

Analysis and prediction of the 2019 novel coronavirus pneumonia epidemic in China based on an individual-based model

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Abstract

We developed a stochastic model to simulate the process of the epidemic of novel coronavirus pneumonia in China. The study provides valuable reference to understand the transmission mechanism of the novel coronavirus and evaluate the influence of intervention measures. We established a stochastic individual-based model, and simulated the whole process of occurrence, development, and control of the epidemic, and the infectors and patients leaving Hubei Province before the traffic was closed. Additionally, the R_0 and the number of infectors and patients who left Hubei were estimated using the coordinate descent algorithm. The median R_0 at the initial stage of the epidemic predicted by the model was 4.97 (95% confidence interval [CI], 4.82- 5.17). Before the traffic lockdown in Hubei, an estimated 2000 (95% CI, 1982–2030) infectors and patients left Hubei and traveled throughout the country. The model estimated that as of March 15, the cumulative number of laboratory-confirmed patients in Hubei and other provinces would reach 42,739 (95% CI, 32734-55472) and 12,870 (95% CI, 11520-14572), respectively. If the government had taken prevention and control measures 1 day later, the cumulative number of laboratory-confirmed patients in the whole country would increase by 32.1%. If the lockdown of Hubei was taken 1 day in advance, it is estimated that the cumulative number of laboratory-confirmed patients in other provinces would decrease by 7.7%. The stochastic model could fit the officially issued data well and simulate the evolution process of the epidemic. Intervention measurements nationwide have effectively curbed human-to-human transmission of the virus.

Background

Since December 8, 2019, patients with fever, cough, myalgia, and fatigue have successively emerged in Wuhan of Hubei Province in Central China [1-3]. They had pneumonia with abnormal findings on chest computed tomography[2,3]. On December 31, 2019, the National Health Commission (NHC), Wuhan Health Commission, and Chinese Center for Disease Control and Prevention (CDC) launched an investigation into the epidemic and found that several patients had an exposure history to the Huanan Seafood Market [1]. On January 1, 2020, this market was closed [1]. On January 8, the CDC officially issued a novel coronavirus (coronavirus disease 2019 [COVID-19]) as the causative pathogen for the outbreak [1,4,5]. On January 23, to prevent the epidemic from spreading to the whole country, Wuhan closed roads, railways, and flights leading to other places and prohibited all people from leaving [6]. One day later, all traffic to and from Hubei was closed. On January 25, the national leading group for epidemic response was established [7]. Drawing on the experience of severe acute respiratory syndrome (SARS) prevention and control, the epidemic prevention and control measures was rapidly implemented nationwide under the unified leadership of the central government.

After the outbreak of the COVID-19 epidemic, epidemiologists have used various mathematical models to conduct epidemiological studies. For example, Wu et al. established the Susceptible-Exposed-Infectious-Recovered (SEIR) model, with an estimated R_0 of 2.68 [8], and Du et al. estimated that there would be 12,400 infectors in Wuhan by January 22 using a simple model of exponential growth coupled with a stochastic model [9]. These studies have played a positive role in people's understanding of the

epidemiological characteristics. However, most studies have only calculated R_0 at the initial stage of the epidemic regardless, if this value changed with the progress of intervention measures. Moreover, several models do not perform quantitative analysis on the association between the number of new infectors per day and the number of laboratory-confirmed patients or the impact of Hubei's lockdown and the government's intervention measures on the epidemic nationwide.

In this study, an individual-based model was established based on the idea of randomization, which reproduced the whole process of occurrence, development, and control of the epidemic. This model can overcome the limitations of the traditional SEIR model and has unique advantages. First, the parameters of the stochastic model for each infector are randomly assigned according to certain probability distribution rules. Second, the stochastic model can flexibly set the activities of infectors, including randomly selecting some infectors and patients to travel to other provinces before Hubei is locked down. Third, the stochastic model can also simulate aggregated epidemics and super-disseminators. For example, when it is running on a computer, some infectors will occasionally spread with a high density in a short period or spread in large quantities to susceptible persons. Finally, the randomization model can calculate the fluctuation ranges of the numbers of new and accumulative patients through repeated calculations, helping people predict various possibilities of epidemic development. The various features show that the stochastic model can reproduce the reality more truly and predict the developmental trend of the epidemic more accurately through more flexible details than the other models could. It has scientific reference value for people to assess the epidemic situation and evaluate the effects of intervention measures.

Methods

Data

From January 20, the NHC and the Hubei Provincial Health Commission (HHC) have issued the numbers of new laboratory-confirmed patients across the country and in Hubei, respectively, on a daily basis [10,11]. According to the Diagnosis and Treatment Plan for Novel Coronavirus Pneumonia (5th Edition) [12], the number of laboratory-confirmed patients in Hubei was no longer issued separately by the HHC. Although the 6th edition of the plan issued on February 18 requires release of laboratory-confirmed patients separately [13], we cannot obtain this number in Hubei from February 16 to February 18. Therefore, we have no choice but to use this number before February 15 as the training data in Hubei and other provinces. Basic parameters can be obtained from the literature published by the CDC [1], as shown in Table 1.

