Effects of control measures and their impacts on COVID-19 transmission dynamics

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Research Article

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Abstract

Governments around the world have grappled with the COVID-19 pandemic for more than a year. Control measures such as social distancing, use of face masks in public places, business and school closures, city or transportation lockdowns, mass gathering bans, population education and engagement, contact tracing, and improved mass testing protocols are being used to contain the pandemic. Currently, there are no studies to date that rank the effectiveness of these measures, resulting in government responses that may be uncoordinated and inefficient. In this study, we developed a Discrete Time Markov Chain model that captures the above control measures and ranks them. We found that the importance of the measures changes over time and depends on the stage of transmission dynamics, as well as the ecological environment. For example, contact tracing is a powerful measure to effectively control the pandemic, however, our results show that while it is indeed helpful during the early stages of the pandemic, it is much less important after a vaccination program takes effect. Besides, our model improved the standard SEIR compartmental model by taking into account the dynamic temporal transmission and recovery probabilities along with considering a portion of the population that will not comply with government-mandated control measures. If implemented, our novel and unique model may assist many countries in pandemic control decisions.

Introduction

Different countries have used different control strategies to combat the COVID-19 pandemic. China and New Zealand implemented a seal and eradicate strategy whereby they quickly applied strict measures very early to stop local transmission, and then sealed their borders to protect the epidemic from reoccurring. The United States and UK chose to strike a balance between controlling the pandemic and its economic impacts by implementing various measures to keep the effective reproduction rate, R_t, low while implementing advanced vaccination programs to achieve population level immunity. Widely-accepted control measures for the pandemic control are social distancing, face masks, business and school closures, city or transportation lockdowns, mass gathering bans, population education and engagement, contact tracing, vaccination programs, viral testing advancements, and targeted mass testing. To formulate an effective control strategy, decision-makers must understand the impact of each control measure on transmission dynamics and identify the control measures that should put more focus on and allocate more resources into.

Huang et al.[1] presented an SEIR compartmental model and showed that quarantine and isolation measures, as well as testing delays, could cause the largest difference in numbers of daily confirmed cases. Zhang et al.[2] found that limiting the mobility of the general population was more important than fast detection and isolation during the early stages of the outbreak in mainland China. Liu et al.[3] found that earlier and stricter lockdown implementation yielded better control than later or more relaxed measures. Indeed, many researchers focus on specific control measures and show their positive benefit, however, they have not aggregated all of these measures into a single model to see their interaction and

compare their relative benefits. In this paper, we develop a Discrete Time Markov Chain model that captures the most, if not all, widely accepted control measures and ranks them so the policymakers can appropriately allocate resources to the most beneficial measures.

Model

Some studies[4,5] use a Markov Chain model with four states (Healthy, Active, Recovered, and Death) to model COVID-19 evolution. Although having few states makes the model easy to manage, these models fail to accurately capture other important dynamics of the epidemic, such as the chance of viral transmission and the likelihood of recovery, both of which fluctuate depending on the length of time an individual patient has been symptomatic. Our proposed model has numerous states to capture this temporal information, and therefore appropriately model dynamic transmission and recovery probabilities.

Our model also accounts for the portion of the population that will not comply with government-mandated control measures by classifying populations as either “cooperative” or “uncooperative.” With effective communication and promotional campaigns, a government might be able to improve the proportion of cooperative people, k_o.

There is a significant portion of asymptomatic cases. Most asymptomatic cases will never be detected but can still spread the virus similar to symptomatic patients. Moreover, those with mild symptoms that have recovered by themselves may not get tested, also contributing to the undetected rate in the population. These two types are classified as the “undetected infected” class. There may also be some infected person, possibly with mild symptoms, who did not comply with self-isolation. Those who did not self-isolate were also assigned to the undetected infected class because they may go out and spread the virus like undetected infected individuals. Thus, the undetected infected class includes asymptomatic and mild symptom cases who do not get tested and those that tested positive but failed to isolate themselves. Recent studies have estimated asymptomatic cases to anywhere from 4% to 52% [6, 7, 8, 9, 10, 11]. Without loss of generality, we set the asymptomatic proportion at 35% and implement a control parameter, k_d, as a percentage adjustment to the asymptomatic proportion to allow manipulation of asymptomatic and symptomatic detection and isolation. Therefore, the proportion of undetected infected over total infected is 35% - k_d. For example, if we can detect 30% of asymptomatic cases and isolate 80% of symptomatic case, we have k_d = (30% × 35%) – (20% × 65%) = -2.5%. We estimate that k_d can range from -10% to 30%, depending on the effectiveness of the control measures being implemented.

Our Discrete Time Markov Chain model at time t has the following states:

SC_t = Susceptible and cooperative with control measure on day t
SU_t = Susceptible and uncooperative with control measure on day t
UC^i_t = Undetected infected for i days and cooperative with control measure on day t
UU^i_t = Undetected infected for i days and uncooperative with control measure on day t

TC^i_t = Detected or will be detected infected for i days and cooperative with control measure on day t
TU^i_t = Detected or will be detected infected for i days and uncooperative with control measure on day t
M_t = Cumulative immune on day t
V_t = Cumulative vaccinated on day t
D_t = Cumulative dead on day t,

where i = 1, …, I, and I is the maximum number of days[1] that an infected person can transmit the virus. In other words, $f_u(i)$ and $f_d(i)$ should be negligible when $i > I$.

The probability for an infected individual to spread the virus after becoming infected for i days follows the temporal transmission probability mass functions, $f_u(i)$ and $f_d(i)$, for undetected and detected infected individuals, respectively. Let R_0 be the basic reproduction number, i.e. the expected number of cases directly generated by one infected individual. Let us define an aggregated epidemic control measure $k_r(t)$ as the measures implemented on day t that directly affect the reproduction number, such as mask wearing, social distancing, and lockdown. For example, Oraby[5] found that lockdown reduces R_0 by 64-85% across 155 countries. By design, only the cooperative populations will implement this $k_r(t)$ measure while the uncooperative populations will not. Hence, the expected number of new cases generated from the contagious population on day t can be calculated as $E_t = (S_i\, UC^i_t\, f_u(i) + S_i\, TC^i_t\, f_d(i)) \times R_0\, k_r(t) + (S_i\, UU^i_t\, f_u(i) + S_i\, TU^i_t\, f_d(i)) \times R_0$.

For a country with a population size N, the number of newly-infected individuals on day $t+1$ can be computed as $UC^1_{t+1} = E_t \times SC_t/(N-D_t) \times (35\% - k_d)$, $UU^1_{t+1} = E_t \times SU_t/(N-D_t) \times (35\% - k_d)$, $TC^1_{t+1} = E_t \times SC_t/(N-D_t) \times (65\% + k_d)$, and $TU^1_{t+1} = E_t \times SU_t/(N-D_t) \times (65\% + k_d)$. The number of susceptible individuals on day $t+1$, SC_{t+1} and SU_{t+1}, are then to be reduced by the newly-infected cases accordingly. Infected states will transition into the next day infected states where $UC^{i+1}_{t+1} = UC^i_t$, $UU^{i+1}_{t+1} = UU^i_t$, $TC^{i+1}_{t+1} = TC^i_t$, and $TU^{i+1}_{t+1} = TU^i_t$, for all t and i =1,…, I-1.
Undetected cases are asymptomatic or mildly symptomatic, therefore we assume they will all recover and become immune. For detected cases, some of them will die. Recent global case fatality rate (CFR)[12] is 2.71%. Hence, the probability that patients in the detected group will die is assumed to be 2.71% and the remaining 97.29% will recover. The estimated CFR of 2.71% is also in a reasonable range with other studies.[2] As a result, the immune state M_{t+1} equals $M_t + (UC^I_t + UU^I_t) + 97.29\%\ (TC^I_t + TU^I_t)$ and the death state D_{t+1} equals $D_t + 2.71\%\ (TC^I_t + TU^I_t)$.

