PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	The role of efficient testing and contact tracing in mitigating the COVID-19 pandemic: A network modeling study
AUTHORS	Hu, Yiying; Guo, Jianying; Li, Guanqiao; Lu, Xi; Li, Xiang; Zhang, Yuan; Cong, Lin; Kang, Yanni; Jia, Xiaoyu; Shi, Xuanling; Xie, Guotong; Zhang, Linqi

VERSION 1 – REVIEW

REVIEWER	Nagarajan, Karikalan ICMR-National Institute for Research in Tuberculosis
REVIEW RETURNED	22-Nov-2020

GENERAL COMMENTS	The authors have undertaken a network modeling study to assess the efficiency of different testing and contact tracing scenarios for Covid-19 using simulation and real world data. The study finding are interesting and important which highlights that early testing could be a game changer in containing the spread of infection and mortality when compared to late stage efforts. This findings could be very potential for nations which are undergoing or expecting the second wave of Covid-19. Yet there are some important reservations I hold in terms of the proposed network modeling methods which the authors refer to and some of the results they have arrived and interpreted. The authors conclude that this is a network based modeling . They have utilized an R package for generating network model based on exponential random graph models. Real world data from Nordic countries have been used to test the assumptions. Here are my comments 1)The authors have to detail more on the network assumptions which they have considered in the exercise. What were the network parameters which were considered in the model? There are references to network size, edge density and network density which are considered but no detailed description is provided anaywhere. Again the authors say in limitations that "all simulations were conducted in a closed population… and Network sizes were also limited by computing complexity" Said this limitation, I am sceptical that whether this could be considered a network model? The authors need to justify that what is novel about the methods they have used when compared to published network modelling studies in Covid-19. Am providing a reference for the authors to relate and validate their network method

(McCombs A, Kadelka C (2020) A model-based evaluation of the efficacy of COVID-19 social distancing, testing and hospital triage policies. PLoS Comput Biol 16(10): e1008388)

2) Figure B depicts a simple hypothetical network graph. It doesn't covey anything additional about network structure s or assumptions used in the study.

3) Is there any other studies in Covid-19 which have used CoTECT model? The authors must cite and discuss those studies.

4) A hypothetical population of 3000 is used for 300 days. Is it due to the limitation of modelling complexity or purposive? Please provide a separate table for all network parameters used in the modeling?

5) I am not clear about the transmission rate and efficiency equation? How did the authors conclude the validity of such assumptions? Is this an in-built assumption in CoTECT as referred by authors? Please discuss on this more and provide references.Is this transmission rate comparable with the real world epidemiological transmission rate of Covid-19?

6) What were the assumptions and parameters used for testing strategies? Was there any sensitivity and specificity assumptions for the testing? This holds lot of impact for the proposed model.

7) The findings show that scenario -1 was the best which could be able to avert more infections and a whooping 92% deaths if the a/symptomatic were tested in a four day window period. Such huge difference evokes a sense of simplification of the complexity of the pandemic. Is there any country or region which had achieved this? The authors refer to China as an example, still the time delay of responding to the pandemic with mass testing was still lengthier for China (not surely within 4 days) . This needs to be discussed with published figures from Chinese studies otherwise this conclusion of authors would be speculative.

8) Sensitivity analysis alters only one scenario of baseline population. Could other key parameters could be checked for their impacts on the outcomes.

REVIEWER	LOPES-JÚNIOR, LUÍS CARLOS
	Universidade Federal do Espirito Santo, Nursing Department
REVIEW RETURNED	24-Dec-2020

GENERAL COMMENTS	First of all, I would like to thank you for the opportunity to review this interesting manuscript and congratulate the authors for this well-designed and highly relevant epidemiological study, mainly in the current pandemic context.
	The paper fills an important gap in the scientific literature, since previous studies generally emphasize that volume of tests is important in containment of the COVID-19 epidemic, but, still, few studies quantify how the efficiency of testing and tracing.
	This epidemiological study aimed to provide a comprehensive and quantitative assessment of the key factors of testing and contact tracing, which might aid in implementing more effective measures to contain the pandemic. The authors have developed a novel

individual-level network model with key parameters obtained from recent studies, to quantify impacts of efficiency of testing and tracing.

