

A dynamic model of the Coronavirus Disease 2019 outbreak to analyze the effectiveness of control measures

Shuhang Yang, PhD^{a,*}, Yu Liu, MS^b, Ke Chen, MD^c, Tong Li, MS^d, Yi Huang, PhD^e, Xiaolei Chen, MS^f, Pengfang Qi, MS^g, Yazhi Xu, BS^h, Feifei Yu, MSⁱ, Yuling Yang, PhD^j, Youhua Chen, PhD^k

Abstract

The World Health Organization (WHO) classified the spread of COVID-19 (Coronavirus Disease 2019) as a global pandemic in March. Scholars predict that the pandemic will continue into the coming winter and will become a seasonal epidemic in the following year. Therefore, the identification of effective control measures becomes extremely important. Although many reports have been published since the COVID-19 outbreak, no studies have identified the relative effectiveness of a combination of control measures implemented in Wuhan and other areas in China. To this end, a retrospective analysis by the collection and modeling of an unprecedented number of epidemiology records in China of the early stage of the outbreaks can be valuable.

In this study, we developed a new dynamic model to describe the spread of COVID-19 and to quantify the effectiveness of control measures. The transmission rate, daily close contacts, and the average time from onset to isolation were identified as crucial factors in viral spreading. Moreover, the capacity of a local health-care system is identified as a threshold to control an outbreak in its early stage. We took these factors as controlling parameters in our model. The parameters are estimated based on epidemiological reports from national and local Center for Disease Control (CDCs).

A retrospective simulation showed the effectiveness of combinations of 4 major control measures implemented in Wuhan: hospital isolation, social distancing, self-protection by wearing masks, and extensive medical testing. Further analysis indicated critical intervention conditions and times required to control an outbreak in the early stage. Our simulations showed that South Korea has kept the spread of COVID-19 at a low level through extensive medical testing. Furthermore, a predictive simulation for Italy indicated that Italy would contain the outbreak in late May under strict social distancing.

In our general analysis, no single measure could contain a COVID-19 outbreak once a health-care system is overloaded. Extensive medical testing could keep viral spreading at a low level. Wearing masks functions as favorably as social distancing but with much lower socioeconomic costs.

Abbreviations: CDC = Center for Disease Control, COVID-19 = Coronavirus Disease 2019, SEIR model = Susceptible-Exposed-Infectious-Recovered-Susceptible model, WHO = World Health Organization.

Keywords: control measures, Coronavirus Disease 2019, critical time, dynamic model, retrospective analysis

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^aYau Mathematical Science Center, Tsinghua University, ^bHuaHuiChangTian(Beijing) Information Technology Co., Ltd., ^cSchool of Nursing, Lanzhou University, Lanzhou, ^dChengdu University of Information Technology, ^eDepartment of Medicine, University of Chicago, Chicago, Illinois, ^fLudong University, Yantai, ^gAnhui University of Finance and Economics, Hefei, ^hLiaoning University of Technology, Jinzhou, ⁱOcean University of China, Qingdao, ^jJiangsu Key Laboratory of Urban Underground Engineering & Environmental Safety, Southeast University, Nanjing, ^kCAS Key Laboratory of Mountain Ecological Restoration and Bioresource Utilization & Ecological Restoration and Biodiversity Conservation Key Laboratory of Sichuan Province, Chengdu Institute of Biology, Chinese Academy of Sciences, Chengdu, China.

* Correspondence: Shuhang Yang, Yau Mathematical Science Center, Tsinghua University, Beijing 100086, China (e-mail: yangsh018@mail.tsinghua.edu.cn).

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1. Introduction

Coronavirus Disease 2019 (COVID-19) was recorded in December 2019 in a seafood market in Wuhan. However, its human-to-human transmission potential was unknown, and the pathogen was not identified for approximately 1 month.^[1] On Jan 20, 2020, Dr. Nanshan Zhong made a public announcement that the novel coronavirus can spread among humans.^[2] Two days later, strict control measures were carried out in Wuhan,^[3] and were soon implemented all over China.^[4] Control measures mainly included adding isolation wards, social distancing, wearing masks, and extensive nucleic-acid testing. Meanwhile, the local governments and the Center for Disease Control (CDC) began to record the tracks of confirmed cases and reported the records to public. All these efforts have effects on the spreading of COVID-19, and China contained its COVID-19 spreading in the middle of March.^[5]

However, the COVID-19 outbreak escalated in Europe in late February and in North America in March and it has spread worldwide at present. Almost all the affected countries took similar control measures as China did but at different levels. For example, South Korea carried out extensive medical testing^[6] and contained the spread of the virus at a low level.^[7] Italy implemented lock down procedures across the whole country on March 09.^[8] An estimation of the effectiveness of control measures became important for making intervention policies.

Several studies have reviewed and predicted COVID-19 spreading based on dynamical models, such as Susceptible-Exposed-Infectious-Recovered-Susceptible (SEIR).^[9,10] However, the SEIR model is more applicable for long term predictions when a certain percent of the population has recovered or become resistant. Previous and recent works have analyzed the effectiveness of control measures.^[11,12] However, few models have considered the capacity of health care as a crucial parameter for modeling and predicting virus spreading. We developed a dynamic model to describe an outbreak during approximately the first 3 months. The parameters of our dynamic model are directly connected to the implementation of control measures and the capacity of local health-care systems. Model simulations quantified the effectiveness of each measure and indicated the importance of medical capacity in the early stage of the outbreak.

2. Methods

2.1. Dynamic model

We considered the variables and parameters in Tables 1 and 2 and Fig. 1. Our dynamic model is based on the recurrence relations among the variables, which are functions of time t . The total population $Z(t)$ on day t decreases by the number of deaths on the previous day. The number of deaths is relatively small compared with the total population, so we regard $Z(t)=Z$ as a constant number. Here, we did not consider the travel of people. Here we did not take newborn population into consideration, since our following simulations have a typical time span 3 months.

We regarded recovered individuals as no longer susceptible to infection. Then, we have the relation between the susceptible population size $S(t)$ and the infected population size $I(t)$,

$$S(t) = Z - I(t). \quad (1)$$

The initial infection is an important parameter $I(0)=I_0$. Here, we assume the initial time point $t=0$ to be one average incubation period before the first confirmed case was reported.

We consider the onset (showing symptoms) but not isolated individuals to be resources of infection. We further divided this group into 2 parts: onset but not confirmed, whose population size on day t is denoted by $O(t)$, and confirmed but not isolated, whose population size on day t is denoted by $A(t)$. On day $t-1$, there were $O(t-1)+A(t-1)$ individuals who were contagious and not isolated, with an average daily close contacts r . An additional factor $S(t-1)/Z$ was introduced, which is the ratio of susceptible to total population. Therefore, a daily increase in infections on day t was estimated as

$$\Delta I(t) = \frac{r\beta[O(t-1) + A(t-1)]S(t-1)}{Z}. \quad (2)$$

This is the most important recursive relation in our dynamic model. It indicates the extend of virus spreading. We regarded the infected but not onset individuals as not contagious. There has been research to assess asymptomatic transmission,^[11] but we have not yet found sufficient supporting data. However, the onset patients would not be contagious indefinitely. In the situation of a

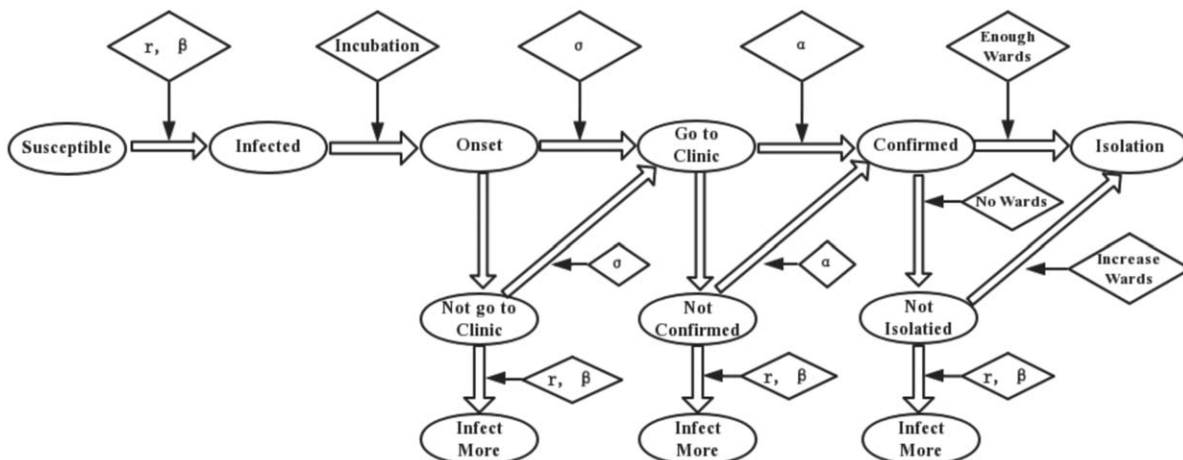


Figure 1. Chart of variables and parameters.

