Different transmission dynamics of COVID-19 and influenza suggest the relative efficiency of isolation/quarantine and social distancing against COVID-19 in China

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Summary

According to a comparative study of the transmission dynamics of seasonal influenza and COVID-19 in China, we evaluated the efficiency of isolation/quarantine and social distancing against COVID-19 transmission, and found that isolation/quarantine alone could not contain COVID-19 pandemic effectively.

Abstract

Background Non-pharmaceutical interventions (NPIs) against Coronavirus Disease 2019 (COVID-19) are vital to reducing the transmission risks. However, the relative efficiency of social distancing against COVID-19 remains controversial, since social distancing and isolation/quarantine were implemented almost at the same time in China.

Methods In this study, surveillance data of COVID-19 and seasonal influenza in the year 2018-2020 were used to quantify the relative efficiency of NPIs against COVID-19 in China, since isolation/quarantine was not used for the influenza epidemics. Given that the relative age-dependent susceptibility to influenza and COVID-19 may vary, an age-structured *Susceptible-Infected-Recovered* model was built to explore the efficiency of social distancing against COVID-19 under different population susceptibility scenarios.

Results The mean effective reproductive number, R_t , of COVID-19 before NPIs was 2.12 (95% confidential interval (CI): 2.02-2.21). By March 11, 2020, the overall reduction in R_t of COVID-19 was 66.1% (95% CI: 60.1%-71.2%). In the epidemiological year 2019/20, influenza transmissibility reduced by 34.6% (95% CI: 31.3%-38.2%) compared with that in the epidemiological year 2018/19. Under the observed contact patterns changes in China, social distancing had similar efficiency against COVID-19 in three different scenarios. By assuming same efficiency of social distancing against seasonal influenza and COVID-19 transmission, isolation/quarantine and social distancing could lead to a 48.1% (95% CI: 35.4%-58.1%) and 34.6% (95% CI: 31.3%-38.2%) reduction of the transmissibility of COVID-19.

Conclusions Though isolation/quarantine is more effective than social distancing, given that typical basic reproductive number of COVID-19 is 2-3, isolation/quarantine alone could not contain the COVID-19 pandemic effectively in China.

Keywords: COVID-19; influenza; effective reproductive number; Non-pharmaceutical interventions; efficiency.

Background

Implementing the most effective interventions has become a top public health priority in the ongoing Coronavirus Disease 2019 (COVID-19) pandemic. Before a highly efficacious vaccine that is accepted by the majority of the population or an antiviral drug is available, only non-pharmaceutical interventions (NPIs) could substantially control infection transmission, based on lessons learned from previous outbreaks, including severe acute respiratory syndrome (SARS), Ebola and the pandemic H1N1 2009.⁰⁻³ However, the relative efficiency of different NPIs remains controversial. To suppress the COVID-19 pandemic in China, the Chinese government implemented a set of NPIs, including not only the classical isolation of the confirmed/suspected cases and quarantine of their close contacts in special facilities, but also unprecedented measures like strict community containments with social distancing.⁴ To date, the COVID-19 pandemic has been under control in China. Since different NPIs were implemented almost at the same time, it is difficult to directly quantify the relative efficiency of each individual NPI. Nonetheless, efforts are being made to address this critical question about the relative efficiency of particular NPIs for COVID-19. This is particularly important and time-sensitive as countries around the world devise strategies to rapidly respond to the pandemic.

One potential way to assess the relative efficiency of NPIs for COVID-19 is to use data and knowledge about a concurrent and similarly transmitted disease: influenza. Both influenza and COVID-19 are highly contagious respiratory infection diseases, and in China, the seasonal influenza epidemics always peak in January–February,⁵ the COVID-19 pandemic which peaked in January 2020, also covered a period that overlapped with the flu season in China. On the one hand, some NPIs that were implemented against COVID-19, such as school and workplace closures, have already been proven to be effective to control influenza transmission.^{6,7} On the other hand, some other NPIs were specifically implemented for

COVID-19, including immediate isolation of the COVID-19 confirmed cases, and quarantine of their close contacts in dedicated quarantine facilities. This situation provides a good opportunity to explore the relative efficacy of different NPIs against the COVID-19 pandemic, by simply assuming a similar transmission mode and efficiency of NPIs against influenza and COVID-19.

