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Brief report

Resurgence of different influenza types in China and the US in 2021

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Abstract: Various nonpharmaceutical interventions (NPIs) were implemented to alleviate the COVID-19 pandemic since its outbreak. The transmission dynamics of other respiratory infectious diseases, such as seasonal influenza, were also affected by these interventions. The drastic decline of seasonal influenza caused by such interventions would result in waning of population immunity and may trigger the seasonal influenza epidemic with the lift of restrictions during the post-pandemic era. We obtained weekly influenza laboratory confirmations from FluNet to analyse the resurgence patterns of seasonal influenza in China and the US. Our analysis showed that due to the impact of NPIs including travel restrictions between countries, the influenza resurgence was caused by influenza virus A in the US while by influenza virus B in China.

Keywords: seasonal influenza; COVID-19; influenza virus A and B; China and the US

1. Introduction

Seasonal influenza circulation often occurs simultaneously in all parts of the world and causes substantial morbidity and mortality. In general, seasonal epidemics mainly emerge during winter in temperate regions, while in tropical regions seasonal influenza is more irregular that may occur throughout the year. What is unexplained is that the expected 2020−2021 flu season did not occur as the level of flu activity remained extremely low both in the United States (the US) and globally, despite high levels of testing and prevalence of COVID-19 [1,2]. The flu virus may fail to trigger large-scale epidemics as exposure to the influenza virus could build up the population immunity and reduce the number of susceptible individuals below a critical threshold level [3]. On the contrary, waning of immunity and a large number of susceptible individuals due to the emergence of new flu strain may

trigger large-scale flu epidemics and even flu pandemic.

The drastic waning of immunity, which is caused by the dramatic decline of seasonal influenza, couples with the lift of COVID-19 restrictions raises the concern whether a more severe flu season would come this winter. Ali et al. [4] estimated the effect of public health and social measures (PHSMs) for COVID-19 on influenza viruses transmission and applied a data-driven simulation to predict the upcoming influenza season. Their results suggest the potential for a substantial infection burden for upcoming influenza seasons. In this study, we mainly focus on the resurgence patterns of seasonal influenza in China and the US to compare the prevalence of different influenza virus variants for the upcoming influenza seasons.

2. Materials and methods

Our analysis is based on the data collected from FluNet [5], which is a global web-based influenza surveillance tool initiated by World Health Organization (WHO). The data derived from FluNet contains reported cases from unspecified influenza subtypes. Therefore, we need to manually classify them into influenza A subtypes and influenza B lineages. The detailed classification procedure is shown in Supplementary Material: 1. Classification Method.

3. Results

As shown in Figure 1, the grey curves represent past flu cases of the years 2014−2019 whilst blue bolded lines are flu cases of the years 2020 to 2022. The background comprised of grey curves, which is overlapping over several years, gives us a clear idea of pre-pandemic influenza levels. Influenza A pandemic in the US came back at the tail of 2021, with a violent upsurge and peaked in a short period, then it fell and peaked again in 2022. Meanwhile, all B lineages have disappeared since a sharp fall in the first quarter of 2020. The pattern for influenza A and influenza B in China is quite opposite to that seen in the US. A sudden drop occurred for influenza B virus at the beginning of 2020, then resurged in 2021, the following was a drastic increase to the summit in 2022 and again fell. However, Influenza A viruses drastically declined to zero in 2020 and remained undetected until a minor resurge in 2022. This opposite pattern of influenza A & B in the US and China indicates the different origins of new strains of influenza A & B (The recent data and transmission patterns of influenza A and B viruses can be seen in Supplementary Material Figure S1).

As observed in Figure 2, the spread of influenza was severely suppressed during the COVID-19 pandemic. We can also see that a wave of AH3 has come back and swept most of the world including the US, due to gradually resumed global mobility since the middle of 2021. Nevertheless, Mainland China's strict border policy made non-locally emerged influenza strains (e.g., AH3) difficult to invade, while locally emerged strain (e.g., B/Victoria) avoided a strain competition situation and caused a large outbreak in Mainland China. B/Yamagata nearly disappeared in China with influenza B return, though B/Victoria viruses caused almost all cases during the COVID-19 pandemic. The detailed transmission patterns of AH1N1, AH3, B/Yamagata and B/Victoria in China and the US are shown in Supplementary Material Figures S2 and S3, respectively. Further, we found a wave of AH3, which started (likely) in India that swept the globe and hit Mainland China only in the middle of 2022. We speculated the different 'post-pandemic' peak time of AH3 and B/Victoria was due to their source of emergence and China's strict border policy.

