

RESEARCH

Multi-chain Fudan-CCDC model for COVID-19 — a revisit to Singapore's case

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Background: COVID-19 has been impacting on the whole world critically and constantly since late December 2019. Rapidly increasing infections has raised intense worldwide attention. How to model the evolution of COVID-19 effectively and efficiently is of great significance for prevention and control.

Methods: We propose the multi-chain Fudan-CCDC model based on the original single-chain model in [Shao *et al.* 2020] to describe the evolution of COVID-19 in Singapore. Multi-chains can be considered as the superposition of several single chains with different characteristics. We identify the parameters of models by minimizing the penalty function.

Results: The numerical simulation results exhibit the multi-chain model performs well on data fitting. Though unsteady the increments are, they could still fall within the range of $\pm 30\%$ fluctuation from simulation results.

Conclusion: The multi-chain Fudan-CCDC model provides an effective way to early detect the appearance of imported infectors and super spreaders and forecast a second outbreak. It can also explain the data from those countries where the single-chain model shows deviation from the data.

Keywords: COVID-19; Singapore; multi-chain Fudan-CCDC model

Author summary: The COVID-19 pandemic has aroused global concern. Timely judgment and accurate estimation play an essential role in epidemic prevention and control. We propose one multi-chain Fudan-CCDC model and use the model to fit the curve of infected cases. Two important rates are considered in the model: one is the infection rate and the other is the isolation rate, moreover, the multi-chain property is constructed to reflect the outbreaks in different time. By identifying different transmission chains, our model explains the epidemic multi-chain evolution in Singapore, and suggests the great importance of controlling the imported cases.

INTRODUCTION

The Fudan-CCDC model [1–3] was proposed by Cheng's group at Fudan University to study the evolution of COVID-19. The model took advantages of the time delay process introduced by the TDD-NCP model [4–9] proposed previously also by Cheng's group, and developed new convolution kernels for the time delay terms by applying several time distributions acquired from an important paper [10] by CCDC (China Center for Disease

Control and Prevention). Both the TDD-NCP model and the Fudan-CCDC model are single-chain models and have been performed well in analyzing the evolution of COVID-19 in China, and its early stage of global transmission [11,12].

The multi-chain model was put forward and developed in the context of the second outbreak in some regions. We first had this idea when analyzing the epidemic situation of South Korea. In Fig. 1, there was a sudden turn in growth rate, which inferred that a stronger transmission

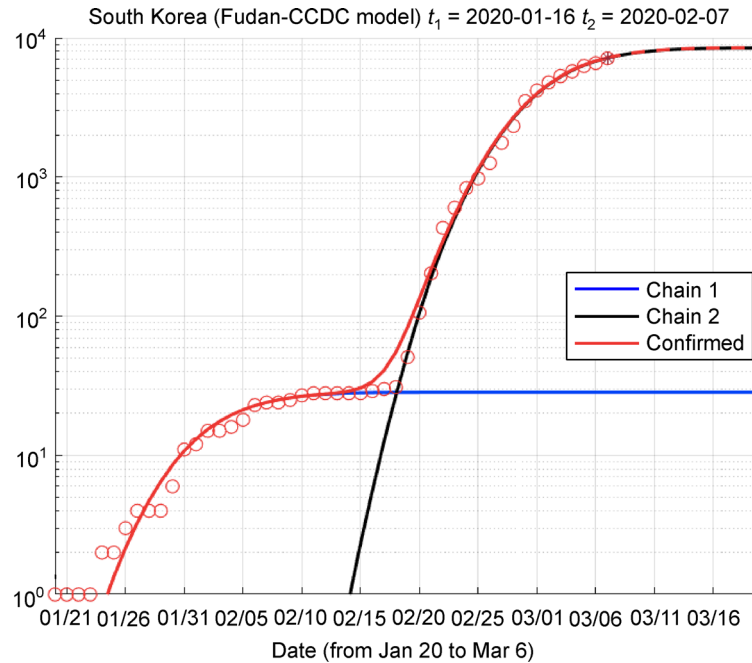


Figure 1. Semi-log plot of data fitting for South Korea, suggesting two chains in transmission. Red circles: data, daily number of cumulative confirmed cases in South Korea, Jan 20 to Mar 6; Red line: curve fitting for data; blue line: the first chain; black line: the second chain. The red, blue, black lines are all estimated by the model.

chain might have emerged.

With the further spread of the global pandemic, such a sudden change in growth rate has been observed in the cases of other countries as well. And the curves fitted by the Fudan-CCDC model sometimes deviate from the data. Singapore is one of the examples. We had studied Singapore's case in [12], and based on the data till Feb 25, we concluded that Singapore had been successful in disease prevention and control. Since then, our group has

been continually tracking the data. Unexpectedly, in late February, a sudden rise occurred (Fig. 2B).

We show in Fig. 2 the curve fitting for Singapore's data by the Fudan-CCDC model, on Feb 17 and Mar 1, respectively. We see in Fig. 2A that on Feb 17, the Fudan-CCDC model had predicted that the increment of confirmed cases would be zero on Feb 27, and remained stable for the next ten days. However, on the crucial day Feb 27, an unexpected rise occurred in Singapore's data

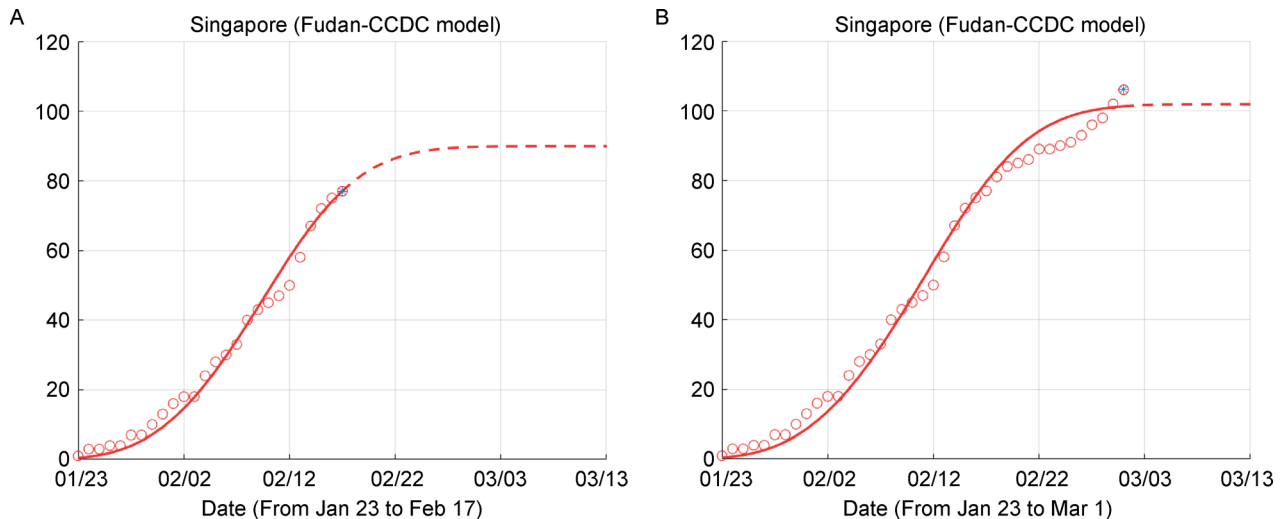


Figure 2. Data fitting for Singapore. (A) Jan 23 to Feb 17; (B) Jan 23 to Mar 1. Red circles: data, the daily number of cumulative confirmed cases in Singapore; red line: curve fitting for data; dotted line: predictions.