Model establishment

1. Assumptions for model establishment

We set some preconditions for the model: First, patients are infectious only after disease onset, and asymptomatic infectors are not considered infection sources. This is because we rely on the definition of

infection source in the 6th edition of the diagnosis and treatment plan [13] and refer to the infectivity characteristics of patients with SARS caused by coronaviruses [14]. Moreover, only patients seeking medical attention can be diagnosed, while patients with asymptomatic infection not seeking medical attention are excluded in the laboratory-confirmed patients of the model. Second, since novel coronavirus pneumonia is a new infectious disease and people have no immunity, all close contacts are considered susceptible. Third, the number of susceptible persons infected by one infector follows Poisson distribution with the R_0 as the mean value. Fourth, Hubei and other provinces have similar $R_0(t)$. This is because the national prevention and control measures have been implemented under the unified leadership, and the implementation of intervention measures in all regions has been similar and synchronous [7].

2. Establishment of the $R_0(t)$

According to the temporal distribution of new laboratory-confirmed patients, we predicted that before the intervention measures were initiated, the virus would continuously spread along with daily contact among people, and the R_0 would continue to remain high during this period. After the intervention measures were initiated, not only the effective contact frequency among people would be significantly reduced but also the infection period of patients would be significantly shortened due to the active screening, therefore, the R_0 in this stage would show a downward trend. According to the abovementioned assumptions, we first listed various possibilities for the $R_0(t)$. Subsequently, we substituted each possible function into a computer program to fit with the training data, and after several tests, the function having the best fitting effect with the training data was finally identified.

3. Establishment of the model according to different developmental stages of the epidemic

In the process of model establishment, we divided the epidemic into three stages according to its occurrence, development, and control processes and designed the computer program according to the characteristics of different stages:

The first stage is the emission period of the epidemic from early December 2019 to January 1, 2020 when the Huanan Seafood Market was closed. The main epidemic features at this stage are as follows: First, animal infection sources in the market continued to spread the virus to humans, leading to the successive appearance of patients with pneumonia [15]; second, these patients were also new infection sources, spreading the virus to other close contacts. In the model, the human infection sources at the early stage of the epidemic were 50 patients with a exposure history to the market and 27 patients with unknown causes before the closure of this market, based on the CDC's findings of investigation [1]. Time of infection, time of seeking medical attention, time of transmission to other susceptible persons, their R_0 , and other information were calculated and stored in a matrix.

The second stage is the development period of the epidemic from January 1, 2020 to January 25, 2020 when Chinese government created a leading group to respond to the epidemic and coordinate the national epidemic prevention and control. The first characteristic of this stage is that people did not adapt

effective protection, resulting in the transmission of the virus among people, and the epidemic began to spread. The second characteristic is that it was during the Spring Festival travel rush in China, and some infectors left Hubei and traveled to all regions of the country and even abroad. Therefore, we randomly selected some of the infectors and patients as the infection sources who arrived at other provinces before Hubei was locked down entirely on January 24. Since then, all the new infectors throughout the country except those in Hubei were infected by these infection sources.

The third stage is the control period of the epidemic, starting from January 25, 2020. The government has strictly implemented a series of powerful measures which have gradually curbed the spread of the epidemic [5]. In the different developmental stages of the epidemic, we assigned the R_0 values to patients according to their time points of disease onset; hence, the epidemic developmental trend changes with the $R_0(t)$.

4. Coordinate descent algorithm

We used the coordinate descent algorithm to obtain the parameters, which is an efficient optimization method of solving extreme values in machine learning [16]. We took the quadratic sum function of the difference between the daily new laboratory-confirmed patients estimated by the model and the corresponding data issued by the government as the objective function. We took the four parameters in the model, namely, a , b , and t of the R_0 and the number of patients and infectors, who left Hubei before it was locked down, namely, m , as the parameters to be estimated (Table 1). Subsequently, we conducted a numerical calculation using the coordinate descent algorithm to obtain the values of the parameters when the objective function reaches the minimum value.

Sensitivity analysis

Partial rank correlation coefficient (PRCC) combined with Latin hypercube sampling was used for the sensitivity analysis to evaluate the influence of the three parameters of R_0 infection period on the model output (the total number of accumulative laboratory-confirmed patients nationwide until March 10, 2020). A standard correlation coefficient, ρ , for the parameter and model output was calculated [17,18]. Details of the coordinate descent algorithm and sensitivity analysis are shown in the supplementary material.

Results

Transmission chain

We randomly selected a patient with a exposure history to the Huanan Seafood Market, found that 802 individuals were infected due to his transmission, and visualized the transmission network (Figure 1). Among these people, the most infectious one could infect 9 susceptible persons and was considered as the super- disseminator in the model.

$R_0(t)$

After testing all possible $R_0(t)$ functions, it was finally determined that the best fitting effect can be obtained when the R_0 remains constant first and subsequently decreases exponentially. Figure 2 shows the changes of the $R_0(t)$ over time. From early December 2019 to January 16, 2020, the $R_0(t)$ stayed constant with a median of 4.97 (95% confidence interval [CI]: 4.82-5.17). Since then, the $R_0(t)$ has shown a rapid downward trend, decreasing to less than 1 by January 27.

Numbers of new laboratory-confirmed patients and new infectors

Figure 3A shows that the peak number of new laboratory-confirmed patients in Hubei predicted by the model was observed on February 6, with an average number of 2953 (95%CI, 2103-4088), while the peak number of new infectors was observed 11 days in advance and was 3563 (95%CI, 2554-4992). Figure 3B shows that the peak number of new laboratory-confirmed patients in other provinces was observed on February 3, with an average number of 918 (95%CI, 808-1049), while the peak number of new infectors was observed 11 days in advance and was 1084 (95%CI, 947-1248). On January 24, due to the blockade of Hubei, the number of new infectors exported to other provinces decreased.

