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A switching dynamic model based on phased COVID-19 data in Chongqing and its evaluation

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ARTICLE INFO	A B S T R A C T
Keywords: COVID-19 Imported cases First-level emergency response Switching dynamic model	Objectives: Although COVID-19 has been controlled in China, the risk of invasion of imported cases remains. We aimed to characterize the impact of the number of imported cases and the implementation of first-level emergency response (FLER) policy. Methods: A SCQIHR switching model was constructed and verified by the complete phased data of COVID-19 in Chongqing in 2020. Then it was used to investigate the impact of the number of imported cases and the timing of FLER. Lastly, it was evaluated by three actual scenarios in Chongqing in 2021. Results: The proposed model can fit the multidimensional time series well. After the implementation of FLER, the mean effective reproduction number, contact rate and misdetection rate were decreased significantly, but the quarantine rate for close contacts and isolation rate for non-hospitalized infectious cases were increased significantly. The peaks of quarantined close contacts and hospitalized infectious cases increased linearly with the increase of the number of imported cases and the lag of FLER time, which was verified by three actual scenarios in Chongqing in 2021. Conclusions: These findings can provide guidance for local public health policy-making and allocation of medical resources, reduce the impact of COVID-19 on the local population.

1. Introduction

The cumulative number of confirmed cases of novel coronavirus disease (COVID-19) worldwide has exceeded 200 million, causing more than 4 million deaths. COVID-19 has become the pandemic with the greatest impact on human society and the economy in the past century (World Health Organization, 2021).

Chongqing, one of the four municipalities under the direct administration of the central government of China and 870 miles west of Wuhan, has a resident population of 31.2 million. Since the end of 2019, approximately 100,000 migrants (including but not limited to migrants from Wuhan) have flowed into Chongqing; migration was more frequent before the Spring Festival in 2020. At the beginning of the COVID-19 outbreak, some experts predicted that Chongqing would become the second hotspot. On January 18, 2020, the first imported case was reported in Chongqing. As of February 24, 2020, a total of 576 cases of COVID-19 were confirmed in Chongqing. Owing to the strict prevention and control interventions (PCIs) adopted by the Chinese government, such as home quarantine, community surveillance, increased social distancing, and centralized quarantine of individuals with suspected cases, COVID-19 in China was controlled by the end of February 2020, and the last individual with a confirmed case in Chongqing was discharged after recovery at the end of April 2020.

However, the great challenge China currently faces is a sharp increase in imported cases resulting from the return of a large number of foreign residents (Russell et al., 2021; Xinhua, 2021a). Additionally, the continuous emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants has aroused widespread concern. On May 26, 2021, Guangdong Province, a coastal province in South China and 1300 miles southeast of Chongqing, reported two newly confirmed cases of local transmission and four asymptomatic cases, which were subsequently determined to be caused by the Delta variant of SARS-CoV-2.

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The local government immediately adopted strict PCIs and eventually screened and confirmed a total of 140 COVID-19 cases (Zheng, 2021a; Zheng, 2021b). In addition, individuals positive for the Delta variant of SARS-CoV-2, as detected by routine nucleic acid testing at Nanjing Lukou Airport on July 20, 2021, led to a new round of cluster infections in Nanjing, Yangzhou, and Zhangjiajie (Cang, 2021; Xinhua, 2021b). To control the spread of the Delta variant, most local governments have adopted stringent measures, such as large-scale nucleic acid testing and travel bans, which have required considerable human effort and financial resources. Therefore, it is imperative to assess the impact of the number of imported cases and the timing of the implementation of the first-level emergency response (FLER) policy on COVID-19.

Mathematical models are basic tools that can be used to better understand the progress of the pandemic and to evaluate the effectiveness of prevention and control strategies. In the early stage of COVID-19, Chinazzi et al. established an SLIR (susceptible, latent, infectious and removed) model to predict the impact of travel restrictions on the domestic and international spread (Chinazzi et al., 2020). Tang et al. evaluated the impact of quarantine measures for close contacts and confirmed cases on trends for the first wave of the COVID-19 outbreak in China (Tang et al., 2020). We have used the SQIR (susceptible, quarantine, infected, and recovered) model to evaluate the impact of PCIs on the COVID-19 outbreak in Chongqing and Guizhou (Dai et al., 2020). However, we did not assess the impact of the number of imported cases and the timing of FLER implementation on the progression of the pandemic or conduct in-depth studies on the effects of cryptic transmission caused by undiagnosed infected individuals on the pandemic.