(see Fig. 2B), which caused our vigilance. Till Mar 1, this new upward trend was so obvious that it could not be explained by the single chain Fudan-CCDC model any longer. Therefore, we began to consider the application of the multi-chain Fudan-CCDC model, and revisit Singapore's case.

RESULTS

There are two important parameters in our model, one is the infection rate β , which depicts the speed of virus transmission, and the other is the isolation rate ℓ , which is related to the strength of government measures and the public's awareness of prevention.

The two-chain and three-chain models until Apr 4

Figures 3 and 4 show the evolutions of COVID-19 in Singapore and its possible future trends, based on the two-chain model. The scattered red circles are the data: the number of cumulative confirmed cases (Fig. 3) and its increment (Fig. 4) from Jan 23 to Apr 4. In Fig. 3, we illustrate the four “most optimized” fitting curves (in solid lines) for the data, and their predictions (in dotted lines) by the model, in the order of red, green, blue and purple, respectively. For the convenience to recognize, the ‘very most optimized’ fitting curve is drawn in a full solid red line, including its prediction. Details of the optimization methods are described in the section “Materials and methods”. We can see from Fig. 3A that based on the two-chain model, Singapore is expected to have zero increment of confirmed cases on Apr 26, and the total number of infections will be around 1500, if no other

transmission chains arise in the future. Figure 3B is the semi-log form of Fig. 3A, and it clearly demonstrates the good curve fitting of the sudden rise in growth rate around Mar 3.

Figure 4A shows the fitting for the daily increment based on the two-chain Fudan CCDC model. There are two peaks in the curves, suggesting possible new sources of transmission. Then we single out the “most optimized” curve (the red line) in Fig. 4B. We see that most of the data fall in this area, indicating the effectiveness of the model. Besides, the two chains are shown in green and blue dotted lines, respectively.

Now we consider the three-chain Fudan-CCDC model. Figures 5 and 6 show the epidemic evolution in Singapore based on the three-chain model. The legends are the same as in the previous context. We can see from Fig. 5A that under the three-chain model, Singapore is expected to have zero increment of confirmed cases on May 4, and the total number of infections will be around 1,900, if no other chains of transmission arise in the future.

In addition, we find that the end date of COVID-19 based on the three-chain model is later than that based on the two-chain model, and the number of total infected is also significantly higher. This is because the time of zero increment will now arrive until all the transmission chains come to end.

Warning a possible new outbreak in Singapore on Apr 12

Figures 7 and 8 show predictions of the cumulative and incremental confirmed cases in Singapore based on the multi-chain model, with data observed from Jan 23 to

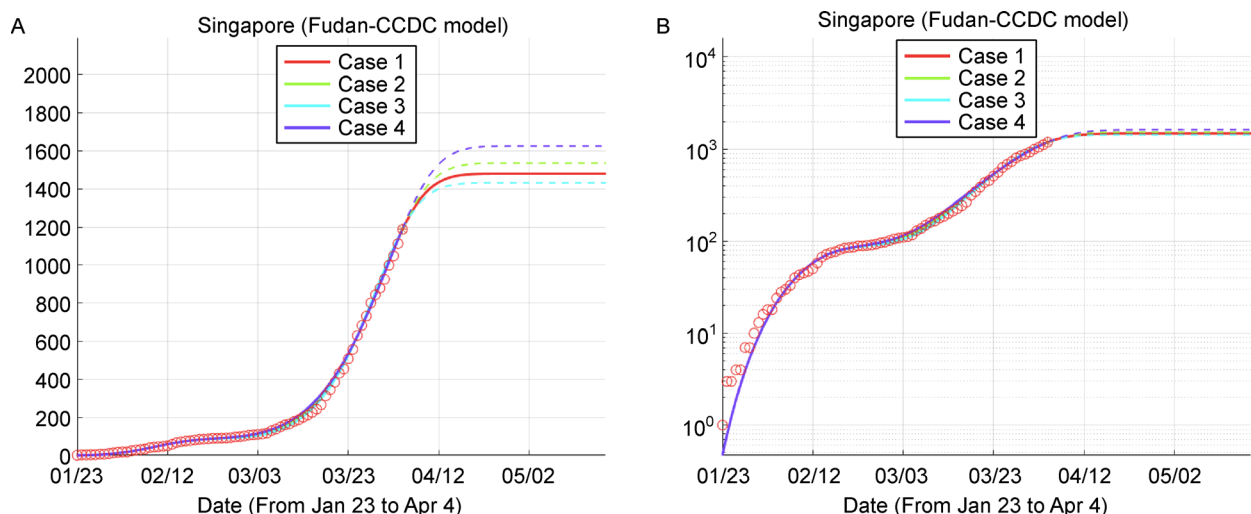


Figure 3. Evolution of COVID-19 based on the two-chain Fudan-CCDC model, Jan 23 – Apr 4. (A) Evolution of number of cumulative confirmed cases based on the two-chain Fudan-CCDC model. Red circles: data; red, green, blue and purple lines: the four ‘most optimized’ fitting curves and their predictions. (B) The semi-log form of panel A.