One important control measure is contact tracing. We define control parameters k_l as *tracing delay*, the time between the isolation of a known case and isolation of its contacts, and k_c as *contact tracing coverage*, the proportion of contacts detected and isolated. k_c then equals the percentage of cases that conduct contact tracing multiplied by the proportion of contacts that can be isolated over all traced contacts. Lastly, one of the most effective control measures is vaccination. Vaccination coverage being

administered up to time t is $k_v(t)$, which is equal to the percentage of the population that has received vaccination up to time t multiplied by vaccine efficacy (i.e., 95% for Moderna[13] and Pfizer-BioNTech[14] and 72% for Johnson & Johnson[15]). Additional details about contact tracing and vaccination modeling can be found in the methods section.

Footnotes:

[1] In the methods section, we show that $I = 21$.

[2] Wu et al.[24] found that for those that have symptoms, 81% have mild to moderate symptoms, while 14% have severe symptoms and 5% are critically ill. Assuming 10–25% of severe symptoms and 100% of critical symptoms are in ICU, this 2.71% CFR translates into 42.34–31.88% ICU death rate (= 2.71/(5+0.1*14), which is in line with the ICU death rates reported in previous studies. For less crowded health systems, Chen et al.[25] showed that a 22% death rate among ICU patients and Gold et al.[26] provides ICU death rate in a range of 37–48.7%. In a crowded health system. However, the ICU death rate can be as high as 78% [27].

Case Studies

Case study I: The United States as of March 21, 2021

As an example, we applied our model with recent data from the United States. As of March 21, 2021, there are 81,415,769 people[16] who received a COVID-19 vaccination. Because the current US population[17] is 331,002,651, the percentage of the population that has received at least one dose of the vaccine is 24.6%. At this time, the United States vaccination capacity is following an exponential growth rate with an average daily growth rate of 0.5% over the last 10 days, derived from [18]. According to a survey[18], 47.2% of people are willing to take a COVID-19 vaccination if it was available to them. Hence, we should not expect $k_v(t)$ to go near 1.0 easily. Therefore, we assume for a base case that the vaccination program will continue at a 0.5% growth rate until it reaches 60% of the population. In the worst-case scenario, the program will continue with a 0.5% growth rate until it reaches 45% of the population. In the best-case scenario, the program will continue with a 0.55% growth rate until it reaches 75% of the population. Because more than 98% of vaccines administered[18] in the United States are Moderna or Pfizer/BioNTech, which are 95% effective, we will assume the United States has a vaccine efficacy of 95%.

Gramlich's 2018 survey[19] revealed that 75% of Americans would cooperate with each other in a crisis. This number is also consistent with the results of a survey[20] about mask use in March 2021. Hence, 75% will be the baseline for k_o, with 50% and 95% for worst and best case scenarios, respectively.

Based on current CDC recommendations,[21] for the purpose of advancing public health planning, the best estimate of R_0 to use in our model is 2.5. We then fit the parameters with actual data to obtain the baseline of a control measure $k_r(t)$. By minimizing the sum of square error in fitting the seven day moving average of new case numbers from actual historical data and predictive model for the past three weeks, we found that a stationary $k_r(t)$ at 0.4354 gives the best fit. As a result, our baseline for $k_r(t)$ is 0.4354. Table 1 shows a summary of control parameters and their assumptions.

Table 1: Summary of control measure parameters and their assumptions

Estimation of control measure parameters	worst case	base case	best case
Proportion of detected case by inform mild symptom to come test for free and easy and/or advance testing in target areas/groups, k_d	-10%	-5%	10%
Contact tracing delay, k_l	5	3	1
Contact tracing coverage, k_c	10%	20%	50%
Vaccination coverage at time t, which is equal to vaccination effectiveness y% times x% of vaccinated population, $k_v(t)$	0.5% growth till 45%	0.5% growth till 60%	0.55% growth till 75%
Reduce lag time for isolation after symptom onset (testing delay), k_g	5	3	1
Increase cooperative proportion, k_o	50%	75%	95%
Reduce $R0$ by encourage mask, distancing, avoid mass gathering, closing of places/transportation, and lockdown, $k_r(t)$	0.8708	0.4354	0.2177

The United States is quite advanced in its vaccination program because as of March 21, 2021, nearly 25% of its population has received at least one dose of the vaccine. Figure 1 shows the number of daily new cases, under the baseline, worst case, and best case for control measure k_r. In the baseline, when k_r = 0.4354, it will take 136 days to get zero new cases. If a lockdown is imposed, and k_r becomes 0.2177, then it will shorten this duration to only 95 days. When k_r is at 0.8708 (e.g. people meeting twice as frequently) the number of new cases transitions to an upward trend but later descends in mid-May when the percentage of the population vaccinated increases, increasing the duration to 275 days.

Extend Data Fig. 1 shows the number of daily new cases, under different vaccination program scenarios. All three scenarios would not yield any significant difference concerning the daily new case numbers. With a 0.55% daily growth rate and a limit of 75%, it would take 124 days until there are zero new cases, while with a 0.5% daily growth rate and a limit of 45%, the duration will increase to 160 days. If the vaccination program stops on March 22, 2021, then the number of daily new cases will still go down if the control measure level is maintained as previously. This is a result of the effective reproduction rate R_e being less than 1.0 due to the 25% vaccination coverage, but the duration until zero new case increases to 289 days. There is a herd immunity threshold[22] required to control the transmission of the virus. However, we show that the benefit of vaccination can be attained immeidately without having to wait to reach the herd immunity threshold, as long as the control measures to keep R_t down continue to be enforced.

Discussion

Fig. 2 is a tornado diagram displaying the number of days required to achieve no new cases from both the best and worst case scenarios for each control measure. For example, reducing $k_r(t)$ to 0.2177 (best case) results in 95 days to zero new cases, while increasing $k_r(t)$ to 0.8708 (worst case) results in 275 days to zero new cases. The diagram shows that, in the United States, where the vaccination program is quite advanced, in order to further improve the speed of pandemic control, policymakers should focus on (1) lowering the effective reproduction even more or at least keep it at the base level by effectively inform the people to maintain social distancing and facemask wearing habits, (2) improving population cooperation through education and engagement, and (3) reducing testing delays. On the contrary, the contact tracing program and asymptomatic detection now have minimal impact on the control speed and becomes less of a priority (e.g. only an 11 day decrease, by improving these parameters).

Case study II: Thailand as of January 6, 2021

To understand the effects of the control measures in a different environment, we applied the model with parameters estimated from Thailand data as of January 6, 2021. Table 2 shows the worst-case, baseline, and best-case scenarios used in the analysis.

Table 2: Summary of control measure parameters and their assumptions

Estimation of control measure parameters	worst case	base case	best case
Improving asymptomatic detection, k_d	-10%	-5%	10%
Reducing contact tracing delay, k_l	5	3	1
Increasing contact tracing coverage, k_c	10%	33.3%	50%
Vaccination program, $k_v(t)$	2 mil Sinovac by May	2 mil Sinovac by May, 26 mil AstraZeneca by Dec	2 mil Sinovac by May, 61 mil AstraZeneca by Dec
Reducing testing delay, k_g	5	3	1
Population education and engagement, k_o	65%	93.7%	95%
Reducing reproduction rate, $k_r(t)$	1	0.6	0.2

By fitting with the actual data and $k_r(t)$ set at 1.0, we found that R_0 for the 2nd wave in Thailand was 2.026. Thus, the worst case scenario for $k_r(t)$ is 1.0 which is the same level as the no new case period immediately preceeding the start of the second wave. Rotejanaprasert et al.[23] estimated R_t in Bangkok and showed that it can drop to as low as 0.5 on May 1, 2020. This implies $k_r(t)$ = 0.2, which is the same level as when Thailand was in lockdown during April/May 2020. For the base case scenario, we assume an intermediate $k_r(t)$ of 0.6.

