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 January 25, 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. Results The basic reproduction number falls between 2.8 to 3.3 by using the real-time reports on the number of 2019-nCoV infected cases from People's Daily in China, and falls between 3.2 and 3.9 on the basis of the predicted number of infected cases from colleagues. Conclusions   The early transmission ability of 2019-nCoV is closed to or slightly higher than SARS. It is a controllable disease with moderate-high transmissibility. Timely and effective control measures are needed to suppress the further transmissions.

【 Key words 】 2019 novel coronavirus (2019-nCoV); basic reproduction number; epidemiology

The transmission of pneumonia associated with novel coronavirus (2019-nCoV) 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 an entirely 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 assume that the infected individuals whose onset time of symptoms no later than January 25, 2020 are resulted from the free propagation, i.e., the transmission is without interventions. Regarding the reports of real-time data of 2019-nCoV situation jointed by the People's Daily in China [2] and DXY.cn (an online community for health care professionals) [3], as well as the estimated number of 2019-nCoV infections from the research group led by the Northeastern University [4] (these two data sources are later abbreviated as People's Daily Reports and Northeastern University Reports), we estimate the basic reproduction number of 2019-nCoV based on the susceptible–exposed–infected–removed (SEIR) compartment model.

Methods

This article intends to estimate the basic reproduction number under the situation of free propagation, which is the initial stage of the spread of 2019-nCoV without the interventions. Most Chinese people are aware of the outbreak of 2019-nCoV by the mainstream media after January 21, 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 2:40am on January 22, 2020. Thus the public awareness and effective interventions are absent when the time is prior to this point. As the median value of the incubation period of SARS is 6.4 days (95% CI 5.2-7.7 days) [5], and the 2019-nCoV incubation period is 5.1 days according to a recent report on a few confirmed cases [6], we infer that the confirmed cases before January 25, 2020 are infected during the free propagation of 2019-nCoV. Meanwhile, the confirmed cases after January 25 are not suitable for the analyses since the cases are generated in the following days are not during the free propagation.

We use the susceptible–exposed–infected–removed (SEIR) compartment model [7] to characterize the early spreading of 2019-nCoV, where each individual can 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 will turn to be an exposed individual with probability β if she/he contacts with an infected individual, an exposed individual has a probability γ_1 to become infected, and an infected will be removed with probability γ_2. The dynamical process of SEIR thus can be described as

$$\frac{dS(t)}{dt} = -\frac{\beta S(t)I(t)}{N},$$

$$\frac{dE(t)}{dt} = \frac{\beta S(t)I(t)}{N} - \gamma_1 E(t),$$

$$\frac{dI(t)}{dt} = \gamma_1 E(t) - \gamma_2 I(t),$$

$$\frac{dR(t)}{dt} = \gamma_2 I(t),$$

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, 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 is negligible compared with the total population, that is, when t approaches 0, $S(t)$ approaches to N. The basic reproduction number can then be approximated as [8]:

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

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 can be rewritten as

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

Results

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

According to the real-time dynamic data of 2019-nCoV by the People's Daily Reports, there are 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 [4][9][10]. If we ignore this situation and suppose that there a fraction q of the suspected cases will 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 is 41/59=0.695), then the number of cases with symptoms on January 25 is $Y(t) = 2032 \times 0.695 + 1408 = 2820$. Note that, the real number of cases is probably much larger than 2820. We consider this number as the optimistic situation (the lower bound of the number of cases having onset of symptoms). If we take the Northeastern University Reports [4] as the reference, there will be about 4,050 cases on January 20, 2020, and about 12,700 cases on January 24, 2020. This result is mainly based on the number of confirmed cases in overseas which are 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 are also very preliminary and some reports [9][10] show similar results to the Northeastern University Reports [4]. Read *et al.* [10] inferred that the actual number of confirmed cases was only 5.1%, including the cases without symptoms. If only 5% of symptomatic infections are detected (more pessimistic than the results of [10]), then according to the confirmed cases (1408) by January 25, the number of cases with

symptoms is 28160, ten times larger than the optimistic one. We use 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 aetiology, as $t=1$. In fact, t might be slightly earlier than December 8, since the symptoms may 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 $t=1$. Based on the above analysis, we mainly use $Y(48)=2820$ from the People's Daily Reports, and $Y(43)=4050$, $Y(47)=12700$ form the Northeastern University Reports [4].

