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When to lift the lockdown in Hubei province during COVID-19 epidemic? An insight from a patch model and multiple source data



Xiaodan Sun ^a, Yanni Xiao ^{a,*}, Xiangting Ji ^b

^a School of Mathematics and Statistics, Xi'an Jiaotong University, Xi'an 710049, China

^b Baidu Inc., Beijing 100094, China

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ABSTRACT

After diagnosed in Wuhan, COVID-19 spread quickly in mainland China. Though the epidemic in regions outside Hubei in mainland China has maintained a degree of control, evaluating the effectiveness and timeliness of intervention strategies, and predicting the transmission risk of work resumption as well as lifting the lockdown in Hubei province remain urgent. A patch model reflecting the mobility of population between Hubei and regions outside Hubei is formulated, and parameterized based on multiple source data for Hubei and regions outside Hubei. The effective reproduction numbers for Hubei and regions outside Hubei are estimated as 3.59 and 3.26 before Jan 23rd, 2020, but decrease quickly since then and drop below 1 after Jan 31st and Jan 28th, 2020. It is predicted that the new infections in Hubei province will decrease to very low level in mid-March, and the final size is estimated to be about 68,500 cases. The simulations reveal that contact rate after work resumption or lifting the lockdown in Hubei plays a critical role in affecting the epidemic. If the contact rate could be kept at a relatively low level, work resumption starting as early as on March 2nd in Hubei province may not induce the secondary outbreak, and the daily new infectious cases can be controlled at a low level if the lockdown in Hubei is lifted after March 9th, otherwise both work resumption and lifting the lockdown in Hubei should be postponed.

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1. Introduction

After diagnosed in Wuhan of Hubei province, COVID-19 spread quickly from Wuhan to surrounding cities, regions outside Hubei in mainland China. By January 22nd, 2020, 571 cases were reported by 25 provinces in mainland China (National Health Commission of the People's Republic of China, 2020). From January 23rd, 2020 Chinese government triggered a series of prevention and control strategies to prevent disease from spreading, including the lockdown of Wuhan, travel restrictions and calling for staying at home during Spring Festival holidays. However, lots of infections or latent individuals have already been imported into regions outside Hubei because of the large volume of travels during Spring festival migrations, resulting in spatially spreading of COVID-19 epidemic in mainland China.

Recently the COVID-19 epidemic in mainland China is weakening with enhanced prevention and control strategies. When to return to work/study and how to manage the orderly work resumption become the challenging problems. Some local govern-

ments have already divided the provinces into different areas according to the epidemic situation of the region itself, and the areas with low epidemic level are allowed to restore production or normal social order. However, determining the date of work resumption is not only dependent on the epidemic situation of the region itself but also the epidemic of other regions as well as migration rate. Then it is essential to accurately estimate the epidemic situations of a region and other regions and investigate the impacts of various dates of work resumption with weakened control measures on the potential outbreak.

Predicting the epidemic of Hubei, estimating the number of cases in regions outside Hubei imported from Hubei province, and investigating the time of work resumption and lifting the lockdown in Hubei by linking reported data of Hubei and regions outside Hubei as well as the mobility of population between Hubei and regions outside Hubei are very important and fall within the scope of this study. There are some early studies which have estimated the epidemic in Hubei or Wuhan by using the reported data and population movement data (Wu et al., 2020; Cao et al., 2020; Jung et al., 2020; Sanche et al., 2020). Some mathematical modelling studies have estimated the epidemic in Hubei or mainland China without considering the mobility of population between

* Corresponding author.

E-mail address: yxiao@mail.xjtu.edu.cn (Y. Xiao).

Hubei and regions outside Hubei or without considering the time varying interventions (Tang et al., 2020; Tang et al., 2020; Tang et al., 2020; Shen et al., 2020; Wang et al., 2020). Note that the Wuhan government began to screen all the suspected cases on February 8 and increased the diagnosis rate from suspected cases greatly (Health Commission of Hubei Province, 2020). How to quantify the changing or time-dependent detection rate or contact rate and evaluate the epidemic more precisely is challenging.

In this study, we shall formulate a two-patchy mathematical model with one patch denoting Hubei province and the other representing regions outside Hubei in mainland China. The two patches connected to each other because of the travelling of population between Hubei and regions outside Hubei in mainland China. Based on the daily reported data for the epidemic in Hubei and regions outside Hubei, as well as the mobility data between Hubei and regions outside Hubei we shall focus on the estimation of the epidemic in Hubei and the effect of work resumption and lifting the lockdown at Hubei province on the epidemic in Hubei and regions outside Hubei in mainland China.

2. Methods

2.1. The model

A two-patchy model is formulated with one patch denoting Hubei province and the other being the regions outside Hubei in mainland China. Before Jan 23th, 2020, these two patches are connected with each other due to the mobility of population between Hubei and regions outside Hubei. Then, the two patches become isolated as the lockdown measure is implemented. After lifting the lockdown in Hubei province, the two patches will be connected again. For convenience, the subscript h and c represent the corresponding quantity in Hubei and regions outside Hubei in mainland China. Susceptibles in Hubei S_h (or regions outside Hubei S_c), may be infected when contacting with the infectious population in Hubei I_h (or regions outside Hubei I_c). After infected, the individual will firstly stay in the latent class, E_h and E_c , and then become infectious I_h and I_c . The infectious population may be diagnosed and confirmed with COVID-19 (Q_h and Q_c) directly, or move to the suspected class Y_h^l and Y_c^l , and then be confirmed with COVID-19. Such kind of suspected individuals are in fact already infected, thus this class is also called as suspected and infected class. The susceptibles may move to suspected but uninfected class Y_h^s and Y_c^s because of common fever or pneumonia, and the suspected but uninfected population may also move back to the susceptibles class after screening. The confirmed population will either recover (R_h and R_c) or dead. The susceptibles, latent population and infectious population may travel between Hubei and regions outside Hubei at a certain probability. Since the confirmed and suspected population will be quarantined, we do not consider the mobility rate for people in these classes. Fig. 1 shows the flow chart of the model, while Eqs. (1) and (2) describe the model equations for Hubei and regions outside Hubei, respectively.

$$\begin{aligned} \frac{dS_h}{dt} &= -\frac{\beta C_h(t) S_h I_h}{N_h} + \delta_h^s(t) Y_h^s - m S_h + r_i(t) S_c - r_e(t) S_h, \\ \frac{dE_h}{dt} &= \frac{\beta C_h(t) S_h I_h}{N_h} - \sigma E_h + r_i(t) E_c - r_e(t) E_h, \\ \frac{dI_h}{dt} &= \sigma E_h - \delta_h^l I_h + r_i(t) I_c - r_e(t) I_h, \\ \frac{dY_h^s}{dt} &= m S_h - \delta_h^s(t) Y_h^s, \\ \frac{dY_h^l}{dt} &= \delta_h^l (1 - q) I_h - \delta_h^y(t) Y_h^l, \\ \frac{dQ_h}{dt} &= \delta_h^l q I_h + \delta_h^y(t) Y_h^l - \gamma_h Q_h - \alpha_h Q_h, \\ \frac{dR_h}{dt} &= \gamma_h Q_h. \end{aligned} \quad (1)$$

$$\begin{aligned} \frac{dS_c}{dt} &= -\frac{\beta C_c(t) S_c I_c}{N_c} + \delta_c^s Y_c^s - m S_c + r_e(t) S_h - r_i(t) S_c, \\ \frac{dE_c}{dt} &= \frac{\beta C_c(t) S_c I_c}{N_c} - \sigma E_c + r_e(t) E_h - r_i(t) E_c, \\ \frac{dI_c}{dt} &= \sigma E_c - \delta_c^l I_c + r_e(t) I_h - r_i(t) I_c, \\ \frac{dY_c^s}{dt} &= m S_c - \delta_c^s Y_c^s, \\ \frac{dY_c^l}{dt} &= \delta_c^l (1 - q) I_c - \delta_c^y Y_c^l, \\ \frac{dQ_c}{dt} &= \delta_c^l q I_c + \delta_c^y Y_c^l - \gamma_c Q_c - \alpha_c Q_c, \\ \frac{dR_c}{dt} &= \gamma_c Q_c. \end{aligned} \quad (2)$$

