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Preliminary prediction of the basic reproduction number of the Wuhan novel coronavirus 2019-nCoV

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Abstract

Objectives: To estimate the basic reproduction number of the Wuhan novel coronavirus (2019-nCoV).

Methods: Based on the susceptible-exposed-infected-removed (SEIR) compartment model and the assumption that the infectious cases with symptoms occurred before 26 January, 2020 are resulted from free propagation without intervention, we estimate the basic reproduction number of 2019-nCoV according to the reported confirmed cases and suspected cases, as well as the theoretical estimated number of infected cases by other research teams, together with some epidemiological determinants learned from the severe acute respiratory syndrome (SARS).

Results: The basic reproduction number fall between 2.8 and 3.3 by using the real-time reports on the number of 2019-nCoV-infected cases from People's Daily in China and fall between 3.2 and 3.9 on the basis of the predicted number of infected cases from international colleagues.

Conclusions: The early transmission ability of 2019-nCoV is close to or slightly higher than SARS. It is a controllable disease with moderate to high transmissibility. Timely and effective control measures are needed to prevent the further transmissions.

KEYWORDS

2019 novel coronavirus (2019-nCoV), basic reproduction number, epidemiology

1 | INTRODUCTION

The transmission of pneumonia associated with the Novel Coronavirus Pneumonia (NCP) originated in Wuhan city has not yet been effectively

blocked. In the meanwhile, the number of confirmed and suspected cases is increasing rapidly. Estimating the epidemiological determinants of 2019-nCoV is significant and urgent regarding the assessment of epidemic transmissibility, the prediction of future trend of epidemic

spreading, as well as the design of control measures. The basic reproduction number is the most important parameter to determine the intrinsic transmissibility, defined as the average number of secondary infectious cases generated by an index case in a completely susceptible population without any interventions.¹ During the outbreak of an epidemic, due to interventions and control measures from government, reaction of personal behaviors (sterilizing, wearing masks, washing hands, reducing contacts, etc.), the depletion of susceptible populations, and the seasonality of transmissibility, the basic reproduction number is generalized to the effective reproduction number, which is defined as the average number of secondary cases generated by an infectious case at time t , and is denoted by R_t . The epidemic is considered to be under control when $R_t < 1$.

We assumed that the infected individuals whose onset time of symptoms no later than January 25, 2020 were resulted from the free propagation, that is, the transmission was without interventions. Regarding the reports of real-time data of 2019-nCoV situation jointly by the People's Daily in China (<https://3g.dxy.cn/newh5/view/pneumonia?scene=2&clicktime=1579583352&enterid=1579583352&from=timeline&isappinstalled=0>) and DXY.cn (an online community for health care professionals; <https://m.weibo.cn/u/2803301701>), as well as the estimated number of 2019-nCoV infections from the research group led by the Northeastern University² (these two data sources are later abbreviated as People's Daily Reports and Northeastern University Reports), we estimated the basic reproduction number of 2019-nCoV based on the susceptible-exposed-infected-removed (SEIR) compartment model.

2 | METHODS

This article was intended to estimate the basic reproduction number under the situation of free propagation, which was the initial stage of the spread of 2019-nCoV without the interventions. Most Chinese people were aware of the outbreak of 2019-nCoV by the mainstream media after 20 January 2020. The Hubei government released the announcement about strengthening the prevention and control measures against 2019-nCoV, and launched the second-level public health emergency response at 2:40 AM on January 22, 2020. Thus, the public awareness and effective interventions were absent when the time was prior to this point. As the median value of the incubation period of SARS was 6.4 days (95% CI 5.2 to 7.7 days)³, and the 2019-nCoV incubation period was 5.1 days according to a recent report on a few confirmed cases,⁴ we inferred that the confirmed cases before January 26, 2020 were infected during the free propagation of 2019-nCoV. Meanwhile, the confirmed cases after January 25 were not suitable for the analyses since the cases were generated in the following days were not during the free propagation.