Fig. 3 shows the daily new case numbers when similar lockdown measures implemented in April 2020 ($k_r(t)$ = 0.2) were re-implemented after the second wave was detected for 2, 9, and 16 days delay. The graph shows that the longer the control measure was delayed, the longer the duration required to achieve

zero new daily cases. For example, if the lockdown was implemented in 2, 9, 16, and 25 days, then it would take 30, 43, 55, and 67 days, respectively, to bring the number of new cases to zero.

As seen from Fig. 4, even though Thailand's vaccination program lags behind many other nations, if it implements a medium control level k_r at 0.6, it will begin to see a positive effect of the vaccination program when k_v reaches 5%, corresponding to 4.6 million people having received the vaccine. At this point, the number of daily new cases will start to descend. This is because the effective reproduction rate is near 1, meaning that a minor reduction in the susceptible population would be satisfactory to decrease the effective reproduction rate to less than 1.

Discussion

The tornado diagram of Thailand in Fig. 5 indicates that, even though Thailand currently has a low number of new cases, it will take more than a year to get zero new cases if all control measures are kept at baseline. Some serious effort is required in order to improve some, if not all, of these control measures. Most benefits would be obtained from implementing measures that reduce reproduction rate and/or testing delay, such as (1) mass gathering bans, (2) increasing the number of mobile testing units particularly for those who live/work in highly-populated areas, and (3) quickly, practically, and effectively isolating those with positive test results so that they can no longer spread the virus. In addition, contact tracing and asymptomatic detection ability still need to be implemented and improved. Moving any of these parameters from worst-case to best-case levels will decrease the amount of time to zero cases by more than 100 days. Most importantly, there are three measures, reducing the reproduction rate, increasing cooperation levels, and implementing vaccination programs, that require special attention to ensure that they do not fall to their worst-case scenario otherwise the pandemic can get out of control.

Conclusion

In conclusion, we presented a Discrete Time Markov Chain model that enhances the standard SEIR compartmental model by taking into account various control measures, the dynamic temporal transmission and recovery probabilities, and different cooperation levels of the population. We implemented the model in two cases, the United States and Thailand, to find the relative effectiveness of various control measures. The model identified that the United States should put more focus on lowering the effective reproduction, improving population cooperation, and reducing testing delays and less focus on contact tracing program and asymptomatic detection. The model also identified that Thailand should focus on all measures with special attention to reducing the reproduction rate, increasing population cooperation, and implementing vaccination programs.

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Methods

Temporal transmission probability of undetected cases

The undetected group includes asymptomatic cases, cases with mild symptoms but untested, and cases with mild symptoms and positive test results but failed to isolate themselves. Zou[28] found that the viral load detected in asymptomatic patients was similar to that of symptomatic patients. We assume they have the same generation time profile as symptomatic cases and used Weibull distribution estimated from Ferretti et al.[29] They used maximum likelihood estimates to infer generation time distribution and fit a Weibull distribution with a mean of 5.5 days and a standard deviation of 1.8 days. This translates to a Weibull distribution with a shape parameter of 1.6749 and a scale parameter of 6.1577. We apply this distribution to R_0 to assign the probability that one infected person can spread the virus to other persons each day, as shown in Fig 1.

Temporal transmission probability of detected cases

For detected cases, to estimate the probability that an infected person can spread the virus each day, we combine incubation period distribution[3] estimated from Lauer et al.[30] with the infectious profile[4] estimated from He et al.[31] and updated by Ashcroft et al.[32] to deduce generation time, as shown in Table 1. The rows in the table represent possible cases with different incubation periods, that can range from 1 to 21 days, with associated probabilities from Lauer et al.[30] shown in the first column. Each row illustrates the probability that an infected person with a given incubation period will transmit the virus each day during the course of the infection. The infectiousness profile data are from He et al.[31] and updated by Ashcroft et al.[32]. The “weighted average” row shows the incubation probability-weighted average of the infectiousness probabilities. The normalized numbers are shown in the “normalized” row to make the probabilities sum to one. Note that we cut the tail of the infectiousness profile after 21 days because, when multiplying with incubation period probability, the results are negligible. Hence, we assume that the maximum number of days that an infected person can transmit the virus, I, is 21. If an infected person does not recover in 21 days, he/she should be hospitalized and should no longer be able to transmit the virus.

Table 1: Estimation of temporal transmission probability. Column day numbers represent the incubation period and the row day numbers represent infectiousness probability distribution.

	Probability	Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
days till symptom onset (incubation period)	0.01%	1	14.98%	14.44%	12.18%	9.07%	6.01%	3.57%	1.92%	0.93%	0.42%	0.17%	0.06%	0.02%	0.01%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
	1.32%	2	13.41%	14.96%	14.44%	12.18%	9.07%	6.01%	3.57%	1.92%	0.93%	0.42%	0.17%	0.06%	0.02%	0.01%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
	9.25%	3	10.28%	13.41%	14.96%	14.44%	12.18%	9.07%	6.01%	3.57%	1.92%	0.93%	0.42%	0.17%	0.06%	0.02%	0.01%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
	18.15%	4	6.65%	10.28%	13.41%	14.96%	14.44%	12.18%	9.07%	6.01%	3.57%	1.92%	0.93%	0.42%	0.17%	0.06%	0.02%	0.01%	0.00%	0.00%	0.00%	0.00%	0.00%
	20.17%	5	3.58%	6.65%	10.28%	13.41%	14.96%	14.44%	12.18%	9.07%	6.01%	3.57%	1.92%	0.93%	0.42%	0.17%	0.06%	0.02%	0.01%	0.00%	0.00%	0.00%	0.00%
	16.96%	6	1.57%	3.58%	6.65%	10.28%	13.41%	14.96%	14.44%	12.18%	9.07%	6.01%	3.57%	1.92%	0.93%	0.42%	0.17%	0.06%	0.02%	0.01%	0.00%	0.00%	0.00%
	12.30%	7	0.56%	1.57%	3.58%	6.63%	10.28%	13.41%	14.96%	14.44%	12.18%	9.07%	6.01%	3.57%	1.92%	0.93%	0.42%	0.17%	0.06%	0.02%	0.01%	0.00%	0.00%
	8.21%	8	0.13%	0.56%	1.57%	3.58%	6.65%	10.28%	13.41%	14.96%	14.44%	12.18%	9.07%	6.01%	3.57%	1.92%	0.93%	0.42%	0.17%	0.06%	0.02%	0.01%	0.00%
	5.24%	9	0.03%	0.15%	0.56%	1.57%	3.58%	6.65%	10.28%	13.41%	14.96%	14.44%	12.18%	9.07%	6.01%	3.57%	1.92%	0.93%	0.42%	0.17%	0.06%	0.02%	0.01%
	3.25%	10	0.01%	0.03%	0.15%	0.56%	1.57%	3.58%	6.65%	10.28%	13.41%	14.96%	14.44%	12.18%	9.07%	6.01%	3.57%	1.92%	0.93%	0.42%	0.17%	0.06%	0.02%
	1.99%	11	0.00%	0.01%	0.03%	0.13%	0.56%	1.57%	3.58%	6.65%	10.28%	13.41%	14.96%	14.44%	12.18%	9.07%	6.01%	3.57%	1.92%	0.93%	0.42%	0.17%	0.06%
	1.22%	12	0.00%	0.00%	0.01%	0.03%	0.15%	0.56%	1.57%	3.58%	6.65%	10.28%	13.41%	14.96%	14.44%	12.18%	9.07%	6.01%	3.57%	1.92%	0.93%	0.42%	0.17%
	0.74%	13	0.00%	0.00%	0.00%	0.01%	0.03%	0.15%	0.56%	1.57%	3.58%	6.65%	10.28%	13.41%	14.96%	14.44%	12.18%	9.07%	6.01%	3.57%	1.92%	0.93%	0.42%
	0.45%	14	0.00%	0.00%	0.00%	0.00%	0.01%	0.03%	0.13%	0.56%	1.57%	3.58%	6.65%	10.28%	13.41%	14.96%	14.44%	12.18%	9.07%	6.01%	3.57%	1.92%	0.93%
	0.28%	15	0.00%	0.00%	0.00%	0.00%	0.00%	0.01%	0.03%	0.15%	0.56%	1.57%	3.58%	6.65%	10.28%	13.41%	14.96%	14.44%	12.18%	9.07%	6.01%	3.57%	1.92%
	0.17%	16	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.01%	0.03%	0.15%	0.56%	1.57%	3.58%	6.65%	10.28%	13.41%	14.96%	14.44%	12.18%	9.07%	6.01%	3.57%
	0.11%	17	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.01%	0.03%	0.15%	0.56%	1.57%	3.58%	6.65%	10.28%	13.41%	14.96%	14.44%	12.18%	9.07%	6.01%
	0.07%	18	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.01%	0.03%	0.15%	0.56%	1.57%	3.58%	6.65%	10.28%	13.41%	14.96%	14.44%	12.18%	9.07%
	0.04%	19	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.01%	0.03%	0.15%	0.56%	1.57%	3.58%	6.65%	10.28%	13.41%	14.96%	14.44%	12.18%
	0.03%	20	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.01%	0.03%	0.15%	0.56%	1.57%	3.58%	6.65%	10.28%	13.41%	14.96%	14.44%
	0.02%	21	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.01%	0.03%	0.15%	0.56%	1.57%	3.58%	6.65%	10.28%	13.41%	14.96%
	weighted average		3.41%	5.50%	7.82%	9.88%	11.22%	11.58%	10.95%	9.57%	7.81%	6.00%	4.37%	3.05%	2.05%	1.34%	0.86%	0.54%	0.34%	0.21%	0.13%	0.08%	0.05%
	normalized		3.52%	5.69%	8.08%	10.21%	11.60%	11.96%	11.31%	9.89%	8.07%	6.20%	4.52%	3.15%	2.12%	1.39%	0.89%	0.56%	0.35%	0.22%	0.13%	0.08%	0.05%

