

The Estimate of the Basic Reproduction Number for Novel Coronavirus disease (COVID-19): A Systematic Review and Meta-Analysis

Running title: The Estimate of The Basic Reproduction Number COVID-19

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Abstract

Objectives: The outbreak of the 2019 novel coronavirus disease (COVID-19) infection is one of the main public health challenges in the world. Because of high transmissibility, the COVID-19 causes many morbidities and mortality in the main parts of the world. The true estimation of the basic reproduction number (R_0) can be beneficial in terms of prevention programs. Because of the present controversy among the original researches about this issue, the current systematic review and meta-analysis aimed to estimate the pooled R_0 for COVID-19 in the current outbreak.

Methods: International databases, (including Google Scholar, Science Direct, PubMed, and Scopus) were searched to obtain the studies conducted regarding the reproductive number of COVID-19. Articles were searched using the following keywords: "COVID-19" and "basic reproduction number" or " R_0 ". The Heterogeneity of between studies was assessed using the I^2 index, Cochran's Q test and T^2 . The random-effects model was used to estimate the R_0 in this study.

Results: The mean of reported R_0 in articles was calculated as 3.38 ± 1.40 with a range of 1.9 to 6.49. According to the results of the random-effects model, the Pooled R_0 for COVID-19 was estimated as 3.32(2.81-3.82). According to the results of meta-regression analysis, the type of used models in estimating R_0 does not have a significant effect on heterogeneity between studies (P: 0.18)

Conclusion: Considering the estimated R_0 for COVID-19, reducing the number of contacts within the population is inevitable to control the epidemic. The estimated overall R_0 was more than WHO estimates.

Keywords: Basic Reproduction Number, COVID-19, Meta-Analysis

INTRODUCTION

In December 2019, a series of pneumonia cases without any identified causes appeared in Wuhan, Hubei, China, with clinical symptoms similar to viral pneumonia [1-3]. Most of the mentioned reported cases worked or lived around the local Huanan seafood wholesale market, where live animals were also sold there [4]. This new human infected virus named by WHO as the 2019 novel coronavirus (COVID-19) [5]. Because of high contagiousness and morbidity, this infection considered by WHO as a global urgency [6]. Because of the high transmissibility of this viral infection, up to 26 Jan 2020 more than 2000 confirmed cases of COVID-19 were identified in China mainly in Wuhan province [7]. Also as of Feb 15, 2020, about 66580 cases with 1524 deaths reported from China [8]. The human to human transmission of this infectious disease was confirmed [9] and this infection reported from countries other than China [10]. Because of the high infectiousness ability of this virus among the suspect population, the calculation of basic reproduction number (R_0), is essential in terms of prevention measures [1]. The R_0 is an epidemiologic metric that can use to assess the contagiousness feature of infectious agents. This index presents the average number of new cases generated by an infected person [11, 12]. The higher amount of R_0 refers to more contagiousness of infectious agents. Since the epidemic began in China, numerous papers have been published. Because the results of various studies so far have been done in this regard are somewhat different and controversial, the current systematic review and meta-analysis aimed to estimate the pooled R_0 for the COVID-19 outbreak, using the original articles published during 2020.

METHODS

Search strategy

This systematic review and meta-analysis performed to estimate pooled R_0 of COVID-19 in articles published in international journals. International databases, (including Google Scholar, Science Direct, PubMed, and Scopus) were searched to obtain the studies conducted regarding the reproductive number of COVID-19. Articles were searched using the keywords "COVID-19" AND "basic reproduction number" OR " R_0 ".

Study selection and data extraction

In the current study, all studies in 2020 which estimated R_0 for COVID-19 were entered into the meta-analysis. The information such as the name of first authors, country, year of study, model of estimation R_0 and estimated R_0 value (with 95% confidence interval) were extracted from the articles.