The outbound travel rate from Hubei province to regions outside Hubei is $r_e(t)$, and the inbound travel rate from regions outside Hubei to Hubei province is $r_i(t)$ at time t . β is the transmission probability per contact. The contact rate in Hubei and regions outside Hubei are both piecewise functions which are proposed by Tang et al. (Tang et al., 2020; Tang et al., 2020), and denoted by $c_h(t)$ and $c_c(t)$, as shown in Eqs. (3) and (4), respectively.

$$c_h(t) = \begin{cases} c_h^0, & \text{before Jan 23rd,} \\ (c_h^0 - c_h^b) e^{-r_h(t-t_{23})} + c_h^b, & \text{after Jan 23rd.} \end{cases} \quad (3)$$

$$c_c(t) = \begin{cases} c_c^0, & \text{before Jan 23rd,} \\ (c_c^0 - c_c^b) e^{-r_c(t-t_{23})} + c_c^b, & \text{after Jan 23rd.} \end{cases} \quad (4)$$

It is assumed that before Jan 23rd, the contact rate for Hubei and regions outside Hubei are both constants, denoted by c_h^0 and c_c^0 , respectively. After Jan 23rd, both contact rates decrease exponentially with the exponential decreasing rates being r_h and r_c . And the smallest contact rates are c_h^b and c_c^b for Hubei and regions outside Hubei. For convenience, initial and smallest transmission rates are further defined as $\beta_h^0 \triangleq \beta c_h^0$, $\beta_h^b \triangleq \beta c_h^b$ and $\beta_c^0 \triangleq \beta c_c^0$, $\beta_c^b \triangleq \beta c_c^b$ for Hubei and regions outside Hubei. The latent period is assumed to be $1/\sigma$ after infected. The diagnosis rates for infectious population are δ_h^l and δ_c^l , among those diagnosed population a proportion q is confirmed with COVID-19, and a proportion $1 - q$ moves to the suspected and infected class. Due to the fact that Hubei government amplifies the screening of suspected population greatly after Feb 8th, there will be an extra confirmation rate from the suspected and infected population to confirmed population. Thus, the confirmation rate for the suspected and infected population in Hubei province is also a piecewise function, which is described as follows.

$$\delta_h^y(t) = \begin{cases} \delta_h^{y_0}, & \text{before Feb 8th,} \\ \delta_h^{y_0} + \delta_h^{y_b}, & \text{after Feb 8th.} \end{cases} \quad (5)$$

As the screening policy for regions outside Hubei is stable, the confirmation rate is assumed as a constant δ_c^y . Since it is difficult to differentiate whether the suspected population is real infected, it is assumed that the exclusion rate for the suspected but uninfected population (denoted by $\delta_h^s(t)$ and δ_c^s) are consistent with those suspected and infected population, that is $\delta_h^s(t) \equiv \delta_h^y(t)$ and $\delta_c^s = \delta_c^y$. The recover rate and disease-induced death rate for the confirmed cases are γ_h, γ_c and α_h, α_c , respectively. Definitions of all the parameters involved in the model are listed in Table 1.

The effective reproduction numbers for Hubei and regions outside Hubei can be calculated without considering the mobility of population between these two patches. As the model structures for both patches are identical, in the following, only the detailed derivation procedure of the effective reproduction number for Hubei patch is given. We firstly calculate the basic reproduction number when all the involved parameters are constants by using the next generation matrix method (Van and Watmough, 2002;

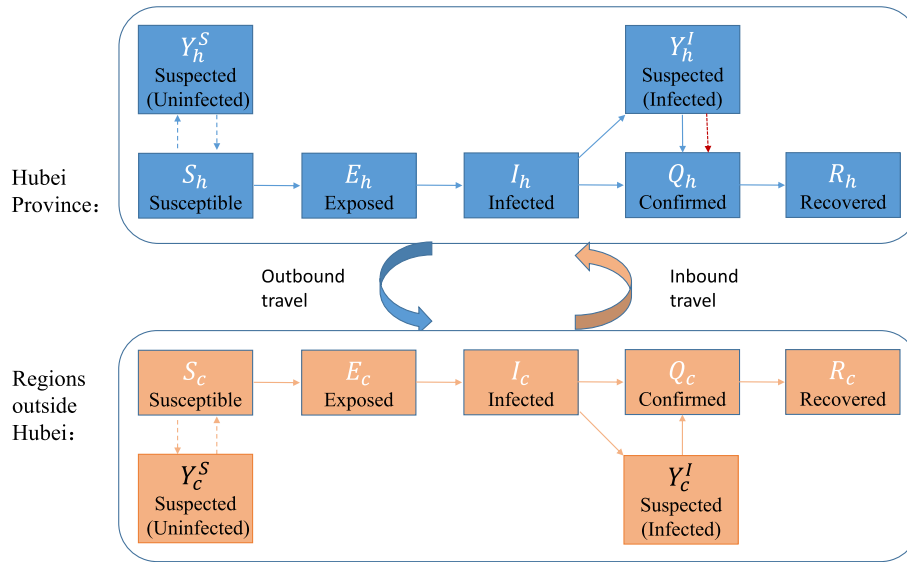


Fig. 1. The flow chart of the model. The red dotted line from suspected and infected class to confirmed class in Hubei patch denotes the extra confirmation rate after Feb 8th, 2020 in Hubei province.

Table 1
Parameter and initial values.

