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## Evaluating the effectiveness of control measures in multiple regions during the early phase of the COVID-19 pandemic in 2020



Zengmiao Wang<sup>a,\*</sup>, Jason Whittington<sup>b</sup>, Hsiang-Yu Yuan<sup>c</sup>, Hui Miao<sup>d</sup>, Huaiyu Tian<sup>a</sup>, Nils Chr. Stenseth<sup>b,\*</sup>

<sup>a</sup>State Key Laboratory of Remote Sensing Science, Center for Global Change and Public Health, College of Global Change and Earth System Science, Beijing Normal University, Beijing 100091, China

<sup>b</sup>Centre for Ecological and Evolutionary Synthesis (CEES), Department of Biosciences, University of Oslo, Oslo N-0315, Norway

<sup>c</sup>Department of Biomedical Sciences, Jockey Club College of Veterinary Medicine and Life Sciences, City University of Hong Kong, Hong Kong 999077, China

<sup>d</sup>Department of Statistics, College of Art and Science, Ohio State University, Columbus, OH 43210, USA

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### ABSTRACT

The number of COVID-19 confirmed cases rapidly grew since the SARS-CoV-2 virus was identified in late 2019. Due to the high transmissibility of this virus, more countries are experiencing the repeated waves of the COVID-19 pandemic. However, with limited manufacturing and distribution of vaccines, control measures might still be the most critical measures to contain outbreaks worldwide. Therefore, evaluating the effectiveness of various control measures is necessary to inform policymakers and improve future preparedness. In addition, there is an ongoing need to enhance our understanding of the epidemiological parameters and the transmission patterns for a better response to the COVID-19 pandemic. This review focuses on how various models were applied to guide the COVID-19 response by estimating key epidemiologic parameters and evaluating the effectiveness of control measures. We also discuss the insights obtained from the prediction of COVID-19 trajectories under different control measures scenarios.

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### 1. Introduction

On 31 December 2019, a novel coronavirus (severe acute respiratory syndrome coronavirus 2, SARS-CoV-2, although the name still in debate [1]) was reported [2,3]. However, due to the high human-to-human transmissibility (the basic reproductive number,  $R_0$  2.2–2.7 [4]), more than 175 million cases were reported, with 3 million deaths due to coronavirus disease 2019 (COVID-19) worldwide by June 2021 [5]. In addition, the transmission also through asymptomatic cases [6] makes the disease control more challenging [7,8] because many of them are not identified and isolated.

With the improvement in the case definition of COVID-19 [9,10] and fast-growing accumulated cases, we gradually understood the transmissibility and severity of this virus in the first wave of China [11]; many models are employed to provide timely and quantitative support. The choice of the models depends on the specific questions that need to be addressed. During the early stage of the pandemic,

especially for a novel pathogen, the first question is to know the epidemiological parameters, e.g., the basic reproduction number ( $R_0$ ) and serial interval. With these parameters, we will learn how fast an infectious disease will spread without any control and what will happen if the interventions are introduced. Transmission-dynamic models have been most widely used to estimate these parameters. Different differential equations are used to divide the population into separate compartments based on epidemiological status (for example, S for susceptible, E for exposed, I for infectious, and R for recovered in an SEIR model).

The following questions deal with how to treat infected patients and prevent others from getting infected. The development of drugs [12–16] is in progress, but for now, no drugs show significance in clinical outcomes [17–20]. COVID-19 patients maintained SARS-CoV-2-specific IgG and neutralizing antibodies five or six months after infection [21,22], providing effective signs for prevention from reinfection and vaccination strategy [23]. Although the COVID-19 vaccines show safety and high protection against COVID-19 [24–33], they will not be available widely soon due to limitations in manufacturing and distribution. Besides, it is still unknown how long the vaccines can protect us from the SARS-CoV-2 virus. Repeated outbreaks can occur if immunity can also maintain several months. Therefore, control measures are still significant measures to reduce transmission in the foreseeable future. The intensities of control measures vary greatly, from relatively

\* Corresponding authors: State Key Laboratory of Remote Sensing Science, Center for Global Change and Public Health, College of Global Change and Earth System Science, Beijing Normal University, Beijing 100091, China (Zengmiao Wang); Centre for Ecological and Evolutionary Synthesis (CEES), Department of Biosciences, University of Oslo, Oslo N-0315, Norway (Nils Chr. Stenseth).