In this study, the transmission dynamics of seasonal influenza and COVID-19 were studies and compared to evaluate the relative efficiency of NPIs against COVID-19 in China.

Methods

Data sources

The weekly reports of influenza surveillance data from April 2018 to March 2020, originally provided by the Chinese National Influenza Center (CNIC), were downloaded from the WHO Flunet. More detailed information about the dataset is in the Supplementary 1. In accordance with earlier studies,^{8,9} a count more precisely representing the influenza infections was used in this study, the weekly incidence rate (henceforth, "incidence rate") of influenza, The weekly incidence rate was calculated by multiplying the influenza-like illness (ILI) rate among patients visiting sentinel hospitals by the viral detection positive rate. The weekly incidence rate was then interpolated to daily incidence rate using splines.⁷ Given the seasonality of seasonal influenza in China, the epidemiological annual cycle was defined as the period from April 1 to March 31, 2019).⁵ Daily number of newly confirmed COVID-19 cases by onset date from December 1, 2019 to March 11, 2020 in China were from China Centers for Disease Control and Prevention. The indicators of influenza and COVID-19 activities are shown in Figure 1 and Figure 2.

Interventions

Though from January 1, 2020, the Huanan seafood wholesale market, where the COVID-19 was firstly discovered, was closed, community-wide implementation of NPIs against COVID-19 began on January 23, 2020, when the first three provinces began a 1-level response, and within the following two days, 27 additional provinces began a 1-level response (Figure 3). In this study, it was assumed that NPIs against COVID-19 began on January 23, 2020.

The NPIs used in China to contain COVID-19 transmission included isolation and quarantine, social distancing, and community containment measures.¹⁰ Isolation/ quarantine is the isolation of the confirmed COVID-19 cases and/or all suspected cases, and quarantine of their close contacts during the incubation period in special quarantine facilities. Social distancing is designed to reduce interactions between people in a broader community, while community containment is also designed to reduce personal interaction, but applied to an entire community.¹⁰ Supplementary 2 described the national level social distance interventions in detail. Since both social distancing and community containment are used to reduce interaction between people, and in China, the social distancing interventions are implemented throughout the country. In this study, NPIs implemented in China were classified in the following two categories:

<u>Intervention 1:</u> Isolation and quarantine, i.e. isolation of the confirmed COVID-19 cases and/or all suspected cases, and quarantine of their close contacts during the incubation period in special quarantine facilities. <u>Intervention 2</u>: Social distancing. The aim of social distancing was to reduce interactions between people. As disease transmitted by respiratory droplets required a certain proximity of people, so in theory, social distancing of people will reduce influenza and COVID-19 transmission.

Models

The efficiency of NPIs against influenza and COVID-19 was evaluated based on changes of the effective reproductive number, R_t , which represents the mean number of secondary cases that were infected by a primary case of infection at time t. Time-varying estimates of the effective reproductive number were made using the R package EpiEstim, assuming a mean serial interval of 4.7 days and a standard deviation of 2.9 days for COVID-19,¹¹ and a mean serial interval of 2.85 days and a standard deviation of 0.93 days for influenza.¹² Changes in transmissibility were evaluated by comparing the R_t values before and after NPIs. All analyses were conducted with R version 3.6.3.

The impact of interventions against COVID-19 was estimated by fitting a regression model for R_t . Based on epidemic theory, $R_t = R_0 S_t e^{\gamma B(t)}$,¹³ where R_0 is the basic reproductive number, S_t is the proportion of susceptible individuals, B(t) is an index of intervention, defined as B(t)=1 during the intervention period and B(t) = 0 during the non-intervention period, γ is a coefficient representing the effect of interventions on infection transmission (γ <0 indicates reduced transmissibility during the intervention period), and the overall efficiency is estimated by 1- e^{γ} . For COVID-19, since the number of infectors was marginal compared with the total population in China, and almost the entire population is susceptible to COVID-19, it was assumed that $S_t = 1$. By using the log-linear multivariable regression model, the parameter γ could be estimated. Denoting the efficiency of social distancing and isolation/quarantine on reducing the infection transmissibility to be e_s and e_i respectively. Assuming that social distancing and isolation/quarantine are independent to containing infection transmission, then the overall efficiency of social distancing and isolation/quarantine could be $1-(1-e_s)(1-e_i)$.

