RESEARCH ARTICLE



Implication of backward contact tracing in the presence of

overdispersed transmission in COVID-19 outbreaks [version 1;

peer review: 2 approved]

Akira Endo¹⁻³,

Centre for the Mathematical Modelling of Infectious Diseases COVID-19 Working Group,

Quentin J. Leclerc^{1,3}, Gwenan M. Knight^{1,3}, Graham F. Medley^{3,4}, Katherine E. Atkins^{1,3,5}, Sebastian Funk^{1,3}, Adam J. Kucharski^{1,3}

¹Department of Infectious Disease Epidemiology, London School of Hygiene & Tropical Medicine, London, WC1E 7HT, UK ²The Alan Turing Institute, London, NW1 2DB, UK

³Centre for the Mathematical Modelling of Infectious Diseases, London School of Hygiene & Tropical Medicine, London, WC1E 7HT, UK

⁴Department of Global Health and Development, London School of Hygiene & Tropical Medicine, London, WC1E 7HT, UK ⁵Centre for Global Health Research, Usher Institute, University of Edinburgh, Edinburgh, EH16 4UX, UK

Reviewer Status 💙 🗸			
Invited Reviewers 1 n 1 1 report report report report report yof Warwick, Coventry, UK versity of Warwick, Coventry, UK ports and responses or comment can be found at the end of the an	s 2 eport ick, versity, ts on the rticle.		
	ver Status Invited Reviewer 1 n 1 20 report r rard Hill (D, University of Warw entry, UK rersity of Warwick, Coventry, UK rersity of Warwick, Coventry, UK rersity of Warwick, Coventry, UK roorts and responses or commen can be found at the end of the a		

Keywords

COVID-19, SARS-CoV-2, contact tracing, backward tracing, overdispersion



This article is included in the Coronavirus

(COVID-19) collection.

Corresponding author: Akira Endo (akira.endo@lshtm.ac.uk)

Author roles: Endo A: Conceptualization, Formal Analysis, Investigation, Methodology, Software, Visualization, Writing – Original Draft Preparation; Leclerc QJ: Investigation, Writing – Review & Editing; Knight GM: Writing – Review & Editing; Medley GF: Writing – Review & Editing; Atkins KE: Writing – Review & Editing; Funk S: Conceptualization, Supervision, Writing – Review & Editing; Kucharski AJ: Conceptualization, Supervision, Writing – Review & Editing

Competing interests: AE received a research grant from Taisho Pharmaceutical Co., Ltd.

Grant information: SF [210758] and AJK [206250] are supported by the Wellcome Trust. AE is financially supported by The Nakajima Foundation and The Alan Turing Institute. QJL is supported by Medical Research Council London Intercollegiate Doctoral Training Program studentship (grant no. MR/N013638/1). GMK is supported by UK Medical Research Council (grant: MR/P014658/1). GFM is supported by NTD Modelling Consortium by the Bill and Melinda Gates Foundation (OPP1184344). KEA is supported by European Research Council Starting Grant (Action number 757688).

The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Copyright: © 2020 Endo A *et al*. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

How to cite this article: Endo A, Centre for the Mathematical Modelling of Infectious Diseases COVID-19 Working Group, Leclerc QJ *et al.* Implication of backward contact tracing in the presence of overdispersed transmission in COVID-19 outbreaks [version 1; peer review: 2 approved] Wellcome Open Research 2020, 5:239 https://doi.org/10.12688/wellcomeopenres.16344.1

First published: 13 Oct 2020, 5:239 https://doi.org/10.12688/wellcomeopenres.16344.1

Introduction

Isolation of symptomatic cases and tracing and quarantine of their contacts is a staple public health control measure, and has the potential to prevent the need for stringent physical distancing policies that result in detrimental impacts on the society (e.g., civil lockdowns)^{1,2}. By identifying and quarantining those who have been recently in contact with infected individuals, epidemic control may be achieved without broad restrictions on the general population. Contact tracing is typically triggered by a confirmed index case identified via symptom-based surveillance. Contacts of this index case are identified via interviews by public health officials (manual contact tracing) or by tracking proximity records on digital devices (digital contact tracing), and asked to quarantine in order to prevent further transmissions.

Contact tracing often targets 'downstream' individuals, who may have been infected by the index case ('forward tracing'); i.e. those who have been in contact with the index case after the index case likely became infectious (often assumed as 2 days before illness onset for COVID-19^{3,4}). However, 'backward tracing' can also be used to identify the upstream primary case who infected the index case (or a setting or event at which the index case was infected) by retracing history of contact to the likely point of exposure up to the upper bound of incubation period. For example, contact history of 14 days prior to symptom onset is collected in Japan, where backward tracing has been operated from the early phase of the COVID-19 outbreak^{5,6}. If this primary case is identified, a larger fraction of the transmission chain can be detected by forward tracing each of the contacts of this primary case.