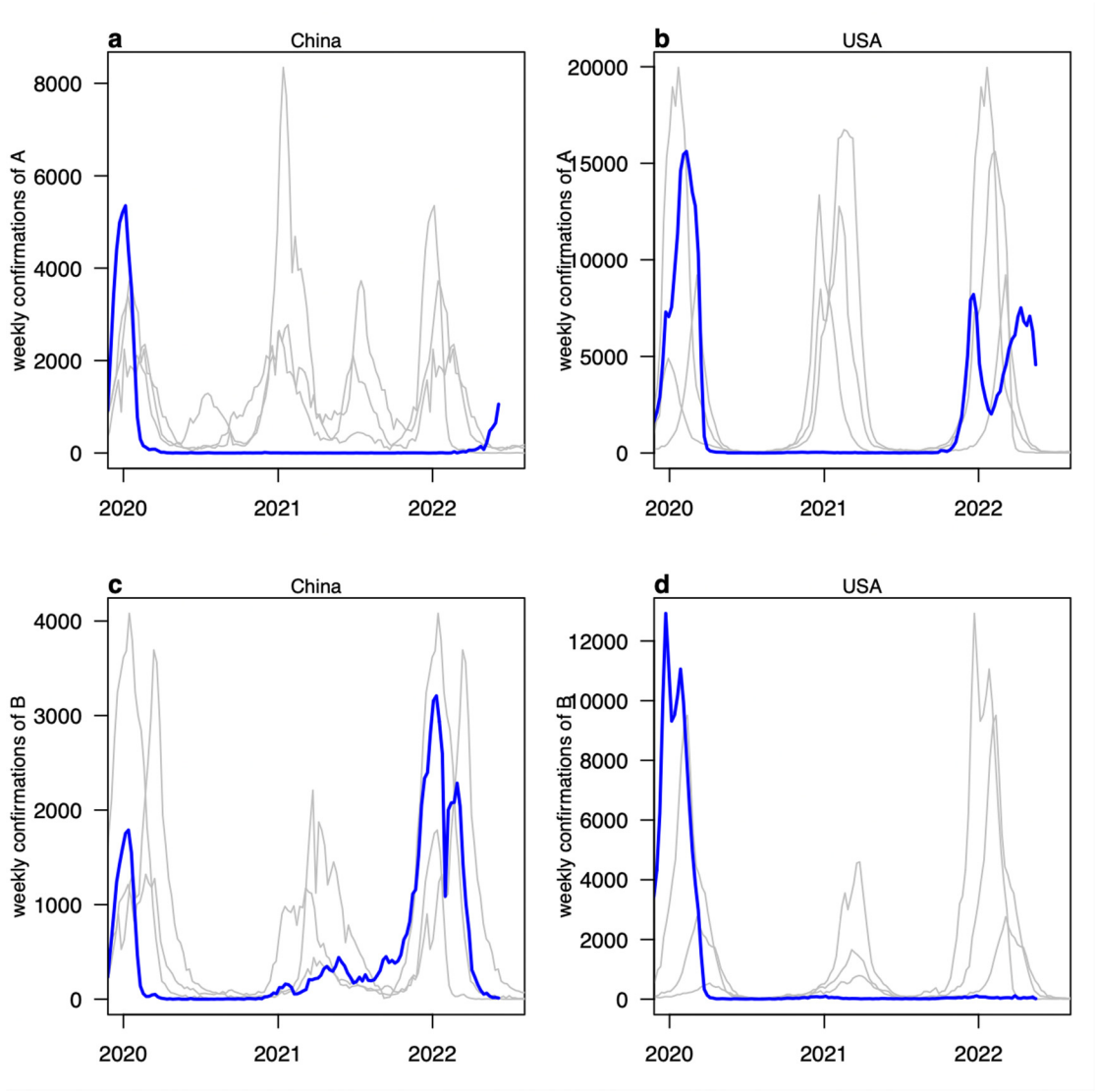

Figure 1. Comparison of Influenza A and Influenza B cases between the US and China. The upper plots are influenza A cases and the lower are influenza B cases. The grey curves are past flu cases of the years 2014−2019 whilst blue bolded lines are flu cases of the years 2020 to 2022. Each x-coordinate point shares 4 y-values, where a blue point indicates x-coordinate corresponding cases and the other three grey points provide information for the exact past 2, 4 and 6 years.