I am sure that this is a novel paper with a topic that will be of great interest for BMJ Open readers. I have some few comments, suggestions in order to strengthen the potential contribution of this topic in any revision the author(s) might undertake.

Minor Revision:

There are some relevant outputs about this particular topic that were not quoted in the introduction. Please, check out both references published in the BMJ Open.

doi: 10.1136/bmjopen-2020-040413
doi: 10.1136/bmjopen-2020-039426

I suggest extending the discussion section a little further because its results are very interesting and impressive and deserve to be discussed further. Consider adding two more paragraphs before presenting study limitations

Ad hoc consultant 1

VERSION 1 – AUTHOR RESPONSE

Reviewer1#
1.
1.1 The authors have to detail more on the network assumptions which they have considered in the exercise. What were the network parameters which were considered in the model?

We thank the reviewer for the constructive suggestion. The following are the details on the network assumptions that we added to the revised manuscript in the method section:
"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 with the desired likelihood of connection conditional on the graph with specific network properties. 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) model, 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) 1, developed by Holland and Leinhardt2 3. "

"Our assumptions and network parameters are aligned with ERGMs, which are listed in supplemental Table S2."

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) that make contact with many other nodes at a given day

0%-3% assumed

Isolation Number of nodes (individuals) who does not make any contact with others on a given day 0%-3% assumed

Infection probability for symptomatic patient （I） The 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） The probability of an exposed but asymptomatic individual passes the COVID-19 to another one based on an existed edge between them 20% Adjusted according to reported R0

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

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

"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 the SE rate and act times, which are 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 . 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."

1.2 There are references to network size, edge density and network density which are considered but no detailed description is provided anywhere.

Thanks for pointing out the questions. Network size is the number of nodes (people) in the network, we have tested the influence of network size in our sensitivity analysis. Theoretically, since we are evaluating an efficiency control measure that will impact every possible node(people) in the network, the number of nodes shall not have a significant influence on the result within a limit. The efficiency is defined as an average waiting time instead of total test kits in demand in our study. Other parameters like edge density are based on a social network study4, which implies several close contacts an average citizen will have in their daily lives. Therefore, edge density can vary between different communities due to culture, season, and other reasons. More sensitivity analysis about these parameters has been addressed and updated on the supplemental material (Table S2).

1.3 Again, the authors say in limitations that "all simulations were conducted in a closed population… and Network sizes were also limited by computing complexity" Said this limitation, I am sceptical that whether this could be considered a network model?

Thank you for giving this problem careful consideration. A close population in our study means we do not consider the infection between two networks or new birth and death happened within the population. All these assumptions shall not change the conclusion nor the assumption. We had modified our description of the main text to avoid misunderstanding from readers.

1.4 The authors need to justify that what is novel about the methods they have used when compared to published network modelling studies in Covid-19. Am providing a reference for the authors to relate and validate their network method (McCombs A, Kadelka C (2020) A model-based evaluation of the efficacy of COVID-19 social distancing, testing and hospital triage policies. PLoS Comput Biol 16(10): e1008388)

Compare to the current study. We provided a unique perspective of describing the effect of efficiently testing and contact tracing. The structure of CoTECT is specially designed for evaluating test and contact tracing measurements. Furthermore, the three testing scenarios were inspired by Beijing's success story. Beijing is a megacity with over 21 million population. The difficulty of suppressing the outbreak surpassed many others, while it still proved its ability by highly efficient epidemiology work. Thanks for providing us with a useful reference. We have added the following description of our novelty in the introduction:

"McCombs A et al. 5. compared strategies of different testing priorities (people with high-risk/low-risk are tested. First, people with symptoms that appeared recently/earlier are tested first) under the condition that the maximum test volume per day is fixed. Adam J Kucharski et al. 6. 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. 7. explored whether testing included all identified contacts or only those with symptoms affected reproductive number. However, we emphasize the efficiency (or timeliness) of testing, which is not necessarily related to the total amount of testing, so we reasoned for novel factors, strategies, and model structure."

