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A network modeling study highlights the critical role of efficient testing and contact tracing in mitigating COVID-19 pandemic

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Abstract

Background:

Previous studies generally emphasize that volume of tests is important in containment of the COVID-19 epidemic. Still, few studies q*uantify how the efficiency of testing and tracing* (average time interval from infection to quarantine of each individual) affect the epidemic, especially at the individual level.

Methods:

We developed a novel individual-level network model with key parameters obtained from recent studies, to quantify impacts of efficiency of testing and tracing. It *distinguishes infection from confirmation by* integrating a stage T as confirmed by testing and quarantined. Stages such as pre-symptomatic (E), asymptomatic (I), symptomatic (Is), death with (F) or without (f) test confirmation are also included. Three scenarios were evaluated in a closed population of 3000 individuals to mimic community-level dynamic. Real-world data from four Nordic countries were also analyzed.

Results:

1) Shortening the time interval between Is and T from 12 days to 4 days results in an 85.2% reduction in infections and 88.8% decrease in deaths. 2) Testing and tracing regardless of symptoms (7-day interval for Is to T, E/I to T interval change correspondingly) reduces 35.7 % of infections and 46.2% of deaths compared to testing Is alone. 3) A 10-day versus a 50-day delay to implement efficient testing and tracing reduces infections and deaths by 35.2% and 44.6%. The results were robust to sensitivity analyses. Analysis of the real-world data shows that tests per case in early-stage epidemics is important in reducing confirmed cases and fatality rates.

Conclusions:

Reducing testing delays in all symptomatic and pre- and asymptomatic cases is an effective containment strategy for COVID-19 outbreaks. These results provide professionals and policy makers with quantitative evidence on the critical value of efficiency in developing testing and contact tracing strategies.

Strengths and limitations of this study

1. This work provides a new perspective to evaluate testing and tracing effect besides tests volume at the individual level, which is the efficiency of testing and tracing (define as the average time interval for each case from initial infection to test confirmation and quarantine).

2. We quantified effects of different efficiency of testing and tracing and verified its important role in the control of COVID-19 epidemic.

3. This novel model can distinguish between the actual number of infections and confirmed cases, and can differentiate pre- and asymptomatic from symptomatic cases, and can be

further optimized to assess the effectiveness of various interventions in controlling COVID-19.

4. Limitations of this work include that all simulations were conducted in a closed population and did not account for inter-community social activity. Network sizes were also limited by computing complexity.

5. Confounders such as differences in population ageing level, medical resources, and lockdown procedures could be considered in our model in future work.

Introduction

Coronavirus disease 2019 (COVID-19) has posed serious public health challenges worldwide since December 2019.Warnings of recurrence are alarming as lockdown measures are being lifted, and there is no guarantee that large-scale testing alone will control the pandemic. We believe that testing policies must factor in efficiency (reducing the average time interval from initial infection to test confirmation and quarantine). Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is more contagious and has longer incubation time than either SARS-CoV and MERS-CoV [1], and can transmit during the incubation period[2,3,4,5,6]. About a third of SARS-CoV-2 infectors in Spain remain asymptomatic[7] and contagious. If the efficiency of testing and contact tracing is low, transmission via latent, pre- and asymptomatic infected individuals may lead to more severe spread, and some transmission models applied to previous epidemic are not suitable for SARS-CoV-2. Furthermore, many models do not quantify the efficiency.

The impact of test and quarantine interventions has been widely evaluated using different models. Some findings highlighted the volume of testing, contact tracing strategy, or combination of different interventions[8,9,10,11,12,13-18]. However, few focused on how efficiency of testing or contact tracing limit disease spread, and the degree to which testing efficiency and contact tracing policies contribute to containment efficacy remains unclear.

In this study, we developed a novel network model, CoTECT, based on R package Epimodel[19] to evaluate how testing and contact tracing efficiency affects the spread of the epidemic. CoTECT incorporates confirmed and unconfirmed infections, including the symptomatic, pre- or asymptomatic, or deceased, to simulate how the efficiency of testing and quarantine impacts epidemic outcomes. We simulated three different scenarios with controlled variables that aimed to eliminate confounding factors. Analysis of real-world data from four Nordic countries revealed that delays in counter measures adversely affect the outcome of epidemic. We provide a comprehensive and quantitative assessment of the key factors of testing and contact tracing, which will assist us in implementing more effective measures to contain the pandemic.

Methods

CoTECT simulation model

CoTECT is a stochastic epidemiological network model built on exponential random graphs[20]. It allows the user to construct a flexible network [21]with the desired likelihood of connection conditional on the graph with specific network properties [22 23].

Based on traditional Susceptible-Exposed-Infectious-Recovered (SEIR) structure, we designed the CoTECT model with eight compartments (Figure 1):

1. Susceptible individuals (S);
2. Exposed to the virus (E), cases in incubation period. E cases are infectious based the biological characteristics of SARS-CoV-2;
3. Infections without observable symptoms (I). Some I cases become symptomatic and transfer to the Is compartment.
4. Infectious and symptomatic cases (Is) are more likely to appear in the T compartment than I or E cases, as symptomatic cases are easier to detect.
5. Test-positive cases with quarantine (T); we assumed all cases confirmed by testing were immediately quarantined.
6. Test-positive fatalities (F);
7. Fatality without a positive test confirmation (f);
8. Recovered cases (R).

Full details are shown in Figure 1.

All arrows represent transmission rate from one compartment to the other, such as from Is to T denoted as Is-T rate.

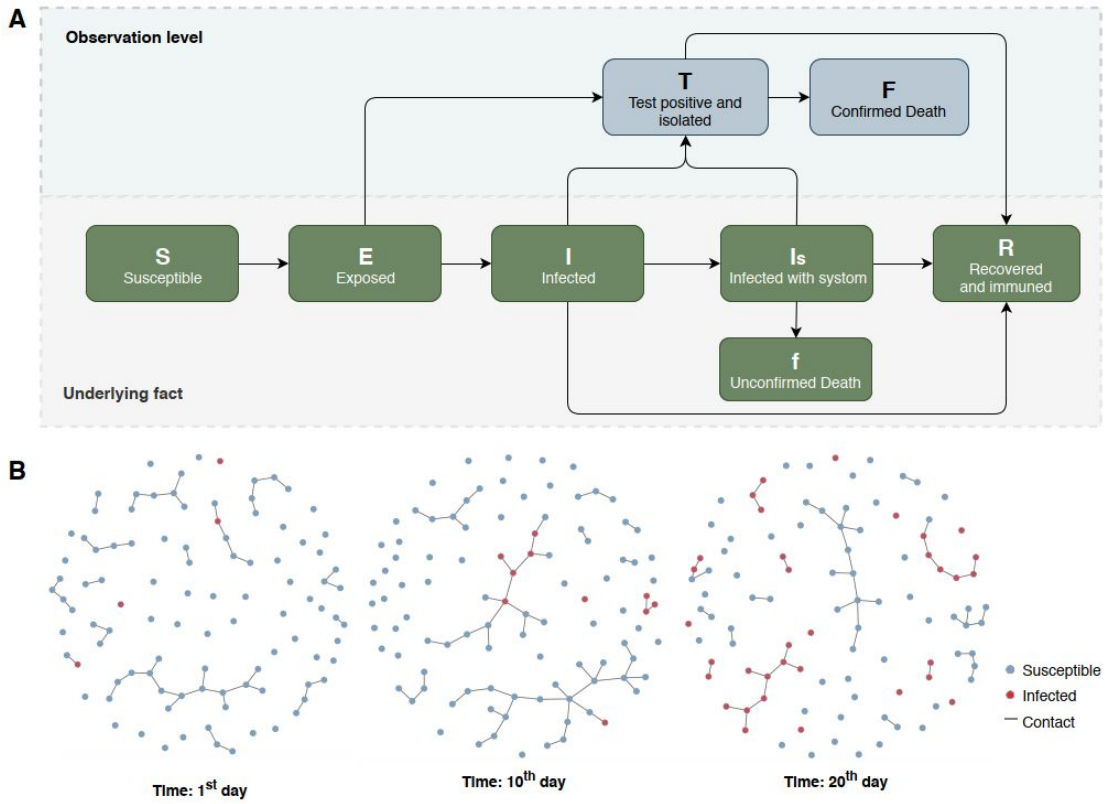

Figure 1. Introduction of the CoTECT model. (A) Structure of the network-based epidemiological model CoTECT. (B) Abbreviated version of the infection network progression. Snapshots shown are days 0, 10 and 20 after the first infected individual. Red and blue dots represent infected and susceptible individuals, respectively. Strings represent contact relationships.

Parameter settings

We parameterized the model using published values from multiple references [24,25,26,27,28], most of which were cases-level data statistics [4,29,30,31]. The parameters including incubation period [32][3], average time from onset to severe case [26], and average recovery times [30] for mild or severe cases are shown in Table S1. Sampled parameters were set at different grades within different scenarios, while fixed parameters remained constant across all experiments. A hypothetical population of 3,000 people over 300 days was used. The basic reproductive number (R0) of the baseline model was 2.2 by adjusting the edge density, maximum connection number and probability of transmission between connected nodes. Testing and tracing efficiencies were defined as an average of each individual's waiting interval from exposed/infected/symptom onset to test confirmation and quarantine. Efficiency is translated as transmission rate in CoTECT (IsT rate, IT rate, ET rate is the reciprocal of the waiting interval). For example, an average 7-day waiting time from symptom onset to quarantine is corresponding to 1/7 transmission rate.

In all experiment setting, the efficiency parameters (IsT rate, IT rate, ET rate) are set correspondingly. The time interval from E to I was six days, based on average of 6.4 days [3,6,25,28] from exposure to infection (incubation period). Therefore, the denominator of the IT rate is usually six days more than that of ET rate. The same logic applied to the IsT rate. Nevertheless, efficient contact tracing will boost both IT and ET rates.

Experiment setting

Baseline model is set as worst condition with no testing and contact tracing, therefore no quarantine measurements conducted. as mentioned above, with R0 is set over 1, the majority of the population will eventually get infected. on top of it, we simulated different combination of interventions as preliminary experiments to compare with the baseline. 1) four weeks delayed reaction (with no testing and contact tracing before the fourth week). And test only open to symptomatic cases; 2) four weeks delayed reaction with test for symptomatic, pre- and asymptomatic cases; 3) two weeks delayed reaction with test for symptomatic, pre- and asymptomatic cases.

We designed three scenarios to investigate the significance of testing efficiency. There was only one changing condition with other variables consistent across each scenario. The average of the 20 experiments was used as the final result. The key outcome indicators include cumulative infection, peak daily infections, peak daily confirmation and quarantine, cumulative confirmed cases and deaths, and CFR.

1) Scenario-1 simulated five different test efficiency levels, represented by five scales of daily transmission rates from Is to T (IsT rate) as 1/4, 1/6, 1/8, 1/10, 1/12. The daily transmission rate from I to T (IT rate) and from E to T (ET rate) changed along with IsT rate.

2) Scenario-2 quantified the importance of efficient contact tracing. Due to asymptomatic transmissibility, contact tracing is critical for effective containment. Tracing efficiency is represented by either the IT or ET rate. Therefore, we designed the simulations with fixed IsT rate (1/7) and different IT (1/12, 1/19, 0) or ET(1/117, 1/24, 0) rates.

3) Scenario-3 was designed based on analyses of real-world data showing that response times have varied greatly worldwide. Many countries were not well prepared for the pandemic, and targeted testing and contact tracing measures were often not implemented until after many confirmed case fatalities. We therefore simulated different public health responses delays in CoTECT. Five experiments were conducted with fixed IsT, IT and ET rates. The delays applied were 10, 20, 30, 40 and 50 days. Before the responses, we set the transmission rate from E,I and Is compartments to T as 0.

Sensitivity analysis

We evaluated transmission progression under conditions with no testing or contact tracing in place for varying population sizes. For all experiments, the mean basic reproduction number was set as an average of 2.2. Network density and relationship duration between nodes were consistent across all experiments.

Patient and Public Involvement

Patients and the public were not involved in this study.

Results

We carried out preliminary experiments to show how the CoTECT model simulates the transmission under different conditions of testing and contact tracing, and then demonstrated in detail the impacts of overall testing and contact tracing efficiency, contact tracing efficiency for pre- and asymptomatic cases, and delayed implementation of efficient testing and contact tracing on disease transmission.

Preliminary results of CoTECT simulation

We first defined the baseline model as the worst-case scenario with no epidemiological interventions conducted in a closed population. The baseline R0 was 2.2, according to the average R0 estimated [33] from 177 countries and territories [34]. (Figure 2A), aligned with previously published studies [26]. Then we compared the baseline model with different combinations of testing and contact tracing interventions to evaluate their respective impact on disease transmission. The infection curve is shown in Figure 2B. We assumed each community responded a minimum of several weeks after first infection. The dark blue line shows the outcome for a delay of four weeks and testing only symptomatic cases. Total infections, peak

daily infections and total deaths were reduced by 13.2%, 43.7% and 27.3%, respectively, compared to baseline. The navy line shows the outcome for an open test policy with efficient contact tracing. Total infections, peak daily infections and total deaths decreased by 23.4%, 43.1% and 41.3%, respectively, compared to baseline. The light blue line shows the outcome for a delay of two weeks after the first infection. Total infections, peak daily infections and total deaths decreased by 44.1%, 75.8% and 61.0%, respectively, compared to baseline.

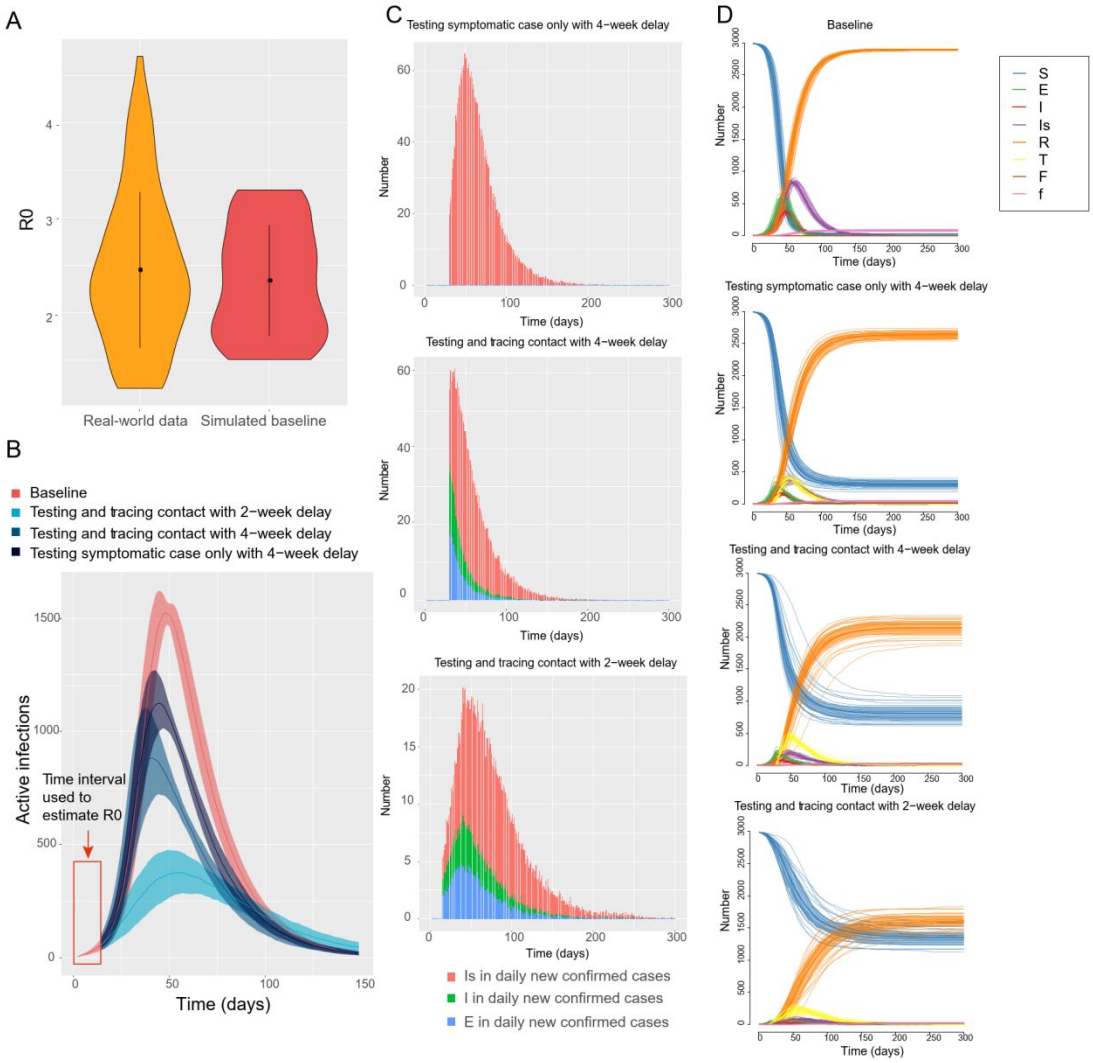

Figure 2. Epidemic transmission for the baseline and intervention models. (A) Violin plots of R0 distributions for the real-world data and baseline model. (B) Infection curves for the baseline and different intervention models. (C) Daily new symptomatic, pre- and asymptomatic cases confirmed by testing. (D) Compartment trends for the different models.

Daily new symptomatic, pre- and asymptomatic cases confirmed by testing in three conditions are shown in Figure 2C. Compared with condition-1 (only testing symptomatic cases with 4-week delay), condition-2 (testing and tracing pre- and asymptomatic contacts with 4-week delay) could reduce 24.8% of total confirmed cases (from 125 to 94), and 26.5% of 94

confirmed cases were diagnosed before symptom onset (E+I). Condition-3 (testing and tracing contacts with 2-week delay) could reduce 51.2% of total confirmed cases (from 125 to 61), 33.6% of 61 confirmed cases were diagnosed before symptom onset (E+I). Moreover, compared to condition-2, Condition-3 also reduced daily peak confirmed Is, I, and E cases by 65.8% (from 38 to 13), 75.0% (from 16 to 4), and 75.0% (from 20 to 5), respectively. We further demonstrated trends of all compartments in baseline and different conditions (Figure 2D). Compared to baseline, as infections decreased in 3 conditions, the S individuals (those remain uninfected) of condition-1, -2, -3 were 6.6, 11.6, and 20.7 times of S individuals of baseline model after 300 days of the epidemic, respectively. Meanwhile, 27.7%, 41.5%, and 61.2 % of deaths (confirmed and unconfirmed by testing) of baseline model were saved in condition-1, -2, -3, respectively. These results indicate that reduced time to action and better identification of pre- and asymptomatic cases are critical factors in flattening the infection curve and decreasing the deaths.

Impacts of overall testing and contact tracing efficiency to all infectors

Three scenarios were designed to quantify the impacts of different testing interventions on transmission. The outcome indicators included final cumulative infections (R+F+f), peak daily infections (E+I+Is), peak daily test-positive cases with quarantine (T), cumulative test positive (T) cases, total fatalities and CFR.

Scenario-1 evaluated the impact of overall testing and contact tracing efficiency by simulating five different levels of test efficiency, represented by five scales of daily transmission rate or average IsT rate. The intervals from symptom onset to positive test with quarantine were 4, 6, 8, 10 and 12 days. The corresponding IsT rates were 1/4, 1/6, 1/8, 1/10 and 1/12, thus reflecting different testing efficiencies. This scenario assumes that contact tracing efficiency changed with the IsT rate, and therefore latent, asymptomatic cases could also be tested. We found that longer public health response delays (i.e., lower IsT rates) resulted in higher peak daily new transmitters, peak daily new diagnoses and overall cumulative infections. In addition, the number of diagnosed and undiagnosed fatalities and the proportion of undiagnosed fatalities increased as IsT rates declined, indicating that fewer tests and slower response times resulted in worse the epidemic outcomes. We decreased the IsT delay from 12 to 4 days in two days intervals and found that, compared to baseline, total infections decreased by 20.5%, 29.2%, 39.0%, 57.0% and 88.3%, respectively, and total deaths decreased by 36.0%, 46.7%, 52.2%, 70.6% and 92.8%, respectively. Peak daily infections across the five experiments increased linearly as IsT rates decreased (Table 1, Figure 3A).

Table 1: Baseline and Scenario-1, -2 and -3 model outcomes

	Delay (days) to targeted testing and contact tracing (T delay)	Average waiting interval (days) from Is to T (1/IsT rate)	Average waiting interval (days) to from I to T (1/IT rate)	Total infections	Peak daily infections	Peak daily test confirmation	Total deaths	Proportion of unconfirmed deaths in total deaths
Baseline	No testing	No IsT transformation	No IT transformation	2933.6	1553.2	0	78.1	100%
Scenario -1	0	4	Yes	344.3	48.7	38.1	5.6	36%
		6		1261.4	181.8	128.3	23	39%
		8		1789	328.5	208.9	37.3	49%
		10		2077.3	425	251.8	41.6	54%
		12		2330.8	581	318.3	50	56%
Scenario -2	0	7	No IT transformation	2510.9	800.4	315	57.2	67%
			13	1941.2	396.6	213	38.1	51%
			11	1614.6	285.5	168.9	30.8	45%
Scenario -3	10	7	Yes	1857.6	360.1	233.4	37.2	46%
	20			1922.6	456.2	294.4	37.8	49%
	30			2272.3	764.1	455.5	45.2	55%
	40			2649.8	1129.5	543	58.6	71%
	50			2866.7	1231.6	400.5	67.1	82%

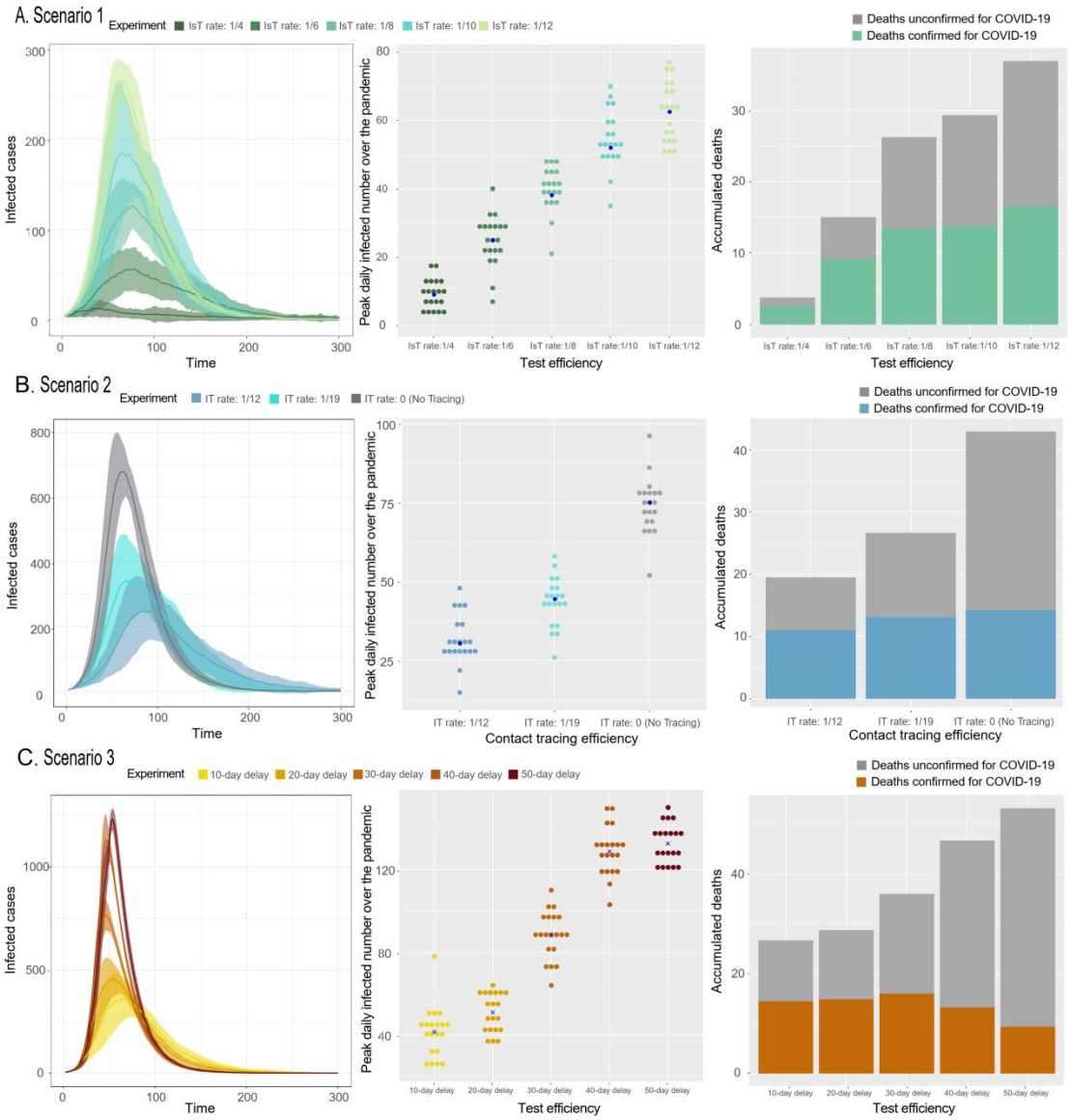

Figure 3: Scenario-1, Two and Three outcomes. Total infections over time, peak daily infections for different public health response strategies (each dot represents a simulation) and accumulated deaths (both confirmed and unconfirmed cases) for (A) Scenario-1, (B) Scenario-2 and (C) Scenario-3.

