Time is of the essence: impact of delays on effectiveness of contact tracing for COVID-19

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Summary

Background

With confirmed cases of COVID-19 declining in many countries, lockdown measures are gradually being lifted. However, even if most social distancing measures are continued, other public health measures will be needed to control the epidemic. Contact tracing either via conventional methods or via mobile app technology is central to control strategies during de-escalation of social distancing. It is therefore essential to identify key factors for a contact tracing strategy (CTS) to be successful.

Methods

We evaluated the impact of timeliness and completeness in various steps of a CTS using a stochastic mathematical model with explicit time delays between time of infection, symptom onset, diagnosis by testing, and isolation. The model also includes tracing of close contacts (e.g. household members) and casual contacts with different delays and coverages. We computed effective reproduction numbers of a CTS (R_{cts}) for a population with social distancing measures and various scenarios for isolation of index cases and tracing and quarantine of its contacts.

Findings

In the best-case scenario (testing and tracing delays of 0 days and tracing coverage of 100%) the effective reproduction number will be reduced with 50% from 1.2 (with social distancing only) to 0.6 (R_{cts}) by contact tracing. A testing delay of 3 days requires tracing delay or

coverage to be at most 1 day or at least 80% to keep R_{cts} below 1, with the R_{cts} reduction being 15% and 17%, respectively. With a testing delay of 4 days, even the most efficient CTS cannot reach R_{cts} values below 1. The effect of minimizing tracing delay (e.g., with app-based technology) declines with declining coverage of app use, but app-based tracing remains more effective than conventional contact tracing even with 20% coverage. The proportion of transmissions per index case that can be prevented depending on testing and tracing delay and isolation of index cases ranges from above 80% in the best-case scenario (testing and tracing delays of 0 days) to 40% and 17% with testing delays of 3 and 5 days, respectively.

Interpretation

Minimizing testing delay is of key importance for the effectiveness of CTS. Optimizing testing and tracing coverage and minimizing tracing delays, for instance with app-based technology further enhances effectiveness of CTS, with a potential to prevent up to 80% of all transmissions. The process of conventional contact tracing should be reviewed and streamlined, while mobile app technology may offer a tool for gaining speed in the process.

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Research in context

Evidence before this study

As of 8 May 2020, the novel coronavirus (SARS-CoV-2) has spread globally and has caused more than 263,000 confirmed deaths of COVID-19 worldwide. In the absence of effective medicines and vaccines, many countries have implemented strict measures of social distancing, thereby reducing transmission and bringing the epidemic under control. For lifting these measures, adequate tools are needed to deal with possible newly arising transmission clusters. Strategies including isolation of confirmed and suspected cases, and identification and quarantining of their contacts are considered a key part of the response during de-escalation of social distancing. As a substantial portion of transmission may occur before the onset of symptoms and before cases can be isolated, it is unclear how successful contact tracing strategies (CTS) can be in reducing onward transmission.

Added value of this study

We performed a systematic analysis of the various steps required in the process of testing and diagnosing an index case as well as tracing and isolation possible secondary cases of the index case. We then used a stochastic transmission model which makes a distinction between close contacts (e.g. household members) and casual contacts to assess which steps and (possible) delays are crucial in determining the effectiveness of CTS. We evaluated how delays and the level of contact tracing coverage influence the effective reproduction number, and how fast CTS needs to be to keep the reproduction number below 1. We also analyzed what proportion of onward transmission can be prevented for short delays and high contact tracing coverage. Assuming that around 40% of transmission occurs before symptom onset, we found that keeping the time between symptom onset and isolation of an index case short (<3 days) is imperative for a successful CTS. This implies that the process leading from symptom onset to receiving a positive test should be minimized by providing sufficient and easily accessible testing facilities. In addition, reducing contact-tracing delays also helps to keep the reproduction number below 1.

Implications of all the available evidence

Our analyses highlight that CTS will only contribute to containment of COVID-19 if it can be organised in a way that time delays in the process from symptom onset to isolation of the index case and his/her contacts are very short. The process of conventional contact tracing should be reviewed and streamlined, while mobile app technology may offer a tool for gaining speed in the process.