In addition, since population susceptibility to influenza and COVID-19 varies, the efficiency of social distancing against influenza and COVID-19 might also vary. In this study, an agestructured Susceptible-Infected-Recovered (SIR) model was built, in which population were divided into three groups: (1) the young, with age less than 18 years old, (2) adults, age between 18 and 60, and (3) the old, with age more than 60 years old. The percentage of the young, adults and the old are 16.9%, 71.2% and 11.9% respectively in China.¹⁴ More detailed information about the age-structured SIR model was in the Supplementary 3.

The contact rates before and after NPIs in China were from Zhang et al.¹⁵ Generally, daily contacts were reduced 7-8-fold during the COVID-19 intervention period.¹⁵

The relative susceptibility (γ_i) to influenza of the children, adult and elderly was assumed to be 2:1:2,¹⁶ since the children and elderly are at high risk from influenza. For COVID-19, since some study reported that the susceptibility increases with age,¹⁵ some study showed that the susceptibility did not change with age.¹⁷ We considered the following three scenarios. Scenario 1: The relative susceptibility to COVID-19 did not change with age, and of three age groups were assumed to be 1:1:1. <u>Scenario 2</u>: The relative susceptibility to COVID-19 increased with age, and of three age groups were assumed to be 1:2:4.

<u>Scenario 3</u>: The relative susceptibility to COVID-19 of three age groups were assumed to be 2:1:2, same with seasonal influenza.

Results

Though the effective reproductive number in the epidemiological years 2019/20 is a little lower than that in the year 2018/19, the trend in the 2-month study period in the epidemiological years 2019/20 is similar to that in the year 2018/19 before the implementation of NPIs against COVID-19 on January 23, 2020 (Figure 4a). After the implementation of NPIs, in the first two weeks, R_t of influenza did not decrease (Figure 4a). This seems unexpected, there were following reasons. Following NPIs implementation, the total number of hospitalizations declined sharply (Figure 1a). Furthermore, since some of the symptoms of COVID-19 confirmed/suspected cases were similar to those seen in influenza cases, such as fever and cough, the ILI rate during the first two weeks after NPIs would be expected to be much higher than the real situation (Figure 1b). Therefore, the incidence rate of influenza, which was calculated by multiplying the ILI rate among patients visiting sentinel hospitals by the viral detection positive rate during this period, would also be expected to be higher than the real situation. After the first two weeks following NPIs implementation, when the ILI rate was close to that in the year 2018/19 (Figure 1b), the estimated R_t declined quickly then (Figure 4a).

To evaluate the efficiency of social distancing against influenza transmission in the epidemiological years 2019/20, the changes of R_t of seasonal influenza in the epidemiological

years 2019/20 were compared with these in 2018/19. In the epidemiological years 2018/19, the estimated mean effective reproductive number, R_t , of seasonal influenza epidemic during the two weeks just before the school winter holiday was 1.12 (95% confidential interval (CI): 1.10-1.15) (Phase 1). When the Chinese school winter holiday began, R_t decreased to 0.98 (95% CI: 0.96, 1.00) (Phase 2). After school resumed, the mean reproductive number increased to 1.01 (95% CI: 0.99-1.02) (Phase 5). In the epidemiological year 2019/20, the effective reproductive number, R_t , of seasonal influenza showed similar trend before the implement of NPIs against COVID-19. In phase 4 and 5, the school did not resume two weeks after the Chinese New Year Eve due to the COVID-19 pandemic, R_t did not increase but decreased more (Figure 4a). In Phase 5, the mean R_t was 0.66 (95% CI: 0.63-0.68). Compared with the same period in the epidemiological year 2018/19, R_t reduced by 34.6% (95% CI: 31.3%-38.2%). We hypothesize this 34.6% reduction of the influenza transmissibility was achieved due to the social distancing measures used to control the COVID-19 pandemic.

For the COVID-19 pandemic, we began the estimation of R_t from December 15, 2020, since before December 15, 2020, the daily number of new cases was few and volatile, so the estimated R_t also fluctuated a lot. Before any interventions, the mean effective reproductive number was 2.12 (95% CI: 2.02-2.21) (Figure 4b). After January 23, 2020, when a set of **NPIs** were implemented, the effective reproductive number showed a sustained, declining trend. After 11 days of NPIs deployment, the effective reproductive number was less than one. This suggested that the NPIs implemented in China were effective to control the COVID-19 pandemic. On March 11, 48 days after the NPIs deployment, the effective reproductive number was only 0.41 (95% CI: 0.36-0.46). According to the regression analysis, by March 11, 2020, the overall reduction in COVID-19 transmissibility with NPIs was 66.1% (95% CI: 60.1%-71.2%) (*p*<0.001).

