COVID-19 epidemic outside China: 34 founders and exponential growth

Yi Li,¹,² Meng Liang,¹ Xianhong Yin,¹ Xiaoyu Liu,¹ Meng Hao,¹ Zixin Hu,¹ Yi Wang,¹ Li Jin¹,²,³

ABSTRACT
COVID-19 raised tension both within China and internationally. Here, we used mathematical modeling to predict the trend of patient diagnosis outside China in future, with the aim of easing anxiety regarding the emergent situation. According to all diagnosis number from WHO website and combining with the transmission mode of infectious diseases, the mathematical model was fitted to predict future trend of outbreak. Daily diagnosis numbers from countries outside China were downloaded from WHO situation reports. The data used for this analysis were collected from January 21, 2020 and currently end at February 28, 2020. A simple regression model was developed based on these numbers, as follows: \[
\log_{10}(N_i + 34) = 0.0515 \times t + 2.075, \]
where \(N_i\) is the total diagnosed patient till the \(i\)-th day and \(t=1\) at February 1, 2020. Based on this model, we estimate that there were approximately 34 undetected founder patients at the beginning of the spread of COVID-19 outside China. The global trend was approximately exponential, with an increase rate of 10-fold every 19 days. Through establishment of this model, we call for worldwide strong public health actions, with reference to the experiences learned from China and Singapore.

INTRODUCTION
In early December of 2019, pneumonia cases of unknown cause emerged in Wuhan, the capital of Hubei province, China.¹ A novel coronavirus (now named SARS-CoV-2) was verified and identified as the seventh member of the enveloped RNA coronaviruses (subgenus, Sarbecovirus; subfamily, Orthocoronavirinae) using high-throughput sequencing²–⁴ as the cause of the disease, which is referred to as COVID-19. Based on the evidence from early transmission dynamics, human-to-human transmission in hospital and family settings had been accumulating¹–⁷ and occurred among close contacts since the middle of December 2019.⁸ According to WHO statistics, the accumulated number of diagnosed patients in China on August 08, 2020 was 89,057.⁹ COVID-19 raised tension both within China and internationally. Since the first case of COVID-19 pneumonia was reported from Wuhan, COVID-19 was rapidly diagnosed in patients in other Chinese cities and in neighboring countries, including Thailand, South Korea, Japan, and even a few Western countries.¹⁰–¹² On January 13, 2020, the Ministry of Public Health of Thailand reported the first imported case of laboratory-confirmed novel coronavirus (COVID-19).¹³ After that, surges in cases of COVID-19 in Italy, Japan, and Iran also heightened fears that the world is on the brink of a pandemic. Therefore, on February 28, the WHO increased the assessment of the risk of spread and impact of COVID-19 to very high at the global level. Approximately 19,187,943 reported cases and 716,075 deaths of COVID-19 have been reported to date August 08,
2020.9 The USA, Brazil, and India are currently the three most affected countries.14

Recently, considerable research resource has been devoted to conducting detailed analysis of the spread of the COVID-19 epidemic.15 16 Several parallel studies have reported that the estimated reproductive number (R0) of COVID-19 is higher than that of SARS, based on different models.17–19 Considering the superspreaders (P), hospitalized (H), and fatality class (F), an ad hoc compartmental mathematical model of the COVID-19 has been established to describe the reality of the Wuhan outbreak and predict the daily number of the confirmed cases.20 Several studies used deep learning to forecast COVID-19 infections.21 22

The disease transmission model predicted the gravity of COVID-19 in Canada using the long short-term memory (LSTM) networks.23 Data-driven estimation methods like LSTM and curve fitting were also used to evaluate the number of COVID-19 cases in India for the next 30 days and the effect of preventive measures.24

Given the limited number of data points and the complexity of the real-life situation, a simple model is expected to be more accurate for describing the spread of the virus (see Discussion section). In this study, we propose a “log-plus” model to predict the situation, which only requires daily number of total diagnoses outside China. This model assumes that there were some unobserved founder patients at the beginning of viral spread outside China and subsequent exponential growth. Despite the simplicity of our model, it fits the data well (R2=0.991). This prediction has potential practical and socially applicable significance and provides evidence that can enhance public health interventions to avoid severe outbreaks.