E-mail addresses: [wangzengmiao@bnu.edu.cn](mailto:wangzengmiao@bnu.edu.cn) (Zengmiao Wang), [n.c.stenseth@mn.uio.no](mailto:n.c.stenseth@mn.uio.no) (Nils Chr. Stenseth).

flexible ones (for example, social distancing) to very stringent approaches (for example, lockdown). The effects of these control measures on COVID-19 transmission also vary correspondingly. It is important to quantify these effects quickly to inform the policy-makers to address the ongoing outbreaks. Therefore, various models are used to assess the effectiveness of different control measures [34–36] and evaluate the intervention strategies under different scenarios [37–41].

To focus on how the models were applied to guide the COVID-19 pandemic response, we summarize the recent estimations of some key epidemiologic parameters and evaluate the effectiveness of control measures using various models in this review. We also discuss the insights obtained from the predictions of the trajectories of COVID-19 under different control measures scenarios, with the genomics and applications in the COVID-19 pandemic also summarized.

## 2. The parameters estimation in the early stage of the COVID-19 pandemic

For the parameter estimation, the reproduction number (the average number of secondary cases each case generates) is of primary interest (see Table 1 for the definitions of epidemiological characteristics). It indicates that the disease continues to grow if the value is more than 1 and reduces in frequency but may die out if it is smaller than 1. Thus, this is the first important parameter usually assessed about the disease and directly indicates control measures.

In the early stage of the COVID-19 pandemic, diverse models with different assumptions were used to estimate the  $R_0$  of the SARS-CoV-2 virus across regions/countries. Insightful results were obtained based on the COVID-19 case surveillance data. Using the model formulated renewal equations,  $R_0$  was about 2.2 by January 22, 2020, in Wuhan [42]. By modelling the transmission with a Poisson process, this parameter in Wuhan was reported to be 2.7–4.0 before December 31, 2019 [43] and above 3.0 before January 26, 2020 [44]. In Niger, it fluctuated between 0.4 and 3.0, with a wide 95% CI before March 17, 2020, using the same Poisson process transmission model [45]. Following the classic susceptible-exposed-infectious-recovered (SEIR) model,  $R_0$  was 2.68 in Wuhan by January 25, 2020 [46] and 3.15 before the introduction of the emergency response on January 23, 2020, at the province level in China [47]. With the extension of a classic SEIR model to seven compartments (adding pre-symptomatic infectious, unascertained infectious, and isolation in hospital compartments),  $R_0$  was estimated to be 3.54 before control measures were taken in Wuhan [48]. The susceptible-infectious-recovered (SIR) model (similar to the SEIR model, but without E compartment) stratified by age groups and contact patterns were also proposed, and  $R_0$  was 1.0–4.0 before interventions for Wuhan and Shanghai, China [49]. With the spread of this virus to the world, the  $R_0$  was estimated at an international scale. In Japan, it was reported to be 4.66, calculated from a susceptible-infectious-recovered-deceased (SIRD) model [50]. Based on the likelihood-based estimation procedure for severe acute respiratory syndrome (SARS) [51],  $R_0$  was 4.02 on March 17 in the United States [52] and about 2.0 on March 20, 2020, in Canada [53]. Case surveillance data suffers from the limited PCR testing capacity or the undocumented infection [54–56], especially for the emergence of a novel pathogen. Considering that, Flaxman et al. [57] proposed a set of statistical models (death model and infection model) based on death data to estimate  $R_0$ . They performed a comprehensive analysis by including the countries of Europe.  $R_0$  was estimated to be 3.8 (95%CI: 2.4–5.6) on average across all European countries. Although the variance of  $R_0$  exists from different models or regions, all of them were larger than 1 (see Table 2 for  $R_0$  before and after control measures). This was a consistent indication that the outbreak of

**Table 1**  
Common terms for epidemiological characteristics and their definitions.

Term	Definition
Attack rate	A kind of incidence rate that measures the proportion of persons in a narrowly defined population observed for a limited period of time, such as during an epidemic
Basic reproduction number	The average number of secondary cases each primary case generates
Case-fatality rate	The rate of death among people who already have a condition
Effective reproduction number	The average number of new infections caused by a single infected individual at time $t$ in the partially susceptible population
Generation time	The time duration from the onset of infectiousness in a primary case to the onset of infectiousness in a secondary case infected by the primary case
Incubation time	The time from exposure to a disease to when the first signs or symptoms of the disease occur
Primary case	A person who acquires a disease from an exposure, for example, to contaminated food
Secondary attack rate	A measure of the frequency of new cases of a disease among the contacts of known cases
Secondary case	A person who gets a disease from exposure to a primary case
Serial interval	The duration of time between onset of symptoms in a primary case and a secondary case

SARS-CoV-2 would worsen, and actions should be taken to prevent the spread of this virus.