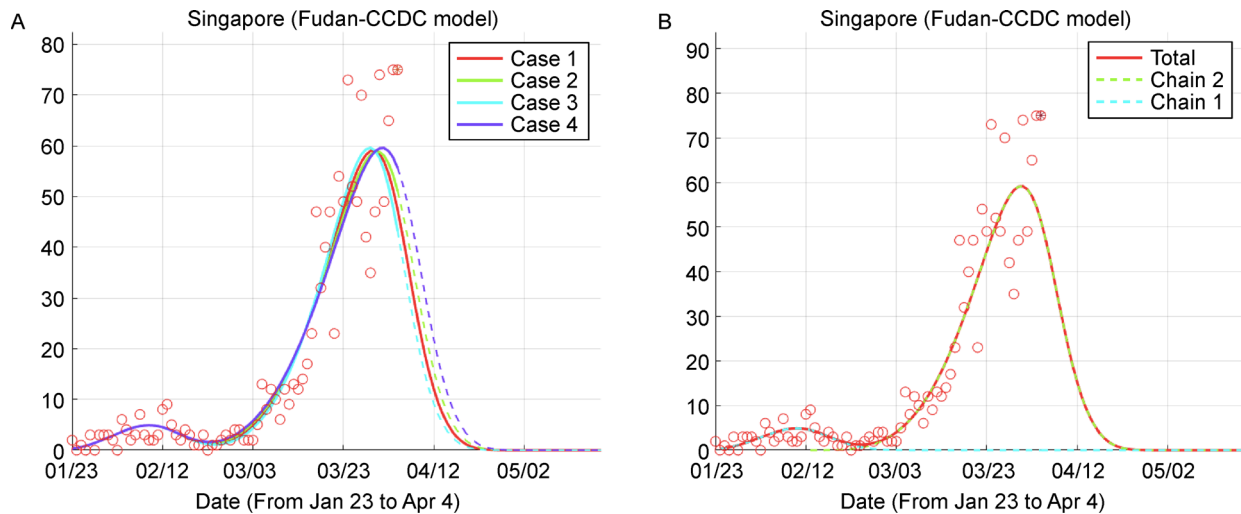


Figure 4. Evolution of the increment of confirmed cases based on the two-chain Fudan-CCDC model. (A) Red circles: data; Red, green, blue and purple lines: the four “most optimized” fitting curves and their predictions. (B) Red circles: data; red line: the “very most optimized” fitting curve; blue dotted line: the first chain; green dotted line: the second chain.

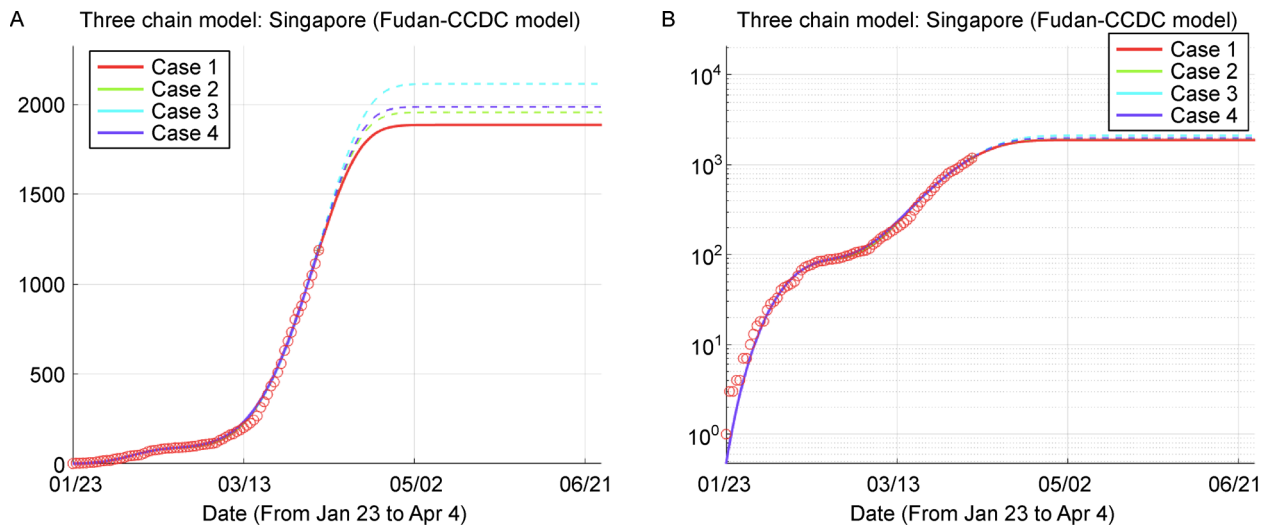


Figure 5. Evolution of COVID-19 based on the three-chain Fudan-CCDC model, Jan 23 – Apr 4. (A) Evolution of number of cumulative confirmed cases based on the three-chain Fudan-CCDC model. (B) The semi-log form of panel A. The legends are the same as in Fig. 3.

Apr 12. Table 1 presents Parameters for two-chain model and three-chain model, with data observed from Jan 23 to Apr 12.

The predictions of the two-chain model and the three-chain model both show an uncontrollable trend of the epidemic. These two models both pass on the information that Singapore might be faced with a very risky situation of rapidly increasing cases. Therefore, strong measures are urgently needed to contain the epidemic.

On April 12, we observed that in our prediction both the two-chain model and the three-chain model did not

converge, and we predicted a wave of outbreaks in Singapore. The later evolution indeed corroborated that.

Two-stage ℓ assumption for the fourth chain

Figure 9A is plotted based on data from Jan 23 to Apr 12, which shows an unstopping trend. The model performs a precise prediction on evolution of 10 days later. Due to quarantine measurements of the government, the increment of confirmed cases drops gradually from Apr 23. We hereby introduced the assumption of two-stage ℓ for the

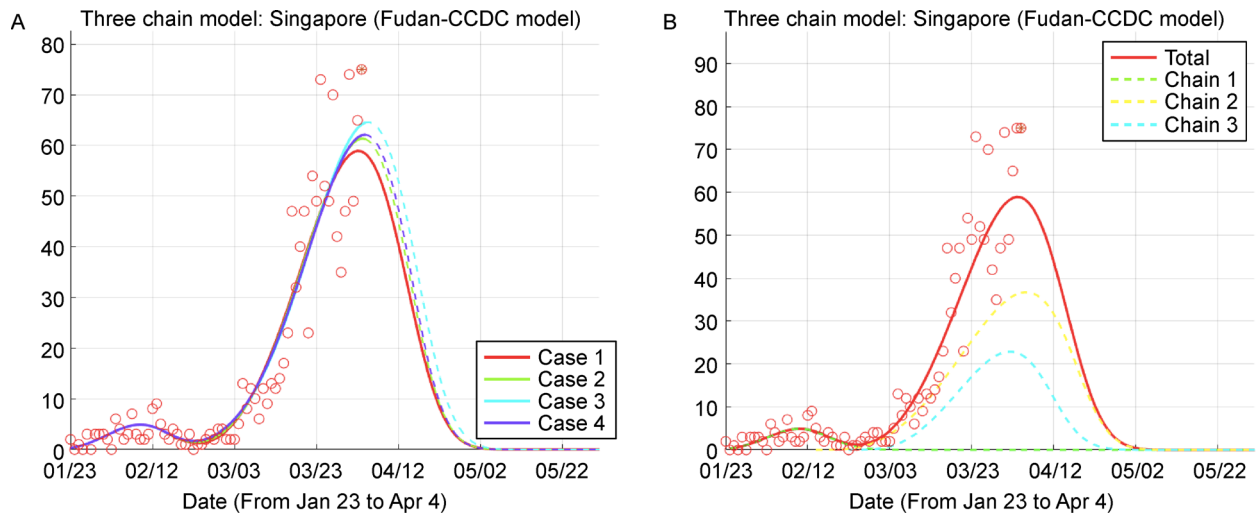


Figure 6. Evolution of the increment of confirmed cases based on the three-chain Fudan-CCDC model. The legends are the same as in Fig. 4.