Impacts of contact tracing efficiency for pre- and asymptomatic cases

Scenario-2 evaluated the impact of tracing efficiency for pre- and asymptomatic cases by simulating different IT and ET rates with a fixed IsT rate. Contact tracing for Covid-19 is critical due to the transmissibility of pre- and asymptomatic infections. The IT and ET rates reflect contract tracing efficiency. In this scenario, the probability that latent and asymptomatic (or mild) cases would be tested and isolated (ET and IT rate) was adjusted by 0, 1/13 and 1/11. The fixed IsT rate was 1/7, which assumed 7 days waiting interval from onset to quarantine. The results showed that larger ET and IT rates resulted in fewer overall infections, confirmed cases and confirmed and unconfirmed fatalities. More efficient contact tracing (12-day delay

from infected to testing for I cases) would prevent 36% of cumulative infections, 64% of peak daily infections, 46% of peak daily confirmed cases and 46% of total deaths compared to no contact tracing. Less efficient contact tracing (as a 19-day delay from infected to testing for I cases) only prevented 23% of cumulative infections, 50% of peak daily infections, 32% of peak daily confirmed cases and 33% of total fatalities compared to no contact tracing. Thus, more efficient contact tracing resulted in overall fewer infections (Table 1, Figure 3B).

Impacts of delayed implementation of efficient testing and contact tracing

Scenario-3 evaluated the impact of delayed implementation of efficient testing and contact tracing. The delay intervals between the first infection and implementation of targeted testing were set as 10, 20, 30, 40 and 50 days. We found that cumulative infections and fatalities increased with increasing delay intervals. Compared to 50-day delay, delays of 10, 20, 30 and 40 days reduced total infections by35.2%, 32.9%, 20.7% and 7.6%, respectively, and total deaths by 44.6%, 43.7%, 32.6% and 12.7%, respectively. The increase in peak daily transmitters as delay interval increased followed a sigmoid-shape curve (Table 1, Figure 3C). Clearly, implementation of a prompt testing response within 20 days of first infection had much more impact than after 20 days.

The important impacts of prompt reaction for testing are not only presented in our simulation, but also observed in real-world data. The measures for sufficiency testing were the number of tests conducted per confirmed case (TPC) and tests per million people (TPM). Here, efficiency is measured as the time interval between infection and positive Covid19 test, and sufficient testing capacity, estimated by TPC and TPM, is therefore a prerequisite for efficiency. Decreasing TPC trends indicate that disease transmission is outpacing testing and efficiency is decreasing. The three indicators of epidemic control were CFR, confirmed cases per million people (CPM) and deaths per million people (DPM).

We selected four Nordic countries with similar medical resources, population aging level, geography and climate for comparison (Figure 4). Day 0 was the day when daily DPM reached 0.1. Norway, Finland and Denmark experienced similar proportion of lockdown duration in first 70 days, and TPC trends over the first 70 days all increased. From Day 0 to 14, TPC was highest in Norway, followed by Finland and Denmark. Between Day 15 and 70, even though the TPCs in Norway and Finland were similar, the CFR in Norway (2.8%) was lower than in Finland (4.6%). This implies that the early-outbreak TPC values are a bigger factor than later TPC in controlling the epidemic. Denmark had the lowest early-outbreak TPC of the above three countries. Even though its TPC later grew dramatically and far exceeded those of Norway and Finland, its CFR (4.9%) was higher than either Norway or Finland. We also observed that overall TPM in Denmark from Days 0 and 70 was 2.7 times those of Norway and Finland. This implies that early-stage TPC may have a greater influence on the overall CFR than late-stage TPC, in consistent with our hypothesis that early testing plays a critical role, without which, testing efforts must be heavily increased as transmission rates worsen. In Sweden, TPC gradually decreased. Sweden's CFR (12%) was the highest of all four countries. This indicates

that failure to implement early-stage sufficient targeted testing may not be remedied by increasing testing in the later period.

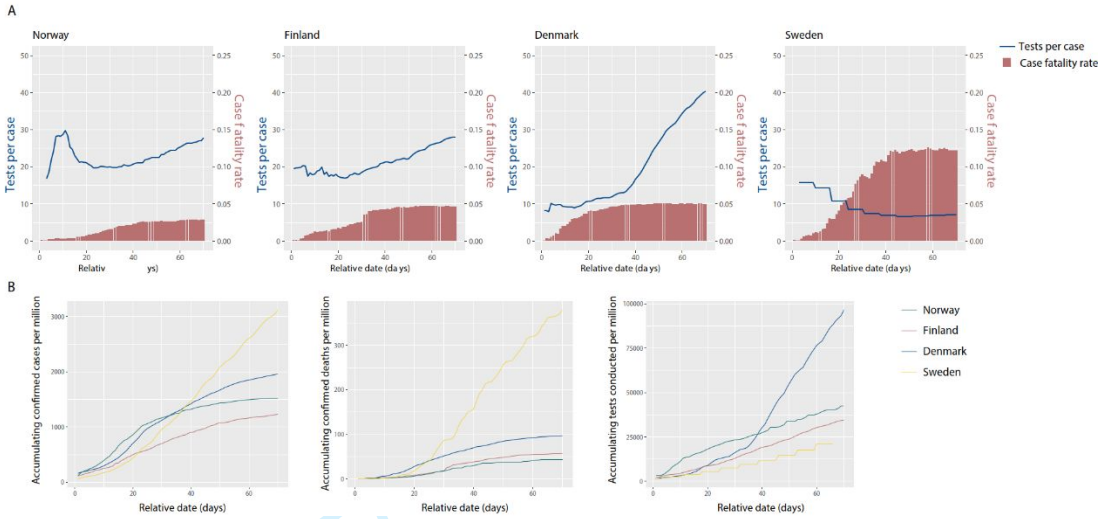

Figure 4: CFR, CPM and DPM trends in representative countries with different TPC and TPM levels.

(A) Accumulating CFR by COVID-19 and the TPC for 4 countries, starting by the day since daily new deaths due to COVID-19 reached 0.1 per million. (B) Accumulating cases, deaths, and tests per million of COVID-19 of 4 countries.

Sensitivity Analysis

Using sensitivity analyses, we compared baseline models with population sizes of 1000, 2000, 3000, 4000 and 5000. The proportions of cumulative infections, peak daily infections and cumulative deaths were similar across all five models. However, variation was much greater between the 1000 and 2000 population models than between population models of 3000 or more. These findings were our rational for using a representative population model of 3000 (Figure S1, Table S2).

Discussion

Our model quantifies how testing and contact tracing efficiency can influence the transmission and indicates that early, efficient testing and contact tracing can reduce disease transmission and mitigate overall fatalities. We believe it is critical to consider the transmission rates from pre- and asymptomatic cases in simulation models, which is the daily probability for an infected person to become confirmed and quarantined. Public health leaders should implement testing and contact tracing as soon as possible after cases are identified to minimize transmission rates over the course of an outbreak. It is reported that testing, tracing and targeted quarantine are more economical approaches in the long term[35].

The mean waiting time from receive COVID-19 test to confirmation is 4.1 days in the United States, which is reported to be disadvantageous to epidemic control [36]. According to Scenario-1, 4-day extra waiting interval will cause tremendous difference in total infection and death. Another example of the value of efficient testing is the successful containment of the second outbreak wave in Beijing, China. Highly efficient testing(opened to all, with or without symptoms) and contact tracing began immediately after the first case was identified and disease transmission was effectively controlled within a month[37,38,39,40] (Table S3), in mark contrast to the first outbreak in Wuhan, for which testing was less efficient and containment was slower. Government leader should aim to both increase testing and shorten the time from testing to quarantine.

Limitations of this work include that all simulations were conducted in a closed population and did not account for immigration or inter-community social activity. Network sizes were also limited by computing complexity. Confounders such as differences in population aging level, medical resources, and lockdown procedures could be considered in our model in the future work. we will continue to study the impact of testing and contact tracing efficiency with constraints and countermeasures.

Contributorship statement

Y. Hu designed and directed the project; Y. Hu and J. Guo wrote the article; X. Li, G. Li, X. Lu, Y. Zhang, L. Cong, Y. Kang, and X. Jia aided in data analysis or writing framework. X. Li, X. Shi and G. Xie were supervising the study, L. Zhang were guiding and supervising the study.

Declaration of interests

We declare no competing interests.

Data sharing

Extra data is available by emailing moehu@foxmail.com.

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Supplemental materials

Table S1. Parameter setting for CoTECT

	Transmission route	Parameter definition	Assumed rate	References
Sampled	E-->T	Rate per day at which exposed (E) individuals test positive and enter quarantine status (T)	1/18 (1/15-1/23)	[1] [2] [3]
	I-->T	Rate per day at which infected (I) cases test positive and enter quarantine status (T)	1/12 (1/9-1/17)	[1] [2] [3]
	Is-->T	Rate per day at which symptomatic infected (Is) cases test positive and enter quarantine status (T)	1/7 (1/4,1/6,1/8,1/10,1/12)	[1]
Fixed	I-->Is	Rate per day at which infected (I) cases become symptomatic (Is) cases	1/5	[1]
Fixed	E-->I	Rate per day at which an exposed (E) individual become infected (I) cases	1/6.4	[4]
	I-->R	Rate per day at which infected cases with mild or no symptoms (I) recover and are immunized (R)	1/14	[1] [2]
	Is-->R	Rate per day at which infected cases with severe symptoms (Is) recover and are immunized (R)	1/21	[1] [5]
	T-->R	Rate per day at which quarantined, test-positive (T) cases recover and are immunized (R)	1/17	Assumed
	Is-->F	Death rate per day of infected cases with severe symptoms (Is)	0.002	[2]
	T-->F	Death rate per day of test-positive (T) cases	0.001	[2] [3] [6] [7]

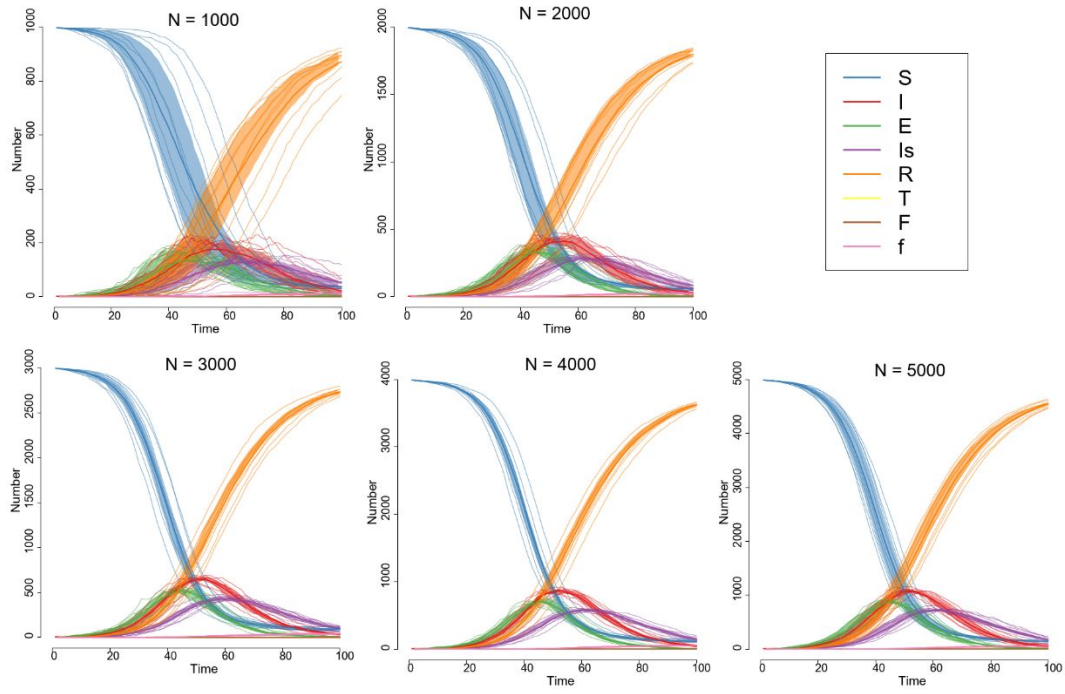

Figure S1: Sensitivity analyses for baseline models of different population sizes (N=1000, 2000, 3000, 4000, and 5000). Curves for each compartment in each model are shown in five graphs and demonstrate similar proportions of people in each compartment in the whole population.

Table S2: Sensitivity analyses for baseline models of different population sizes

Population size	Total infections	Peak daily infections	Proportion of total infections in population whole	Cumulative deaths of unconfirmed cases
1000	883.2	290.9	88.3%	12.1
2000	1826.2	668.5	91.3%	27.4
3000	2769.8	1035	92.3%	39.3
4000	3676	1378.4	91.9%	52.7
5000	4606.9	1716.8	92.1%	60.8

Table S3. Testing efficiency for the second-wave outbreak in Beijing, China

Average time from onset to reporting (first 37 cases)	Percentage of cases confirmed by contact tracing (first 37 cases)	Tests for traced contacts (first ten days)	Daily testing capacity within one month	Test efficiency for cases with fever	Test efficiency for other patients	Test efficiency for other patients	Test efficiency for normal test application	Total confirmed cases	Percentage of cases confirmed by targeted screening tests
2.7 days	68%	2342 thousand	90 to100 thousand	6h	12h	6h	24h	335	52%

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The role of efficient testing and contact tracing in mitigating COVID-19 pandemic: A network modeling study

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Abstract

Objectives

To quantify how the efficiency of testing and tracing (average time interval from infection to quarantine of each individual) affect the COVID-19 epidemic.

Setting

We developed a novel individual-level network model (CoTECT) with key parameters obtained from recent studies to quantify the impacts of testing and tracing efficiency. It distinguishes infection from confirmation by integrating a stage T as confirmed by testing and quarantined. Stages such as pre-symptomatic (E), asymptomatic (I), symptomatic (Is), death with (F) or without (f) test confirmation are also included. Three scenarios were evaluated in a closed population of 3000 individuals to mimic the community-level dynamic. Real-world data from four Nordic countries and Beijing's second outbreak were also analyzed.

Primary and secondary outcome measures

Simulation result: total/peak daily infections and confirmed cases; total deaths (confirmed/unconfirmed by testing), fatalities, case fatality rates. Real-world analysis: confirmed cases and deaths per million people.

Results

1) Shortening the time interval between Is and T from 12 days to 4 days results in an 85.2% reduction in infections and an 88.8% decrease in deaths. 2) Testing and tracing regardless of symptoms (7-day interval for Is to T, E/I to T interval change correspondingly) reduces 35.7 % of infections and 46.2% of deaths compared to testing Is alone. 3) A 10-day versus a 50-day delay to implement efficient testing and tracing reduces infections and deaths by 35.2% and 44.6%. The results were robust to sensitivity analyses. Analysis of the real-world data shows that tests per case in early-stage epidemics are critical in reducing confirmed cases and fatality rates.

Conclusions

Reducing testing delays in all symptomatic and pre- and asymptomatic cases is an effective containment strategy for COVID-19 outbreaks. These results provide professionals and policymakers with quantitative evidence on the critical value of efficiency in developing testing and contact tracing strategies.

Strengths and limitations of this study

1. This work provides a new perspective to evaluate testing and tracing effect besides tests volume at the individual level, which is the efficiency of testing and tracing (define as the average time interval for each case from initial infection to test confirmation and quarantine).

2. We quantified the effects of different testing efficiency and tracing and verified its important role in the control of the COVID-19 epidemic.

3. This graphical model with a novel structure can distinguish between the actual number of infections and confirmed cases, differentiate pre- and asymptomatic from symptomatic patients, and be further optimized to assess the effectiveness of various interventions in controlling COVID-19.

4. Limitations of this work include that all simulations were conducted in a closed population and did not account for inter-community social activity. Network sizes were also limited by computing complexity.

5. Confounders such as differences in population aging level, medical resources, and lockdown procedures could be considered in our model in future work.

Introduction

Coronavirus disease 2019 (COVID-19) has posed severe challenges to the physical and mental health of people worldwide since December 2019[1] . Warnings of recurrence are alarming as lockdown measures are being lifted, and there is no guarantee that large-scale testing alone will control the pandemic. We believe that testing policies must factor efficiency (reducing the average time interval from initial infection to test confirmation and quarantine). Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is more contagious and has a longer incubation time than either SARS-CoV and MERS-CoV [2], and can transmit during the incubation period[3] [4,5,6,7]. About a third of SARS-CoV-2 infectors in Spain remain asymptomatic[8] and contagious. Suppose the efficiency of testing and contact tracing is low. In that case, transmission via latent, pre-and asymptomatic infected individuals may lead to a more severe spread, and some transmission models applied to the previous epidemic are not suitable for SARS-CoV-2. Furthermore, many models do not quantify the influence of efficiency.

The impact of test and quarantine interventions has been widely evaluated using different models. Some findings highlighted the volume of testing, contact tracing strategy, or combination of other interventions[9] [10,11] [12,13,14-19]. For example, Luís Carlos Lopes-Júnior et al. [20]. provided a protocol to evaluate evidence on the influence of the testing capacity for symptomatic individuals in the control of COVID-19, which we referred to in literature research of the effect of testing[20]. McCombs A et al. [21]. compared strategies of different testing priority (people with high-risk/low-risk are tested first, people with symptoms appeared recently/earlier are tested first) under the condition that the maximum test volume per day is fixed. Adam J Kucharski et al. [22]. simulated the effects of random mass testing of 5% of the population each week on transmission reduction and compared it with isolation and tracing effects, without analysis on different testing scenarios. Alyssa Bilinski et al. [13]. explored whether testing included all identified contacts or only those with symptoms affected effective reproductive number. However, few research focused on how the efficiency of testing or contact tracing limits the disease spread and the degree to which testing efficiency and contact tracing policies contribute to containment efficacy. The efficiency (or timeliness) of testing is not necessarily related to the total amount of testing, so we reasoned for novel factors, strategies, and model structure.

In this study, we developed a novel network model, CoTECT, based on R package Epimodel[23] to evaluate how testing and contact tracing efficiency affect the epidemic's spread. CoTECT incorporates confirmed and unconfirmed infections, including the symptomatic, pre-or asymptomatic, or deceased, to simulate how the efficiency of testing and quarantine impacts epidemic outcomes. We simulated three different scenarios with controlled variables that aimed to eliminate confounding factors. Analysis of real-world data from four Nordic countries revealed that delays in countermeasures adversely affect the outcome of the epidemic. We provide a comprehensive and quantitative assessment of the critical factors of testing and contact tracing, which will help us implement more effective measures to contain the pandemic.

Methods

CoTECT simulation model

CoTECT is a self-developed stochastic epidemiological network model built on mathematical modeling of infectious disease dynamics platform with R language called Epimodel, and it allows the user to construct a flexible network [24]with the desired likelihood of connection conditional on the graph with specific network properties [25] [26].

The platform supports stochastic network models developing with self-defined contact mode and interaction between different nodes (stand for individuals), which is different from the ordinary differential equation (compartmental) mode,l which assumes human social activity is based on a large, homogenous, well-mixed population. Instead, every interaction is a stochastic process on CoTECT. The underlying network is called exponential-family random graph models (ERGMs)[27], developed by Holland and Leinhardt 1,2. CoTECT assumes all tests hold the best sensitivity and specificity, which described false-positive and true-negative as a small probability event.

Based on the traditional Susceptible-Exposed-Infectious-Recovered (SEIR) structure, we designed the CoTECT model with eight compartments (Figure 1):

1. Susceptible individuals (S);
2. Exposed to the virus (E), cases in incubation period. E cases are infectious based on the biological characteristics of SARS-CoV-2;
3. Infections without observable symptoms (I). Some I cases become symptomatic and transfer to the Is compartment.
4. Infectious and symptomatic cases (Is) are more likely to appear in the T compartment than I or E cases, as symptomatic cases are easier to detect.
5. Test-positive cases with quarantine (T); we assumed all cases confirmed by testing were immediately quarantined.
6. Test-positive fatalities (F);
7. Fatality without a positive test confirmation (f);
8. Recovered cases (R).

Full details are shown in Figure 1.

All arrows represent transmission rate from one compartment to the other, such as from Is to T denoted as IsT rate.

Infectious happens on the existed edge (real contact) between two nodes (persons) in a given probability. In our model, the infection rate is determined by SE rate and act times, which is the contact times between a susceptible person and an exposed person. The exposed states represent the incubation period with relatively lower transmission ability than infected patients with symptoms. This probability setting is based on the epidemiological characteristics of COVID-19. If the SE rate is p and the average act times is three times, the infection probability between two connected nodes (people) is $1-(1-p)3$. Meanwhile, the edge connecting two nodes is generated and dissolved by a stochastic process with conditions. The conditional probability of an edge forming and dissolving is based on a Bernoulli distribution with the module-specific parameter, and the resulting degree distribution is a binomial mixture [27].

Besides the infection process, all transmission rate from A module to B implies that the mean duration of remaining the A statues. For example, a 0.1 recovery rate (IR rate) indicates a ten days duration of recovery. All transmission of statues of each node is a Bernoulli process in a matter of time. The Basic reproductive number R0 is measured based on the simulated result of changing the number of total infections (E+I+Is+T). We adjusted the network-related parameters to approach a WHO reported R0 of SAR-COV-2 on our baseline model, as shown in Figure-2 A. Figure1-B displayed the stochastic process of the edge generation and desolvation and represented the dynamic change of our social network, which had led to the abbreviation version of the contact network on different time steps

Parameter settings

We parameterized the model using published values from multiple references [28,29,30] [31,32], most of which were cases-level data statistics [5,33,34,35]. The parameters, including incubation period [36] [4], average time from onset to severe case [30], and average recovery times [34] for mild or severe cases, are shown in Table S1. Sampled parameters were set at different grades within different scenarios, while fixed parameters remained constant across all experiments. A hypothetical population of 3,000 people over 300 days was used. Our assumptions and network parameters are aligned with ERGMs, which are listed in supplemental Table 2. The basic reproductive number (R0) of the baseline model was 2.2 by adjusting the edge density, maximum connection number, and probability of transmission between connected nodes (Table S2). Testing and tracing efficiencies were defined as an average of each individual's waiting interval from exposed/infected/symptom onset to test confirmation and quarantine. Efficiency is translated as transmission rate in CoTECT (IsT rate, IT rate, ET rate is the reciprocal of the waiting interval). For example, an average 7-day waiting time from symptom onset to quarantine is corresponding to the 1/7 transmission rate.

The efficiency parameters (IsT rate, IT rate, ET rate) are set correspondingly in all experiment settings. The time interval from E to I was six days, based on an average of 6.4 days [4] [7] [29] [32] from exposure to infection (incubation period). Therefore, the denominator of the IT rate is

usually six days more than that of ET rate. The same logic applied to the IsT rate. Nevertheless, efficient contact tracing will boost both IT and ET rates.