Unlike forward tracing, backward tracing is more effective when the number of onward transmissions is highly variable, because index cases are disproportionately more likely to have been generated by primary cases who also infected others (an example of the "friendship paradox"^{7,8}). Because there is evidence that the number of secondary transmissions of SARS-CoV-2 per case exhibits substantial individual-level variation (i.e. overdispersion), often resulting in so-called superspreading events^{9–11}, a large proportion of infections may be linked to a small proportion of original clusters. As a result, finding and targeting originating clusters in combination with reducing onwards infection may substantially enhance the effectiveness of tracing methods^{12,13}.

In the present study, we explore the incremental effectiveness of combining 'backward' tracing with conventional 'forward' tracing in the presence of overdispersion in SARS-CoV-2 transmission, using a simple branching process model.

Methods

Overdispersion and the coverage of contact tracing

We used a branching process model to compare the performance of forward and backward contact tracing triggered by an index case found by symptom-based surveillance (Figure 1). We enumerate generations of transmission chains linked to the index case so that the index case belongs to generation-1 (G1). Backward tracing first identifies the primary case (G0) that infected the index case and then applies forward tracing to those infected by the primary case (G1). We represent the transmission chains of COVID-19 by a branching process where p(x) denotes the offspring distribution, i.e. the probability mass function of the number of secondary transmissions caused by a single case. If an individual is identified as a primary case, they are more likely to have generated more cases than any random case because the probability that a primary case is identified is proportional to



(A) Forward contact tracing only

(B) Forward + backward contact tracing

Figure 1. Schematic illustration of forward and backward contact tracing. Two cases (index cases #1 and #2) from a transmission tree originating from an (initially) undetected primary case are assumed to be detected by surveillance. Possible results of contact tracing are shown where (A) only forward tracing is performed or (**B**) both forward and backward tracing are performed. Some cases may remain undetected because contact tracing can miss cases.

the number of cases it generates. Therefore, the number of offspring of the identified primary case follows $p(x | G_0) = \frac{xp(x)}{\mathbb{E}(x)}$, where $\mathbb{E}(x) = \sum_{x=0}^{\infty} xp(x)$. The mean number of G1 cases able

to be identified by backward tracing (including the index case)

is
$$\mathbb{E}(x \mid \mathbf{G}_0) = \sum_{x=0}^{\infty} x \frac{xp(x)}{\mathbb{E}(x)} = \frac{\mathbb{E}(x)}{\mathbb{E}(x)} = R(1 + v^2),$$
 where

 $\mathbb{E}(x) = R$ is the reproduction number and v is the coefficient of variation (the standard deviation of x divided by its mean). With a high overdispersion (large v), backward tracing of the index case can substantially increase the number of G1 cases to trace. Conversely, the mean number of cases that can be identified by forward tracing is *R* regardless of the degree of overdispersion.

When we assume p(x) follows a negative-binomial distribution^{10,14} with an overdispersion parameter k, backward tracing on average identifies $\mathbb{E}(x \mid G_0) = R(1 + v^2) = 1 + R\left(1 + \frac{1}{k}\right)$ G1 cases. Existing studies suggest k for SARS-CoV-2 transmission is small and likely to lie within the range of 0.1–0.5^{10,15,16}. A small k indicates that the primary case identified through backward tracing typically generates more secondary cases than does a randomly selected case (i.e. $\mathbb{E}(x \mid G_0) > E(x) = R$).

The higher probability of identifying a large cluster by backward tracing can also be demonstrated by looking at the tail probability of the offspring distribution. Given a negative-binomial offspring distribution $p(x, R, k) = {\binom{x+k-1}{x}} {\binom{R}{R+k}}^x {\binom{k}{R+k}}^k$, the probability that a cluster of secondary infections caused by a

G0 case identified by backward tracing has a size of X or larger is

$$\begin{split} \sum_{x=X}^{\infty} p(x \mid G_0) &= \frac{1}{R} \sum_{x=X}^{\infty} x p(x; R, k) = \sum_{x=X}^{\infty} \binom{x+k-1}{x-1} \binom{R}{R+k}^{x-1} \left(\frac{k}{R+k}\right)^{k+1} \\ &= \sum_{x=X-1}^{\infty} p(x; \frac{k+1}{k} R, k+1). \end{split}$$

For different combinations of the reproduction number R and overdispersion parameter k, we estimated the mean size of an identified cluster in backward tracing and the probability of observing a size of at least 5, 10 and 25.