We also detailed the discussion part that although we did not estimate the total amount of testing required, we found that the earlier and more efficient testing reduced more testing based on our model. CoTECT disassembled the compartment of "infected" into two parts as infected with and without confirmation. It also divided deaths into confirmed and unconfirmed deaths, which was convenient to describe a complete picture under inefficient testing:

"Our study originally evaluated the effects of efficiency of testing and contact tracing (proposing a new definition of test efficiency: average waiting time for each individual) on Covid-19 transmission. Compared with previous studies, which mostly emphasized the amount of testing, we did not limit our study 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, reducing testing demand. Many studies already proved some test strategies could release the pressure of test kits shortage. 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. "

2. Figure B depicts a simple hypothetical network graph. It doesn't covey anything additional about network structures or assumptions used in the study.

Figure1-B displayed the stochastic process of edge generation and dissolution. The difference shown in the three subplots represents the dynamic edge change of our social network over time. It is a vivid presentation of everyday social activities. We have extended the figure described in the article.

"Figure1-B displayed the stochastic process of the edge generation and desolvation, and represented the dynamic change of our social network, which had shown the abbreviation version of the contact network on different time steps."

3. Is there any other studies in Covid-19 which have used CoTECT model? The authors must cite and discuss those studies.

Thanks for pointing out this question. CoTECT is a self-developed model named CoTECT. There are no other studies in Covid-19 that used our model yet. But we do encourage more research developed about this kind of simulation study in the future. However, a few studies are using the same platform.

There is Jennes et.a8l simulated a cruise background transmission on Epimodel. Lopez et.al9 proposed a massive diagnostic test strategy applied in Spain, which mainly focused on how the transmission changed as network parameters changed. Murhaf et al. 10. estimated the volume of infections for Saudi Arabia pandemic on top of EpiModel. Churches et al. 11. sought to rapidly develop a flexible, freely available simulation model for other researchers based on the Epimodel platform.

4. A hypothetical population of 3000 is used for 300 days. Is it due to the limitation of modelling complexity or purposive? Please provide a separate table for all network parameter

Thanks for the kind reminder. The modelling complexity exposed due to the increased complexity of our model structure. Following the reviewer's comments, we've provided a sensitivity analysis and found that the influence of population size is neglectable. A more explicit table has been added (Table S2).

5. I am not clear about the transmission rate and efficiency equation? How did the authors conclude the validity of such assumptions? Is this an in-built assumption in CoTECT as referred by authors? Please discuss on this more and provide references. Is this transmission rate comparable with the real world epidemiological transmission rate of Covid-19?

Thank you for raising an important point here. Transmission rate from one status to the other statues of the same node is based on a Bernoulli distribution where the expected waiting time to change is where p denotes the distribution's expected value. And we have added this explanation to the main text as follows:

"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-day average 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. "

But infectious probability (transmission rate from S to E) is applied only on the existed edge (real contact) between two nodes (persons). The validation of the assumption is built with the network model's mechanism, which is justified more explicitly on the method reference 3.

6. What were the assumptions and parameters used for testing strategies? Was there any sensitivity and specificity assumptions for the testing? This holds a lot of impact for the proposed model.

Thanks for pointing this out, we have addressed this issue in the supplemental material:

" 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 who were 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."

7. The findings show that scenario -1 was the best which could be able to avert more infections and a

whooping 92% deaths if the a/symptomatic were tested in a four day window period. Such huge difference evokes a sense of simplification of the complexity of the pandemic. Is there any country or region which had achieved this? The authors refer to China as an example, still the time delay of responding to the pandemic with mass testing was still lengthier for China (not surely within 4 days) . This needs to be discussed with published figures from Chinese studies otherwise this conclusion of authors would be speculative.

Thanks for the comment. To our knowledge, China has achieved the period from symptom onset to reporting less than four days12-14. 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 an added Table S5 in supplemental materials. 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 senario as four days. According to another cohort study in Beijing 14, 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. This was added to the supplemental material (Table S4, S5).