Experiment setting

The baseline model is set as the worst condition with no testing and contact tracing. Therefore no quarantine measurements were conducted. As mentioned above, with R0 being set over 1, most of the population will eventually get infected. On top of it, we simulated different combinations of interventions as preliminary experiments to compare with the baseline. 1) four weeks delayed reaction (with no testing and contact tracing before the fourth week). And test only open to symptomatic cases; 2) four weeks delayed response with the test for symptomatic, pre-and asymptomatic patients; 3) two weeks delayed reaction with the test for symptomatic, pre-and asymptomatic cases.

We designed three scenarios to investigate the significance of testing efficiency. There was only one changing condition with other variables consistent across each scenario. The average of the 20 experiments was used as the final result. The critical outcome indicators include cumulative infection, peak daily infections, peak daily confirmation and quarantine, cumulative confirmed cases and deaths, and CFR.

1) Scenario-1 simulated five different test efficiency levels, represented by five scales of daily transmission rates from Is to T (IsT rate) as 1/4, 1/6, 1/8, 1/10, 1/12. The daily transmission rate from I to T (IT rate) and from E to T (ET rate) changed along with IsT rate.

2) Scenario-2 quantified the importance of efficient contact tracing. Due to asymptomatic transmissibility, contact tracing is critical for effective containment. Tracing efficiency is represented by either the IT or ET rate. Therefore, we designed the simulations with fixed IsT rate (1/7) and different IT (1/12, 1/19, 0) or ET(1/117, 1/24, 0) rates.

3) Scenario-3 was designed based on real-world data analyses showing that response times have significantly varied worldwide. Many countries were not well prepared for the pandemic, and targeted testing and contact tracing measures were often not implemented until after many confirmed case fatalities. We, therefore, simulated different public health response delays in CoTECT. Five experiments were conducted with fixed IsT, IT, and ET rates. The delays applied were 10, 20, 30, 40, and 50 days. Before the responses, we set the transmission rate from E, I, and Is compartments to T as 0.

Sensitivity analysis

We evaluated transmission progression under conditions with no testing or contact tracing in place for varying population sizes. For all experiments, the mean basic reproduction number was set as an average of 2.2. Network density and relationship duration between nodes were consistent across all experiments.

The sensitivity analysis also included tests on network-related parameters, which describe the disease transmission model's underlying social activity pattern. In our study, the simulation

model built upon a graph model consist of edges and nodes. The edge between two nodes reflects a relatively close contact could transmit the disease with a certain probability. In CoTECT, the edges can be interpreted as a face to face conversation or share a uber ride. Unlike the sensitivity analysis about the population size, which emphasizes the unchanged infection ratio and transmission rate under different network sizes, the network-related parameter test will demonstrate how these parameters impact the disease transmission.

We tested each edges' mean duration (contact), concurrent edges (how many simultaneous contacts happened per day), and the whole network's density. These results are included in supplemental materials (Figure S1, Table S3). As mentioned in the main text, the final set of these parameters are tuned based on the simulated baseline's R0(basic reproductive number).

Patient and Public Involvement

Patients and the public were not involved in this study.

Results

We carried out preliminary experiments to show how the CoTECT model simulates the transmission under different testing conditions and contact tracing. We then demonstrated in detail the impacts of comprehensive testing and contact tracing efficiency, contact tracing efficiency for pre-and asymptomatic cases, and delayed implementation of efficient testing and contact tracing on disease transmission.

Preliminary results of CoTECT simulation

We first defined the baseline model as the worst-case scenario with no epidemiological interventions conducted in a closed population. The baseline R0 was 2.2, according to the average R0 estimated[37] from 177 countries and territories[38]. (Figure 2A), aligned with previously published studies[30]. Then we compared the baseline model with different combinations of testing and contact tracing interventions to evaluate their respective impact on disease transmission. The infection curve is shown in Figure 2B. We assumed each community responded a minimum of several weeks after the first infection. The dark blue line indicates the outcome for a delay of four weeks and testing only symptomatic cases. Total infections, peak daily infections, and total deaths were reduced by 13.2%, 43.7%, and 27.3%, respectively, compared to baseline. The navy line shows the outcome of an open test policy with efficient contact tracing. Total infections, peak daily infections, and total deaths decreased by 23.4%, 43.1,% and 41.3%, respectively, compared to baseline. The light blue line shows the outcome for a delay of two weeks after the first infection. Total infections, peak daily infections, and total deaths decreased by 44.1%, 75.8,% and 61.0%, respectively, compared to baseline.

Daily new symptomatic,pre-andd asymptomatic cases confirmed by testing in three conditions are shown in Figure 2C. Compared with condition-1 (only testing symptomatic cases with 4-week delay), condition-2 (testing and tracing pre- and asymptomatic contacts with 4-week delay) could reduce 24.8% of total confirmed cases (from 125 to 94), and 26.5% of 94

confirmed cases were diagnosed before symptom onset (E+I). Condition-3 (testing and tracing contacts with a 2-week delay) could reduce 51.2% of total confirmed cases (from 125 to 61), 33.6% of 61 confirmed cases were diagnosed before symptom onset (E+I). Moreover, compared to condition-2, Condition-3 also reduced daily peak confirmed Is, I, and E cases by 65.8% (from 38 to 13), 75.0% (from 16 to 4), and 75.0% (from 20 to 5), respectively. We further demonstrated trends of all compartments in baseline and different conditions (Figure 2D). Compared to baseline, as infections decreased in 3 conditions, the S individuals (those who remain uninfected) of condition-1, -2, -3 were 6.6, 11.6, and 20.7 times of S individuals of baseline model after 300 days of the epidemic, respectively. Meanwhile, 27.7%, 41.5%, and 61.2 % of deaths (confirmed and unconfirmed by testing) of the baseline model were saved in condition-1, -2, -3, respectively. These results indicate that reduced time to action and better identification of pre-and asymptomatic cases are critical factors in flattening the infection curve and decreasing the deaths.

Impacts of overall testing and contact tracing efficiency to all infectors

Three scenarios were designed to quantify the impacts of different testing interventions on transmission. The outcome indicators included final cumulative infections (R+F+f), peak daily infections (E+I+Is), peak daily test-positive cases with quarantine (T), cumulative test positive (T) cases, total fatalities, and CFR.

Scenario-1 evaluated the impact of overall testing and contact tracing efficiency by simulating five different levels of test efficiency, represented by five scales of daily transmission rate or average IsT rate. The intervals from symptom onset to positive test with quarantine were 4, 6, 8, 10, and 12 days. The corresponding IsT rates were 1/4, 1/6, 1/8, 1/10, and 1/12, thus reflecting different testing efficiencies. This scenario assumes that contact tracing efficiency changed with the IsT rate, and therefore latent, asymptomatic cases could also be tested. We found that longer public health response delays (i.e., lower IsT rates) resulted in higher peak daily new transmitters, peak daily new diagnoses, and overall cumulative infections. Besides, the number of diagnosed and undiagnosed fatalities and the proportion of undiagnosed fatalities increased as IsT rates declined, indicating that fewer tests and slower response times resulted in worse epidemic outcomes. We decreased the IsT delay from 12 to 4 days in two days intervals and found that, compared to baseline, total infections decreased by 20.5%, 29.2%, 39.0%, 57.0% and 88.3%, respectively, and total deaths decreased by 36.0%, 46.7%, 52.2%, 70.6% and 92.8%, respectively. Peak daily infections across the five experiments increased linearly as IsT rates decreased (Table 1, Figure 3A).

Table 1: Baseline and Scenario-1, -2, and -3 model outcomes

	Delay (days) to targeted testing and contact tracing (T delay)	Average waiting interval (days) from Is to T (1/IsT rate)	Average waiting interval (days) to from I to T (1/IT rate)	Total infections	Peak daily infections	Peak daily test confirmation	Total deaths	The proportion of unconfirmed deaths in total deaths
Baseline	No testing	No IsT transformation	No IT transformation	2933.6	1553.2	0	78.1	100%
Scenario -1	0	4	Yes	344.3	48.7	38.1	5.6	36%
		6		1261.4	181.8	128.3	23	39%
		8		1789	328.5	208.9	37.3	49%
		10		2077.3	425	251.8	41.6	54%
		12		2330.8	581	318.3	50	56%
Scenario -2	0	7	No IT transformation	2510.9	800.4	315	57.2	67%
			13	1941.2	396.6	213	38.1	51%
			11	1614.6	285.5	168.9	30.8	45%
Scenario -3	10	7	Yes	1857.6	360.1	233.4	37.2	46%
	20			1922.6	456.2	294.4	37.8	49%
	30			2272.3	764.1	455.5	45.2	55%
	40			2649.8	1129.5	543	58.6	71%
	50			2866.7	1231.6	400.5	67.1	82%

Impacts of contact tracing efficiency for pre-and asymptomatic cases

Scenario-2 evaluated the impact of tracing efficiency for pre-and asymptomatic cases by simulating different IT and ET rates with a fixed IsT rate. Contact tracing for Covid-19 is critical due to the transmissibility of pre-and asymptomatic infections. The IT and ET rates reflect contract tracing efficiency. In this scenario, the probability that latent and asymptomatic (or mild) cases would be tested and isolated (ET and IT rate) was adjusted by 0, 1/13, and 1/11.

The fixed IsT rate was 1/7, which assumed seven days waiting for an interval from onset to quarantine. The results showed that larger ET and IT rates resulted in fewer overall infections, confirmed cases, and confirmed and unconfirmed fatalities. More efficient contact tracing (12-day delay from infected to testing for I cases) would prevent 36% of cumulative infections, 64% of peak daily infections, 46% of peak daily confirmed cases, and 46% of total deaths compared to no contact tracing. Less efficient contact tracing (as a 19-day delay from infected to testing for I patients) prevented 23% of cumulative infections, 50% of peak daily infections, 32% of peak daily confirmed cases, and 33% of total fatalities compared to no contact tracing. Thus, more efficient contact tracing resulted in fewer infections (Table 1, Figure 3B).

Impacts of delayed implementation of efficient testing and contact tracing

Scenario-3 evaluated the impact of delayed implementation of efficient testing and contact tracing. The delay intervals between the first infection and implementation of targeted testing were set as 10, 20, 30, 40, and 50 days. We found that cumulative infections and fatalities increased with increasing delay intervals. Compared to 50-day delay, delays of 10, 20, 30 and 40 days reduced total infections by 35.2%, 32.9%, 20.7% and 7.6%, respectively, and total deaths by 44.6%, 43.7%, 32.6% and 12.7%, respectively. The increase in peak daily transmitters as delay interval increased followed a sigmoid-shape curve (Table 1, Figure 3C). Clearly, implementing a prompt testing response within 20 days of the first infection had much more impact than response 20 days later.

The critical impacts of prompt reaction for testing are presented in our simulation and observed in real-world data. The sufficiency testing measures were the number of tests conducted per confirmed case (TPC) and tests per million people (TPM). Here, efficiency is measured as the time interval between infection and positive Covid19 test, and sufficient testing capacity, estimated by TPC and TPM, is a prerequisite for efficiency. Decreasing TPC trends indicate that disease transmission is outpacing testing, and efficiency is decreasing. The three indicators of epidemic control were CFR, confirmed cases per million people (CPM), and deaths per million people (DPM).

We selected four Nordic countries with similar medical resources, population aging level, geography, and climate for comparison (Figure 4). Day 0 was the day when daily DPM reached 0.1. Norway, Finland, and Denmark experienced a similar proportion of lockdown duration in the first 70 days, and TPC trends over the early 70 days all increased. From Day 0 to 14, TPC was highest in Norway, followed by Finland and Denmark. Between Day 15 and 70, even though the TPCs in Norway and Finland were similar, the CFR in Norway (2.8%) was lower than in Finland (4.6%). This implies that the early-outbreak TPC values are a more significant factor than later TPC in controlling the epidemic. Denmark had the lowest early-outbreak TPC of the above three countries. Even though its TPC later grew dramatically and far exceeded those of Norway and Finland, its CFR (4.9%) was higher than either Norway or Finland. We also observed that overall TPM in Denmark from Days 0 and 70 was 2.7 times those of Norway and Finland. This implies that early-stage TPC may have a more significant influence on the overall CFR than late-stage TPC, consistent with our hypothesis that early testing plays a

critical role, without which, testing efforts must be heavily increased as transmission rates worsen. In Sweden, TPC gradually decreased. Sweden's CFR (12%) was the highest of all four countries. This indicates that early-stage insufficient testing might not be saved by increasing testing volume in the later period.

Sensitivity Analysis

Using sensitivity analyses, we compared baseline models with population sizes of 1000, 2000, 3000, 4000, and 5000. The proportions of cumulative infections, peak daily infections, and cumulative deaths were similar across all five models. However, variation was much more significant between the 1000 and 2000 population models than between population models of 3000 or more. These findings were our rationale for using a representative population model of 3000 (Figure S1, Table S3).

Sensitivity analysis of network-related parameters emphasis how does the structure of social network impacts disease transmission. The density of the network will directly impact disease transmission speed (FigureS1, Table S3). The extremely low density is difficult to maintain nowadays. We can expect to see it happened in a lockdown town in a short period. Decreasing the number of concurrent nodes with fixed density will skew the infection number curve. It also affects the variance since nodes with concurrent become a critical node that can spread the disease to many other nodes. The duration of edges indicates the stability of the relationship between two nodes. The result revealed that the increase of the stability would flatten the infection curve. It is clear that if we only contact the same group of people repeatedly, the possibility of being infected will drop.

Discussion

Our model quantifies how testing and contact tracing efficiency can influence the transmission of COVID-19 and indicates that early, efficient testing and contact tracing can reduce disease transmission and mitigate overall fatalities. We believe it is critical to consider the transmission rates from pre-and asymptomatic cases in simulation models, which is the daily probability for an infected person to become confirmed and quarantined. Public health leaders should implement testing and contact tracing as soon as possible after cases are identified to minimize transmission rates for an outbreak. Our results provide professionals and policymakers with quantitative evidence on the critical value of efficiency in developing testing and contact tracing strategies, especially instructive for nations undergoing or expecting the second/third wave of Covid-19.

Compared with previous studies, which mostly emphasized the amount of testing, we did not limit our analysis to estimate the fixed total amount of testing required since the capacity of testing changed over time. Instead, we revealed that earlier and more efficient testing could reduce the number of infections, therefore reduce testing demand. Many studies already[39] proved some test strategies could release the pressure of test kits shortage[40]. However, we focused more on the waiting time of exposed people receive their test results (efficiency of testing and contact tracing). The methodology novelty was reflected in the model structure and

scenario design. CoTECT can measure the timeliness of test measures taken for each individual to a macro perspective outcome.

The mathematical pattern of communicating disease transmission is well studied, while researchers still unable to precisely predict how large a novel infectious disease will impact a given population. It is because the outcome is decided by both human intervention and virus activities. It is better describing as a dynamic process where humans are racing with the virus. We learned from Beijing's successful story that efficient testing, tracking, and quarantine could save millions of lives from COVID-19. This study inductively assumes that Beijing's valuable experience can be summarized as an efficient test and tracing work. And then, we tested our assumption on a well-designed individual-based contact network model. It is reported that testing, tracing, and targeted quarantine are more economical approaches in the long term[41]. Efficient testing and tracing require hard work and maintains vigilance for a long time. However, the reward is much more attempting.

The mean waiting time from receiving the COVID-19 test to confirmation is 4.1 days in the United States, which is reported to be disadvantageous to epidemic control [42]. According to Scenario-1, a 4-day extra waiting interval will cause a tremendous difference in total infection and death. Another example of the value of efficient testing is the successful containment of the second outbreak wave in Beijing, China. Highly efficient testing(opened to all, with or without symptoms) and contact tracing began immediately after the first case was identified[43] [44,45] [46] (Table S4,S5), in mark contrast to the first outbreak in Wuhan testing was less efficient, and containment was slower. Government leaders should aim to both increase testing and shorten the time from testing to quarantine.

Besides test efficiency for each individual, the prompt reaction (including contact tracing, quarantine, and lockdown) of the pandemic in the early stage (first month since the first case) will save many infections even in a close population. If we consider the distance of cities and border check, an exponential number of people will be protected by locking the specific town early. Although many countries have built an advanced epidemic surveillance report system, the inadequate use and insufficient emphasis require more attention.

The size of the population is irrelevant to the disease transmission rate. Therefore, our main conclusion could generalize to different circumstances, from megacity like Beijing to every small village. China has adopted a prompt reaction with the efficient test. Furthermore, this highly efficient work requirement has become a policy applied in every corner of Mainland China. Since 2020 March, there is an apparent under-controlled situation observed in China, and even the medical resource (hospital bed, ICU, physician number per capita [47]) is much less than a developed country like Germany and United States.

Our experiment and real-world data justified the pandemic's magic weapon as fast and alert actions instead of a massive test capacity. With medical research development, we sincerely expect a quicker and more solid vaccine development process in the future. However, before the vaccine was delivered to everyone, the best lesson we learned from COVID-19 is still the

efficiency test, contact tracing, and quarantine, which required close cooperation between the government, the public health sector, and people living in this country. Admit the new virus's dangers are the critical first step to survive this pandemic [48].

Limitations of this work include that all simulations were conducted in a 3000 population-and did not account for immigration or inter-community social activity. Network sizes were also limited by computing complexity. Confounders such as differences in population aging level, medical resources, and lockdown procedures could be considered in our future work model. Besides, the model cannot estimate the socio-economic resources required for efficient testing.We will continue to study the impact of testing and contact tracing efficiency with constraints and countermeasures and improve our model in the future.

Contributorship statement

Y. Hu designed and directed the project; Y. Hu and J. Guo wrote the article; X. Li, G. Li, X. Lu, Y. Zhang, L. Cong, Y. Kang, and X. Jia aided in data analysis or writing framework. X. Li, X. Shi, and G. Xie were supervising the study, L. Zhang was guiding and supervising the study. All authors meet the ICMJE criteria for authorship.

Declaration of interests

We declare no competing interests.

Data sharing

Data are available in a public, open access repository. Data are available upon reasonable request. Data are available by emailing moehu@foxmail.com.

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Figure Legend

Figure 1. Introduction of the CoTECT model. (A) Structure of the network-based epidemiological model CoTECT. (B) Abbreviated version of the infection network progression. Snapshots shown are days 0, 10 and 20 after the first infected individual. Red and blue dots represent infected and susceptible individuals, respectively. Strings represent contact relationships.

Figure 2. Epidemic transmission for the baseline and intervention models. (A) Violin plots of R0 distributions for the real-world data and baseline model. (B) Infection curves for the baseline and different intervention models. (C) Daily new symptomatic, pre- and asymptomatic cases confirmed by testing. (D) Compartment trends for the different models.

Figure 3: Scenario-1, Two and Three outcomes. Total infections over time, peak daily infections for different public health response strategies (each dot represents a simulation) and accumulated deaths (both confirmed and unconfirmed cases) for (A) Scenario-1, (B) Scenario-2 and (C) Scenario-3.

Figure 4: CFR, CPM and DPM trends in representative countries with different TPC and TPM levels.
(A) Accumulating CFR by COVID-19 and the TPC for 4 countries, starting by the day since daily new deaths due to COVID-19 reached 0.1 per million. (B) Accumulating cases, deaths, and tests per million of COVID-19 of 4 countries.

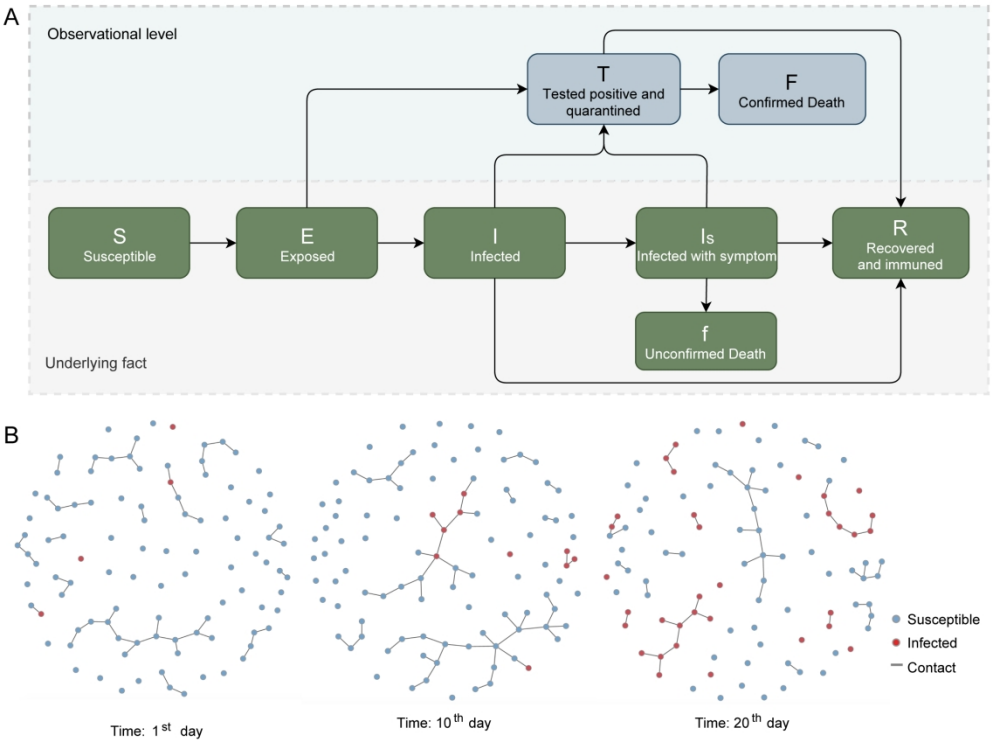
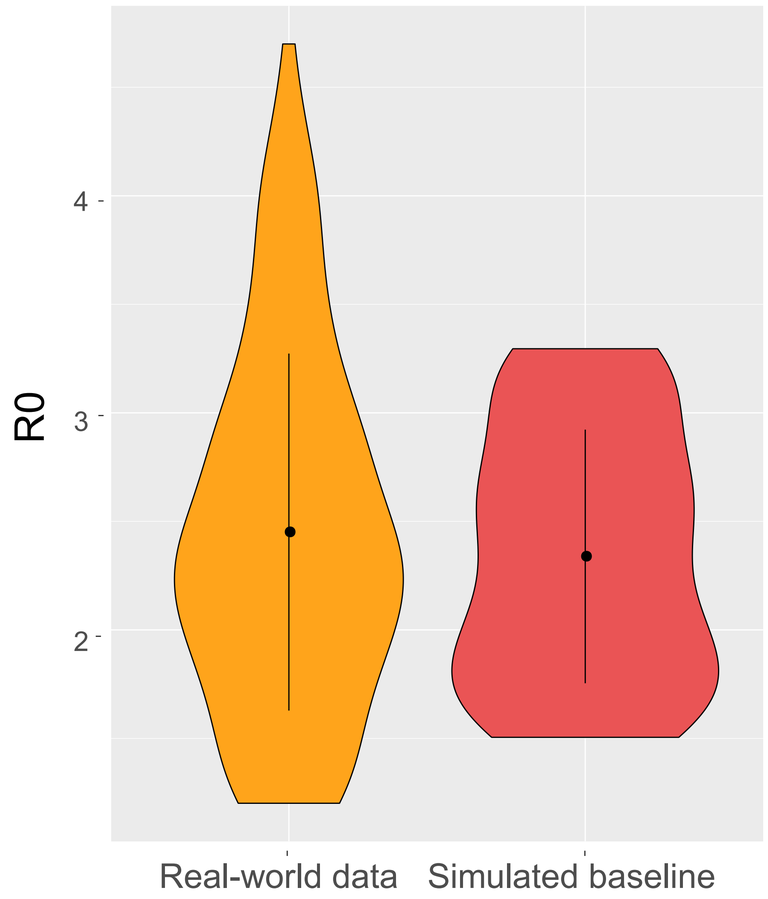
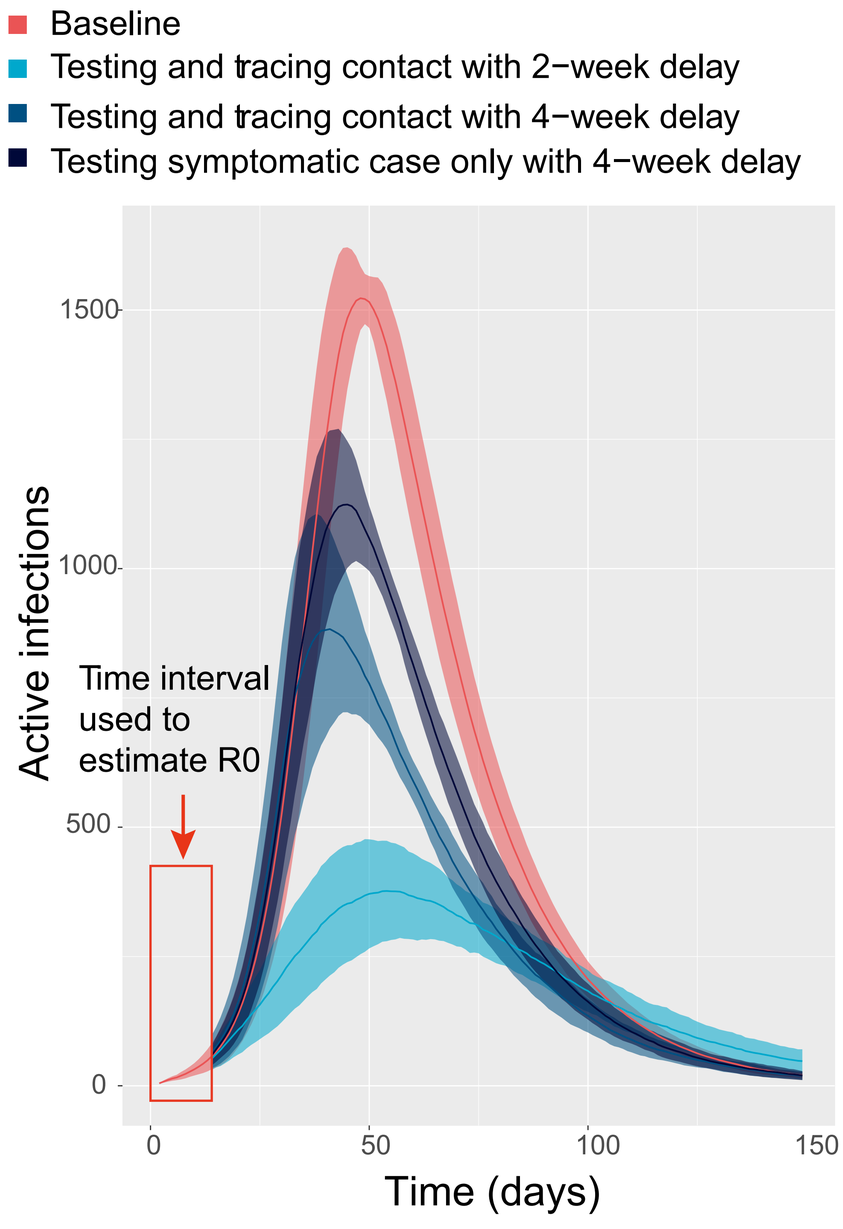


Figure 1. Introduction of the CoTECT model. (A) Structure of the network-based epidemiological model CoTECT. (B) Abbreviated version of the infection network progression. Snapshots shown are days 0, 10 and 20 after the first infected individual. Red and blue dots represent infected and susceptible individuals, respectively. Strings represent contact relationships.