To evaluate and analyze the risk of imported cases, according to the risk of cryptic transmission through undiagnosed individuals, we first constructed a new SCQIHR (Susceptible, close Contacts, Quarantined close contacts, non-hospitalized Infectious cases [infected but not realize he/she is infected, and not be isolated and diagnosed], Hospitalized infectious cases [isolated and receiving treatment], Removed [including death and discharged cases]) model. Then, based on phased data from retrospective reports by the Chongqing Municipal Center for Disease Control and Prevention in 2020, we obtained five time series. After that, the multidimensional time series were used to estimate the undetermined parameters in the model. Finally, the impact of the number of imported cases and the timing of FLER implementation on COVID-19 was investigated using the constructed model, and the simulation results were evaluated by three actual scenarios caused by imported cases in Chongqing in 2021.

2. Methods

2.1. Data sources

We retrospectively collected data for 576 COVID-19 cases confirmed by the Chongqing Municipal Health Commission and the Chongqing Municipal Center for Disease Control and Prevention between January 18, 2020, and April 29, 2020; among the confirmed cases, 173 were cases imported from Wuhan and other places, and 403 cases involved local transmission (67 cases of local transmission originated in Wuhan; however, the infected individuals did not develop symptoms until they arrived in Chongqing, and therefore, the cases were classified as local transmission). COVID-19 has been divided into five types: mild, moderate, severe, critical cases, and asymptomatic cases, but Chinese Centers for Disease Control reported asymptomatic cases, only accounts for 1.2% of total number of confirmed cases (China, 2020) and no asymptomatic infected cases were reported in the first wave of the COVID-19 outbreak in Chongqing, so they were not considered for modeling. We treated them as infected cases who can only go to hospital or be quarantined in the three actual scenarios of PCIs.

For all laboratory-confirmed cases, we obtained data on the onset of symptoms, and the records of quarantine, hospitalization and discharge, by tracing their medical history and screening medical records. The onset of symptoms was determined by time of self-report onset of fever, cough, or other respiratory symptoms. For all close contacts, the date of quarantine was also recorded. Based on the main epidemiological characteristics of and PCIs for COVID-19, the population in Chongqing was classified into six epidemiological statuses: S (susceptible subjects), C (close contacts), Q (quarantined close contacts), I (non-hospitalized infectious cases, infected but do not realize they were infected), H (hospitalized infectious cases, infected and receive treatment), and R (removed cases). The interactions among these epidemiological statuses are shown in Fig. 1. Individuals (S) contacted with an infected case (I) flow into close contacts population (C). The close contact (C) develops clinical symptoms but does not realize being infected, he/she then became an infected case (I). The close contact (C) can also be quarantined (Q) by timely contact tracing. The infected case (I) is hospitalized (H) until contact tracing or seeking medical assistance. If the quarantined close contact (Q) develops clinical symptoms, he/she will be sent to designated hospital for isolation and treatment (H). Otherwise, he/ she will be back to susceptible population (S) after a period of quarantine. Eventually, all infected cases (I) and hospitalized cases (H) will flow to removed population (R) due to recovery or death. Thus, the six epidemiological statuses distinguish between guarantined and unguarantined populations (C and Q) and between non-hospitalized and hospitalized cases (I and H). The imported cases from Wuhan were denoted as Z.

We then summarized the records of all confirmed cases and quarantined individuals, and gave the time lines of epidemiological status changes for four typical cases in Fig. 2 for better illustrating PCIs of COVID-19 in Chongqing. We firstly demonstrated the epidemiological status change $S \rightarrow C \rightarrow I \rightarrow H \rightarrow R$. Case 1 was firstly closely contacted with an infected individual on January 3 (S \rightarrow C) and 8 days later, he/she developed clinical symptoms ($C \rightarrow I$), but did not realize he/she was infected. Until January 19, case 1 was isolated and treated at designated hospitals $(I \rightarrow H)$ resulting from contact tracing or seeking medical assistance, and eventually he/she was being discharged after 21 days treatment ($H \rightarrow R$). Secondly, case 2 was used to illustrate the epidemiological status change $S \rightarrow C \rightarrow Q \rightarrow H \rightarrow R$. Different from case 1, case 2 was directly moved from C to Q, because case 2 was guarantined by immediate contact tracing. Then case 2 was sent to hospital for treatment on January 25 ($Q \rightarrow H$). Thirdly, case 3 was used to show the epidemiological status change $S \rightarrow C \rightarrow Q \rightarrow S$. Case 3 differs from case 2 in that during quarantine case 2 was not infected and several days later was released to susceptible group. Lastly, case 4 was employed to show the epidemiological status change $Z \rightarrow I \rightarrow H \rightarrow R$. Case 4 was imported to Chongqing on January 5, but he/she was isolated and treated in the designated hospital until January 18. After 15 days treatment, case 4 was released to R (removed group).