Simulation of the effectiveness of forward and backward contact tracing

Using our simple branching process model with a negative-binomial offspring distribution, we assessed the potential effectiveness of forward and backward contact tracing. We assumed that contact tracing is triggered by the detection of an index case whose primary case is initially unknown so that our simulation would guide decision making at the operational level (i.e. whether it is worthwhile to implement contact tracing when a case is found). We compared two scenarios: forward tracing only and the combination of forward and backward tracing (Figure 1). In the forward only scenario, G2 cases resulting from an index case are potentially traced and quarantined; in the combined scenario, more G1 cases can be identified through backward tracing of the primary infection and thus a larger number of G2 cases can be traced and quarantined. As the infectious period of G1 cases is likely to have already passed when they are identified by contact tracing because tracing only starts after the index case is confirmed, we assumed that secondary transmissions caused by G1 cases would not be prevented and that only G2 cases successfully traced could be put in quarantine (which confers a relative reduction c in transmission). To account for potential limitations in the effectiveness of contact tracing, we assumed that the primary case is identified with probability band that each offspring of identified cases are traced with probability q. G1 cases not traced may be independently found by symptom-based surveillance; we accounted for such independent case finding with a detection probability d (although we excluded backward tracing triggered by these cases from analysis), which is expected to be low due to frequent subclinical infections¹⁷. All parameters used for simulation are listed in Table 1.

We estimated the expected number of G3 cases averted and defined the effectiveness of contact tracing by the relative reduction in the total number of G3 cases. Assuming a negative-binomial branching process with a mean R and overdispersion parameter k, the mean total number of generation 3 cases given an index case found by surveillance is

$$C_{3} = \sum_{x_{0},x_{1},x_{2}=0}^{\infty} x_{0}x_{1}x_{2}p(x_{0} \mid G_{0})p(x_{1})p(x_{2}) = \mathbb{E}(x \mid G_{0})\mathbb{E}(x)^{2} = R^{2}\left(1 + R\left(1 + \frac{1}{k}\right)\right).$$

In the forward only scenario, the expected number of G1 cases excluding

the initially found index case is $\mathbb{E}(x \mid G_0) - 1 = R\left(1 + \frac{1}{k}\right)$, of which proportion *d* is independently detected by symptom-based surveillance. Therefore, the total number of G1 cases targeted

by forward tracing (including the index case) is $1 + Rd\left(1 + \frac{1}{k}\right)$.

Of the secondary cases generated by these G1 cases (*R* cases each on average), proportion *q* are successfully traced, i.e. Rq(1+Rd(1+1/k)) G2 cases are traced and asked to quarantine on average. The effective reproduction number of quarantined G2 cases is assumed to be R(1-c); therefore, the estimated number of G3 cases averted is given as

$$\Delta_{\rm F} = R^2 qc \left(1 + Rd \left(1 + \frac{1}{k} \right) \right).$$

In the combined (forward + backward) scenario, G1 cases can also be detected by backward tracing. Of the mean $R\left(1+\frac{1}{k}\right)$

G1 cases potentially under the scope of backward tracing, proportion (1 - d)(1 - bq) will remain undetected either by backward tracing or independent detection. As a result, (1-(1-d)(1-bq)) R(1+1/k) G1 cases are identified on average in addition to the index case, leading to tracing of Rq(1+(1-(1-d)(1-bq))R(1+1/k)) G2 cases. By asking these traced G2 cases to quarantine, G3 cases are expected to be averted by

Parameter	Notation	Assumed value in Figure 2 and <i>Extended data</i> , Figures S1 and S2 ¹⁸
Reproduction number	R	1.2, 2.5
Overdispersion parameter	k	0.2, 0.5
Relative reduction in transmission due to quarantine	С	0.2 – 1.0
Probability of identifying the primary (G0) case by backward tracing	b	0.5, 0.8
Probability of identifying each offspring of an already identified case	q	0.0- 1.0
Probability of a G1 case identified by surveillance independently of contact tracing	d	0.1, 0.2

Table 1. Parameter notations and values assumed in simulation.

$$\Delta_{\rm F+B} = R^2 qc \left[1 + (1 - R(1 - d)(1 - bq)) \left(1 + \frac{1}{k} \right) \right].$$

The effectiveness of contact tracing in the forward and combined scenarios are obtained as $\frac{\Delta_{\rm F}}{C_3}$ and $\frac{\Delta_{\rm F+B}}{C_3}$, respectively. The simulation was implemented in R-3.6.1. The replication code and *Extended data* are reposited on GitHub (https://github. com/akira-endo/COVID19_backwardtracing) and archived with Zenodo¹⁸.