In many cases, we can improve the control of pandemics by imposing isolation after detection. This is usually done by quarantine, hospitalization, or self-isolation. We define the lag between the time an infected person develops symptoms and the time that he/she is isolated as *testing delay* or k_g, which can vary from 0 to 7 days[34] while the infectiousness probabilities after k_g day from the onset will be set to zero. The example truncated probabilities with k_g = 3 are shown in Table 2. The truncated probability numbers are then normalized with the factor from no isolation cases because isolation after detection should have no impact on the transmission probability before isolation.

Table 2: Estimation of temporal transmission probability assuming that infected persons are isolated 3 days after symptom onset. Column day numbers represent the incubation period and the row day numbers represent infectiousness probability distribution.

	Probability	Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
days till symptom onset (incubation period)	0.01%	1	14.98%	14.44%	12.18%																		
	1.32%	2	13.41%	14.96%	14.44%	12.18%																	
	9.25%	3	10.28%	13.41%	14.96%	14.44%	12.18%																
	18.15%	4	6.65%	10.28%	13.41%	14.96%	14.44%	12.18%															
	20.17%	5	3.58%	6.65%	10.28%	13.41%	14.96%	14.44%	12.18%														
	16.96%	6	1.57%	3.58%	6.65%	10.28%	13.41%	14.96%	14.44%	12.18%													
	12.30%	7	0.56%	1.57%	3.58%	6.63%	10.28%	13.41%	14.96%	14.44%	12.18%												
	8.21%	8	0.13%	0.56%	1.57%	3.58%	6.65%	10.28%	13.41%	14.96%	14.44%	12.18%											
	5.24%	9	0.03%	0.15%	0.56%	1.57%	3.58%	6.65%	10.28%	13.41%	14.96%	14.44%	12.18%										
	3.25%	10	0.01%	0.03%	0.15%	0.56%	1.57%	3.58%	6.63%	10.28%	13.41%	14.96%	14.44%	12.18%									
	1.99%	11	0.00%	0.01%	0.03%	0.13%	0.56%	1.57%	3.58%	6.65%	10.28%	13.41%	14.96%	14.44%	12.18%								
	1.22%	12	0.00%	0.00%	0.01%	0.03%	0.15%	0.56%	1.57%	3.58%	6.65%	10.28%	13.41%	14.96%	14.44%	12.18%							
	0.74%	13	0.00%	0.00%	0.00%	0.01%	0.03%	0.15%	0.56%	1.57%	3.58%	6.65%	10.28%	13.41%	14.96%	14.44%	12.18%						
	0.45%	14	0.00%	0.00%	0.00%	0.00%	0.01%	0.03%	0.13%	0.56%	1.57%	3.58%	6.65%	10.28%	13.41%	14.96%	14.44%	12.18%					
	0.28%	15	0.00%	0.00%	0.00%	0.00%	0.00%	0.01%	0.03%	0.15%	0.56%	1.57%	3.58%	6.65%	10.28%	13.41%	14.96%	14.44%	12.18%				
	0.17%	16	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.01%	0.03%	0.15%	0.56%	1.57%	3.58%	6.65%	10.28%	13.41%	14.96%	14.44%	12.18%			
	0.11%	17	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.01%	0.03%	0.15%	0.56%	1.57%	3.58%	6.65%	10.28%	13.41%	14.96%	14.44%	12.18%		
	0.07%	18	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.01%	0.03%	0.15%	0.56%	1.57%	3.58%	6.65%	10.28%	13.41%	14.96%	14.44%	12.18%	
	0.04%	19	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.01%	0.03%	0.15%	0.56%	1.57%	3.58%	6.65%	10.28%	13.41%	14.96%	14.44%	12.18%
	0.03%	20	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.01%	0.03%	0.15%	0.56%	1.57%	3.58%	6.65%	10.28%	13.41%	14.96%	14.44%
	0.02%	21	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.01%	0.03%	0.15%	0.56%	1.57%	3.58%	6.65%	10.28%	13.41%	14.96%
	weighted average		3.41%	5.50%	7.82%	9.88%	11.10%	10.66%	8.70%	6.30%	4.22%	2.71%	1.69%	1.04%	0.64%	0.39%	0.24%	0.15%	0.09%	0.06%	0.03%	0.02%	0.01%
	normalized		3.52%	5.69%	8.08%	10.21%	11.47%	11.02%	8.99%	6.51%	4.37%	2.80%	1.75%	1.07%	0.66%	0.40%	0.25%	0.15%	0.09%	0.06%	0.04%	0.02%	0.01%

The results of the cases with 1–3 days of isolation after symptom onset are shown in Fig. 1.

Contract tracing modeling

We define incubation period distribution, which is estimated from Lauer et al.[30] as *P*, where *p(j)* represents the probability that the incubation period is *j* days. Suppose a detected infected individual has an incubation period of *j* days, the time that he/she will be isolated is $j+k_g$ days, and the time that proportion k_c of his/her contacts will be isolated is $j+k_g+k_l$ days. On a given day *t*, the expected numbers of patients with *j* days incubation period that will be detected and isolated on that day are $p(j)\,TC_t^{j+k_g}$ for the cooperative group and $p(j)\,TU_t^{j+k_g}$ for the uncooperative group. The number of contacts that they may have transmitted the virus to, after having the virus for *i* days, can be computed as $p(j)\,TC_t^{j+k_g}R_0\,f_d(i)\,k_r(t-(j+k_g)+i)+p(j)\,TU_t^{j+k_g}R_0 f_d(i)$. It will take k_l days until their contacts are isolated. As a result, on day *t*, contact tracing will reduce the number of contagious people in each state of the Markov chain as follows.

$$UC_t^{j+k_g+k_l-i} = UC_t^{j+k_g+k_l-i} - k_c \cdot \left(\frac{SC_{t-k_l-(j+k_g)+i}}{N-D_{t-k_l-(j+k_g)+i}}\right)\cdot(35\%-k_d)\cdot \left(p(j)\,TC_{t-k_l}^{j+k_g}R_0\,f_d(i)\,k_r\left(t-k_l-(j+k_g)+i\right)+p(j)\,TU_{t-k_l}^{j+k_g}R_0 f_d(i)\right). \quad (1)$$

for all j=1, …, 21-k_g and for all i= max(1, k_l+ j + k_g – I), …, min(I, j+kg -1).