We collected the Q(t), I(t), H(t), and R(t) by counting the number of individuals in the corresponding epidemiological status at day t. In addition, Z(t) is the number of newly imported cases from Wuhan city and the $Q_c(t)$ is the cumulative number of released quarantined close contacts at day t. since it is difficult to find out the exact date of close contact for most individuals, we did not collect C(t). The six phased time series (Z(t), Q(t), I(t), H(t), R(t) and $Q_c(t)$) are shown in Fig. 3.

2.2. Model

Fig. 1 depicts the flowchart for the transmission among six epidemiological groups (*S*, *C*, *Q*, *I*, *H*, *R*). Through the implementation of close contact tracing, close contacts are quarantined until he or she is hospitalized or released to the susceptible group.

Since January 24, 2020, due to the issuance of FLER, all provinces in China, including Chongqing, have gradually implemented and strengthened prevention and control measures for the pandemic. Measures such as community monitoring, the tracing and quarantine of close contacts, the detection of infectious cases, and the isolation of hospitalized cases have gradually escalated. Therefore, based on the number



Fig. 1. Flowchart of COVID-19 transmission in populations. S represents susceptible, C corresponds to close contacts but no detection, Q signifies quarantined close contacts, I represents non-hospitalized infectious cases, H denotes hospitalized infectious cases, R indicates removed cases, and Z represents imported cases.

of close contacts of confirmed cases before and after the implementation of FLER (Fig. S1), the PCI parameters (β , k_1 , k_2 and ε , see Table S1 for details) can be divided into phase 1 (before FLER implementation, i.e., January 1 to January 24, 2020) and phase 2 (after FLER implementation, i.e., after January 24, 2020). Furthermore, using the significant negative correlation between hospital admission time and length of hospital stay (Fig. S2), we can conclude that February 10, 2020 was the time point at which the parameter $\gamma_{\rm H}$ (see Table S1 for details) changes, which was consistent with the fact that emergency medical institutions started in Chongqing in 2020 (Liang et al., 2020). As a result, the proposed SCQIHR dynamic model becomes a switching model, and the detailed model equations, parameters and initial conditions are described in "Model description" subsection of the Supplementary.

2.3. Model fitting

In order to simultaneously estimate the undetermined parameters in the model (S1) based on the five time series' data, the adaptive Metropolis–Hastings algorithm was used to execute the Markov Chain Monte Carlo (MCMC) process (Haario et al., 2006) and to minimize the cost function vector (S2), see "Cost function" subsection in Supplementary for details. Thus, the estimated values for the model parameters and their standard deviations were obtained (Table S1 and Fig. S3).

2.4. Effective reproduction number

In accordance with the literature (Xu et al., 2020), the mean and standard deviation (5.2 \pm 5.3) of the serial interval for COVID-19 were obtained. Then, the effective reproduction number R_t can be computed by R package epiEstim (Cori et al., 2013), and the mean effective reproduction number before and after the implementation of FLER was computed and statistically compared.

2.5. Statistical analysis

Kolmogorov–Smirnov test was used to analyze the normality of the data. Normally distributed data are expressed as the mean \pm standard deviation; otherwise, they are expressed as the median and quartile. Independent-samples *t*-test was used to compare the difference between the mean effective reproduction number before and after the implementation of FLER, while one-sample *t*-test was used to compare with the threshold value of one. Wilcoxon rank sum test was used to compare the differences between the number of close contacts and four estimated parameters (β , k_1 , k_2 , and ε) before and after the implementation of FLER. Pearson correlation coefficient was used to analyze the correlation between admission time and length of hospital stay. Statistical

analysis was performed using IBM SPSS (version 22.0). P < 0.05 indicates that difference is statistically significant.