Introduction

As the first wave of the SARS-CoV-2 has reached its peak of cases in many countries, societies are preparing so-called exit-strategies from the COVID-19 lockdown, while still successfully controlling transmission. Contact tracing, in combination with testing and quarantine or isolation of the contacts, is considered a key component in a phase when lockdown measures are gradually lifted[1-8] This requires upscaling of conventional contact tracing capacity. The potential of mobile apps to support contact tracing is widely discussed and such technology has been used in several Asian countries that have successfully reduced case numbers[9-14]. Yet, many uncertainties remain on the optimal process of contact tracing with conventional methods and/or mobile applications, on the timing of testing for current or past infection, and on the required coverage of contact tracing needed. As a result, predicting the effects of contact tracing, and predicting whether and at which level of virus circulation contact tracing can sufficiently control remaining transmission is difficult.

Modelling studies have demonstrated how mobile applications can increase effectiveness of contact tracing, compared to conventional approaches for contact tracing, but effectiveness depends on what proportion of the population will use the app consistently and for a sufficiently long period of time[9].

In previous work, we have investigated the impact of timeliness and completeness of case reporting for the effectiveness of surveillance and interventions[15-17], and we quantified the timeliness of contact tracing of infected passengers during an airline flight for the 2009 pandemic influenza[18]. In all of these studies, the timing of various steps in the monitoring and intervention chain emerged as one of the key factors for effectiveness of a public health response. Usually, there are identifiable delays in the response chain that may be critical to the overall effectiveness of a strategy.

Here we analyze in detail the process chain of identifying index cases by symptom-reporting followed by testing, and subsequent contact tracing, with the aim to inform policy makers on the relative importance of key steps in the process. We use a mathematical model that reflects the various steps and delays in the test and contact tracing process to quantify the impact of delays on the effective reproduction number and the fraction of onward transmission prevented per diagnosed index case[5,19].

Time delays in contact tracing

Our starting point is an assumed effective reproduction number (R_e) for COVID-19 of around 1, describing a situation with “social distancing but measures lifted to some extent”. We then quantify the relative contribution of the individual components of a contact trace strategy (CTS) required to bring and maintain the effective reproduction number with CTS (R_{CTS}) to a value below 1. For simplicity we do not include transmission in healthcare settings.

We break down the process of contact tracing in two different steps (Table 1 and Figure 1).

- An index case acquires infection (at time T_0), then after a short latent period becomes infectious (at time T_1), and finally symptomatic (at time T_2), which is here defined as “being eligible for testing”. Subsequently a proportion of all symptomatic subjects gets tested and diagnosed (at time T_3). The time between T_2 and T_3 is called the “testing delay” ($D_1 = T_3 - T_2$), and may vary between 0 and 5 days, and in this period individuals might self-quarantine. We refer to the proportion of all symptomatically infected subjects that is tested as testing coverage and vary it from 20% to 100%. After being diagnosed, we assume index cases are quarantined with no further transmission.

- The second step is tracing contacts of the index, which occurs at time T_4. A fraction of those contacts will be quarantined, with effectiveness ranging from 0%-100%. For simplicity we assume that contacts in quarantine do not spread. The time between T_3 and T_4 is the “tracing delay” ($D_2 = T_4 – T_3$), which may range from 0 (for instance with app technology) to 4 days (with conventional approaches). In this step, tracing coverage is defined as the proportion of contacts detected, which either depends on the capacity of conventional approaches (ranging from 40% to 80%) or on the fraction of the population using suitable app technology for screening (ranging from 40% to 80%).

Figure 1: Schematic of the contact tracing process and its time delays.