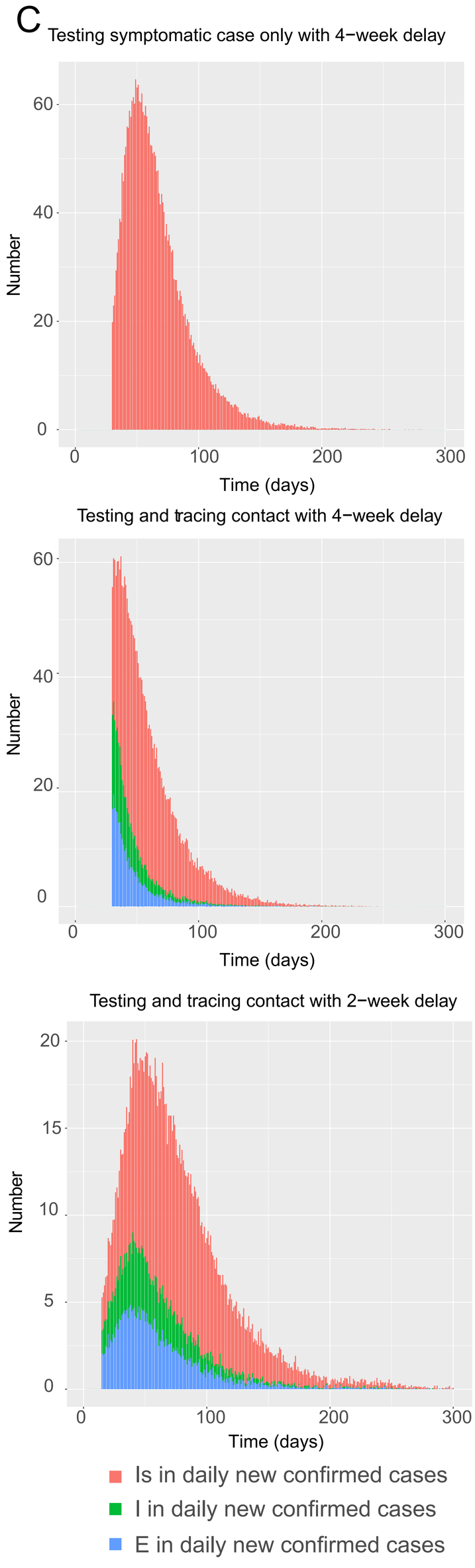
A


R0
4
3
2
Real-world data
Simulated baseline

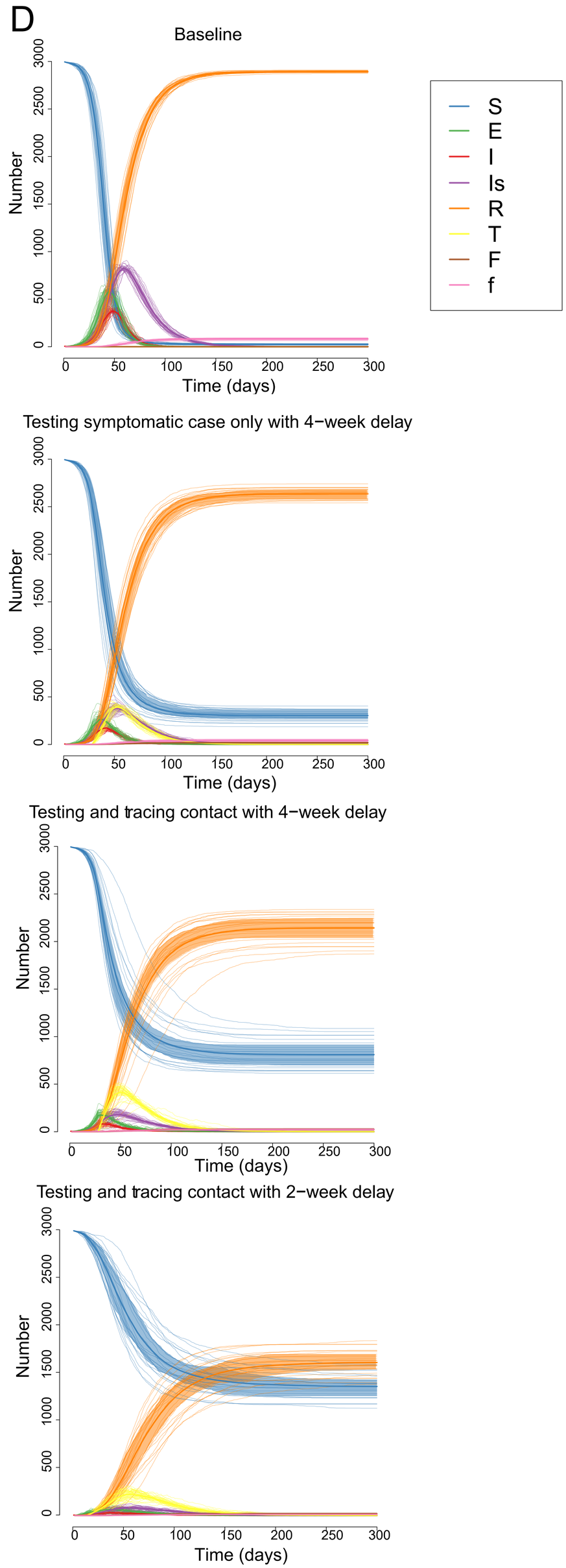
B

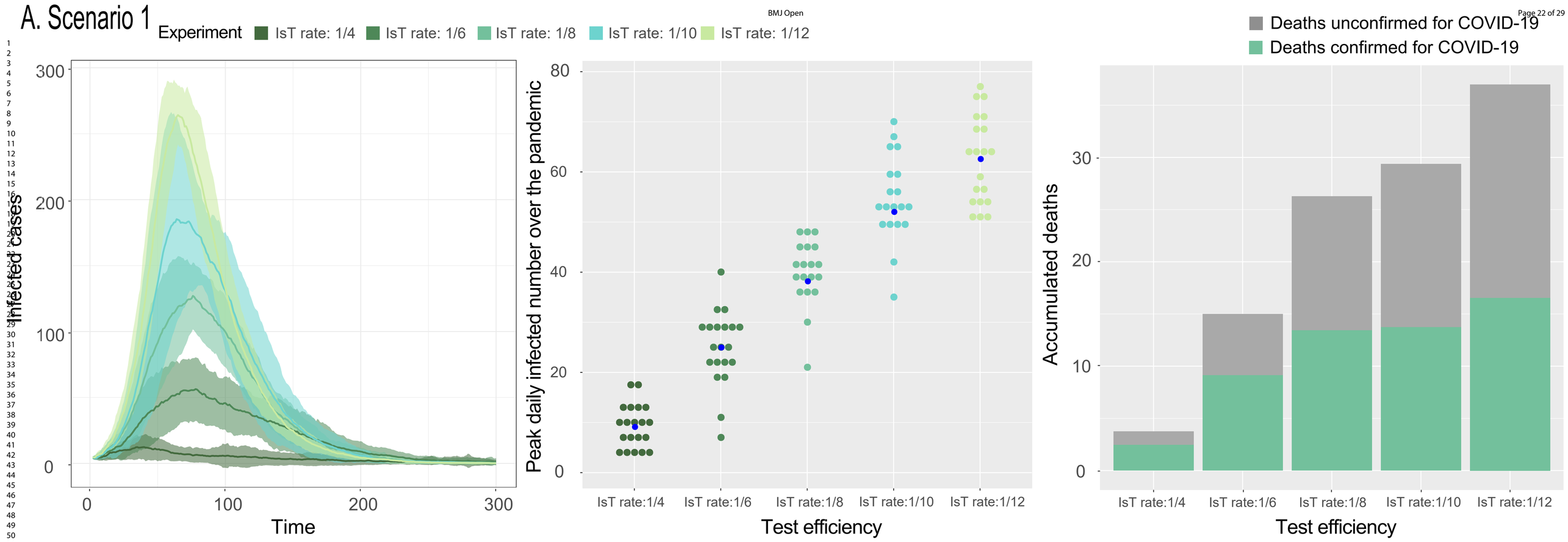

Baseline
Testing and tracing contact with 2−week delay
Testing and tracing contact with 4−week delay
Testing symptomatic case only with 4−week delay
Active infections
1500
1000
500
0
Time interval
used to
estimate R0
0
50
100
150
Time (days)

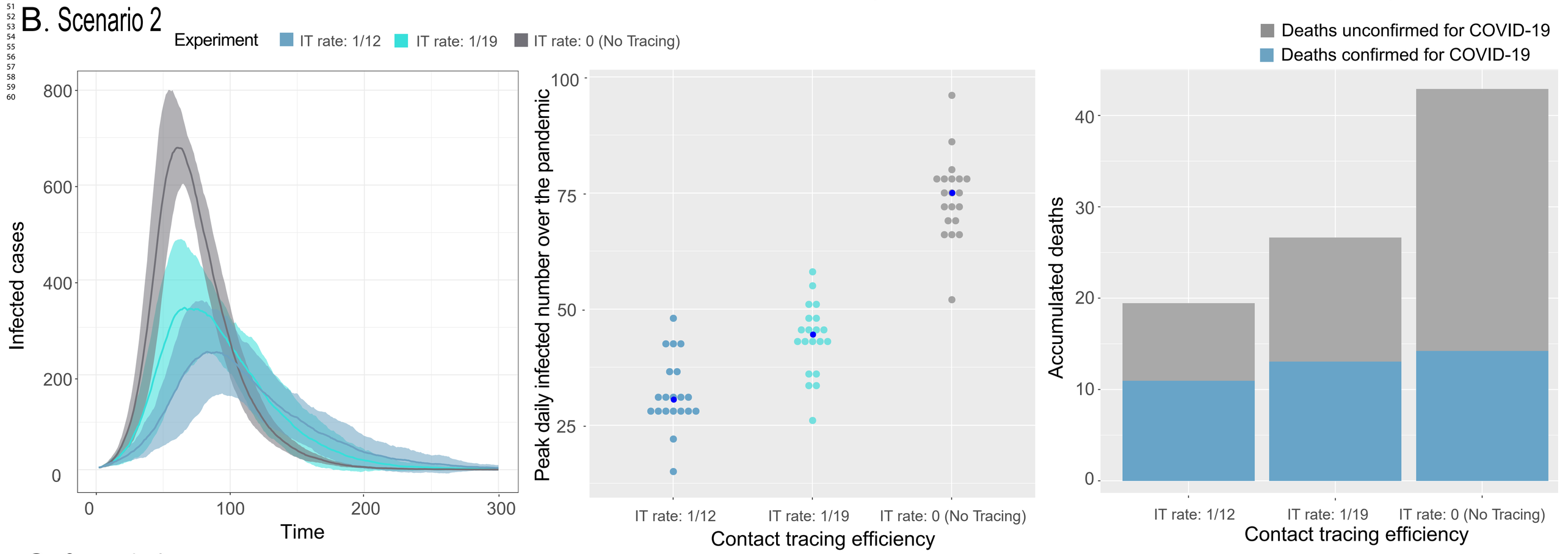
C

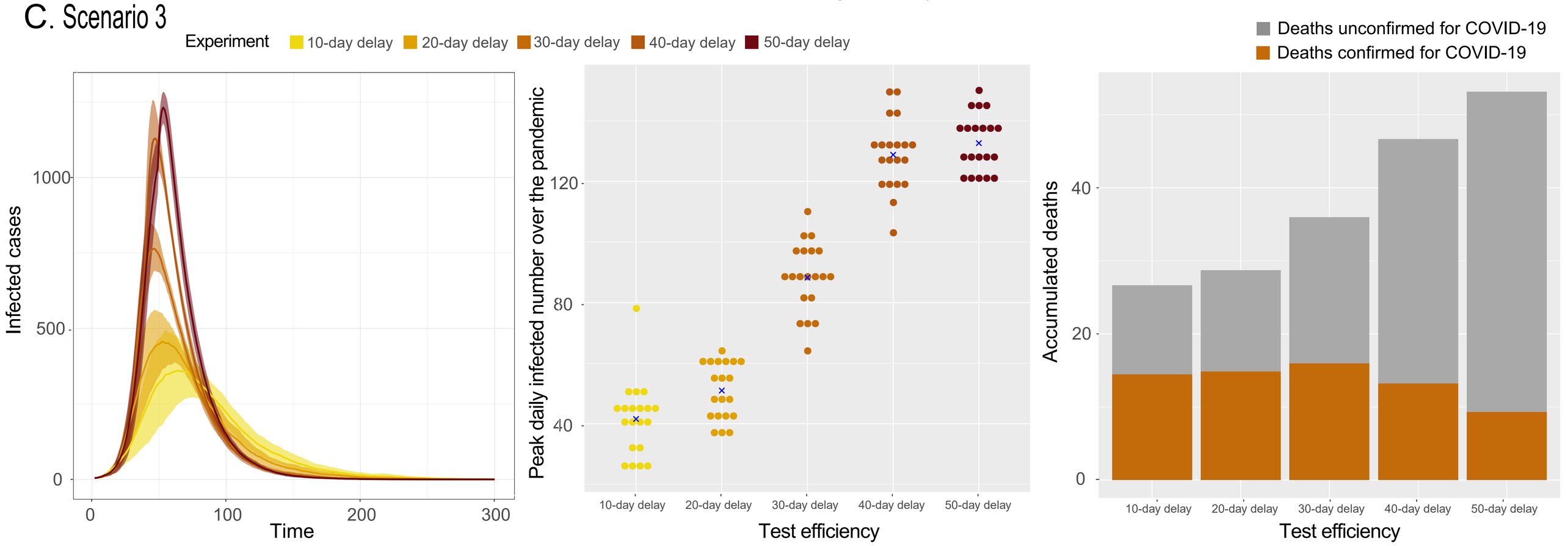

Testing symptomatic case only with 4−week delay
Number
60
40
20
0
0
100
200
300
Time (days)
Testing and tracing contact with 4−week delay
Number
60
40
20
0
0
100
200
300
Time (days)
Testing and tracing contact with 2−week delay
Number
20
15
10
5
0
0
100
200
300
Time (days)
Is in daily new confirmed cases
I in daily new confirmed cases
E in daily new confirmed cases

D

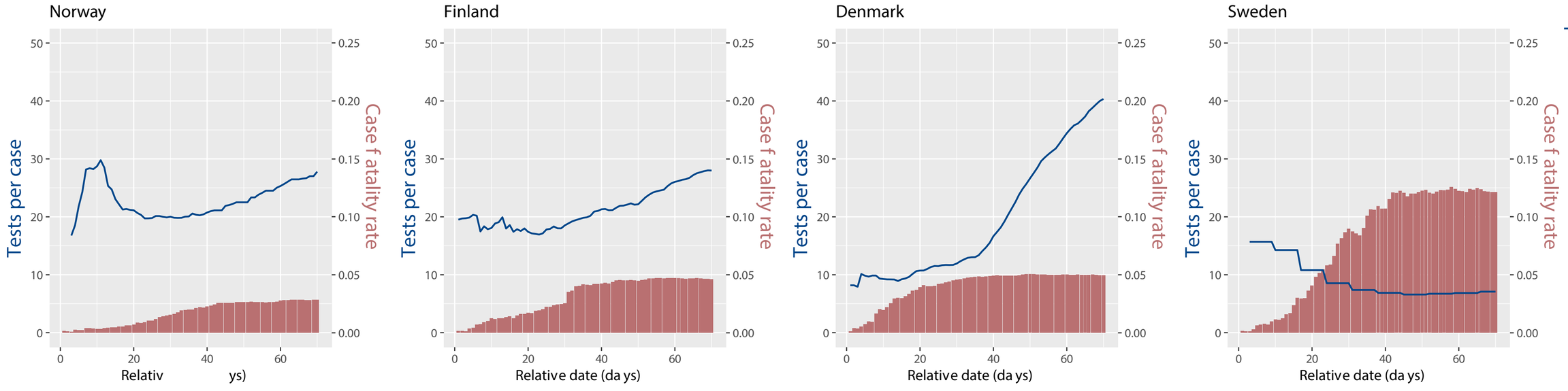

Baseline
Number
3000
2500
2000
1500
1000
500
0
0
50
100
150
200
250
300
Time (days)
S
E
I
Is
R
T
F
f
Testing symptomatic case only with 4−week delay
Number
Time (days)
Testing and tracing contact with 4−week delay
Number
Time (days)
Testing and tracing contact with 2−week delay
Number
Time (days)


A. Scenario 1
Experiment
IsT rate: 1/4
IsT rate: 1/6
IsT rate: 1/8
IsT rate: 1/10
IsT rate: 1/12
Infected cases
Time
Peak daily infected number over the pandemic
IsT rate:1/4
IsT rate:1/6
IsT rate:1/8
IsT rate:1/10
IsT rate:1/12
Test efficiency
Deaths unconfirmed for COVID-19
Deaths confirmed for COVID-19
Accumulated deaths
Test efficiency


B. Scenario 2
Experiment
IT rate: 1/12
IT rate: 1/19
IT rate: 0 (No Tracing)
Infected cases
Time
Peak daily infected number over the pandemic
IT rate: 1/12
IT rate: 1/19
IT rate: 0 (No Tracing)
Contact tracing efficiency
Deaths unconfirmed for COVID-19
Deaths confirmed for COVID-19
Accumulated deaths
Contact tracing efficiency


C. Scenario 3
Experiment
10-day delay
20-day delay
30-day delay
40-day delay
50-day delay
Infected cases
Time
Peak daily infected number over the pandemic
10-day delay
20-day delay
30-day delay
40-day delay
50-day delay
Test efficiency
Deaths unconfirmed for COVID-19
Deaths confirmed for COVID-19
Accumulated deaths
Test efficiency

A



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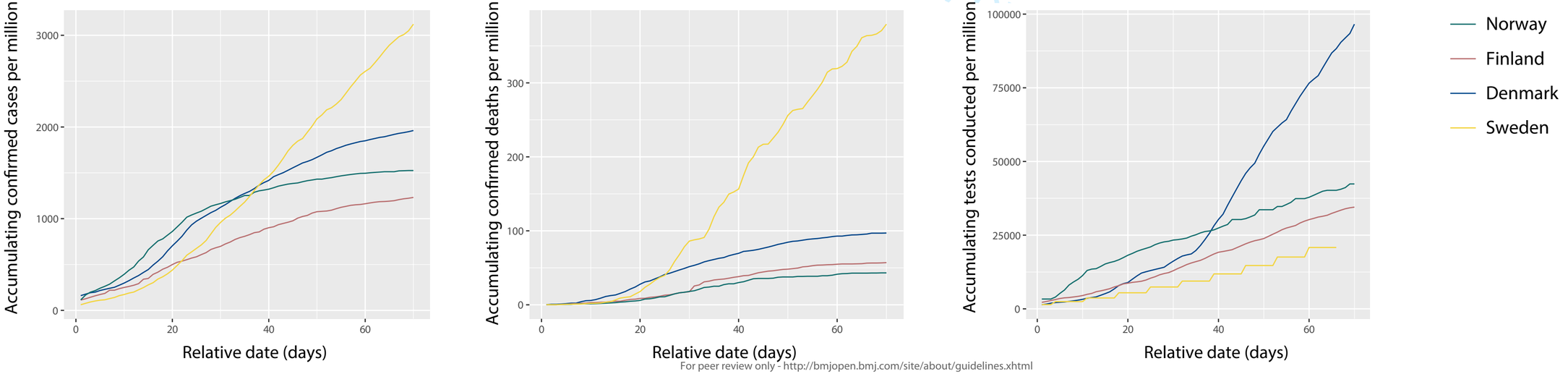
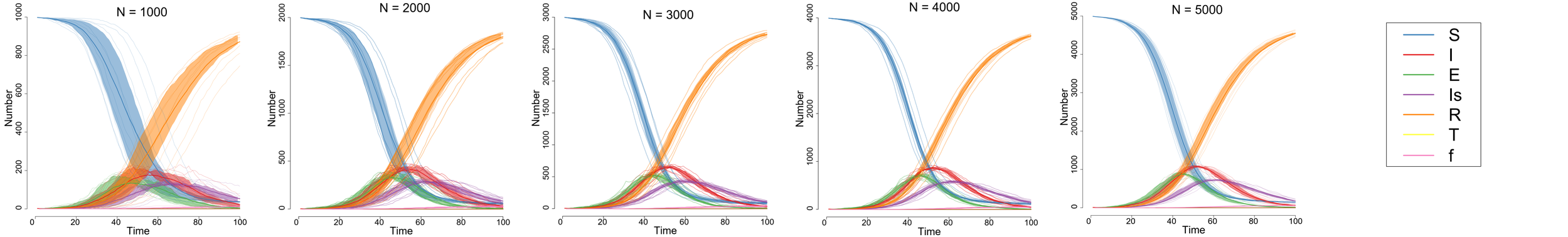


