The effectiveness of quarantine and isolation determine the trend of the COVID-19 epidemics in the final phase of the current outbreak in China

Biao Tang, Fan Xia, Sanyi Tang, Nicola Luigi Bragazzi, Qian Li, Xiaodan Sun, Juhua Liang, Yanni Xiao, Jianhong Wu

PII: S1201-9712(20)30137-5

DOI: https://doi.org/10.1016/j.ijid.2020.03.018

Reference: IJID 4024

To appear in: International Journal of Infectious Diseases

Received Date: 18 February 2020

Revised Date: 4 March 2020

Accepted Date: 6 March 2020

Please cite this article as: Tang B, Xia F, Tang S, Bragazzi NL, Li Q, Sun X, Liang J, Xiao Y, Wu J, The effectiveness of quarantine and isolation determine the trend of the COVID-19 epidemics in the final phase of the current outbreak in China, *International Journal of Infectious Diseases* (2020), doi: https://doi.org/10.1016/j.ijid.2020.03.018

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2019 Published by Elsevier.



# The effectiveness of quarantine and isolation determine the trend of the COVID-19 epidemics in the final phase of the current outbreak in China

Biao Tang <sup>1,2</sup>, Fan Xia <sup>1,4</sup>, Sanyi Tang <sup>3</sup>, Nicola Luigi Bragazzi <sup>2</sup>, Qian Li <sup>2,4</sup>, Xiaodan Sun <sup>1,4</sup>, Juhua Liang <sup>3</sup>, Yanni Xiao <sup>1,4,\*</sup> and Jianhong Wu <sup>1,2,5,\*</sup>

- <sup>1</sup> The Interdisplinary Research Center for Mathematics and Life Sciences, Xi'an Jiaotong University, Xi'an 710049, People's Republic of China
- <sup>2</sup> Laboratory for Industrial and Applied Mathematics, Department of Mathematics and Statistics, York University, Toronto, Ontario, Canada, M3J 1P3
- <sup>3</sup> School of Mathematics and Information Science, Shaanxi Normal University, Xi'an, 710119, People's Republic of China
- School of Mathematics and Statistics, Xi'an Jiaotong University, Xi'an 710049, People's Republic of China
- Fields-CQAM Laboratory of Mathematics for Public Health, York University, Toronto, Ontario, Canada, M3J 1P3

The first four authors made the same contributions.

\* Correspondence: yxiao@mail.xjtu.edu.cn, wujh@yorku.ca

#### Highlights

 Since January 23<sup>rd</sup> 2020, stringent measures for controlling the novel coronavirus epidemics have been enforced and strengthened in mainland China.

- Most infected cases have been quarantined or put in suspected class, which has been ignored in existing models.
- Results of our model show that the trend of the epidemics mainly depends on quarantined and suspected cases.
- It is important to continue enhancing the quarantine and isolation strategy and improving the detection rate in mainland China.

#### **Summary**

**OBJECTIVES**: Since January 23<sup>rd</sup> 2020, stringent measures for controlling the novel coronavirus epidemics have been gradually enforced and strengthened in mainland China. The detection and diagnosis have been improved as well. However, the daily reported cases staying in a high level make the epidemics trend prediction difficult.

**METHODS**: Since the traditional SEIR model does not evaluate the effectiveness of control strategies, a novel model in line with the current epidemics process and control measures was proposed, utilizing multisource datasets including cumulative number of reported, death, quarantined and suspected cases.

**RESULTS**: Results show that the trend of the epidemics mainly depends on quarantined and suspected cases. The predicted cumulative numbers of quarantined and suspected cases nearly reached static states and their inflection points have already been achieved, with the epidemics peak coming soon. The estimated effective reproduction numbers using model-free and model-based methods are decreasing, as well as new infections, while new reported cases are increasing. Most infected cases have been quarantined or put in suspected class, which has been ignored in existing models.

**CONCLUSIONS**: The uncertainty analyses reveal that the epidemics is still uncertain and it is important to continue enhancing the quarantine and isolation strategy and improving the detection rate in mainland China.

Keywords: coronavirus; multi-source data; mathematical model; SEIR model

#### Introduction

Early identifying signature features of an outbreak can provide policy- and decision-makers with timely information to implement effective interventions.<sup>1,2</sup> Recently, a novel coronavirus (COVID-19) outbreak has occurred in Wuhan, Hubei, China, and has spread out to neighboring countries.<sup>3-5</sup>

During the early stages, the prediction of the COVID-19 epidemics by means of transmission dynamics models relies on the cumulative number of reported cases or the number of newly reported ones. The dynamical impact of the increasingly strong measures of the Chinese government has not been fully captured. Unprecedented interventions, including strict contact tracing, quarantine of entire towns/cities and travel restrictions, have added and will add further uncertainty to the analysis of the epidemics.

When enforcing such measures to a sample of 100 people, at least 9 of these may be found infected. Nearly 50% of infected people are confirmed from suspected cases.<sup>6</sup> It is unfeasible to predict the impact of the COVID-19 epidemics without taking into account the effects of the

recently implemented measures. Estimates based on transmission dynamics models not including quarantined/suspected cases, as well as the cumulative reported cases from these compartments, cannot be used for informing public health policies.<sup>7</sup>

Since January 23<sup>rd</sup> 2020, after the implementation of the lock-down strategy in Wuhan, all other Chinese provinces have adopted similar measures. Nevertheless, the number of recently reported cases has increased faster than before, because of the incubation period of the virus, or the introduction of new screening/testing measures. Moreover, the diagnosis and treatment procedures have been simplified, and the detection effort has been strengthened.<sup>8</sup>

As such, the classical SEIR model cannot be used to depict and fit the data. The evolutionary trend of the epidemics depends on the strength of interventions, especially on the scale of quarantined and suspected populations. It is necessary to devise a dynamic model with suspected compartment incorporating prevention and control strategies to predict the trend of the COVID-19 epidemics based on multiple data sources and assess the efficacy of control strategies. We also incorporate the model-free method to estimate the effective number and to verify the declining trend of new infections.