An earlier version of this article can be found on medRxiv (DOI: https://doi.org/10.1101/2020.08.01.20166595).

Results

Larger clusters are likely to be detected through backward tracing in the presence of overdispersion

The estimated mean and the tail probabilities of the secondary transmissions caused by a primary case identified via backward contact tracing suggests the potential strength of this tracing approach (Table 2). With a substantial individual-level variation in the number of secondary transmissions per case, characterised by a small overdispersion parameter k of a negative-binomial distribution ranging 0.1-0.5, backward tracing typically leads to a primary case generating 3-10 times more infections than a randomly chosen case (whose mean defines the reproduction number R). The tail probabilities, ranging from 25% to 88% (Table 2), suggest that backward tracing is likely to find a relatively large cluster (≥5) under the plausible parameter settings. These values are striking because the probability of finding such clusters in forward tracing will be much lower. In a case of R = 1.2 and k = 0.2, only 6% of random cases results in 5 or more secondary infections, as opposed to 53% of primary cases identified by backward tracing.

Backward tracing typically results in multiple-fold increases in the overall effectiveness of contact tracing

Using a branching process model, we simulated the effectiveness of contact tracing. Across plausible ranges of parameter values, we found that introducing backward tracing in addition to forward tracing increased the effectiveness of contact tracing by a factor of 2-3 (Figure 2 and *Extended data*, S1 and S2¹⁸). Although the relative improvement in effectiveness by introducing backward tracing is similar between different values of k (0.2 and 0.5), the coverage of backward tracing scales up with overdispersion. We found that a higher degree of overdispersion (i.e. small k) resulted in a larger absolute number of cases averted by backward tracing (Figure 3 and *Extended data*, S3). In the presence of substantial overdispersion (k = 0.1), backward tracing is expected to avert 2–3 times more G3 cases than it does in a less-dispersed outbreak (k = 0.5).

Discussion

Using a simple branching process model, we showed that backward contact tracing has the potential to identify a large proportion of infections because of the observed overdispersion in COVID-19 transmission. For each index cases detected, forward tracing alone can, on average, identify at most the mean number of secondary infections (i.e. R). In contrast, backward tracing increases this maximum number of traceable individuals by a factor of 2-3, as index cases are more likely to come from clusters than a case is to generate a cluster. Furthermore, backward tracing contributes to epidemiological understanding of highrisk settings because transmission events with a common source are more likely to be identified. While standard tracing mostly focuses on forward tracing^{3,4}, there has been increasing interest in a possible combination of forward and backward tracing to control COVID-19^{13,19}. Our results provide further evidence for this approach by quantifying the possible benefit of backward tracing, especially when the offspring distribution is highly variable, as is the case with SARS-CoV-2.

There are a number of operational challenges to implementing such contact tracing approaches. Since the number of contacts that lead to transmission is likely to be only a fraction of total contacts experienced by detected cases, expanding the coverage of contact tracing may involve a substantial logistical burden^{20,21}. With a longer timeline of contact history to be interviewed, recall bias may affect the success rate of backward tracing. In

Reproduction number (<i>R</i>)	Overdispersion parameter (<i>k</i>)	Mean number of transmissions from primary case (E(x G ₀))	Probability $(x \ge 5 G_0)$	Probability $(x \ge 10 G_0)$	Probability $(x \ge 25 G_0)$
0.8	0.1	9.8	67%	39%	7%
	0.2	5.8	49%	18%	0.7%
	0.3	4.5	38%	9%	0.1%
	0.4	3.8	30%	5%	0.02%
	0.5	3.4	25%	3%	0.003%
1.2	0.1	14.2	77%	53%	17%
	0.2	8.2	62%	32%	4%
	0.3	6.2	53%	20%	0.9%
	0.4	5.2	45%	13%	0.2%
	0.5	4.6	40%	9%	0.07%
2.5	0.1	28.5	88%	74%	43%
	0.2	16.0	81%	59%	21%
	0.3	11.8	75%	48%	11%
	0.4	9.8	71%	40%	6%
	0.5	8.5	67%	34%	3%

Table 2. Characteristics of transmissions from a primary case identified by backward contact tracing for different combinations of the reproduction number (*R*) and overdispersion parameter (*k*).

 $\mathbb{E}(x \mid G_0)$: the mean number of offspring generated by a primary case identified by backward tracing (G0 case). Note that this is larger than the mean number of offspring of a random case.

