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Isolation and Contact Tracing Can Tip the Scale to Containment of COVID-19 in Populations With Social Distancing

Supplementary Appendix

Our analyses are based on a model first developed for ring vaccination for smallpox (Kretzschmar et al., 2004), which we adapted to describe the spread of COVID-19 with isolation and contact tracing (Kretzschmar et al., 2020a). The model describes transmission with a discrete time branching process, and keeps track of numbers of latent and infectious individuals, numbers of diagnosed cases, and numbers of isolated infected individuals. The model distinguishes between close contacts (e.g. in the household) and other non-household contacts. Figure 1 of the main text gives a schematic overview of transmission and contact tracing in the model.

We use the following notation:

- $E_{t,\tau}$ is the number of persons infected at time $t-\tau$, who are still latently infected (i.e. infected but not yet infectious) at time t.
- $I_{t,\tau}$ is the number of persons who became infectious at time $t-\tau$, who are still infectious and not isolated at time t.
- $Q_{t,\tau}$ is the number of persons who because infectious at time $t-\tau$, who are in isolation at time t.
- D_E is the maximum duration of the latent period. The default value is 3 days.
- D_I is the duration of the infectious period (including persons in isolation). The default value is 10 days, with variable infectivity over the course of the infectious period. See below for details.

The time dynamics of the model is implemented as a set of difference equations with a time step of 1 day. In this study, we did not use time dependent simulations, therefore we will not describe the time dependent model further. A precise formulation of the equations for the time dependent model can be found in Kretzschmar et al. (2004), and some results for the time dependent evolution of an COVID-19 outbreak are given in our earlier manuscript (Kretzschmar et al., 2020b).

A.1 Natural history of infection

The probability of moving from the latent to the infectious state on day τ of the latent period is given by $P_I(\tau)$ ($\tau = 1, ..., D_E$.). Throughout, we take $D_E = 3$ and

$$P_I(\tau) = \begin{cases} 0.5 & \text{if } \tau = 1 \\ 0.7 & \text{if } \tau = 2 \\ 1.0 & \text{if } \tau = 3\,. \end{cases} \tag{S1}$$

This means that after day 1 of the latent period, 50% of all infecteds become infectious, after day 2 a total of 85% have become infectious, and after day 3, 100% have entered to infectious state. The average

duration of the latent period is therefore (0.5 x 2) + ((1-0.5) x 0.7 x 3) + ((1-0.5) x (1-0.7) x 4) = 2.65 days. The probability of transmission upon contact on day τ of the infectious period $P_T(\tau)$ was modelled in a similar vein with a discretized Gamma distribution with parameters estimated from published data (see Table 1 of the main text). With these parameters, infectivity peaks around 5 days after infection, and about 43.7% of transmission occurs before symptom onset. The probability of developing symptoms on day τ of the infectious period $P_S(\tau)$ was modelled with a discretized Lognormal distribution (He et al., 2020; Ashcroft et al., 2020) (see Table 1 of the main text). Here, we made the additional assumption that 20% of infected persons never develop symptoms (Mizumoto et al., 2020; Buitrago-Garcia et al., 2020). Details of the estimation procedure are given in the Supplementary Information of our earlier study (Kretzschmar et al., 2020a).

A.2 Contact distributions

For household contacts we assume that the number of contacts per day follows a Poisson distribution with mean $\mu_1 = 2.15$. For non-household contacts, we assume that the number of contacts per day is distributed according to a negative binomial distribution with parameters n and p. We denote the mean of this distribution by μ_2. We chose these parameters such that the total mean daily contact number $\mu_1 + \mu_2$ and its standard deviation are approximately equal to the daily number of contacts (13.85) and standard deviation (10.54) reported for the Netherlands in the Polymod study (Mossong et al., 2008).

For the transmission process, it is possible that contact persons are already infected at some point during the infectious period of the index case. To account for the probability of a contact person still being susceptible at day τ of the infectious period of the index case, we defined the saturation functions S_h and S_c for household and non-household contacts as follows

$$S_h(\tau) = \prod_{i=1}^{\tau-1} (1 - P_T(i)) \tag{S2}$$

and

$$S_c(\tau) = \prod_{i=1}^{\tau-1} (1 - qP_T(i)) \,, \tag{S3}$$

where q denotes the reduction factor of transmission in non-household contacts as compared to household contacts.

