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

Yi Li,[1,2] Meng Liang,[1] Xianhong Yin [ID],[1] Xiaoyu Liu,[1] Meng Hao,[1] Zixin Hu,[1] Yi Wang,[1] Li Jin[1,2,3]

[1]Ministry of Education Key Laboratory of Contemporary Anthropology, Human Phenome Institute, School of Life Sciences, Fudan University, Shanghai, China
[2]Institute for Six-sector Economy, Fudan University, Shanghai, China
[3]Research Institute of Data Sciences, Fudan University, Shanghai, China

Correspondence to
Li Jin and Yi Wang, School of Life Sciences & Institute of Data Sciences, Fudan University, Shanghai, China; lijin@fudan.edu.cn, wangyi_fudan@fudan.edu.cn

YL and ML contributed equally.

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: $\log_{10}(N_t + 34) = 0.0515 \times t + 2.075$, where N_t 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 sequencing[2–4] 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 accumulating[5–7] 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

Significance of this study

What is already known about this subject?
► A novel coronavirus was verified and identified as the seventh member of the enveloped RNA coronaviruses as the cause of the disease, which is referred to as COVID-19.
► COVID-19 raised tension both within China and internationally.
► Considering the complexity of the real-life situation, a simple model is expected to be more accurate for describing the spread of the virus.

What are the new findings?
► A "log-plus" model has been established to predict the situation, which only requires daily number of total diagnoses outside China.
► There have been about 34 unobserved founder patients of COVID-19 at the beginning of spread outside China.
► The global trend is approximately exponential, at a rate of 10-fold every 19 days.

How might these results change the focus of research or clinical practice?
► As a 10-fold increase in patient numbers of COVID-19 every 19 days has been estimated, we call for strong public health actions worldwide.

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-2019 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 ($R^2=0.991$). 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 WHO daily diagnosis number outside China

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).
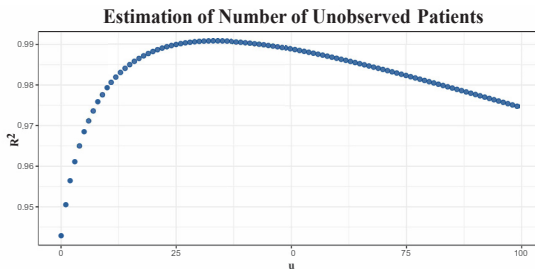
Figure 1 Estimation of u parameter by enumeration.

Global trend model

Next, we plotted $log_{10}\left(N_t + 34\right)$ 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
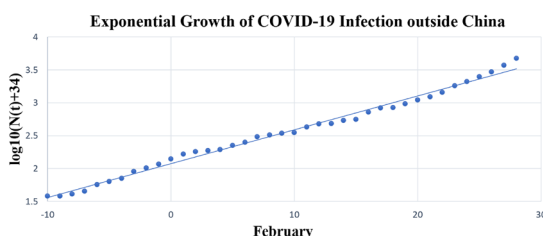
already present before, or parallel with, the outbreak in Wuhan.

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.

ORCID iD
Xianhong Yin http://orcid.org/0000-0002-4021-1617

Figure 2 Exponential growth of COVID-19 infection outside China.

REFERENCES

1 Huang C, Wang Y, Li X, *et al*. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395:497–506.
2 Lu R, Zhao X, Li J, *et al*. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *The Lancet* 2020;395:565–74.
3 WHO. WHO Director-General's remarks at the media briefing on 2019-nCoV on 11 February 2020, 2020. Available: https://www.who.int/dg/speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-2019-ncov-on-11-february-2020
4 Zhu N, Zhang D, Wang W, *et al*. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med Overseas Ed* 2020;382:727–33.

5 Chan JF-W, Yuan S, Kok K-H, *et al*. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet* 2020;395:514–23.

6 Phan LT, Nguyen TV, Luong QC, *et al*. Importation and human-to-human transmission of a novel coronavirus in Vietnam. *N Engl J Med* 2020;382:872–4.