Probability ($x \ge n \mid G_0$): the probability that the number of offspring generated by a G0 case is n or greater.

practice, interviewed cases might be asked not only for specific individuals they know to have contacted but also for a history of locations or events visited, as happens during outbreak investigations so that those who were present can be notified and/or tested. Backward tracing can in effect be viewed as an outbreak investigation process in which new cases and their contacts can be routinely linked via their shared exposure events, supported by cross-referencing over epidemiological, diagnostic and quarantine datasets, with additionally identified infections triggering further tracing. Due to the difficulty in determining the direction of transmission, backward tracing may find a cluster of cases rather than a single primary case. However, our results still apply as long as subsequent forward tracing is conducted for all of the identified cases.

Our model makes some simplifying assumptions. Delays in confirmation and tracing were such that only generation-2 (G2) cases were assumed to be traced and quarantined before becoming infectious. In reality, cases are identified at different points in time and the reduction in infectiousness may be partial if cases are quarantined after becoming infectious (which can be a concern for backward tracing with an additional generation to trace).

To allow intuitive comparison, the effectiveness of tracing was measured by the proportion of G3 cases averted given an index case detected by surveillance, and long-term dynamics were not considered. We believe our focus on assessing the effectiveness of a single practice of contact tracing triggered by a detected case is more relevant to operational-level decision making given finite resources. We also did not consider in our model that independently detected multiple index cases may have the same primary case, which can cause duplicated effort of backward tracing. However, such duplication may be minimised if information of each index case is shared among health officials; moreover, overlapping backward tracing still has a benefit because it increases confidence in the identification of primary cases or infection settings.

With these limitations, our results suggest a significant potential benefit to backward tracing, which should be balanced against finite resources. Because backward tracing is operationally a set of forward tracing measures targeting multiple G1 cases in parallel, additional effectiveness requires a proportional amount of effort, in addition to the 'overhead' investigation effort to identify other G1 cases. Cost-effectiveness analysis



Figure 2. The estimated effectiveness of forward and backward contact tracing for different parameter values. Left panels (**A**, **D**, **G**): the effectiveness (the proportion of G3 cases averted) of forward tracing alone; middle panels (**B**, **E**, **H**): the effectiveness of a combination of forward and backward tracing; right panels (**C**, **F**, **I**): incremental effectiveness by combining backward tracing with forward tracing. Colours represent the relative reduction in transmission from G2 cases if traced and held in quarantine. *R*: the reproduction number; *k*: overdispersion parameter; *q*: proportion of secondary infections caused by a detected case successful traced; *c*: relative reduction in transmission from quarantined cases; *b*: probability of successful identification of the primary case; *d*: probability of detection of generation-2 (G2) cases independent of contact tracing.

Figure 3. The estimated absolute number of generation-3 (G3) cases averted by forward and backward contact tracing. Left panels (**A**, **D**, **G**): the number of cases averted by forward tracing alone; middle panels (**B**, **E**, **H**): the number of cases averted by a combination of forward and backward tracing; right panels (**C**, **F**, **I**): additional cases averted by combining backward tracing with forward tracing. Colours represent the assumed reproduction number *R*. *R*: the reproduction number; *k*: overdispersion parameter; *q*: proportion of secondary infections caused by a detected case successful traced; *c*: relative reduction in transmission from quarantined cases; *b*: probability of successful identification of the primary case; *d*: probability of detection of generation-2 (G2) cases independent of contact tracing.

combined with finer-scale dynamic modelling would help further identify the conditions under which backward tracing is most efficient and feasible.

Data availability

Underlying data

All data underlying the results are available as part of the article and no additional source data are required.

Extended data

Zenodo: akira-endo/COVID19_backwardtracing: Implication of backward contact tracing in the presence of overdispersed transmission in COVID-19 outbreaks. https://doi.org/10.5281/zenodo.4062208¹⁸.

Supplementary text 'COVID19_backwardtracing.html' contains the following supplementary figures (files stored in subfolder 'figs'), which are also available on GitHub:

- Figure S1: The estimated effectiveness with R = 2.5.
- Figure S2: The estimated effectiveness with R = 1.2 and d = 0.5.
- Figure S3: The number of generation 3 cases averted with 60% success rate of tracing and 60% relative reduction in transmission during quarantine.

Software availability

The reproducible code is available from: https://github.com/ akira-endo/COVID19_backwardtracing.

Archived repository at time of publication: https://doi. org/10.5281/zenodo.4062208¹⁸.