A



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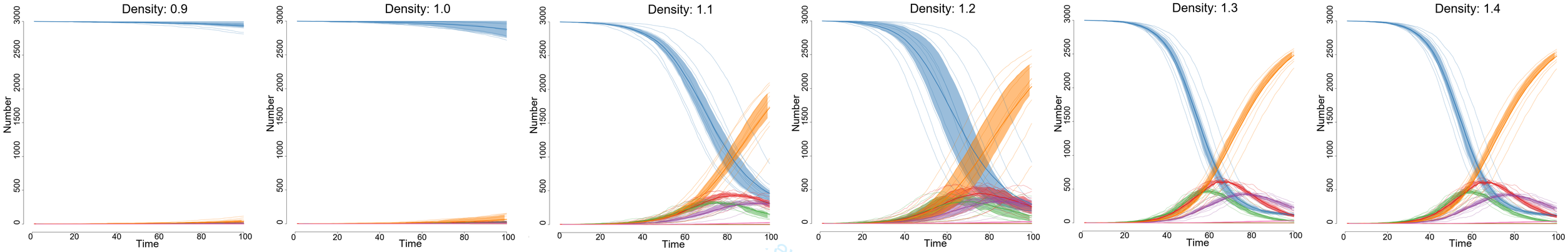

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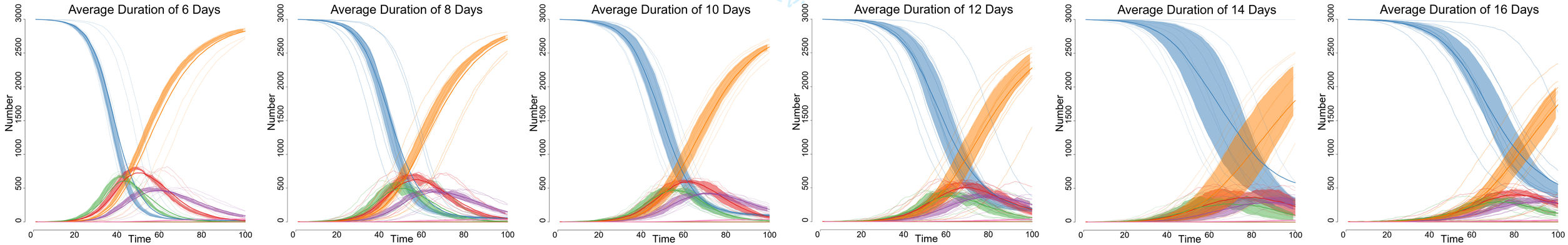

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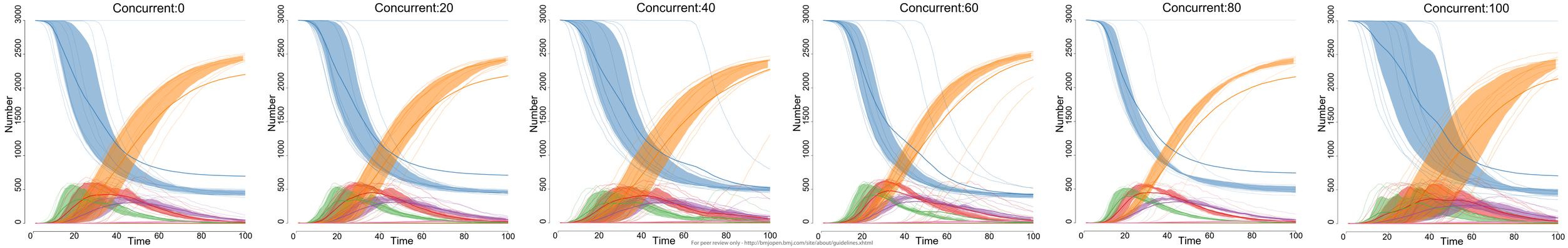

Supplemental materials

Model Assumptions

CoTECT assumes all tests hold the best sensitivity and specificity, which described false-positive and true-negative as a small probability event. When a small probability event happened, people exposed to the virus did not change to a tested and quarantined status in an expected period. Yet, this possibility is more than zero during the simulation. If the test sensitivity and specificity drop down, we can prolong the expected waiting time to test and self-quarantine in CoTECT. However, the test model(T) is a self-quarantine status that prevents 100% of infections from the confirmed cases, which is relied on a strong assumption. Furthermore, since the model was built based on a Bernoulli distribution, it is plausible that some infected people skipped from self-quarantine get self-recovery instead (Table S1, S2).

Table S1. Setting of transmission rates for CoTECT

	Transmission rate	Parameter definition	Assumed rate	References
Sampled	E-->T	Rate per day at which exposed (E) individuals test positive and enter quarantine status (T)	1/18 (1/15-1/23)	[1 2 3]
	I-->T	Rate per day at which infected (I) cases test positive and enter quarantine status (T)	1/12 (1/9-1/17)	[1 2 3]
	Is-->T	Rate per day at which symptomatic infected (Is) cases test positive and enter quarantine status (T)	1/7 (1/4,1/6,1/8,1/10,1/12)	[1]
Fixed	I-->Is	Rate per day at which infected (I) cases become symptomatic (Is) cases	1/5	[1]
Fixed	E-->I	Rate per day at which an exposed (E) individual become infected (I) cases	1/6.4	[4]
	I-->R	Rate per day at which infected cases with mild or no symptoms (I) recover and are immunized (R)	1/14	[1 2]

	Is-->R	Rate per day at which infected cases with severe symptoms (Is) recover and are immunized (R)	1/21	[1 5]
	T-->R	Rate per day at which quarantined, test-positive (T) cases recover and are immunized (R)	1/17	Assumed
	Is-->F	Death rate per day of infected cases with severe symptoms (Is)	0.002	[2]
	T-->F	Death rate per day of test-positive (T) cases	0.001	[2 3 6 7]

Table S2. Parameter setting for CoTECT network framework

Parameter	Definition	Value	Reference
Density	Density of whole social network.	1.3	Adjusted according to reported R0 (corresponding with infection probability and contact times)
Concurrent	Number of nodes (individuals) which contact many other nodes at a given day	0%-3%	Assumed
Isolation	Number of nodes (individuals) who does not make any contact with others at a given day	0%-3%	Assumed
Infection probability for symptomatic patient （I）	Probability of an infected individual passes the COVID-19 to another one based on an existed edge between them	30%	Adjusted according to reported R0
Infection probability for asymptomatic patient （E）	Probability of an exposed but asymptomatic individual passes the COVID-19 to another one based on a existed edge between them	20%	Adjusted according to reported R0
Contact times between I	Average contact times between two	3	Adjusted according to reported R0

	connected individuals (one is infected) in a given day		
Contact times between E	Average contact times between two connected individuals (one is exposed) in a given day	3	Adjusted according to reported R0

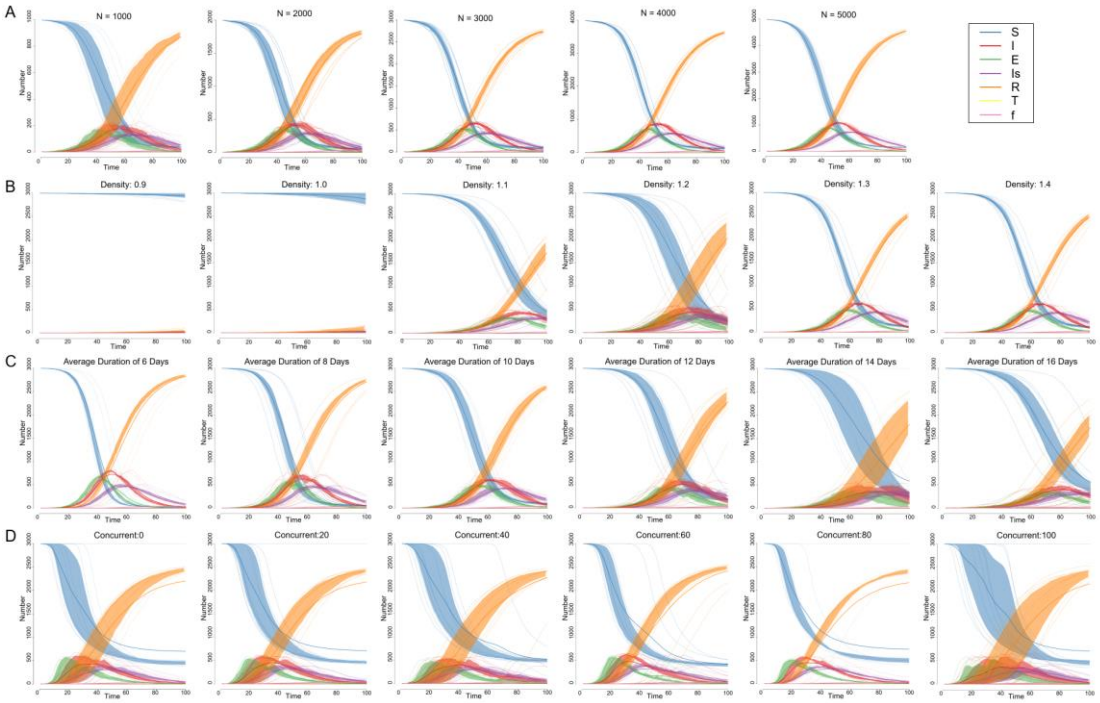

Figure S1: Sensitivity analyses for baseline models of different (A) population sizes (N=1000, 2000, 3000, 4000, and 5000), (B) densities (0.9, 1.0, … ,1.4), (C) average duration (6 days, 8 days, …, 16 days), and (D) concurrent nodes (0, 20, …, 100). Curves for each compartment in each model are shown in the graphs and demonstrate similar proportions of people in each compartment in the whole population for different population sizes.

Table S3: Sensitivity analyses for baseline models of different population sizes, densities, average duration, and concurrent nodes.

Parameters	Values	Total infections	Peak daily infections	Proportion of total infections in whole population	Cumulative deaths of unconfirmed cases
Population size	1000	883.2	290.9	88.3%	12.1
	2000	1826.2	668.5	91.3%	27.4
	3000	2769.8	1035	92.3%	39.3

	4000	3676	1378.4	91.9%	52.7
	5000	4606.9	1716.8	92.1%	60.8
Density	0.9	42.5	2.5	1.42%	0.2
	1.0	66.4	4.4	2.21%	0.8
	1.1	1754.6	61	58.49%	25
	1.2	2053.8	61.7	68.46%	26.1
	1.3	2510.2	99.9	83.67%	31.5
	1.4	2747.6	106.8	91.59%	37.5
Average duration (Days)	6	2864.4	130	95.48%	40.3
	8	2741.3	102.4	91.38%	38.3
	10	2627.7	93.4	87.59%	38.7
	12	2310.4	73.8	77.01%	32.8
	14	1823.8	52.2	60.79%	24.5
	16	1755.3	59.4	58.51%	22.1
Concurrent nodes	0	2229.3	77.1	74.31%	30.1
	20	2210.4	86.7	73.68%	33.8
	40	2302.2	67.7	76.74%	30.8
	60	2444.8	93.2	81.49%	31.6
	80	2189.8	92.9	72.99%	29.6
	100	2167.6	69.5	72.25%	27.5

Estimation of IsT rate based on real-world data

According to the public information about the epidemic investigation, we calculated the average time from onset to reporting of the first 23 symptomatic cases in the second-wave outbreak of Covid-19 to be 2.7 days (Table S4), with case data displayed in Table S5. 2.7 days is shorter than four days we set in scenario-1, therefore, it is realistic and feasible to set the window period of the best scenario as four days. According to another cohort study in Beijing [8], China, the median time interval from illness onset to laboratory confirmation is seven days (4.7–10.2), so a four day window period is rational (Table S4, S5).

Table S4. Testing efficiency for the second-wave outbreak in Beijing, China

Average time from onset to reporting (first 37 cases)	Percentage of cases confirmed by contact tracing (first 37 cases)	Tests for traced contacts (first ten days)	Daily testing capacity within one month	Test efficiency for cases with fever	Test efficiency for other patients	Test efficiency for other patients	Test efficiency for normal test application	Total confirmed cases	Percentage of cases confirmed by targeted screening tests
2.7 days	68%	2342 thousand	90 to100 thousand	6h	12h	6h	24h	335	52%

Table S5. Average time from onset to reporting, and means of reporting of first 37 cases for the second-wave outbreak in Beijing, China[8]

Number of cases	Symptom	Days from onset to reporting	Means of reporting
1	fever	0	initiative
2	fever	4	initiative
3	fever	5	initiative
4	fever	4	initiative
5	fever	1	initiative
6	fever	5	initiative
7	fever	2	initiative
8	no	NA	tracing
9	no	NA	tracing
10	muscle soreness	3	tracing
11	sore throat	2	tracing
12	fever	0	initiative
13	headache	8	tracing
14	no	NA	tracing
15	no	NA	tracing
16	sore throat	1	tracing
17	fever	4	tracing
18	fever	0	initiative
19	cough	1	tracing
20	sneeze	2	tracing
21	fever	2	tracing
22	sneeze	8	tracing
23	headache	1	tracing
24	no	NA	tracing
25	fever	1	initiative
26	fever	4	initiative
27	fever	2	tracing
28	no	NA	tracing

29	dry throat	2	tracing
30	no	NA	tracing
31	no	NA	tracing
32	no	NA	tracing
33	no	NA	tracing
34	no	NA	tracing
35	no	NA	tracing
36	no	NA	tracing
37	no	NA	initiative
Average		**2.7**	

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The role of efficient testing and contact tracing in mitigating the COVID-19 pandemic: A network modeling study

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Abstract

Objectives

This study quantified how the efficiency of testing and contact tracing impacts the spread of COVID-19. The average time interval between infection and quarantine, whether asymptomatic cases are tested, and initial delays to beginning a testing and tracing program were investigated.

Setting

We developed a novel individual-level network model, called CoTECT, using key parameters from recent studies to quantify the impacts of testing and tracing efficiency. The model distinguishes infection from confirmation by integrating a 'T' compartment, which represents infections confirmed by testing and quarantine. The compartments of presymptomatic (E), asymptomatic (I), symptomatic (Is), and death with (F) or without (f) test confirmation were also included in the model. Three scenarios were evaluated in a closed population of 3,000 individuals to mimic community-level dynamics. Real-world data from four Nordic countries were also analyzed.

Primary and secondary outcome measures

Simulation result: total/peak daily infections and confirmed cases; total deaths (confirmed/unconfirmed by testing), fatalities, and the case fatality rate. Real-world analysis: confirmed cases and deaths per million people.

Results

1) Shortening the duration between Is and T from 12 to 4 days reduces infections by 85.2% and deaths by 88.8%. 2) Testing and tracing regardless of symptoms reduces infections by 35.7% and deaths by 46.2% compared with testing only symptomatic cases. 3) Reducing the delay to implementing a testing and tracing program from 50 to 10 days reduces infections by 35.2% and deaths by 44.6%. These results were robust to sensitivity analysis. An analysis of real-world data showed that tests per case early in the pandemic is critical for reducing confirmed cases and the fatality rate.

Conclusions

Reducing testing delays will help to contain outbreaks. These results provide policymakers with quantitative evidence of efficiency as a critical value in developing testing and contact tracing strategies.

Strengths and limitations of this study

1. This work provides efficiency as a new perspective when evaluating the impact of testing and tracing from three aspects: 1) the average time interval between infection and test confirmation/quarantine; 2) whether contacts of both symptomatic and asymptomatic infectors undergo testing and contact tracing; and 3) the delay to initiating testing and contact tracing after the first infection early in the outbreak.

2. We quantified the effects of different testing and tracing efficiencies using a self-designed model with a novel structure, and verified their important role in the control of the COVID-19 pandemic.

3. This model is highly practicable, because the ideal average wait time between infection and quarantine can be simulated, and this value can be measured in practice for policymakers to assess whether their actions are efficient.

4. A limitation of this work is that all simulations were conducted in a closed population that did not account for inter-community social activity.

5. Impacts of differences in population age ranges, medical resources, and lockdown measures could be considered in this model in future work.

Introduction

Coronavirus disease 2019 (COVID-19) has posed severe challenges to the physical and mental health of people worldwide since its outbreak in December 2019[1]. New waves of cases in Asia, South America, and the European Union continue to occur in the first quarter of 2021. It takes long-time effort to achieve global herd immunity, especially when new strains predominate[2-4]. In this condition, testing cases and tracing and quarantining their contacts is still a key non-pharmaceutical intervention. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is more contagious and has a longer incubation time than SARS-CoV or MERS-CoV[5] and can be transmitted during the incubation period[6 7 8 9 10]. For example, approximately one-third of SARS-CoV-2 infectors in Spain were asymptomatic[11] and contagious. Transmission via latent, presymptomatic, and asymptomatic infected individuals may lead to more rapid spread. Due to the rapid spread of the epidemic and asymptomatic transmission, higher requirements are put forward for testing and tracing. Not only is a large number of tests necessary, but more importantly, efficiency of testing and tracing must be improved. Otherwise, it is difficult to avoid the epidemic rebound before herd immunity is achieved. Therefore, it is crucial to quantify the efficiency of the testing and contact tracing (i.e., the timeliness of testing and tracing). This efficiency is related to three aspects: 1) the average time interval from infection to test confirmation and quarantine; 2) whether symptomatic, asymptomatic, and

presymptomatic infectors are tested and traced; and 3) the delay to initiating testing and contact tracing after the first infection early in the outbreak.

The impact of testing and contact tracing (including quarantine) has been widely evaluated by various models. However, previous studies have focused on quantifying the volume of testing or the percentage of infections that should be traced, or they have highlighted a combination of other interventions[12 13,14 15,16,17-22]. Few studies have quantified how the efficiency of testing and contact tracing limits disease spread. Lopes-Júnior et al.[23] published a protocol to evaluate the influence of testing capacity for symptomatic individuals on the control of COVID-19. We referred to this protocol and searched PubMed and Google Scholar in our literature review for studies evaluating the effect of testing and contact tracing through March 2021. We identified 14 modeling studies were closely related to our work, but most of them did not investigate the effects on epidemic control of the time interval between infection and quarantine or delays to the implementation of testing and tracing procedures. Six of these 14 studies[12 13 24-26 27] only determined the percentage of infections or contacts that needed to be tested and traced to stop the pandemic, but their models were not designed to quantify the effect of testing and tracing delays. For example, Ferretti et al. [27] concluded the contact tracing work could be overwhelming based on the transmission speed and active social interaction. Therefore, they compromised to strategies which covering only part of the contacts, and the assumptions were fit only for the exponential phase of the pandemic. Keeling et al.[25] found that 71% of contacts needed to be traced to reduce the basic reproductive number (R0) below 1 or to relax social-distancing interventions, but these studies did not mention tracing efficiency (i.e., the time interval needed for tracing). Other four articles [12 13 24 26] also identified the proportion of contacts that should be traced. But because the number of infections is unknown in the real world, the usefulness for policymakers of these studies is limited. Five studies[28 29 30 31 32] were simulations of specific environments (a university campus, care homes, and Dane County in the United States, and the United States); thus, their generalizability of their findings is limited. Three studies[33 26 16]focused on policies of testing and tracing. For instance, McCombs et al.[33] compared different testing priority strategies (e.g., people with high-risk or low-risk are tested first, people with recent/early symptoms are tested first) under the condition that the maximum test volume per day is fixed. Kucharski et al.[26] simulated the effect on transmission reduction of randomly mass testing 5% of the population each week and compared it with the effects of isolation and tracing, but the authors did not analyze different testing scenarios. Bilinski et al.[16] explored whether testing that includes all identified contacts or only those with symptoms alters the effective reproductive number. However, these models do not quantify the impacts of testing and tracing efficiency, which is a vital factor independent of the total amount of testing and tracing.

To quantify the impacts of testing and tracing efficiency on COVID-19 containment and supplement the deficiencies of existing research, we developed a novel individual-level network model, called CoTECT (Testing Efficiency and Contact Tracing model for COVID-19). Traditional population-level models cannot evaluate the time interval between infection and quarantine for each individual, and they do not define the interaction mode between individuals. Although some individual-level models have been developed, they are not directly suitable for modeling testing efficiency in

COVID-19 transmission[34],because infectivity of SARS-Cov2 during incubation period was not considered, and confirmed cases were not distinguished from infections. CoTECT distinguishes between confirmed and unconfirmed infections by integrating a T compartment, which refers to those who are confirmed to be infected by testing and then quarantined. The model also incorporates the following compartments: presymptomatic (E), asymptomatic (I), symptomatic (Is), and death with (F) or without (f) test confirmation. Regarding three aspects of efficiency, we simulated three scenarios using controlled variables with the aim of eliminating confounding factors, and investigated the average time interval between infection and quarantine, whether asymptomatic cases are tested, and initial delays to beginning a testing and tracing program. Other key parameters used in our model were obtained from recent studies. Our model uses novel factors, strategies, and a unique model structure to evaluate how the efficiency of testing and contact tracing impacts the spread of COVID-19. An analysis of real-world data from four Nordic countries (with other similar confounders) revealed that delays in countermeasures adversely affect pandemic progression. Data from the second outbreak in Beijing were used to verify the importance of shorting the time interval between infection and quarantine. We provide a comprehensive and quantitative assessment of the critical factors related to testing and contact tracing that will help implement more effective measures to contain the pandemic.

Methods

CoTECT simulation model

CoTECT is a stochastic epidemiological network model that we developed specifically to evaluate how the efficiency of testing and contact tracing impacts the outcome of COVID-19 spread. The model was built with the R language and is based on EpiModel, a platform that can mathematically model infectious disease dynamics, allowing the user to construct a flexible network[35] with the desired likelihood of connections conditional on specific network properties[36 37]. The compartments and parameters were set in accordance with recent COVID-19 research. EpiModel supports stochastic network models developed with self-defined contact modes and interactions between different nodes (i.e., different individuals). This differs from the typical differential equation (compartmental) mode, which assumes that human social activity is based on a large, homogenous, well-mixed population. By contrast, every interaction is a stochastic process in CoTECT. The underlying network is an exponential-family random graph model (ERGM)[38], developed by Holland and Leinhardt.

Building on the traditional Susceptible-Exposed-Infectious-Recovered (SEIR) structure, we designed the CoTECT model with eight compartments (Figure 1):

1. Susceptible individuals (S)

2. Individuals exposed to the virus (E) (i.e., cases in the incubation period). E cases are considered to be infectious based on the biological characteristics of SARS-CoV-2.

3. Infected individuals who do not have observable symptoms (I). Some I cases become symptomatic and transfer to the Is compartment.

4. Infected symptomatic cases (Is) are more likely to appear in the T compartment than I or E cases, as symptomatic cases are easier to detect.

5. Test-positive cases who are quarantined (T). We assumed all cases confirmed by testing are immediately quarantined.

6. Test-positive fatalities (F)

7. Fatalities without a positive test confirmation (f)

8. Recovered cases (R)

A schematic of the model is provided in Figure 1. Arrows represent the transmission rate from one compartment to another, such as from Is to T, denoted as the IsT rate.

Infection occurs at the existing edge (real contact) between two nodes (people), with a given probability. In our model, the infection rate is determined by the SE rate and the times of contact between a susceptible person and an exposed person. SE rate related to the probability of a susceptible person become exposed (E) under the condition of existed connection with another infected nodes (E, I or Is). The exposed compartment represents the incubation period and contains individuals with a lower transmission ability than symptomatic, infected cases. This probability setting is based on the epidemiological characteristics of COVID-19. If the SE rate is p and the average times of contact is three, the infection probability between two connected nodes (people) is $1 - (1 - p)^3$. Meanwhile, the edge connecting two nodes is generated and dissolved by a stochastic process with particular conditions. The conditional probability of an edge forming and dissolving is based on a Bernoulli distribution of the module-specific parameter, and the resulting distribution is a binomial mixture[38]. After infection, the status transmission rate (the combined IsT, IT, and ET rate) is the reciprocal of the waiting interval). For example, an average 7 day waiting time from symptom onset to quarantine corresponds to a 1/7 transmission rate.