METHODS

Data

Daily numbers of COVID-19 diagnoses in countries outside China were downloaded from WHO situation reports (https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports). The data used in this analysis start on January 21, 2020 and end at February 28, 2020.

Model

Data were first explored by plotting log-transformed daily case numbers. A linear trend was observed in more recent data, while the fit was relatively poor for earlier time points. The presence of some undetected founder patients at the early time points were considered. Based on exploratory analysis and mathematical intuition, we proposed the following model:

\[ \log_{10}(N_t + u) = a \times t + b \]

where \( N_t \) is the number of patients diagnosed outside China, according to WHO, on the \( t \)-th day, \( t=1 \) on February 1; \( u \) is the number of unobserved founder patients at the beginning of spread outside China; and \( a \) and \( b \) are simple linear regression parameters. We enumerated \( u \) from 0 to 100, with step size 1. For each \( u \), we calculated Pearson’s correlation (R^2) between \( t \) and \( \log_{10}(N_t + u) \), and selected the \( \hat{u} \) that maximized R^2 and estimated corresponding \( \hat{a} \) and \( \hat{b} \), using a simple linear regression between \( t \) and \( \log_{10}(N_t + \hat{u}) \).

Table 1

| Date     | \( t \) | \( N_t \) | \( \log_{10}(N_t+34) \) | Model fit |
|----------|--------|----------|------------------------|-----------|
| January 21 | –10    | 4        | 1.580                  | 1.559     |
| January 22 | –9     | 4        | 1.580                  | 1.611     |
| January 23 | –8     | 7        | 1.613                  | 1.662     |
| January 24 | –7     | 11       | 1.653                  | 1.714     |
| January 25 | –6     | 23       | 1.756                  | 1.765     |
| January 26 | –5     | 29       | 1.799                  | 1.817     |
| January 27 | –4     | 37       | 1.851                  | 1.868     |
| January 28 | –3     | 56       | 1.954                  | 1.920     |
| January 29 | –2     | 68       | 2.009                  | 1.971     |
| January 30 | –1     | 82       | 2.064                  | 2.023     |
| January 31 | 0      | 106      | 2.146                  | 2.075     |
| February 1 | 1      | 132      | 2.220                  | 2.126     |
| February 2 | 2      | 146      | 2.255                  | 2.178     |
| February 3 | 3      | 153      | 2.272                  | 2.229     |
| February 4 | 4      | 159      | 2.286                  | 2.281     |
| February 5 | 5      | 191      | 2.352                  | 2.332     |
| February 6 | 6      | 216      | 2.398                  | 2.384     |
| February 7 | 7      | 270      | 2.483                  | 2.435     |
| February 8 | 8      | 288      | 2.508                  | 2.487     |
| February 9 | 9      | 307      | 2.533                  | 2.538     |
| February 10 | 10     | 319      | 2.548                  | 2.590     |
| February 11 | 11     | 395      | 2.632                  | 2.641     |
| February 12 | 12     | 441      | 2.677                  | 2.693     |
| February 13 | 13     | 447      | 2.682                  | 2.744     |
| February 14 | 14     | 505      | 2.732                  | 2.796     |
| February 15 | 15     | 526      | 2.748                  | 2.847     |
| February 16 | 16     | 683      | 2.856                  | 2.899     |
| February 17 | 17     | 794      | 2.918                  | 2.950     |
| February 18 | 18     | 804      | 2.923                  | 3.002     |
| February 19 | 19     | 924      | 2.981                  | 3.053     |
| February 20 | 20     | 1073     | 3.044                  | 3.105     |
| February 21 | 21     | 1200     | 3.091                  | 3.156     |
| February 22 | 22     | 1402     | 3.157                  | 3.208     |
| February 23 | 23     | 1769     | 3.256                  | 3.259     |
| February 24 | 24     | 2069     | 3.323                  | 3.311     |
| February 25 | 25     | 2459     | 3.397                  | 3.362     |
| February 26 | 26     | 2918     | 3.470                  | 3.414     |
| February 27 | 27     | 3664     | 3.568                  | 3.466     |
| February 28 | 28     | 4691     | 3.674                  | 3.517     |