According to Refs. [5][11], the value of ρ for SARS is in the range of [0.5, 0.8], we take $\rho = 0.65$ in the absence of more references. In the sensitivity analysis, we will consider ρ from 0.5 to 1. As the formula $\rho(1-\rho)$ is symmetry, the range, i.e., [0.5,1], covers all possible values of ρ. Lipsitch *et al.* [12] showed that the average of T_g is 8.4 days for SARS, while in the early outbreaks T_g is higher (the average value is 10.0 days), and they suggested the sensitivity analysis interval as $T_g \in [8,12]$. Imai *et al.* [13] claim that the case study reported in Ref. [6] indicates that 2019-nCoV has a much shorter T_g. However, we cannot yet obtain any solid estimation about the value of T_g as the number of samples is too small the questionnary survey does not sufficiently cover the interests about genration time. Therefore, we mainly concentrate on $T_g = 8.4$ (days) and $T_g = 10.0$ (days), and take sensitivity analysis with the same interval [10, 14] as suggested by Ref. [12].

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	12700	47	3.34
Northeastern University Reports	10.0	12700	47	3.93

As shown in Table 1, the basic reproduction number falls between 2.8 to 3.3 based on the People's Daily Reports, and falls between 3.2 and 3.9 on the basis of the Northeastern University Reports [4]. The estimated value of R_0 by the Reports of the Northeastern University is similar to the value estimated by Read *et al.* [10], which is in the range of [3.6,4.0]. Our estimated values are higher than the ones ([2.1,3.5], with a median value 2.6) by Imai *et al.* [13]. In accordance with the currently preliminary estimations, the transmissibility of 2019-nCoV is close to SARS. For example, the basic reproduction number of SARS by Lipsitch *et al.* [12] is [2.2, 3.6], and the average basic

reproduction number of SARS by Riely *et al.* [14] is 2.7 (the 95% CI is [2.2,3.7]), but if considering the superspreading events, this average value rises up to 3.4. The basic reproduction number of SARS by Wallinga and Teunis [15] is from 3.1 to 4.2, which is not lower than our pessimistic result. Therefore, if we rely on the People's Daily Reports, the basic reproduction number of 2019-nCoV is 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 is only slightly higher than SARS. It is a controllable disease with moderate-high transmissibility. Concerning the previous experiences in fighting with SARS, the spreading of 2019-nCoV could be quickly reduced (probably in two or three weeks) through timely and effective control measures by government.
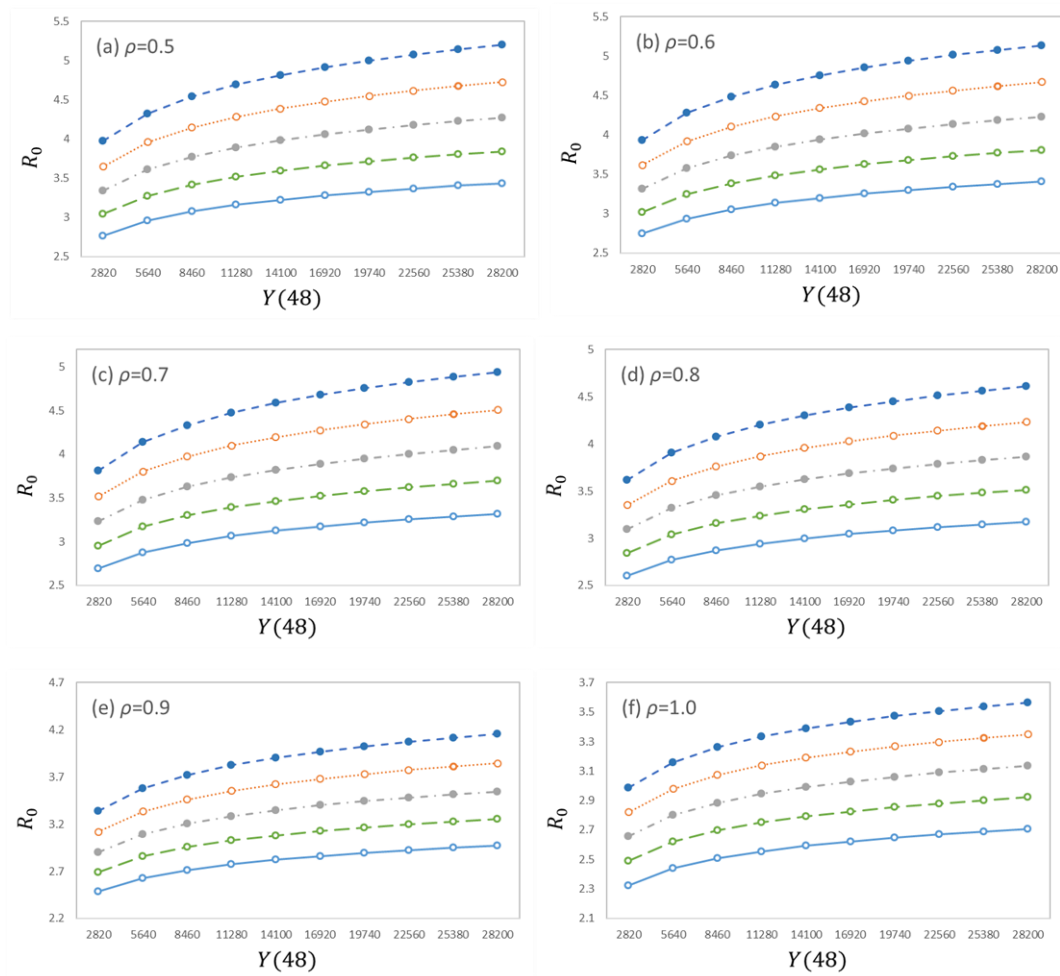
Figure 1. Impacts of different key parameters on the estimated basic reproduction numbers. The x-axis is the number of cases with symptoms on day 48, figures (a)-(f) correspond to the six different scenarios for $\rho = 0.5, 0.6, 0.7, 0.8, 0.9, 1$ **, the five curves in each figure from top to bottom correspond to the five different cases for** $T_g = 12, 11, 10, 9, 8$ **.**