7 JT W, Leung K, Leung GM. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modeling study. *Lancet* 2020.

8 Li Q, Guan X, Wu P, *et al*. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med* 2020;382:1199–207.

9 WHO. Coronavirus disease (COVID-19) Situation Report – 201, 2020. Available: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200808-covid-19-sitrep-201.pdf?sfvrsn=121bb855_2

10 Kim H. *Outbreak of novel coronavirus (COVID-19): what is the role of radiologists?* 2020.

11 Shao N, Pan H, Li X, *et al*. CoVID-19 in Japan: what could happen in the future? *MedRxiv* 2020.

12 Ryu S, Ali ST, Lim J, *et al*. The estimate of infected individuals of the 2019-Novel coronavirus in South Korea by incoming international students from the countries of risk of 2019-Novel coronavirus: a simulation study. *MedRxiv* 2020.

13 WHO. Coronavirus disease 2019 (COVID-19) situation report – 38. Available: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200227-sitrep-38-covid-19.pdf?sfvrsn=9f98940c_2

14 Ilie O-D, Cojocariu R-O, Ciobica A, *et al*. Forecasting the spreading of COVID-19 across nine countries from Europe, Asia, and the American continents using the ARIMA models. *Microorganisms* 2020;8:1158.

15 Shao N, Cheng J, Chen W. The reproductive number R0 of COVID-19 based on estimate of a statistical time delay dynamical system. *MedRxiv* 2020.

16 Zhao Q, Chen Y, Small DS. Analysis of the epidemic growth of the early 2019-nCoV outbreak using internationally confirmed cases. *MedRxiv* 2020.

17 Xiong H, Yan H. Simulating the infected population and spread trend of 2019-nCov under different policy by EIR model. *SSRN Journal* 2020.

18 Mizumoto K, Kagaya K, Chowell G. Early epidemiological assessment of the transmission potential and virulence of 2019 novel coronavirus in Wuhan City: China, 2019-2020. *MedRxiv* 2020.

19 Zhao S, Lin Q, Ran J, *et al*. Preliminary estimation of the basic reproduction number of novel coronavirus (2019-nCoV) in China, from 2019 to 2020: a data-driven analysis in the early phase of the outbreak. *Int J Infect Dis* 2020;92:214–7.

20 Ndaïrou F, Area I, Nieto JJ, *et al*. Mathematical modeling of COVID-19 transmission dynamics with a case study of Wuhan. *Chaos Solitons Fractals* 2020;135:109846.

21 Jiang W, Schotten HD. Deep learning for fading channel prediction. *IEEE Open J Commun Soc* 2020;1:320–32.

22 Huang CJ, Chen YH, Ma Y, *et al*. Multiple-input deep convolutional neural network model for covid-19 forecasting in China. *MedRxiv* 2020.

23 Chimmula VKR, Zhang L. Time series forecasting of COVID-19 transmission in Canada using LSTM networks. *Chaos Solitons Fractals* 2020;135:109864.

24 Tomar A, Gupta N. Prediction for the spread of COVID-19 in India and effectiveness of preventive measures. *Sci Total Environ* 2020;728:138762.

25 Business Insider. The number of coronavirus cases outside China could jump tenfold every 19 days without 'strong intervention,' a study says, 2020. Available: https://www.businessinsider.nl/coronavirus-outside-china-tenfold-increase-19-days-strong-intervention-study-2020-3/

26 Yahoo News. The number of coronavirus cases outside China could jump tenfold every 19 days without 'strong intervention,' a study says, 2020. Available: https://news.yahoo.com/number-coronavirus-cases-outside-china-171856791.html

27 Tsiotas D, Magafas L. The effect of Anti-COVID-19 policies on the evolution of the disease: a complex network analysis of the successful case of Greece. *Physics* 2020;2:325–39.

28 Igor N, Ihor K, Gerhard DCoronavirus pandemic dynamics in March, 2020. What can we expect in April? Available: https://www.researchgate.net/publication/340385105_Coronavirus_pandemic_dynamics_in_March_2020_What_can_we_expect_in_April

29 Rossman H, Keshet A, Shilo S, *et al*. A framework for identifying regional outbreak and spread of COVID-19 from one-minute population-wide surveys. *Nature Medicine* 2020:1–4.