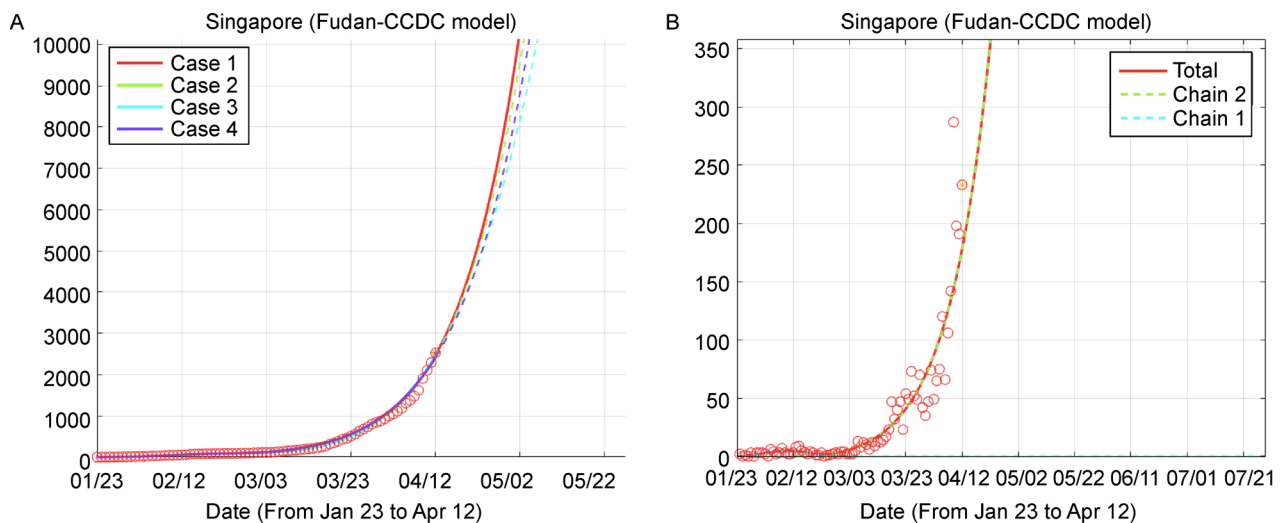


Figure 7. Evolution of COVID-19 based on the two-chain Fudan-CCDC model, Jan 23 – Apr 12. (A) Number of cumulative confirmed cases. (B) Increment (daily confirmed cases).

fourth chain and applied the modified parameter in analysis on Apr 30, shown in Fig. 9B.

Parameter values are obtained by data fitting with optimization programs, which are collected in Table 2.

Comparison of models with different chain numbers

With the data of Jan 23–Mar 19, we conducted experiments on models with different chain numbers to see the difference among the models with different chain numbers, and the results are shown in Figs. 10 and 11.

Here we list the parameters in Table 2 or the multi-

chain model based on the data from Jan 23 to May 31.

New two-chain model with two-stage parameters

Though the evolution of the epidemic so far can be well fitted by the multi-chain model, the drawback is obvious that more chains would be needed if more cases appear. Here we introduce new two-chain model. The difference is that the parameters β and ℓ are both two-stages, that is to say, β and ℓ will be changed at some time t_c in every chain (see Table 3).

Figure 12A and B (the semi-log plot) shows that the number of cumulative confirmed cases can be fitted well

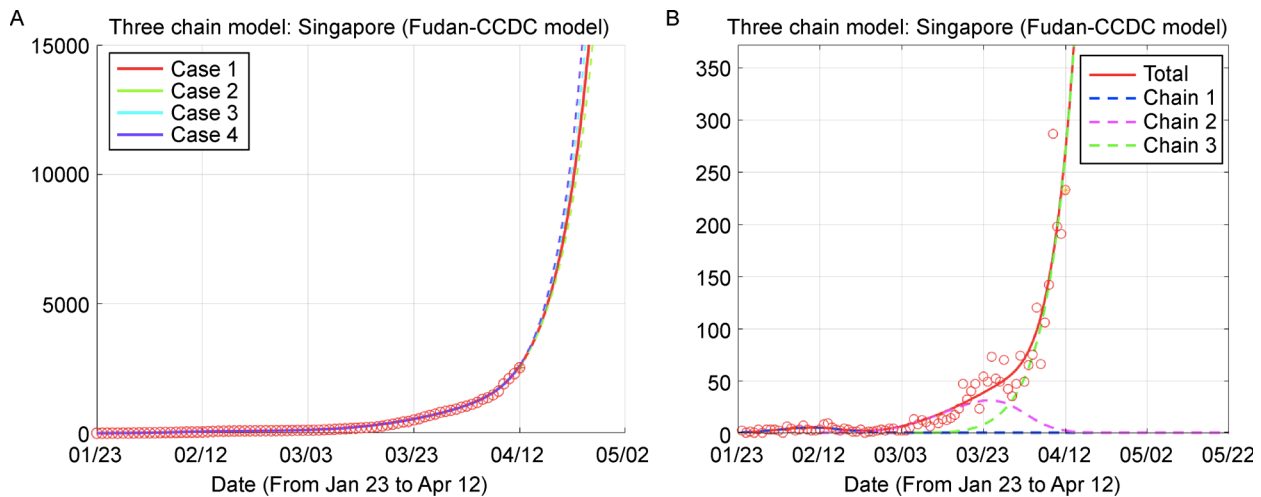


Figure 8. Evolution of COVID-19 based on the three-chain Fudan-CCDC model, Jan 23 – Apr 12. (A) Number of cumulative confirmed cases. (B) Increment (daily confirmed cases).