Besides  $R_0$ , other parameters are also of interest and estimated using statistical methods, including incubation time, serial interval, generation time, and attack rate. The mean incubation period for the time window from December 24, 2019, to February 17, 2020, was estimated to be 5.2 days (95%CI: 1.8–12.4), and the mean serial interval at 5.1 days (1.3–11.6) outside Hubei Province, China [58]. The generation time was 4.6 (95%CI: 4.2–5.1) days based on the data from Jan. 1, 2020, to Feb. 11, 2020, in China [59]. The attack rate of health care workers in Wuhan was about 11.9% [60], and the secondary attack rate among household contacts was 12.4% (95%CI: 9.8–15.4) [61]. Some other characteristics of COVID-19 were also significant and estimated. For example, rates of symptomatic cases, medical consultations, hospitalizations, and deaths in Wuhan from December 1, 2019, to March 31, 2020, were estimated to be 796 (95%CI: 703–977), 489 (95%CI: 472–509), 370 (95%CI: 358–384), and 36.2 (95%CI: 35.0–37.3) per 100,000 persons, respectively [62]. By March 2, 2020, The overall estimated case-fatality rate was 3.6% (1.1–7.2) [63]. After the COVID-19 pandemic was under control, the overall hospitalized case fatality rate (CFR.) in China was estimated to be 4.6% (95%CI: 4.5%–4.8%) [64], and the overall symptomatic case fatality risk of COVID-19 in Wuhan became 1.4% (0.9%–2.1%) [65]. Clinical characteristics were also reported [66]. These epidemiological parameters enable us to deepen our understanding of this disease that provided vital information to policymakers.

## 3. Search strategy and selection criteria

We used google scholar to search the literature related to the effectiveness of control measures published from December 1, 2019, to December 30, 2020, in each country. The following keywords were used: non-pharmaceutical interventions (or NPIs, control measures), name of the country, and COVID-19 (or SARS-CoV-2). To include all possible control measures, we did not specify the control measures

**Table 2**

The reproduction number of COVID-19 before and after the introduction of control measures for the countries. The time and type of conducting the control measures was defined in the corresponding reference.

The reproduction number	Before control measures	After control measures	Data Type	Model	Time	Reference
China	1 ~ 4	<1	The daily case data	The classic SEIR model, the model formulated with the use of renewal equations, Poisson process, the extension of a classic SEIR model to seven compartments, the SIR model stratified by age groups and contact patterns	12/8/2019 to 3/8/2020	[42–44,46–49]
Niger	0.4 ~ 3	Around 1	The daily case data	Poisson process	3/19/2020 to 7/4/2020	[45]
Japan	4.66	1.79	The daily case data	A susceptible-infectious-recovered-deceased model	1/22/2020 to 5/14/2020	[50]
United States	4.02	1.51	The daily case data	The likelihood-based estimation procedure	3/17/2020 to 4/1/2020	[52]
Canada	2	<1	The daily case data	The likelihood-based estimation procedure	3/20/2020 to 6/10/2020	[53]
France	4 ~ 5	<1	The death data	A set of statistical models (death model and infection model)	2/2020 to 5/4/2020	[57]
Italy	3 ~ 4	<1	The death data	*	*	[57]
Spain	4 ~ 6	<1	The death data	*	*	[57]
UK	Around 4	<1	The death data	*	*	[57]
Belgium	4 ~ 6	<1	The death data	*	*	[57]
Germany	3 ~ 5	<1	The death data	*	*	[57]
Sweden	2 ~ 3	<1	The death data	*	*	[57]
Switzerland	3 ~ 4	<1	The death data	*	*	[57]
Austria	3 ~ 5	<1	The death data	*	*	[57]
Norway	2 ~ 4	<1	The death data	*	*	[57]
Denmark	3 ~ 5	<1	The death data	*	*	[57]

\*Same with above one.

for each country. Instead, titles and abstracts of papers published in English were screened, meeting that a model (either a statistical or a mathematical model) was used to evaluate the effectiveness of implemented control measures on COVID-19 for countries. We excluded studies that evaluated the effects of control measures related to economics, other diseases, or the optimal control measure strategies.

#### 4. The evaluation of the effects of control measures using various models

##### 4.1. The different control measures and related effectiveness

On January 23, 2020, the first lockdown strategy in the world to prevent the dispersal of COVID-19 was implemented in Wuhan, China. At the same time, other types of control measures, such as case isolation, suspending public transport, closed down schools and entertainment venues, and banning public gatherings, were also applied. Additionally, the highest level of emergency for public health response was initialized nationally in China to prepare against outbreaks in other regions. In the pioneering analysis of evaluating the control measures' effectiveness in Wuhan, the Wuhan shutdown was related to the delayed arrival of COVID-19 in different cities in China by 2.91 days [47,67]. Wuhan's 'travel restriction' strategy showed a more marked effect on the international scale, where case importations were reduced by nearly 80% until mid-February [68].