Table 1
Variables with associated epidemiological meanings used in the dynamic model.

Variables	
t	Time, in days
$Z(t)$	Total population
$S(t)$	Total number of susceptible individuals
$I(t)$	Accumulated number of infected individuals
$L(t)$	Accumulated number of individuals in incubation
$O(t)$	Accumulated number of individuals onset but not confirmed
$C(t)$	Daily increased number of confirmed cases
$A(t)$	Accumulated confirmed but not isolated cases
$H(t)$	Daily number of hospitalized individuals
$W(t)$	Remaining isolation wards of a health-care system
$D(t)$	Daily deaths in hospital
$R(t)$	Daily recovered patients from hospital

lasting medical emergency (defined below), we assumed that the individuals in $A(t)$ will remain contagious for an additional 7 days.

We assumed infected individuals will be onset after one average incubation period. Recall that $O(t)$ is the total number of onset but not confirmed individuals. Therefore, on day t , $O(t)$ will have a increase by $\Delta I(t - T_{in})$. Also, $O(t)$ decreases by the number of confirmations on day $t-1$. We denote the number of infected individuals confirmed on day t by $C(t)$. Then, the change in $O(t)$ on day t is:

$$\Delta O(t) = \Delta I(t - T_{in}) - C(t - 1). \quad (3)$$

Let σ be the probability for an onset infected individual to go for a clinical consultation in a single day and α be the probability for a patient to be confirmed after clinical consultation in a single day. Then, we have:

$$C(t) = \sigma \alpha O(t). \quad (4)$$

This relation represents how fast we can identify and isolate an infected individual. We denote the latent population size by $L(t)$. We estimate that the number of people in the incubation period on day t is the number of infected on day t subtracted from the number of infected individuals one average incubation period ago:

$$L(t) = I(t) - I(t - T_{in}). \quad (5)$$

We denote the hospitalized population size with $H(t)$. There are 2 situations to discuss. If the available wards are sufficient and all the newly confirmed cases can be isolated and treated, we have

$$H(t) = C(t). \quad (6)$$

If the daily confirmed cases on day t , $C(t)$, are more than the remaining wards on day $t-1$, $W(t-1)$, then not all the confirmed cases can be treated and isolated. We call such situation an emergency of the health-care system. Under emergency conditions, $H(t)$ equals the sum of the daily number of recoveries from the hospital $R(t)$, deaths in hospital $D(t)$, and remaining wards on the previous day $W(t-1)$:

$$H(t) = D(t) + R(t) + W(t - 1). \quad (7)$$

Here, daily recovery and death (in Hospital) population sizes $R(t)$ and $D(t)$ are estimated as

$$R(t) = r_{re} H(t - T_{re}), \quad (8)$$

$$D(t) = r_d H(t - T_d), \quad (9)$$

where r_{re} and r_d are the rates of recovery and deaths in the hospital, and T_{re} and T_d are the average periods of in-hospital recovery and death, respectively. We did not consider self-recoveries and non-hospitalized deaths since the self-recovery rate and not-in-hospital death rate are unknown yet. Our model focuses on the early stage of an outbreak, so the self-recovery portion is relatively small.

We denote the remaining isolation wards on day t by $W(t)$. The initial capacity of the health-care system is a crucial parameter $W_0 = W(0)$. The number of in-hospital recoveries and deaths will increase the remaining wards on the next day, and the hospitalization will decrease $W(t)$. Therefore, the change in $W(t)$ on day t is

$$\Delta W(t) = R(t - 1) + D(t - 1) - H(t - 1). \quad (10)$$

If daily confirmed cases are more than the available isolation wards, $A(t)$ starts to accumulate:

$$\Delta A(t) = C(t - 1) - H(t - 1). \quad (11)$$

The accumulation of $A(t)$ will speed up the spread of virus as shown in $\Delta I(t)$.

In our model, we only considered symptomatic transmissions. We derived a formula for the basic reproduction number, $R_0 = r \beta n_0$, where n_0 is the average time interval from onset to isolation. Given the daily probability to see a doctor σ we can calculate the average time n_1 from onset to medical consultation as the mathematical expression:

$$n_1 = \sum_i i \sigma (1 - \sigma)^{i-1} = 1/\sigma \quad (12)$$

The time n_2 is defined in Table 2 as the average time interval for an individual between first medical consultation to being hospitalized. Similar calculation gives $n_2 = 1/\alpha$. Since $n_0 = n_1 +$

Table 2
Parameters with associated epidemiological meanings used in the dynamic model.

Parameters	
r	Average daily close contacts per person
β	Transmission rate
σ	Daily possibility for an onset patient to go to a clinic
α	Daily possibility for an infected to be confirmed
n_1	Average time from onset to first medical consultation
n_2	Average time from going to clinic to isolation
r_{re}	Rate of recovery from hospital
r_d	Rate of death in hospital
T_{in}	Average incubation period
T_{re}	Average time of recovery from hospital
T_d	Average time of death in hospital
T_{em}	Time of emergency of a health-care system

n_2 , we derived another formula of the basic reproduction number,

$$R_0 = r\beta(1/\sigma + 1/\alpha). \quad (13)$$

2.2. Control measures

We listed major control measures and analyzed how each measure works in terms of parameter configurations.

- Measure 1: adding isolation wards.

Infections increase much faster during emergency of the health-care system. Adding additional isolation wards will delay the time to reach emergency status.^[13]

- Measure 2: social distancing.

Social distancing means a decrease in daily close contacts r . Recall that $\Delta I(t)$ contains r as a coefficient, so this measure will contain virus spread proportionally.^[14,15]

- Measure 3: self-protecting.

Wearing a mask and washing hands could be the most economic but effective ways to protect oneself from being infected. This measure can drop the transmission rate β .^[16,17]

- Measure 4: extensive medical testing and quickly confirmation.

This measure is to reduce the 2 average times n_1 and n_2 , or equivalently to increase σ and α .

2.3. Assumptions

Here we summarize our assumptions in our dynamic model.

1. The total population $Z(t)$ is constant, not changing with time.
2. We regarded the recovered individuals no longer susceptible.
3. In our model, we only considered symptomatic transmissions, that is, we regard the onset (showing symptoms) individuals as infection resources rather the incubation individuals.
4. We didn't consider self-recovery and not-in-hospital death cases.
5. We assume that an individual would be contagious for 14 days from being onset.

2.4. Data sources and ethical issue

The main data sources are national and regional CDCs in China. The daily numbers of confirmed cases in Wuhan, Henan,

Guangxi, Liaoning, Tianjin, Shenzhen, and Chongqing are published by regional CDCs.^[18,19,20] We performed statistical analysis on the average times from onset to isolation based on information contained in regional CDC reports. We collected the number of isolation wards and Fang Cang hospital wards from a report by the Wuhan government.^[21]

The data of Italy and South Korea we collected is from the website: <https://statistichecoronavirus.it/coronavirus-italia/?from=singlemessag&isappinstalled=0>

There is no ethical issue. All the data are available to the public.