With the contact pattern changes before and after the COVID-19 pandemic in China, we quantified the efficiency of the social distancing interventions against COVID-19 transmission in three scenarios. The same reduction in contact rates led to the reduction in the R_t of COVID-19 by 70.6%, 71.4% and 70.2% respectively in three scenarios (Table 1). It's reasonable that when the adult is less susceptible to COVID-19 (Scenario 3), social distancing is less effective. With different assumptions of population susceptibility to COVID-19, the efficiencies of contact rates reduction may vary, but the differences are moderate. This is partly due to that the strict NPIs implemented in China, the contact rates in all 3-age groups decreased sharply. Here we have to stress that the estimated reduction of R_t from contact rate changes is not comparable with the estimation from the daily number of confirmed COVID-19 cases, because the latter is an average reduction over the study period, while the former is the reduction at two time points: one before NPIs, one after NPIs.

According to the above analysis, it's found that population susceptibility to an infection may have limited effect on the efficiency of social distancing against infection transmission with the reported contact rates changes from literatures. Thus by assuming the same efficiency of social distancing against seasonal influenza and COVID-19, i.e. social distancing could reduce 34.6% (95% CI: 31.3%-38.2%) of transmissibility of COVID-19. Since by March 11, 2020, the overall reduction in COVID-19 transmissibility with NPIs was 66.1% (95% CI: 60.1%-71.2%), we could estimate that isolation/quarantine led to a 48.1% (95% CI: 35.4%-58.1%) reduction of the transmissibility of COVID-19.

Discussion

This study estimated the basic reproductive number for COVID-19 as 2.12 (95% CI: 2.02-2.21), which is close to 2.2-2.68 reported in the literature.^{18,19} This reproductive number is much higher than that of seasonal influenza, which is 1.28 (interquartile range: 1.19–1.37),²⁰ so it is more difficult to control COVID-19 than influenza. The estimated reduction in the reproductive number of seasonal influenza epidemic during the Chinese school winter holiday alone was 12.5% (95% CI: 9.1%-16.5%, Phase 2 VS Phase 1) in the years 2018/19, which coincided with studies in Hong Kong SAR, China and South Korea. ^{6,7,13,21} In the year 2019/20, the reproductive number reduced by 34.6% (95% CI: 31.3%-38.2%), which is much higher than previous years. This is consistent with the study in Hong Kong SAR, P.R. China, where the effective reproductive number of seasonal influenza reduced by 44% in the epidemiological year 2019/20 during the COVID-19 pandemic period.²¹ The difference in the reduction between epidemiological 2019/20 and 2018/19 may be explained by the fact that in the epidemiological year 2019/20, to contain COVID-19, there were not only school closures, but also public event cancellations, public transport closures, mandates to wear masks in public areas, and so on.

Social distancing interventions have been shown to be effective against COVID-19.²² In three scenarios, social distancing has similar efficiency against COVID-19 transmission. The estimated 48.1% reduction of transmissibility due to isolation/quarantine intervention coincides with the results from a retrospective cohort study in Guangzhou, China, in which it was estimated that prompt isolation/quarantine only reduced 20-50% of the effective reproductive number of COVID-19 in Guangzhou.²³ Given that the typical basic reproductive number of COVID-19 was 2-3, isolation/quarantine alone is not enough to contain COVID-

19 transmission in China. In contrast, isolation and quarantine was effective for SARS in 2003.¹⁰ The reason could be that viral shedding peaks at 6-11 days after onset of illness, enabling early isolation before massive transmission.¹⁰ By contrast, for COVID-19, because pre-symptomatic and asymptomatic cases were estimated to contribute 44-53% of transmission,^{24,25} it was not surprising that isolation and quarantine alone could not contain the COVID-19 pandemic in China.