Parameter or Initial values	Definitions	Mean value		Source
		Hubei	Other regions	
$\beta_{c_h}(t)$ ($\beta_{c_c}(t)$)	Transmission coefficient	-	-	see text
β	Transmission probability per contact	-	-	see text
$c_h^0(c_c^0)$	Initial contact rate	-	-	see text
$c_h^l(c_c^l)$	Smallest contact rate	-	-	see text
$\beta_h^0(\beta_c^0)$	Initial transmission rate	0.7182	0.9202	Estimated
$\beta_h^l(\beta_c^l)$	Smallest transmission rate	0.0021	0.0021	Estimated
$r_h(r_c)$	Exponential decreasing rate of contact rate	0.1609	0.2377	Estimated
$1/\sigma$	Latent period	4.2	4.2	(Sanche et al., 2020)
m	Suspected rate for the susceptibles	$5.9857e-07$	$5.9857e-07$	Estimated
q	Confirmation proportion immediately after diagnosed	0.0928	0.0928	Estimated
$\delta_h^l(\delta_c^l)$	Diagnosis rate	0.2001	0.2820	Estimated
$\delta_h^y(t)(\delta_c^y)$	Confirmation rate from suspected and infected class	-	0.3005	Estimated
$\delta_h^{y_0}$	Initial confirmation rate from suspected and infected class	0.1391	-	Estimated
$\delta_h^{y_1}$	Extra confirmation rate from suspected and infected class	0.3104	-	Estimated
$\delta_h^s(t)(\delta_c^s)$	Exclusion rate from suspected but uninfected class	$\delta_h^y(t)$	δ_c^y	Estimated
$\gamma_h(\gamma_c)$	Recover rate	1/11.5	1/11.5	(Sanche et al., 2020)
$\alpha_h(\alpha_c)$	Disease induced death rate	0.0048	$8.7240e-04$	Estimated
$r_i(t)$	move in mobility rate	variable	variable	see text
$r_e(t)$	move out mobility rate	variable	variable	see text
$S_h(0)(S_c(0))$	Initial Susceptibles	$5.9170e+07$	$1.3362e+09$	(National Bureau of Statistics of China, 2019)
$E_h(0)(E_c(0))$	Initial latent population	84.9992	0	Estimated
$I_h(0)(I_c(0))$	Initial infectious population	104	0	(Epidemiology Working Group for NCIP Epidemic Response, 2020)
$Y_h^l(0)(Y_c^l(0))$	Initial suspected and infected population	0	0	Data
$Y_h^s(0)(Y_c^s(0))$	Initial suspected but uninfected population	0	0	Data
$Q_h(0)(Q_c(0))$	Initial confirmed cases	27	0	Data
$R_h(0)(R_c(0))$	Initial recovered cases	0	0	Data

Diekmann et al., 2010). The linearized infection subsystem for Hubei patch is

$$\begin{aligned} \frac{dE_h}{dt} &= \beta C_h I_h - \sigma E_h, \\ \frac{dI_h}{dt} &= \sigma E_h - \delta_h^l I_h, \\ \frac{dY_h^l}{dt} &= \delta_h^l (1 - q) I_h - \delta_h^y Y_h^l, \\ \frac{dQ_h}{dt} &= \delta_h^l q I_h + \delta_h^y Y_h^l - \gamma_h Q_h - \alpha_h Q_h. \end{aligned} \tag{6}$$

Thus, the transmission and transition matrix can be given as

$$F = \begin{pmatrix} 0 & \beta C_h & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}, V = \begin{pmatrix} \sigma & 0 & 0 & 0 \\ -\sigma & \delta_h^l & 0 & 0 \\ 0 & -\delta_h^l (1 - q) & \delta_h^y & 0 \\ 0 & -\delta_h^l q & -\delta_h^y & \gamma_h + \alpha_h \end{pmatrix}. \tag{7}$$

The basic reproduction number is the dominant eigenvalue of matrix FV^{-1} ,

$$\rho(FV^{-1}) = \frac{\beta C_h}{\delta_h^l}.$$

Thus, the effective reproduction number for Hubei patch and regions outside Hubei patch are

$$R_t = \begin{cases} \frac{\beta C_h(t)}{\delta_h^l}, & \text{Hubei province,} \\ \frac{\beta C_c(t)}{\delta_c^l}, & \text{Regions outside Hubei.} \end{cases} \tag{8}$$

2.2. The data

COVID-19 reported data. The data is collected from the website of National Health Commission of the People’s Republic of China (National Health Commission of the People’s Republic of China, 2020) and Health Commission of Hubei Province (Health Commission of Hubei Province, 2020), on which the number of daily new/cumulative cases and new/cumulative deaths for both Hubei province and Mainland China are reported every day from Jan 11th, 2020. By which we can calculate the number of such cases for regions outside Hubei easily. Since there are no new cases reported from Jan 11th to 15th, the data from Jan 16th are used in this article. The number of daily reported new confirmed cases and daily new deaths for Hubei and regions outside Hubei from Jan 16th to Feb 21st are described in Fig. 2 (A) and (B). Meanwhile, the number of existing suspected cases in Hubei province from Feb 8th to Feb 21st are collected, which is illustrated in Fig. 2 (C). The number of daily new suspected cases can also be obtained for mainland China from Jan 22nd, as shown in Fig. 2 (D).

Mobility data We collect the mobility index between Wuhan and other regions except for Wuhan from Baidu Migration (Baidu, 2020), Fig. 3(A) shows the mobility index between Wuhan and other regions from Jan 1st to Jan 23rd. Fig. 3(B) illustrates the proportions of within-province travel among the total outbound and inbound travel of Wuhan.

2.3. Parameters and initial values

We firstly determine some parameter and initial values by references and reported data, then estimate the remaining parameters and initial values by using Least Square Method. So as to avoid the temporal autocorrelations in the cumulative data (King et al., 2015), the daily new reported cases, deaths in Hubei and regions outside Hubei, the existing suspected cases in Hubei province from Feb 8th to Feb 21st, and the daily new suspected cases in mainland China are used to estimate the unknown parameters.

Since most of the infectious cases before Dec 31st, 2019 are linked to Huanan market (Li et al., 2020), we consider the disease spreading after Dec 31st, 2019. Thus, the initial value for each class should be the corresponding value on Dec 31st, 2019. According to the reported data, we can determine the initial values for the suspected class, confirmed class and recovered class for Hubei province. The Epidemiology Working Group for NCIP Epidemic Response of Chinese CDC (Epidemiology Working Group for NCIP Epidemic Response, 2020) published that 104 cases are symptomatic before Dec 31st, 2019, that is $I_h(0) = 104$. Meanwhile, the initial values for all the classes other than the susceptible class in regions outside Hubei should be very small, thus are assumed to be 0. The initial values for susceptible classes for Hubei and regions outside Hubei can be regard as the total population in Hubei and regions outside Hubei, respectively, which are obtained from China Statistical Yearbook (National Bureau of Statistics of China, 2019). The mean duration of the latent period is determined according to the estimation by Sanche et al. (Sanche et al., 2020), i.e. $\sigma = 1/4.2$. Sanche et al. (Sanche et al., 2020) also estimated that the duration from initial hospital admittance to discharge is 11.5 days, thus the recovery rates are $\gamma_h = 1/11.5, \gamma_c = 1/11.5$. As strong correlations exist, it is difficult to estimate the transmission probability per contact and the contact rate simultaneously, thus we estimate the transmission rates $\beta_h^0, \beta_h^b, \beta_c^0, \beta_c^b$ instead.

By the mobility data we can calculate the number of travelers between Wuhan and regions outside Hubei (Sanche et al., 2020). The mobility rate for people in latent and infectious class between Hubei and regions outside Hubei is calculated according to the mobility data of Wuhan. The reason is described as follows: 1, Wuhan is the capital of Hubei province and is also the transportation hub of China, most of the travel between Hubei and regions outside Hubei are in fact the travel between Wuhan and regions outside Hubei; 2, most infected cases are located in Wuhan before Jan 23rd, thus the travel between other cities in Hubei and regions outside Hubei has little effect on the disease transmission from Hubei to regions outside Hubei, especially for the importation of infected cases of regions outside Hubei. We calculate the outbound and inbound mobility rate at time t as $r_e(t) = \frac{m_e(t)}{N_1}$, and $r_i(t) = \frac{m_i(t)}{N_2}$, where $m_e(t)$ and $m_i(t)$ are the number of persons move out from Wuhan and move into Wuhan from regions outside Hubei, and N_1 and N_2 are the total population in Wuhan city and regions outside Hubei, respectively. As Wuhan and nearby cities in Hubei province are quarantined successively from Jan 23rd, we do not consider the population mobility between Hubei and regions outside Hubei after Jan 23rd. Considering the fact that almost the same number of susceptibles move into or move out from Hubei every day, thus has little effect on the number of susceptibles in Hubei and regions outside Hubei, we ignore the mobility between susceptibles in Hubei and regions outside Hubei.