Cumulative number of laboratory-confirmed patients

Figure 4A shows that the cumulative number of laboratory-confirmed patients in Hubei predicted by the model reached 42,739 on March 15 (95% CI, 32734-55472). Figure 4B shows that the cumulative number of laboratory-confirmed patients in other provinces predicted by the model reached 12,870 on March 15 (95% CI, 11520-14572).

Numbers of unidentified patients and unidentified infectors

Figure 5A shows the number of unidentified patients in Hubei peaked on February 1 with a median of 13252 (95%CI, 9434-18434). The number of unidentified infectors in Hubei peaked on January 29 with a median of 14524 (95%CI, 13218-16058). Figure 5B shows the number of unidentified patients in other provinces peaked on January 29 with a median of 4100 (95%CI, 3634-4586). The number of unidentified infectors in other provinces peaked on January 26 with a median of 4488 (95%CI, 4274-4687).

Impact of delaying intervention measures and lockdown of Hubei in advance on the epidemic developmental trend

Figure 6A shows the impact of delaying intervention measures on the epidemic nationwide. When the intervention measures were delayed for 1d and 2d, respectively, the peaking time point of the number of new laboratory-confirmed patients in the whole country was postponed by 1d and 2d, respectively, and the cumulative number increased by 32.1% and 73.4% on March 15, respectively. Figure 6B shows that when the lockdown of Hubei was implemented 1d and 2d in advance, respectively, the peaking time point of new laboratory-confirmed patients in other provinces emerged 1d and 1d in advance, respectively, and the cumulative number decreased by 7.7% and 11.6% on March 15, respectively.

Sensitivity analysis

We obtained 500 samples from a uniform distribution for each parameter (a , b , and t of R_0) range, and the PRCCs for the three indexes were 0.87, 0.57, and -0.18, respectively. A value greater than 0 indicates a positive correlation, and a value less than 0 indicates a negative correlation. Values near -1 or +1 indicate that the parameter has a strong impact on the output, whereas values closer to 0 indicate less effect on the output result.

Discussion

First, we will discuss the impacts of the R_0 , new infectors, unidentified patients and unidentified infectors, and the intervention measures on the epidemic, respectively. Finally, we will discuss the limitations of this study.

The R_0 at the initial stage of the epidemic in this study is 4.97, which is not only higher than 2.2 [1] and 2.46 [8] previously published but also higher than 2.87 [20] of SARS. This can reasonably explain why both the growth rate and cumulative number of patients are higher than those of SARS although the Chinese government has taken similar intervention measures as those for SARS. This study found that the R_0 had remained at a high level until January 16, which led to a rapid increase in the number of patients nationwide. After January 16, the R_0 decreased rapidly. This time point is consistent with the time that strict exit screening measures were activated in Wuhan and when people with body temperature $\geq 37.3^\circ\text{C}$ were restricted from leaving [1]. The research results have been verified by facts. The rapid decrease of R_0 is the main reason for the significant decrease in the number of new laboratory-confirmed patients nationwide.

Based on Figure 3, the changes in new infectors are similar to those in new laboratory-confirmed patients, both increasing first and subsequently decreasing. This is because patients are able to infect susceptible persons only in the period after disease onset and before isolation treatment. Therefore, both the number of unidentified patients and $R_0(t)$ will influence the number of new infectors. After February 19th, the laboratory-confirmed patients issued by the HHC were significantly higher than the predictive number by the model. We hypothesized that the reason was as follows: from February 17, Wuhan launched a 3 days dragnet investigation of close contacts with confirmed patients, suspected patients, and patients with fever where novel coronavirus pneumonia could not be ruled out [21]. In addition to Wuhan, since February 18, a comprehensive investigation and verification of patients with fever has also been conducted in Hubei [22]. However, most of the patients with mild illness and asymptomatic infections do not seek medical attention and are diagnosed under normal conditions, so the government's active investigation does not meet the first premise of the model.

Determining the numbers of unidentified infectors and patients helps the government formulate prevention and control plans. However, these numbers cannot be directly counted in practice. We have performed a quantitative analysis on their quantitative association in Figure 5 and found that the number of infectors changes before the number of patients, suggesting that disease onset will occur after a period of time in the infectors. The peaking time points of the two are nearly 4-8 days earlier than the

peaking time point of the issued new laboratory-confirmed patients; thus, the peaking time points of unidentified infectors and patients can be predicted based on the peaking time point of the issued new laboratory-confirmed patients.

It can be seen from Figure 6A that the earlier the intervention measures were implemented, the easier it would be to control the epidemic. To prevent the epidemic from spreading to the whole country, the government blocked all traffic from Hubei to the outside world. Based on Figure 6B, the lockdown of Hubei is conducive to containing the epidemic in the whole country. Although this measure will increase the number of patients in Hubei, it can control the epidemic in the local area, reduce the risk of spreading the epidemic to the whole country, and significantly reduce the cost of fighting the epidemic, thus allowing the country to concentrate national medical forces to support Wuhan and other cities in Hubei.