In addition to the infection process, the transmission rate from A to B implies a mean duration of remaining in the A status before changing to B status. For example, a 0.1 recovery rate (IR rate) indicates a 10 day recovery duration; thus, we defined the efficiency of testing and contact tracing as the time from E to T or from I to T, reflected as the ET rate and the IT rate, respectively. All transmission of status of each node form a Bernoulli distribution over time. The value of R0 is determined based on the simulated result of changing the number of total infections (E+I+Is+T). To approach the SARS-CoV-2 R0 value reported by the WHO, we

adjusted the network-related parameters in our baseline model, as shown in Figure 2A. Figure 1B displays the stochastic process of the edge generation and desolvation, representing the dynamic change of the social network. This dynamic change led to the abbreviated version of the contact network at various time steps.

Parameter settings

The parameters used in the model were taken from published values from multiple sources[39 40 41 42 43], most of which were case-level statistics[8 44 45 46]. The parameters are shown in Table S1 and include the incubation period[47 7], the average time from onset to a severe case[41], and the average recovery time[45] for mild and severe cases. The sampled parameters were set at different grades within the scenarios, while fixed parameters remained constant across all experiments. A hypothetical population of 3,000 people over 300 days was used. Our assumptions and network parameters are in line with ERGMs and are listed in Supplemental Table 2. The R0 of the baseline model was 2.2 and was obtained by adjusting the edge density, maximum number of connections, and probability of transmission between connected nodes (Table S2). Testing and tracing efficiencies were defined as an individual's average duration between exposure, infection, and symptom onset and test confirmation and quarantine. In CoTECT, the efficiency is translated as the transmission rate (the combined IsT, IT, and ET rate is the reciprocal of the waiting interval). For example, an average 7 day waiting time from symptom onset to quarantine corresponds to a 1/7 transmission rate.

The efficiency parameters (IsT rate, IT rate, and ET rate) were linked in all experiments setting according to Table 1. The average time interval from E to I was 6 days; this was based on an average of 6.4 days[7 10 40 43] from exposure to infection (i.e., the incubation period). Therefore, the denominator of the IT rate is typically 6 days greater than that of the ET rate. The same logic applies to the IsT rate. Nevertheless, efficient contact tracing will boost both the IT and ET rates. CoTECT assumes that all COVID-19 tests have optimal sensitivity and specificity; therefore, false positives are described as small probability events.

Experiment setting

Efficient testing and contact tracing is crucial and includes three aspects: 1) the average duration (in days) from exposure to self-quarantine for each individual during the pandemic; 2) whether symptomatic, asymptomatic, and presymptomatic infectors are tested and traced; and 3) the delay to initiating testing and contact tracing after the first infection early in the outbreak. To quantify the impacts of different efficiency of testing and tracing on transmission, CoTECT was used to simulate three different scenarios and one baseline scenario. The critical outcome indicators were cumulative infection (R+F+f), peak daily infections (E+I+Is), peak daily test-positive cases with quarantine (T), cumulative test-positive cases, total fatalities, and case fatality rate (CFR).

The baseline scenario is the worst-case condition in which no testing or contact tracing is conducted. Thus, no quarantine measurements were carried out in this model. When the R0 is

greater than 1, most of the population will eventually become infected. Using these assumptions, we also simulated different combinations of interventions as preliminary experiments to compare with the baseline scenario: 1) A 4 week delay in response (with no testing or contact tracing before the fourth week), and testing of symptomatic cases only; 2) A 4 week delay in response after which symptomatic, presymptomatic, and asymptomatic cases are tested; and 3) A 2 week delay in response after which symptomatic, presymptomatic, and asymptomatic cases are tested.

We designed the following three scenarios to investigate the importance of testing efficiency from three aspects. Only one condition was changed, with the other variables remaining consistent in each scenario. The average of 20 randomly-repeated experiments was taken as the final result.

1) Scenario 1 evaluated the impact of overall testing and contact tracing efficiency by simulating five different levels of test efficiency, represented by five scales of daily transmission rate or average IsT rate. The intervals from symptom onset to positive test with quarantine were 4, 6, 8, 10, and 12 days. The corresponding IsT rates were 1/4, 1/6, 1/8, 1/10, and 1/12, thus reflecting different testing efficiencies.

2) Scenario-2 evaluated the impact of tracing efficiency for pre-and asymptomatic cases by simulating different IT and ET rates with a fixed IsT rate. Contact tracing for Covid-19 is critical due to the transmissibility of pre-and asymptomatic infections. The IT and ET rates reflect contract tracing efficiency. In this scenario, the probability that latent and asymptomatic (or mild) cases would be tested and isolated (ET and IT rate) was adjusted by 0, 1/13, and 1/11. The fixed IsT rate was 1/7, which assumed seven days waiting for an interval from onset to quarantine.

3) Scenario-3 evaluated the impact of delayed implementation of efficient testing and contact tracing. The response times have varied significantly worldwide. Many countries were not well prepared for the pandemic, and targeted testing and contact tracing measures were often not implemented until after many confirmed case fatalities. Therefore, we simulated different public health response delays in CoTECT. Five experiments were conducted with fixed IsT, IT, and ET rates. The delay intervals between the first infection and implementation of targeted testing were set as 10, 20, 30, 40, and 50 days. The transmission rates from the E, I, and Is compartments to T were set as 0 prior to the response.

Sensitivity analysis

We conducted the sensitivity analysis to elaborate how other factors (network parameters) would impact the transmission process. Firstly, we evaluated transmission progression when no testing or contact tracing was in place for varying population sizes. For the three scenarios, the mean R0 was set as 2.2. The network density and contact duration between nodes were consistent across the main experiments.

Secondly, the sensitivity analysis also included tests of network-related parameters, which describe the disease transmission model's underlying social activity patterns. In our study, the simulation model built upon a graph model consisted of edges and nodes. The edge between two nodes reflects a relatively close contact that could result in disease transmission with a certain probability. In CoTECT, the edges can be interpreted, for example, as face-to-face conversations or sharing a car ride. Unlike the sensitivity analysis of the population size, which uses a constant infection ratio and transmission rate but applies different network sizes, the network-related parameter test demonstrates how these parameters impact disease transmission.

We tested each edge's mean duration (contact), concurrent edges (how many simultaneous contacts happened per day), and the density of the entire network. The results are presented in the supplemental materials (Figure S1, Table S3). As previously mentioned, the final set of these parameters was tuned based on the R0 of the simulated baseline.

Patient and public involvement

No patients or other members of the public were involved in this study.

Results

We carried out preliminary experiments to show how the CoTECT model simulates transmission under different conditions of testing and contact tracing. We then demonstrated how disease transmission is impacted by 1) the efficiency of comprehensive testing and contact tracing, 2) the efficiency of contact tracing for presymptomatic and asymptomatic cases, and 3) delaying the implementation of efficient testing and contact tracing.

Preliminary results of CoTECT simulation

We first defined the baseline model as the worst-case scenario with no epidemiological interventions conducted in a closed population. The baseline R0 was 2.2, according to the average R0 estimated[48] from 177 countries and territories[49]. (Figure 2A), aligned with previously published studies[41]. Then we compared the baseline model with different combinations of testing and contact tracing interventions to evaluate their respective impact on disease transmission. The infection curve is shown in Figure 2B. We assumed each community responded a minimum of several weeks after the first infection. The dark blue line indicates the outcome for a delay of four weeks and testing only symptomatic cases. Total infections, peak daily infections, and total deaths were reduced by 13.2%, 43.7%, and 27.3%, respectively, compared to baseline. The navy line shows the outcome of an open test policy (not only symptomatic cases) with a four-week delay. Total infections, peak daily infections, and total deaths decreased by 23.4%, 43.1% and 41.3%, respectively, compared to baseline. The light blue line shows the outcome for a delay of two weeks after the first infection. Total infections, peak daily infections, and total deaths decreased by 44.1%, 75.8% and 61.0%, respectively, compared to baseline.

Daily new symptomatic, pre-and asymptomatic cases confirmed by testing in three conditions are shown in Figure 2C. Compared with condition-1 (only testing symptomatic cases with 4-week delay), condition-2 (testing and tracing pre- and asymptomatic contacts with 4-week delay) could reduce 24.8% of total confirmed cases (from 125 to 94), and 26.5% of 94 confirmed cases were diagnosed before symptom onset (E+I). Condition-3 (tracing contacts and testing with a 2-week delay) could reduce 51.2% of total confirmed cases (from 125 to 61), 33.6% of 61 confirmed cases were diagnosed before symptom onset (E+I). Moreover, compared to condition-2, Condition-3 also reduced daily peak confirmed Is, I, and E cases by 65.8% (from 38 to 13), 75.0% (from 16 to 4), and 75.0% (from 20 to 5), respectively. We further demonstrated trends of all compartments in baseline and different conditions (Figure 2D). Compared to baseline, as infections decreased in 3 conditions, the S individuals (those who remain uninfected) of condition-1, -2, -3 were 6.6, 11.6, and 20.7 times of S individuals of baseline model after 300 days of the epidemic, respectively. Meanwhile, 27.7%, 41.5%, and 61.2 % of deaths (confirmed and unconfirmed by testing) of the baseline model were saved in condition-1, -2, -3, respectively. These results indicate that reduced time to action and better identification of pre-and asymptomatic cases are critical factors in flattening the infection curve and decreasing the deaths.

Impacts of overall testing and contact tracing efficiency to all infectors

Scenario-1 simulated five different test efficiency levels represented by five different daily transmission rates from Is to T (IsT rate): 1/4, 1/6, 1/8, 1/10, and 1/12. The daily transmission rate from I to T (IT rate) and from E to T (ET rate) changed in accordance with the IsT rate. This scenario assumes that contact tracing efficiency changed with the IsT rate, and therefore latent, asymptomatic cases could also be tested. We found that longer public health response delays (i.e., lower IsT rates) resulted in higher peak daily new transmitters, peak daily new diagnoses, and overall cumulative infections. Besides, the number of diagnosed and undiagnosed fatalities and the proportion of undiagnosed fatalities increased as IsT rates declined, indicating that fewer tests and slower response times resulted in worse epidemic outcomes. We decreased the IsT delay from 12 to 4 days in two days intervals and found that, compared to baseline, total infections decreased by 20.5%, 29.2%, 39.0%, 57.0% and 88.3%, respectively, and total deaths decreased by 36.0%, 46.7%, 52.2%, 70.6% and 92.8%, respectively. Peak daily infections across the five experiments increased linearly as IsT rates decreased (Table 1, Figure 3A).

Impacts of contact tracing efficiency for pre-and asymptomatic cases

Scenario-2 quantified the importance of efficient contact tracing. Owing to asymptomatic transmissibility, contact tracing is critical for effective containment. The tracing efficiency is represented by either the IT or ET rate. Therefore, we designed simulations with a fixed IsT rate (1/7) and varied the IT (1/12, 1/19, 0) and ET rates (1/17, 1/24, 0).The results showed that larger ET and IT rates resulted in fewer overall infections, confirmed cases, and confirmed and unconfirmed fatalities. More efficient contact tracing (12-day delay from infected to testing for I cases) would prevent 36% of cumulative infections, 64% of peak daily infections, 46% of

peak daily confirmed cases, and 46% of total deaths compared to no contact tracing. Less efficient contact tracing (as a 19-day delay from infected to testing for I patients) prevented 23% of cumulative infections, 50% of peak daily infections, 32% of peak daily confirmed cases, and 33% of total fatalities compared to no contact tracing. Thus, more efficient contact tracing resulted in fewer infections (Table 1, Figure 3B).

Impacts of delayed implementation of efficient testing and contact tracing

Scenario-3 evaluated the impact of delayed implementation of efficient testing and contact tracing. We found that cumulative infections and fatalities increased with increasing delay intervals. Compared to 50-day delay, delays of 10, 20, 30 and 40 days reduced total infections by 35.2%, 32.9%, 20.7% and 7.6%, respectively, and total deaths by 44.6%, 43.7%, 32.6% and 12.7%, respectively. The increase in peak daily transmitters as delay interval increased followed a sigmoid-shape curve (Table 1, Figure 3C). Clearly, implementing a prompt testing response within 20 days of the first infection had much more impact than response 20 days later.

The critical impact of the prompt initiation of a testing program is demonstrated in our simulation and is observed in real-world data. Measures of testing sufficiency are the number of tests conducted per confirmed case (TPC) and the number of tests per million people (TPM). Here, efficiency is measured as the average time interval between infection and a positive COVID-19 test. A sufficient testing capacity, estimated by TPC and TPM, is a prerequisite for efficient testing. Decreasing TPC trends indicate that disease transmission is outpacing testing and that efficiency is decreasing. The three indicators of epidemic control are CFR, confirmed cases per million people (CPM), and deaths per million people (DPM).

For comparison, we selected four Nordic countries that have similar medical resources, population age ranges, geography, and climate (Figure 4). Day 0 was defined as the day on which the daily DPM reached 0.1. Norway, Finland, and Denmark experienced a similar lockdown duration in the first 70 days, and the TPC over the first 70 days increased in all countries. From Day 0 to 14, TPC was highest in Norway, followed by Finland and Denmark. Between Day 15 and 70, although the TPCs in Norway and Finland were similar, the CFR in Norway (2.8%) was lower than in Finland (4.6%). This implies that the early outbreak TPC values were a more significant factor than later TPC values in controlling the pandemic. Denmark had the lowest early outbreak TPC of these three countries. Even though its TPC later grew dramatically and far exceeded those of Norway and Finland, its CFR (4.9%) was higher than those of Norway and Finland. We also observed that the overall TPM in Denmark from Day 0 to 70 was 2.7 times those of Norway and Finland. This implies that the early stage TPC may have a more significant influence on the overall CFR than the late-stage TPC, consistent with our hypothesis that early testing plays a critical role, without which testing efforts must be heavily increased as transmission rates worsen. In Sweden, the TPC gradually decreased. Sweden's CFR (12%) was the highest of all four countries. This indicates that insufficient testing in the early stage might not be remedied by subsequently increasing the testing volume.

Sensitivity analysis

To validate the rationality of our model's network settings, we conducted sensitivity analyses using various population sizes and different settings of the parameters related to R0.

We first compared baseline models with population sizes of 1,000, 2,000, 3,000, 4,000, and 5,000. The proportion of cumulative infections, peak daily infections, and cumulative deaths were similar in all five models. However, there was considerably more variation between the 1,000 and 2,000 population models than between the models with population sizes of 3,000 or more. These findings underpinned our rationale for using a representative population of 3,000 (Figure S1, Table S3).

Second, a sensitivity analysis of R0-related parameters emphasized how the structure of a social network impacts disease transmission. In addition to the intrinsic properties of SARS-CoV-2, the value of R0 is determined by three parameters that we studied in the sensitivity analysis: the social network density, concurrent contacts (the number of people a person has contact with), and the average duration of contact between two people. The network density will directly impact the rate of disease spread (Figure S1, Table S3). An extremely low density is difficult to maintain in most areas. However, we can expect that a low density would occur in a town under lockdown for a short period of time. Decreasing the number of concurrent nodes with a fixed density will skew the infection number curve. This also affects the variance, because concurrent nodes become critical nodes that can spread the disease to many other nodes. The duration of an edge indicates the stability of the relationship between two nodes. The results revealed that increased stability would flatten the infection curve. It is clear that if we were to only contact the same group of people repeatedly, the possibility of infection would decrease. The value of R0 changed when the settings of these three parameters were altered. To improve the universality of our model, we selected suitable ranges for these parameters to achieve the average R0 reported in other studies (Figure 2A). The R0 distribution in our baseline simulation corresponded to the average R0 estimated from 177 countries and territories [ref38]. The sensitivity analysis showed the validity of how we regulated parameters that are related to transmission dynamics. For all experiments, the mean R0 was set as 2.2. The network density, concurrent contacts, and the relationship duration between nodes were consistent across all experiments.

Discussion

Principal findings

This work quantified how testing and contact tracing efficiency, investigated as the average duration between infection and quarantine and the delay in testing and tracing close contacts after the first identified infection, can influence COVID-19 transmission. 1) Scenario 1 demonstrates that shortening the average time interval between symptom onset and quarantine from 12 days to 4 days results in an 85.2% reduction in infections and an 88.8% decrease in

deaths. 2) Scenario 2 indicates testing and tracing regardless of symptoms (a 7 day interval for Is to T, with the E/I to T intervals changing accordingly) reduces infections by 35.7% and deaths by 46.2% compared with testing symptomatic cases (Is) alone. 3) Reducing the delay in implementing an efficient testing and tracing program from 50 days to 10 days reduces infections and deaths by 35.2% and 44.6%, respectively. Scenario 3 implies that the delayed implementation of testing and contact tracing will lead to a massive demand in testing capacity, which is also supported by the analysis of data from the four Nordic countries. Thus, efficient testing and contact tracing can reduce disease transmission and the overall number of fatalities.

Strengths and weaknesses of the study

Strengths of this work include: 1) It provides a new perspective on evaluating the effect of testing and tracing in addition to the test volume at the individual level. This new perspective focuses on the efficiency of testing and tracing. Our work indicates that controlling the COVID-19 pandemic requires a rapid response to testing and tracing rather than solely relying on a massive testing capacity. 2) We quantified the effects of different testing and tracing efficiencies using a self-developed model, called CoTECT, as well as real-world data to verify their important role in controlling the COVID-19 pandemic. The model quantified the additional percentage of infections and deaths that would occur when the implementation of these efficient measures is delayed. 3) This model is highly practicable. The ideal average wait time between infection and quarantine was simulated, and this time interval can be measured in practice for policymakers to determine whether their actions are efficient. Our main conclusions can be generalized to different circumstances, from megacities to small villages.

Weaknesses of this study include: 1) All simulations were conducted in a closed population; the model did not account for inter-community social activity. 2) We assumed that nearly 100% of the tests were accurate because false-positive tests result in an unnecessary self-quarantine. We also assumed that no infections would occur after self-quarantine.

Strengths and weaknesses in relation to other studies

While previous studies[12 13 16 24-26 27] have typically emphasized the amount or percentage of infections or contacts that need to be tested and traced, our model simulates the ideal average wait time between infection and quarantine, which is a more practical criterion that is easily measured in real-world epidemiological investigations. In contrast, the percentage or number of infections that need to be tested and traced proposed by other modeling studies are less useful; this is because the true number of infections is difficult to estimate in the real world.

In addition, we did not limit our analysis to estimating a fixed, total amount of testing required, because the capacity of testing changes over time. Instead, we focused on the duration between an exposure event and when an exposed person receives their test result (i.e., the efficiency of testing and contact tracing). We found that more efficient testing can reduce the number of infections and deaths and decrease the fatality rate, and demand in testing capacity will increase as implementation of testing and contact tracing delayed. The testing and contact tracing

capacity should be considered along with the demand for testing, which is related to the total number of infections.

In contrast to models that are suitable only for specific regions and conditions[28 29 30 31 32], our tool has potential to be used for various population sizes and is generalizable to different types of communities. The novelty of this method is reflected in the model's structure and scenario design. Using the timeliness of individual testing, CoTECT can predict macro perspective outcomes.

The weakness of our work in relation to other studies is that age ranges of the population, the medical resources, and lockdown measures were not explicitly adjusted in this model (regarded as controlled variables). Impacts of these variables have been considered in other existed studies[27 15 18 33].

Meaning of the study

Our results provide professionals and policymakers with quantitative evidence showing that efficiency is a critical value in the development of testing and contact tracing strategies. Our model is particularly useful for nations facing a potential second or third wave of COVID-19 or the spread of mutated virus strains or other emerging infectious diseases. We provide a novel tool, CoTECT, that policymakers can use to simulate the effects of delays to implementing testing and tracing systems, which could help them balance the costs with the risks. The model highlights that it is critical to consider the transmission rates from presymptomatic and asymptomatic cases, as well as the time delay between testing and quarantine.

Meaning of our conclusions drew from 3 scenarios is: 1) according to Scenario 1, an extra 4 days of waiting will lead to a considerable difference in total infections and deaths. At one point, the mean wait time between taking a COVID-19 test and receiving the result was 4.1 days in the United States, which is disadvantageous for controlling disease spread[50]. So, our study indicates the government and testers of some countries should improve the efficiency of testing; 2) an example of the value of efficient testing is the successful containment of the second COVID-19 outbreak in Beijing, China. Highly efficient testing (open to all regardless of symptoms) and contact tracing began immediately after the first case was identified[51 52,53 54] and average time from onset to reporting of first 37 cases was 2.7 days (Tables S4 and S5). This is in marked contrast to the first outbreak in Wuhan when testing was less efficient and containment was slower, which verified our scenario 1 and 2. 3) In Scenario 3 we focused on the delay between the first infection and implementation of contact tracing and testing. In the real world, the longer the delay, the higher the initial positive rate would be (the lower TPC), which was analyzed in Nordic countries. We recommend government to increase TPC as soon as possible in the early stage of a pandemic, which is critical in reducing the number of confirmed cases and the fatality rate.

Unanswered questions and future research

Some unanswered questions are: 1) How does inter-community social activity affect our model? 2) How does variables such as population age ranges, medical resources, and lockdown measures lead to different results? 3) Whether the socioeconomic resources required for efficient testing could be estimated? To solve these issues, we will introduce more variables and improve our model to study the impact of testing and contact tracing efficiency under different circumstances of constraints and countermeasures.

Contribution statement

Y. Hu designed and directed the project; Y. Hu and J. Guo wrote the article; X. Li, G. Li, X. Lu, Y. Zhang, L. Cong, Y. Kang, and X. Jia aided in data analysis or writing framework. X. Li, X. Shi, and G. Xie were supervising the study, L. Zhang was guiding and supervising the study. All authors meet the ICMJE criteria for authorship.

Declaration of interests

We declare no competing interests.

Data sharing

Data are available in a public, open access repository. Data are available upon reasonable request. Data are available by emailing moehu@foxmail.com.