2.4. Simulations

We implement simulations to study the effect or work resumption on the epidemic of Hubei and regions outside Hubei, and the effect of time for lifting the lockdown in Hubei on the epidemic of regions outside Hubei. Work resumption will inevitably lead to the increase of contact rate, but the increase of effective contact rate (i.e. the contact that can lead to infection) could be controlled at a certain low level by preventive measures. Therefore, we suppose that the contact rate will increase to different levels after work resumption, then investigate the work resumption time on the epidemic of Hubei province. Similarly, we study the work resumption time on the epidemic of regions outside Hubei.

To study the effect of lifting the lockdown in Hubei on the epidemic of regions outside Hubei, we determine the mobility rate of

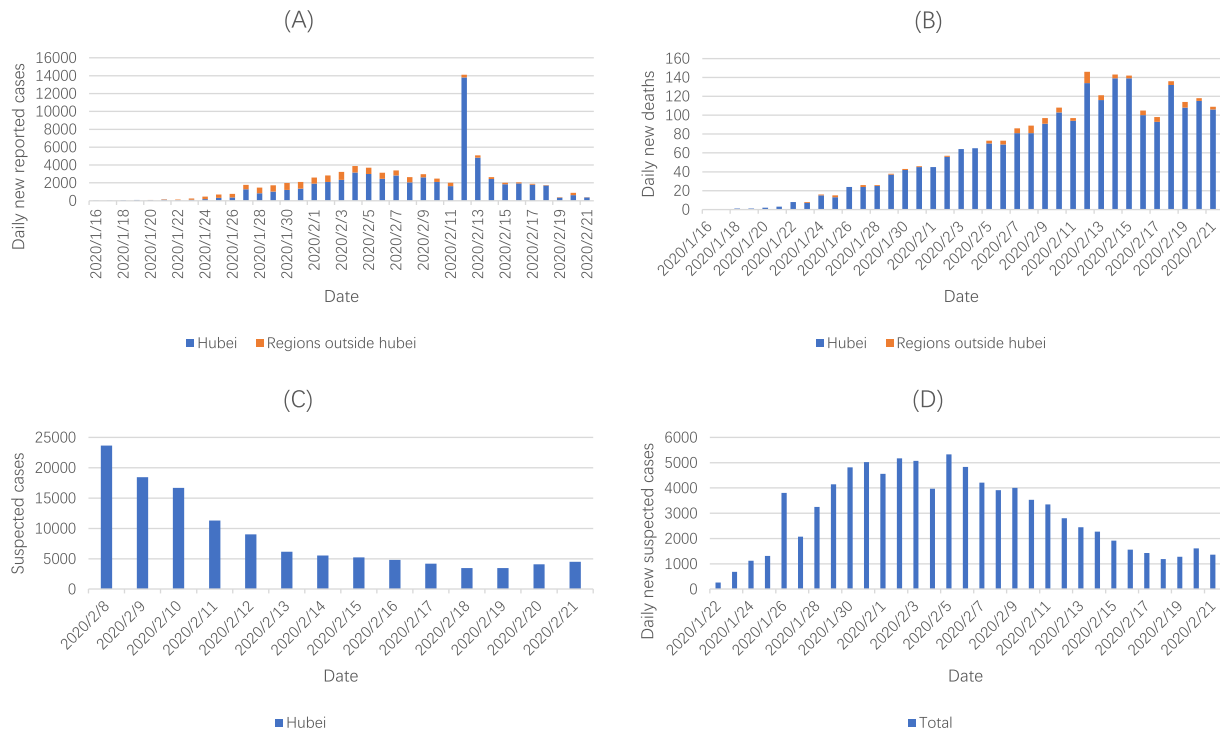


Fig. 2. Daily data for Hubei and regions outside Hubei. (A) new reported cases, (B) new deaths, (C) existing suspected cases in Hubei province, (D) new suspected cases.

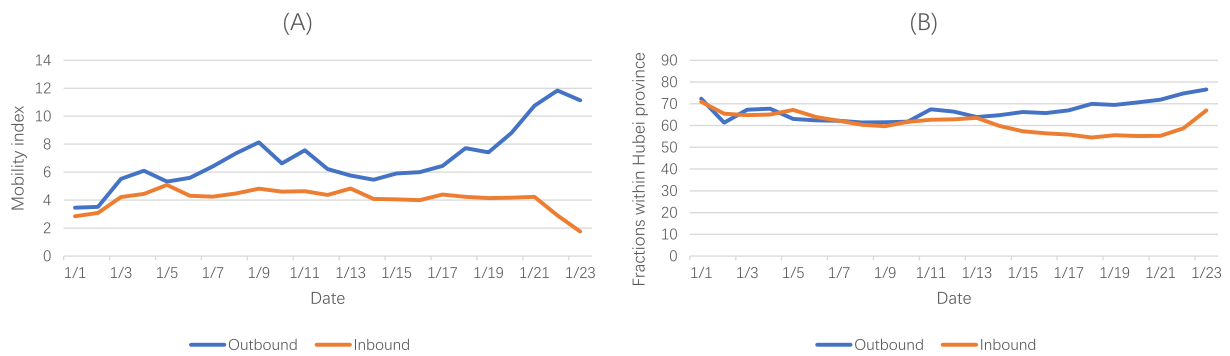


Fig. 3. Mobility indices from and to Wuhan city. (A) the mobility index. (B) the proportion of mobility within Hubei province.

the population between Hubei and regions outside Hubei according to the mean mobility rate before the Chinese new year. As *Chunyun* begins at Jan 10th, 2020, the daily number of people move out from Hubei in the first 14 days after lifting the lockdown is same to the mean daily number of people move into Hubei 14 days before the Jan 23rd, i.e. Jan 10th to Jan 23rd during *Chunyun*. From the 15th day after lifting the lockdown, the daily number of people move out from Hubei is the same with those move in Hubei before Jan 10th, 2020. Also, we study the effect of lifting the lockdown in Hubei on the epidemic of regions outside Hubei with different contact rate levels.

We utilized Matlab R2019 b for windows to implement the parameter estimation as well as the numerical simulations.