Suppose that a contact of an index case was isolated on day *t*. This means that the index case was detected and isolated on day t-k_l. On day t-k_l, the index case has had the virus for $j+k_g$ days, where *j* is his/her incubation period. The first day that he/she got the virus would be day t - k_l - (j+k_g -1). Since then he/she has been potentially spreading the virus for *i* days, i = 1, …., j+k_g-1, corresponding to day t - k_l - (j+k_g -i), from day t - k_l - (j+k_g -1) to day t - k_l - (j+k_g – (j+k_g-1)) = t - k_l –1. Hence, on day *t*, the contact who contracted the virus from the index case on the index case's i^{th} day of infection, which was day t - k_l - (j+k_g -i), would be infected for t – (t - k_l - (j+k_g -i)) = k_l + j + k_g -i days. This explains the superscript of *UC* in Equation (1).

We only considered the cases in which the contact has been infected for less than *I* days (i.e., k_l + j + k_g -i ≤ I) because after *I* days, the virus can no longer be transmitted through contact. Thus, $i \geq k_l + j + k_g - I$ and $i \geq$ max(1, k_l + j + k_g – I). Moreover, the index cases can spread the virus at most *I* days. Hence, $i \leq$ min(I, j+kg -1). This explains the range of *i* in Equation (1).

The reduction in the numbers in states UU_t follows the same form as UC_t in Equation (1), except that *SC* in (1) is replaced by *SU*. The reductions in numbers in states TC_t and TU_t follow the same forms as states UC_t and UU_t, respectively, except the term (35% - k_d) is replaced by term (65% + k_d) to appropriately represent the detected group. Moreover, the sum of reductions from states UC_t and UU_t are added to state M_t because these isolated contagious contacts will no longer be able to transmit the virus. However, only 97.29% of the sum of the reductions from state TC_t and TU_t are added to state M_t because 2.71% of them will die, which in this case, are added to state D_t.

Vaccination modeling

Due to the possibility of reinfection, countries such as the UK[35] and United States[36] and currently provide vaccination to their populations regardless of whether they were previouslly infected. We define m to be the proportion of COVID-19 recovered individuals that can get a vaccination. Based on the current vaccination policy, we assume that $m = 1$. Let k_e be the number of days for the vaccine to give full protection. CDC[37] currently suggests that k_e be 14 days. As a result, the number of people receiving vaccination at time t is $k_v(t)(N-D_t) - k_v(t-1)(N-D_{t-1})$. The population that can receive a vaccination at time t is $N-D_t-V_t-(1-m)M_t$. Therefore, the number of cooperative susceptible individuals SC_t to get the vaccine at time t is $(k_v(t)(N-D_t) - k_v(t-1)(N-D_{t-1}))\bullet SC_t / (N-D_t-V_t-(1-m)M_t)$. These vaccinated individuals would still be susceptible for the next k_e days as they may become infected before the vaccine reaches its maximum protection. We assume that, during the k_e days before the vaccine takes effect, the chance that susceptible individuals become infected is the same regardless of whether they were vaccinated or not. Hence, at time t, the number of cooperative susceptible SC_t will be reduced by $(k_v(t-k_e)(N-D_{t-ke}) - k_v(t-k_e-1)(N-D_{t-ke-1}))\bullet SC_t / (N-D_{t-ke}-V_{t-ke}-(1-m)M_{t-ke})$ and moved to V_t. The number of infected individuals that were vaccinated at time $t-k_e$ is $(k_v(t-k_e)(N-D_{t-ke}) - k_v(t-k_e-1)(N-D_{t-ke-1}))\bullet (SC_{t-ke} - SC_t) / (N-D_{t-ke}-V_{t-ke}-(1-m)M_{t-ke})$, which is subtracted from M_t and moved to V_t. The formula for state SU_t follows the same fashion as SC_t but with SU replacing all SC.

Footnotes:

[3] The incubation period has a median time of 4–5 days[26] from exposure to symptoms onset. Lauer et al.[26] fit the incubation period into log-normal distribution with mean and SD of the natural logarithm of the distribution of 1.621 and 0.418, respectively. The incubation period for COVID-19 is thought to extend to 14 days, with a median time of 4–5 days from exposure to symptoms onset. Lauer et al.[26] reported that 97.5% of people with COVID-19 who have symptoms will do so within 11.5 days of infection.

[4] He et al.[27] fit serial interval distribution with gamma distribution. Together with a log-normal incubation period distribution estimated from Li et al.[33], they inferred that infectiousness started from 12.3 days before symptom onset, peaked at symptom onset, and then declined quickly within 7 days. This aligns with recent advisories by the EU that 10 days after symptom onset would be safe to not be in isolation. Some parameters of the infectious profile were updated in Ashcroft et al.[32]

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Figures

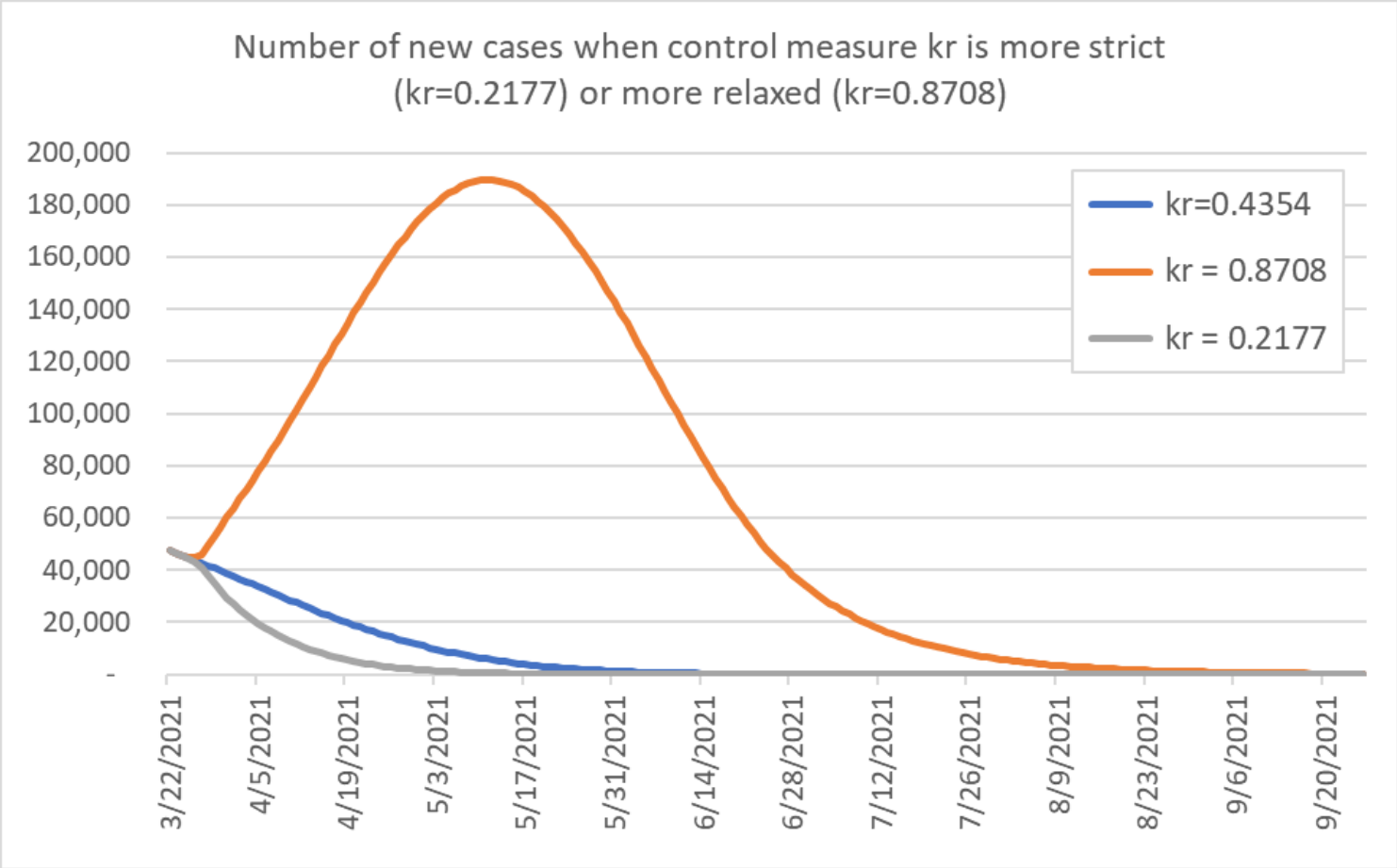

Figure 1

The number of daily new cases, under the base, worst, and best cases of control measure kr.