Table 1 Parameters for two-chain model and three-chain model, Jan 23 – Apr 12

| | The two-chain model | | | The three-chain model | | |
|---------|---------------------|---------|---------|-----------------------|---------|---------|
| | Date | β | ℓ | Date | β | ℓ |
| Chain 1 | Jan 15 | 0.33704 | 0.50507 | Jan 15 | 0.33704 | 0.50507 |
| Chain 2 | Feb 12 | 0.45546 | 0.66223 | Feb 13 | 0.40577 | 0.56929 |
| Chain 3 | — | — | — | Feb 21 | 0.43645 | 0.56929 |

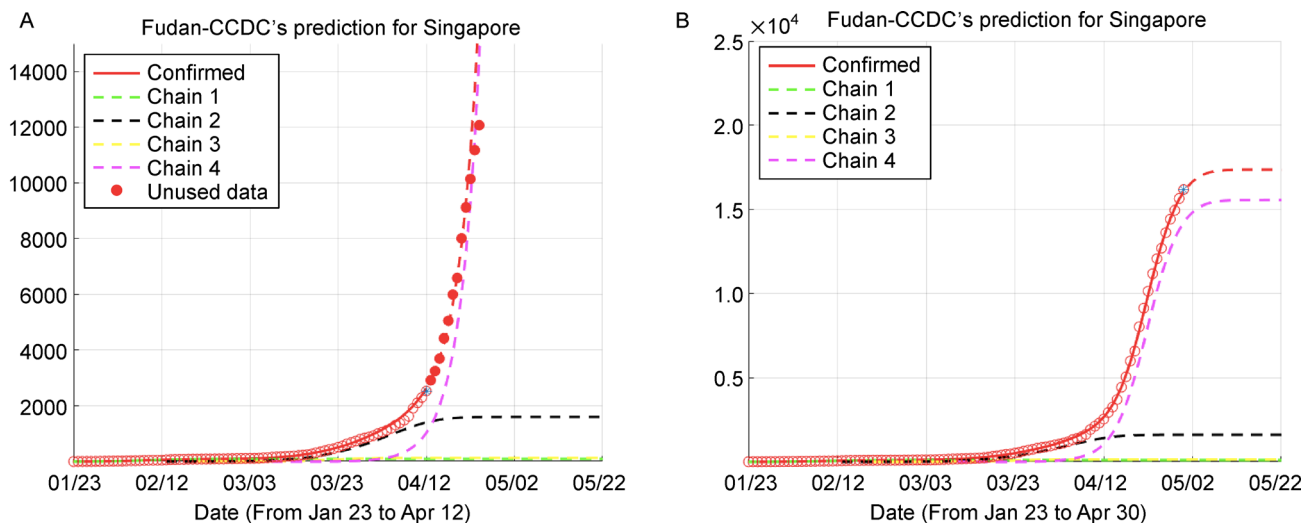


Figure 9. Evolution of COVID-19 based on the multi-chain model. (A) Prediction of three-chain model, where the hollow circle is the public data used in parameter identification, the solid circle is the subsequent trend between Apr 13 and Apr 22. (B) Number of cumulative confirmed cases, with a two-stage model.

by the new chain model. Figure 13A and B (the semi-log plot) shows the fitting for the daily increment based on the new two-chain Fudan CCDC model, where only the new

cases which are great than 10 are plotted. One advantage of the two-stages model is that the trend of the evolution is clear.

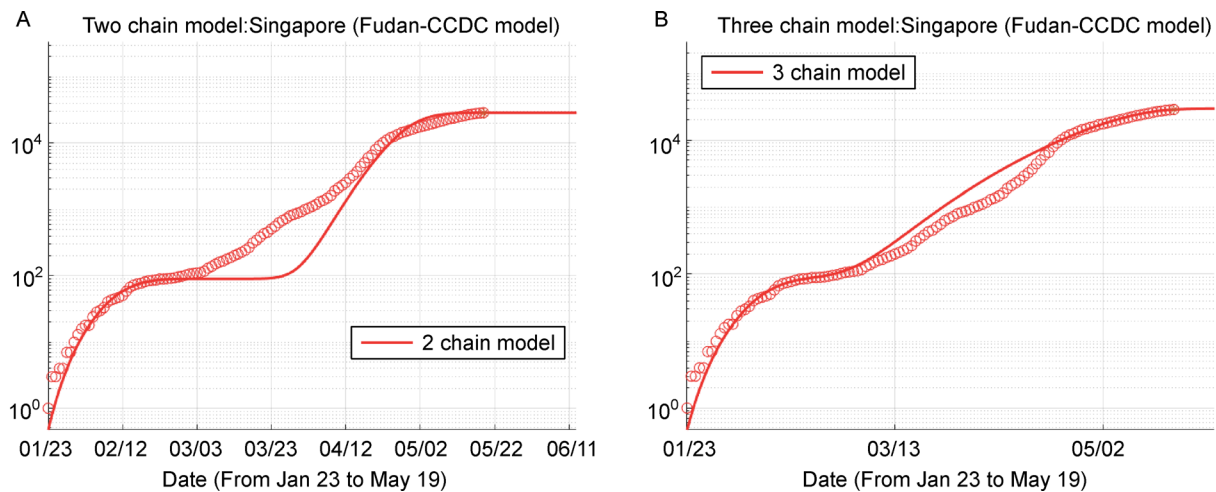


Figure 10. Evolution of COVID-19 based on the multi-chain model, Jan 23 – May 19. (A) Number of cumulative confirmed cases for two-chain model. (B) Number of cumulative confirmed cases for three-chain model.