Availability of source code

The source code of the model is available at: https://github.com/wangyi-fudan/COVID-19_Global_Model

RESULTS

Data table

The WHO daily count of numbers of diagnoses outside China and ‘log-plus’ transformed data, as well as model fit data, are presented in table 1.

Parameter estimation

According to February 28 data, \( \hat{u}, \hat{a}, \) and \( \hat{b} \) were estimated as 34, 0.0515, and 2.075, respectively (figure 1).
Global trend model
Next, we plotted \( \log_{10}(N_t + 34) \) against time to visualize model fitting (figure 2). The \( R^2 \) value for the model was 0.991, indicating an excellent fit.

Future number prediction
The number of COVID-19 diagnoses as of February 28 was 4691. Our model predicts that the number of diagnoses outside China will expand exponentially at a rate of 10-fold every 19 days in the absence of strong public health interventions.

DISCUSSION
In this report, only the total number of diagnoses outside China was analyzed. Country-scale data are also available, but is less complete than the total numbers; hence, we limited our analysis to capture the global trend.

This model is a minimal extension of the “default” exponential growth model, using an estimate of 34 undetected founder patients outside China. An almost perfect model fit (\( R^2=0.991 \)) indicates that the spread of disease does follow our model.

A simple and straightforward linear model has some advantages: (1) it works for small sample sizes, due to limited observation or somewhat imperfect data; (2) it is relatively robust in complex situations, and the virus spreading pattern is complex and varies across the world, hence a simple model can provide coarse-grained trend estimation; and (3) a linear model easier to extrapolate than more complex models (eg, neural networks).

The existence of 34 undetected founder patients is not surprising. Actually, founder patients are those patients who are not reported at the beginning (January 22) of WHO reports. Thus, most of them are not under control and continually contribute to the pandemic. These individuals may have had mild symptoms and thus did not attend hospital; however, we do not preclude that they were already present before, or parallel with, the outbreak in Wuhan.

Based on this model, we estimate that there were approximately 34 undetected founder patients at the beginning of the spread of COVID-19 outside China. This suggests that the disease stably followed an approximate exponential growth model at the very beginning. This situation is dangerous, as we expect a 10-fold increase in patient numbers every 19 days, in the absence of strong intervention. We call for strong public health actions worldwide, referring to the experiences learned from China and Singapore.

The manuscript has been preprinted on the medRxiv (doi: https://doi.org/10.1101/2020.03.01.20029819). It is our pleasure that many researchers and social media care more about the outbreak trend outside China through our manuscript. The results of this article have been read more than 9000 times, picked by seven news outlets, and cited more than 10 times.25–29 We reproduced the disease’s initial spread to the world, which would impose a positive impact on other countries to pay attention to the development of COVID-19 and take powerful measures in time.

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Contributors
YW conceived the idea and wrote the source code. YW,YL, ML, and LJ contributed to the data analysis, generating of tables and figures, and manuscript writing. YL, ML, XX, XL, MH, ZH, YY, and BJ contributed to the theoretical analysis and manuscript revision. All authors contributed to the final revision of the manuscript.

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Competing interests
The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Not required.

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Data availability statement
All data relevant to the study are included in the article or uploaded as supplementary information. The source code of the model is available at https://github.com/xyj-fudan/COVID-19_Global_Model.

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Original research

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