Furthermore, contact numbers can be reduced in a scenario with physical distancing. This is implemented in the model by applying a reduction factor to the means of the distributions. If these factors are denoted by r_h and r_c for household and non-household contacts, the means of the contact number distributions for a physical distancing scenario will be $r_h\mu_1$ and $r_c\mu_2$. If for example $r_h = 0.2$, we say that the number of close contacts is reduced by 80%. In summary, the number of contacts per day of the infectious period is described by a random variable $C(\tau) = C_1(\tau) + C_2(\tau)$, where

$$C_1(\tau) \sim Poisson\left(r_h\mu_1 S_h(\tau)\right) \tag{S4}$$

and

$$C_2(\tau) \sim NegBin\left(r_c n S_c(\tau), p\right) \,. \tag{S5}$$

Here *NegBin* denotes the negative binomial distribution. In the following, $\mu_1(\tau) = r_h\mu_1 S_h(\tau)$ and $\mu_2(\tau) = r_c(np/(1-p))S_c(\tau)$ are used to denote the mean number of contacts on day τ of the infectious period.

A.3 Basic reproduction number

The basic reproduction number for our model can be calculated explicitly (see Diekmann et al. (2013)), and it is given by

$$R_0 = \sum_{\tau=1}^{D_I} (\mu_1(\tau)P_T(\tau) + \mu_2(\tau)qP_T(\tau)) \ , \tag{S6}$$

where q is the factor by which non-household contacts are less transmissible than household contacts. In addition, we denote by $R_0(\tau)$ the number of secondary cases produced on day τ of the infectious period, which is given by the summand in the above equation. Using $R_0(\tau)$, the proportion of onward transmission generated up to day τ of the infectious period is written as follows

$$\rho(\tau) = \frac{1}{R_0} \sum_{i=1}^{\tau} R_0(i) \ . \tag{S7}$$

A.4 Diagnosis, isolation, and contact tracing

The process of diagnosis, isolation, and tracing of contacts is shown schematically in Figure A1. The probability of diagnosis depends on the probability of developing symptoms. However, there can be a delay D_1 between symptom onset and diagnosis. Therefore, the probability of being diagnosed per day of the infectious period is given by $P_D(\tau) = 0$ for $\tau < D_1$, and $P_D(\tau) = P_S(\tau - D_1 + 1)$ for $D_1 \leq \tau \leq D_I$. If not everybody who develops symptoms is tested, the probability of diagnosis is reduced by a factor f_t, which represents the fraction of symptomatic persons who get tested. If, for example, only persons who are using a mobile tracing app get tested, the fraction f_t represents the proportion of the population using the app. In summary

$$P_D(\tau) = \begin{cases} 0, & \text{if } \tau < D_1 \\ f_t P_S(\tau - D_1 + 1) & \text{if } D_1 \leq \tau \leq D_I \ . \end{cases} \tag{S8}$$

The probability that an infected contact person is traced and isolated depends on this person's infector being diagnosed. For a contact person who is infected on day τ of this person;s infector's infectious period, we can compute the probability that the infector is diagnosed on day $\tau + i$ of the infectious period. Tracing then occurs on day $\tau + i + D_2$, where D_2 is the delay between isolation of the index case and successful tracing and isolation of the infected contact person. We assume that tracing is performed within a time window of length w, i.e. contacts that the index case had in the time interval $[\tau + i - w, \tau + i]$ will be identified and traced. On day $\tau + i + D_2$, contacts in the time window $[\tau + i + D_2 - w, \tau + i + D_2]$ can be identified and tested, and if they are infected will be isolated. The proportion of these contacts that are successfully isolated is called the tracing coverage and is denoted by C. This implies that the probability to be traced and isolated for a contact infected on day τ of the index case's infectious period is given by