3. Results

The data fitting results are illustrated in Fig. 4, where (A), (B) and (C) describe the results for daily new reported cases, deaths and existing suspected cases in Hubei province, (D), (E) show the

results for daily new reported cases and deaths in regions outside Hubei, and (F) describe the daily new suspected cases in mainland China. The estimated parameter values and the initial values of the model are listed in Table 1. As shown in Fig. 4, the model fits the real reported data well. Based on the estimation results, the effective reproduction numbers for Hubei and regions outside Hubei can be calculated, which are described in Fig. 5. The basic reproduction number (i.e. the effective reproduction number before Jan 23rd, 2020) for Hubei and regions outside Hubei are 3.59 and 3.26. The high value of the reproduction number indicates that the COVID-19 have relatively strong infectivity. Note that the effective reproduction numbers decrease quickly after Jan 23rd with strengthening prevention and control strategies, and they drop below 1 on Jan 31st and Jan 28th for Hubei and regions outside Hubei, respectively. Our estimation and model fitting results are verified by comparing the predicated cumulative number of cases with the real data, as shown in Fig. 6. It is predicated that the epidemic may be almost controlled in mid- March, and the final accumulative number of cases in Hubei and regions outside Hubei will be about 68,500 cases and 13,900 cases. After verifying our model

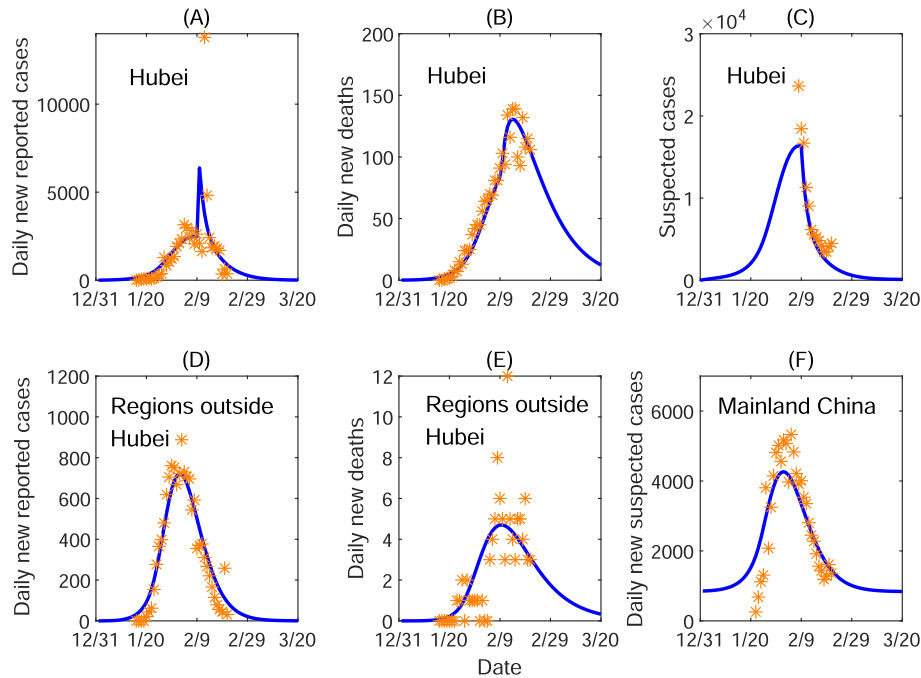


Fig. 4. Data fitting results. (A) daily new reported cases in Hubei province, (B) daily new deaths in Hubei province, (C) existing suspected cases in Hubei province, (D) daily new reported cases in regions outside Hubei, (E) daily new deaths in regions outside Hubei, (F) daily new suspected cases in mainland China. The orange stars illustrate the real data, the blue curves show the model predicting results.

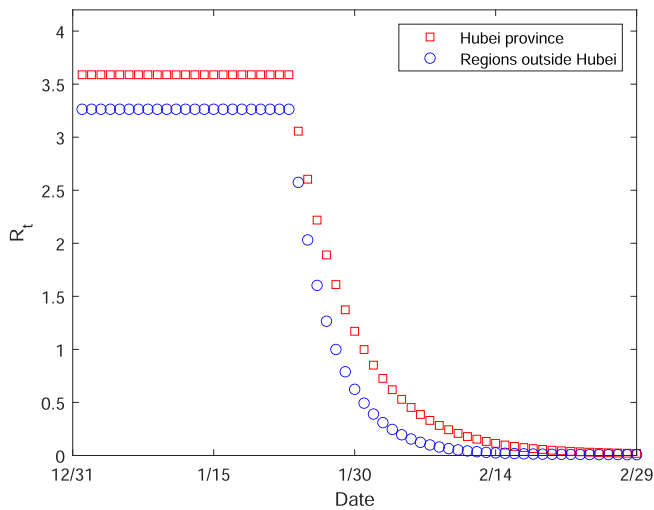


Fig. 5. The effective reproduction number in Hubei and regions outside Hubei.

estimation we can also estimate the epidemic before Jan 23rd 2020 when the novel coronavirus is hardly known and many infections could not be confirmed. It was estimated that about 818 cases in regions outside Hubei, either in the latent or infected classes, were imported from Hubei province before Jan 23rd, 2020.

To investigate the effect of work resumption on epidemic, we initially consider variation in contact rate within each patch (Hubei province or regions outside Hubei as decoupled patch) on the number of daily new infectious cases. Fig. 7 shows the effect of work resumption in Hubei province, thus the variation in contact rate within Hubei patch. Fig. 7 (A) illustrates the result of no work resumption, (B), (C) and (D) describe the results if the contact rate becomes 5%, 10%, 20% of the level before Jan 23rd, 2020. While in each sub-figure, dark, cyan, red, green and blue curve denotes that the work resumption begins on Mar 2nd, Mar 9th, Mar 16th, Mar

23rd and no work resumption, respectively. From Fig. 7 (B) we can get that if the contact rate becomes 5% of the level before Jan 23rd, all the curves do not show significant increase. That is, if the contact rate can keep at a relative low level, work resumption has little effect on the epidemic in Hubei province as long as the time of work resumption is later than March 2nd. If the contact rate becomes 10% of the level before Jan 23rd, as shown in Fig. 7 (C), the dark curve and cyan curves increase quickly and then decrease quickly. While if the contact rate becomes 20% of the level before Jan 23rd, as shown in Fig. 7 (D), the dark and cyan curves increase significantly to much higher levels compared with that of Fig. 7 (C), and the red and green curves increase slightly. But all the curves decrease very slowly in Fig. 7 (D). Fig. 7 (C) and (D) indicate that if the contact rate increase to a higher level after work resumption, there may be another outbreak with both the scale and duration of the outbreak increasing with the contact rate level. In this situation, work resumption should be postpone to Mar 16th or even more later.

Similarly, Fig. 8 describes the effect of work resumption on epidemic in regions outside Hubei, i.e. the variation in contact rate within regions outside Hubei patch. Fig. 8 (A) illustrates the result of no work resumption, (B), (C) and (D) describe the results if the contact rate becomes 5%, 10%, 20% of the level before Jan 23rd. All the curves show similar trends to that of Fig. 7. But the difference is that the amount of daily new infectious cases is sufficiently small, i.e. less than 2 cases, compared with that of Fig. 7, whose daily new infectious cases may increase to more than 40 cases. This indicates that the epidemic in regions outside Hubei has already been controlled at a relatively low level after Mar 2nd, thus work resumption has very little effect on the epidemic in regions outside Hubei if the contact rate could be kept at less than 20% of the level before Jan 23rd.

To examine the impact of lifting the lockdown in Hubei province, we consider the mobility of population between Hubei and regions outside Hubei. At the meantime, the contact rate also increases to different levels after lifting the lockdown in Hubei.