3. Results

3.1. Retrospective analysis and model simulation for the Wuhan outbreak

We divided the time range from December 1, 2019 to March 20, 2020 into 4 stages. The first stage from December 01 to January 01, had no control measures in place. The second stage was from January 01 to January 23, Wuhan JinYinTan Hospital had reported pneumonia of unknown origin at the end of December, and people were becoming aware of the disease.^[22] In the third stage, from January 23 to February 15, strict control measures were implemented,^[3] such as the closing of public places and suspension of school and work. The fourth stage was from February 15 to March 20, when Wuhan began to applying stricter measures, including testing and isolating all potentially infected individuals,^[23] until no more newly reported cases after March 19.^[24]

We assumed that the initial infection is $I_0=5$ and the average daily close contacts $r=14$ without control measures and $r=5$ under strict social distancing. An early report analyzed the first 425 confirmed cases in Wuhan and found that the average time from onset to first health-care consultation was 5.8 days (95% CI 4.3–7.5) from the beginning of December 2019 to January 1, 2020, and 4.6 days (95% CI 4.1–5.1) after January 1, 2020.^[25] Therefore, we chose $\sigma=0.17$ in the first stage and $\sigma=0.22$ in the second. After Dr. Zhong's announcement, people with symptoms were more willing to see a doctor, so we estimated an increased $\sigma=0.5$ after January 23. We estimated the average time n_2 to be approximately 3 days, and equivalently $\alpha=0.3$. We assumed the transmission rate $\beta=0.04$ without medical protection^[14] and β reduced to 0.02 under self-protections.^[16,17] After February 15, extensive medical testing resulted in an increase of in the rate of confirmation, so we assumed $\sigma=0.9$ and $\alpha=0.8$ in the fourth stage. The parameters for the Wuhan retrospective simulations are listed in Table 3.

Table 3
Parameter configurations for simulating the historical COVID-19 outbreak in Wuhan.

Parameters	First stage Dec 01–Jan 01 No measures	Second stage Jan 02–Jan 23 Becoming alert	Third stage Jan 23–Feb 15 All measures	Fourth stage After Feb 15 Stricter measures
r	14	14	5	5
β	0.04	0.04	0.02	0.02
σ	0.17	0.22	0.5	0.9
α	0.3	0.3	0.3	0.8
Derived R_0	5.16	4.41	0.53	0.24

These parameter values were derived from reports and news released from the Wuhan government and CDC.

Here, R_0 is derived by the formula $R_0=r\beta(1/\sigma+1/\alpha)$. The same formula is applied in the following tables.

CDC=Center for Disease Control, COVID-19=Coronavirus Disease 2019.

A report from the Wuhan CDC^[21] gave daily numbers of total and available wards, which we used to determine the number of isolation wards. We performed a linear regression of the number of wards and assumed that the initial number of isolation wards was $W(0)=3000$, and that the total number increased by 800 after January 23. Furthermore, on February 5, the Wuhan government started to build “Fang Cang” hospitals to contain a large number of infected individuals with mild symptoms. We estimated that there were about 2000 increased positions each day in Fang Cang hospitals. A recent article described how Fang Cang hospitals functioned.^[26] We put $W(t)$ an extra increase by 2000 since February 5 for 10 days. We assumed the recovery rate $r_{re}=95\%$, death rate $r_d=5\%$,^[27] average time for recovery $T_{re}=18$ days, average time of death $T_d=15$ days,^[28,29] and average incubation period $T_{in}=5$ days.^[30,31]

Table 4

Comparison of the simulation results with the real historical outbreak cases in Wuhan.

	Simulation	Reported
Total confirmed by Jan 01 ($t=31$)	69	71
Total confirmed by Feb 01 ($t=62$)	18,756	3215
Total confirmed by Mar 01 ($t=91$)	53,017	49,659
Total confirmed by Mar 20 ($t=110$)	53,122	50,005
Highest daily confirmed	6126 on Feb 15	13,436 on Feb 12
Time of no more confirmed	Mar 15	Mar 19

The comparisons between actual cases in Wuhan and the numerical simulation results are shown in Table 4 and Fig. 2A and B. The simulation output showed that the number of

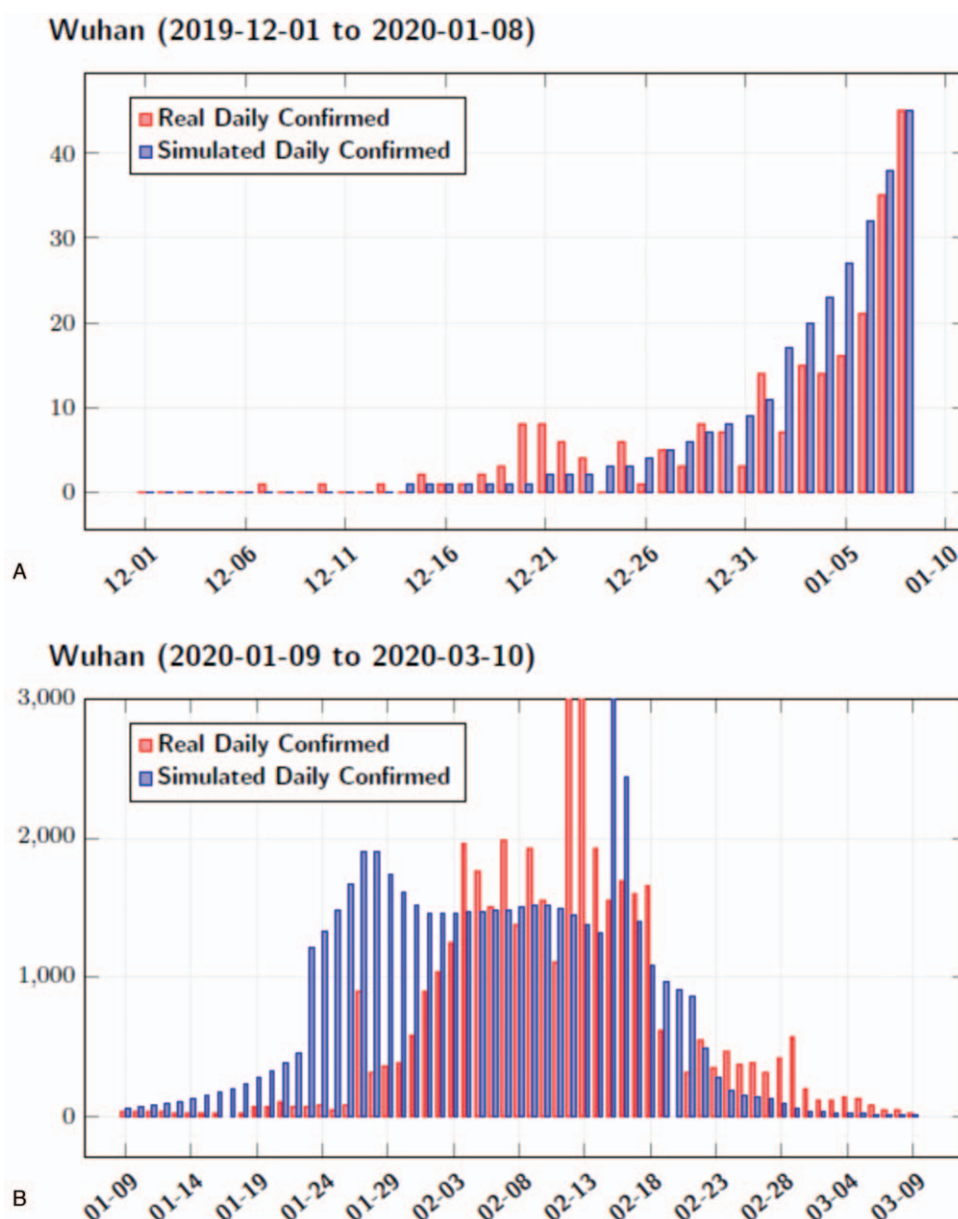


Figure 2. Wuhan retrospective analysis and model simulation results compared with the daily reported cases. A: December 01 to January 08, B: January 09 to March 10.