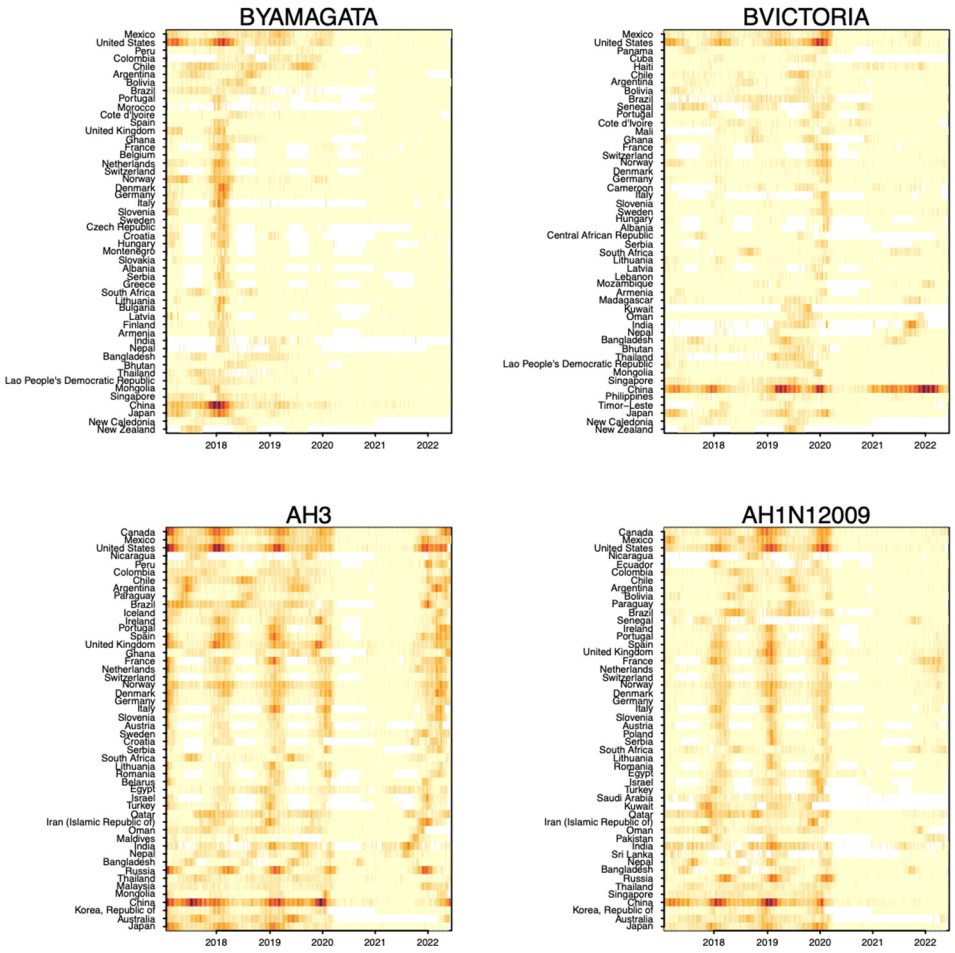

Figure 2. Heat map of four influenza sublineages in 60 countries/regions from June 2017 to June 2022. The COVID-19 pandemic had suppressed the global spread of influenza. But the spread of AH3 has resumed by the middle of 2022. BVIC caused an outbreak at the end of 2021 in Mainland China

4. Discussion and conclusions

Since SARS-CoV-2 emerged and circulated around the world, influenza activity has been lower than that seen before the pandemic. This might be due to the adoption of PHSMs in response to COVID-19. Ali et al. [4] showed a maximum of 1 to 5-fold rise in peak magnitude and 1 to 4-fold rise in epidemic size for the upcoming influenza 2022–23 winter season by a model-based prediction, suggesting a substantially increased infection burden for the upcoming influenza seasons in the northern hemisphere. In order to better understand the possible dominant strains for the upcoming influenza seasons and provide evidence-based public health interventions, our research discussed the pattern of flu reintroduction and resuscitation taking China and the US as an example, after a year-long slumber in the early stages of the COVID-19 pandemic. Our analysis depicted that influenza viruses A and B showed distinct return features in China and the US. The upcoming influenza season may be dominated by influenza B in China while influenza A may dominate the upcoming influenza season in the US, which is unusual. This phenomenon may be attributed to the strict nonpharmaceutical

interventions (NPIs) including border policy in Mainland China and travel restrictions between the two countries during the COVID-19 period [6−10].