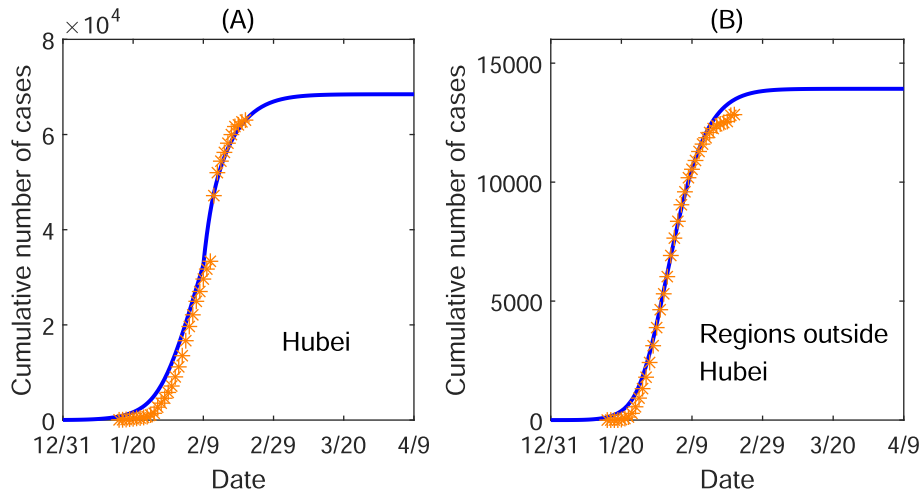


Fig. 6. Comparison between model prediction with real reported data. (A) cumulative number of cases in Hubei province, (B) cumulative number of cases in regions outside Hubei province. The orange stars illustrate the real data, the blue curves show the model predicting results.

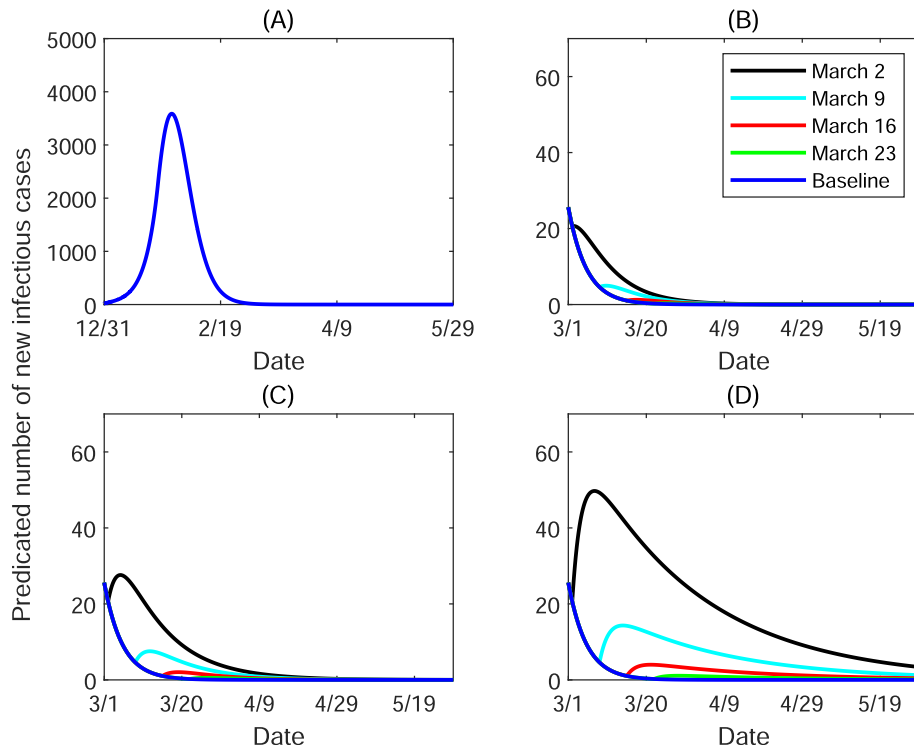


Fig. 7. Effect of work resumption time on the epidemic in Hubei province. (A) shows the result of no work resumption. (B)–(D) show the effect of work resumption. After work resumption, it is assumed that the contact rate becomes (B) 5%, (C) 10%, (D) 20% of the level before Jan 23, 2020. The work resumption time are Mar 2, Mar 9, Mar 16 and Mar 23, which are illustrated in black, cyan, red and green curve, respectively.

We then check the variation of the new infectious cases with the variation of the beginning time of lifting the lockdown in Hubei. Lifting the lockdown in Hubei has little effect on the epidemic of Hubei province, as fewer infected individuals may move into Hubei compared with that move out from Hubei. Here, we mainly focus on the effect of lifting the lockdown in Hubei on the epidemic in regions outside Hubei. The results are shown in Fig. 9 with (A) describing the results of continuing the lockdown in Hubei and no variation in contact rate, (B), (C) and (D) describing the results if the contact rate after lifting the lockdown in Hubei in both patches increasing to 5%, 10% and 20% of the level before Jan 23rd. Dark, cyan, red, green and blue curves in each sub-figure

denote that lockdown in Hubei is lifted on Mar 2nd, Mar 9th, Mar 16th, Mar 23rd and lockdown continues at Hubei, respectively. From Fig. 9 (B)–(D) we can get that all the curves will increase slightly, with the peak of curves decreasing with the postpone of lifting the lockdown in Hubei. Furthermore, the number of new infectious cases increases with the increasing of contact rate after lifting the lockdown in Hubei, which indicates that keeping relatively low contact rate is crucial to avoid a second outbreak of the epidemic in regions outside Hubei after lifting the lockdown in Hubei province. Comparing Fig. 9 with Fig. 8, we can get that though lifting the lockdown in Hubei in March do affect the epidemic in regions outside Hubei, showing as more new infectious

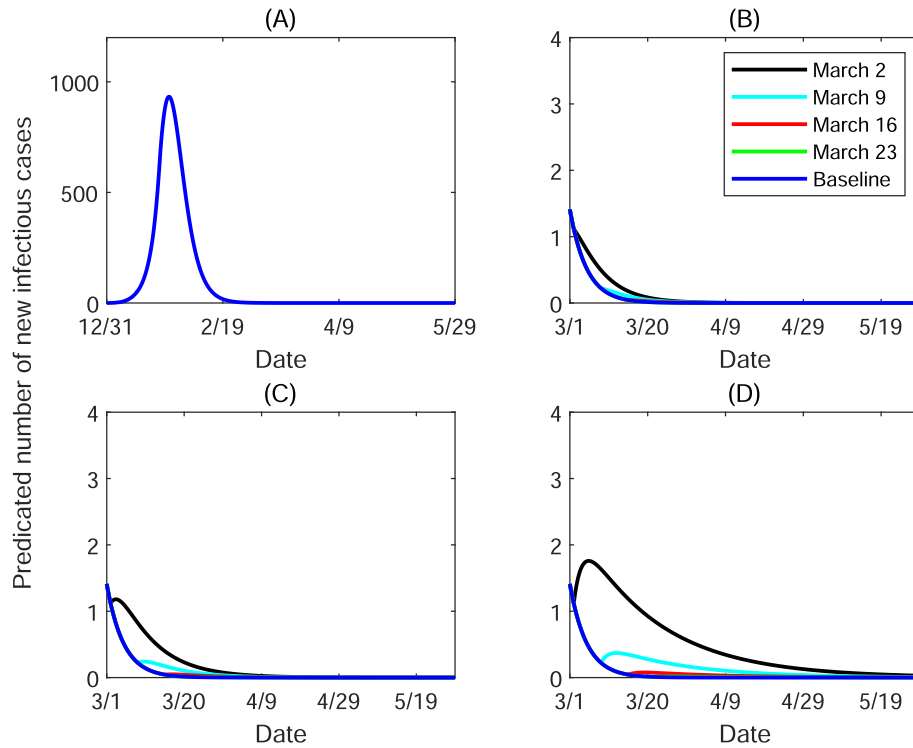


Fig. 8. Effect of work resumption time on the epidemic in regions outside Hubei. (A) shows the result of no work resumption. (B)–(D) show the effect of work resumption. After work resumption, it is assumed that the contact rate becomes (B) 5%, (C) 10%, (D) 20% of the level before Jan 23, 2020. The work resumption time are Mar 2, Mar 9, Mar 16 and Mar 23, which are illustrated in black, cyan, red and green curve, respectively.