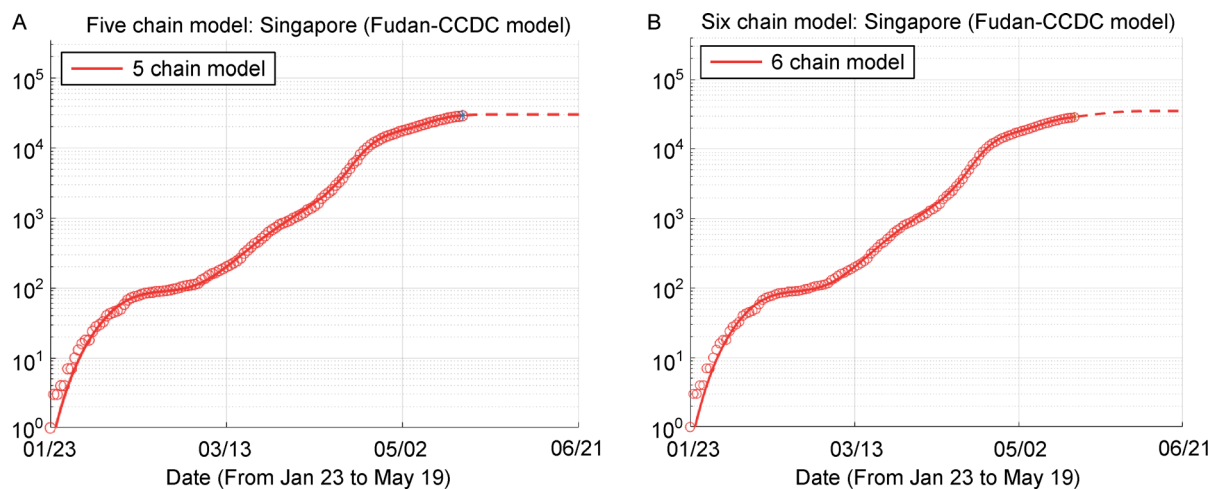


Figure 11. Evolution of COVID-19 based on the multi-chain model, Jan 23 – May 19. (A) Number of cumulative confirmed cases for five-chain model. (B) Number of cumulative confirmed cases for six-chain model.

Table 2 Values of the parameters identified by the multi-chain models, Jan 23 – May 31

| | The six-chain mode | | | The seven-chain mode | | |
|---------|--------------------|---------|---------|----------------------|---------|---------|
| | Date | β | ℓ | Date | β | ℓ |
| Chain 1 | Jan 15 | 0.33704 | 0.50507 | Jan 15 | 0.33704 | 0.50507 |
| Chain 2 | Feb 13 | 0.43894 | 0.62332 | Feb 13 | 0.43894 | 0.62332 |
| Chain 3 | Feb 20 | 0.41690 | 0.62332 | Feb 20 | 0.41690 | 0.62332 |
| Chain 4 | Mar 10 | 0.50293 | 0.62332 | Mar 10 | 0.50293 | 0.62332 |
| | Apr 09 | 0.50293 | 1.7021 | Apr 09 | 0.50293 | 1.7021 |
| Chain 5 | Apr 05 | 0.80367 | 0.62332 | Apr 05 | 0.80413 | 1.7021 |
| Chain 6 | Apr 21 | 0.80074 | 1.7021 | Apr 21 | 0.80313 | 1.7021 |
| Chain 7 | – | – | – | May 7 | 0.79986 | 1.7021 |

Table 3 Parameters for the new two-chain model with two-stages parameters, Jan 23 – June 13

| | β_1 | β_2 | ℓ_1 | ℓ_2 | t_0 | t_c |
|---------|-----------|-----------|----------|----------|------------|------------|
| Chain 1 | 0.2349 | 0.5728 | 0.2444 | 0.8248 | 2019-12-28 | 2020-02-24 |
| Chain 2 | 0.3821 | 0.1443 | 0.000 | 0.1470 | 2020-03-09 | 2020-04-06 |

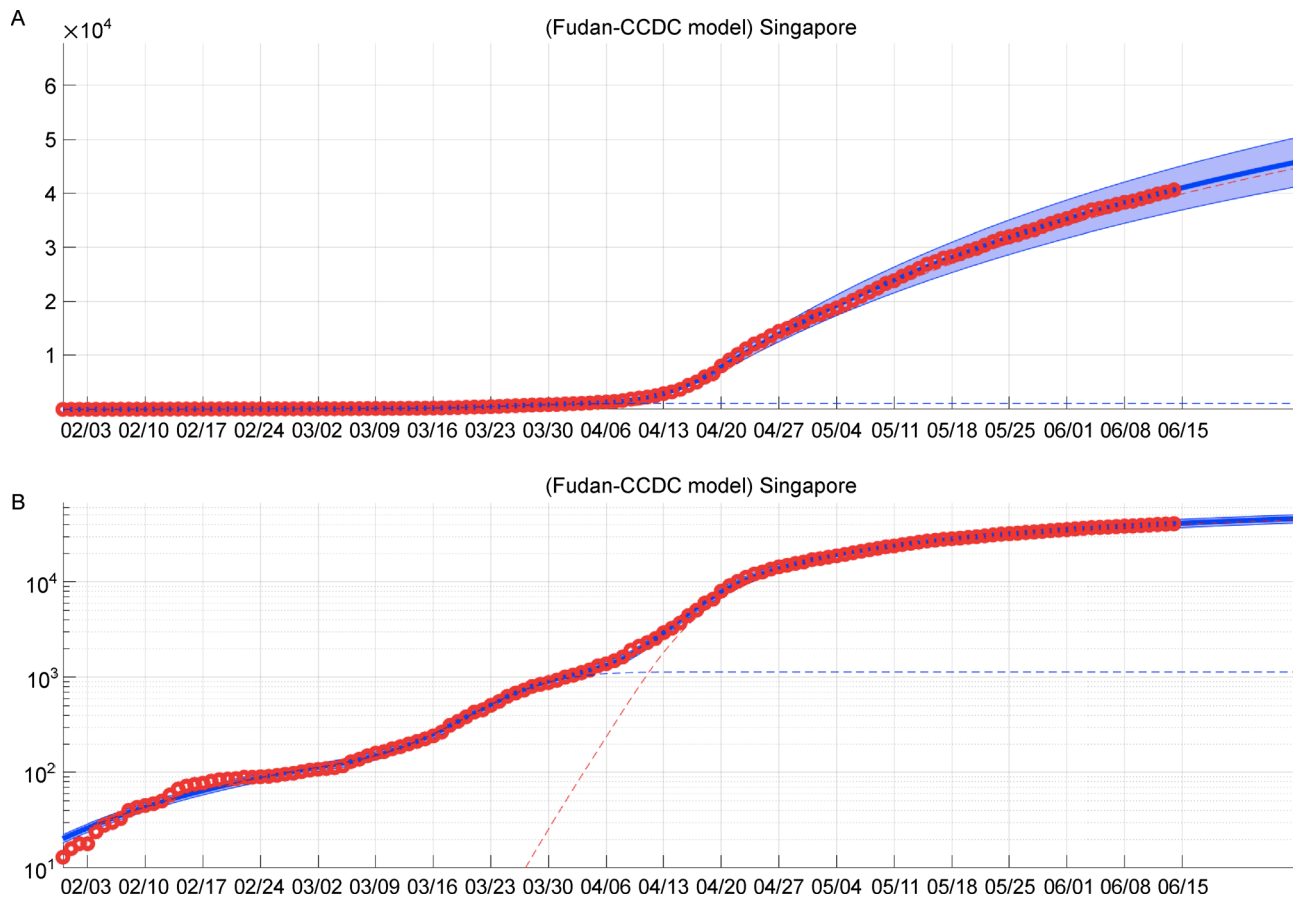


Figure 12. Evolution of COVID-19 based on the new two-chain Fudan-CCDC model, Feb 03 – June 15. (A) Evolution of number of cumulative confirmed cases based on the new two-chain Fudan-CCDC model. Red circles: data; blue lines: fitting curves and their predictions. Light blue area: $\pm 10\%$ fluctuation of the blue line. (B) The semi-log form of panel A.