This study has the following three limitations. First, some asymptomatic infections and patients with mild symptoms who have not sought medical attention have not been counted by the government in the laboratory-confirmed patients; therefore, the number of laboratory-confirmed patients issued by the state is less than the actual number, which would lead to the underestimation of the R_0 . Second, although asymptomatic infections are not the main infection sources, some of them are also infectious. Because the country lacks accurate statistics for this part of the population, we cannot estimate their scale in this study. Hence, a new model investigating this theoretically needs to be established. Third, although the $R_0(t)$ in Hubei is basically similar as that in other provinces, there may be some minor differences, for example, the intervention measures in Hubei were initiated slightly earlier than in other provinces. Moreover, due to the relative shortage of medical resources in Wuhan, some patients might have caused more spread due to the delay in isolation and treatment. These factors may lead to deviations in the model's estimation of the number of patients and infectors.

Conclusions

The model fits well with the official data and is consistent with the facts, suggesting that the model can reasonably reflect the developmental trend of the epidemic and provides a good reference for epidemic analysis in other countries and regions.

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Declarations

Competing interests

The authors declare that they have no competing interests.

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Authors contribution:

Guo ZY designed the study, analyzed the data, and wrote most of the manuscript, including quality assurance and control; Xiao D contributed to writing the manuscript and helped to conduct the literature review.

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Table

Please see the supplementary files section to view the table.

Figures

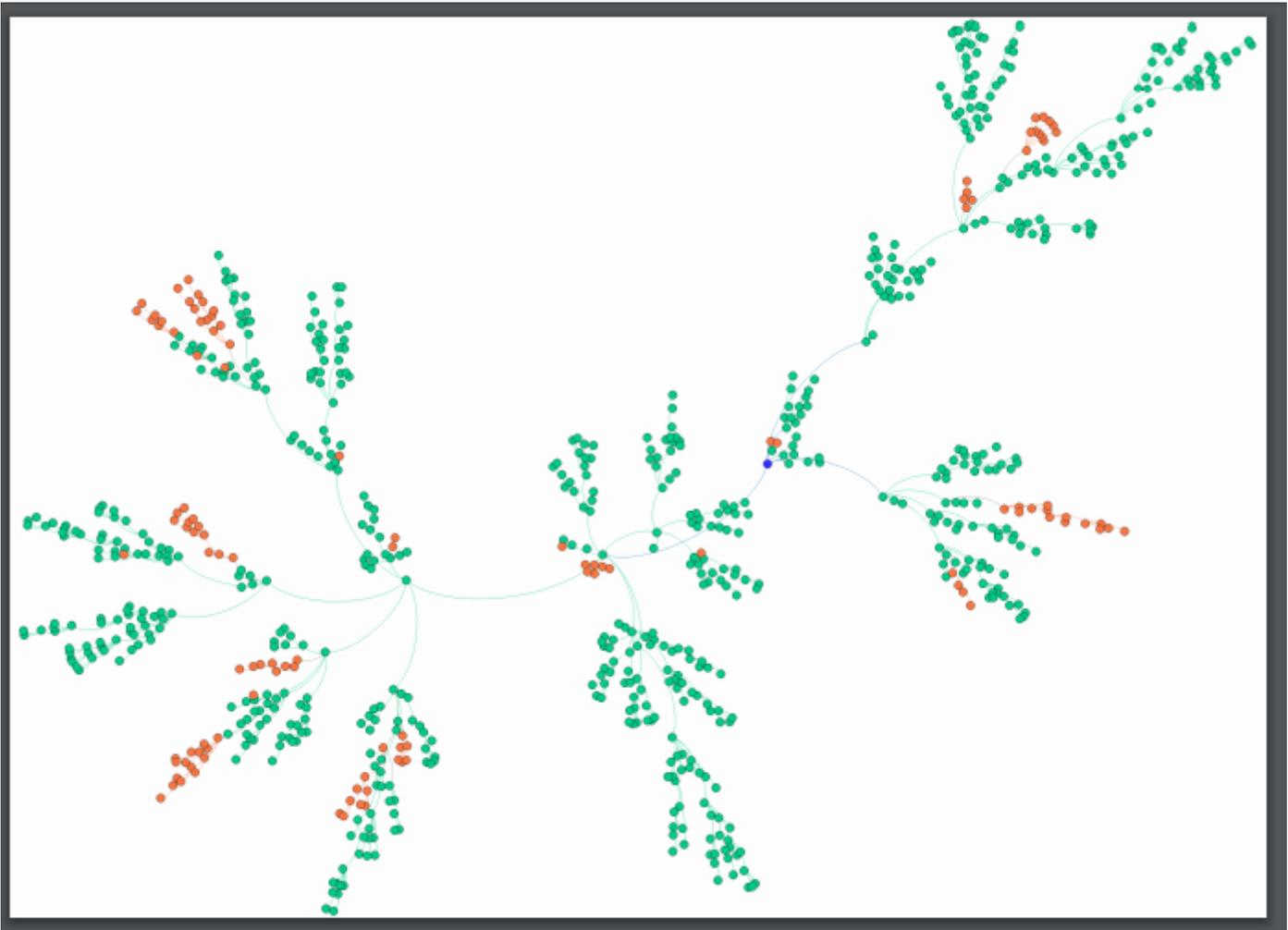


Figure 1

Transmission chain of 802 infectors caused by one infection source Legend: The green circles represent the infectors in Hubei; the red circles represent the infectors in other provinces throughout China; the blue circle represents the first infectious source in the transmission chain; the connection lines represent the transmission associations.