Most countries adopted similar interventions to contain the transmission of COVID-19, such as case-based self-isolation mandates, encouragement of social distancing, banning public events, and ordering school closures and lockdowns. During the 1918 influenza pandemic 100 years ago, similar control measures had also been employed [69,70]. The various control measures [71] showed substantial effects on economics [72] and the physical and mental health of

individuals [73–80]. Therefore, evaluating the effectiveness of timely control measures is recognized as a crucial step to combat this virus.

The time-dependent reproduction number ( $R_t$ ), also called effective reproduction number, was employed to evaluate the effects of combined control measures (see Table 2). For countries, this value was smaller than one after control measures, such as China in Asia [47,48,81], and the 12 countries in Europe and North America [53,57]. But for Japan [50] and the United States [52],  $R_t$  remained higher than 1. Other indicators were also used to illustrate the effect of control measures. Dehning et al. [82] focused on the spreading rate and found that it was 0.09 around 23 March 2020, showing the control measures were effective and new cases began to decline in Germany. Serial intervals were also used to inform the effectiveness of control measures. It was 7.8 days on average in mid-January 2020 and decreased to 2.2 days in early February 2020 in China after implementing control measures on January 23, 2020 [83]. The reduction of those indicators showed that the control measures were adequate to control COVID-19. However, the effectiveness of control measures appeared different in different countries, revealing differences in public response and cooperation with these measures.

Based on the Complexity Science Hub COVID-19 Control Strategies List (CCSL) [71], the control measures are classified into a four-level hierarchical structure, from eight broad themes at level 1 to <2,000 group codes at level 4. With so many different control measures, it is essential to understand each type's effectiveness. A series of studies were conducted based on other models and criteria. In a comprehensive analysis across the 11 European countries, the researchers [57] found that lockdown had a significant identifiable effect on transmission (81% (95%CI: 75%–87%) reduction) of the SARS-CoV-2 virus in terms of  $R_t$  by a set of statistical models (death model and infection model). At the same time, public events bans, school closures, self-isolation, social distancing, etc., did not significantly reduce the transmission of the SARS-CoV-2 virus. Under a stochastic age-structured transmission model, the potential impact of four different control mea-

asures (school closures, physical distancing, shielding of people aged 70 years or older, and self-isolation of symptomatic cases) was assessed to mitigate the related burden of COVID-19 in the U.K. It was concluded that the four interventions were each likely to decrease  $R_t$ , but not sufficiently to prevent ICU demand from exceeding health service capacity, and only the lockdown periods were sufficient to bring  $R_t$  below 1 [84]. The effectiveness of lockdown is consistent with a previous study of interventions [57], and the same conclusion about the importance of lockdowns was also made in France [85,86]. By extended SEIR model (two additional compartments: A, infectious and asymptomatic; F, dead) and variance analysis, Chiu et al. [87] found that the fraction of contacts traced was one of the most significant drivers of variation in  $R_t$  in the United States and other most significant drivers including hygiene effectiveness relative to social distancing, the degree of mitigation during shelter-in-place, and maximum relative increase in contacts from shelter-in-place. They together contribute greater than 50% of the variance in  $R_t$ . The daily growth rate of COVID-19 cases was also used to evaluate the effectiveness of control measures. Lin et al. [88] studied the effect of the “stay-at-home” order from March 16, 2020, to April 10, 2020, at the state level in the United States using Poisson regression. They found that the growth rate had slowed down since March 29, 2020, with an average reduction of 12.8%. Courtemanche et al. [89] employed an event regression study and found that the shelter-in-place orders in the United States had led to statistically significant ( $P < 0.01$ ) reductions in the COVID-19 case. The growth rates reduced by 3.0% after six to ten days, 4.5% after eleven to fifteen days, 5.9% after sixteen to twenty days, and 8.6% from twenty-one days onward. Their study also showed that closing restaurant dining rooms and bars or entertainment centers and gyms led to significant reductions in the growth rate of COVID-19 cases in all periods after introduction. At the same time, public school closure did not affect the daily growth rate. As for mandating face mask use in public, it was reported that this measure was associated with a decline in the daily COVID-19 growth rate by 0.9%, 1.1%, 1.4%, 1.7%, and 2.0% in 1–5, 6–10, 11–15, 16–20, and 21 or more days after state face mask orders were signed, respectively [90].