Statistical analysis

The heterogeneity of between studies was assessed using the I^2 index, Cochran's Q test and T^2 . According to I^2 results the heterogeneity can be classified into three categories which include: $I^2 < 25\%$ (low heterogeneity), $I^2 = 25-75\%$ (average heterogeneity), and $I^2 > 75\%$ (high heterogeneity)[13]. Because of the high amount of I^2 (99.3%), as well as the significance of Cochran's Q ($p < 0.0001$) the random-effects model was used to estimate of reproductive number (R_0) in this study. Also, the univariate Meta-regression analysis was used to assess the effect of different models on heterogeneity between studies. The impact of covariates on the estimated R_0 was assessed by univariate meta-regression analysis. In the current study, just the used Models to estimate R_0 by original researches were considered as a covariate. Data were analyzed by STATA (version 11) software.

Ethics Statement

This paper is a systematic review so it did not need ethical consideration.

RESULTS

We identified 85 studies, of which 23 were duplicates, leaving 62 reports (Figure 1). A total of 55 reports passed the initial screening, and 23 reports passed full-text assessment for eligibility. Reasons for exclusion were as follows: reporting of R_e and instead of R_0 and

insufficient data. Finally, we included 23 studies in this systematic review (Table 1). No studies were excluded due to poor quality. In the current study 29 records that estimated R_0 of COVID-19 were entered to analysis. Studies have used different methods to estimate R_0 for COVID-19. All the studies that were included in the Meta-analysis were done in 2020 in China. The mean of reported R_0 in articles was calculated as 3.38 ± 1.40 with a range of 1.9 to 6.49. More information was shown in Table 1.

Pooled estimation of reproductive number (R_0)

According to the results of the random-effects model, the pooled R_0 for Covid-19 was estimated as 3.32(2.81-3.82). It means each infected person with COVID-19 can transmit the infection to on average 4 susceptible people (Figure and Table 2). There was significant heterogeneity between studies (I^2 :99.3, P of chi 2 test for heterogeneity :< 0.001 and T^2 : 1.72) (Table 2).

Meta-regression

According to the results of meta-regression analysis, the type of models used for estimation of R_0 doesn't have a significant effect on heterogeneity between studies (P: 0.81). The distribution of the estimated R_0 according to different models was shown in Figure 3. The numbers on the x-axis in Figure 3 represent the type of method used in estimating R_0 . The coding is as follows: Stochastic Markov Chain Monte Carlo methods=1, Dynamic Compartmental Model=2, Statistical Exponential Growth Model=3, Statistical Maximum Likelihood Estimation=4, Mathematical Transmission Model=5, Mathematical Incidence Decay, and Exponential Adjustment=6, Stochastic Simulations of Early Outbreak Trajectories=7, Mathematical SEIR-type Epidemiological Model=8, other Mathematical Models=9, Networked Dynamics Meta Population Model =10, Fudan-CCDC Model=11, SEIQ Model=12, Coalescent-based Exponential Growth, and a Birth-Death Skyline Model=13, not mentioned =14.