DISCUSSION

Advantages of the multi-chain Fudan-CCDC model

The multi-chain Fudan-CCDC model has given a better explanation of the epidemic evolution in Singapore, and perhaps other nations as well. Compared to single chain models, the multi-chain Fudan-CCDC model shows the following advantages: (i) It better fits the data in history; (ii) By identifying different sets of parameters for different chains, it is able to simulate the multi-peaks in the daily increment data, which the single-chain models can hardly explain; (iii) It illustrates the importance of controlling the imported cases. Since zero increment depends on when the last chain vanishes, it is difficult to

completely end the epidemic unless all sources of transmission are detected and blocked.

With more chains, the model could better interpret the epidemic and gain more accurate predictions.

Detection of new chains

Now we revisit Fig. 2 to discuss when to introduce new chains. In Fig. 2B, there is an obvious shallow pit around Feb 27 along with the data trend, illustrating that the number of confirmed cases was about to flatten, but rose up again immediately. This shallow pit acts as a signal to consider new chains in the model, warning new sources of transmission. In fact, in Fig. 2A, a shallow pit has already occurred around Feb 12. This pit was not so obvious as

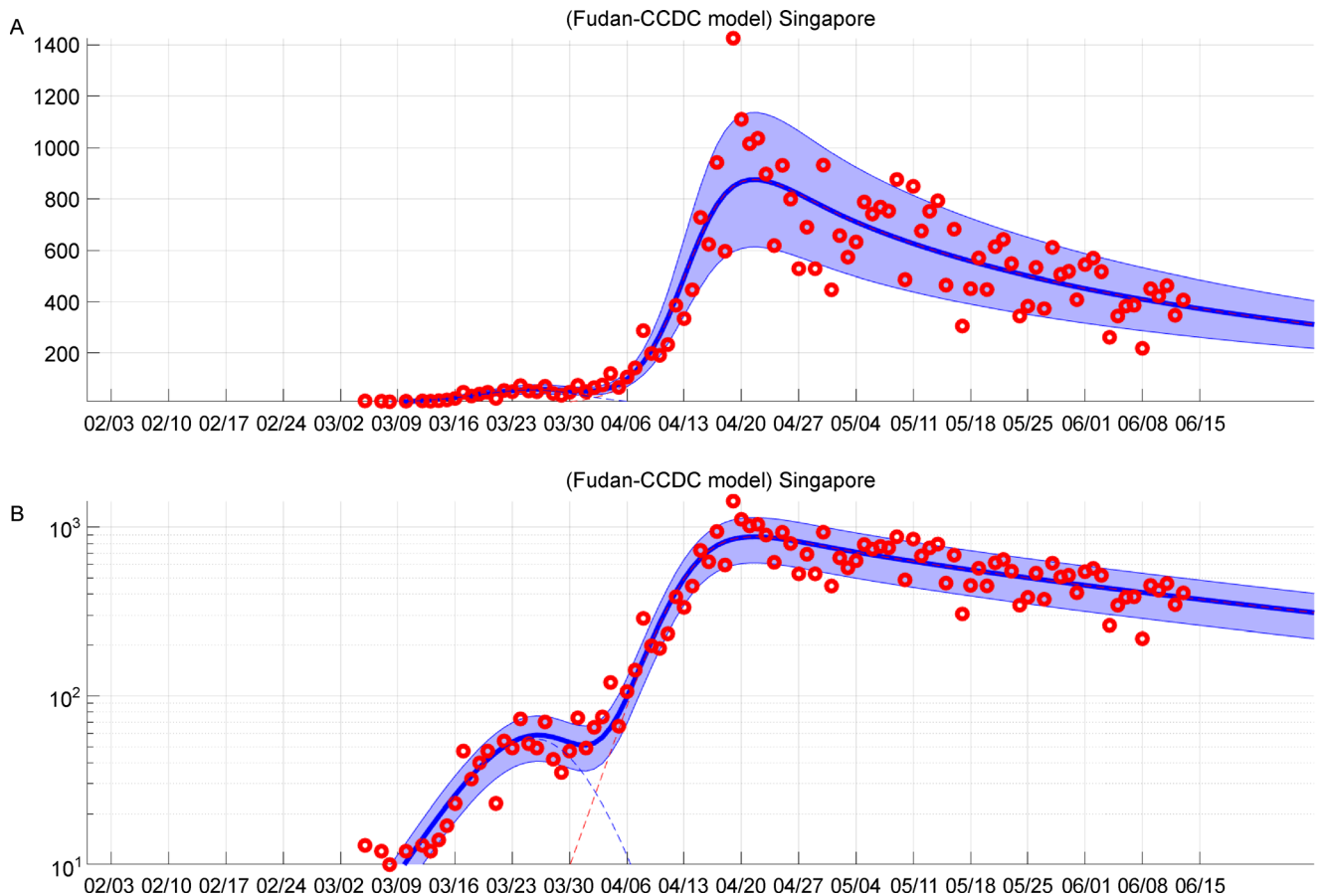


Figure 13. Evolution of COVID-19 increment based on the new two-chain Fudan-CCDC model, Feb 3 – June 15.
(A) Evolution of number of cumulative confirmed cases based on the new two-chain Fudan-CCDC model. Red circles: data; blue lines: fitting curves and their predictions. Light blue area: $\pm 30\%$ fluctuation of the blue line. (B) The semi-log form of panel A.

the next one around Feb 27, and was likely to be treated as fluctuation of the data. Besides, more data are needed to form a new transmission chain. Therefore, carefully detecting and analyzing these shallow pits plays an important role in finding new chains.

Additivity

One may find that the multi-chain model is just an addition of multiple single-chain models. In fact, the single-chain and multi-chain Fudan-CCDC models are both linear ones, so they enjoy the convenience of additivity. For the traditional nonlinear epidemic models such as the SIR and SEIR models, the model also can be linearized, and SEIJR model is developed [13]. The property of additivity is friendly, as it allows us to construct new models of not only multiple chains, but also multiple districts, which might be applicable to other countries.