Although different models and criteria were employed, the conclusion was reached that control measures are adequate to control the transmission of the SARS-CoV-2 (see Table 3 for the evaluated control measures). The lockdown was the most effective one in studies from Wuhan, China to Europe of the various control measures. The importance of early intervention and aggressive control [91], contact tracing [92,93], and face masks [94], and eye protection [95] in combatting the COVID-19 pandemic were also highlighted. In addition, the model also explained the sub-exponential growth of COVID-19 cases before February 2020 in China [96] and the impact of socioeconomic factors on the transmission of this virus [97,98]. An interesting finding is that the control measures reduced not only the transmission of COVID-19 but also other respiratory infectious diseases [99–102].

#### 4.2. The evaluation of control measures integrated with big data: mobility and social media

Big data has been widely used to investigate the COVID-19 transmission in the current pandemic [103–111]. Successful examples include the human-mobility-based transmission-dynamic model. With the assistance of big data and powerful computational resources, a more detailed picture of SARS-CoV-2 dynamics will be available.

Human movement is responsible for spreading infectious diseases, and data on movement patterns have been successfully applied to understand the transmission of infectious diseases [112–116]. Previous studies have shown that the spread of COVID-19 from Hubei Province to other provinces of China was driven primarily by human mobility [117–122]. Multiple transmission-dynamic models are needed to inte-

grate the mobility data for the areas of interest in general. The mobility from one place to another is incorporated into the transmission-dynamic models for these two regions and represents the compartments flow between these two regions. By taking all the transmission-dynamic models as a whole, related parameters can be estimated. At the exact time, related public health efforts can be quantified, and the control measures can be evaluated. Aggregating mobile phone data in Shenzhen, China to the SEIR model, Zhou et al. [104] found that if intra-city mobility were reduced by 20%, the epidemic peak would have been delayed for about two weeks, with peak incidence decreasing 33%. If the reduction increased to 40%, the peak would be delayed by four weeks and the peak daily incidence reduced by around 66%. A 60% reduction in mobility delayed the peak by 14 weeks and decreased the magnitude of the epidemic by 91% (see Table 4). A study in the U.K. showed that human mobility reduction significantly impacted reducing COVID-19-related deaths [123]. Using COVID-19 data and travel network information, Lai et al. [124] developed a stochastic SEIR framework to simulate different outbreaks and interventions (early detection, isolation of cases, travel restrictions, and contact reductions) across China. They found that the effectiveness of other control measures varied. Early detection and isolation of patients averted more cases than did travel restrictions and contact reductions. However, the combination of these control measures was found to achieve the most vigorous and most rapid effect. Schlosser et al. [125] found that COVID-19 lockdown induces structural changes in mobility networks in Germany while distancing and isolation can flatten the curve with a SIR model integrated with the mobility network. Using data on high-speed train passengers from 19 December 2019 through 6 March 2020 in China, Hu et al. [126] found that COVID-19 has a high transmission risk among train passengers. Still, this risk showed significant differences with co-travel time and seat location. The transmission rate decreased with increasing distance traveled and increased with increasing co-travel time. Besides, smartphone applications through Bluetooth or GPS site to track interaction between individuals are proposed to increase efficiency of contact tracing [127–130].

Information sharing and transmission have dramatically improved due to social media tools, such as Facebook, Twitter, YouTube, and WhatsApp [131]. With these platforms, public health guidelines about COVID-19 reached the world with incredible speed. Based on the penetration of social media, many helpful topics were investigated during the pandemic, such as public attention [132–134], predicting the epidemic outbreak [135,136], and human sentiments [137]. The spatial transmission of COVID-19 in Wuhan, China was also studied using the geo-tagging Sina Weibo data [138].

#### 4.3. Suppression vs. Mitigation

Irrespective of the specific approaches, the critical question is what we can learn from the current pandemic responses. The governments in each country adopted customized control measures strategies to contain the spread of COVID-19 cases based on their politics, economics, and culture, ranging from stringent lockdowns, the “Flatten the curve” approaches, to voluntary control measures. Although control measures vary, they can generally be classified into two groups (see Table 5): 1) Suppression; 2) Mitigation [139]). Suppression aims to reduce  $R_t$  to below one and eliminate human-to-human transmission gradually. Mitigation seeks to slow down the speed of the virus transmission to delay the arrival time of the pandemic peak to have more time to prepare medical supplies and avoid the over-extension of medical resources to minimize avoidable deaths. In terms of which strategies were employed by different countries, China, South Korea, and India opted to focus on suppression, while most other countries pursued mitigation. However, the results of the control measures strategies are still challenging to predict. India employed the Suppression strategy and locked down the whole country from March 25, 2020,