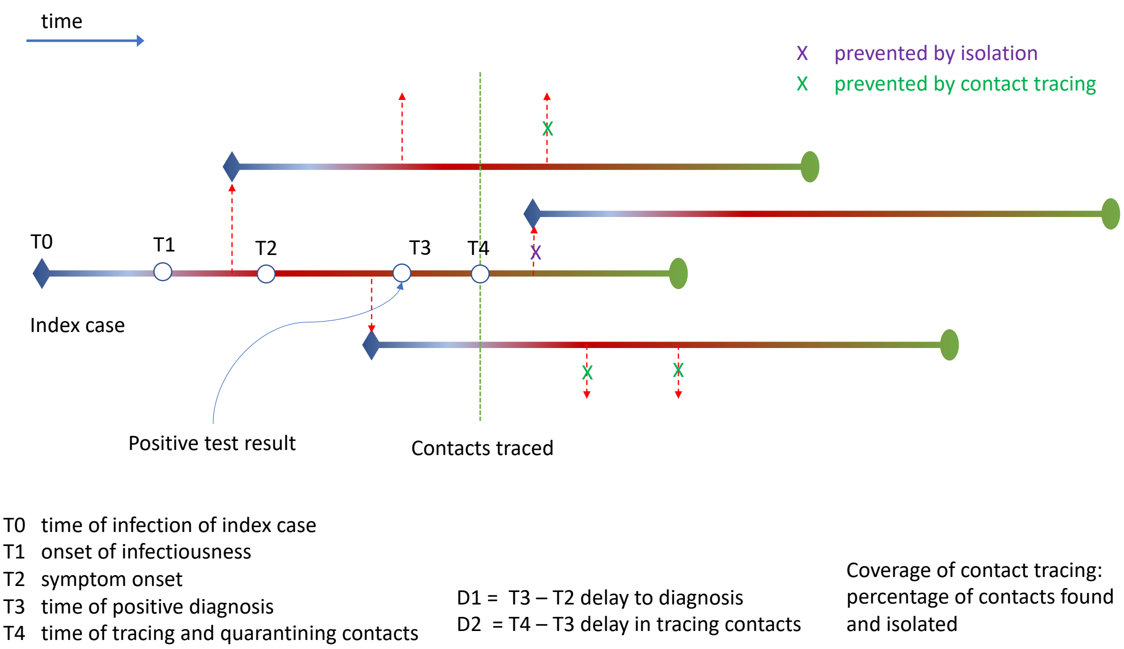


Table 1: Time delays in the test and contact tracing process (see also Figure 1).

Time	Event	Comments	Model implementation
T_0	the time of infection of the index case	Not observed	Start of the latent period, which lasts 1-3 days.
T_1	Time the index case becomes infectious	Proportion of pre-symptomatic transmission may range from 0% to 40% of all transmissions	After 1-3 days after infection, the infectious stage starts, which lasts 10 days with variable infectiousness. About 40% of transmission takes place in the first 2 days of infectiousness[25].
T_2	Time that the index (case) becomes	T_0 until T_2 reflects the time window in which prevention is not possible with CTS	The incubation period in the model is taken in agreement with published literature[21].

	symptomatic, and eligible for testing		
T_3	Time that index (case) is tested positive	T_2 until T_3 is the testing delay, which may range from 0-5 days The proportion being tested varies from 0-100% During this period we expect subjects to self-quarantine, with effectiveness ranging from 0%-100%	After a testing delay D_1 after symptom onset, an individual receives a positive test result and gets isolated. If an individual self isolates immediately, D_1=0. After isolation, no transmission takes place.
T_4	Time that contacts of index case are traced and quarantined.	T_3 until T_4 is the tracing delay, which may range from 0 (for instance with app technology) to 4 days (with current GGD approach). Here we can also vary the proportion with short post-test-delay (those with apps) and not.	After a tracing delay D_2, contacts of the index case are traced and isolated. D_2 and the tracing coverage (proportion of contacts found and isolated) may differ between close and casual contacts. If household contact self-isolate immediately with the index case, it means that D_2=0 and coverage 100% for close contacts. For simplicity we assume that contacts in quarantine do not spread.

The best-case scenario is that all eligible for testing are immediately tested (coverage 100%) with a very fast test result (test-delay 1 day), followed by immediate tracing (trace delay 0 days) of all contacts (coverage 100%), that immediately adhere to quarantine measures. More realistic scenarios include testing and tracing delays, with suboptimal testing and tracing coverages and suboptimal adherence to quarantining and testing.

Impact on effectiveness on population level

To analyse the impact of these time delays on the effectiveness of contact tracing we use a model first described in Kretzschmar et al[19], which was recently adapted for SARS-CoV-2[5]. The stochastic model describes an epidemic in its early phase as a branching process. Starting from a small set of initially infected individuals, the model calculates the numbers of latently infected persons, infectious persons, and persons that are diagnosed and isolated in time steps of one day. Latent infection, infectivity during the infectious period, and daily contact rates are quantified using distributions taken from published data.[20-24] We distinguish between close contacts (e.g. household contacts, but also other high-risk contacts) and casual contacts, which differ in the risk of acquiring infection from the index case. Also, the time required for tracing and quarantining contacts and the coverage of tracing may differ between these types of contacts and between different CTS (i.e., conventional contact tracing versus mobile app supported contact tracing). Intervention effectiveness is determined by the daily probability of an index case being diagnosed by testing during the infectious period, and depends on various delays in the process of tracing household and non-household contacts, respectively, and on the proportions of contacts that can be traced and isolated (see Figure 1). We assume that isolation is perfect, i.e. that isolated persons do not transmit any longer. The model is described by a set of difference equations, and allows for explicit computation of the basic reproduction number R_0, the effective reproduction number under social-distancing interventions R_e and the effective reproduction number with CTS (R_{cts}). The model was coded in Mathematica 12.1.