We used the SEIR compartment model⁵ to characterize the early spreading of 2019-nCoV, where each individual could be in one of the following four states: susceptible (S), exposed (E, being infected but without infectiousness), infected (I, with infectiousness), and removed

(R). At each time step (in days in later analyses), a susceptible individual would turn to be an exposed individual with probability β if she/he contacts with an infected individual, an exposed individual had a probability γ_1 to become infected, and an infected would be removed with probability γ_2 . The dynamical process of SEIR thus could be described as:

$$\begin{aligned}\frac{dS(t)}{dt} &= -\frac{\beta S(t)I(t)}{N}, \\ \frac{dE(t)}{dt} &= \frac{\beta S(t)I(t)}{N} - \gamma_1 E(t), \\ \frac{dI(t)}{dt} &= \gamma_1 E(t) - \gamma_2 I(t), \\ \frac{dR(t)}{dt} &= \gamma_2 I(t),\end{aligned}$$

where $S(t)$, $E(t)$, $I(t)$, and $R(t)$, respectively, represent the number of individuals in the susceptible, exposed, infectious, and recovered states at time t , and N is the total number of individuals in the system such that $N = S(t) + E(t) + I(t) + R(t)$. The infected population during early transmission was negligible compared with the total population, that is, when t approaches 0, $S(t)$ approaches to N . The basic reproduction number could then be approximated as⁶:

$$R_0 = \left(1 + \frac{\lambda}{\gamma_1}\right) \left(1 + \frac{\lambda}{\gamma_2}\right),$$

where $\lambda = \ln Y(t)/t$ is the growth rate of the early exponential growth and $Y(t)$ is the number of infected people with symptom by time t . The exposed period and the infection period could be expressed as $T_E = 1/\gamma_1$ and $T_I = 1/\gamma_2$. Generation time could then be approximated as $T_g = T_E + T_I$. Denote by $\rho = T_E/T_g$ the ratio of exposed period to generation time, the basic reproduction number could be rewritten as

$$R_0 = 1 + \lambda T_g + \rho(1 - \rho)(\lambda T_g)^2.$$

3 | RESULTS

To estimate R_0 , the parameters λ , ρ , and T_g were needed, where λ was determined by $Y(t)$. Below was the detailed discussion about these three parameters.

According to the real-time dynamic data of 2019-nCoV by the People's Daily Reports, there were 1408 confirmed cases and 2032 suspected cases by the time of 23:59 on January 25, 2020. In reality, there should be a certain fraction of infected people with symptoms having not been found.^{2,7,8} If we ignored this situation and suppose that there will be a fraction q of the suspected cases would be confirmed further (on the basis of an early report that 41 of the 59 suspected cases were eventually confirmed, the reference value of q was $41/59 = 0.695$), then the number of cases with symptoms on 25 January was $Y(t) = 2032 \times 0.695 + 1408 = 2820$. Note that the real number of cases was probably much larger than 2820. We considered this number as the optimistic situation (the lower bound of the number of cases having onset of symptoms). If we took the Northeastern University Reports² as the reference, there would be about 4050 cases on

TABLE 1 The basic reproduction numbers and the corresponding key parameters

Data sources	T_g	$Y(t)$	t	R_0
People's Daily Reports	8.4	2820	48	2.83
People's Daily Reports	10.0	2820	48	3.28
Northeastern University Reports	8.4	4050	43	3.22
Northeastern University Reports	10.0	4050	43	3.78
Northeastern University Reports	8.4	12 700	47	3.34
Northeastern University Reports	10.0	12 700	47	3.93

January 20, 2020, and about 12 700 cases on January 24, 2020. This result was mainly based on the number of confirmed cases in overseas that were exported from Wuhan. Even though there might be a large bias due to the highly limited samples, it should be seriously considered as all other methods were also very preliminary and some reports^{7,8} showed similar results to the Northeastern University Reports.² Read et al⁸ inferred that the actual number of confirmed cases was only 5.1%, including the cases without symptoms. If only 5% of symptomatic infections were detected (more pessimistic than the results of Read's study⁸), then according to the confirmed cases (1408) by January 25, the number of cases with symptoms was 28 160, 10 times larger than the optimistic one. We used it as the upper bound of $Y(t)$ in sensitivity analysis. We set the date December 8, 2019, the presence time of the first pneumonia of unknown etiology, as $t = 0$. In fact, t might be slightly earlier than December 8, since the symptoms might have appeared for some time before to the hospital. Hence, the estimated basic reproduction number might be a bit higher by using December 8, 2019 as $t = 0$. Based on the above analysis, we mainly used $Y(48) = 2820$ from the People's Daily Reports, and $Y(43) = 4050$, $Y(47) = 12 700$ from the Northeastern University Reports.²