#### **Methods**

#### Data

We obtained data of laboratory-confirmed COVID-19 cases in China from the "National Health Commission" of the People's Republic of China and the Hubei's "Health Commission". 9-11 Data information includes the newly reported cases, the cumulative number of reported confirmed cases,

the cumulative number of cured cases, the number of death cases, and the cumulative numbers of quarantined/suspected cases (Figure 1). The number of quarantined cases does not include the number of suspected cases although the suspected cases have been isolated. Except for Hubei, the mean duration of hospital stays was around 9 days, with the shortest hospitalization duration of 5 days (in Hainan) and the longest hospitalization duration of 12.75 days (in Guangdong). The duration of hospital stays in Hubei was around 20 days, because, on the one hand, more severe patients were found in Hubei, and on the other hand, Wuhan has set stricter discharge standards. In addition to the usual standards of two nucleic acid tests being negative within an interval of 24 hours, Wuhan requires 10-12 days more of observation in the hospital. Since the number of daily cases in hospital is not suitable to identify the model/estimate the parameters, we use cumulative data.

Data used in the present study is reported in Appendix 1.

#### The model

A deterministic SEIR model based on the clinical progression of the disease, epidemiological status of the individuals, and intervention measures was proposed (Figure 2). We stratify the populations as susceptible (S), exposed (E), infected (I), hospitalized (H) and recovered (R) compartments, and we further stratify the population to quarantined susceptible  $(S_q)$ , and quarantined suspected individuals (B). We extend our model structure, (P) including the quarantined suspected compartment, which consists of exposed infectious individuals resulting from contact tracing and individuals with common fever needing clinical medication.

By enforcing contact tracing, a proportion, q, of individuals exposed to the virus is quarantined, and can either move to the compartment B or  $S_q$ , depending on whether they are effectively infected or not, <sup>14,15</sup> while the other proportion, I-q, consists of individuals exposed to the virus who are missed from contact tracing and move to the exposed compartment E once effectively infected or stay in compartment S otherwise.

Let the transmission probability be  $\beta$  and the contact rate be c. Then, the quarantined individuals, if infected (or uninfected), move to the compartment B (or  $S_q$ ) at a rate of  $\beta cq$  (or  $(1-\beta)cq$ )). Those who are not quarantined, if infected, will move to the compartment E at a rate of  $\beta c(1-q)$ . Let constant m be the transition rate from susceptible class to the suspected compartment via general clinical medication due to fever or illness-like symptoms.

Data on suspected individuals and also most of confirmed cases come from this compartment. The suspected individuals leave this compartment at a rate of b, with a proportion, f, if has been confirmed to be infected by the COVID-19, going to the hospitalized compartment, whilst the other proportion, 1-f, has been proven to be not infected by the COVID-19 and goes back to the susceptible class once recovery (Table 1).

$$\begin{cases} S' = -\frac{\left(\beta c(t) + c(t)q(t)(1-\beta)\right)SI}{N} - mS + \lambda S_q + b(1-f)B, \\ E' = \frac{\beta c(t)(1-q(t))SI}{N} - \sigma E, \\ I' = \sigma E - \left(\delta_I(t) + \alpha + \gamma_I\right)I, \\ B' = \frac{\beta c(t)q(t)SI}{N} + mS - bB, \\ S_q' = \frac{(1-\beta)c(t)q(t)SI}{N} - \lambda S_q, \\ H' = \delta_I(t)I + bfB - (\alpha + \gamma_H)H, \\ R' = \gamma_I I + \gamma_H H. \end{cases}$$

The contact rate c(t) is a decreasing function with respect to time t:

# <u>Journal Pre-proof</u>

$$c(t) = (c_0 - c_b)e^{-r_1t} + c_b$$

where  $c_0$  denotes the contact rate on January 23<sup>rd</sup> 2020) with  $c(0) = c_0$ ,  $c_b$  denotes the minimum contact rate under the current control strategies with  $\lim_{t\to\infty} c(t) = c_b$ , where  $c_b < c_0$ ,  $r_1$  denotes the contact rate modeled as exponential decreasing rate, assuming that the contacts are decreasing gradually considering the implementation of interventions.

q(t) is an increasing function with respect to time t:

$$q(t) = (q_0 - q_m)e^{-r_2t} + q_m$$

where  $q_0$  is the initial quarantined rate of exposed individuals with  $q(0) = q_0$ ,  $q_m$  is the maximum quarantined rate under the current control strategies with  $\lim_{t\to\infty}q(t)=q_m$  and  $q_m>q_0$ , and  $q_0$ , and  $q_0$  is the quarantined rate modeled as exponential increasing rate. This function reflects the gradually enhanced contact tracing.

The transition rate  $\delta_I(t)$  is an increasing function with respect to time t, the period of diagnosis  $1/\delta_I(t)$  is a decreasing function of t:

$$\frac{1}{\delta_I(t)} = \left(\frac{1}{\delta_{I0}} - \frac{1}{\delta_{If}}\right) e^{-r_3 t} + \frac{1}{\delta_{If}},$$

where  $\delta_{I0}$  is the initial diagnose rate,  $\delta_{If}$  is the fastest diagnose rate, and  $r_3$  is the exponential decreasing rate of the detection period.  $\delta_I(0) = \delta_{I0}$  and  $\lim_{t\to\infty} \delta_I(t) = \delta_{If}$  with  $\delta_{If} > \delta_{I0}$ . Then, we define the effective reproduction number as

$$R(t) = \frac{\beta c(t)(1 - q(t))}{\delta_I(t) + \alpha + \gamma_I}.$$

#### Model-free estimation for $R_0$ and $R_t$

Taking one day as a time unit and assuming December  $31^{st}$  2019 to be the time start point, i.e., t = 0 let  $W_t^c$  and  $N_t^c$  be the number of confirmed cases at time t in Wuhan and in China,

respectively. Let  $W_t^o$  and  $N_t^o$  be the number of patients eventually confirmed and with illness onset at time t in Wuhan and in China. T represents the duration from onset to confirmation for a patient eventually confirmed with  $P_T$  as probability distribution.