**Table 3**  
The evaluated control measures and the used models.

Evaluated control measures	Effect	Region	Model	Time	Reference
Lockdown Public events School closure Self-isolation Social distancing encouraged	81% (75%–87%) relative reduction in $R_t$ < 5% relative reduction in $R_t$	11 European countries	A set of statistical models (death model and infection model)	2/2020 to 5/4/2020	[57]
School closures Physical distancing Shielding of people aged 70 years or older Self-isolation of symptomatic cases	Each could cause insufficient reduction in $R_t$ . The combined intervention is more effective ( $R_t < 1$ )	UK	A stochastic age-structured transmission model	12/2019 to 5/11/2020	[84]
Lockdown	77% reduction in reproductive number.	France	A suite of modeling analyses	3/17/2020 to 5/11/2020	[85]
Social distancing Testing Contact tracing	They together contribute >50% of variance in $R_t$	US	An extended SEIR model (two additional compartments: A, infectious and asymptomatic; F, dead)	3/19/2020 to 7/22/2020	[87]
Stay-at-home	The growth rate had slowed down since March 29, 2020 with an average reduction of 12.8%	US	Poisson regression	1/21/2020 to 4/10/2020	[88]
Shelter-in-place orders Bans on large gatherings Restaurant or entertainment center closures Public school closures	Significant reductions in the growth rate of COVID-19 cases Significant reductions in the growth rate of COVID-19 cases No effect on the daily growth rate of COVID-19 cases	US	An event study regression	3/1/2020 to 4/27/2020	[89]
Face masks or covers	A decline in the daily COVID-19 growth rate by 0.9%, 1.1%, 1.4%, 1.7%, and 2.0% in 1–5, 6–10, 11–15, 16–20, and 21 or more days after state face mask orders were signed, respectively	US	An event study regression	3/31/2020 to 5/22/2020	[90]
Lockdown The Wuhan travel restriction The national emergency response	Reduced the number of cases in other cities across China Prevented almost all of travel movement and markedly reduced the number of exportations of COVID-19 from Wuhan A delay in epidemic growth and a reduction in case numbers during the first 50 days of the COVID-19 epidemic in China	China	SEIR model; Regression analysis;	12/31/2019 to 2/9/2020	[47]
Early detection Isolation of cases Travel restrictions	The number of cases of COVID-19 could have been reduced by 66% (IQR 50%–82%), 86% (81%–90%) or 95% (93%–97%), respectively NA If population contact resumed to normal levels, the lifting of travel restrictions might cause case numbers to rise again	China	The stochastic SEIR model	1/23/2020 to 4/13/2020	[124]
Contact reductions	Maintaining social distancing even to a limited extent (for example, a 25% reduction in contact between individuals on average) through to late April would help to ensure control of COVID-19 in epicenters such as Wuhan				

**Table 4**  
The influence of mobility reduction on epidemic peak and epidemic peak incidence.

Mobility reduction	Epidemic peak	Peak incidence	Time	Reference
20%	Delayed by about 2 weeks	Reduced by around 33%	1/10/2020 to 2/20/2020	[104]
40%	Delayed by 4 weeks	Reduced by around 66%		
60%	Delayed by 14 weeks	Reduced by 91%		

to May 31, 2020. Yet,  $R_t$  is still above 1 for most states in India, except Gujarat [140]. Sweden took a unique approach of not implementing strict closures instead of relying on personal responsibility. Despite such loose control measures,  $R_t$  was strikingly below 1 [57]. A study [141] showed that mild mandates overlaid with voluntary standards could achieve results highly similar to late-onset strict orders in an individual-based model. The data from Google and Apple reported an 18%–33% decrease in the workplace during April [141,142] in Sweden supports this conclusion. The phenomenon in India and Sweden may be caused by several factors, such as differences in population density, the degree of policy implementation, the willingness of public

cooperation, and the quality of health services. If the public follows the guidelines well, lockdown may be unnecessary.

## 5. Integration of modelling results into decision making

Another essential feature from modeling is that we can predict the trajectory of COVID-19 under different control measures scenarios and appropriately inform policy-makers (see Table 6). According to the stochastic SEIR model from a previous study [124], if population contact were to resume to normal levels, the lifting of travel restrictions might lead to another wave of infections. Thus, maintaining social dis-

**Table 5**  
Two strategy categories of control measures and their related countries.

Strategy	Goal	Country	Reference
Mitigation	Reducing peak healthcare demand while protecting those most at risk of severe disease from infection. ( $R_t < 1$ )	China, India, South Korea	[139]
Suppression	Reducing case numbers to low levels and maintaining that situation indefinitely.	Most of other country (e.g., Sweden, US)	[139,141,142]