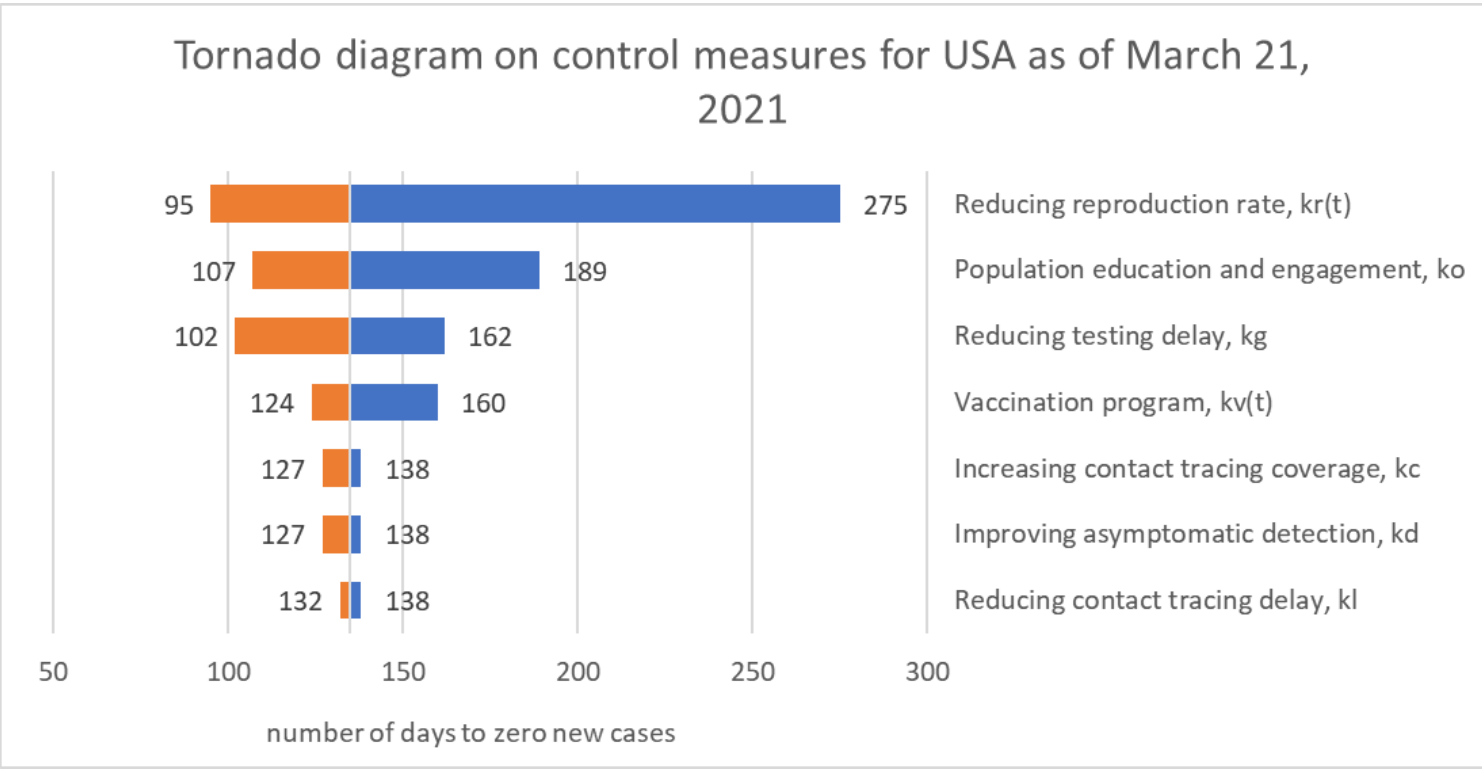

Figure 2

Tornado diagram on control measures for USA case study

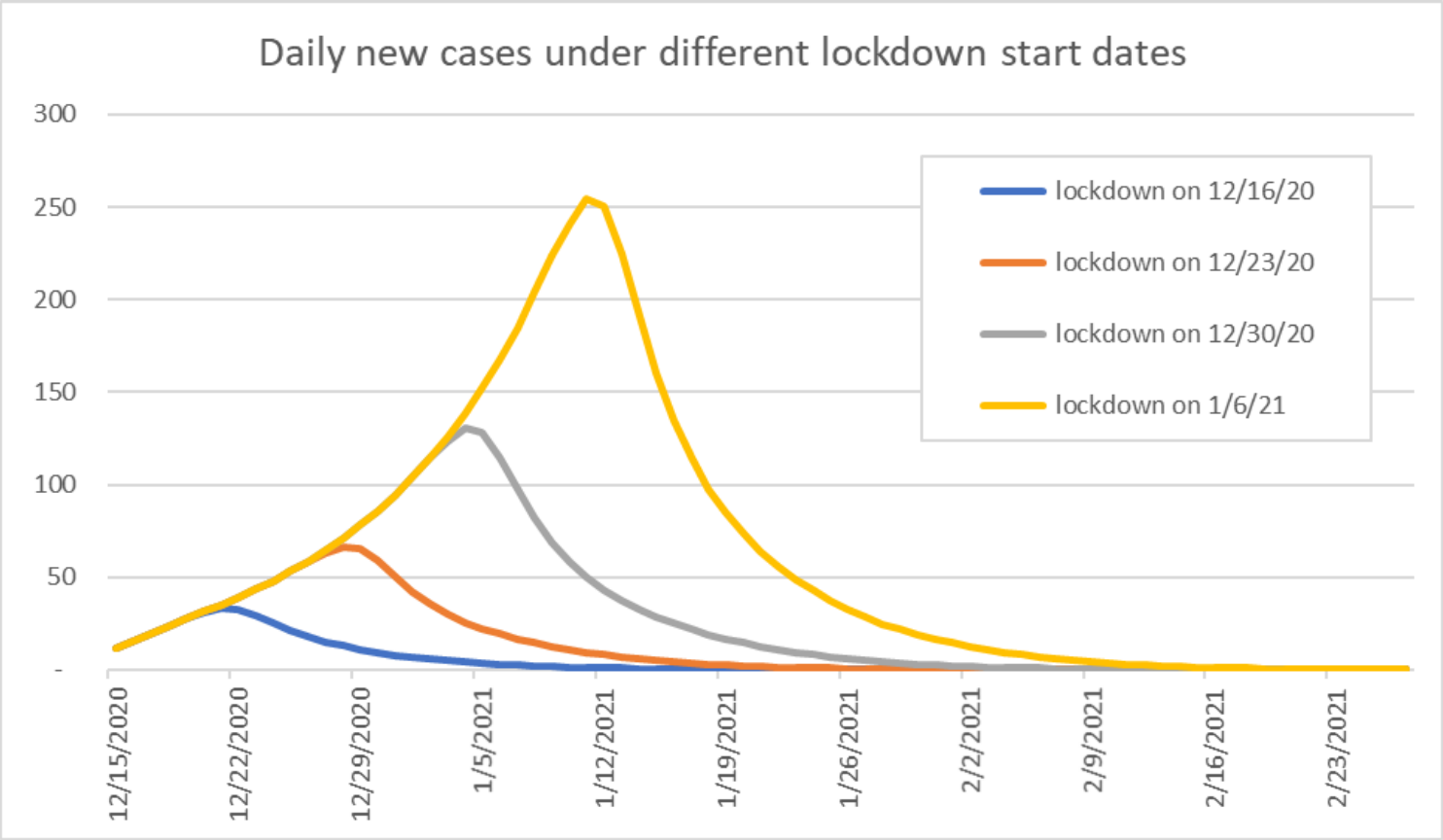

Figure 3

Daily new cases under different lockdown start dates

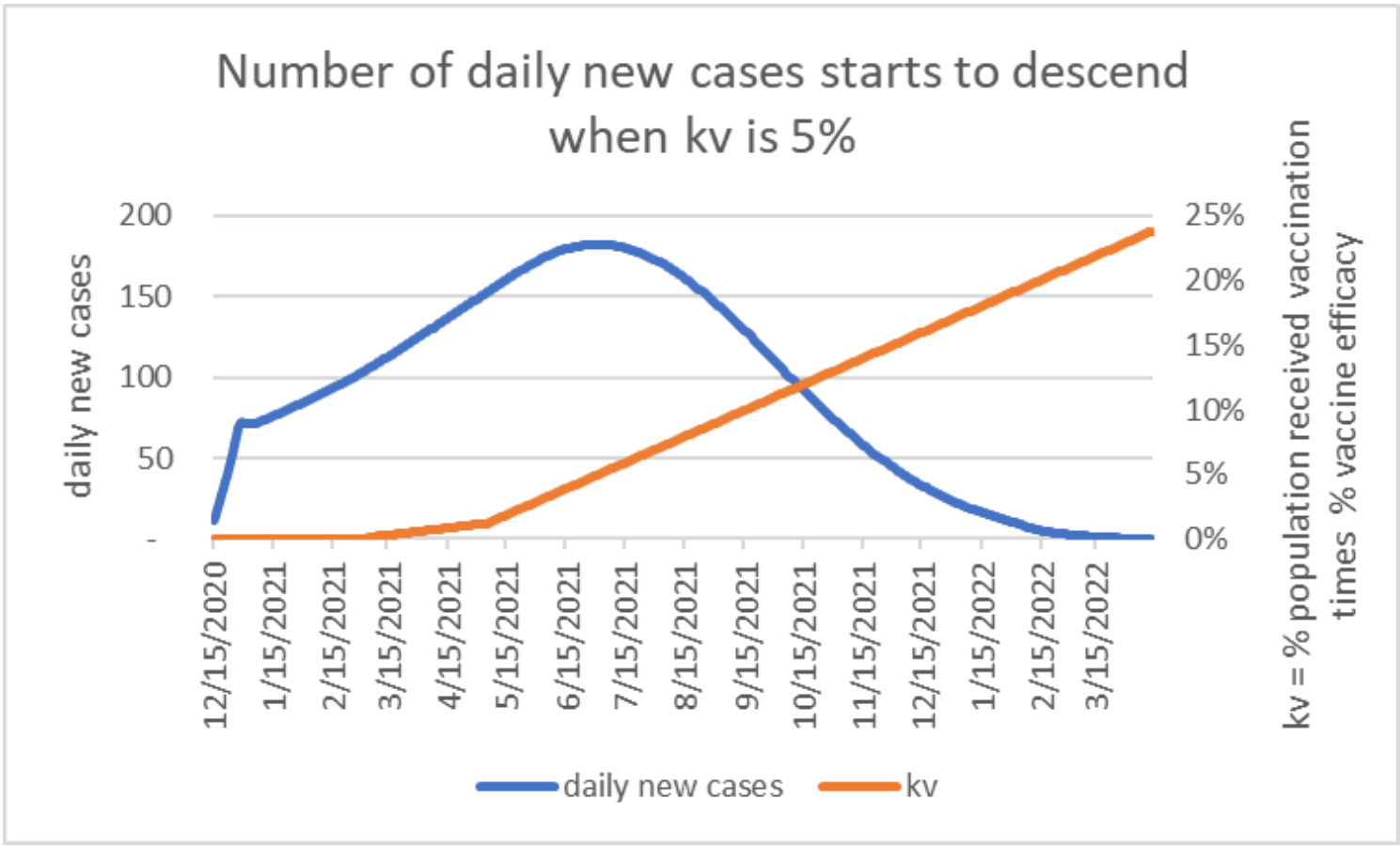

Figure 4