The value of ρ for SARS was in the range of [0.5, 0.8], we took $\rho = 0.65$ in the absence of more studies.^{3,9} In the sensitivity analysis, we would consider ρ from 0.5 to 1. As the formula $\rho(1 - \rho)$ was symmetry, the range, that is, [0.5, 1], covers all possible values of ρ . Lipsitch et al¹⁰ showed that the average of T_g is 8.4 days for SARS, while in the early outbreaks T_g was higher (the average value was 10.0 days), and they suggested the sensitivity analysis interval as $T_g \in [8, 12]$. Imai et al¹¹ claimed that the case study reported in Chan's research⁴ indicated that 2019-nCoV has a much shorter T_g . However, we could not yet obtain any solid estimation about the value of T_g as the number of samples was too small and the questionnaire survey did not sufficiently cover the interests about generation time. Therefore, we mainly concentrated on $T_g = 8.4$ (days) and $T_g = 10.0$ (days), and took sensitivity analysis with the same interval^{8,12} as suggested by Lipsitch et al.¹⁰

As shown in Table 1, the basic reproduction number fell between 2.8 and 3.3 based on the People's Daily Reports and fell between 3.2 and 3.9 on the basis of the Northeastern University Reports.² The estimated value of R_0 by the Reports of the Northeastern University was similar to the value estimated by Read et al,⁸ which was in the range of [3.6, 4.0]. Our estimated values were higher than the ones ([2.1, 3.5], with a median value 2.6) by Imai et al.¹¹ In accordance

with the currently preliminary estimations, the transmissibility of 2019-nCoV was close to SARS. For example, the basic reproduction number of SARS by Lipsitch et al¹⁰ was [2.2, 3.6], and the average basic reproduction number of SARS by Riely et al¹² was 2.7 (95% CI 2.2 to 3.7), but if considering the superspreading events, this average value increased up to 3.4. The basic reproduction number of SARS by Wallinga and Teunis¹³ was from 3.1 to 4.2, which was not lower than our pessimistic result. Therefore, if we rely on the People's Daily Reports, the basic reproduction number of 2019-nCoV was not higher than SARS, or even slightly lower than the basic reproduction number of SARS predicted by some other research teams. Even with the more predictions by the Northeastern University Reports, the basic reproduction number of 2019-nCoV was only slightly higher than SARS. It was a controllable disease with moderate to high transmissibility. Concerning the previous experiences in fighting with SARS, the spreading of 2019-nCoV could be quickly reduced (probably in 2 or 3 weeks) through timely and effective control measures by government.

Figure 1 shows the sensitivity analysis of the three key parameters. Under the worst case ($Y(48) = 28 016$, $\rho = 0.5$, $T_g = 12$), the estimated R_0 was 5.2; under the best case ($Y(48) = 2820$, $\rho = 1.0$, $T_g = 8$), the estimated R_0 was 2.3. Because R_0 was sensitive to the generation time, with the accumulation of epidemiological survey data, the estimation of generation time would be more accurate, thus providing a more precise estimation of the basic reproduction number.

4 | DISCUSSION

Considering the extreme cases, the basic reproduction number was in the range of [2.3, 5.2], but we thought it should be in the range of [2.8, 3.9]. Based on the data of the People's Daily Reports, the prediction of the basic reproduction number was in the range of 2.8 and 3.3, and this range became [3.2, 3.9] when the data were based on the Northeastern University Reports.² Even with the pessimistic estimation, the basic reproduction number of 2019-nCoV was only slightly higher than SARS, fully equipped with controllable condition. Many known basic reproduction numbers were higher than 2019-nCoV, for example, Zika virus was 1.4-6.6,¹⁴ Middle East respiratory syndrome was 2.0-6.7,¹⁵ and smallpox was 3.5-6.0.¹⁶ In other words, 2019-nCoV does not have particularly outstanding transmissibility.