8. Sensitivity analysis alters only one scenario of baseline population. Could other key parameters could be checked for their impacts on the outcomes.

Thanks for the suggestion. We have added sensitibity analysis of three more parameters such as network density, concurrent nodes number and duration of edges to the main text and supplemental materials (Figure S1, Table S2, S3), and explained in the main text in the results section. Still, we set parameters fixed in our experiment according to previous research.

"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 S2, 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)."

"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."

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.

Reviewer: 2#

1. There are some relevant outputs about this particular topic that were not quoted in the introduction. Please, check out both references published in the BMJ Open.

doi: 10.1136/bmjopen-2020-040413
doi: 10.1136/bmjopen-2020-039426

We thank the reviewer for the constructive suggestion. We're pleased to add more references to the introduction, including the ones that the Reviewer 2 suggested as follows:

"Coronavirus disease 2019 (COVID-19) has posed severe challenges to the physical and mental health of people worldwide since December 2019. "
……
"For example, Luís Carlos Lopes-Júnior et al. 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. McCombs A et al. 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. simulated the effects of random mass testing of 5% of the population each week on transmission reduction. They compared it with the impact of isolation and tracing, without analysis on different testing scenarios. Alyssa Bilinski et al. explored whether testing included all identified contacts or only those with symptoms affected effective reproductive number. However, few researches 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."

2. I suggest extending the discussion section a little further because its results are very interesting and impressive and deserve to be discussed further. Consider adding two more paragraphs before presenting study limitations

Thanks for the suggestion. We have improved the discussion, covering a statement of the principal findings, the study's meaning, possible explanations and implications for policymakers, and unanswered questions and future research. Please check the main text in detail:

"Compared with previous studies, which mostly emphasized the amount of testing, we did not limit our study to estimate the fixed total amount of testing required, since the capacity of testing changed along the time. Instead, we revealed that earlier and more efficient testing could reduce the number of infections, therefore reduce testing demand. Many studies already proved some test strategies could release the pressure of test kits shortage. 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."
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"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."

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"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 future model. "

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accessed June 2020.

REVIEWER	Nagarajan, Karikalan ICMR-National Institute for Research in Tuberculosis
REVIEW RETURNED	11-Mar-2021

GENERAL COMMENTS	The authors say that efficiency of covid-19 testing has been assessed in only few studies. But there have been many modelling studies available as of now. Appropriate references needs to be added to justify the claim. Why choose nordic countries real world data ?and what is the time line ? is this data still relevant? this is very crucial since the pandemic scenario had changed largely now. Authors have to clarify that in what way the findings add value to the existing research on covid. In what way using an existing CoTECT package could be considered a novelty? does the real world data had any unique contact network information and thus studied? Sensitivity analysis need to elaborated more. how the model was validated ? I suggest a better and updated literature review and methodology to justify the need for this study.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

Dr. Karikalan Nagarajan, ICMR-National Institute for Research in Tuberculosis

Comments to the Author:

1. The authors say that efficiency of covid-19 testing has been assessed in only few studies. But there have been many modelling studies available as of now. Appropriate references needs to be added to justify the claim.

Thank you for constructive suggestion. We updated literature review in the introduction section and references were added. We searched PubMed and Google Scholar for literature through March 2021 using the terms ("COVID-19" OR "coronavirus disease 2019" OR "SARS-CoV-2" OR "severe acute respiratory syndrome coronavirus 2" OR "2019-NCoV" OR "2019 novel coronavirus") AND ("contact tracing" OR "contact-tracing" OR "tracing contact" OR "testing") AND ("efficiency" OR "efficient" OR "inefficient" OR "effectiveness" OR "effective" OR "inefficient" OR "delay"). We identified 1,848 studies, including 92 modeling studies among which 14 were closely related to our work.

"Most of these 14 studies 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] 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."

The comparison of part of literatures was listed in the attached table "comparison of part of literatures.xlsx".

2. Why choose Nordic countries real world data? and what is the time line ? is this data still relevant? this is very crucial since the pandemic scenario had changed largely now. Authors have to clarify that in what way the findings add value to the existing research on COVID.