Daily new cases under vaccination program base case

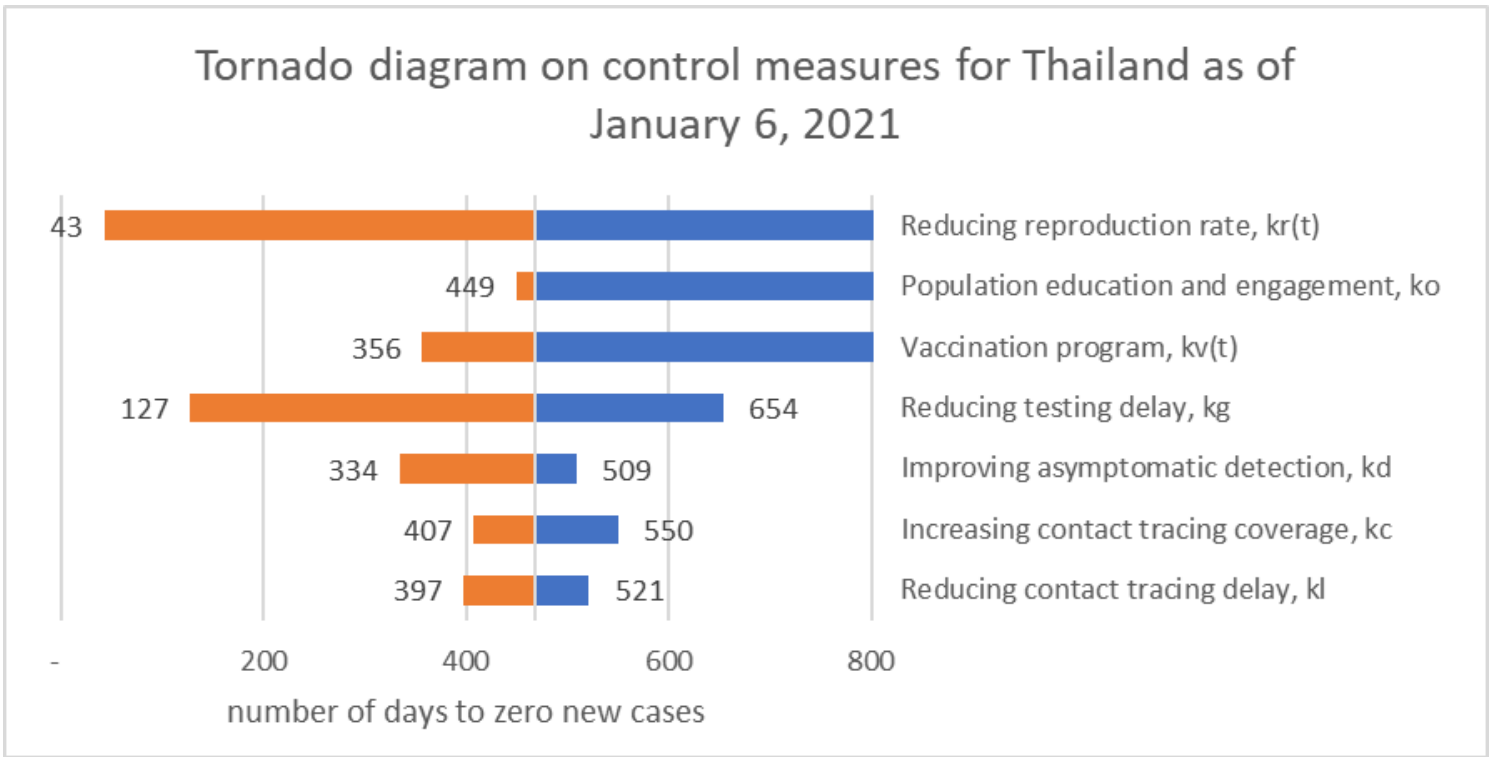

Figure 5

Tornado diagram on control measures for Thailand case study

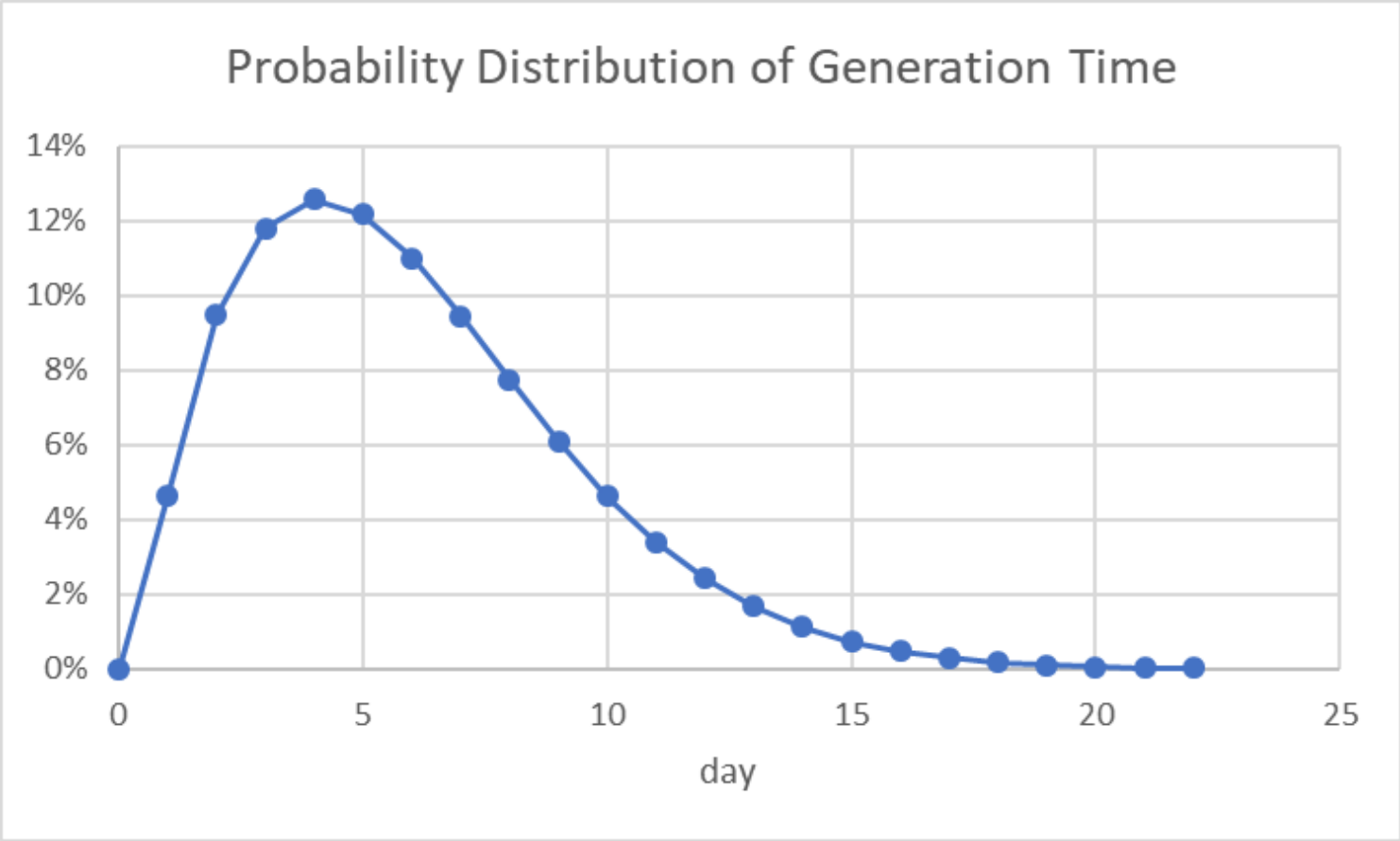

Figure 6

Discretization of probability distribution