Figure 1 shows the sensitivity analysis of the three key parameters. Under the worst case ($Y(48) = 28016$, $\rho = 0.5$, $T_g = 12$), the estimated R_0 is 5.2; under the best case ($Y(48) = 2820$,

$\rho = 1.0, T_g = 8$), the estimated R_0 is 2.3. Because R_0 is 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.

Discussions

Considering the extreme cases, the basic reproduction number is in the range [2.3, 5.2], but we think it should be in the range [2.8, 3.9]. Based on the data of the People's Daily Reports, the prediction of the basic reproduction number is in the range of 2.8 and 3.3, and this range becomes [3.2, 3.9] when the data is based on the Reports the Northeastern University [4]. Even with the pessimistic estimation, the basic reproduction number of 2019-nCoV is only slightly higher than SARS, fully equipped with controllable condition. Many known basic reproduction numbers are higher than 2019-nCoV. For example, Zika virus is 1.4-6.6 [16], Middle East respiratory syndrome is 2.0-6.7 [17], and smallpox is 3.5-6.0 [18]. In a word, 2019-nCoV does not have particularly outstanding transmissibility.

The value of basic reproduction number is 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 will further improve the quality of the estimation of R_0. The number of confirmed cases obtained from different sources varies widely. Since a significant proportion of patients with 2019-nCoV have mild symptoms, which could be healed without entering the hospital, there may be a large number of patients not in the official confirmed list. Consequently, we suggest 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). Our model assumes that the individuals in exposed state do not have or have very lower-level infectiousness (according to SARS), however, it is possible that for 2019-nCoV, individuals in the exposed state still have considerable infectiousness. Such possible difference is already taken into account by varying the value of ρ.

It needs to be emphasized that the method used in this article is 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 [19-22].

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 are to reduce these parameters, and to eventually make the effective reproduction number R_t below 1. According to our results, if $k\beta D$ can be reduced

by 3/4 (to its 1/4), 2019-nCoV can be effectively controlled. Staying at home and cancelled meetings can decrease the frequency of contacts between infected and susceptible individuals. Wearing masks and washing hands can 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 are needed, which would shorten the effective infectious time period *D*. Restrictions on transportation, extension of winter holiday, and the cancellation of various conferences also aim 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 have the same mobility as healthy people in principle. There are also some preliminary epidemiological findings suggesting that infected cases have 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 will suppress the effects caused by mild symptoms and exposed state with infectiousness. Relying on the Chinese experiences in fighting with SARS, we believe that 2019-nCoV will be effectively controlled soon.

In summarize, 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-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.

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