\* Although the intervention strategies are summarized into two categories, it is hard to decide the category for each country, since most of the control measures are the combination of mitigation and suppression strategies.

tancing, Chang et al. [143] proposed a metapopulation susceptible–exposed–infectious–removed (SEIR) model that integrates fine-grained, dynamic mobility networks in ten of the largest U.S. metropolitan areas. According to their model, a small minority of ‘super-spreaders points of interest (such as restaurants and religious establishments) account for a large majority of the infections, and restricting the maximum occupancy at each end of interest is more effective than uniformly reducing mobility. The IHME COVID-19 Forecasting Team [144] uses a deterministic SEIR (susceptible, exposed, infectious, and recovered) model to predict possible trajectories of COVID-19 in the United States from 22 September 2020 through 28 February 2021. They found that the universal mask use (95% mask use in public) could be sufficient to avert the worst effects of epidemic resurgences in many states. This strategy could save an additional 129,574 (85,284–170,867) lives from September 22, 2020, through the end of February 2021, or another 95,814 (60,731–133,077) lives, assuming 85% of mask-wearing, when compared to the current social distancing mandates. Using mobility and case data, Ruktanonchai et al. [145] indicated that appropriate coordination could significantly improve the likelihood of eliminating community transmission throughout Europe.

## 6. The application of genomics in COVID-19

With the development of next-generation sequencing technology, the SARS-CoV-2 genome was quickly released and shared [146]. The

work to trace the zoonotic origin of SARS-CoV-2 was also performed using the methods from the genomics field. Although the genome sequence showed that this novel virus has high similarity to the bat coronavirus RaTG13 with an overall genome sequence identity of 96.2% [147], there is a possibility of decades of evolutionary divergence between them [148]. The SARS-CoV-2 virus was closely related to SARS-like coronaviruses [146]. SARS-CoV-2 affects more regions within a shorter time than SARS-CoV, infecting older people with a higher probability [149]. However, the pathway of transmission from zoonotic reservoirs to humans is still unknown. Therefore, multi-source discipline methods (for example, geography and molecular epidemiology) and multi-source data (for example, human mobility and sequences from wild animals) are needed.

By now, there have been over 250,000 SARS-CoV-2 genome sequences deposited worldwide [150]. The most common SARS-CoV-2 virus clusters/clades in a region/country can be identified from a phylogenetic analysis of these sequences. The mutation diversity of the SARS-CoV-2 virus can be monitored [151] to identify the virus with greater transmissibility or pathogenicity (see Table 7). For example, the SARS-CoV-2 D614G variant is prevalent globally and transmits significantly faster, and displays increase competitive fitness than the wild-type virus in hamsters [152]. During the early stage of the COVID-19 pandemic in Washington state in the United States, researchers found that 84% of viral cases analyzed were grouped into a clade with SNPs of C8782T, C17747T, A17858G, C18060T, and T28144C, 9% were grouped into a smaller clade, and the rest of the viral cases were distributed across the phylogenetic tree [153]. Using the sequences from May 20, 2020, Yang et al. [154] found that the clade, featuring SNPs 241T, 3037T, 14408T, 23404G, 25563T, and 1059T, was dominant (~51.07%) in most states of the United States. In Brazil, 490 sequences collected from December 24, 2019, to April 30, 2020, were classified into three clades [155]. The first clade (38% of Brazilian strains) was featured with a nucleotide substitution (G25088T) in the spike protein in São Paulo state. The second clade (34%) had two SNPs in ORF6 (T27299C) and nucleoprotein (T29148C), and the third clade (4%) was especially prevalent in the Ceará state. It showed that 80% of secondary infections traced back to 15% of SARS-CoV-2 primary infections, indicating the heterogeneity in the transmission of COVID-19 [156]. Similarly, the super-spreading events in Boston also revealed high heterogeneity according

**Table 6**  
Predicted the trajectory of COVID-19 under different control measures scenarios.

Control measures	Scenario	Result	Time	Model	Reference
Contact reduction	Resume population contact to normal level	Another wave of infection	1/23/2020 to 4/13/2020	Stochastic SEIR	[124]
Social distance	Limited extend through late April 2020	Ensuring control of COVID-19		Stochastic SEIR	[124]
Mobility	Restricting the maximum occupancy at each high-risk point of interests	More effective control decision	3/1/2020 to 5/9/2020	Metapopulation SEIR	[143]
Mobility	Uniformly reducing mobility from neighbourhoods to point of interests	Less effective control decision		Metapopulation SEIR	[143]
Mask	95% mask use in public	Less death compared to current social distancing mandates; Sufficient to ameliorate the worst effects of epidemic resurgences in many states	9/22/2020 to 2/28/2021	Deterministic SEIR	[144]
Mask	85% mask use in public	Less death compared to current social distancing mandates		Deterministic SEIR	[144]
Lockdown coordination	Appropriate coordination through communities in Europe	The improvement of the likelihood of eliminating community transmission throughout Europe	1/28/2020 to 4/6/2020	Model with mobility and case data	[145]