Table 5**Simulation for an early intervention in Wuhan (Measures 2, 3, and 4).**

Parameters	A strict intervention		A mild intervention	
	Dec 01–Jan 01 No measure	After Jan 02 Measure 2, 3, 4	Dec 01–Jan 01 No measure	After Jan 02 Measure 2, 3, 4
r	14	5	14	10
β	0.04	0.02	0.04	0.02
σ	0.17	0.8	0.17	0.8
α	0.3	0.3	0.3	0.3
Derived R_0	5.16	0.46	5.16	0.92
Total infections	1370		4584	
No confirmed case on	$t=95$ days		$t=297$ days	

We suppose that control measures had been implemented on Jan 02 in Wuhan.

infections in 90 days were $I(90)=53,079$ compared with the reported 49,659 confirmed cases on March 01.^[32] In the simulation, the spread was contained and the number of infections stabilized at 53,122 in total on $t=103$ d. In the actual situation, the total number of confirmed cases stabilized at 50,333. The model simulation showed that on March 15 ($t=103$ day), there was no additional confirmed cases. The real situation is that on March 16, 17, and 18, only 1 confirmed case was reported each day, and since March 19 ($t=107$ days) Wuhan has reported 0 confirmed cases.^[24] Our simulation projected approximately 10,000 infections on January 17 to 18, compared with the estimated 4000 infections (uncertainty range: 1000–9700) reported by the Imperial College group.^[33]

3.2. A critical time for Wuhan

We performed simulations assuming that control measures had been implemented on January 02 in Wuhan, which is approximately 3 weeks before the control measures actually took place. The parameters are listed in Table 5. We tested 2 scenarios: strict social distancing $r=5$ and mild social distancing $r=10$. The isolation wards are enough to hospitalize all the patients and no emergency of the health-care system occurs in either simulation, so Measure 1 is not needed. We kept $\alpha=0.3$ low, considering that there may not be enough equipment and kits immediately after the outbreak begins. Simulations show that a strict social distancing, plus wearing masks and extensive medical testing ($\sigma=0.8$), could contain the outbreak and the spread would be stopped in 3 months with a total number of infections about 1400. Mild social distancing could contain the outbreak at a low level but the spread will last for 10 months with about 4500 total infections, as shown in Table 5.

We also simulated a series of situations with delayed intervention times of several days, see Table 6. This series of simulations showed that if interventions had been applied after January 25, the infections would have a large increase. Control measures implemented later than January 25 would not contain the outbreak in Wuhan in 3 months. In this scenario, strict social

quarantine must last for a longer time, and social side effects would become significant.

Such simulations results indicate that there is a time point crucial to control the outbreak in its early stage. If control measures were carried out before this time point, the spreading will be kept in a low level, such as situations in East Asian and European countries. Missing this time point, a pandemic could be widely spread even under control measures. We call this time point the critical time. From our simulations, we found that the critical time for Wuhan is January 25.

3.3. Other provinces and cities outside Hubei

We collected daily local CDC reports from over 300 cities outside of Hubei Province. Reports from cities outside Hubei contain more epidemiological information than those from Hubei. We analyzed the reports of confirmed cases in Henan Province,^[18] Guangxi Province, Liaoning Province, Tianjin City,^[19] Chongqing City, and Shenzhen City.^[20] We found that the average times from onset to isolation decreased after January 25, see Table 7. Such a decrease indicates the effectiveness of preventative policies. The statistical analysis results are used to estimate parameters in model simulations for these areas.

The local CDC reports also distinguished imported cases from locally infected cases. Instead of setting an initial infections value, we added the daily imported infections into our model on the corresponding dates. We set $r=15$, $\beta=0.04$ before January 25, and $r=5$, $\beta=0.02$ after January 25. The parameters σ and α were estimated based on the average time n_0 from onset to isolation before and after January 25. Model simulation results and reported data are compared in Fig. 3.

3.4. Italy and South Korea

We performed retrospective and predictive simulations for the COVID-19 outbreak in Italy and South Korea. The parameters were estimated based on the control measures implemented by local government and on reported data. For Italy, we set $r=15$,

Table 6**Simulations of delayed interventions and the critical time (Jan 25) for Wuhan (all measures).**

Time to intervene	Jan 23	Jan 24	Jan 25	Jan 26	Jan 27
Accumulated infections in 90 days $I(90)$	53,096	63,679	81,603	104,611	131,834
Latent on the 90th day $L(90)$	93	181	705	1391	2281
Can the outbreak be contained to a low level in 3 months?	Yes	Yes	No	No	No

Table 7
Statistical analysis of local CDC reports of Henan, Liaoning, and Guangxi Provinces and Tianjin, Shenzhen, and Chongqing cities.

		Before Jan 25	After Jan 25
Henan Province			
Total confirmed cases	1232		
Imported cases	499		
Average time from onset to isolation		5.51 days (4.91–6.11), n=227	2.92 days (2.68–3.17), n=699
Liaoning Province			
Total confirmed cases	125		
Imported cases	65		
Average time from onset to isolation		4.21 days (2.78–5.64), n=33	1.77 days (1.14–2.39), n=64
Guangxi Province			
Total confirmed cases	236		
Imported cases	47		
Average time from onset to isolation		3.75 days (2.59–4.90), n=63	1.75days (1.34–2.16), n=143
Tianjin City			
Total confirmed cases	135		
Imported cases	25		
Average time from onset to isolation		2.59 days (0.64,4.54), n=22	1.63 days (1.02,2.23), n=70
Shenzhen City			
Total confirmed cases	421		
Imported cases	350		
Average time from onset to isolation		4.97 days (4.38–5.55), n=172	3.13 days (2.71–5.84), n=233
Chongqing City			
Total confirmed cases	576		
Imported cases	203		
Average time from onset to isolation		5.91 days (4.73,7.10), n=149	2.85 days (2.12,3.59), n=230
Data are presented as means (95% CI), n			

CDC=Center for Disease Control; CI=confidence interval.

$\beta=0.04$, $\sigma=0.2$, and $\alpha=0.3$ before March 09, and set $r=10$, $\beta=0.03$, $\sigma=0.5$, and $\alpha=0.8$ after March 09 when the control measures were carried out all over Italy.^[8] Then, the corresponding $R_0=5.0$ before March 09 and $R_0=0.98$ after March 09 was derived using the formula $R_0=r \beta(1/\sigma+1/\alpha)$. The simulation results and reported data are compared in Fig. 4A. If we further put $r=5$ after March 26, corresponding to $R_0=0.49$, we predicted that Italy would contain the COVID-19 spreading in the late May with approximately 190,000 as shown in Fig. 4A.

In the simulation for South Korea, we set January 20 as $t=0$, and on February 26 ($t=37$) South Korea implemented control measures: suspending all schools, prohibiting mass gatherings, and providing masks and extensive medical testing.^[6] Based on these measures, we set $I_0=6$, $r=20$, $\beta=0.04$, $\sigma=0.3$, and $\alpha=0.3$ before February 25 and set $r=14$, $\beta=0.02$, $\sigma=0.5$, and $\alpha=0.9$ after February 25. Here, we assumed r values higher than those of Wuhan considering that South Korea has a denser population and did not suspend work. The corresponding $R_0=5.33$ before February 26 and $R_0=0.87$ after February 26 were derived. The simulation predicted a total number of infections of 9522 on March 27 compared with the actual number of 9331 infections (see Fig. 4B).

3.5. The effectiveness and criticality of control measures

As long as a regional health-care system is overloaded, infections increase rapidly. Therefore, early interventions before T_{em} are crucial to contain an outbreak or to keep it at a low level. Here, we designate spreading at a low level if there is not an emergency of the health-care system in the 3-months period. We also found that there is a critical time in the early stage, after which, a certain level of measures would not prevent an outbreak. Similar to our analysis of the critical time in the retrospective simulation for

Wuhan, we also analyzed critical times for general scenarios. Such analysis could be indicative of the extent that a local government must implement control measures and how much risk a certain area is facing.

We consider the following cases, suppose the initial infection $I(0)$ is 5, total number of isolation wards $W(0)$ is 1000, transmission rate $\beta=0.04$, $\sigma=0.3$, and $\alpha=0.3$. We compared the simulation results given no interventions and each of the 4 control measures in Table 8. We also analyzed critical times for different combinations of control measures to be implemented (see Table 9). Figure 5 shows the effectiveness compared among different control measures. Figure 6 shows the simulated daily confirmed cases if control measures were implemented 1 day before the critical day, on the critical day, and 1 day after the critical day.