Our analysis showed that there were distinct differences between changes in influenza activity in the US and China which was consistent with previous studies [11,12]. Influenza activity declined earlier in China than in the US (Figure 1) during the 2019−2020 flu season. This might be due to that China was the first country to take strict measures to mitigate COVID-19. The nationwide implementation of NPIs in response to COVID-19, including border restrictions, school closures, social distancing and mask-wearing, may substantially reduce the transmission of influenza as well [13]. These findings suggest that public health and social measures might be useful during the influenza seasons.

The dominant influenza subtypes shifted before and after the COVID-19 outbreak. Before the outbreak, influenza A subtypes (e.g., AH3, A1H12009) dominated in China, while after the outbreak, influenza B virus, mainly the B/Victoria strain dominated. On the contrary, influenza A dominated in the US after the outbreak of COVID-19 (Figures 2, S2 and S3). And there were also novel influenza A subtypes detected in humans during the 2021–22 influenza season [14]. Influenza A(H3N2) was reported to be the predominant virus throughout the 2021–22 influenza season in the US, while the number of influenza B viruses, e.g., B/Victoria, and B/Yamagata viruses reported was very small. It appeared that there was a global disappearance of B/Yamagata viruses during the COVID-19 pandemic [15]. Though the precise driven factors for the possible extinction of B/Yamagata are unknown, there are speculations that the inherent vulnerability of this lineage (B/Yamagata viruses have a lower effective reproductive number), global circulation pattern of the viruses in different susceptible populations (B/Yamagata viruses disproportionately affects adults whose mobility was largely restricted due to COVID-19 pandemic), along with prolonged use of a well-matched influenza vaccine for B/Yamagata, may have together enabled massive suppression of B/Yamagata during the pandemic. This shift in influenza type and subtype dominance may have important implications for influenza prevention and public health interventions. Given the possible loss of immunity (strain specific) in the population, the decreased influenza activity and circulation over the past few years may affect the severity of the upcoming influenza season, as shown in Ali et al. estimation [4].

Vaccination is one of the most effective measures in influenza control. Identifying and developing effective universal vaccines in the context of the potential extinction of B/Yamagata, as well as timely influenza vaccination program in the general population and the targeted population (e.g., children and older adults), are of primary importance after influenza's long-term absence. This is complemented by NPIs, which together could minimize the potentially severe consequences of seasonal influenza in the future.

Annual flu vaccination is recommended by CDC for the people who are older than 6 months and do not have contraindications. The overall flu vaccination rate for persons 6 months and older is around 40% to 55% in the US during the recent 10 flu seasons [16]. And only minor fluctuations in flu vaccination rate are observed during the COVID-19 pandemic. On the contrary, the flu vaccination rate is very low in China. Unfortunately, we could not directly access the China annual vaccination rate data from the official website. However, the studies conducted to estimate the flu vaccination rate in China could give us a glance at it. The estimated average vaccination rate was 1.5–2.2% between 2004 and 2014 in China [17]. Another study [18] estimated a 2.4% vaccination rate from a national cross-sectional study. We couldn't find any studies about the recent vaccination rate and its fluctuation during the COVID-19 pandemic in China. One possible hypothesis is that the vaccination rate remains at a low level and doesn't fluctuate too much during the COVID-19 pandemic in China.

Then the flu vaccination rate doesn't fluctuate too much during the COVID-19 pandemic in both countries. Thus, we can hardly say that the COVID-19 pandemic has a huge impact on flu vaccination. This again verifies that lower influenza activity mainly attributes to the adoption of PHSMs in response to COVID-19. Moreover, since the vaccine uptake has been consistent, the vaccine cannot explain why one strain/subtype dominates and the other strain/subtype disappears. The most likely mechanism we think could be PHSMs or the travel restrictions prevent the strain importation.

Our analysis clearly showed the shift in influenza type and subtype dominance in different countries. Although influenza activity is decreasing and circulation is low during the COVID-19 pandemic, remaining vigilant for influenza infections, performing sufficient testing for seasonal influenza viruses, and monitoring for novel influenza virus strains are still important. Better understanding of virus evolution, human susceptibility, ecological and social interactions are key to responding to the next pandemic.

Conflict of interest

The authors declare there is no conflict of interest.

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