**Table 7**  
The dominant variants in different regions.

Dominant variant	Proportion	Region	Reference
D614G	NA	Global	[152]
SNPs of C8782T, C17747T, A17858G, C18060T, and T28144C	84%	Washington, US	[153]
SNPs 241T, 3037T, 14408T, 23404G, 25563T and 1059T	51%	US	[154]
G25088T	38%	Brazil	[155]

to the phylogenetic analysis [157]. A long-term projection was also obtained from a deterministic model of multiyear interactions between existing coronaviruses for the United States [158]. Emerging new COVID-19 lineages, such as B.1.1.7 [160] and P.1 [161], have shown higher transmissibility than the existing ones. A recent study in France shows that current vaccination rates may not be sufficient to compensate for the increased transmissibility of B.1.1.7 [159], which indicates that the control measures are still needed. Although the vaccines are being rolled out, a disturbing question is whether the vaccines are still effective against new lineages. For example, B.1.351 may be associated with immune escape [160,161]. If this is true, it seems that we need rely on control measures. Considering the rapid evolution of SARS-CoV-2, suitable control measures will be proposed based on the prediction and the current status of SARS-CoV-2 clades [159,162–165].

## 7. Summary and suggestions

This review discusses how the models (such as SIS, SIR, and SEIR) can be applied to guide COVID-19 response [47,50]. Based on these models, we summarize the estimations of some key epidemiology parameters and evaluate the effectiveness of control measures. Using the available data type and the experience of the modelers, the statistical model is another option [52,53]. In terms of evaluating the effectiveness of control measures, most researchers adopt the use of transmission-dynamic models. Conclusions from models are consistent that the control measures were effective [166,167], and lockdown is the most effective way to mitigate the spread of the virus [168]. However, the effectiveness of control measures was evaluated in only a small proportion of countries. We suggest that more studies may be needed for more countries to complete the control measures, especially for low-income countries. With the complete characterization of the SARS-CoV-2 virus, more effective strategies can be applied to combat this virus.

We also discuss the insights obtained from predictions of the trajectories of COVID-19 under different control measures scenarios. By a phylogenetic tree analysis, we can get the complete picture of SARS-CoV-2 clades worldwide and monitor the mutation diversity to guard against the emergence of new strains using the massive genome sequence data. The transmission dynamics of COVID-19 are complicated, which is influenced by the nature of the virus [169–171], human behaviour [172], and meteorological factors [173–175]. Due to the difficulty in theory and computation, models have to simplify this process and focus on specific elements. Better data is needed [67] to get a more realistic model. More attention should be paid to inappropriate assumptions and the misinterpretation of data or results, especially for emerging infectious diseases with limited prior knowledge.

Based on the study, we proposed some suggestions for policymakers to contain the COVID-19 outbreak. First, if the COVID-19 situation is complicated, a lockdown policy may be employed to cut the transmission chain and bring  $R_t$  under one as soon as possible. And supplemented actions should be taken to curtail the spreading of the virus

indeed. Second, the measures should be taken as quickly as possible in case of missing the control window. Since more contagious COVID-19 lineages are emerging, it seems that not much time is left if the more contagious COVID-19 clans seed in a region. Third, improving the public understanding of COVID-19 may increase general compliance with the control strategy. The individuals may be self-isolated when they realized the danger of the invisible enemy.

Although we tried to normalize and summarize the results from previous research, due to the variation of the data sources and models, the comparison of results from the literature may have left some unavoidable bias in this review. Furthermore, the evaluation of the effectiveness of control measures may be affected by other factors (e.g., the political environment and citizen consciousness) that were not considered in most of the previous research. Finally, whether the outcomes of control measures can be replicated in other parts of the world still needs further investigation.

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## Conflict of interest statement

The authors declare that there are no conflicts of interest.

## Author contributions

**Zengmiao Wang:** Data Curation, Investigation, Conceptualization, Writing – Original Draft, Writing - Review & Editing. **Jason Whittington:** Writing - Review & Editing. **Hsiang-Yu Yuan:** Writing - Review & Editing. **Hui Miao:** Data Curation, Investigation. **Huaiyu Tian:** Conceptualization. **Nils Chr. Stenseth:** Supervision.

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