$$P_{ct}(\tau) = \sum_{i=\tau}^{Min(D_I, \tau+w)} C\phi(i)P_D(i) \ , \tag{S9}$$

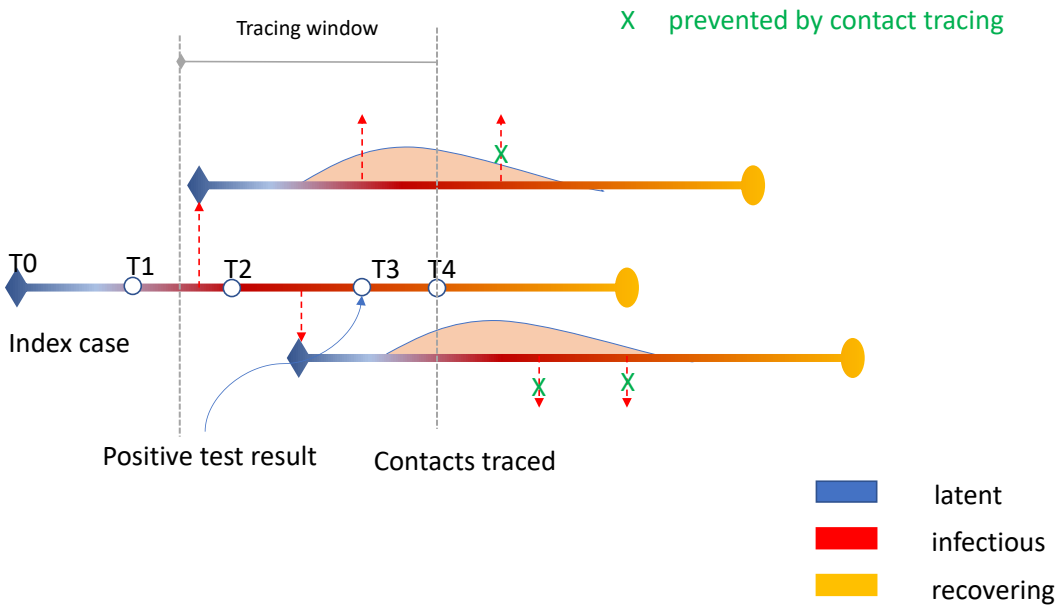

Figure A1. *Schematic of the infection time line of an index case, and cases prevented by contact tracing. The red area under the curve represents the probability distribution of onward transmission of the infected contacts. The part of the distribution to the right of the dashed line marked "contacts traced" can be prevented by isolating these contacts. For explanations of the time points $T_0, ..., T_4$ see Table A1.*

where

$$\phi(\tau) = \prod_{i=1}^{\tau-1}(1 - P_D(i)) \tag{S10}$$

is the probability that an infected index case is not yet diagnosed on day τ of the infectious period.

An infected contact person may already have infected others at the moment they are traced and isolated. This means that we may only prevent a fraction of the potential onward transmissions of that contact person. To account for that, we introduced a weighting function $\lambda(\sigma)$, that describes the fraction of onward transmission that has occurred on day σ after infection of the contact person. Here σ can run from 1 to $D_I + w$, because the moment tracing of a contact person takes place can be from 1 day after infection up to $D_I + w$ days after infection. The latter occurs when the contact person was infected on the first day of the index case's infectious period, the index case was diagnosed on the last day of his infectious period, and the tracing delay equals the window period. If the tracing delay is longer than the window period, no contacts will be traced.

The proportion of onward transmissions an infected contact person has already generated on day σ since acquiring infection can be computed as

$$\lambda\left(\sigma\right) = \sum_{i=1}^{D_E}\prod_{j=1}^{i-1}(1 - P_I(j))P_I(i)\rho(\sigma - i)\ , \tag{S11}$$

which implies that the proportion that can be prevented is $1 - \lambda(\sigma)$. A contact person, who is infected on day τ of the index case's infectious period, may be traced between $\tau + 1$ and $D_I + D_2$ days after that. If $D_I + D_2 - w < \tau$ the contact will be isolated.

Combining λ with the probability of diagnosis of the index case enables us to calculate the tracing probability as follows

$$\psi(\tau) = \sum_{i=\tau}^{D_I} \phi(i) P_D(i) C(1 - \lambda(\tau + i + D_2)) \, . \tag{S12}$$

Therefore, tracing the contact will decrease the effective reproduction number by a factor $1 - \psi(\tau)$. As delay and coverage may differ between household and non-household contacts, we distinguish between $\psi_h(\tau)$ and $\psi_c(\tau)$.

Table A1. Description of events during contact tracing.

Time	Event	Comments	Model implementation
$\mathbf{T_0}$	Time of infection of the index case.	Not observed	Start of the latent period, which lasts 1-3 days. Per day of the latent period, an infected person moves to the infectious period with a given probability.
$\mathbf{T_1}$	Time the index case becomes infectious.	Presymptomatic transmission may take place from time T_1 onwards.	After 1-3 days after infection, the infectious stage starts, which lasts 10 days with variable infectiousness. Between 33% and 50% of transmission takes place before symptoms onset (He et al., 2020).
$\mathbf{T_2}$	Time that the index case becomes symptomatic and eligible for testing.	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 (Li et al., 2020; He et al., 2020).
$\mathbf{T_3}$	Time that the index case is tested positive.	T_2 until T_3 is the testing delay, which may range from 0-7 days.	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.
$\mathbf{T_4}$	Time that contacts of the 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 3 days (with manual tracing).	After a tracing delay D_2, contacts of the index case are traced, and infected contacts are isolated. D_2 and the tracing coverage (proportion of contacts found and isolated) may differ between household and non-household contacts. If all household contacts self-isolate immediately with the index case, it means that $D_2 = 0$ and coverage is 100% for those contacts.