Since both COVID-19 and seasonal influenza are respiratory infections and have similar transmission routes, including droplet and contact transmission,²⁶ in this study, we assumed that social distancing had similar effects against COVID-19 and influenza transmission. While some of the epidemiological characteristics of COVID-19 and influenza vary, which may affect the role of social distancing in infection dynamics. For example, the mean incubation period of COVID-19 is much longer than that of influenza (4 days²⁷ VS 1.4 days²⁸). Besides, for COVID-19, about half of secondary cases were infected during the index cases' presymptomatic stage,²⁴ while for influenza, there is scant evidence that presymptomatic individuals play a role in the transmission.²⁹ In addition, population almost had no preexisting immunity against COVID-19, while some people may have preexisting immunity against influenza as seasonal influenza epidemics occurs annually.

There were four major limitations in this study. First, we only estimated the effective reproductive number of COVID-19 by March 11, 2020, when the COVID-19 pandemic in China was near the end, but still continuing, which means that if after March 11, 2020, the reproductive number continue to reduce, the overall reduction of COVID-19 transmissibility would be more than 66.1% as we estimated. This suggests that the efficiency of

isolation/quarantine would be underestimated. The use of more time series data of COVID-19, if available, could address this limitation. The second major limitation is the assumption that social distancing and isolation/quarantine are independent to containing infection transmission. Isolation/quarantine interventions aimed at reducing the interaction between susceptible and infected individuals, while social distancing aimed at reducing interaction between individuals, which means social distancing could also reduce the interaction between susceptible and infected individuals, so social distancing and isolation/quarantine are not completely independent. The third one is the interpolation of daily incidence rates of influenza from the weekly data. The daily variation in influenza transmissibility might have been reduced because of this interpolation. The use of daily data of influenza, if available, would address this limitation. The last one is about the the surveillance data. For both influenza and COVID-19, the data came from a nationwide, however, 1bout 55% of COVID-19 cases were from Wuhan. So in Wuhan with stricter NPIs implemented, it is not surprising that NPIs in Wuhan reducing the effective reproductive number by 96.0% as of 8 March 2020,³⁰ higher than the nationwide average reduction estimated in this study, i.e. 81% as of 11 March 2020. Because most COVID-19 cases concentrated in Wuhan City, using the nationwide surveillance data to estimate the efficiency of NPIs against COVID-19 might lead to an underestimate.

In conclusion, by March 11, 2020, social distancing and isolation/quarantine led to a 34.6% and 48.1% reduction of COVID-19 transmissibility, respectively. Considering that the typical basic reproductive number is 2-3 for COVID -19, isolation/quarantine alone is not enough to contain the COVID-19 pandemic in China.

Notes

Acknowledgements

This project was supported by National Key R&D Program of China (Grant No. 2020YFC0840900), Shenzhen Science and Technology Program (Grant No. KQTD20180411143323605), the grants from Zhejiang Natural Science Foundation (Grant No. LQ20H260009). We are grateful for the World Health Organization (WHO Flunet) and Chinese National Influenza Center (CNIC, Weekly report) providing the influenza surveillance data.

Author's contributions

HL, YS and YL conceived and designed the study. YS and YL supervised the study. XW³ MX, YX collected data. HL cleaned and analysed the data. HL wrote the drafts of the manuscript. YL, YS, BC XD, XW^{1,2} commented on and revised drafts of the manuscript. YS, YL, and HL interpreted the findings. All authors read and approved the final report.

Declaration of interests

All authors declare no competing interests.

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Table

 Table 1. Efficiency of social distancing isolation/quarantine and against COVID-19

Interventions	Percentage reduction of the effective reproductive number		
	Scenario 1	Scenario 2	Scenario 3
Social distancing	70.6%	71.4%	70.2%

Figure legends

Figure 1. Weekly indicators of seasonal influenza activity in China in the epidemiological years 2018/19 and 2019/20; (a) number of visitors to hospital, (b) ILI rate, (c) incidence rate.

Figure 2. Daily number of confirmed COVID-19 cases by onset date from December 2 to March 11, 2020. After March 11, 2020, the number of confirmed cases reached at a very low level.

Figure. 3. Timeline of the discovery of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causing COVID-19 and interventions implemented in China, from 31 December 2019.

Figure 4. Daily effective reproductive number of infections. (a) seasonal influenza in the epidemiological years 2018/19 and2019/20, the daily effective reproductive number of influenza with 95% confidential interval is in the Supplementary 4; (b) COVID-19 pandemic, with grey area representing the 95% confidential interval.



Figure 1A



Figure 1B



Figure 1C



Figure 2



Figure 3







Figure 4B