4. Discussion

4.1. Comparison between simulations and historical outbreak patterns

The retrospective simulation for Wuhan was shifted approximately 10 days ahead of the reported numbers (see Fig. 2B). One reason could be that, in a mathematical model, effects appear provided that we change the configuration of parameters. In reality, preventative measures take some time to be carried out. The second reason is that the dates of reported cases were several days later than the date of medical confirmation, as we observed while reading the CDC reports. Another possible explanation is that we fixed the beginning time $t=0$ as December 01, 2020 and the initial infection $I(0)=5$. A delay of the beginning time or a reduction of the initial infection would push the simulation results forward along the time axis. Therefore, we could make a

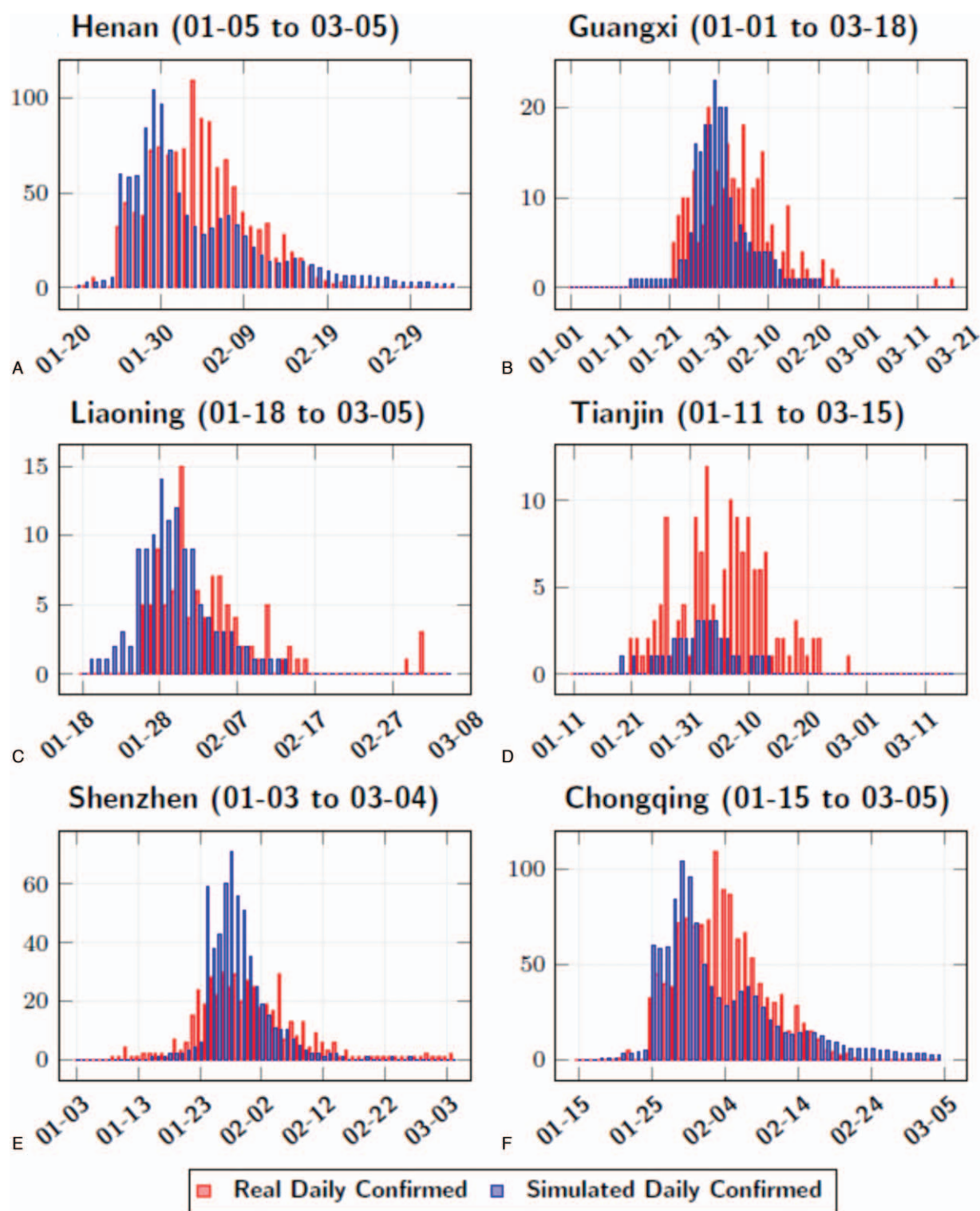


Figure 3. Retrospective simulations for provinces and cities outside Hubei. A: Henan Province; B: Guangxi Province; C: Liaoning Province; D: Tianjin City; E: Shenzhen City; F: Chongqing City.

more accurate estimation of the beginning time and the initial infections of the COVID-19 outbreak by model fitting.

For Henan, Liaoning, and Guangxi Provinces, the simulation results showed several days ahead of the reported data as we have seen for the Wuhan retrospective simulation. For Shenzhen City, the times from the simulation results and the reported data

matched, but the simulation predicted more infections than those reported. The simulation results for Tianjin predicted much lower infections than reported. The reason for this outcome could be that there were several clusters of infections in Tianjin.^[34,35] Our simulations showed the effectiveness of the timely implementations of control measures in provinces outside Hubei.^[36]

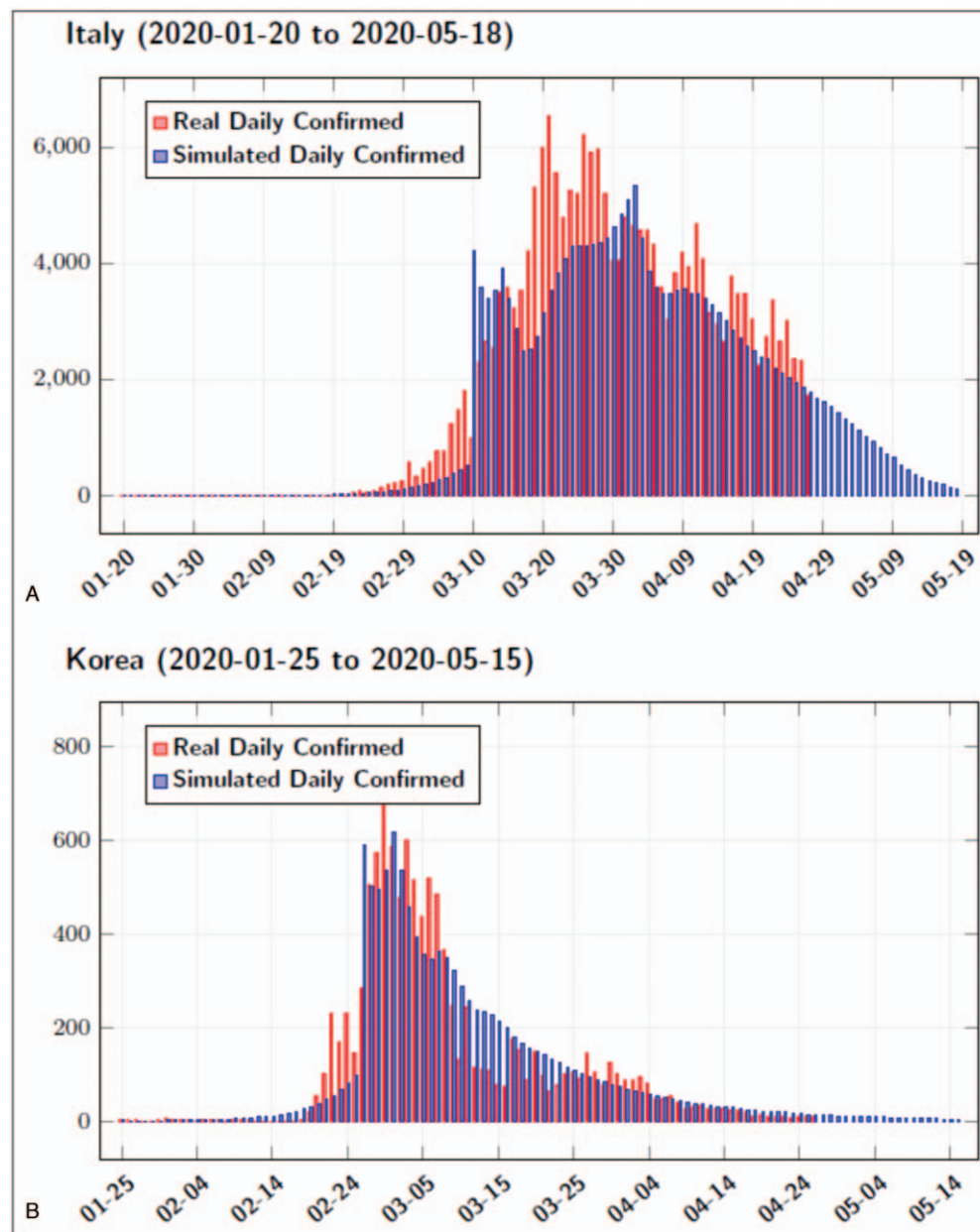


Figure 4. Retrospective and predictive model simulations compared with reported daily confirmed cases for Italy and South Korea. A: Italy, simulation from January 20 to May 18, reported case from January 20 to April 27, B: South Korea, simulation from January 25 to May 18, reported case from January 25 to April 27.