Parameter settings

We assumed that without social distancing individuals have on average 4 close contacts per day and around 9 casual contacts per day, with certain stochastic variability. The distributions were fitted to data from the Polymod study[23]. Transmission probability per contact for close contacts was taken to be 4 times higher than for casual contacts. Symptomatic and asymptomatic cases were assumed to be equally infectious. Overall, the transmission probability was calibrated to a basic reproduction number of $R_0 = 2.5$. For the social distancing, we assumed that close contacts were reduced by 40% and casual contacts by 70%. The resulting effective reproduction number was $R_e = 1.2$. Without further interventions, the doubling time of the epidemic would be around 19 days.

Scenarios modelled

We analyzed the impact of various testing and tracing delays and tracing coverage on the effective reproduction number R_{cts} while keeping the testing coverage at 100%. For comparison, we also considered the strategy where symptomatic individuals get tested and isolated, without subsequent tracing (R_{iso}). We varied the testing delay D_1 between 0 and 7 days, the tracing delay D_2 between 0 and 3 days, and tracing coverages between 0% and 100%. Tracing delays and coverages were allowed to differ between close contacts and casual contacts.

We then compared the effectiveness of conventional CTS with a scenario that reflects mobile app technology for alerting subjects to be tested and for tracing contacts. Differences between these strategies were taken as follows. The testing delay (D_1) is reduced with app technology. With conventional CTS symptomatic individuals need to decide to seek health care to get tested, and we assume that with app technology symptomatic subjects get alerted and can be tested without health care interference, for instance in specific test facilities for app users. For conventional CTS we assume suboptimal coverage in identifying contacts from the week before diagnosis by testing due to recall bias, especially for casual contacts. For CTS with mobile app technology we assume 100% tracing coverage of the proportion of subjects using app technology. For simplicity we assume 100% compliance with quarantining. We assume that tracing goes back for 7 days before the positive test result. The exact parameter values for this comparison are shown in Table 2.

Next, we quantified the impact of coverage of testing and app use on the effectiveness of CTS. We varied the percentage of app users in the population between 20% and 80%. We first considered the situation that testing is provided for 100% of persons with symptoms independent of app use, and app use only influences the fraction of contacts that are traced. Alternatively, we considered the situation that only app users with symptoms are tested (i.e. testing coverage varies between 20% and 80%) and coverage of tracing also depends on fraction of app use, i.e. varies as the testing coverage.

Finally, we quantified the fraction of transmissions of an index person that can be prevented, and the contribution to the fraction prevented from isolation and from tracing contacts with decreasing delays. The number of onward transmissions of an index case is by definition described by the effective reproduction number of the realized scenario. Therefore, the difference of reproduction numbers between two intervention scenarios under the condition that an index case is diagnosed, will describe the fraction of onward transmissions prevented.

For contact persons, this is the fraction of the total infectivity that lies after the time of isolation, i.e. the part of infectiousness that is prevented by contact tracing. In other words, a contact person who is detected and isolated before the start of his infectious period is a fully prevented transmission, while a contact person who is only traced and identified after 70% of his infectivity has passed, is counted as 0.3 of a prevented onward transmission.

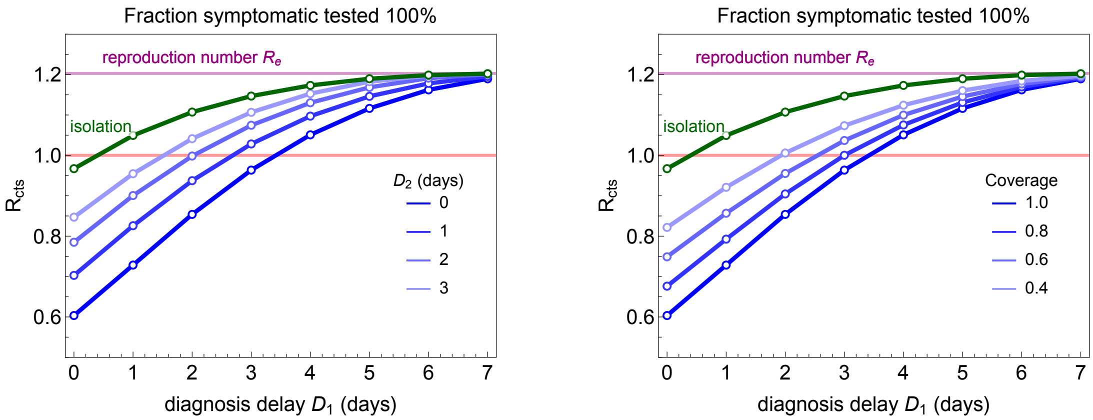
Table 2: Comparison Conventional CT and Mobile app CT