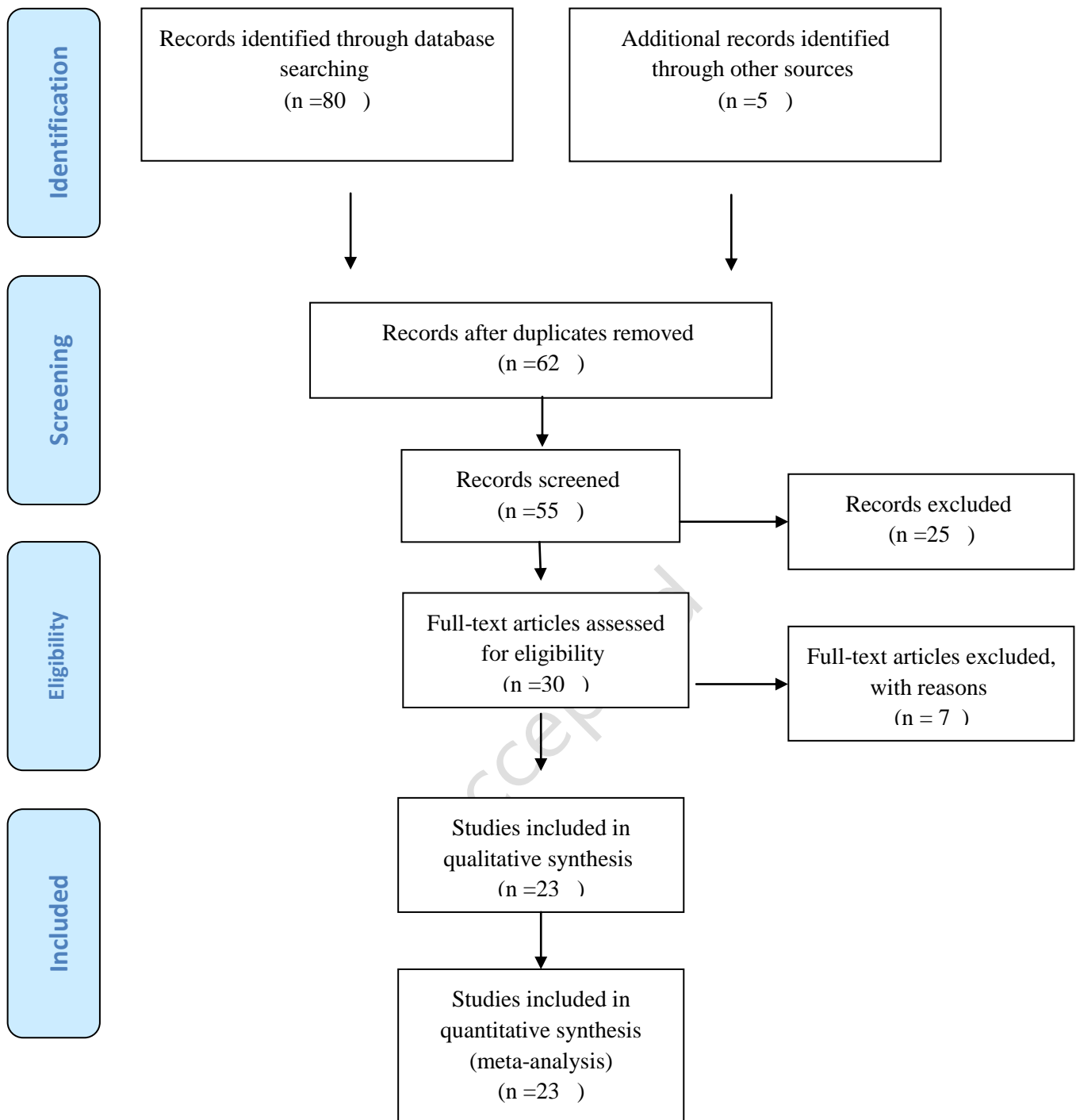


Figure1. PRISMA Flow Diagram for included studies in current meta-analysis

Table 1. Descriptive characteristics of entered records in the meta-analysis

first author	Year	Country	Model	Reproductive number	LCL	UCL
Joseph T Wu et al[14]	2020	China	MCMC	2.68	2.47	2.86
Mingwang Shen et al[15]	2020	China	Dynamic Compartmental Model	6.49	6.31	6.66
Tao Liu et al[16]	2020	China	Statistical Exponential Growth Model	2.90	2.32	3.63
Tao Liu et al[16]	2020	China	Statistical Maximum Likelihood Estimation	2.92	2.28	3.67
Jonathan M. Read et al[17]	2020	China	Mathematical Transmission Model	3.11	2.39	4.13
Maimuna Majumder et al[18]	2020	China	IDEA	2.55	2.00	3.10
WHO[11]	2020	China	Mathematical Model	1.95	1.40	2.50
Shi Zhao et al[19]	2020	China	Statistical Exponential Growth Model	2.24	1.96	2.55
Shi Zhao et al[19]	2020	China	Statistical Exponential Growth Model	3.58	2.89	4.39
Natsuko Imai[20]	2020	China	Mathematical Model	2.50	1.50	3.50
Julien Riou and Christian L. Althaus[21]	2020	China	Stochastic Simulations of Early Outbreak Trajectories	2.20	1.40	3.80
Tang, Biao et al.[22]	2020	China	Mathematical SEIR-Type Epidemiological Model	6.47	5.71	7.23
Qun Li et al[23]	2020	China	Statistical Exponential Growth Model	2.20	1.40	3.90