3. Results

3.1. Fitting of the data from the Chongqing COVID-19 report

The best fitting results of SCQIHR switching model were obtained (Fig. 4). The model fitting results almost completely overlap with the known five time series, validating the accuracy of the SCQIHR model.

As seen in Fig. 4, since the onset of symptoms for the first imported case on January 1, 2020, the number of close contacts and non-hospitalized infectious cases in Chongqing increased significantly and peaked on January 24. After FLER was issued, close contacts were quickly traced and quarantined, and non-hospitalized infectious cases were quickly quarantined and identified through large-scale screening. The number of quarantined close contacts and hospitalized cases increased significantly and peaked in early February. Across time, close contacts were gradually released to the susceptible group after strict quarantine. With improvements in COVID-19 diagnosis and treatment technologies, the number of hospitalized cases decreased sharply after February 10, and the epidemic in Chongqing diminished, which is consistent with the results reported in previous study (Dai et al., 2020).

3.2. Evaluation of the PCIs for the COVID-19 outbreak in Chongqing before and after the implementation of FLER

We first compared the values of four PCI parameters (β , k_1 , k_2 and ε) before and after the implementation of FLER (January 24, 2020). The results indicated that after the implementation of FLER, the contact rate β and misdetection rate ε were decreased significantly (Fig. 5(A), 5(C), P < 0.05), but the quarantine rate for close contacts k_1 and the isolation rate for non-hospitalized infectious cases k_2 were increased significantly (Fig. 5(B), 5(D), P < 0.05), confirming the effectiveness of strict PCIs in Chongqing after the implementation of FLER.

On the daily effective reproduction number $R_{\rm b}$ Fig. S4 shows its variation curve as well as the daily incidence curve for COVID-19 in Chongqing in 2020. The results indicated that there were significant difference in the mean effective reproduction number before (6.49 \pm 1.00) and after (0.84 \pm 0.04) the implementation of FLER (P < 0.05), which once again confirms the effectiveness of strict PCIs in Chongqing.

3.3. Simulation and practical application of PCIs based on different numbers of imported cases and FLER implementation dates

Using the estimated parameters, we simulated that if strict PCIs were



Fig. 2. The time lines of epidemiological state changes for four cases. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

adopted earlier, the peak number of quarantined and hospitalized cases would be lower and the number of quarantined cases would peak earlier (Figure S5AB). However, if strict PCIs were delayed, there would be a rapid and substantial increase in the cumulative number of quarantined close contacts and hospitalized cases (Figure S5CD).

Because the diagnosis and treatment technologies for COVID-19 have markedly improved, we fixed the parameter γ_H at 0.0862. To analyze the applicability of the model in the prevention and control of COVID-19,

we assumed the following epidemic scenario: all imported cases arrived on day 0, and the model parameters before and after the implementation of FLER remained the same as the above estimated parameter values, i.e., the PCIs were the same as those in 2020. Using quarantined close contacts and hospitalized cases as response variables, we simulated series of COVID-19 epidemic trends using different numbers of imported cases and FLER implementation dates. The results indicated that with the increase in the number of imported cases, the



Fig. 3. Time series of the complete phased data of COVID-19 in Chongqing in 2020. Daily imported cases (Z(t)), daily quarantined close contacts (Q(t)), daily non-hospitalized infectious cases (I(t)), daily hospitalized infectious cases (I(t)), daily hospitalized infectious cases (H(t)), cumulative removed cases (R(t)) and close contacts released from quarantine ($Q_c(t)$). The red dashed line indicates the issuance date of the first-level emergency response. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

peak number of quarantined close contacts and hospitalized cases also increase significantly. Under different FLER implementation dates, the cumulative number of quarantined close contacts and hospitalized cases showed significant linear relationships with the number of imported cases (Fig. 6).

Last, the model was applied in three actual scenarios of imported cases in Chongqing in 2021.

In the first actual scenario, there were 2 imported cases. The imported cases arrived in Jiangjin County, Chongqing, from Shaanxi Province, on July 27, 2021. Three days after the diagnosis was confirmed, the local government immediately adopted strict PCIs. A total of 207 close contacts were quarantined, and no cases of local transmission were identified. As seen in Fig. 6, the cumulative number of quarantined close contacts estimated by the model was 178 (95% CI [154, 223]), a finding that is consistent with the actual reported number of quarantined close contacts. However, the estimated cumulative number of hospitalized cases (4.55, 95% CI [3.88, 5.81]) was slightly higher than the actual reported number of hospitalized cases.