Table 8

Comparison among different control measures.

	No intervention	Add wards	Mild social distance	Strict social distance	Wear masks	Increase testing	Extensive testing
r	15	15	10	5	15	15	15
β	0.04	0.04	0.04	0.04	0.02	0.04	0.04
σ	0.3	0.3	0.3	0.3	0.3	0.5	0.8
α	0.3	0.3	0.3	0.3	0.3	0.5	0.9
Add wards	0	100/d	0	0	0	0	0
Derived R_0	4	4	2.67	1.33	2	2.40	1.42
Emergency day	46 d	58d	58d	106d	71 d	59d	No emergency
Infected in 60 days	83,000	60,581	5412	221	1408	2747	25
Outbreak controlled	No	No	No	Low level	No	No	Yes

All the measures are implemented from $t=0$ days.

Table 9**Critical times to intervene for several combinations of control measures required to contain the outbreak in 3 months.**

	Test	Dis and Test	Mask and Test	Dis and Mask	Dis, Mask, and Test
r	15	5	15	5	5
β	0.04	0.04	0.02	0.02	0.02
σ	0.8	0.8	0.8	0.3	0.8
α	0.9	0.9	0.9	0.3	0.9
Derived R_0	1.42	0.47	0.71	0.67	0.24
Critical time	31d	36d	35d	35d	38d
Intervene 1 day before the critical time					
$I(90)$	2065	2015	1515	3876	2198
Epidemic stops	200d	87d	90d	Low level	84d
Intervene on the day of critical time					
$I(90)$	9767	30,364	37,045	4653	6670
T_{em}	61d	41d	42d	65d	41d

Dis=social distancing, Mask=wearing masks, Test=extensive medical testing.

The simulation results for Italy and South Korea matched the reported cases well. Our simulations verified the success of South Korea in containing COVID-19 spread by extensive medical testing and mask wearing, and predicted that Italy would stop the outbreak by continuing strict social distancing until late May.

4.2. Effectiveness of control measures and early warning

The simulation results in Table 8 and Fig. 5 show that strict social distancing or extensive medical testing could contain an outbreak to a low level or control it altogether. However, we assumed these measures were implemented from the very beginning of the epidemic, which is not realistic. We present the results of combinations of measures that can contain an outbreak. As we analyzed the times for control measures to be implemented, we also found the critical times for each combination of measures (see Table 9). The analysis of the critical times indicates that early interventions are crucial and that the effects of control measures would be greatly different if implemented merely a single day late: from containing an outbreak in 3 months to emergency in 2 months (see Fig. 6).

Our model quantified the risk that a local health-care system faces from a COVID-19 outbreak by determining the emergency time. Given the current number of infections and remaining capacity of a regional health-care system, our model can be indicative of how soon and to what extent a combination of control measures are necessary to suppress an outbreak. A previous report^[37] estimated the health-care capacities for COVID-19 infections in 182 countries by analyzing the International Health Regulations annual reports. Our model, together with the data on the health-care system capacities of countries can provide early warnings for countries experiencing the threat of COVID-19 outbreaks.

4.3. Limitation and applicability

1. We regard the local total population $Z(t)$ as a constant not changing with time. First of all, the number of death is relatively small compared with the total population. For example, there are 3869 reported deaths compared with about 10 million total population in Wuhan. We didn't consider newborn as well, since our simulations have a time span from 30 to 100 days.

One factor could be taken into consideration in our future work: the traveling population. Relevant data were collected and studied in the work.^[38]

2. There are several reports about recovered individuals had a positive test result after their recovery. But we haven't found any studied cases on such group about their infectiousness.
3. We did not consider self-recovery and non-hospital death of patients, who will not remain infectious long-term. However, we did not find supporting data to estimate the rates and average times to self-recovery and non-hospital death. Taking these factors into consideration will be part of our future work. In the early stage, 60 days since the first case was reported, for example, most of the patients can be isolated and treated in hospitals. For example, in Wuhan the emergency time of the health-care system is about 50 days after the first case reported. A typical time from showing symptoms to recovery or death is about 15 to 20 days. So our model would be applicable in the first 2 to 3 months since the first case is reported.

We assumed that all the infected patient are supposed to be hospitalized. However, a recent work^[39] estimated about 50% to 80% infected are necessary to be hospitalized. Then, patients with mild symptoms could be treated and isolated at home. This fact will postpone the emergency of the health-care system for several days. However, as we found by simulations and in as a previous work^[40] has shown, even the best health-care systems will be overloaded without further control measures.

4. We performed a long-term simulation for Italy, and to fix the issue mentioned above, we assumed an individual would be contagious for 14 days from being onset. Our simulation results are applicable for providing early warnings and making intervening policies in the early stage.
5. Another limitation of our model is that we only considered symptomatic transmission. We did not consider transmission from asymptomatic infected individuals. However, recent reports and studies have found evidence for asymptomatic transmissions.^[40,41] The asymptomatic transmission rate was also studied and estimated by a recent work.^[11]

4.4. Importance of the data from regional CDCs in China

Since January 25 the social-net workers of local governments and employees of regional CDCs outside Hubei Province in China have collected and reported epidemiological information of