For k different days  $t_1, \ldots, t_2(t_2 - t_1 + 1 = k)$ ,  $N_j^0$  is assumed to follow the Poisson distribution with mean  $\lambda_j$ , which is the parameter to be estimated, given the number of confirmed cases  $N_{s_1}^c, \ldots, N_{s_2}^c$  on days  $s_1, \ldots, s_2(s_2 - s_1 + 1 = m)$  and the probability  $p_{ij} = P(i - j \le i - j + 1)$  that a patient with illness onset on day j will be confirmed on day i. For each j,  $q_j = \sum_{i=max\{j,s_1\}}^{s_2} p_{ij}$  is positive, with at least a fraction of patients with illness onset on day j and confirmed during the period  $s_1, \ldots, s_2$ . Parameters  $(\lambda_{t_1}, \ldots, \lambda_{t_2})$  can be estimated by  $N_{s_1}^c, \ldots, N_{s_2}^c$  and  $p_{ij}$ through deconvolution method (the Richardson-Lucy iterative algorithm):  $^{16-18}$ 

$$N_i^{c(n)} = \sum_{j=t_1}^i p_{ij} \cdot \lambda_j^{(n)} \tag{1}$$

$$\lambda_j^{(n+1)} = \frac{\lambda_j^{(n)}}{q_j} \cdot \sum_{i=\max\{j,s_1\}}^{s_2} \frac{p_{ij} \cdot N_i^c}{N_i^{c(n)}}$$
 (2)

where  $N_i^{c(n)}$  and  $\lambda_j^{(n)}$  are fitted values of  $N_i^c$  and  $\lambda_j$  in the n<sup>th</sup> iteration respectively. We stop the iteration when the error of fitting

$$\chi^{2} = \frac{1}{m} \sum_{i=s_{1}}^{s_{2}} \frac{(N_{i}^{c(n)} - N_{i}^{c})^{2}}{N_{i}^{c(n)}}$$
(3)

gets small and the values of  $\ \lambda_{t_1}^{(n)},\ldots,\lambda_{t_2}^n$  are reasonable.

Because the method above requires at least a fraction of patients with illness onset on day j and confirmed during the period  $s_1, \ldots, s_2$ , we can determine the proper  $t_1$  and  $t_2$  such that  $q_i > 0$  for  $t_1 \le j \le t_2$  in terms of the distribution T.

 $N_j^0$  for  $j < t_1$  is estimated as follows: let  $T_0$  and  $T_c$  be the dates of a patient with illness onset and confirmed. Let  $W_t^{0|T_c < s}$  and  $N_t^{0|T_c < s}$  be the number of patients who are confirmed at

or before time S and with illness onset at time t in Wuhan and in China, and let  $P(T \le h|T_c = s)$  be the probability that a patient was confirmed at time s and h days after illness onset, which is the probability that a patient was confirmed at time s and with illness onset being the interval [s-h,s]. Let  $P(T \le h|T_0 = s)$  be the probability that a patient was confirmed h days after the illness onset on time s. Then

$$N_t^{0|T_c \le s} - W_t^{0|T_c \le s} = \sum_{i=0}^{s-t} (N_{t+i}^c - W_{t+i}^c) \cdot P(i \le T \le i+1|T_c = t+i) \tag{4}$$

$$N_t^{0|T_c \le s} = N_t^0 \cdot P(T \le s - t|T_0 = t) \tag{5}$$

We use equations (4) and (5) to estimate  $N_t^0$  for  $t \leq t_1$ . To estimate the daily number of cases with illness onset in the period December  $8^{\text{th}}$  2019-February  $2^{\text{nd}}$  2020 in China,  $\{N_t^o\}_{t=-23}^{33}$ , (Figure 1(B)), we performed two steps: 1) we have used the daily number of confirmed cases from January  $17^{\text{th}}$  2020 to February  $3^{\text{rd}}$  2020 in China  $\{N_t^c\}_{t=17}^{34}$  and the distribution  $P_T$  to estimate the daily number of patients with illness onset from January  $4^{\text{th}}$ -February  $2^{\text{nd}}$  2020  $\{N_t^o\}_{t=4}^{33}$ ; 2) we have used the daily number of confirmed cases before or on January  $2^{\text{nd}}$  2020 in China and in Wuhan  $\{N_t^c\}_{t\leq 22}$  and  $\{W_t^c\}_{t\leq 22}$ ), the daily number of cases with illness onset before January  $2^{\text{nd}}$  and confirmed before January  $2^{\text{nd}}$  in Wuhan  $\{W_t^o|_{T_c\leq 22}\}_{t=-23}^{22}$  and the distribution  $P(T \leq h|_{T_c} = s)$  and  $P(T \leq h|_{T_o} = t)$  to estimate the daily number of cases with illness onset  $\{N_t^o\}_{t=-23}^3$  from December  $8^{\text{th}}$  2019 to January  $3^{\text{rd}}$  2020. We use the method based on the following renewal equation to estimate  $R_0$  and  $R_t$ .  $1^{19,20}$  Let  $f_t$  be the number of new cases on day t, and let  $g_\tau = G(\tau) - G(\tau - 1)$  be the discretized distribution of the serial interval with  $G(\tau)$  being the cumulative distribution function:

$$E(j_t) = R_0 \sum_{\tau=1}^{t-1} g_{\tau} j_{t-\tau} \tag{6}$$

The number of new cases follows the Poisson distribution. The distribution of the serial interval is modeled as a gamma distribution with mean of 7.5 days and standard deviation of 3.4 days.<sup>21</sup> For  $R_t$  we have

$$E(j_t) = R_t \sum_{\tau=1}^{t-1} g_{\tau} j_{t-\tau}$$
 (7)

We estimate  $R_0$  and  $R_t$  based on the illness onset data per day  $N_t^0$  (which is used to replace  $j_t$ ).