The value of basic reproduction number was most sensitive to the generation time T_g , and thus we hope the more accurate estimation of the generation time based on the accumulation of epidemiological survey data would further improve the quality of the estimation of R_0 . The number of confirmed cases obtained from different sources varied widely. Since a significant proportion of patients with 2019-nCoV had mild symptoms, which could be healed without entering the hospital, there might be a large number of patients not in the official confirmed list. Consequently, we suggested it to be more prudent. For example, the design of control measure should refer to the more pessimistic estimation (based on the Northeastern University Reports) rather than the more optimistic one (based on the People's Daily Reports).

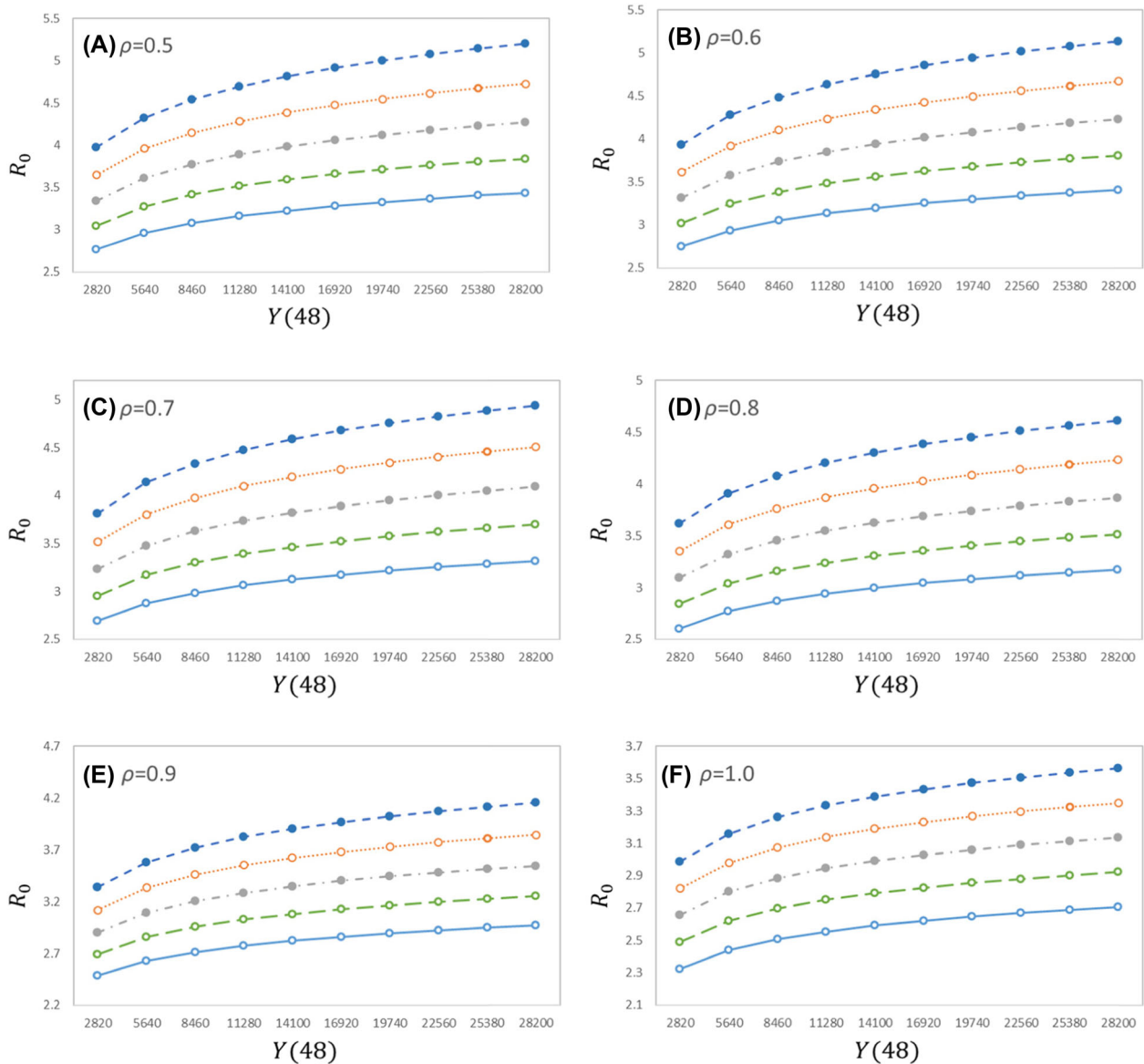


FIGURE 1 Impacts of different key parameters on the estimated basic reproduction numbers. The x-axis is the number of cases with symptoms at $t = 48$; (A)–(F) correspond to the six different scenarios for $\rho = 0.5, 0.6, 0.7, 0.8, 0.9, 1$, the five curves in each figure from top to bottom correspond to the five different cases for $T_g = 12, 11, 10, 9, 8$

Our model assumes that the individuals in exposed state did not have or have very lower level infectiousness (according to SARS), however, it was possible that for 2019-nCoV, individuals in the exposed state still had considerable infectiousness. Such possible difference was already taken into account by varying the value of ρ .

It was needed to be emphasized that the method used in this article was a preliminary estimation under the premise of largely insufficient data. In order to have a better estimation of the basic reproduction number and effective reproduction number, as well as predicting the trend of epidemic transmission, we not only need to know precise epidemiological determinants, but also need to improve the model itself by further considering the diversity in susceptibilities and contact probabilities of people in different ages and genders, the

different spreading mechanisms in hospitals and communities, the effects of regional population density and human mobility, and so on.^{17–20}