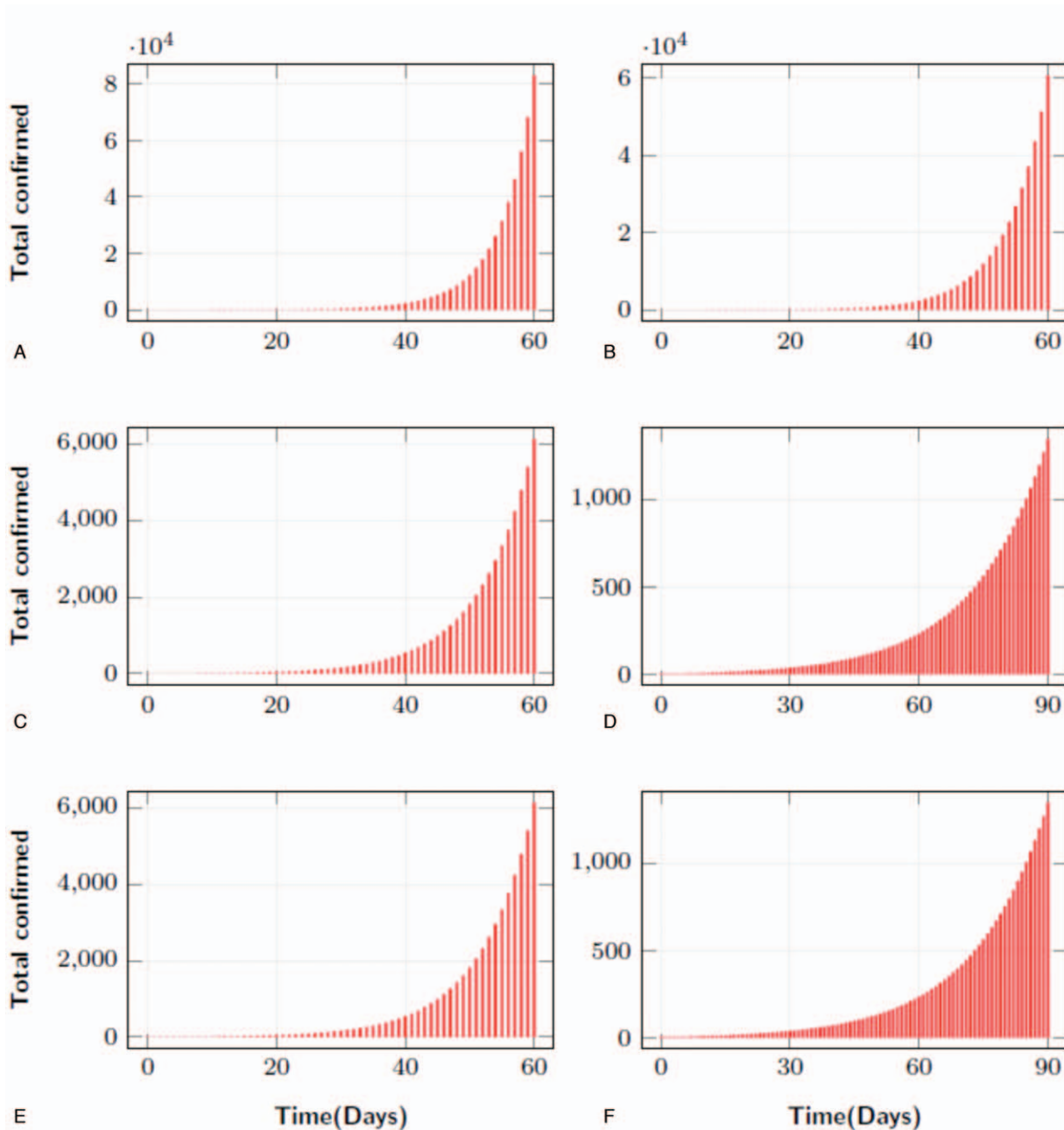


Figure 5. Comparison among different control measures (all implemented from $t=0$ day). A: No intervention, B: Increasing health-care system capacity (+100 wards per day), C: Mild social distancing ($r=10$), D: Strict social distancing ($r=5$), E: Wearing masks ($\beta=0.02$), F: Mild tests ($\alpha=\sigma=0.5$).

almost every confirmed case. Such information makes many epidemiological studies on COVID-19 possible. For example, an analysis of the effectiveness of control measures outside Hubei Province in China was recently reported. In their paper^[42] the average time from symptom onset to first health-care consultation, which is n_1 in our paper, and from first health-care consultation to hospital admission, which is n_2 in our paper, were analyzed statistically including 8579 confirmed cases reported national-wide. We analyzed the epidemiological information for separate provinces and cities, considering that the control measures were implemented at different levels in different areas.

We applied our data analysis results in model simulations to quantify the effectiveness of control measures outside Hubei Province.

All the above analyses cannot be done if regional CDCs in China are not functional or the outbreak case data are not released to the public. To this end, our study benefited from the important role of regional CDCs in China in monitoring and managing the detection and control of COVID-19 outbreaks. Moreover, we encourage regional CDCs in other countries to also share their epidemiological data to promote more in-depth public health research on the COVID-19 transmission mechanisms.

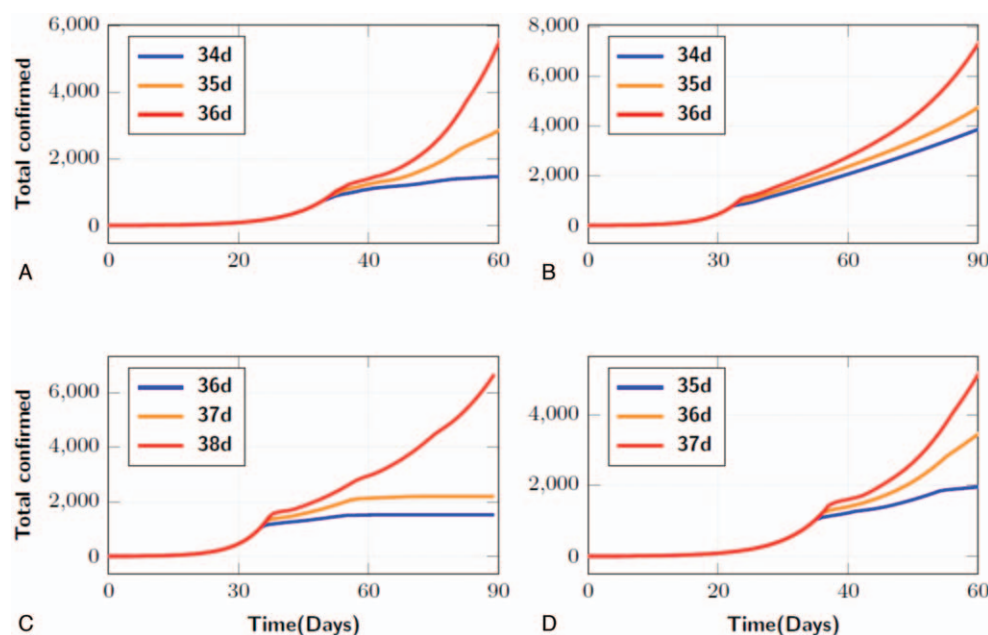


Figure 6. Critical times for different combinations of control measures. A: Extensive medical testing and wearing masks, B: Wearing masks and strict social distancing, C: Wearing masks, strict social distancing, and extensive medical testing, D: Strict social distancing and extensive medical testing. Blue: Intervening 1 day before the critical day, Yellow: Intervening on the critical day, Red: Intervening 1 day after the critical day.

4.5. Socioeconomic factors and preventative policies

The impacts of Covid-19 are not limited to health-care systems but have effects on all aspects of a society. People of lower socioeconomic status, especially in developing countries, would have higher risks. Long-term strict social distancing will cause a large increase in unemployment. Developing countries usually have a more fragile health-care system and a denser population, which implies a higher risk of an outbreak. Therefore, intervention policies must be made with consideration of complex situations. We suggest that a combination of mild social distancing, wearing masks, and extensive medical testing could be efficient, economic, and realistic for a long term intervention policy until a vaccine is invented.

5. Conclusions

Our dynamic simulations indicate that no single measure could contain a COVID-19 outbreak once a health-care system is overloaded. Early interventions have great effectiveness and there is a critical time to contain COVID-19 spread at a low level. Missing the critical time, the local health-care system would be soon overloaded, and the local government must plan long-term control measures. Adding isolation wards can delay the emergency time but cannot contain an outbreak. Social distancing is effective but has high social costs. Wearing a mask works as well as social distancing with a much lower costs. Extensive medical testing, as what South Korea have done, could keep the spread at a low level but would not end an epidemic completely in a short period.

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Author contributions

Conceptualization: Shuhang Yang, Yu Liu.

Data curation: Shuhang Yang, Yu Liu, Ke Chen, Xiaolei Chen, Pengfang Qi, Yazhi Xu, Feifei Yu, Yuling Yang.

Formal analysis: Shuhang Yang, Ke Chen, Tong Li, Yi Huang, Yazhi Xu, Feifei Yu, Yuling Yang.

Investigation: Ke Chen, Tong Li, Yi Huang, Xiaolei Chen, Pengfang Qi, Yuling Yang.

Software: Yu Liu.

Supervision: Youhua Chen.

Visualization: Yi Huang.

Writing – original draft: Shuhang Yang.

Writing – review & editing: Youhua Chen.

References

- [1] HUBEI.GOV.CN. Wuhan CDC reported the pneumonia epidemic; 2019. Available at: http://wjw.wuhan.gov.cn/xwzx_28/gsgg/202004/t20200430_1199576.shtml. (Accessed January 21, 2020).
- [2] HUBEI.GOV.CN. A high-level expert group of the national health commission answered questions on COVID-19; 2020. Available at: http://www.hubei.gov.cn/zxjy/rdhy/202001/t20200121_2013408.shtml. (Accessed January 21, 2020).
- [3] HUBEI.GOV.CN. Wuhan implemented the control of people entering and leaving Wuhan to curb the spread of the epidemic; 2020. Available at: http://www.hubei.gov.cn/zhuanti/2020/gzxxgzbd/zxtb/202001/t20200121_2013644.shtml. (Accessed January 21, 2020).
- [4] National Health Commission of the People's Republic of China. State health commission general office on strengthening the primary medical and health institutions novel coronavirus infected pneumonia epidemic prevention and control work notice interpretation; 2020. Available at: <http://www.nhc.gov.cn/xcs/fkdt/202001/36c4168c6c8a4e5a89562f2504d97a45.shtml>. (Accessed January 26, 2020).
- [5] Guancha.cn. National health commission: on the whole, the current epidemic peak has passed; 2020. Available at: https://www.guancha.cn/politics/2020_03_12_541304.shtml. (Accessed March 12, 2020).