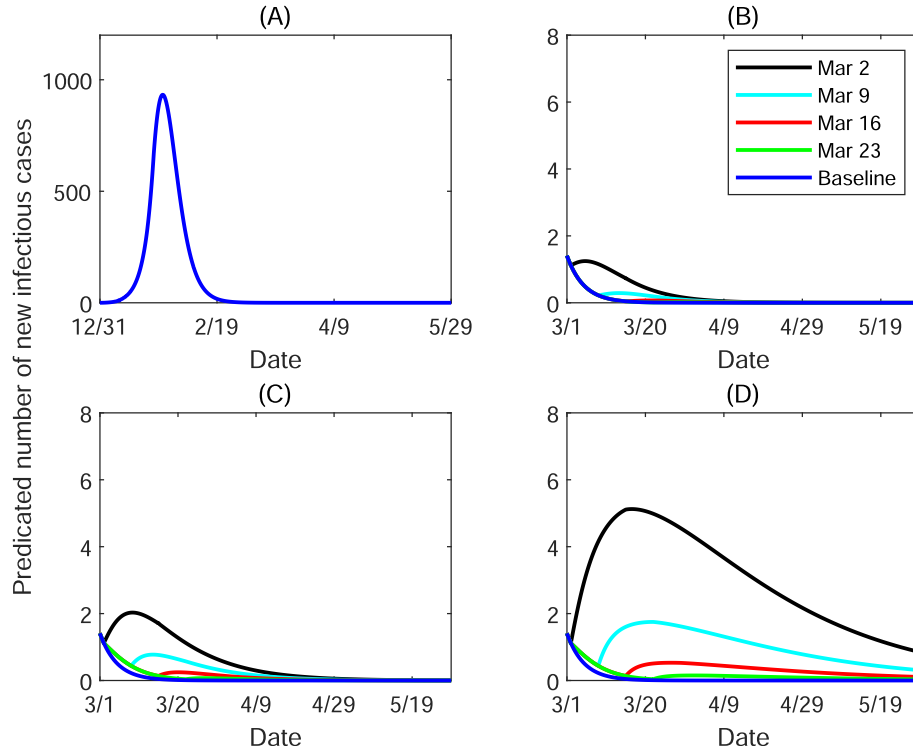


Fig. 9. Effect of lifting the lockdown in Hubei on the epidemic in regions outside Hubei. (A) shows the results of continuing lockdown measure. (B)–(D) show the results for lifting the lockdown in Hubei. After lifting the lockdown in Hubei, it is assumed that the contact rate becomes (B) 5%, (C) 10%, (D) 20% of the level before Jan 23, 2020. The time of lifting the lockdown in Hubei are Mar 2, Mar 9, Mar 16 and Mar 23, which are illustrated in black, cyan, red and green curve, respectively.

cases after lifting the lockdown, the daily number of new infections can be controlled at low level if the contact rate could be kept

below 20% of the level before Jan 23rd. If we intuitively choose the daily number of new infectious cases being no more than 5

Table 2
Ranges of the parameters for sensitivity analysis.

Parameter	Ranges	Parameter	Ranges
m	[1e-8, 1e-6]	q	[0.05, 0.5]
β_h^0	[0.6, 1]	β_c^0	[0.6, 1]
β_c^0	[1e-4, 0.1]	β_h^b	[1e-4, 0.1]
r_h	[0.05, 0.5]	r_c	[0.05, 0.5]
$\delta_h^{y_0}$	[0.1, 0.4]	δ_c^y	[0.1, 1]
$\delta_h^{y_b}$	[0.1, 0.6]	-	-
δ_h^l	[0.125, 0.6]	δ_c^l	[0.125, 0.6]
α_h	[1e-4, 1e-2]	α_c	[1e-4, 1e-2]

cases as a criterion, lockdown in Hubei should lift after Mar 9th if the contact rate could be kept at 20% of the level before Jan 23rd. In other words, if the contact rate can be kept at no more than 20% of the level before Jan 23rd, lift the lockdown in Hubei after Mar 9th will not induce large scale second outbreak in regions outside Hubei.

As there are lots of unknown parameters involved in the model, variations of the parameters may affect the trend of the epidemic greatly. To study the sensitivity of the unknown parameters on the model prediction results, we conduct Latin Hypercube Sampling (LHS) and Partial Rank Correlation Coefficients (PRCCs) analysis. All the parameter values are sampled from uniform distributions with the ranges given by experience, which are listed in Table 2. The results of the sensitivity analysis are illustrated in Fig. 10, where (A) and (B) denote the variations of the base-10 logarithm of the cumulative number of confirmed cases in Hubei and regions outside Hubei, respectively. From Figure (A) and (B) we can get that the cumulative number of cases both in Hubei and regions outside Hubei will reach the steady stage before early April, and the base-10 logarithm of the final sizes vary greatly from 0 to 6 and 0 to 4 for Hubei and regions outside Hubei, respectively. Fig. 10 (C) and (D) illustrate the PRCCs for the dependence of cumulative number of confirmed cases in April 1st in Hubei and

regions outside Hubei on each parameter. As shown in Fig. 10 (C), the initial and smallest transmission rates β_h^0, β_h^b , exponential decreasing rate of the contact rate r_h , diagnosis rate δ_h^l and disease induced death rate α_h affect the epidemic in Hubei province greatly, while all the parameters involved in regions outside Hubei patch has relatively little effect on the epidemic in Hubei province. As shown in Fig. 10 (C), the transmission rates (β_h^0, β_h^b) and disease related death rate (α_h) have positive effect, while the decreasing rate of the contact rate (r_h) and diagnosis rate (δ_h^l) have negative effect on the epidemic, which indicates the importance of reducing the transmission rates and disease related death rate, and increasing the diagnosis rate for disease control. Similar results are obtained for the epidemic in regions outside Hubei, as shown in Fig. 10 (D), the initial and smallest transmission rates β_c^0, β_c^b , exponential decreasing rate of the contact rate r_c , diagnosis rate δ_c^l and disease induced death rate α_c within regions outside Hubei patch have great effects on the epidemic. It needs to be noticed that the initial transmission rate β_h^0 and diagnosis rate δ_h^l in Hubei patch also affect the epidemic in regions outside Hubei greatly. This happens due to the fact that lots of infected individuals move out from Hubei to regions outside Hubei before Jan 23rd, the epidemic in Hubei before Jan 23rd plays an important role in the disease transmission in regions outside Hubei.