Sheng Zhang et al[24]	2020	China	Statistical Maximum Likelihood Estimation	2.28	2.06	2.52
Mingwang Shen et al[15]	2020	China	Mathematical Model	4.71	4.50	4.92
Zhanwei Du et al[25]	2020	China	Statistica Exponential Growth Model	1.90	1.47	2.59
Kamalich Muniz-Rodriguez et al[26]	2020	China	Statistica Exponential Growth Model	3.30	3.10	4.20
Can Zhou[27]	2020	China	SEIR Model	2.12	2.04	2.18
Tao Liu[28]	2020	China	Statistical Exponential Growth Model	4.50	4.40	4.60
Tao Liu[28]	2020	China	Statistical Exponential Growth Model	4.40	4.30	4.60
Ruiyun Li et al[29]	2020	China	Networked Dynamic Metapopulation Model	2.23	1.77	3.00
Sang Woo Park et al[30]	2020	China	MCMC	3.10	2.10	5.70
Nian Shao et al[31]	2020	China	Fudan-CCDC Mode	3.32	3.25	3.40
Huijuan Zhou et al[32]	2020	China	SEIQ Model	5.50	5.30	5.80
Alessia Lai et al[33]	2020	China	Coalescent-Based Exponential Growth And a Birth-Death Skyline Method	2.60	2.10	5.10
Sung-mok Jung et al[9]	2020	China	MCMC	2.10	2.00	2.20
Sung-mok Jung et al[9]	2020	China	MCMC	3.20	2.70	3.70
Steven Sanche et al[34]	2020	China	Statistical Exponential Growth Model	6.30	3.30	11.30
Steven Sanche et al[34]	2020	China	Statistical Exponential Growth Model	4.70	2.80	7.60