	Conventional CT	Mobile app CT
Testing coverage	100%	100%
Time to (self)-isolation (D_1)	4 days	0 day
Time to trace close contacts (D_2)	3 days	0 day
Time to trace other contacts	3 days	0 day
Tracing coverage close contacts	80%	100%
Tracing coverage casual contacts	50%	100%
Time traced back	7 days	7 days

Results

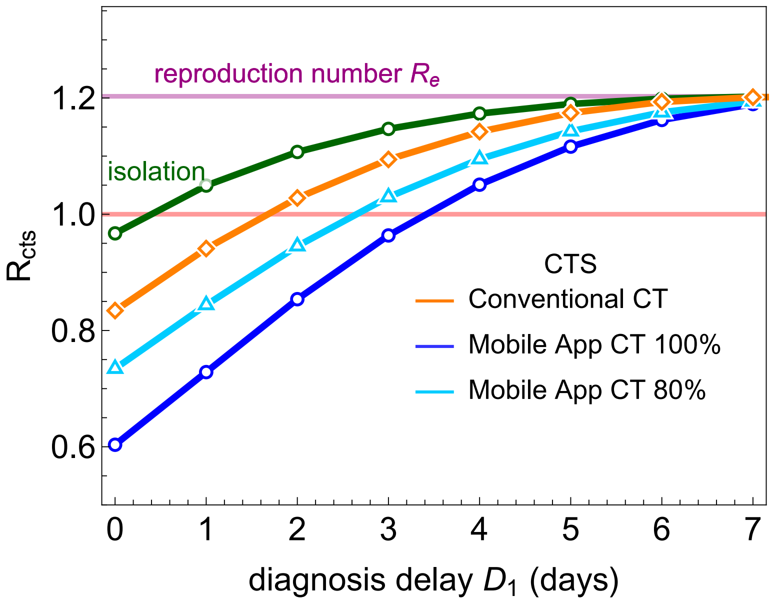
In the best-case scenario, if all infectious persons that develop symptoms are tested and isolated within 1 day after symptom onset the effective reproduction number R_e will decline from 1.2 to R_{iso} = 0.97, without contact tracing (Figure 2). Contact tracing will further decrease the reproduction number to R_{cts}=0.6 in the best case. In the optimal scenario – a testing delay of 0 days and a tracing delay of 0 days and a tracing coverage of 100%, the additional reduction of R_{cts} is 50%. Yet, with a diagnosis delay of 3 days, tracing delay or tracing coverage should be at most 1 day or at least 80% to keep R_{cts} below 1. In these scenarios the reduction of R_{cts} compared to the best-case scenario is 15% and 17%. With a testing delay of 4 days, even the most efficient contact tracing cannot reach R_{cts} values below 1.

Figure 2: Impact of contact tracing on the effective reproduction number depending on various delays and tracing coverages. In these analyses, 100% of those who develop symptoms get tested. For comparison the reproduction number R_{iso} with only isolation of index cases without contact tracing is plotted (green). (A) Influence of varying tracing delay D_1 on the x-axis. The curves plotted in blue show varying tracing delays D_2; (B) Here the tracing coverage is varied in the curves plotted in blue, while there is assumed to be no delay in tracing the contacts.



We assumed that conventional CTS has longer tracing delay and lower tracing coverage than CTS based on app technology which results in marked differences in R_{cts} for the whole range of testing delay (Figure 3). With conventional CTS, R_{cts} would remain above 1, if the testing delay exceeds 2 days, whereas contact tracing based on app technology could still keep R_{cts} below 1, as long as testing and tracing coverage would be at least 80%. If the testing delay reaches 5 days or more, app technology adds little effectiveness to conventional CTS or just isolating symptomatic cases.