In the second actual scenario, an imported case of asymptomatic infection arrived in Fengjie County, Chongqing, from Hubei Province on July 31, 2021. Three days after diagnosis, the local government immediately adopted strict PCIs and quarantined 51 close contacts; no cases of local transmission were identified. As seen in Fig. 6, the cumulative number of quarantined close contacts estimated by the model was 89 (95% CI [76, 110]), and the cumulative number of hospitalized cases estimated by the model was 2.30 (95% CI [1.95, 2.90]); both estimates were slightly higher than the actual reported data.

Recently, on October 22, 2021, an imported case travelled from

Gansu Province to Chongqing, and causing an outbreak. Then he travelled to Chengdu where he became symptomatic and was diagnosed 11 days later (November 2, 2021). Based on the prediction of our model, there will be 7.69 (95% CI [5.98, 10.31]) hospitalized cases and 339 (95% CI [271, 447]) quarantined close contacts in total. Finally, six confirmed cases and five asymptomatic infections have been officially confirmed in this outbreak, which is just within the prediction range of our model. However, a total of 1242 close contacts were quarantined after this epidemic, which is slighter higher than the results of our model. The possible reason may be that the infected strain was Delta variant of SARS-CoV-2, which is thought to more transmissible than previous variants (Earnest et al., 2021). Thus the local government implemented more strict measures and quarantined more close contacts, resulting in the increased number of cumulative quarantined close contacts.

4. Discussion

Based on retrospective report data provided by the Chongqing Municipal Center for Disease Control and Prevention in 2020, we constructed a new SCQIHR switching model to explore the impact of imported cases and FLER implementation dates on COVID-19 in Chongqing. The results indicate that strict PCIs can significantly reduce the effective reproduction number, increase the tracing and quarantining rates for close contacts and the diagnosis and isolation rates for non-hospitalized infectious cases, and reduce the contact rate and misdetection rate, thus facilitating quick epidemic control. The simulation results indicate that if strict PCIs are implemented 10 days in advance,



Fig. 4. Illustration of the fitting result of model (1) in Chongqing. The solid blue line represents the model-predicted daily data, and the actual data are shown as red points. Light blue areas represent the 95% confidence interval (CIs) of model predictions. *S*(*t*), susceptible; *C*(*t*), close contacts; *Q*(*t*), quarantined close contacts; *I*(*t*), non-hospitalized infectious cases; *H*(*t*), hospitalized infectious cases; *R*(*t*), removed cases; *Q*_c(*t*), accumulative close contacts released from quarantine. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

the number of infected cases will be reduced by half; however, if the implementation of strict PCIs is delayed by 10 days, the cumulative number of infectious cases will increase by 5 times. The simulation results also indicate that the scale of the epidemic exhibits a significant linear relationship with the number of imported cases.

The prevention and control policies implemented by the government and medical institutions are multifaceted and include the quarantine of close contacts, the isolation of infectious cases, the implementation of large-scale nucleic acid testing, the strengthening of nosocomial infection management, the prevention of nosocomial infection, the control of infection sources, the strict prevention of imported cases, the control of transmission routes, the protection of susceptible populations, etc. (Liang et al., 2020). In this study, the beneficial effects of strict PCIs can be explained by the significant increases in tracing and quarantining rates for close contacts, the diagnosis and quarantine rates for nonhospitalized infectious cases, and the recovery rates and significant decreases in the rate of contact between susceptible subjects and nonhospitalized infectious cases and the misdetection rate in the later period. These results are consistent with previous epidemiological survey results in other provinces of mainland China and in other countries (Giordano et al., 2020; Li et al., 2020; Tang et al., 2020). Tang et al. conclude that the tracing and quarantine of close contacts and isolation of infectious cases are two basic measures that determine COVID-19 trends and that a long time may be required to fully control the epidemic (Tang et al., 2020). A study conducted in Italy also showed that restrictive social distancing measures combined with large-scale testing and the tracing and quarantine of close contacts can limit COVID-19, further revealing the key role of strict measures (Giordano et al., 2020). The results of this study showed that the mean effective reproduction number decreased rapidly after implementation of FLER, which is consistent with the fact that COVID-19 was well controlled in Chongqing in February 2020.