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Table 1: Baseline and Scenario-1, -2, and -3 model outcomes

	Delay (days) to targeted testing and contact tracing (T delay)	Average waiting interval (days) from Is to T (1/IsT rate)	Average waiting interval (days) to from I to T (1/IT rate)	Total infections	Peak daily infections	Peak daily test confirmation	Total deaths	The proportion of unconfirmed deaths in total deaths
Baseline	No testing	No IsT transformation	No IT transformation	2933.6	1553.2	0	78.1	100%
Scenario -1	0	4	Yes	344.3	48.7	38.1	5.6	36%
		6		1261.4	181.8	128.3	23	39%
		8		1789	328.5	208.9	37.3	49%
		10		2077.3	425	251.8	41.6	54%
		12		2330.8	581	318.3	50	56%
Scenario -2	0	7	No IT transformation	2510.9	800.4	315	57.2	67%
			13	1941.2	396.6	213	38.1	51%
			11	1614.6	285.5	168.9	30.8	45%
Scenario -3	10	7	Yes	1857.6	360.1	233.4	37.2	46%
	20			1922.6	456.2	294.4	37.8	49%
	30			2272.3	764.1	455.5	45.2	55%
	40			2649.8	1129.5	543	58.6	71%
	50			2866.7	1231.6	400.5	67.1	82%

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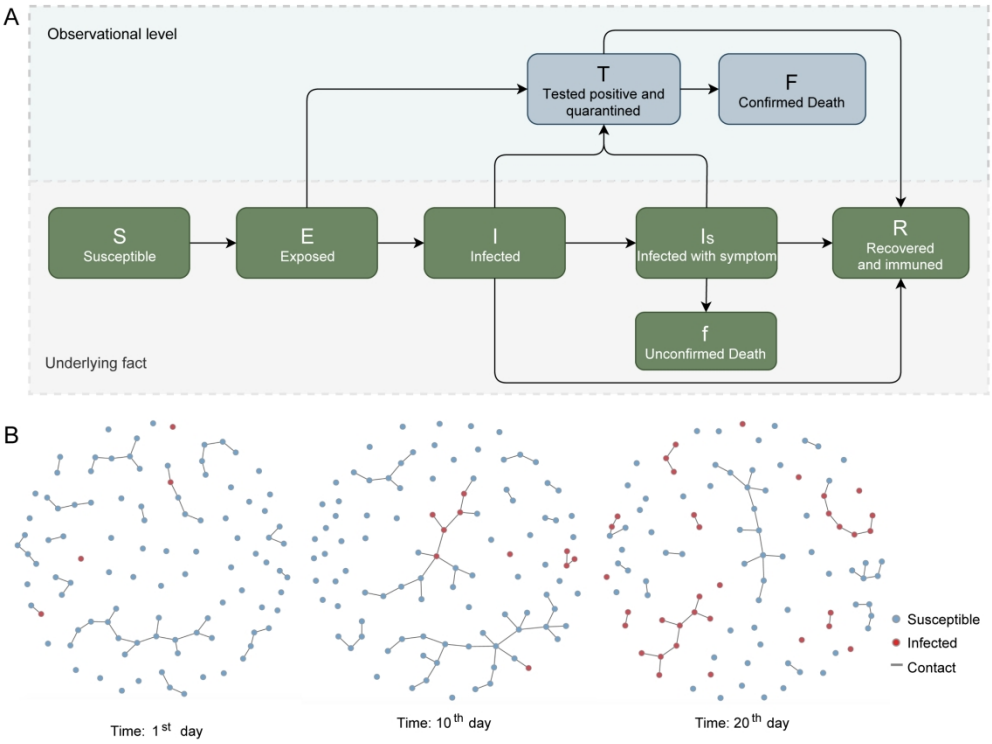
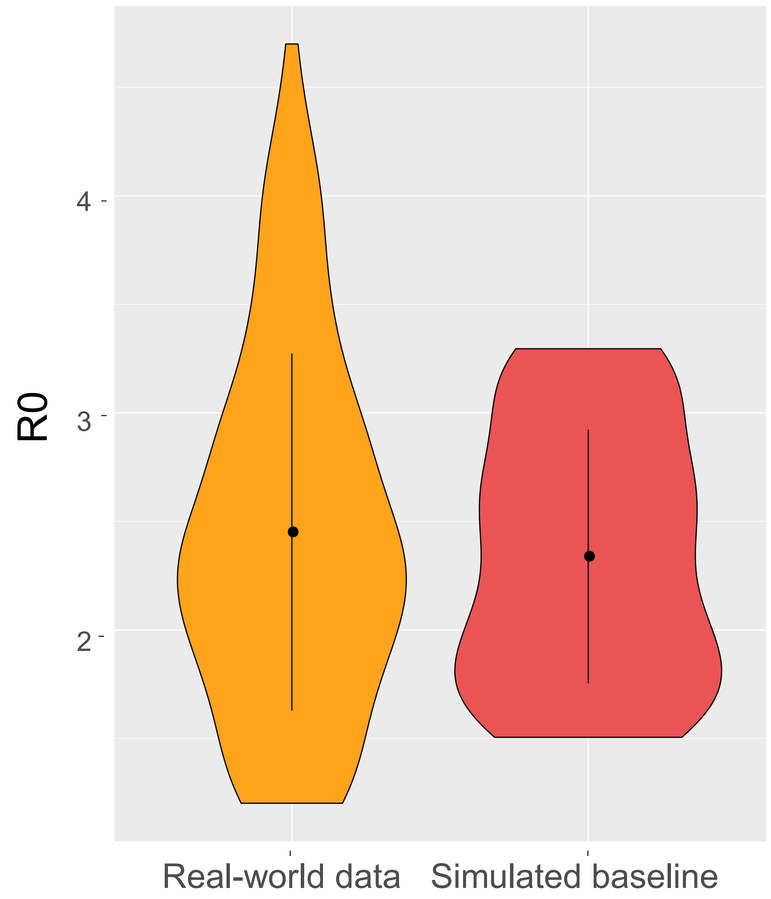
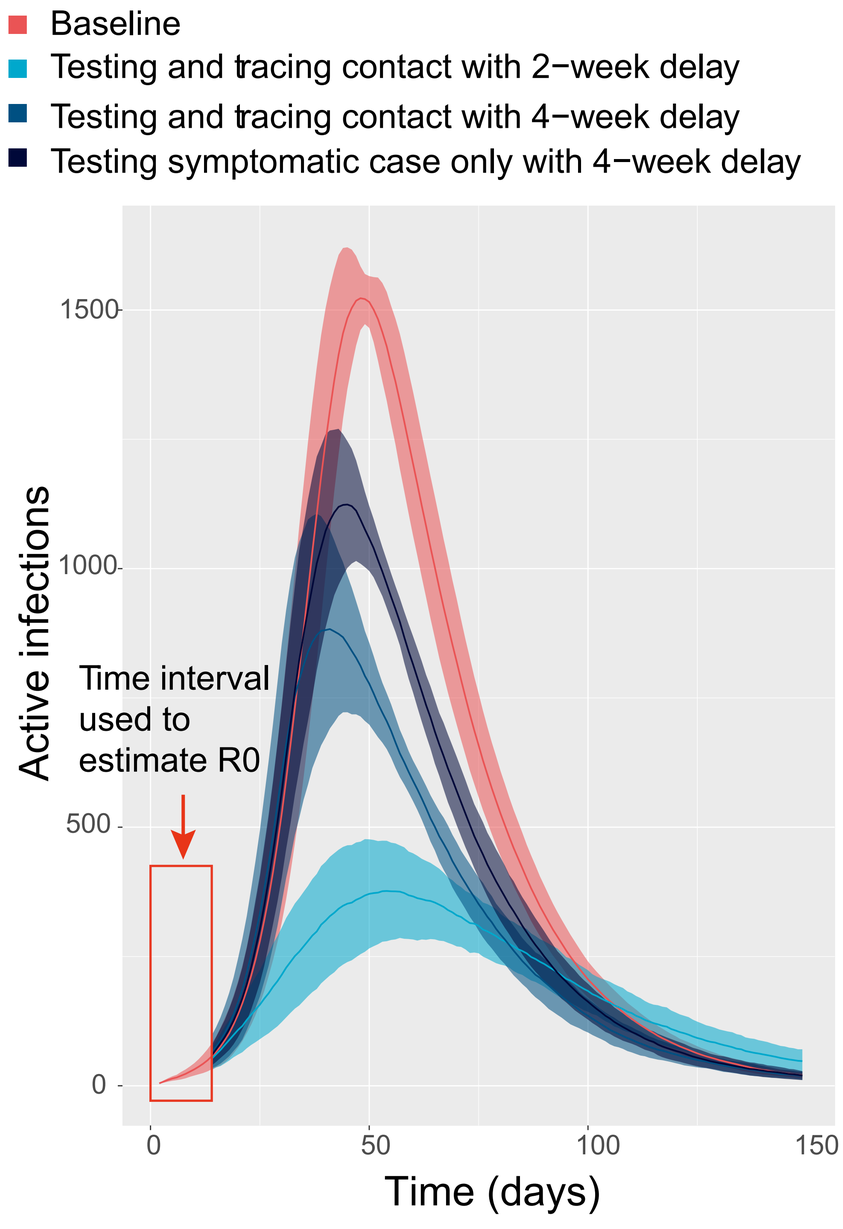


Figure 1. Introduction of the CoTECT model. (A) Structure of the network-based epidemiological model CoTECT. (B) Abbreviated version of the infection network progression. Snapshots shown are days 0, 10 and 20 after the first infected individual. Red and blue dots represent infected and susceptible individuals, respectively. Strings represent contact relationships.

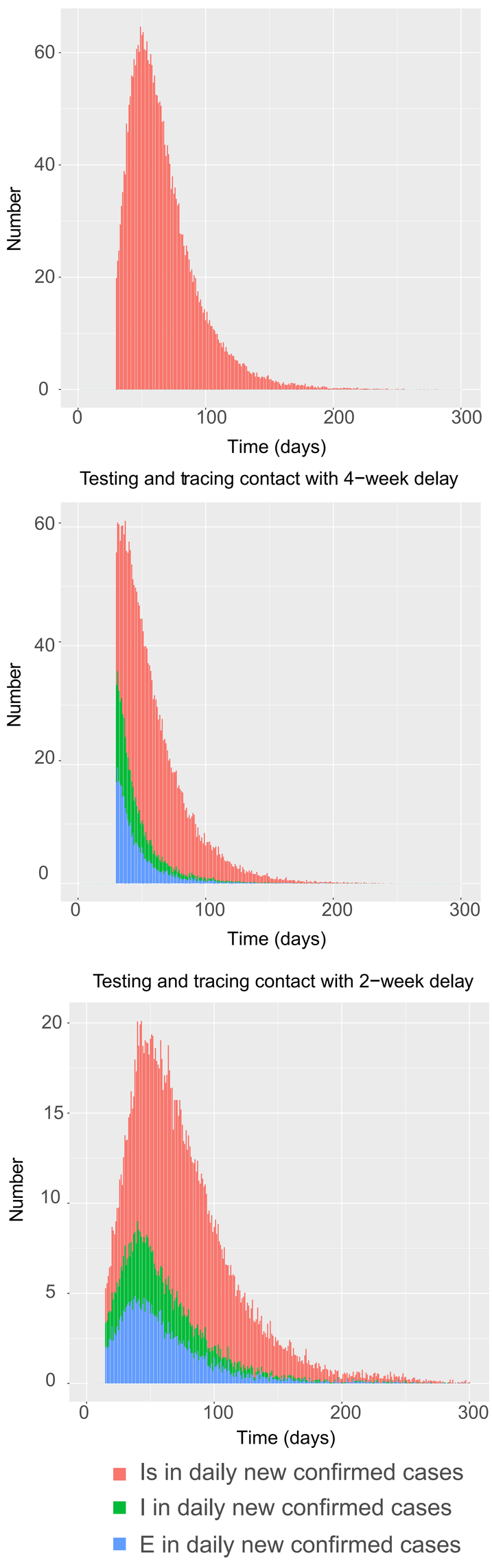
A


R0
4
3
2
Real-world data
Simulated baseline

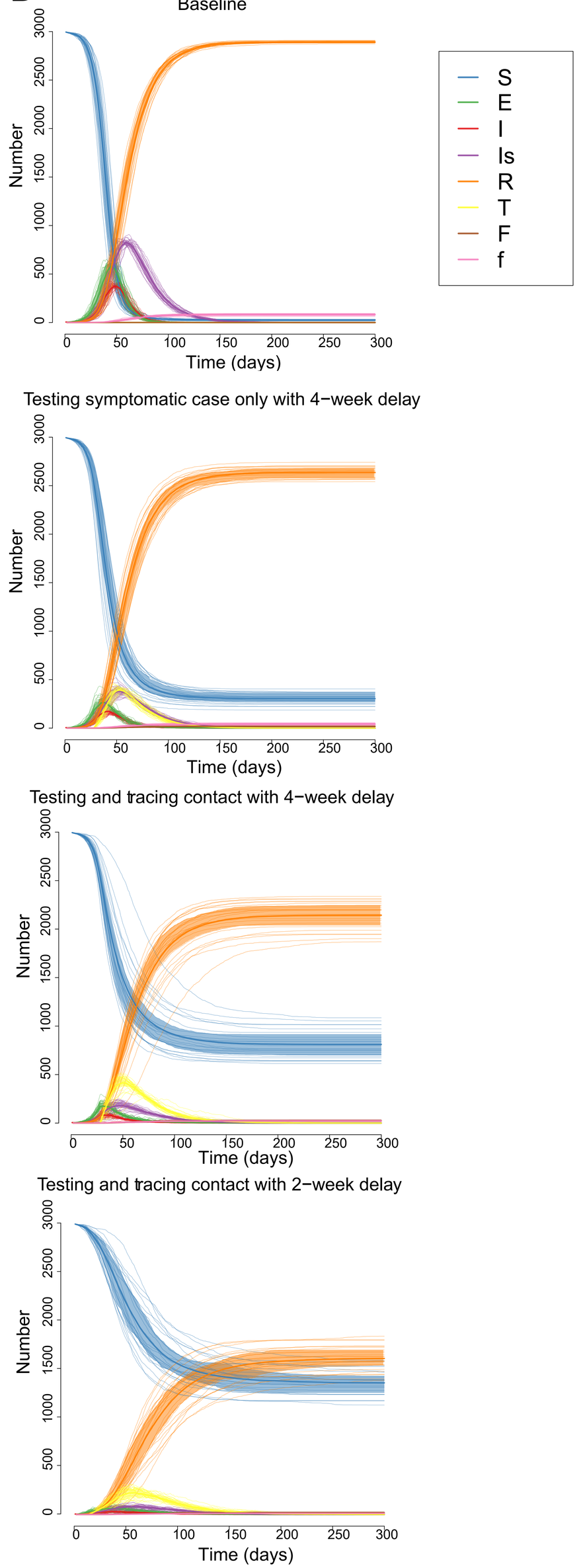
B

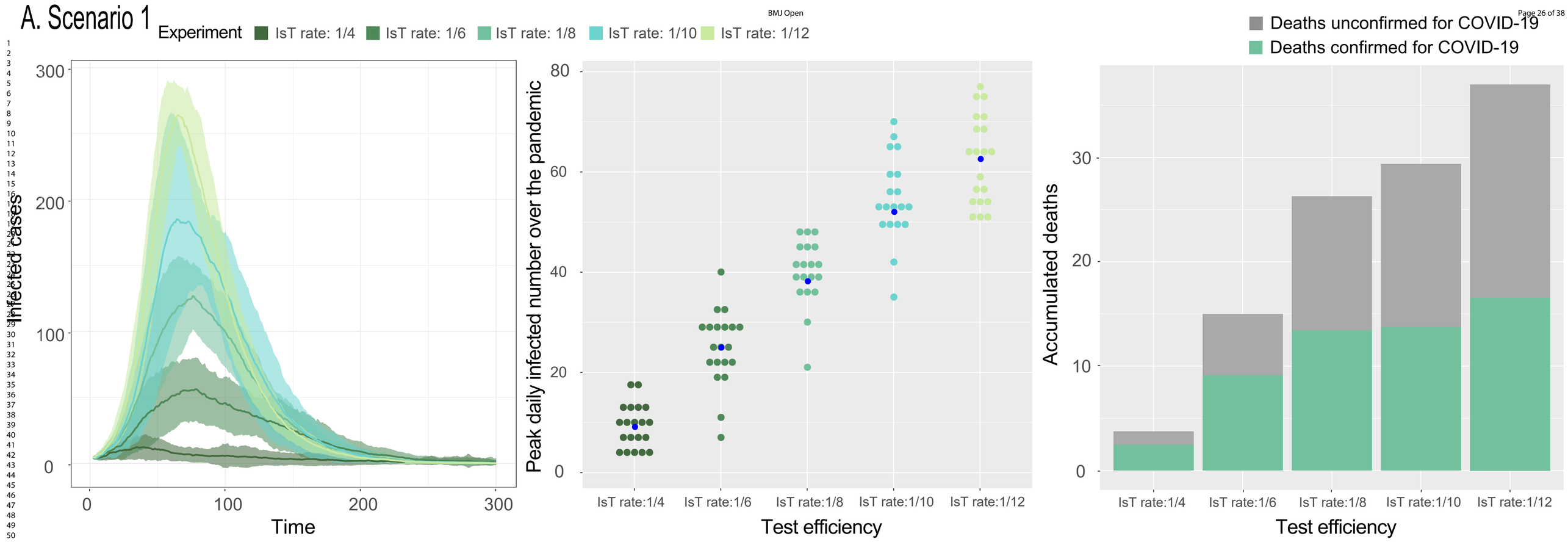

Baseline
Testing and tracing contact with 2−week delay
Testing and tracing contact with 4−week delay
Testing symptomatic case only with 4−week delay
Active infections
Time interval used to estimate R0
Time (days)

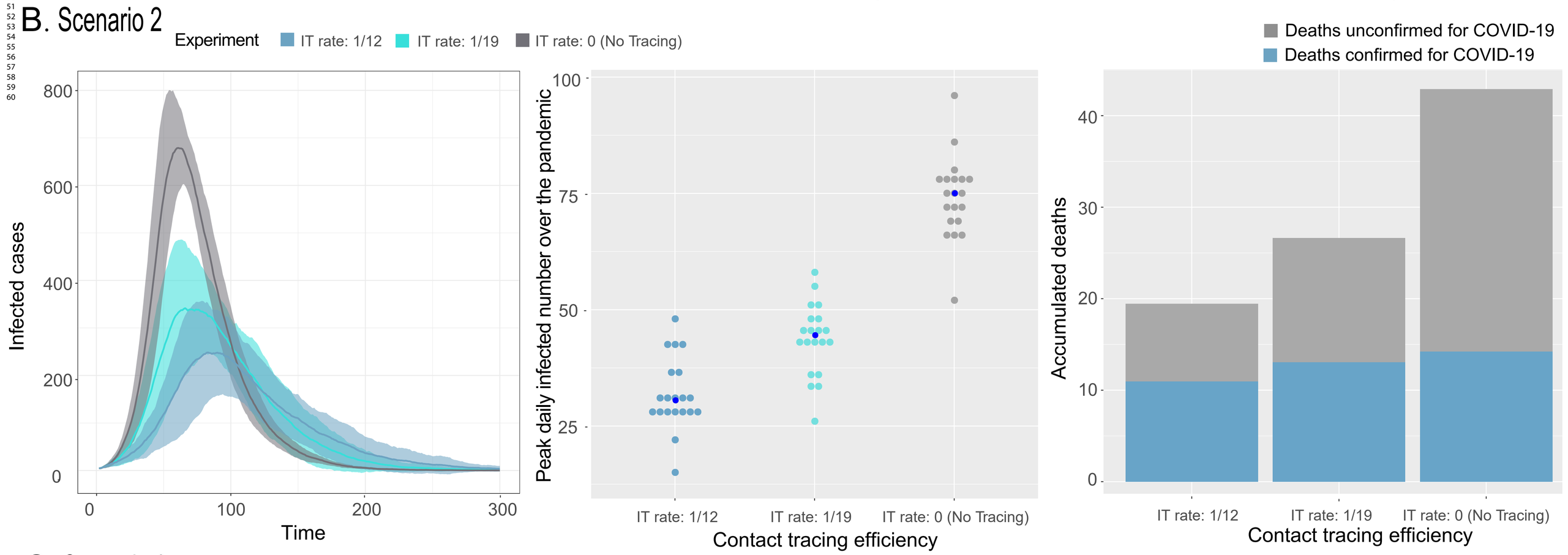
C

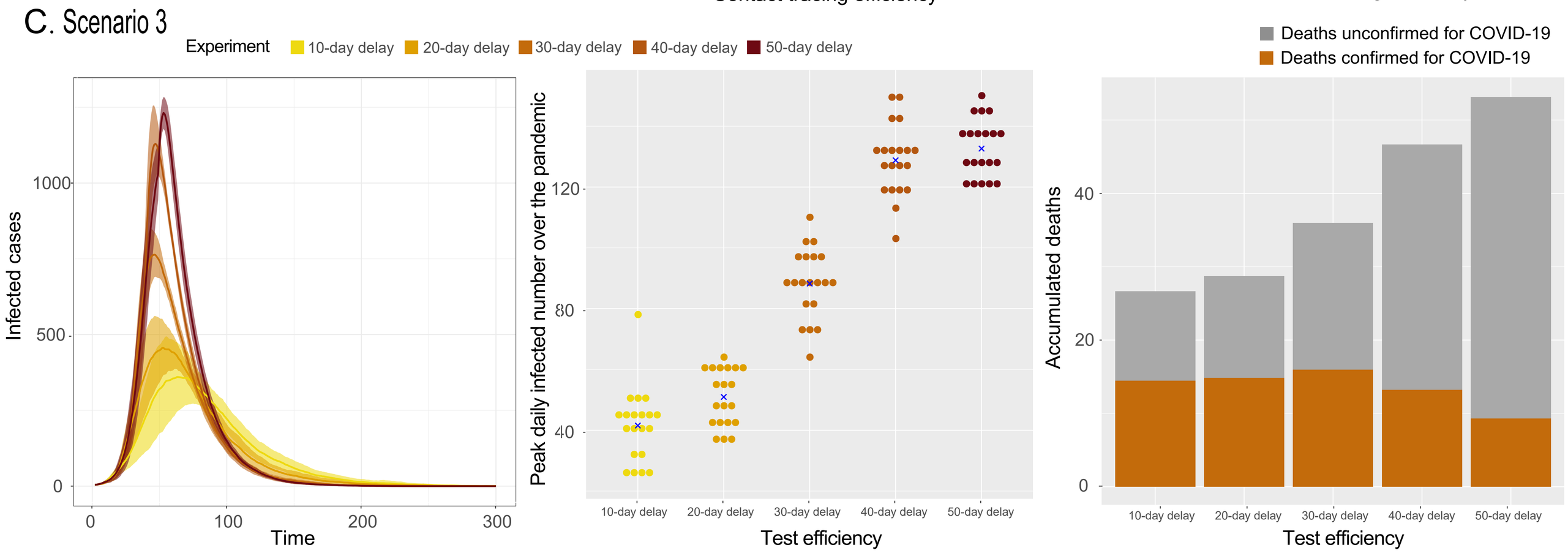

Testing symptomatic case only with 4−week delay
Number
Time (days)
Testing and tracing contact with 4−week delay
Testing and tracing contact with 2−week delay
Is in daily new confirmed cases
I in daily new confirmed cases
E in daily new confirmed cases

D

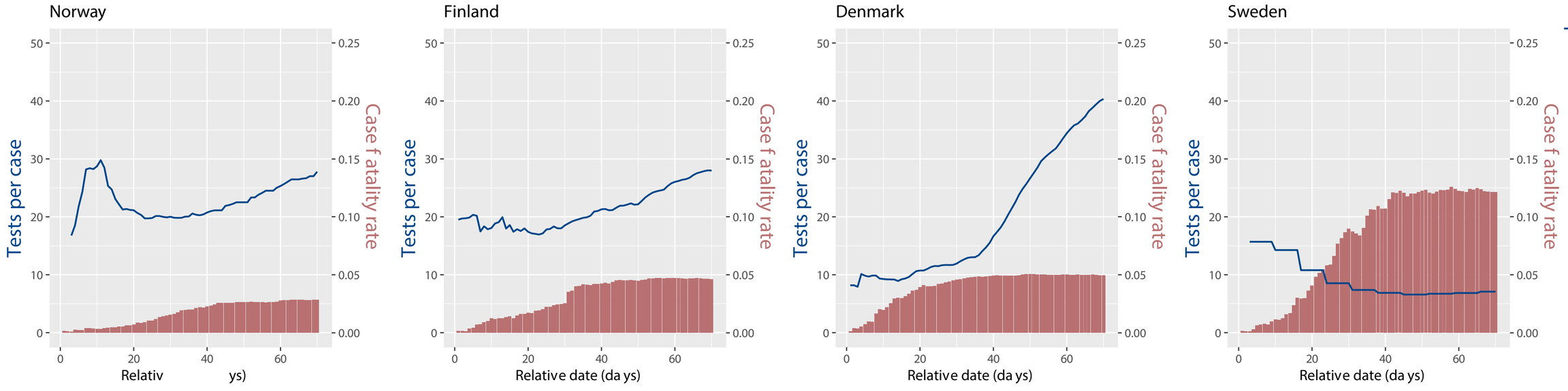

Baseline
Number
Time (days)
S
E
I
Is
R
T
F
f
Testing symptomatic case only with 4−week delay
Testing and tracing contact with 4−week delay
Testing and tracing contact with 2−week delay


A. Scenario 1
Experiment
IsT rate: 1/4
IsT rate: 1/6
IsT rate: 1/8
IsT rate: 1/10
IsT rate: 1/12
Infected cases
Time
Peak daily infected number over the pandemic
IsT rate:1/4
IsT rate:1/6
IsT rate:1/8
IsT rate:1/10
IsT rate:1/12
Test efficiency
Deaths unconfirmed for COVID-19
Deaths confirmed for COVID-19
Accumulated deaths
Test efficiency