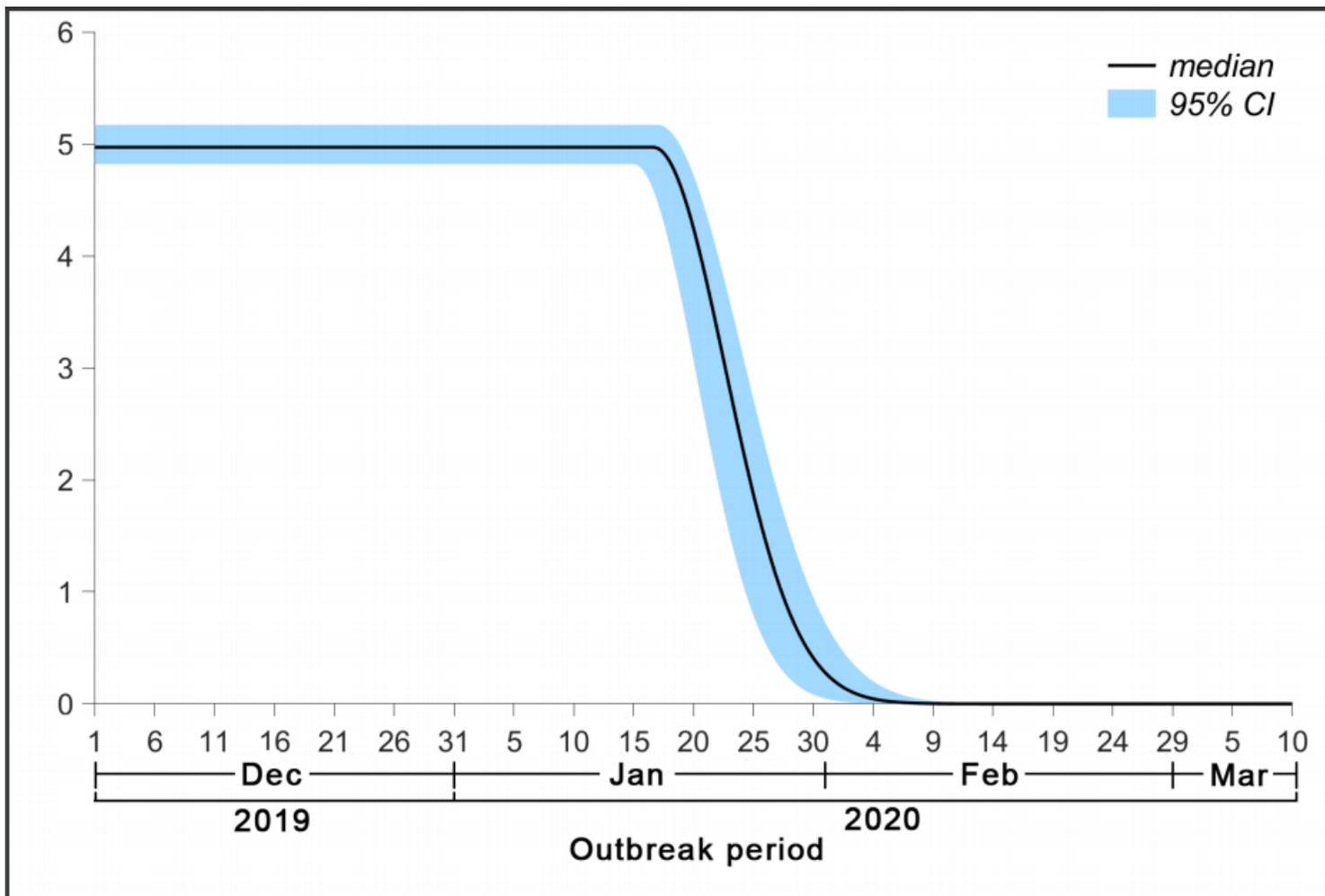


Figure 2

Temporal distribution of the $R_0(t)$ Legend: The solid line represents the median value of the $R_0(t)$, and the blue area represents the 95% confidence interval.