From the dynamic perspective, $R_0 = k\beta D$, where k is the average number of contacts to susceptible individuals of an infected individual per day, β is the transmission probability through a contact between an infected individual and a susceptible individual, and D is the effective time period allowing an infected individual to infect susceptible individuals. The government's control policy and individuals' prevention behaviors were to reduce these parameters, and to eventually make the effective reproduction number R_t below 1. According to our results, if $k\beta D$ could be reduced by 3/4 (to its 1/4), 2019-nCoV could be effectively controlled. Staying at home and cancelled meetings could

decrease the frequency of contacts between infected and susceptible individuals. Wearing masks and washing hands could reduce the transmission probability β . If the individuals exhibit the suspected symptoms or have contacts with the high-risk groups, the corresponding medical observation and the isolation with other individuals were needed, which would shorten the effective infectious time period D . Restrictions on transportation, extension of winter holiday, and the cancellation of various conferences also aimed at reducing the effective reproductive number. Based on the preliminary information, a considerable amount of people infected with 2019-nCoV only show mild symptoms, and thus they had the same mobility as healthy people in principle. There were also some preliminary epidemiological findings suggesting that infected cases had infectiousness during the exposed period. These reasons, together with the delayed responses by Wuhan government, lead to a fiercer outbreak of 2019-nCoV than SARS. On the contrary, reducing the traveling and avoiding the meetings, in the meanwhile, wearing masks and washing hands frequently would suppress the effects caused by mild symptoms and exposed state with infectiousness. Relying on the Chinese experiences in fighting with SARS, we believed that 2019-nCoV would be effectively controlled soon.

In conclusion, the SEIR model is employed to describe the dynamical process of 2019-nCoV spreading, and based on the collected data of 2019-nCoV, the basic reproduction number is predicted in this article a little higher than the SARS, which suggests that 2019-nCoV is of a moderate to high transmissibility. In order to control the further extension of 2019-nCoV quickly, more effective and timely control measures are required. In the process of prediction, some parameters related to the early stage of SARS transmission were used, and meanwhile it shows that the basic reproduction number is a little sensitive to the generation time. Thus, the microscopic survey about the transmission processes is needed to further improve the quality of predictions.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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