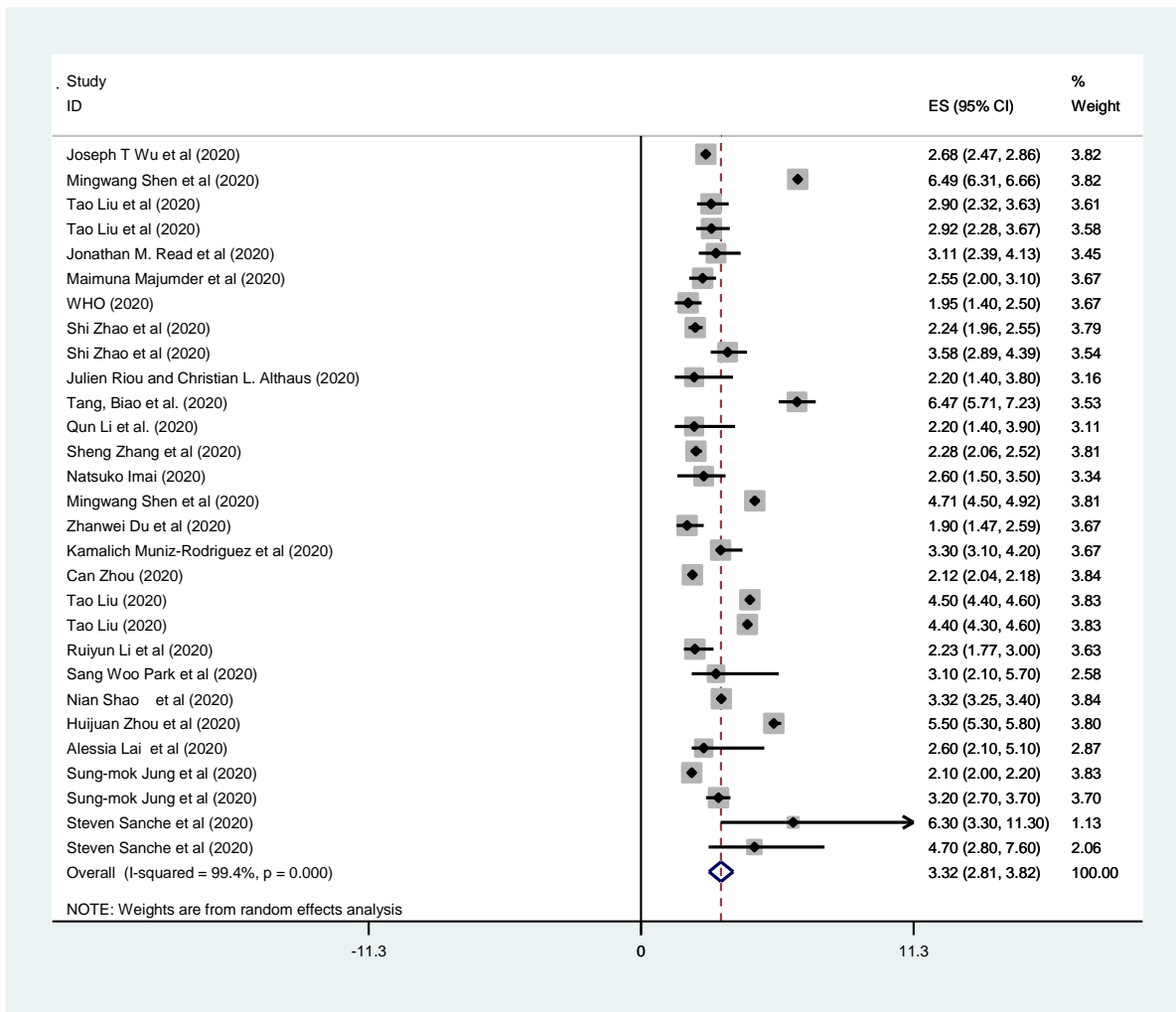


Figure2. Forest plot of the pooled basic reproductive number (R_0) for COVID-19

Table2. Pooled Estimation of reproductive number (R_0) for COVID-19

Pooled Estimate(95% CI)	Q	I ²	T ²
3.32(2.81-3.82)	<0.001	99.3	1.72

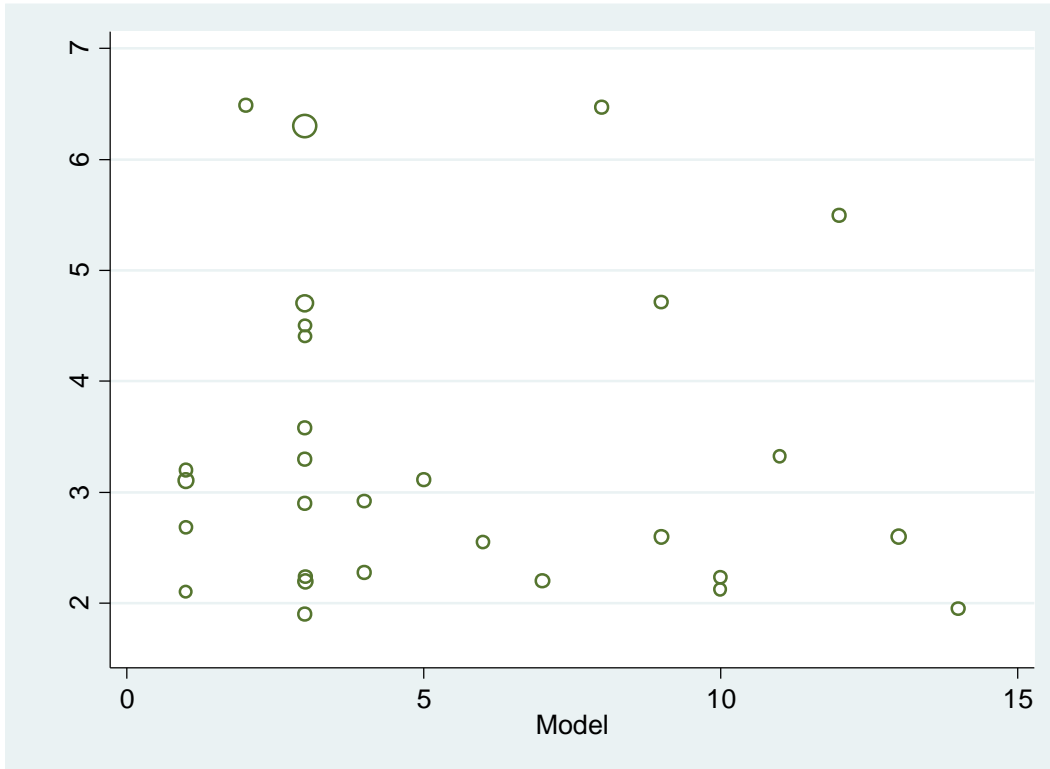


Figure3. The distribution of estimated R_0 according to different models.