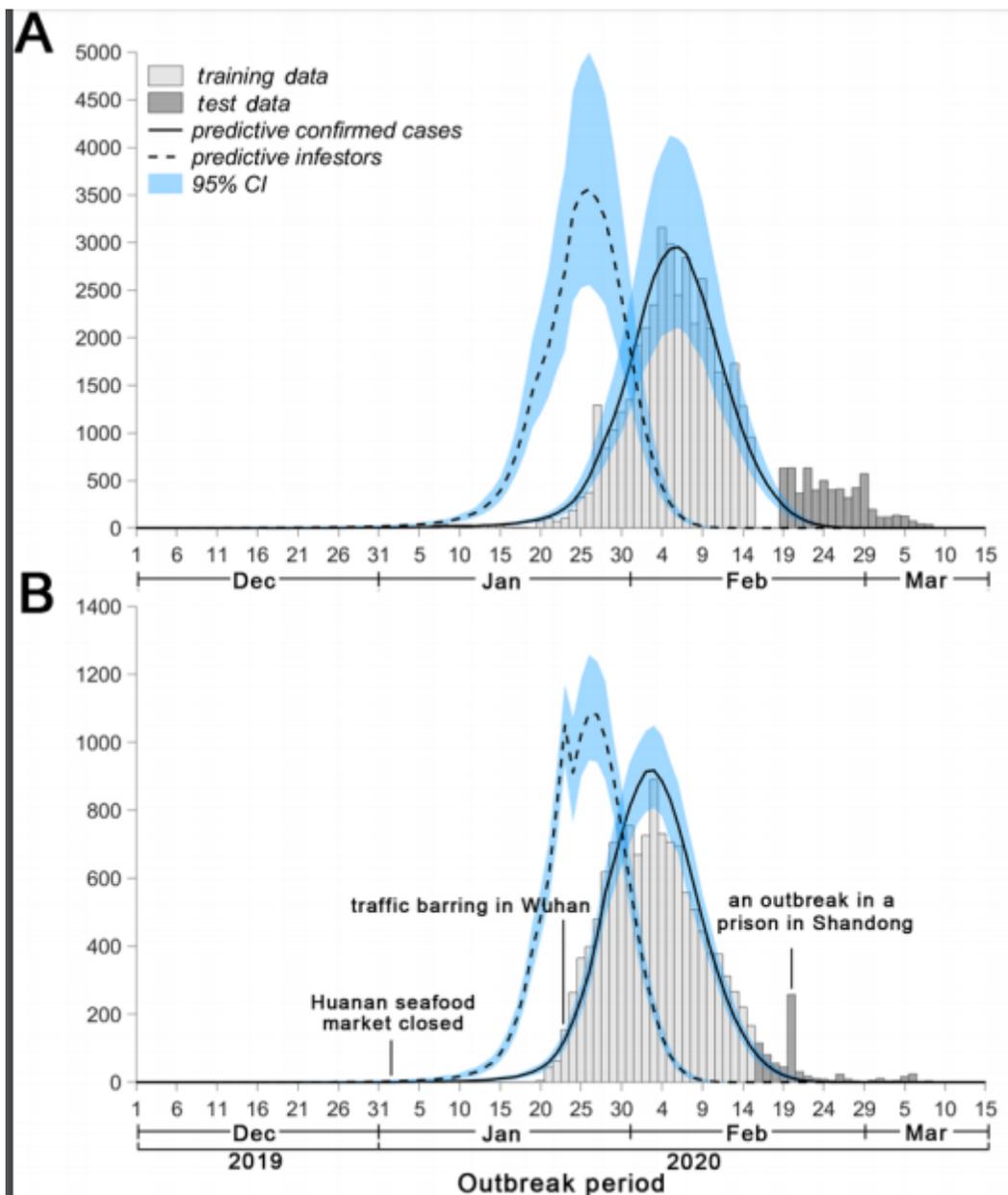


Figure 3

Numbers of new laboratory-confirmed patients and new infectors estimated by the model Legend: Histogram A represents the number of new laboratory-confirmed patients in Hubei issued by the government, and the solid and dashed lines represent the numbers of new laboratory-confirmed patients and new infectors in Hubei estimated by the model, respectively. From February 16 to 18, the number of new laboratory-confirmed patients in Hubei could not be obtained, because the number of new laboratory-confirmed patients and clinical diagnosis patients was simultaneously released by the HHC. Histogram B represents the number of new laboratory-confirmed patients in other provinces issued by the government. The abrupt rise in this number on February 20th was due to a clustering epidemic in a prison in Shandong Province [19]. The solid and dashed lines represent the number of new laboratory-confirmed patients and the number of new infectors in other provinces estimated by the model, respectively.