Figure 3: Comparison of a conventional and mobile app CTS. For parameter values, see table 2. We assumed that ascertainment is 100% for the conventional CTS and 100% and 80% for the mobile app CTS.



The reductions of R_e (based on social distancing) achieved by isolation only, conventional CTS, and mobile app-based CTS is shown in figure 4. For isolation only and for conventional CTS we assumed a delay of 4 days between symptom onset and isolation of the index case. The relative reductions are independent of the level of R_e, as there is a linear relationship between the various reproduction numbers. Conventional CTS, even if applied for all infected subjects with symptoms is 45% less effective than mobile app-based CTS, due to longer tracing delays and lower tracing coverage.

The effectiveness of app-based technology declines with lower fractions of persons using it (Figure 5). Yet, it remains more effective than conventional contact tracing even with 20%

coverage, due to its inherent speed. In Figure 5a we assume that all symptomatic persons get tested, and then vary coverage of app use. In Figure 5b, we assume that only app users who develop symptoms get diagnosed, and that only app users get traced and isolated. Even with low coverage there is a reduction of R_e, due to fast tracing of a small part of te population. Depending on R_e, such an approach might be sufficient to reduce R_{cts} to levels below 1.

In Figure 6, we quantified proportions of transmissions per index case that can be prevented depending on testing delay, as well as the contributions of isolation of index cases and tracing of contacts. In the best-case scenario (testing and tracing delay being 0 days) more than 80% of transmissions can be prevented if coverage of infected persons being tested is 100%.

Figure 4: The reduction of the effective reproduction number for various CTS. The reproduction number with CTS, R_{cts}, is shown as a percentage of the reproduction number where only social distancing is implemented (R_e). For the isolation scenario and conventional tracing scenario we assumed that there is a delay of 4 days between symptom onset and isolation of the index case.

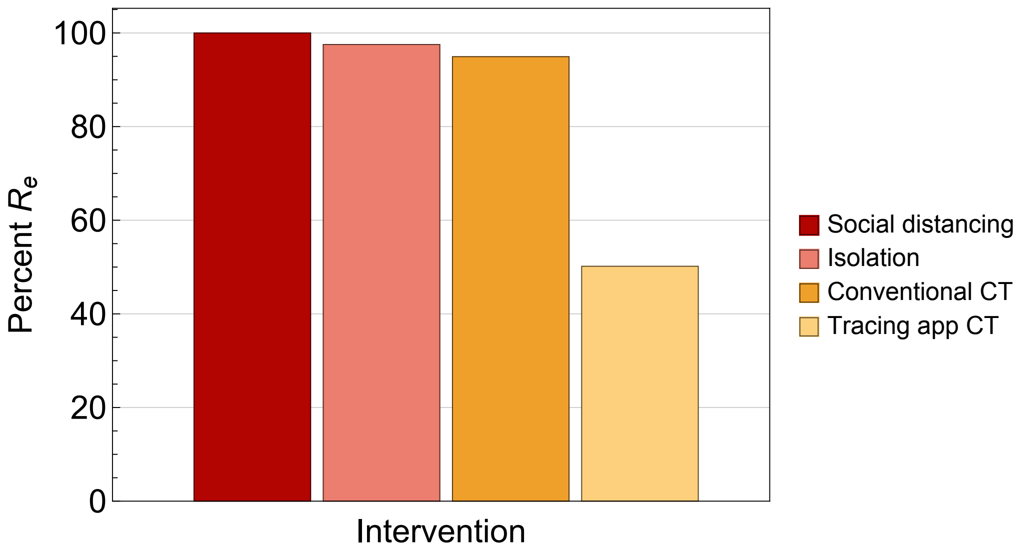
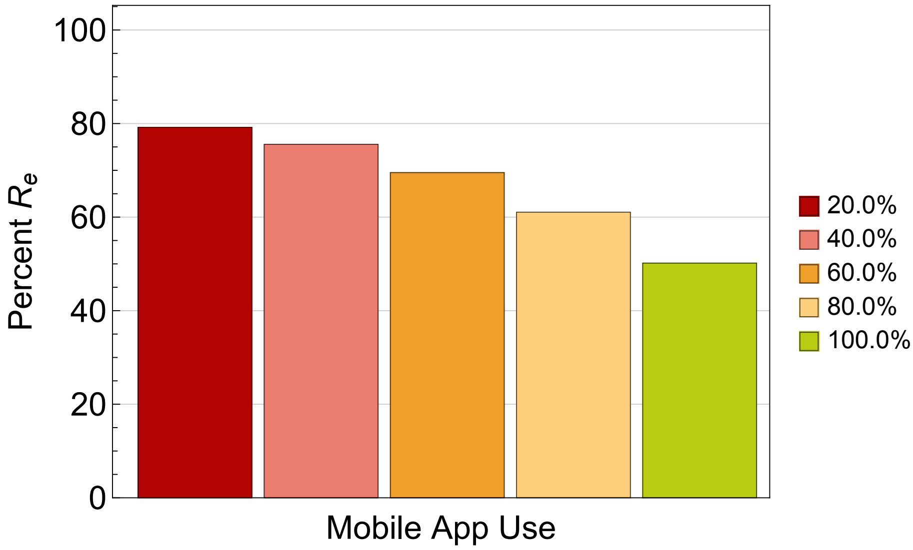