License: MIT

Members of the Centre for Mathematical Modelling of Infectious Diseases (CMMID) COVID-19 Working Group (random order):

Billy J Quilty, Matthew Quaife, Amy Gimma, Charlie Diamond, Rosalind M Eggo, Kiesha Prem, W John Edmunds, Fiona Yueqian Sun, Emily S Nightingale, James W Rudge, Simon R Procter, Rein M G J Houben, Sophie R Meakin, Christopher I Jarvis, James D Munday, Kevin van Zandvoort, Georgia R Gore-Langton, Stéphane Hué, Thibaut Jombart, Damien C Tully, Samuel Clifford, Nicholas G. Davies, Kathleen O'Reilly, Sam Abbott, C Julian Villabona-Arenas, Rachel Lowe, Megan Auzenbergs, David Simons, Nikos I Bosse, Jon C Emery, Yang Liu, Stefan Flasche, Mark Jit, Hamish P Gibbs, Joel Hellewell, Carl A B Pearson, Alicia Rosello, Timothy W Russell, Anna M Foss, Arminder K Deol, Oliver Brady, Petra Klepac

CMMID COVID-19 Working Group funding statements. Billy J Quilty (NIHR: 16/137/109 & 16/136/46), Matthew Quaife (ERC Starting Grant: 757699, B&MGF: INV-001754), Amy Gimma (Global Challenges Research Fund: ES/P010873/1), Charlie Diamond (NIHR: 16/137/109), Rosalind M Eggo (HDR UK: MR/S003975/1, UK MRC: MC_PC 19065), Kiesha Prem (B&MGF: INV-003174, European Commission: 101003688), W John Edmunds (European Commission: 101003688, UK MRC: MC-PC 19065), Fiona Yueqian Sun (NIHR: 16/137/109), Emily S Nightingale (B&MGF: OPP1183986), James W Rudge (DTRA: HDTRA1-18-1-0051), Simon R Procter (B&MGF: OPP1180644), Rein M G J Houben (ERC Starting Grant: #757699), Sophie R Meakin (Wellcome Trust: 210758/Z/18/Z), Christopher I Jarvis (Global Challenges Research Fund: ES/P010873/1), James D Munday (Wellcome Trust: 210758/Z/18/Z), Kevin van Zandvoort (Elrha R2HC/UK DFID/Wellcome Trust/NIHR, DFID/Wellcome Trust: Epidemic Preparedness Coronavirus research programme 221303/Z/20/Z), Georgia R Gore-Langton (UK MRC: LID DTP MR/N013638/1), Thibaut Jombart (Global Challenges Research Fund: ES/P010873/1, UK Public Health Rapid Support Team, NIHR: Health Protection Research Unit for Modelling Methodology HPRU-2012-10096, UK MRC: MC-PC 19065), Samuel Clifford (Wellcome Trust: 208812/Z/17/Z, UK MRC: MC-PC 19065), Nicholas G. Davies (NIHR: Health Protection Research Unit for Immunisation NIHR200929), Kathleen O'Reilly (B&MGF: OPP1191821), Sam Abbott (Wellcome Trust: 210758/Z/18/Z), Rachel Lowe (Royal Society: Dorothy Hodgkin Fellowship), Megan Auzenbergs (B&MGF: OPP1191821), David Simons (BBSRC LIDP: BB/M009513/1), Nikos I Bosse (Wellcome Trust: 210758/Z/18/Z), Jon C Emery (ERC Starting Grant: #757699), Yang Liu (B&MGF: INV-003174, NIHR: 16/137/109, European Commission: 101003688), Stefan Flasche (Wellcome Trust: 208812/Z/17/Z), Mark Jit (B&MGF: INV-003174; NIHR: 16/137/109, NIHR200929; European Commission: 101003688), Hamish P Gibbs (UK DHSC/UK Aid/NIHR: ITCRZ 03010), Joel Hellewell (Wellcome Trust: 210758/Z/18/ Z), Carl A B Pearson (B&MGF: NTD Modelling Consortium OPP1184344, DFID/Wellcome Trust: Epidemic Preparedness Coronavirus research programme 221303/Z/20/Z), Alicia Rosello (NIHR: PR-OD-1017-20002), Timothy W Russell (Wellcome Trust: 206250/Z/17/Z), Oliver Brady (Wellcome Trust: 206471/Z/17/Z), Petra Klepac (Royal Society: RP\EA\180004, European Commission: 101003688)

References

 Ferretti L, Wymant C, Kendall M, et al.: Quantifying SARS-CoV-2 transmission suggests epidemic control with digital contact tracing. Science. 2020; 368(6491): eabb6936.
 PubMed Abstract | Publisher Full Text | Free Full Text

 Kucharski AJ, Klepac P, Conlan AJK, et al.: Effectiveness of isolation, testing, contact tracing, and physical distancing on reducing transmission of SARS-CoV-2 in different settings: a mathematical modelling study. Lancet Infect Dis. 2020; 20(10): 1151–1160. PubMed Abstract | Publisher Full Text | Free Full Text

 World Health Organization: Contact tracing in the context of COVID-19: Interim guidance. 2020. Reference Source