#### **Results**

#### Model-free estimation of the basic/effective reproduction numbers

To estimate the onset-to-confirmation distribution  $P_T$ , we have collected detailed information of some patients confirmed before January 30<sup>th</sup> 2020 from the Health Commissions of different cities, including dates of illness onset and dates of confirmation. We use the data of these patients with illness onset before January 20<sup>th</sup> (ten days prior to the latest onset date of the patients in the data) to avoid underestimating T.

By fitting a Weibull distribution on the illness onset data before January 30<sup>th</sup>, we estimate  $P_T$  to be Weibull distributed (mean 7.67, standard deviation 2.88). By fitting a Weibull distribution on the data of cases confirmed on day s we estimate  $P(T \le h|T_c = s)$  to be Weibull distributed with mean 5.29 and standard deviation 3.48 for s = 20,21,22. From the literature<sup>21</sup>  $P(T \le h|T_0 = t)$  was assumed to follow a Weibull distribution with mean 12.5 and standard deviation 7.5 for  $t \le 0$  and a Weibull distribution with mean 9.1 and standard deviation 4.18 for  $1 \le t \le 3$ .

We chose  $(S_1, ... S_2) = (17, ... 34)$  (January 17<sup>th</sup>-February 3<sup>rd</sup>) to estimate  $N_{t_1}^0, ..., N_{t_2}^0$ . According to  $P_T$  we calculate that  $q_j > 0$  for  $4 \le j \le 33$  and  $q_j = 0$  for other j. Then we can determine  $(t_1, ..., t_2) = (4, ..., 33)$  (January 4<sup>th</sup>-February 2<sup>nd</sup>) and estimate  $\{N_t^0\}_{t=t_1}^{t_2}$ . We got  $\{W_t^{0|T_c \le 22}\}_{t=-23}^{22}$  from the literature,  $S_t^0$  we chose  $S_t^0 = 22$  in formula (4). We obtain  $S_t^0 = 32$  for  $S_t^0 = 20$ , (Figure 3), and hence we only need to estimate the distribution  $S_t^0 = 32$  for  $S_t^0 = 20$ , 21,22. Therefore, then  $S_t^0 = 32$  can be estimated by formula (4) and formula (5).

We estimate the daily number of cases with illness onset on the day from December  $8^{th}$ , 2019 to February  $2^{nd}$ , 2020 in China,  $\{N_t^0\}_{t=-23}^{33}$ , (Figure 3(B)). The number of daily illness onset cases grew exponentially before January  $20^{th}$  2020, and continued to grow but with a lower rate after January  $20^{th}$  2020. Then it increased with a constant rate since the growth looks like a straight line (Figure 3(B)). We used the data on cases with illness onset before January  $4^{th}$ ,  $\{N_t^0\}_{t=-23}^{33}$ , to estimate the basic reproduction number  $R_0$ , which was 3.27 (95% confidence interval [2.98, 3.58]). To investigate the variation of the basic reproduction number and its relationship with the serial interval, sensitivity analysis is carried out by changing the mean of the serial interval from 3 to 12 days. We examine the variation in  $R_0$  with the serial interval (Figure 3(C)). The basic reproduction number  $R_0$  increases in parallel with the serial interval. According to recent papers,  $R_0$  increases in parallel with the serial interval. According to recent papers,  $R_0$  increases in parallel with the serial interval creates. The mean of median serial interval was estimated to range from 3 to 6 days, the corresponding value of estimated  $R_0$  is between 1.45 and 2.43 (Figure 3(C)).

Further we use the number of cases with illness onset on day t in China,  $\{N_t^0\}_{t=-23}^{33}$ , to estimate the effective reproduction number  $R_t$  (Figure 4(A)). It has a peak around January 20<sup>th</sup> and begins

to decrease after January 20<sup>th</sup>. It is worth noting that  $R_t$  started to be stable from late January and was still above 1. By repeating the above process, we also estimated the data on cases with illness onset in the Hubei Province between December 8<sup>th</sup>-February 2<sup>nd</sup> and based on that we further estimated the effective reproduction number  $R_t$  for Hubei (Figure 4(B)). It follows from Figure 3(B) that the data on cases with illness onset for Hubei is quite similar to that for China before mid-January. From Figure 4(B) the effective reproduction number  $R_t$  for Hubei shows a declining trend, which decreases quicker than that for mainland China, compared with Figure 4(A). The number of cases with illness onset in Hubei may peak earlier than in mainland China. From Figure 4(B) there was a small peak around January 12<sup>th</sup> 2020 which induces a relatively small and late main peak in Hubei, compared to Figure 4(A).

#### Prediction from the dynamic model

By simultaneously fitting the proposed model to the four columns of data of cumulative reported, death, quarantined and suspected cases, we obtain the estimations for the unknown parameters and initial conditions. The best fitting result is shown in Figure 5 (black curves). From Figure 5 the inflection points of cumulative quarantined and suspected population have been basically reached, while the cumulative number of reported cases nearly reaches its inflection point, which implies that the COVID-19 epidemic will nearly peak. Comparing the results in Figure 5(A-D), the number of quarantined/suspected cases peak earlier than the number of reported cases. Increasing the minimum contact rate  $c_b$  leads to an increase in the cumulative number of reported cases, the cumulative numbers of quarantined and suspected cases. An increase in individuals' movement

and/or weakening intervention measures (i.e.,  $c_b$  becomes larger) result in more cumulative reported, quarantined, suspected cases and postpone the epidemic peak (Figure 5(A-D)). From Figure 5 (C-D, G-H) increasing the detection rate by three times while halving the confirmation ratio will result in high cumulative numbers of quarantined and suspected cases. In such a scenario, the number of cumulative reported cases exhibits a great decline, by comparing Figure 5 (A) and (E), Figure 5 (B) and (F)), i.e., the blue curves in Figure 5 (E-F) stabilize at lower values than the black curves do, which means that increasing detection rate by four times, even decreasing the confirmation ratio by half, can lower down the final cumulative reported cases and bring forward the epidemic peak. Continuing to enhance the quarantine and isolation strategy, improving detection rate, decreasing the confirmation ratio, are beneficial for mitigating the burden of the infection.