Thanks. Nordic data were used to verify the scenario-3 in our three scenarios. 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 tests per confirmed case), which was analyzed in Nordic countries. We chose the four Nordic countries for comparison because confounders such as medical resources, population aging level, geography were similar in these countries, but the testing and tracing policies were different. Timeline of data of Nordic countries were the early stage of the pandemic when daily deaths per million population reached 0.1. The data were used to underline our conclusion drew from Scenario 3, which was analysis of the early stage of the epidemic, so the data were relevant. Even now, our findings are still applicable to the early stages of recurrence of local outbreak. From China's experience, even if the epidemic is temporarily controlled, it may still recur in a local area, and rapid response is still of practical significance for the subsequent outbreaks.

Aside from scenario 3, other two scenarios are also relevant nowadays. Because scenario 1 quantified how waiting time for each infector to get tested and quarantined dramatically affect epidemic results, and scenario 2 quantifies the crucial role of testing and tracing both symptomatic and asymptomatic in COVID-19 containment. These finds are still instructive as new waves of cases occur in many countries recently.

We have clarified the added value of our findings to the existing research on COVID in the introduction and discussion sections as follows:

"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…... 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."

"**Strengths and weaknesses in relation to other studies**

While previous studies[12 13 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."

3. In what way using an existing CoTECT package could be considered a novelty? does the real world data had any unique contact network information and thus studied?

Thank you for pointing out the lack of explanation of the novelty of the CoTECT model. CoTECT is a novel individual-level network model developed by ourselves, it is designed especially for quantifying the impacts of testing and tracing efficiency on COVID-19 containment. We have further clarified the novelty in the introduction section accordingly: "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[33],because infectivity of SARS-Cov2 during incubation period was not considered, and confirmed cases were not distinguished from infections." So, we proposed novel factors, strategies, and model structure compared with previous researches. EpiModel package was only used as basis to develop our new model, we upgraded it to adapt to our issues.

key parameters of our model were obtained from real-word studies to assure the rationality.To make the conclusion generalized to a different community, we parameterized the network with the social pattern according to published values from multiple references 28,29,30,31,32 , most of which were statistics of cases-level data 5,33,34,35.

4. Sensitivity analysis needs to elaborate more. how the model was validated?

Thanks for the suggestion. elaborated sensitivity analysis has added to the results.

" To validate the rationality of network setting of our model, we did sensitivity analysis for varying population sizes, and for different setting of parameters related to R0.

Firstly, 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).

Secondly, sensitivity analysis of R0-related parameters emphasized how the structure of social network impacts disease transmission. In addition to intrinsic properties of SARS-Cov2, the R0 was determined by three parameters that we studied in sensitivity analysis, including density of social network, concurrent (the number of people a person has contact with), and average duration of contact between two people. 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 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 infection will drop. R0 changed as different settings of these three parameters. In order to improve the universality of our model, we need to set a suitable a range for these parameters to make R0 achieve the average level of R0 reported in other studies (figure 2A), the distribution of R0 of our baseline simulation is corresponding to the average R0 estimated from 177 countries and territories. In a word, sensitivity analysis showed how we regulated parameters that are related to transmission dynamics, for all experiments, the mean R0 was set as an average of 2.2. Network density, concurrent and relationship duration between nodes were consistent across all experiments."

5. I suggest a better and updated literature review and methodology to justify the need for this study.

Thanks, we updated literature review and methodology in the introduction as mentioned in the answers to the question 1 and 2 above.

"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[11] [12,13] [14,15,16-21]. Few studies have quantified how the efficiency of testing and contact tracing limits disease spread……We referred to this protocol in our literature search for studies evaluating the effect of testing[22] and searched PubMed and Google Scholar for related literature through March 2021. We identified 14modeling 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……

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[33],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…... 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…..."

VERSION 3 – REVIEW

REVIEWER	Nagarajan, Karikalan
	ICMR-National Institute for Research in Tuberculosis

REVIEW RETURNED	31-May-2021

GENERAL COMMENTS	The authors have addressed all the major queries raised and improved the quality of the manuscript. I consider this as acceptable.