- Centers for Disease Control and Prevention: Health Departments: Interim Guidance on Developing a COVID-19 Case Investigation & Contact Tracing Plan. 2020. Reference Source
- National Institute of Infectious Diseases: [Implementation guideline for active epidemiological surveillance of novel coronavirus disease cases (tentative): addendum regarding implementation of rapid identification of cluster cases] (Japanese). 2020. Reference Source
- Jindai K, Furuse Y, Oshitani H: [Novel coronavirus disease cluster intervention] (Japanese). Infect Agents Surveill Rep. 2020; 41: 108–110.
- Salathe M, Kazandjieva M, Lee JW, et al.: A high-resolution human contact network for infectious disease transmission. Proc Natl Acad Sci. 2010; 107(51): 22020-22025.
 PubMed Abstract | Publisher Full Text | Free Full Text
- Allard A, Moore C, Scarpino SV, *et al.*: The role of directionality, heterogeneity and correlations in epidemic risk and spread. 2020. Reference Source
- Liu Y, Eggo RM, Kucharski AJ: Secondary attack rate and superspreading events for SARS-CoV-2. Lancet. 2020; 395(10227): e47.
 PubMed Abstract | Publisher Full Text | Free Full Text
- Endo A, Centre for the Mathematical Modelling of Infectious Diseases COVID-19 Working Group, Abbott S, et al.: Estimating the overdispersion in COVID-19 transmission using outbreak sizes outside China [version 3; peer review: 2 approved]. Wellcome Open Res. 2020; 5: 67.
 PubMed Abstract | Publisher Full Text | Free Full Text
- Leclerc QJ, Fuller NM, Knight LE, et al.: What settings have been linked to SARS-CoV-2 transmission clusters? [version 2; peer review: 2 approved]. Wellcome Open Res. 2020; 5: 83.
 PubMed Abstract | Publisher Full Text | Free Full Text
- Klinkenberg D, Fraser C, Heesterbeek H: The effectiveness of contact tracing in emerging epidemics. Getz W, editor. *PLoS One.* 2006; 1(1): e12. PubMed Abstract | Publisher Full Text | Free Full Text

- Bradshaw WJ, Alley EC, Huggins JH, et al.: Bidirectional contact tracing dramatically improves COVID-19 control. medRxiv. 2020. Publisher Full Text
- Lloyd-Smith JO, Schreiber SJ, Kopp PE, et al.: Superspreading and the effect of individual variation on disease emergence. Nature. 2005; 438(7066): 355–359.
- PubMed Abstract | Publisher Full Text | Free Full Text
- Lau MSY, Grenfell B, Nelson K, et al.: Characterizing super-spreading events and age-specific infectiousness of SARS-CoV-2 transmission in Georgia, USA. medRxiv. 2020. Publisher Full Text
- Adam D, Wu P, Wong J, et al.: Clustering and superspreading potential of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections in Hong Kong. Prepr (Version 1) available Res Sq. 2020. Publisher Full Text
- Oran DP, Topol EJ: Prevalence of Asymptomatic SARS-CoV-2 Infection : A Narrative Review. Ann Intern Med. 2020; 173(5): 362–367.
 PubMed Abstract | Publisher Full Text | Free Full Text
- Endo A: akira-endo/COVID19_backwardtracing: Implication of backward contact tracing in the presence of overdispersed transmission in COVID-19 outbreaks (Version 1.01). Zenodo. 2020. http://www.doi.org/10.5281/zenodo.4062208
- Scientific Pandemic Influenza Group on Modelling Operational sub-group: SPI-M-0: Consensus Statement on COVID-19, 3 June 2020. 2020. Reference Source
- Keeling MJ, Hollingsworth TD, Read JM: Efficacy of contact tracing for the containment of the 2019 novel coronavirus (COVID-19). J Epidemiol Community Health. 2020; 74(10): 861–866.
 PubMed Abstract | Publisher Full Text | Free Full Text
- Hellewell J, Abbott S, Gimma A, et al.: Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts. Lancet Glob Heal. 2020; 8(4): e488-e496.
 PubMed Abstract | Publisher Full Text | Free Full Text

Open Peer Review

Current Peer Review Status:

Version 1

Reviewer Report 03 November 2020

https://doi.org/10.21956/wellcomeopenres.17971.r40876

© **2020 Winter A.** This is an open access peer review report distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Amy Winter 匝

Department of Epidemiology, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, USA

Thank you for the opportunity to review "Implication of backward contact tracing in the presence of overdispersed transmission in COVID-19 outbreaks." The authors conduct a straightforward branching process simulation to evaluate the additional impact of backwards contact tracing in conjunction with the conventional forward contact tracing. The motivation for the paper builds on our epidemiological understanding of over-dispersion in the transmission of COVID-19, meaning that index cases are disproportionately more likely to result from primary cases that also infected other individuals. As a result, using backwards contact tracing to identify primary cases and their contacts across 2-3 generations expands the potential for contact tracing to identify and isolate more infectious cases beyond forward contract tracing alone.