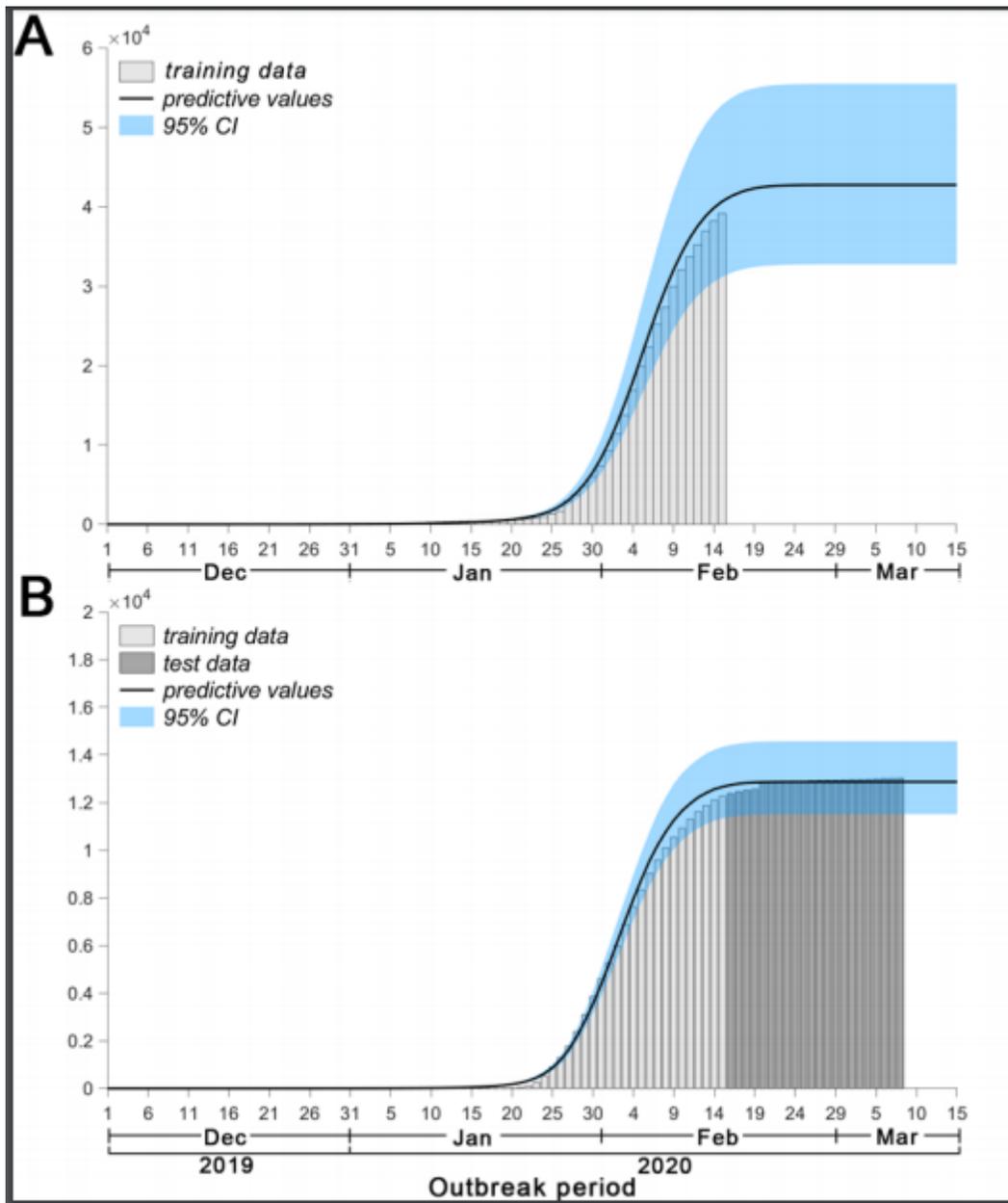


Figure 4

Cumulative number of new laboratory-confirmed patients estimated by the model Legend: A represents the cumulative number of new laboratory-confirmed patients in Hubei estimated by the model. B represents the cumulative number of new laboratory-confirmed patients in other provinces estimated by the model.

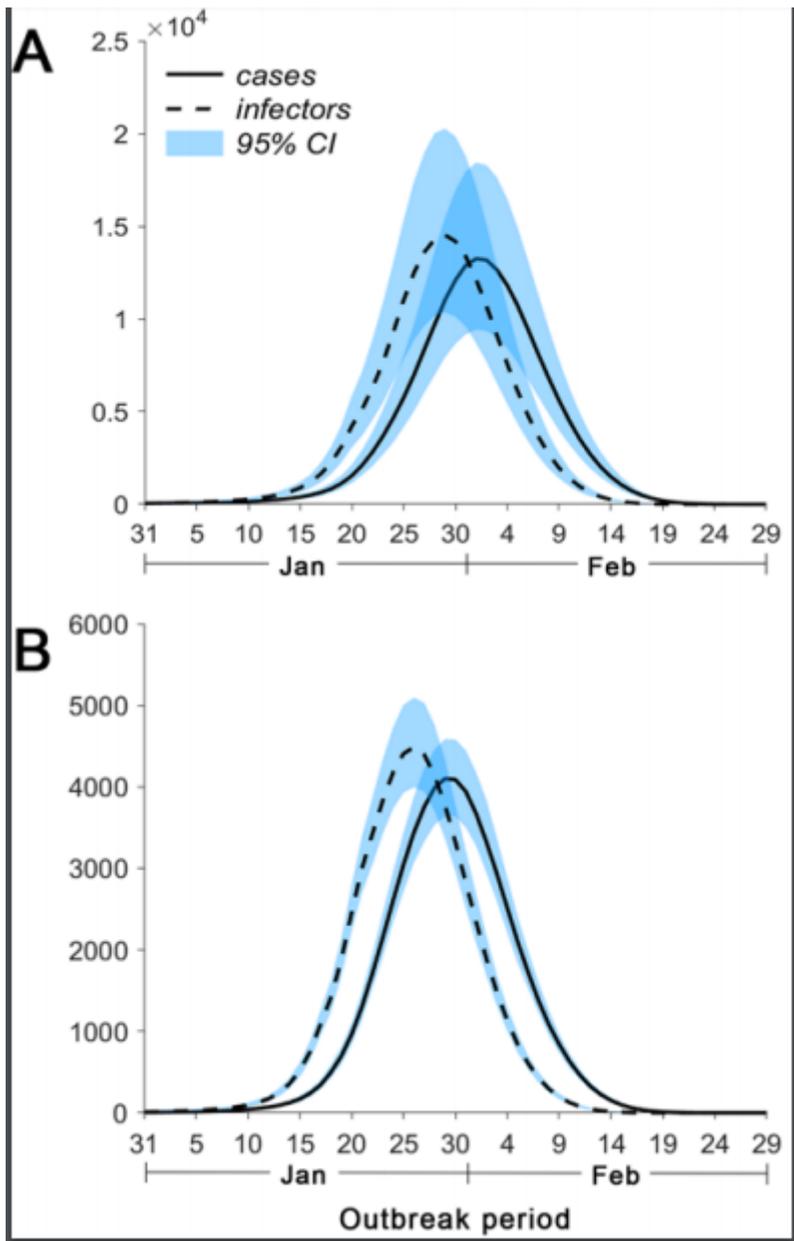


Figure 5

Unidentified patients and infectors estimated by the model Legend: A. The solid and dashed lines represent the numbers of unidentified patients and unidentified infectors in Hubei estimated by the model, respectively. B. The solid and dashed lines represent the numbers of unidentified patients and unidentified infectors in other provinces estimated by the model, respectively.