4. Discussion

It is essential to examine the early epidemic situation of COVID-19 by using late and relatively accurate reported data. This can not only provide the evaluation of the effectiveness and timeliness of public health intervention strategies but also predict the transmission risk of population flow due to returning back to work/study. A two-patchy model, which describes the mobility of population between Hubei and regions outside Hubei in mainland China, is formulated to estimate the epidemic in Hubei province and try to

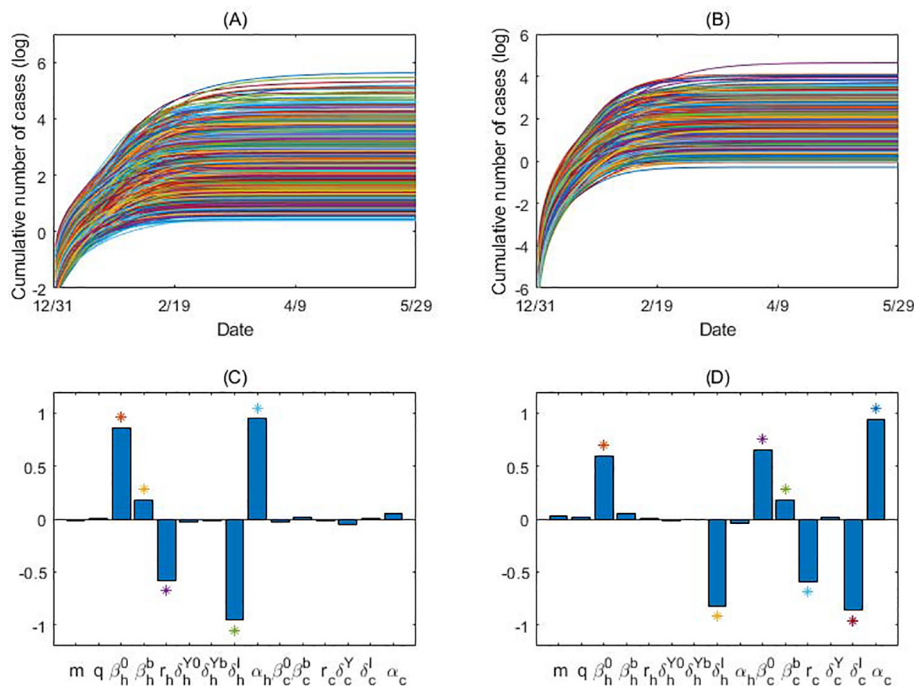


Fig. 10. Sensitivity analysis. (A) variations of the logarithm cumulative number of confirmed cases in Hubei province. (B) variations of the logarithm cumulative number of confirmed cases in regions outside Hubei. (C) Partial Rank Correlation Coefficients (PRCC) for the dependence of cumulative number of cases in April 1st in Hubei province on each parameter. (D) Partial Rank Correlation Coefficients (PRCC) for the dependence of cumulative number of cases in April 1st in regions outside Hubei on each parameter.

investigate the time of work resumption and lifting the lockdown measure of Hubei province. Similar model approach for considering population movement between Hubei and regions outside Hubei can be found in former study (Sanche et al., 2020), in which the authors investigated the rapid spread of COVID-19 in early stages. Our model reflects the effect of time varying interventions on the transmission rate, thus may characterize the epidemic more precisely. The model is parameterized by fitting 6 columns of reported data from Jan 16th to Feb 21st 2020 including daily new reported cases, new deaths and etc for Hubei province and regions outside Hubei. As the number of daily reported cases begin to include the clinically diagnosed cases on Feb 12nd, 2020, both the number of new and cumulative reported cases have big jumps on that day. We do not consider this changing in the model in this article, thus it is difficult to fit the number of new/cumulative reported cases both before and after Feb 12nd well. To predict the epidemic accurately, more efforts are made to fit the epidemic after Feb 12nd well, thus the estimations before Feb 12nd are slightly larger than the reported data. Especially, the estimated epidemic situation in Hubei before Jan 23rd, 2020 is more serious than the reported data indicated, as shown in Fig. 4 (A) and Fig. 6 (A). The effective reproduction numbers for both Hubei and regions outside Hubei are very high before Jan 23rd, and decrease quickly after Jan 23rd, and become less than 1 after Jan 31st and Jan 2th. It is estimated that the reproduction number before Jan 23rd is as high as 3.59 and 3.26 for Hubei and regions outside Hubei, respectively, which follow the ranges obtained by former researchers (Wu et al., 2020; Cao et al., 2020; Tang et al., 2020; Shen et al., 2020; Li et al., 2020; Riou and Althaus, 2020; Read et al., 2020; Zhao et al., 2020; Liu et al., 2020). It is estimated that the epidemic in Hubei and regions outside Hubei may be almost controlled at early- to mid-March, the final size of the epidemic in Hubei and regions outside Hubei are estimated to be about 68,500 cases and 13,900 cases, and about 818 cases in regions outside Hubei are exported from Hubei before Jan 23rd.

We investigate the impact of the work resumption and lifting the lockdown in Hubei province on the potential second outbreak. We consider two scenarios: 1) changing contact rates within each patch at different time points, and 2) different time of lifting the lockdown in Hubei with various contact rates. Main results can be concluded as follows. In Hubei province, if the strict interventions are implemented after work resumption, i.e. keep the contact rate at relatively low level, work resumption after March 2nd has little effect on the epidemic of Hubei province. However, if the contact rate increases to higher levels after work resumption, another outbreak may appear, and the scale and duration of the outbreak increases with the contact rate level. In regions outside Hubei province, work resumption may increase the daily number of new infectious cases but at a relative low level if the intervention measures implemented suitably after work resumption. Lifting the lockdown in Hubei province in March may cause an increase of the new infectious cases in regions outside Hubei. But the contact rate after lifting the lockdown plays a vital role on the scale of second outbreak. If relatively strict interventions are implemented after lifting the lockdown, the daily number of new infectious cases can be controlled to less than 5 cases if lift the lockdown after Mar 9th. In conclusion, strict interventions for maintaining the contact rate at a relatively low level is critical to avoid a second outbreak of the epidemic after work resumption or lifting the lockdown in Hubei province.

As many unknown parameters involved in the model, sensitivity analysis is implemented to see the variation of the epidemic curve when parameters vary, which further indicates the importance for reducing the transmission rate and increasing the diagnosis rate on the disease control. Nevertheless, there are also limitations for this study. We do not fit the data for daily new

cured cases but use the recovery rate estimated by former study (Sanche et al., 2020), as the cure rates in different regions and stages, and for different age groups change a lot, it is difficult to fit the daily data for cured cases and deaths simultaneously. Furthermore, it is assumed that all the infected cases will not transmit the disease after diagnosis, no matter of immediate confirmation with COVID-19 or moving to the suspected class, thus the cure rate in fact has little effect on the disease transmission.

CRediT authorship contribution statement

Xiaodan Sun: Methodology, Software, Investigation, Formal analysis, Writing - original draft, Writing - review & editing. **Yanni Xiao:** Conceptualization, Methodology, Supervision, Writing - review & editing. **Xiangting Ji:** Methodology, Investigation.

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