Repeating the above process based on real and generated data for Hubei gives similar results reported in Figure 6 (there is no data on suspected cases in Hubei). From Figure 6 (A-C) doubling the minimum contact rate  $c_b$  leads to an increase in the cumulative number of reported, quarantined, and suspected cases. Similar to Figure 5(A-C), increasing the minimum contact rate  $c_b$  induces a significant increase in the number of quarantined cases, comparing Figure 6(C) to Figure 5(C). More people may be quarantined if the contact rate becomes greater in Hubei.

The important factors making the prediction difficult are the lag in cases reporting and the randomness of the monitoring data. To examine the randomness of multi-source data and their influence on model prediction, we assume the cumulative reported, death, suspected and cumulative quarantined cases follow a Poisson distribution with the intraday cumulative number as the key parameter, and we randomly generate 1000 columns of datasets for fitting. We then

obtain the mean value and 95% confidence interval of key indicators including epidemic situation, daily reproduction ratio, peak time or inflection point (Figure 7). Due to the characteristics of the cumulative data, we here only show the 95% of the unilateral upper confidence limit and interval in Figure 7. The number of cumulative quarantined cases tends to be stable while the other three types of cumulative population sizes exhibit great randomness, implying that a random event (such as a sudden cluster infection) may lead to a rapid increase in the numbers of cumulative reported cases, deaths and suspected cases. Moreover, the fitting curve of the cumulative death cases with the real data is located in the middle of 95% unilateral upper confidence interval. The number of cumulative death cases due to the COVID-19 infection is highly uncertain where the improvement of treatment level may significantly reduce the fatality rate.

Similarly, on the basis of real data and 1000 columns of generated data we plot the curve of hospital notifications, (Figure 8(A) for China and (D) for Hubei). The hospital notifications will peak around February 8<sup>th</sup> 2020, and the peak time for the Hubei province may be one day early. The values of the hospital notifications in Figure 8 (A) and (D) are much smaller than those reported by the National Health Commission of China,<sup>11</sup> due to the very restrictive discharge conditions in Hubei. From Figure 8 (B) and (E), the estimated effective reproduction number based on the real data almost coincides with the mean values for both China and Hubei, while the effective reproduction number in the Hubei province is always larger than that the value for mainland China. From Figure 8(A) and Figure 8(B), the COVID-19 epidemics in China is highly uncertain. Figure 8(C) and (F) give the estimated contact rate c(t), quarantined rate q(t) and diagnose rate  $\delta_I(t)$ , showing that the contact rate curve for Hubei decreases faster than that for

mainland China with a smaller  $c_b$ . The quick decrease of the contact rate, the gradual increase of quarantined diagnosed cases rates indicate that the restrictive measures in China have been strengthened since January  $23^{\rm rd}$  2020.

#### Discussion

Since January 23<sup>rd</sup> 2020 the Chinese government has implemented several measures. Recent data show that most of reported cases come from suspected individuals. This implies that the changing trends of cumulative quarantined and suspected cases greatly influence the trend of the COVID-19 epidemics. The cumulative numbers of quarantined and suspected cases nearly tend to stabilize, since their inflection points have already been achieved. The COVID-19 epidemics will peak in the near future.

The existing models either use the data of only confirmed cases or data of both confirmed and death cases, with most of model predictions ignoring the effects of quarantine and isolation. Here we extend a previously developed model by including new compartments, and utilizing more data of quarantined and suspected cases, to make predictions and perform assessment and risk analysis. Based on our prediction, the number of cumulative confirmed cases is near to its inflection point and the COVID-19 infection will peak soon. The trend of the COVID-19 epidemics in Hubei and China depends on cumulative quarantined and suspected cases, in terms of variations of detection rate and the confirmation ratio for these two compartments.

Therefore, our model is consistent with the current epidemics development and in line with the prevention measures implemented in mainland China. The effective reproduction numbers are

quite large before January 24<sup>th</sup> 2020, suggesting that the population movement before the Spring Festival, especially the outflow of the population before the lock-down of Wuhan, has been an important factor resulting in the COVID-19 epidemics. The effective reproduction numbers show a declining trend, meaning that new infections have largely been decreasing, while new reported cases have been increasing significantly during February 3<sup>rd</sup> to February 7<sup>th</sup> 2020. Most cases were quarantined or became suspected cases.

The strong measures implemented have reduced the effective reproduction number. These interventions may take a longer time to be effective as the second and third generations of infected people are exposed in succession. After the first wave of the Spring festival, the flow of people increased the risk of spreading the novel coronavirus. The uncertainty of the national epidemics is higher than that of Hubei, so the evolutionary trend of the epidemics still needs attention in the future in terms of population migration or possible infection clusters on the way.

Tables.

Table 1: Parameter estimates for the 2019-nCov epidemics in Wuhan, China.