In conclusion, the multi-chain Fudan-CCDC model is suitable for Singapore. It has made possible the early detection of imported infectors and super spreaders, and is

able to suggest timely adjustment for epidemic control. Based on the experiences in Singapore, it is very difficult to control the transmission since the infected people will increase exponentially even if very small infected ones are not be isolated or treated, and it is important to trace the curve of the cases.

MATERIALS AND METHODS

In this section, we introduce two models, the single-chain Fudan-CCDC model and the multi-chain Fudan-CCDC model respectively. The single-chain Fudan-CCDC model describes the evolution of COVID-19 based on the assumption that all the new cases originate from the initial source, *i.e.*, there is only one chain of transmission. And the multi-chain Fudan-CCDC model assumes that due to new imported cases, new super spreaders, or the different transmission characteristics of different regions, there may be two or more single chains of transmission in the country.

The single-chain Fudan-CCDC model

As is mentioned in [1–3,11,12], our single-chain Fudan-CCDC model is as follows:

$$\begin{aligned} I(k+1) &= I(k) + \beta I_0(k), \\ J(k+1) &= J(k) + \beta \sum_i I_0(k-i) f_4(i), \\ G(k+1) &= G(k) + \ell \sum_i I_0(k-i) f_2(i) \\ &\quad - \ell \sum_i I_0(k-i) f_4(i), \\ I_0(k) &= I(k) - J(k) - G(k), \end{aligned}$$

where $I(k)$ and $J(k)$ represent the cumulative infected people and the cumulative confirmed cases at day k , respectively, and $G(k)$ is the instant (not cumulative) number of infected isolated not yet confirmed by the hospital. The infected ones are put into isolation once they show illness symptoms, and the newly confirmed should be removed from the isolated group. $I_0(k)$ is the number of people who are potentially infectious to healthy ones—they are infected actually but not in quarantine or hospitalization. β and ℓ represent the infection rate and the isolation rate respectively, which may be changed in different time periods. Some transition probabilities are used in our model: $f_2(k)$ and $f_4(k)$ are the transition probabilities from infection to illness onset, and from infection to hospitalization, respectively. Here we reconstruct them from one important paper [10] by CCDC:

- $f_2(t)$: the transition probability from infection to illness onset is one log-normal distribution of

$$f_2(t) = \frac{0.5977}{t} e^{-1.105(\ln(t) - 1.417)^2},$$

- $f_3(t)$: the transition probability from illness onset to hospitalization is one Weibull distribution of

$$f_3(t) = 0.005557 t^{1.641} e^{-0.002105 t^{2.641}},$$

- $f_4(t)$: the transition probability from infection to hospitalization, which can be calculated via the convolution of $f_2(t)$ and $f_3(t)$, and may be approximated by

$$\begin{aligned} f_4(t) &= f_2 * f_3(t) \\ &\approx 0.06244 e^{-\left(\frac{t-10.87}{5.378}\right)^2} + 0.03322 e^{-\left(\frac{t-15.97}{6.9}\right)^2}. \end{aligned}$$

In the implementation, the supports of f_2 and f_4 is set by 21 days and 42 days respectively [10]. This time delay dynamic system is applicable to simulations of COVID-19 in the countries where community transmission exists, while the kernels like $f_2(k)$ and $f_4(k)$ might vary from countries to countries.

The model can be used to fit the reported numbers of the cumulative confirmed cases and predict the evolution of epidemic, and the details can be found in [1–3,11,12].

The multi-chain Fudan-CCDC model

In the multi-chain Fudan-CCDC model, the final epidemic transmission chain is the superposition of several single chains:

$$\begin{aligned} I^m(k+1) &= I^m(k) + \beta^m I_0^m(k), \\ J^m(k+1) &= J^m(k) + \beta^m \sum_i I_0^m(k-i) f_4(i), \\ G^m(k+1) &= G^m(k) + \ell^m \sum_i I_0^m(k-i) f_2(i) \\ &\quad - \ell^m \sum_i I_0^m(k-i) f_4(i), \\ I_0^m(k) &= I^m(k) - J^m(k) - G^m(k), \end{aligned}$$

and we obtain the sum forms:

$$I = \sum I^m, J = \sum J^m, G = \sum G^m, m = 1, 2, 3, \dots, M,$$

where t^m is the start time of the m -th source.

Specifically, we have applied the two-chain and the three-chain models to analyze the situations in Singapore. We suppose that there is a new chain when a sudden turn appears in the curve of reported confirmed cases. For both the two-chain model and the three-chain model, infection rate β and isolation rate ℓ of the first chain are obtained by fitting data before a specific time node. The differences lie in assumptions and parameters to be identified.

Optimization method for parameter identification

Parameter identification is an optimization process. There are two kinds of decision variables in this optimization, time nodes t and the model parameters. We suppose that more recent data have more importance and efficiency for us to predict the trend. So we established the objective function as follows:

$$\min_{t, \beta, \ell} f(\beta, \ell; t)$$

where

$$f(\beta, \ell; t) = \omega \frac{\|J - data\|_2}{\|data\|_2} + \frac{\|\max(J - data, 0)\|_{1,t}}{\|data\|_{1,t}}.$$

Note that the first term is to minimize the difference between values of data and simulations, *i.e.*, the empirical risk and the second term is to minimize the structural risk. ω is the weight of the penalty term, and t contains only t^2 in the two-chain model, and (t^2, t^3) in the three-chain model.

Time nodes. Since public data are discrete along time and time nodes are dates, the grid searching method could be used to obtain the minimum value of the objective function. As characteristics of the first chain is known, so we only need to do grid searching of other chains.

Model parameters. The parameter optimization is solved by a constrained optimization problem solver.

Therefore, the whole process of optimization can be summarized as the following three steps: determine all possible time nodes; calculate the minimum of objective function for cases of different time nodes; obtain the optimal time nodes and model parameters.

Data and materials availability

The data employed in this paper are acquired from WIND (like Bloomberg), and the situation reports of the World Health Organization (<https://www.who.int>). All the data can be accessed publicly. No other data are used in this paper.

AUTHOR CONTRIBUTIONS

The algorithms are implemented by H. P., which are based on the single-chain model implemented by N. S., and designed by W. C. All authors conceived the study, carried out the analysis, discussed the results, drafted the first manuscript, critically read and revised the manuscript, and gave final approval for publication.

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COMPLIANCE WITH ETHICS GUIDELINES

The authors Hanshuang Pan, Nian Shao, Yue Yan, Xinyue Luo, Shufen Wang, Ling Ye, Jin Cheng and Wenbin Chen declare that they have no conflict of interests.

All procedures performed in studies were in accordance with the ethical standards of the institution or practice at which the studies were conducted, and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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