DISCUSSION

It is necessary to estimate the amount of R_0 to determine the severity and size of the epidemic, as well as to design appropriate interventions and responses to protect the population against disease and to control of the epidemic [35]. The estimated R_0 value is important in infectious disease epidemiology because the force of infection could be reduced by $1 - 1/R_0$ to eliminate the disease outbreak. For example, at $R_0 = 2.5$ this fraction is 60%, but at $R_0 = 3.2$ this fraction is 68.7%. Mathematical models play an important role in decision making during outbreak control [36]. Our systematic review and meta-Analysis found the overall R_0 to be 3.32(2.81-3.82), which is more than WHO estimates of 1.4 to 2.5(11) but similar to results of a former review with 12 articles that have had been conducted in China (11). Our estimation is similar in comparison with the R_0 values of the SARS epidemics ($R_0 = 4.91$) in Beijing, China [37], and MERS in Jeddah ($R_0 = 3.5-6.7$), Saudi Arabia [38]. Such a high R_0 indicates that the virus can go through at least three–four generations of transmission [22]. Similar to reviews of R_0 for other pathogens [39-41] our result highlight that R_0 is not an intrinsic value characteristic of a given pathogen, but rather describes the transmissibility of that pathogen within the specific population and setting under study. The estimated R_0 depends on some

issues such as the social and demographical variables, estimation method used, and the validity of the underlying assumptions and the biology of the infectious agent. For example, the frequency of contacts may depend on population size and cultural issues. These factors can vary across regions. In addition, estimates of R_0 may be somewhat error-prone due to some reasons such as data insufficiency and short onset time period. The more studies are done and the more data is produced, the hope is that this error will be reduced. Our results showed that there was significant heterogeneity between studies ($I^2:99.3$, P of χ^2 test for heterogeneity < 0.001 and $T^2: 1.72$). One reason for this issue is that it is hard to calculate the exact number of infected cases during an outbreak. The variability in R_0 values reported by different studies indicates that precisely estimating of R_0 is rather difficult. Also, the R_0 can be affected by environmental factors and modeling methodology [12]. There are lots of calculation methods for R_0 [42]. Our review was restricted to Chinese articles. For other countries surveillance data is needed to either calculate R_0 value or R_0 estimates extrapolate from a comparable setting.

Consideration of the reasons for reporting high levels of R_0 in some studies also seems necessary. Modeling assumptions may be one reason for this issue. Usually, high R_0 values are calculated in the early stages of the epidemic, because of the small sample size as well as the lack of awareness about the disease and inadequate preventive measures. Since the number and patterns of people's contacts in different populations vary because of some reasons, such as the general culture and the level of literacy in the community, the value of R_0 varies among different populations, or even among subgroups of a single population. In fact, the total value of R_0 in a population is the average of the R_0 subtypes of that community. It is therefore important to note that even if the total R_0 value in a population is low (even less than 1), the likelihood of transmission in some subgroups of that population may still be high. Given the rapid spread of the disease, the dependency of the effectiveness of control measures to some factors such as the frequency of asymptomatic infections and the potential for disease transmission before symptoms onset, COVID-19 seems to be relatively difficult to control. R_0 is dependent on the population as well as the method of calculation and quantifies the transmissibility of a disease in a population. Our findings suggest that measures such as preventing human population gatherings, restricting the transportation system, closing schools, and universities, etc., may be necessary to control the epidemic.

SUPPLEMENTAL MATERIALS

None

CONFLICT OF INTEREST

The authors have no conflicts of interest associated with the material presented in this paper.

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AUTHOR CONTRIBUTIONS

YA, M S conceived the study design, Search of articles, provided data, led the analysis, prepare drafts of the manuscript, M T data extraction, prepare drafts of the manuscript and final edition. All authors approved final version of manuscript.

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