D	D. (° .'4'	<b>Estimated values</b>	Course		
Parameter	Definitions	Hubei(Std)	China(Std)	Source	
$c_0$	Contact rate at the initial time	14.781	14.781	9	
$c_b$	Minimum contact rate under the current control strategies	5.00(0.0039)	8.00(0.066)	Estimated	
$r_1$	Exponential decreasing rate of contact rate	0.20(0.0067)	0.15(0.0352)	Estimated	
β	Probability of transmission per contact	0.2068(0.0048)	0.1911(0.0175)	Estimated	
$q_0$	Quarantined rate of exposed individuals at the initial time	0.0051(0.0052)	$1.00 \times 10^{-4} (0.0037)$	Estimated	
$q_m$	Maximum quarantined rate of exposed individuals under the current control strategies	0.6297(0.0134)	0.98(0.0087)	Estimated	
$r_2$	Exponential increasing rate of quarantined rate of exposed individuals	0.10(0.00062)	0.1531(0.004)	Estimated	
m	Transition rate of susceptible individuals to the suspected class	$1.00 \times 10^{-6} (1.21 \times 10^{-8})$	$1.0002 \times 10^{-7} (1.58 \times 10^{-8})$	Estimated	
b	Detection rate of the suspected class	0.09(0.000066)	0.07(0.0078)	Estimated	
f	Confirmation ratio: Transition rate of exposed individuals in the suspected class to the quarantined infected class	0.80(0.0032)	0.50(0.0541)	Estimated	
σ	Transition rate of exposed individuals to the infected class	1/7	1/7	9	
λ	Rate at which the quarantined uninfected contacts were released into the wider community	1/14	1/14	9	
$\delta_{I0}$	Initial transition rate of symptomatic infected individuals to the quarantined infected class	0.1326	0.1326	9	
$\delta_{If}$	Fastest diagnose rate	2.5(0.0009)	2.5(0.006)	Estimated	
$r_3$	Exponential decreasing rate of diagnose rate	0.20(0.000139)	0.20(0.093)	Estimated	
$\gamma_I$	Recovery rate of infected individuals	0.33	0.33	9	
$\gamma_H$	Recovery rate of quarantined infected individuals	0.20(0.0045)	0.15(0.0132)	Estimated	
α	Disease-induced death rate	0.013(0.00036)	0.008(0.00017)	Estimated	
Initial	Definitions	Estimated values	Source		
values		Hubei(Std)	China(Std)		
S(0)	Initial susceptible population	$9.00 \times 10^6 (3.52)$	$2.00 \times 10^7 (1.23)$	Estimated	
		$\times 10^5$ )	$\times 10^7$ )		
E(0)	Initial exposed population	$4.00 \times 10^3 (390)$	$9.00 \times 10^{3}$ (	Estimated	
			$2.11\times10^3)$		
I(0)	Initial infected population	935(60)	$1.2405 \times 10^3 (642)$	Estimated	
B(0)	Initial suspected population	800(13)	1072	Data	
$S_q(0)$	Initial quarantined susceptible population	2132	7347	Data	
H(0)	Initial quarantined infected population	494	771	Data	

R(0) Initial recovered population 34 34 Data



Table 2: Control daily reproduction ratio R(t) for the COVID-19 epdemics in Wuhan, China.

Date		Jan. 23	Jan. 24	Jan. 25	Jan. 26	Jan. 27	Jan. 28	Jan. 29	Jan. 30	Jan. 31
<b>P</b> (1)	Hubei	6.3947	5.0024	3.9330	3.1090	2.4722	1.9784	1.5943	1.2946	1.0599
R(t)	China	6.0033	4.5709	3.4774	2.6431	2.0076	1.5243	1.1577	0.8803	0.6709
Date		Feb. 1	Feb. 2	Feb. 3	Feb. 4	Feb. 5	Feb. 6	Feb. 7	Feb. 8	Feb. 9
Date R(t)	Hubei	Feb. 1 0.8755	Feb. 2 0.7302	Feb. 3 0.6153	Feb. 4 0.5241	Feb. 5 0.4515	Feb. 6 0.3935	Feb. 7 0.3470	Feb. 8 0.3096	<b>Feb. 9</b> 0.2794

#### **Funding Source**

This research was funded by the National Natural Science Foundation of China (grant numbers: 11631012 (YX, ST), 61772017 (ST)), and by the Canada Research Chair Program (grant number: 230720 (JW) and the Natural Sciences and Engineering Research Council of Canada (Grant number:105588-2011 (JW).

#### **Ethical Approval**

Waived, since all data utilized are publicly available.

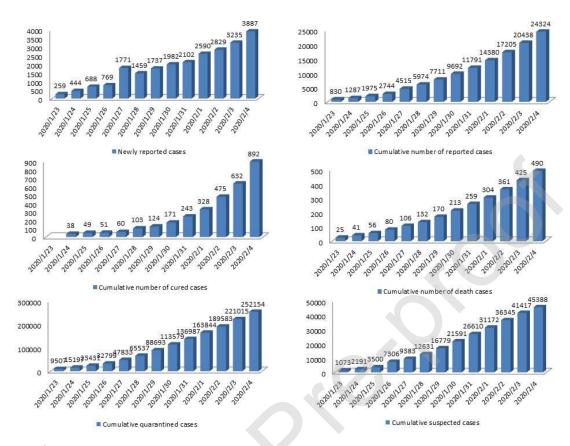
#### **Conflict of Interest**

None.

