–2020 season for (a) northern China, (b) southern China, (c) England, and (d) the United States. (e–h) Weekly percent positivity in 2020–2021 seasons for (e) northern China, (f) southern China, (g) England, and (h) the United States. Shaded area refers to 95%CI.

the maximal weekly percent reduction are much shorter in China than in other areas, which is consistent with the literature on the differentiation of mask behavior among populations [23]. While the short-term effects of mobility mitigation in the four areas were similar, the long-term effects in the influenza seasons could vary substantially. These differences could be due to the differential duration and long-term impact of mobility-related NPIs. Notably, only domestic mobility in China gradually returned to almost normal levels after a falloff in early 2020; international mobility in all four areas remained at much lower levels by Week 28 of 2021 (Fig. S2).

We found that the impact of SARS-CoV-2 interference differed in the four areas, with the effects in southern China and the United States being particularly small. This is probably due to the low transmission of SARS-CoV-2 in the two areas in early 2020, as the extent of viral interference relies heavily on the spread of the intervening virus [15,24]. Of note is the large effect of SARS-CoV-2 interference in Hubei Province, China in the 2019–2020 season, where SARS-CoV-2 community transmission was widespread in most parts of the province. However, it is also possible that the interference depends on the circulating strains [25,26].

This study adds to the literature in several ways. First, despite the wide association of NPIs to mitigate SARS-CoV-2 transmission, to the best of our knowledge, this is the first investigation of their individual effects and SARS-Cov-2 interference in seasonal influenza and in the long term, as the COVID-19 pandemic evolves over one year. Unlike the early detection of the SARS-CoV-2 virus, the virological surveillance system for influenza has been established in many countries and can provide high-quality epidemiological and laboratory data for monitoring and evaluating influenza transmission. We relied on long-term surveillance data to independently estimate the individual effects for each area. Second, we found that mask-wearing is more effective than mobility mitigation in all four areas, although the relative advantage depends on the timing and duration of the NPIs. Given the relatively low cost [27,28], wearing masks for a short period could be considered an accompanying method for influenza vaccination in preparedness for influenza pandemics, or severe seasonal epidemics in populations at higher risk of developing severe complications, or having lower vaccine efficacy [29,30]. Finally, the insight from our study could offer a starting point for understanding SARS-CoV-2 interference in influenza transmission. The results of SARS-CoV-2 interference suggest that the effect varies with the timing of the influenza season and the speed of SARS-CoV-2 community transmission, providing valuable knowledge for facilitating deeper understanding of viral ecology.

This study has several limitations. First, we used the percent positivity reported by laboratory and clinical surveillance systems, but the total number of influenza specimens collected also dropped following the start of NPIs. Nevertheless, the decline coincided with that in the end of the 2019–2020 season when the influenza surveillance naturally decreased; the sampling specimens collected during the 2020–2021 season returned to normal [8]. Second, although in all four areas, no substantial differences in influenza vaccination behavior between the 2019 and 2021 seasons and other recent seasons were found [31–33], in England and the United States, the yearly influenza vaccination uptake increases steadily with small values, which may result in slightly overestimated effects for these two areas. Third, we leveraged the COVID-19 vaccine data to account for the time-varying change in mask-wearing as the COVID-19 pandemic evolves, and the effectiveness of the order may also depend on the type of mask used

[11] and the presence of other personal protection behaviors (e.g., hand hygiene and respiratory etiquette). Fourth, the analysis of SARS-CoV-2 interference relied on virological data in the 2019–2020 influenza season, and extrapolation of the estimates to other seasons may be inaccurate because of the potential distinct circulation strains. Furthermore, our domestic mobility data are collected from mobile phone users and public transport statistics, which may only provide an incomplete picture of human movement change [34]. Although this represents a limitation, in all four areas, the change in domestic mobility patterns during the COVID-19 period closely coincides with the mobility-related NPIs in each area (Fig. S14 and Table S3 in Appendix A). Thus, our results on domestic mobility support the findings on school closures in an earlier study [35]. Finally, although the results at the United States state level are consistent with those for the United States, heterogeneity may still exist in cities across other large study areas.

Influenza's global plummeting provides a great opportunity to understand the individual effects of mask-wearing and mobility mitigation at the policy level and offers a head start on interference from influenza and other respiratory infectious diseases. These findings are valuable for forecasting future influenza seasons [36] and for guiding healthcare policy and the allocation of healthcare resources [37]. Identifying and developing universal influenza vaccines are still of primary importance for influenza control. However, given the relatively low negative impact of wearing masks in relation to the burden of influenza [38,39], our results suggest that wearing masks for a short period could be considered as a coordinated measure to influenza vaccination in preparedness for seasonal and pandemic influenza in populations with low vaccination coverage, or when matched vaccines are not available, calling for a revisit of the role of mask-wearing in the World Health Organization (WHO)'s pandemic influenza intervention guidance [40].

Acknowledgments

This study was supported by grants from the National Natural Science Foundation of China (82041023 and 81773546), the Chinese Academy of Medical Sciences (CAMS) Innovation Fund for Medical Sciences (2020-I2M-1-001), the Chinese Academy of Medical Sciences Fund for Influenza Pandemic Response and Public Health Emergency System (2021P062QG008), the Bill & Melinda Gates Foundation (2021P057QG006), and the Special Fund for Health Development Research of Beijing (2021-1G-3013). The funder of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the manuscript.

Authors' contributions

Xiao-Hua Zhou and Luzhao Feng supervised the study. Shasha Han designed the study. Shasha Han, Ting Zhang, Yan Lyu, and Peixi Dai collected data. Shasha Han, Ting Zhang, and Yan Lyu performed analyses. Shasha Han, Ting Zhang, Yan Lyu, Shengjie Lai, Xiao-Hua Zhou, and Luzhao Feng interpreted the findings. Shasha Han and Ting Zhang wrote the manuscript. Shengjie Lai, Jiandong Zheng, Weizhong Yang, Xiao-Hua Zhou, and Luzhao Feng commented on and revised the manuscript accordingly. All authors have approved the final manuscript as submitted.

Compliance with ethics guidelines

Shasha Han, Ting Zhang, Yan Lyu, Shengjie Lai, Peixi Dai, Jiandong Zheng, Weizhong Yang, Xiao-Hua Zhou, and Luzhao Feng declare that they have no conflict of interest or financial conflicts to disclose.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.eng.2021.12.011.

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