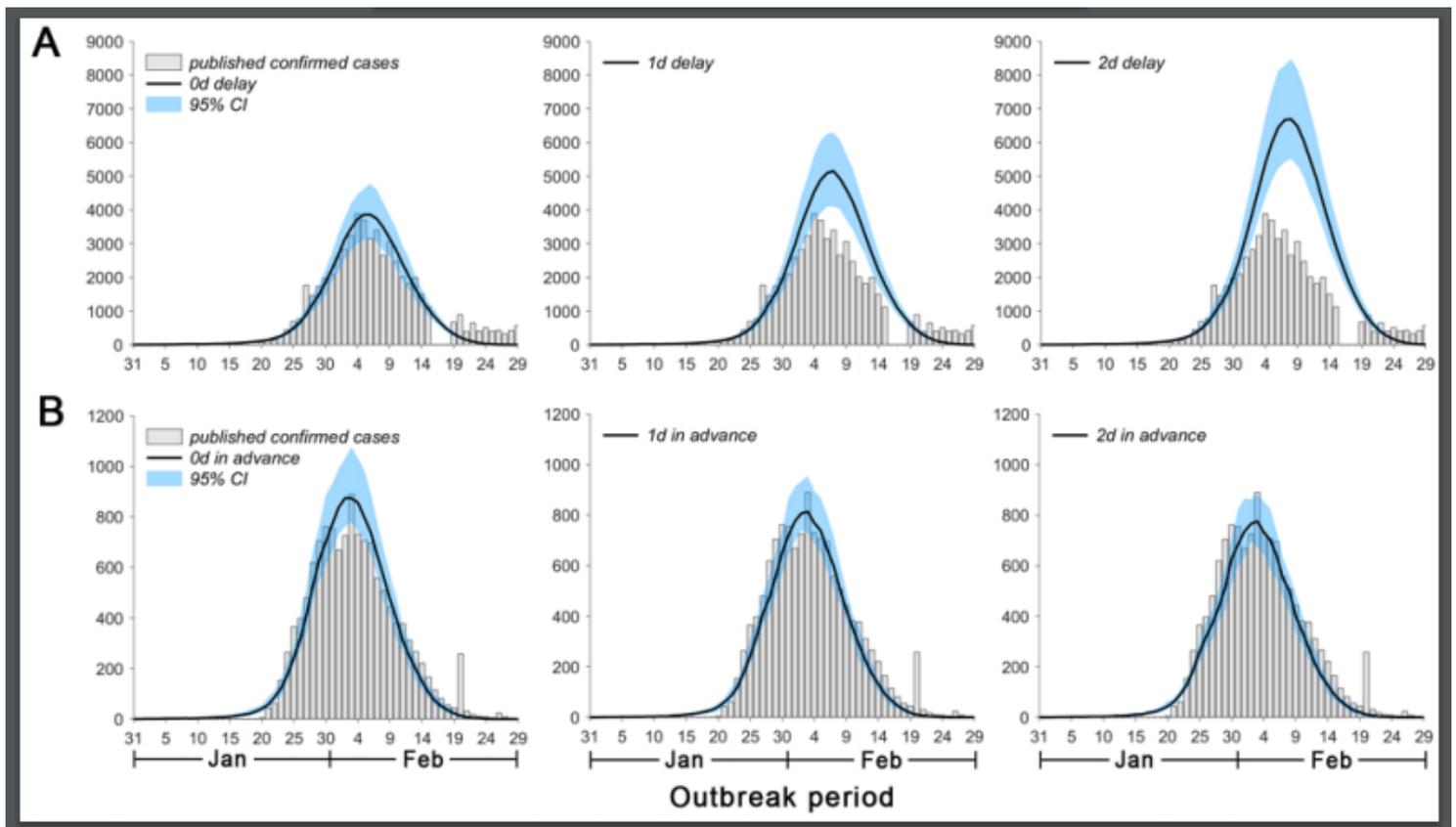


Figure 6

Impacts of delayed intervention measures and lockdown of Hubei in advance on the epidemic developmental trend Legend: A represents the impact of delayed intervention measures on the number of new laboratory-confirmed patients nationwide. The histogram represents the number of new laboratory-confirmed patients nationwide issued by the government, and the solid line indicates the number of new laboratory-confirmed patients nationwide predicted by the model. B represents the impact of lockdown of Hubei in advance on the number of new laboratory-confirmed patients in other provinces. The histogram represents the number of new laboratory-confirmed patients in other provinces issued by the government, and the solid line represents the number of new laboratory-confirmed patients in other provinces predicted by the model. We ensure that the author lists exactly match the tracking system, article file, and supplementary information. The mathematical model is based on published data. Experiments were not part of our study.

Supplementary Files

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