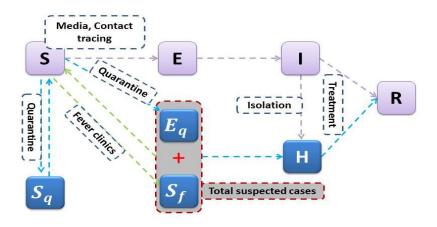
#### References

- 1. Viboud C, Simonsen L, Chowell G. A generalized-growth model to characterize the early ascending phase of infectious disease outbreaks. *Epidemics* 2016; **15**: 27-37.
- 2. Chowell G, Viboud C, Simonsen L, Moghadas SM. Characterizing the reproduction number of epidemics with early subexponential growth dynamics. *J R Soc Interface* 2016; **13** (123).
- 3. Cohen J, Normile D. New SARS-like virus in China triggers alarm. Science 2020; 367: 234-235.
- 4. Lu H, Stratton CW, Tang YW. Outbreak of Pneumonia of Unknown Etiology in Wuhan China: the Mystery and the Miracle. *J Med Virol* 2020 doi: 10.1002/jmv.25678.
- 5. Parry J. China coronavirus: cases surge as official admits human to human transmission. *BMJ* 2020; 368: m236.
- 6. HB.CHINA.COM.CN. http://hb.china.com.cn/2020-01/27/content 41043813.htm?f=pad&a=true [Accessed 4 Feb 2020].
- 7. Tang B, Bragazzi NL, Li Q, Tang S, Xiao Y, Wu J. An updated estimation of the risk of transmission of the novel coronavirus (COVID-19). *Infect Dis Model* 2020.
- 8. National Health Commission of the People's Republic of China. http://www.nhc.gov.cn/xcs/xxgzbd/gzbd\_index.shtml [Accessed 9 Feb 2020].
- 9. Tang B, Wang X, Li Q, et al. Estimation of the Transmission Risk of the COVID-19 and Its Implication for Public Health Interventions. *J Clin Med* 2020; **9**: 462.
- 10. Health Commission of Hubei Province. Available at http://wjw.hubei.gov.cn/bmdt/ztzl/fkxxgzbdgrfyyq/ [Accessed 6 Feb 2020]
- 11. National Health Commission of the People's Republic of China. http://www.nhc.gov.cn/xcs/xxgzbd/gzbd\_index.shtml [Accessed 6 Feb 2020]
- 12. Guanchazhe News. https://baijiahao.baidu.com/s?id=1657591560934072148&wfr=spider&for=pc [Accessed 6 Feb 2020]
- 13. National Health Commission of the People's Republic of China. <a href="http://www.nhc.gov.cn/xcs/xwbd/202002/35990d56cfcb43f4a70d7f9703b113c0.shtml">http://www.nhc.gov.cn/xcs/xwbd/202002/35990d56cfcb43f4a70d7f9703b113c0.shtml</a> [Accessed 4 Feb 2020]
- 14. Castillo-Chavez C, Castillo-Garsow CW, Yakubu A. Mathematical Models of Isolation and Quarantine. *JAMA* 2003; 290: 2876-2877.
- 15. Keeling MJ, Rohnai P. Modeling infectious diseases in humans and animals. Princeton University Press. 2008; p. 313-320.
- 16. Richardson WH. Bayesian-Based Iterative Method of Image Restoration. JOSA 1972; 62 (1): 55–59.
- 17. Lucy LB. (1974). An iterative technique for the rectification of observed distributions. *Astronomical Journal* 1974; **79** (6): 745–754.
- 18. Goldstein E, Dushoff J, Ma J, Plotkin JB, Earn DJ, Lipsitch M. (2009). Reconstructing influenza incidence by deconvolution of daily mortality time series. *Proceedings of the National Academy of Sciences* 2009; **106** (51): 21825-21829.
- 19. Nishiura H, Chowell G. The effective reproduction number as a prelude to statistical estimation of time-dependent epidemic trends. In Mathematical and statistical estimation approaches in epidemiology (pp. 103-121). 2009; Springer, Dordrecht.
- 20. Nishiura H. Correcting the actual reproduction number: a simple method to estimate R0 from early epidemic growth data. *International journal of environmental research and public health* 2010; **7** (1): 291-302.
- 21. Li Q, Guan X, Wu P, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. *N Engl J Med* **2020**, doi: 10.1056/NEJMoa2001316.
- 22. Hiroshi Nishiura,
  Natalie M. Linton, Andrei R. Akhmetzhanov, Serial interval of novel coronavirus (COVID-19) inf ections, medRxiv preprint https://doi.org/10.1101/2020.02.03.20019497
- 23. Zhanwei Du, Lin Wang, Xiaoke Xu, Ye Wu, Benjamin J. Cowling, and Lauren Ancel Meyers, The serial interval of COVID-19 from publicly reported confirmed cases, medRxiv preprint .https://doi.org/10.1101/2020.02.19.20025452

#### Figures.



**Figure 1.** The datasets related to the COVID-19 epidemics including newly reported cases, cumulative number of reported cases, cumulative number of cured cases, cumulative number of death cases, cumulative quarantined cases and cumulative suspected cases.



**Figure 2.** Diagram of the model adopted in the study for simulating the COVID-19 infection. Interventions including intensive contact tracing followed by quarantine and isolation are indicated. The gray compartment means suspected case compartment consisting of contact tracing Eq and fever clinics.

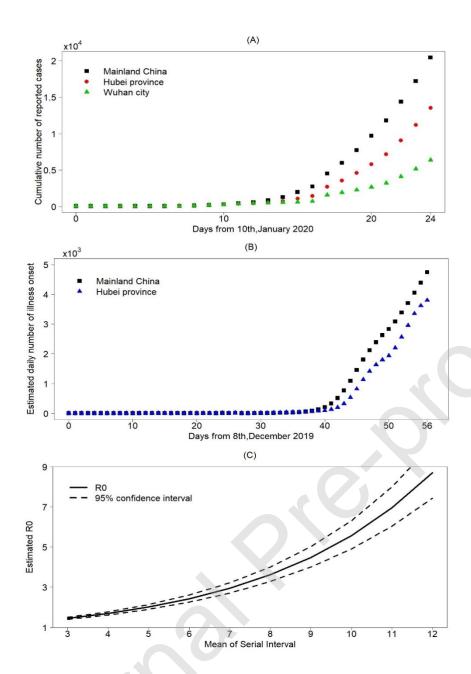
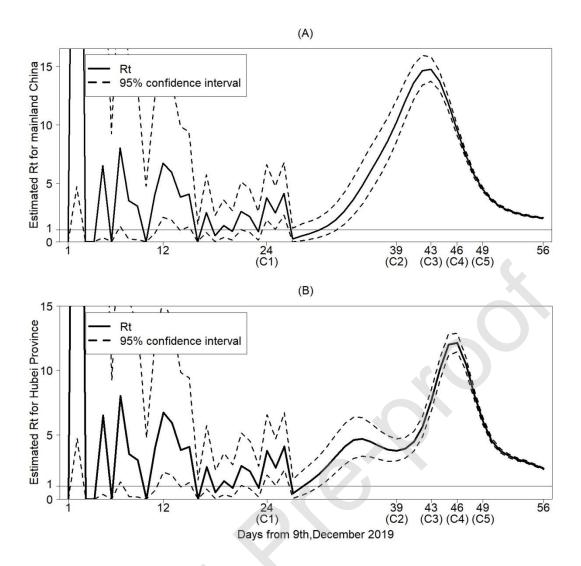
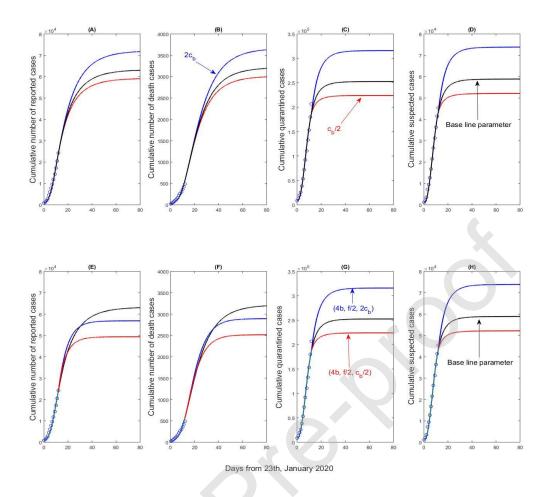