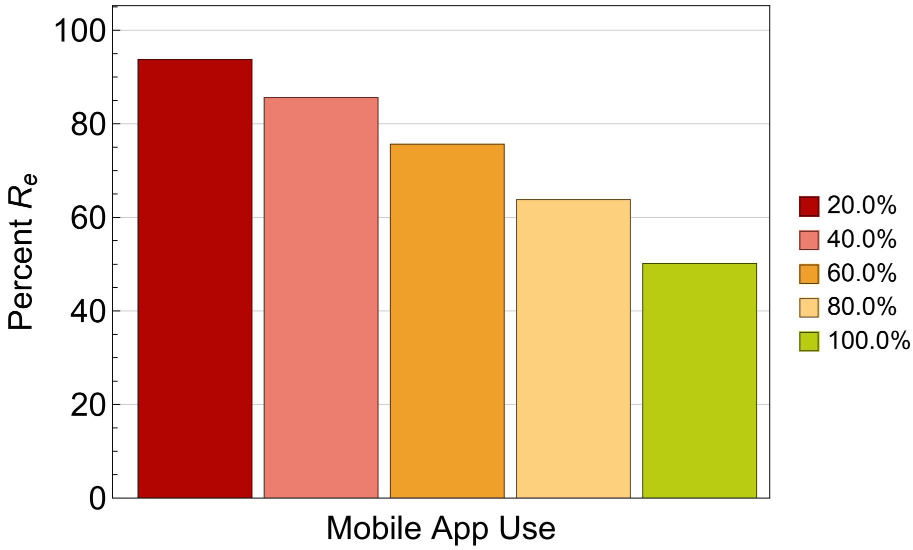
Figure 5: The impact of mobile app use on R_{cts} for varying levels of app use. In (A), we assume that there is also testing of those who do not use the mobile app, so app use only is used for tracing contacts. In (B), only app users, who develop symptoms, are tested.

(A)



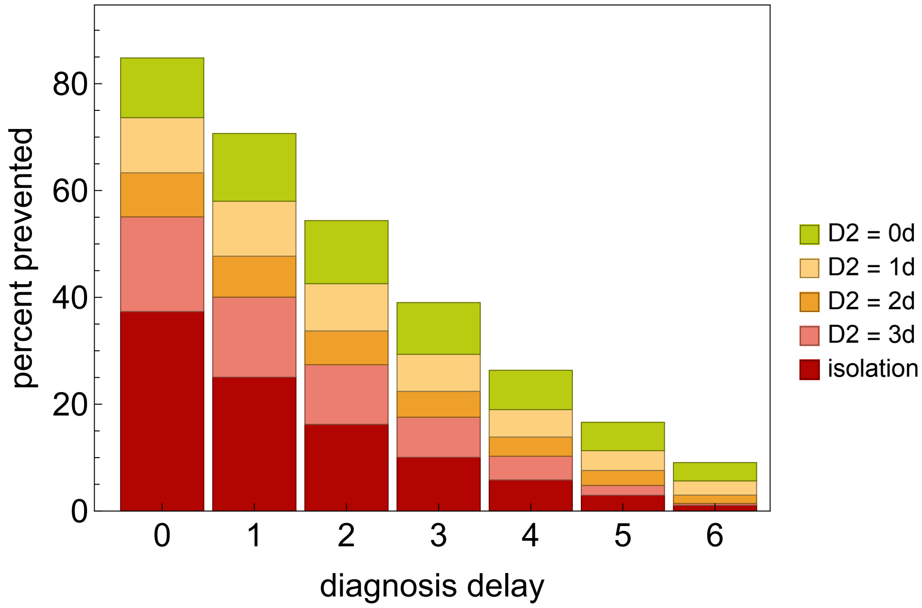
100
80
60
40
20
0
Percent R_e
Mobile App Use
20.0%
40.0%
60.0%
80.0%
100.0%

(B)



100
80
60
40
20
0
Percent R_e
Mobile App Use
20.0%
40.0%
60.0%
80.0%
100.0%

Figure 6: The fraction of onward transmissions prevented by isolation of the index case and his/her infected contacts. The fraction prevented by contact tracing increases with decreasing tracing delay.