- [6] Washington Post. South Korea is doing 10,000 coronavirus tests a day. The U.S. is struggling for even a small fraction of that; 2020. Available at: https://www.washingtonpost.com/world/asia_pacific/coronavirus-test-kits-south-korea-us/2020/03/13/007f14fc-64a1-11ea-8a8e-5c5336b32760_story.html. (Accessed March 13, 2020).
- [7] ScienceMag.org. Coronavirus cases have dropped sharply in South Korea. What's the secret to its success? 2020. Available at: <https://www.sciencemag.org/news/2020/03/coronavirus-cases-have-dropped-sharp-ly-south-korea-whats-secret-its-success>. (Accessed March 18, 2020).
- [8] BBC NEWS. Coronavirus: Italy extends emergency measures nationwide; 2020. Available at: <https://www.bbc.com/news/world-europe-51810673>, (accessed March 10, 2020).
- [9] Wu JT, Leung K, Leung GM. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study. *Lancet* 2020;395: 689–97.
- [10] Kucharski AJ, Russell TW, Diamond C, et al. Early dynamics of transmission and control of COVID-19: a mathematical modelling study. *Lancet Infect Dis* 2020;20:553–8.
- [11] Ferretti L, Wymant C, Kendall M, et al. Quantifying SARS-CoV-2 transmission suggests epidemic control with digital contact tracing. *Science* 2020;368:eabb6936doi: 10.1126/science.abb6936.
- [12] Fraser C, Riley S, Anderson RM, et al. Factors that make an infectious disease outbreak controllable. *Proc Natl Acad Sci USA* 2004;101: 6146–51.
- [13] Tang B, Xia F, Tang SY, et al. The effectiveness of quarantine and isolation determine the trend of the COVID-19 epidemics in the final phase of the current outbreak in China. *Int J Infect Dis* 2020;95:288–93.
- [14] Chen Y, Cheng J, Jiang Y, et al. A time delay dynamic system with external source for the local outbreak of 2019-nCoV. *Appl Anal* 2020;1–2.
- [15] Ferguson NM, Laydon D, Nedjati-Gilani G, et al. Impact of non-pharmaceutical interventions (NPIs) to reduce COVID-19 mortality and healthcare demand. Imperial College COVID-19 Response Team; 2020.
- [16] Leung NHL, Chu DKW, Eunice YC, et al. Respiratory virus shedding in exhaled breath and efficacy of face masks. *Nat Med* 2020;26:676–80.
- [17] Bootsma MC, Ferguson NM. The effect of public health measures on the 1918 influenza pandemic in U.S. cities. *Proc Natl Acad Sci USA* 2007;104:7588–93.
- [18] Health Commission of Henan Province. Update on covid-19 outbreak in Henan province as of 24:00 on March 29; 2020. Available at: <http://hnwsw.gov.cn/contents/858/49159.shtml>. (Accessed March 29, 2020).
- [19] WSJK.TJ.GOV.CN. Tianjin City CDC Daily Reports on Epidemic. Available at: <http://wsjk.tj.gov.cn/col/col14/index.html>. (Accessed April 01, 2020).
- [20] Shenzhen Municipal Health Commission. Epidemic situation of COVID - 19 in Shenzhen city on March 29, 2020; 2020. Available at: http://wjw.sz.gov.cn/yqxx/202003/t20200329_19080681.htm. (Accessed April 5, 2020).
- [21] HUBEI.GOV.CN. Total and Remaining hospital beds in designated hospitals in Wuhan city (February 20, 2020); 2020. Available at: http://www.hubei.gov.cn/zhuanti/2020/gzxxgzbd/zxtb/202002/t20200221_2144312.shtml. (Accessed February 21, 2020).
- [22] Health Commission of the Hubei Province. Hubei: JinYinTan Hospital Dean, the first person who reported the coronavirus epidemic; 2020. Available at: http://wjw.hubei.gov.cn/bmdt/ztl/fkxxgzbdgrfyyq/yxdx/202002/t20200206_2020461.shtml. (Accessed February 6, 2020).
- [23] Wuhan Municipal Health Commission. Wuhan accelerated hospitalizing infected patient into designated hospitals; 2020. Available at: <http://wjw.wuhan.gov.cn/front/web/showDetail/2020021509592>. (Accessed February 15, 2020).
- [24] HUBEI.GOV.CN. Epidemic situation of COVID - 19 in Hubei province on March 19, 2020; 2020. Available at: http://www.hubei.gov.cn/zhuanti/2020/gzxxgzbd/zxtb/202003/t20200320_2185776.shtml. (Accessed March 19, 2020).
- [25] Li Q, Guan XH, Wu P, et al. Early transmission dynamics in Wuhan, china, of novel coronavirus-infected pneumonia. *N Engl J Med* 2020; 382:1199–207.
- [26] Chen SM, Zhang ZJ, Yang JT, et al. Fangcang shelter hospitals: a novel concept for responding to public health emergencies. *Lancet* 2020; 395:1305–14.
- [27] Worldometer. Coronavirus (COVID-19) Mortality Rate; 2020. Available at: <https://www.worldometers.info/coronavirus/coronavirus-death-rate/#ref-9>. (Accessed April 04, 2020).
- [28] Wilson N, Kvalsvig A, Barnard LT, et al. Case-fatality risk estimates for COVID-19 calculated by using a lag time for fatality. *Emerg Infect Dis* 2020;26:1339.
- [29] Zhou F, Yu T, Du RH, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020;Published online March 11.
- [30] Lauer SA, Grantz KH, Bi QF, et al. The incubation period of 2019-nCoV from publicly reported confirmed cases: estimation and application. *Ann Intern Med* 2020;172:577–82.
- [31] Yang Y, Lu QB, Liu MJ, et al. Epidemiological and clinical features of the 2019 novel coronavirus outbreak in China. *BMJ* 2020;Published online Jan 1.
- [32] HUBEI.GOV.CN. Epidemic situation of COVID - 19 in Hubei province on 29 February 2020; 2020. Available at: http://www.hubei.gov.cn/zhuanti/2020/gzxxgzbd/zxtb/202003/t20200301_2164980.shtml. (Accessed March 01, 2020).
- [33] Imai N, Dorigatti I, Cori A, et al. Report 2: Estimating the potential total number of novel Coronavirus cases in Wuhan City, China. Imperial College London COVID-19 Response Team; 2020. Published online Jan 22.
- [34] Tianjin Information and Industry Bureau. 60% of Confirmed Cases in Tianjin Are Due to Family Gatherings; 2020. Available at: <http://gyxxh.tj.gov.cn/ggdt/71026.htm>. (Accessed on April 08, 2020).
- [35] People's Daily, Expert Explain A Cluster Infection in BaoDi Mall Tianjin; 2020. Available at: <https://m.weibo.cn/2803301701/4471289555669490>. (Accessed on April 08, 2020).
- [36] Lai SJ, Ruktanonchai NW, Zhou LC, et al. Effect of non-pharmaceutical interventions to contain COVID-19 in China. *Nature*. 2020.
- [37] Kandel N, Chungong S, Omaar A, et al. Health security capacities in the context of COVID-19 outbreak: an analysis of International Health Regulations annual report data from 182 countries. *Lancet* 2020; 395:1047–53.
- [38] Kraemer M, Yang CH, Plessis L, et al. The effect of human mobility and control measures on the COVID-19 epidemic in China. *Science* 2020; 368:493–7.
- [39] Verity R, Okell LC, Dorigatti I, et al. Estimates of the severity of coronavirus disease 2019: a model-based analysis. *Lancet Infect Dis*. 2020. Published online Mar 30.
- [40] Bai Y, Yao LS, Wei T. Presumed Asymptomatic Carrier Transmission of COVID-19. *JAMA*. 2020;323:1406–7.
- [41] People.cn. A man, returning to Beijing from Wuhan infected his mother and caused 28 people in isolation; 2020. Available at: <http://bj.people.com.cn/BIG5/n2/2020/0403/c14540-33926461.html>. (Accessed April 3, 2020).
- [42] Zhang JJ, Litvinova M, Wang W, et al. Evolving epidemiology and transmission dynamics of coronavirus disease 2019 outside Hubei province, China: a descriptive and modelling study. *Lancet Infect Dis*; 2020. Published online Apr 2.