Figure 3. (A) Cumulative number of confirmed reported cases for mainland China, Hubei province and Wuhan city, (B) Estimated number of illness onset cases for mainland China, Hubei province and Wuhan city, (C) Estimated basic reproduction number  $R_0$ .



**Figure 4.** Estimated effective reproduction number  $R_t$  for mainland China in (A) and for Hubei province in (B). The timings of strategies implemented are as follows: (C1): Huanan Seafood Wholesale Market closed on January  $1^{\rm st}$  2020; (C2): Detection kits for COVID-19 firstly used on January  $16^{\rm th}$  2020; (C3): The Chinese government amended the Law on the Prevention and Treatment of Infectious Diseases to include the COVID-19 as class-B infection but manage it as a class-A infection due to its severity on January  $20^{\rm th}$  2020; (C4): Lock-down strategy in Wuhan implemented on January  $23^{\rm rd}$  2020; (C5): Spring festival holiday extended and self-quarantine measures kept on January  $26^{\rm th}$  2020.



**Figure 5.** Goodness of fit (black curve) and variation in cumulative number of reported cases, cumulative number of death cases, cumulative quarantined cases and cumulative suspected cases with the minimum contact rate ( $C_b$ ), detection rate (b) and the confirmation ratio (f).

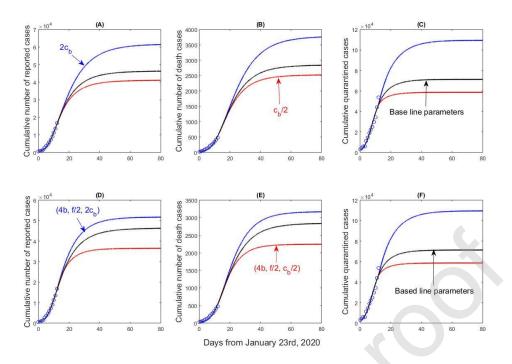


Figure 6. Goodness of fit (black curve) and variation in cumulative number of reported cases, cum ulative number of death cases, and cumulative quarantined cases with the minimum contact rate ( $c_b$ ), detection rate (b) and the confirmation ratio (f) for Hubei Province.

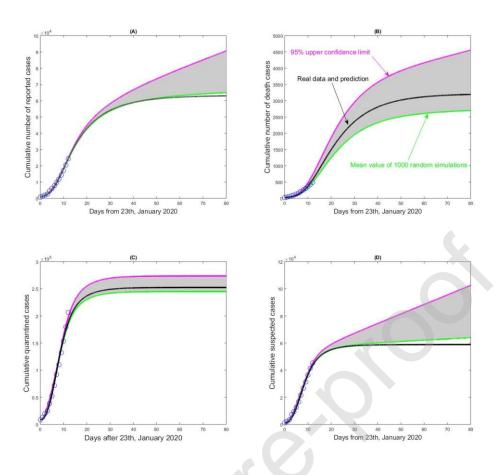
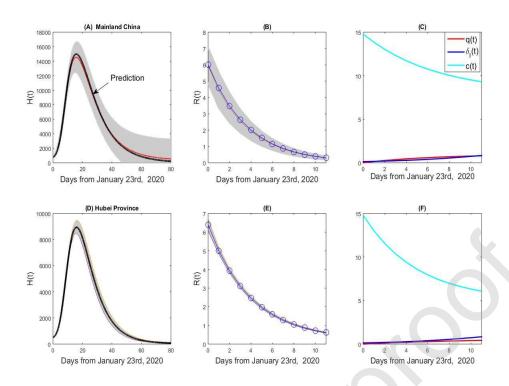


Figure 7. The impact of the randomness of the cumulative reporting data sets including cumulat ive number of reported cases, cumulative number of death cases, cumulative quarantined cases an d cumulative suspected cases on the 2019nCov epidemic in mainland China. The unilateral 95% c onfidence intervals (here 95% upper confidence limits) have been given, and the mean curve and e stimated curve based on the real data sets are marked in each subplot.



**Figure 8.** The hospital notifications, effective reproduction numbers, and estimated contact rate, quarantined rate and diagnose rate curves for mainland China (A-C) and the Hubei province (D-F)

### Appendix.

#### Data information

Date	Cumulative confirmed cases		Cumulati cases	Cumulative death cases		Cumulative quarantined population	
	China	Hubei	China	Hubei	China	Hubei	China
01/23	830	549	25	24	9507	3653	1073
01/24	1287	729	41	39	15197	5682	2191
01/25	1975	1052	56	52	23431	7989	3500
01/26	2744	1423	80	76	32799	10394	7306
01/27	4515	2714	106	100	47833	16904	9383
01/28	5974	3554	132	125	65537	22095	12631
01/29	7711	4586	170	162	88693	28780	16779
01/30	9692	5806	213	204	113579	35144	21591

01/31	11791	7153	259	249	136987	41075	26610	
02/01	14380	9074	304	294	163844	48571	31172	
02/02	17205	11177	361	350	189583	56088	36345	
02/03	20438	13522	425	414	221015	68988	41417	
02/04	24324	16678	490	479	252154	81039	45388	