This study mainly discusses the impact of the number of imported cases and the FLER implementation date on the development of the epidemic. The earlier strict PCIs are implemented, the smaller the final scale of the epidemic. Travel restrictions and other PCIs can be enacted as public health measures by national and international institutions, and the sooner, the better (Li et al., 2020). The simulation results in this



Fig. 5. Comparison of four PCI parameters before and after implementation of the first-level emergency response. (A) contact rate β , (B) quarantine rate k_1 , (C) misdetection rate ε , and (D) isolation rate k_2 . *: P < 0.05.



Fig. 6. Simulation results for cumulative quarantined close contacts (A) and cumulative hospitalized cases (B) using different numbers of imported cases and different FLER implementation dates. The black, red and green points are the three actual reported data points (Chongqing, 2021). FLER, first-level emergency response. The shaded areas represent the 95% CI of the corresponding solid lines. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

study indicate that the implementation of strict PCIs 10 days in advance will reduce the number of quarantined close contacts and hospitalized cases by half. Therefore, once an (imported) infectious case is detected, the early strict PCIs can effectively reduce the utilization of medical resources and the cost of epidemic prevention.

We also found that the final scale of the epidemic is significantly proportional to the number of imported cases. Currently, the number of imported cases is increasing significantly, especially in international tourist centers such as Beijing, Shanghai, Guangzhou, and Chongqing, generating great pressure on epidemic prevention and control (Chen et al., 2020). Furthermore, due to the rapid mutation of SARS-CoV-2, imported cases have caused multiple sporadic outbreaks in China. It is imperative to understand the impact of imported cases on the epidemic. When strict PCIs are implemented, the simulation results indicate

significant linear relationships between the number of imported cases and the prevalence and medical burden. Due to the ongoing COVID-19 pandemic around the world, self-protection awareness and adherence to social distancing have improved (Chen et al., 2020). Governments at all levels are also calling on communities to adopt prevention measures to reduce nonessential contact between residents (Liang et al., 2020). In addition, COVID-19 vaccinations and strict PCIs after outbreaks may be the potential causes of the slight differences between the results simulated by the model and the actual scenarios in 2021.

The PCIs brings great social, economic, political etc. impact on the local population. The strict measures that the local government timely takes controlled the source of infection and cut off the transmission pathways. The number of quarantined close contacts and hospitalized cases was dramatically reduced after a period of strict measures such as the closed management of residential communities, contact tracing, increased isolation rate, and decreased misdetection rate, which saved a considerable amount of medical and social resources. Moreover, local government also enforces contact tracing and published the activity path of confirmed cases anonymously, ensuring the safety and stability of the overall social situation. Initially, the economic impact of COVID-19 on the Chinese economy is huge, but likely transitory. China's policy responses to this shock such as fiscal, monetary and institutional measures make a rapid economic rebound and recently Chongqing becomes one of cities with GDP over 1 trillion yuan (Xinhua, 2022).

The current study still remains some limitations. First, asymptomatic infected cases were not considered in the modeling and treated as symptomatic infection in the three practical scenarios. Thus, we need additional study to investigate their impact on the PCIs of COVID-19. Second, the exact date when a close contact develops clinical symptoms relies on patients' self-reports, which may degrade the reliability of the daily number of non-hospitalized infectious cases (I(t)).

Ethical approvals

No human subjects were involved in this work and therefore ethical approvals were not required for the development of this manuscript.

Credit author statement

Jiang Long: Conceptualization, Methodology, Software, Validation, Investigation, Resources, Data Curation, Writing - Original Draft, Funding acquisition. Chenxi Dai: Conceptualization, Methodology, Software, Validation, Formal analysis, Data Curation, Writing - Original Draft, Writing - Review & Editing. Shanshan Kuang: Investigation, Resources, Data Curation. Han Zhao: Investigation, Resources, Data Curation. Dan Liu: Software, Formal analysis, Data Curation. Qing Luo: Software, Formal analysis, Data Curation. Kaifa Wang: Conceptualization, Methodology, Software, Validation, Formal analysis, Data Curation, Writing - Original Draft, Writing - Review & Editing, Funding acquisition.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.meegid.2022.105270.

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