of generation time estimated from Ferretti et al.25

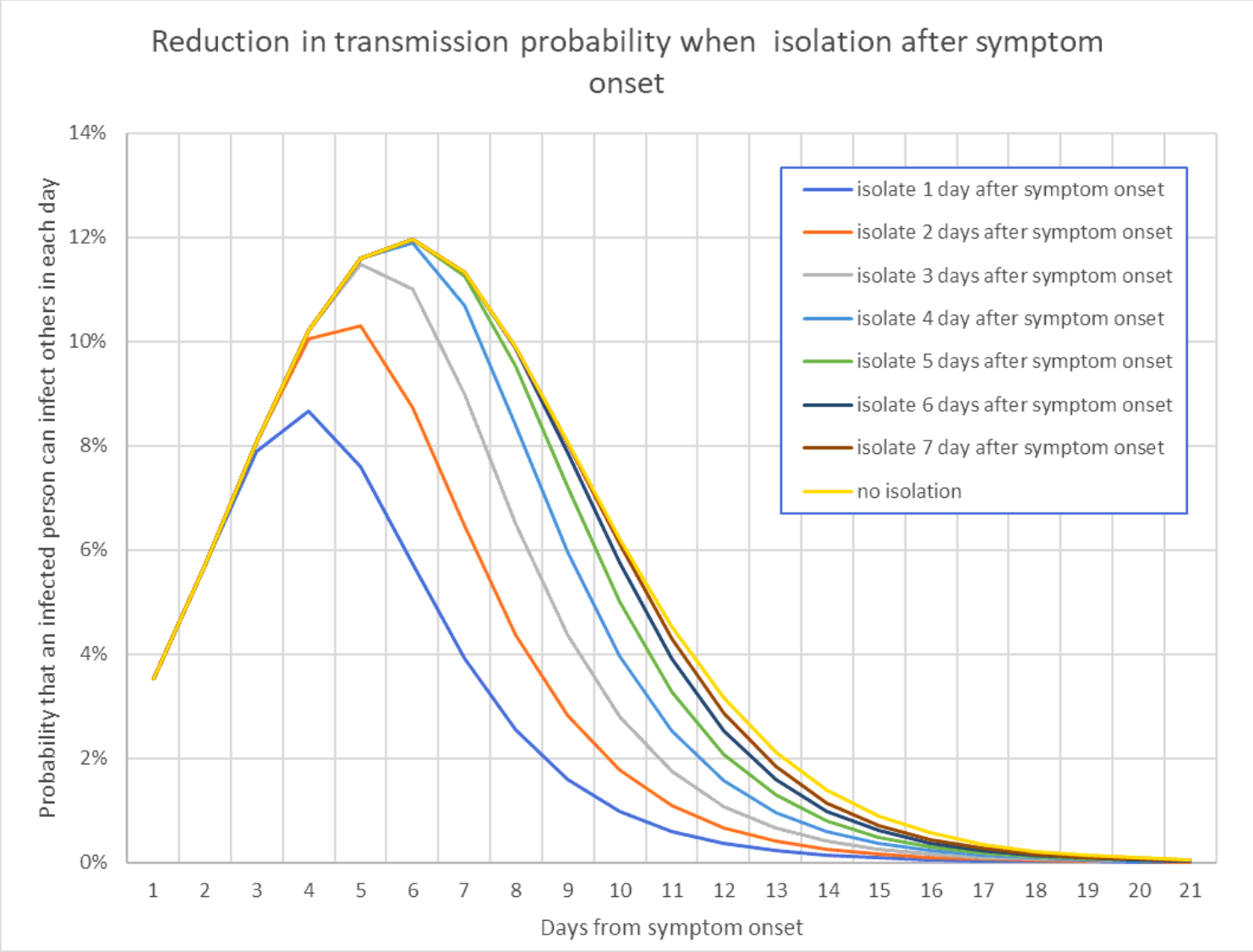

Figure 7

Reduction in transmission probability when isolated after symptom onset

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- ExtendedSupplementalData.docx