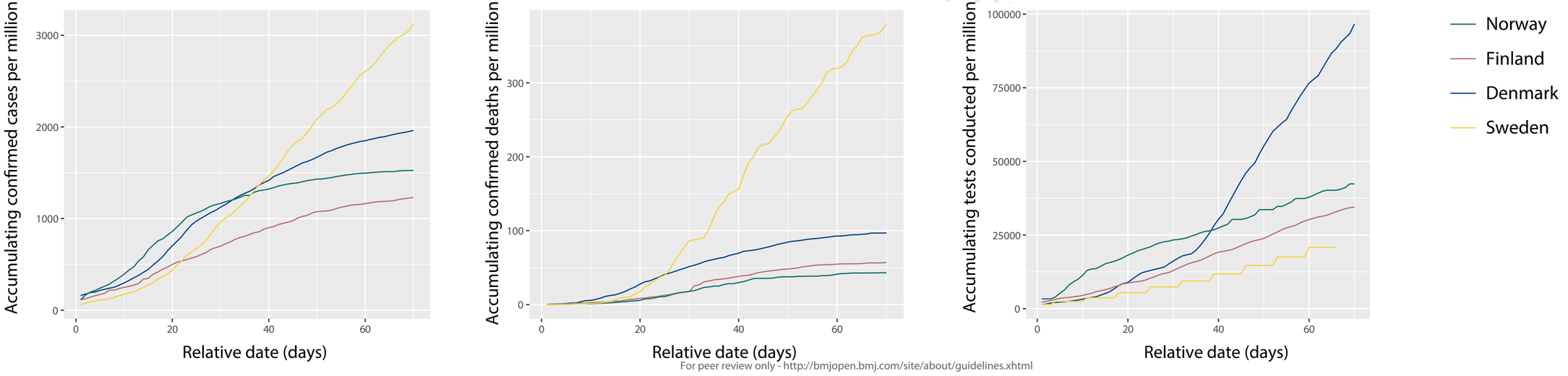

B. Scenario 2
Experiment
IT rate: 1/12
IT rate: 1/19
IT rate: 0 (No Tracing)
Infected cases
Time
Peak daily infected number over the pandemic
IT rate: 1/12
IT rate: 1/19
IT rate: 0 (No Tracing)
Contact tracing efficiency
Deaths unconfirmed for COVID-19
Deaths confirmed for COVID-19
Accumulated deaths
Contact tracing efficiency


C. Scenario 3
Experiment
10-day delay
20-day delay
30-day delay
40-day delay
50-day delay
Infected cases
Time
Peak daily infected number over the pandemic
10-day delay
20-day delay
30-day delay
40-day delay
50-day delay
Test efficiency
Deaths unconfirmed for COVID-19
Deaths confirmed for COVID-19
Accumulated deaths
Test efficiency

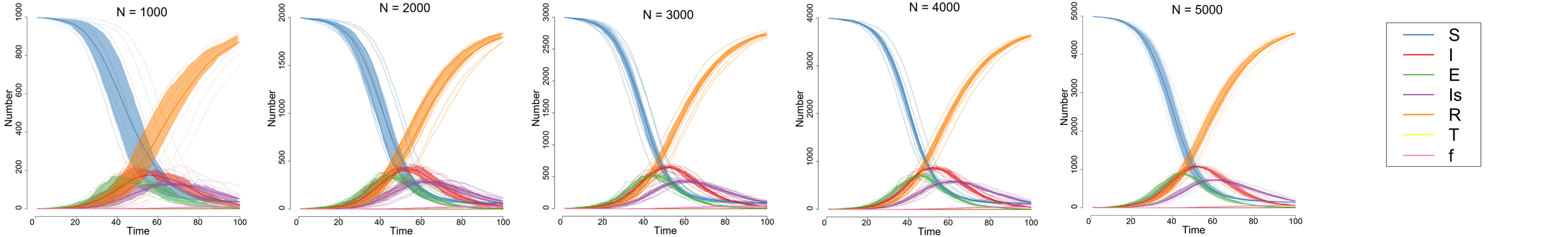
A


Norway
Finland
Denmark
Sweden
Tests per case
Case fatality rate
Tests per case
Case f atality rate
Relativ ys)
Relative date (da ys)
Relative date (da ys)
Relative date (da ys)

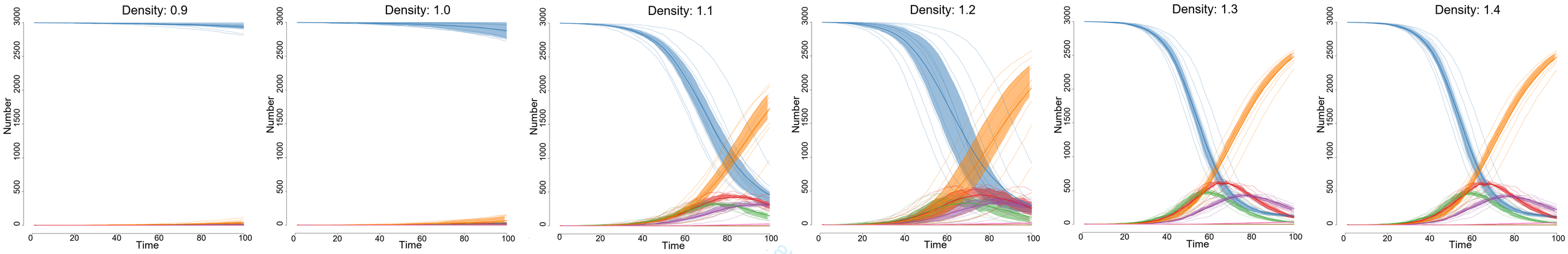
B


Accumulating confirmed cases per million
Relative date (days)
Accumulating confirmed deaths per million
Relative date (days)
Accumulating tests conducted per million
Relative date (days)
Norway
Finland
Denmark
Sweden

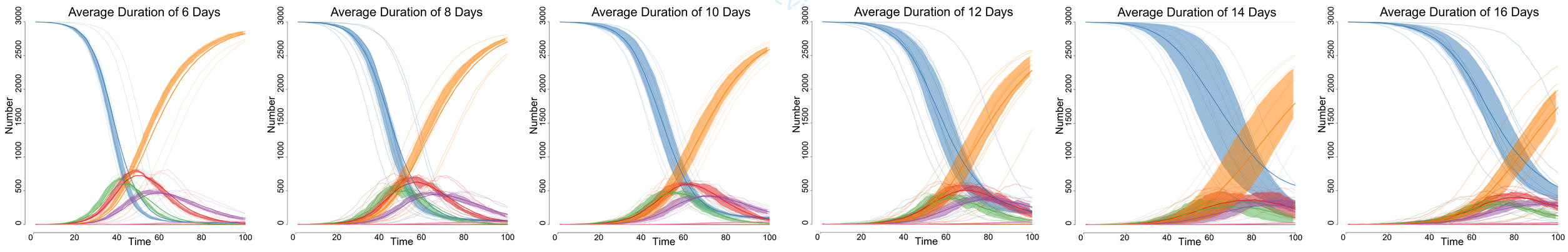
A



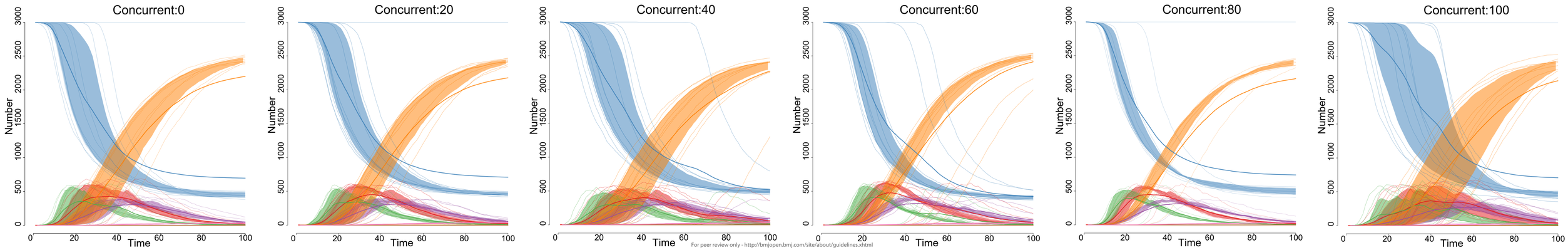
B



C



D



Supplemental materials

Model Assumptions

CoTECT assumes all tests hold the best sensitivity and specificity, which described false-positive and true-negative as a small probability event. When a small probability event happened, people exposed to the virus did not change to a tested and quarantined status in an expected period. Yet, this possibility is more than zero during the simulation. If the test sensitivity and specificity drop down, we can prolong the expected waiting time to test and self-quarantine in CoTECT. However, the test model(T) is a self-quarantine status that prevents 100% of infections from the confirmed cases, which is relied on a strong assumption. Furthermore, since the model was built based on a Bernoulli distribution, it is plausible that some infected people skipped from self-quarantine get self-recovery instead (Table S1, S2).

Table S1. Setting of transmission rates for CoTECT

	Transmission rate	Parameter definition	Assumed rate	References
Sampled	E-->T	Rate per day at which exposed (E) individuals test positive and enter quarantine status (T)	1/18 (1/15-1/23)	[1 2 3]
	I-->T	Rate per day at which infected (I) cases test positive and enter quarantine status (T)	1/12 (1/9-1/17)	[1 2 3]
	Is-->T	Rate per day at which symptomatic infected (Is) cases test positive and enter quarantine status (T)	1/7 (1/4,1/6,1/8,1/10,1/12)	[1]
Fixed	I-->Is	Rate per day at which infected (I) cases become symptomatic (Is) cases	1/5	[1]
Fixed	E-->I	Rate per day at which an exposed (E) individual become infected (I) cases	1/6.4	[4]
	I-->R	Rate per day at which infected cases with mild or no symptoms (I) recover and are immunized (R)	1/14	[1 2]

	Is-->R	Rate per day at which infected cases with severe symptoms (Is) recover and are immunized (R)	1/21	[1 5]
	T-->R	Rate per day at which quarantined, test-positive (T) cases recover and are immunized (R)	1/17	Assumed
	Is-->F	Death rate per day of infected cases with severe symptoms (Is)	0.002	[2]
	T-->F	Death rate per day of test-positive (T) cases	0.001	[2 3 6 7]

Table S2. Parameter setting for CoTECT network framework

Parameter	Definition	Value	Reference
Density	Density of whole social network.	1.3	Adjusted according to reported R0 (corresponding with infection probability and contact times)
Concurrent	Number of nodes (individuals) which contact many other nodes at a given day	0%-3%	Assumed
Isolation	Number of nodes (individuals) who does not make any contact with others at a given day	0%-3%	Assumed
Infection probability for symptomatic patient （I）	Probability of an infected individual passes the COVID-19 to another one based on an existed edge between them	30%	Adjusted according to reported R0
Infection probability for asymptomatic patient （E）	Probability of an exposed but asymptomatic individual passes the COVID-19 to another one based on a existed edge between them	20%	Adjusted according to reported R0
Contact times between I	Average contact times between two	3	Adjusted according to reported R0

	connected individuals (one is infected) in a given day		
Contact times between E	Average contact times between two connected individuals (one is exposed) in a given day	3	Adjusted according to reported R0

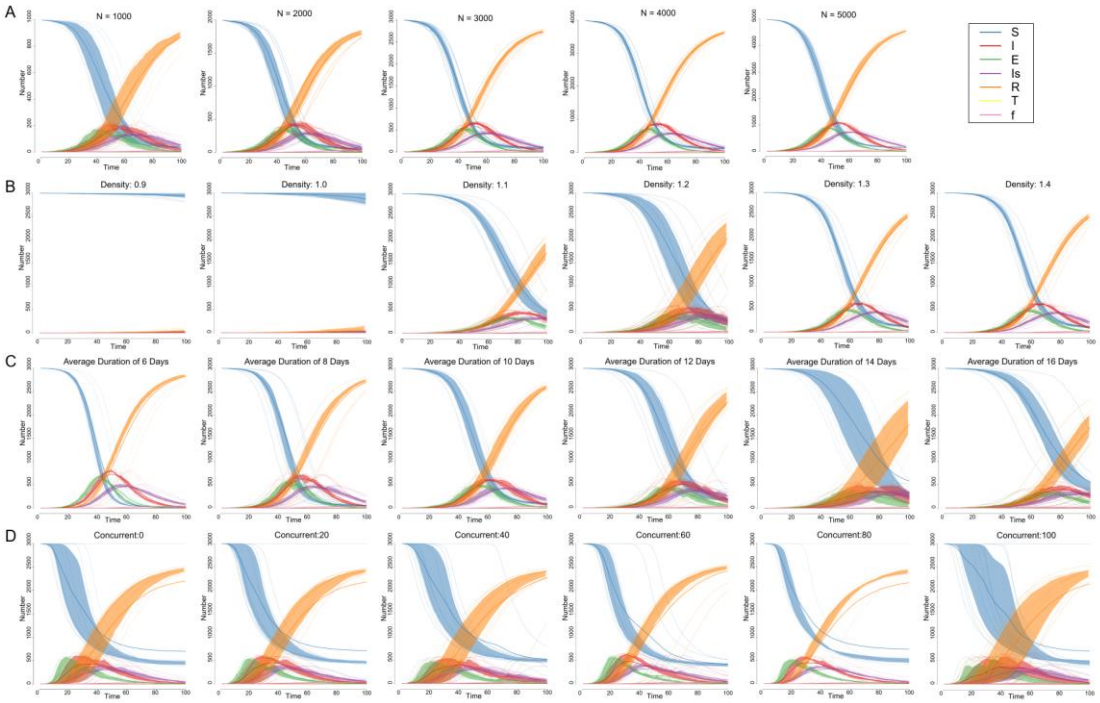


Figure S1: Sensitivity analyses for baseline models of different (A) population sizes (N=1000, 2000, 3000, 4000, and 5000), (B) densities (0.9, 1.0, … ,1.4), (C) average duration (6 days, 8 days, …, 16 days), and (D) concurrent nodes (0, 20, …, 100). Curves for each compartment in each model are shown in the graphs and demonstrate similar proportions of people in each compartment in the whole population for different population sizes.

Table S3: Sensitivity analyses for baseline models of different population sizes, densities, average duration, and concurrent nodes.

Parameters	Values	Total infections	Peak daily infections	Proportion of total infections in whole population	Cumulative deaths of unconfirmed cases
Population size	1000	883.2	290.9	88.3%	12.1
	2000	1826.2	668.5	91.3%	27.4
	3000	2769.8	1035	92.3%	39.3

	4000	3676	1378.4	91.9%	52.7
	5000	4606.9	1716.8	92.1%	60.8
Density	0.9	42.5	2.5	1.42%	0.2
	1.0	66.4	4.4	2.21%	0.8
	1.1	1754.6	61	58.49%	25
	1.2	2053.8	61.7	68.46%	26.1
	1.3	2510.2	99.9	83.67%	31.5
	1.4	2747.6	106.8	91.59%	37.5
Average duration (Days)	6	2864.4	130	95.48%	40.3
	8	2741.3	102.4	91.38%	38.3
	10	2627.7	93.4	87.59%	38.7
	12	2310.4	73.8	77.01%	32.8
	14	1823.8	52.2	60.79%	24.5
	16	1755.3	59.4	58.51%	22.1
Concurrent nodes	0	2229.3	77.1	74.31%	30.1
	20	2210.4	86.7	73.68%	33.8
	40	2302.2	67.7	76.74%	30.8
	60	2444.8	93.2	81.49%	31.6
	80	2189.8	92.9	72.99%	29.6
	100	2167.6	69.5	72.25%	27.5

Estimation of IsT rate based on real-world data

According to the public information about the epidemic investigation, we calculated the average time from onset to reporting of the first 23 symptomatic cases in the second-wave outbreak of Covid-19 to be 2.7 days (Table S4), with case data displayed in Table S5. 2.7 days is shorter than four days we set in scenario-1, therefore, it is realistic and feasible to set the window period of the best scenario as four days. According to another cohort study in Beijing [8], China, the median time interval from illness onset to laboratory confirmation is seven days (4.7–10.2), so a four day window period is rational (Table S4, S5).

Table S4. Testing efficiency for the second-wave outbreak in Beijing, China

Average time from onset to reporting (first 37 cases)	Percentage of cases confirmed by contact tracing (first 37 cases)	Tests for traced contacts (first ten days)	Daily testing capacity within one month	Test efficiency for cases with fever	Test efficiency for other patients	Test efficiency for other patients	Test efficiency for normal test application	Total confirmed cases	Percentage of cases confirmed by targeted screening tests
2.7 days	68%	2342 thousand	90 to100 thousand	6h	12h	6h	24h	335	52%

Table S5. Average time from onset to reporting, and means of reporting of first 37 cases for the second-wave outbreak in Beijing, China[8]

Number of cases	Symptom	Days from onset to reporting	Means of reporting
1	fever	0	initiative
2	fever	4	initiative
3	fever	5	initiative
4	fever	4	initiative
5	fever	1	initiative
6	fever	5	initiative
7	fever	2	initiative
8	no	NA	tracing
9	no	NA	tracing
10	muscle soreness	3	tracing
11	sore throat	2	tracing
12	fever	0	initiative
13	headache	8	tracing
14	no	NA	tracing
15	no	NA	tracing
16	sore throat	1	tracing
17	fever	4	tracing
18	fever	0	initiative
19	cough	1	tracing
20	sneeze	2	tracing
21	fever	2	tracing
22	sneeze	8	tracing
23	headache	1	tracing
24	no	NA	tracing
25	fever	1	initiative
26	fever	4	initiative
27	fever	2	tracing
28	no	NA	tracing

29	dry throat	2	tracing
30	no	NA	tracing
31	no	NA	tracing
32	no	NA	tracing
33	no	NA	tracing
34	no	NA	tracing
35	no	NA	tracing
36	no	NA	tracing
37	no	NA	initiative
Average		**2.7**	

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Strengthening the Reporting of Empirical Simulation Studies (STRESS)
Agent based simulation guidelines STRESS-ABS

Section/Subsection	Item	Recommendation	Reported in the main document
1. Objectives			
Purpose of the model	1.1	Explain the background and rationale for the model.	Abstract, introduction, methods
Model Outputs	1.2	State the qualitative or quantitative system level outputs that emerge from agent interactions within the ABS. Define all quantitative performance measures that are reported, using equations where necessary. Specify how and when they are calculated during the model run along with how any measures of error such as confidence intervals are calculated	Methods
Experimentation Aims	1.3	If the model has been used for experimentation, state the research questions that it was used to answer. a.) Theory driven analysis. – Provide details and reference the theories that are tested within the model. b.) Scenario based analysis – Provide a name and description for each scenario, including a rationale for the choice of scenarios and ensure that item 2.3 (below) is completed. c.) Design of experiments – Provide details of the overall design of the experiments with reference to performance measures and their parameters (provide further details in *data* below). d.) Simulation Optimisation – (if appropriate) Provide full details of what is to be optimised, the parameters that were included and the algorithm(s) that was be used. Where possible provide a citation of the algorithm(s).	Methods
2. Logic			
Base model overview diagram	2.1	Provide one or more of: state chart, process flow or equivalent diagrams to describe the basic logic of the base model to readers. Avoid complicated diagrams in the main text.	Methods, results
Base model logic	2.2	Give details of the base model logic. This could be text to explain the overview diagram along with extra details including ABS product and process patterns. Include details of all intermediate calculations.	Methods, results
Scenario logic	2.3	Give details of any difference in the model logic between the base case model and scenarios. This	Introduction, methods, results

		could be incorporated as text or, where differences are substantial, could be incorporated in the same manner as 2.1.		
Algorithms	2.4	Provide further detail on any algorithms in the model that (for example) mimic complex or manual processes in the real world (i.e. scheduling of arrivals/appointments/operations/maintenance, operation of a conveyor system, machine breakdowns, etc.). Sufficient detail should be included (or referred to in other published work) for the algorithms to be reproducible. Pseudo-code may be used to describe an algorithm.		Introduction, methods, results
Components	2.5	2.5.1. Environment	Describe the environment agents interact within, indicating its structure, and how it is generated. For example, are agents bound within a homogeneous grid, or do they have continuous movement through a detailed landscape incorporating geographic or environmental information?	Methods
		2.5.2. Agents	List all agents and agent groups within the simulation. Include a description of their role in the model, their possible states, state transitions, and all their attributes. Describe all decision-making rules that agents follow in either algorithmic or equation form. Where relevant authors should report: • The data that agents access (I.e. internal attributes or external information from the environment) and how it is used. • The objectives agents seek to achieve. • The algorithms, optimisations, heuristics and rules that agents use to achieve objectives. • How agents work together within a group along with any	Methods

		rules for changes in group membership. • Predictions of future events and adaptive action.	
	2.5.3. Interaction Topology	Describe how agents and agent groupings are connected with each other in the model define: • with whom agents can interact, • how recipients of interactions are selected • what frequency interaction occurs. • How agents handle and assign priorities to concurrent events It is recommended that interactions are described using a combination of equations pseudo-code and logic diagrams. Report how interactions are affected by agent states and the environment state	Methods
	2.5.4 Entry / Exit	Where relevant, define how agents are created and destroyed in the model.	Methods
3. Data			
Data sources	3.1	List and detail all data sources. Sources may include: • Interviews with stakeholders • samples of routinely collected data, • prospectively collected samples for the purpose of the simulation study, • public domain data published in either academic or organisational literature. Provide, where possible, the link and DOI to the data or reference to published literature. All data source descriptions should include details of the sample size, date ranges and use within the study.	Methods

Pre-processing	3.2	Provide details of any data manipulation or filtering that has taken place before its use in the simulation, e.g. interpolation to account for missing data, removal of outliers or filtering of large scale data.	Methods
Input parameters	3.3	List all input parameters in the model, providing a description of each parameter and the values used. For stochastic inputs provide details of any continuous, discrete or empirical distributions used along with all associated parameters. Where applicable define the time/spatial dependence of parameters and any correlation structure. Clearly state: • Base case inputs • Inputs used in experimentation, where different from the base case. • Where optimisation or design of experiments has been used, state the range of values that parameters can take. Where theoretical distributions are used, state how, , these were selected and prioritised above other candidate distributions.	Methods, results
Assumptions	3.4	Where data or knowledge of the real system is unavailable, state and justify the assumptions used to set input parameter values and distributions; agent interactions or behaviour; or model logic.	Methods
4. Experimentation			
Initialisation	4.1	State if a warm-up period has been used, its length and the analysis method used to select it. State what if any initial agent and environmental conditions have been included. For example, the initial agent population size, agent states and attributes, initial agent network structure(s), and resources within the environment. Report whether initialisation of these variables is deterministic or stochastic.	Methods, results
Run length	4.2	Detail the run length of the simulation model and time units.	Methods
Estimation approach	4.3	State if the model is deterministic or stochastic. If the model is stochastic, state the number of replications that have been used. If an alternative estimation method has been used (e.g. batch means), provide full details.	Methods
5. Implementation			

Software or programming language	5.1	State the operating system and version and build number. State the name, version and build number of commercial or open source ABS software that the model is implemented in. State the name and version of general-purpose programming languages used (e.g. Python 3.5.2). Where packages, frameworks and libraries have been used provide all detailed including version numbers.	Methods
Random sampling	5.2	State the algorithm or package used to generate random samples within the software/programming language used e.g. Mersenne Twister or Java.Random version x.y	Methods
Model execution	5.3	If the ABS model has a time component, describe how time is modelled (e.g. fixed time steps or discrete-event). State the order of variable updating within the model. In time-stepped execution state how concurrent events are resolved. If the model is parallel, distributed and/or use grid or cloud computing, etc., state and preferably reference the technology used. For parallel and distributed simulations the time management algorithms used. If the HLA is used then state the version of the standard, which run-time infrastructure (and version), and any supporting documents (FOMs, etc.)	Methods
System Specification	5.4	State the model run time and specification of hardware used. This is particularly important for large scale models that require substantial computing power. For parallel, distributed and/or use grid or cloud computing, etc. state the details of all systems used in the implementation (processors, network, etc.)	Methods
6. Code Access			
Computer Model Sharing Statement	6.1	Describe how someone could obtain the model described in the paper, the simulation software and any other associated software (or hardware) needed to reproduce the results. Provide, where possible, the link and DOIs to these.	Data sharing