Discussion and conclusions

Using a mathematical model that describes the different steps of the CTS for COVID-19 we have quantified the relevance of delays and coverage proportions for controlling transmission of SARS-CoV-2. Based on these analyses we conclude that reducing the testing delay, i.e. shortening the time between symptom onset and test positivity, is the most crucial step. Reducing the tracing delay, i.e. shortening the time of contact tracing, may further enhance the effectiveness of CTS. Yet this additional effect rapidly declines with increasing testing delay. Naturally, the effectiveness of CTS increases when proportions of index subjects detected and contacts traced increase as well. CTS has huge potential to control virus transmission, and thus to alleviate other control measures, but only if all delays are maximally reduced.

There are several obvious factors that can reduce the effectiveness of CTS, such as a large proportion of infectious subjects that remain asymptomatic or are otherwise not ascertained and a large proportion of contacts that cannot be traced. The latter implies that the potential benefits of using app-based technology for contact tracing requires participation of a substantial proportion of the population. Also, app use needs to continue over a long time period, so required continued adherence of app users. Low proportions of participation do not render CTS useless, however, because it could help to locally extinguish clusters before they grow larger. Also, for this purpose, the timeliness and completeness of CTS in local populations should be high to make it successful.

The strength of the approach is that it explicitly takes many details of the contact tracing process into account, such that the key factors can be identified. A limitation of our approach is that it does not take population age-structure into account, which may influence the proportion of asymptomatic cases and the mobile app use coverage. Also, the willingness of an index case or contact person to self-isolate may be different in different age groups. We have also assumed homogeneous mixing of the population, and homogeneous distributed use of app technology for the different coverage levels. Yet, clustering of non-users may have consequences for overall effectiveness of CTS, similar to clustering of non-vaccinated subjects. This is an important aspect to be addressed in subsequent work. The model also ignores that some contacts of the index case may have symptoms before they are traced by CTS. As these contacts may already self-isolate, this lowers the benefits of contact tracing.

Our finding of the crucial importance of the first step of CTS, establishing a diagnosis in subjects with symptoms, has important consequences. It requires an infrastructure for testing, that allows subjects with symptoms to be tested, preferably, within one day of symptom onset. Studies have demonstrated that viral shedding in the respiratory tract is highest at the start of symptoms[25], so early testing will also increase the sensitivity of this approach. To further enhance effectiveness, as many infectious subjects need to be tested, which requires a low threshold for testing. As the clinical symptoms of COVID-19 are mostly mild and heterogeneous, many subjects should be eligible for testing, resulting in a large proportion of subjects with negative test results. Future work should determine the optimal balance between the proportion of test-negatives and the effectiveness of CTS. In our country, testing of ambulatory subjects is coordinated by the public health services and general practitioners. That infrastructure may introduce a considerable delay in testing. To optimize the effectiveness of CTS a different infrastructure with direct access of symptomatic subjects to testing facilities should be considered. Finally, laboratories should be prepared to deliver high-throughput rapid testing.

Our findings also provide strong support to optimize contact tracing. In our country this is now based on establishing a contact between public health officers and index patients, followed by an interview after which contacts are traced. This procedure is labor intensive, time consuming, prone to recall bias and usually takes several days. Optimizing this process with app technology, or any other method achieving the same goal of minimizing tracing delay, will be needed to establish optimal control of transmission. An important advantage of app-based technology is the possibility of performing multiple step tracing, as not only the first-line contacts can be traced, but also their (second-line) contacts and so on. Naturally, the number of contacts than rapidly increases, which increases the number of both correctly and unnecessarily quarantined subjects. Further work will focus on finding an optimal balance for this aspect. In fact, our findings suggest that optimized CTS, with short delays and high coverage for testing and tracing could reduce the reproduction number by 50%, which would allow alleviation of most of the currently implemented control measures.

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