A.5 Effective reproduction numbers and critical tracing coverage

In the case where diagnosis and isolation is possible, the number of secondary cases is reduced. An infected person can only transmit to his contacts on day τ of the infectious period, if he has not been diagnosed and isolated on the previous days of the infectious period, which is given by $\phi(\tau)$. We then define the effective reproduction number with testing and isolation as

$$R_e = \sum_{\tau=1}^{D_I} (\mu_1(\tau) P_T(\tau) + \mu_2(\tau) q P_T(\tau)) \phi(\tau) \, . \tag{S13}$$

Similarly, if contacts of an infected person diagnosed at day τ of the infectious period are traced and isolated, the number of secondary infections is reduced. The main idea of how to calculate the impact of tracing on the reproduction number is the following: at the moment a contact person is infected, we can calculate the probability that the index case will be diagnosed at a later day of his infectious period, and the probability that the contact person will then be found and isolated. Therefore, we can compute by what fraction the onward transmission of the contact person is reduced by tracing and isolation. We here assume that tracing goes back within a time window of length w from the day of diagnosis of the index case. Contact persons who were already infected in a time interval w before diagnosis of the index case will be found and isolated after a delay D_2. At the point of isolation, a fraction $\lambda(\tau)$ of their onward transmissions have already occurred, i.e. only the remaining fraction $1 - \lambda(\tau)$ can be prevented. As explained above, this reduces the effective reproduction number by factors $\psi_h(\tau)$ and $\psi_c(\tau)$. This leads to the definition of the effective reproduction number with tracing as

$$R_e = \sum_{\tau=1}^{D_I} (\mu_1(\tau) P_T(\tau)(1 - \psi_1(\tau)) + \mu_2(\tau) q P_T(\tau)(1 - \psi_2(\tau))) \phi(\tau) \, . \tag{S14}$$

The critical tracing coverage C_{crit} is obtained by computing the smallest non-negative root of the equation

$$R_e = 1 \, , \tag{S15}$$

where C_{crit} enters the equation via the tracing probabilities $\psi(\tau)$. As our model is in essence stochastic, inidividual reproduction numbers can be defined and calculated by Monte Carlo simulations. These can be used to determined the variability of individual reproduction numbers and compare their distribution with the mean values presented here. For details see Kretzschmar et al. (2020a).

A.6 Exponential growth rate and doubling time

We denote by $\epsilon(\tau), \tau = 1, .., D_E$ the probability that an infected individuals moves to the infectious stage exactly on day τ of the latent period. We have

$$\epsilon(\tau) = \prod_{j=1}^{\tau-1} (1 - P_I(j)) P_I(\tau) \, , \tag{S16}$$

so that the exponential growth rate r can be calculated as root of the equation

$$1 = \sum_{j=1}^{D_E} \sum_{\tau=1}^{D_I} e^{-r(j+\tau)} \epsilon(j) (\mu_1(\tau) P_T(\tau) + \mu_2(\tau) q P_T(\tau)) \tag{S17}$$

(see Diekmann et al. (2013)).With the exponential growth rate at hand, the doubling time δ is subsequently computed as

$$\delta = \frac{ln(2)}{r} \,. \tag{S18}$$

Table A2. Description of variables and parameters.

Notation	Description	Note
P_I	Probability of becoming infectious per day of latent period	vector of length D_E
P_T	Probability of transmission upon contact per day of infectious period	vector of length D_I
P_S	Probability of symptom onset per day of infectious period	vector of length D_I
P_D	Probability of being diagnosed per day of infectious period	vector of length D_I
P_{ct}	Probability of contact being traced per day of infectious period of infector	vector of length D_I
$\mu_1(\tau), \mu_2(\tau)$	Mean daily number of contacts for close and casual contacts	vector of length D_I
S_h, S_c	Saturation factors describing reduction of susceptible contacts due to repeated contact	vector of length D_I
r_h, r_c	Reduction factors for physical distancing	fractions
q	Ratio of transmissibility between casual to close contacts	fraction
f_t	Fraction of population who gets tested	fraction
w	Tracing window period	integer (days)
C	Tracing coverage	fraction
$\phi(\tau)$	Probability of not being diagnosed by day τ	vector of length D_I
$\rho(\tau)$	Proportion of onward transmission by day τ	vector of length D_I
$\lambda(\sigma)$	Proportion of onward transmissions by day σ since acquiring infection	vector of length $D_E + D_I$
$\psi(\tau)$	Probability of being traced by day τ of the infectors infectious period	vector of length D_I
$\epsilon(\tau)$	Probability of becoming infectious on day τ of the infectious period	vector of length D_E
r	exponential growth rate	real (1/day)
δ	doubling time	real (days)

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