The objectives and motivation are clearly laid out and addressed in the introduction. Figure 1 is a helpful schematic to demonstrate the difference between forward and backwards contact tracing. The methods are straight forward and appropriate to answer the questions at hand. The authors do a nice job evaluating both the proportion and absolute number of generation 3 cases averted across a range of input parameter values. These sensitivity analyses and resulting multi-paneled figures 2, 3, S, S2, & S3 are critical given heterogeneity in populations, their contacts, and the effectiveness of contact tracing and surveillance systems. Lastly, the conclusions are consistent with the results presented. Overall, that paper was well-written and concise. I believe the conclusions add important nuance to the growing scientific literature around contact tracing for COVID-19 and more generally expand the range of interventions available to public health agencies to control the spread of SARS-CoV-2.

I do not have any suggested revisions.

Is the work clearly and accurately presented and does it cite the current literature? Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others? $\ensuremath{\mathsf{Yes}}$

If applicable, is the statistical analysis and its interpretation appropriate? $\ensuremath{\mathsf{Yes}}$

Are all the source data underlying the results available to ensure full reproducibility? $\ensuremath{\mathsf{Yes}}$

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Seroepidemiology, infectious disease modeling, vaccine preventable diseases, demography.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 22 October 2020

https://doi.org/10.21956/wellcomeopenres.17971.r40878

© **2020 Hill E.** This is an open access peer review report distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Edward Hill 匝

¹ Zeeman Institute: Systems Biology and Infectious Disease Epidemiology Research (SBIDER), University of Warwick, Coventry, UK

² School of Life Sciences, University of Warwick, Coventry, UK

³ Mathematics Institute, University of Warwick, Coventry, UK

In the study, the authors use a branching process model to explore the implication of combining backward contact tracing with forward contact tracing for control of COVID-19. They use the model to estimate: (i) the mean size of an identified cluster in backward contact tracing; (ii) the probability of identifying a large cluster by looking at the tail probabilities of the offspring distribution; (iii) assess contact tracing effectiveness, measured by generation-3 (G3) cases averted. With the observed overdispersion SARS-CoV-2 transmission, the findings suggest backward contact tracing can be an effective tool for outbreak control.

I found the manuscript to be very clear and concise. The study premise is well motivated and the methodological approach is appropriate. Sufficient details are provided, via the manuscript and

supporting code, to enable others to undertake a similar analysis.

Please find below additional line-by-line comments:

Abstract

Results paragraph: It currently reads "a primary case generating 3-10 times more infections than average". Would it be fair to explicitly say 3-10 times more infections than a randomly chosen case (average case)?

Final sentence: Suggest amending "of overdispersion as was observed" to "of overdispersion as is observed".

Introduction

Para 1, L5-8: The sentence beginning "By identifying..." repeats, in my view, much of the information given in the opening sentence and could be removed.

Para 2, L9: Amend "upper bound of incubation period" to "upper bound of the incubation period".

Para 4, L4: Propose repositioning the phrase "using a simple branching process model" to the first line, following "In the present study".

Methods

Check the first usage of G2 and G3 and that the acronyms are introduced alongside the full phrase (i.e. generation-2 (G2), generation-3 (G3)).

Simulation subsection, Para 2, L5: Replace "generation-3" by G3.

Simulation subsection, Para 4, L3: Add "a" ahead of "proportion (1-d)(1-bq)".

Simulation subsection, Para 4, Equation for Δ_{F+B} : I think there is a typo with regards to the placement of the *R* term. Should the expression in the square brackets read 1 + (1-(1-d)(1-bq))R(1 + 1/k)?

Results

Para 1, L7: In the passage "distribution ranging 0.1-0.5", to aid flow of text consider replacing with "distribution ranging between 0.1-0.5".

Para 1, L10-13: I believe the percentage range specified for the tail probabilities are specific to the number of offspring generated by a primary case being five or higher (rather than 10 or higher, or 25 or higher)? If so, making that criteria explicit within the text would reduce the risk of misinterpretation.

Para 2, L2-5: In the description of findings presented in Figures 2, S1, S2, there is a lack of comment on the relationship with the variable *q*.

Discussion

Para 2: To support the discussion on the operational challenges of implementing contact tracing approaches, additional references may be added to reflect how some of the stated issues have

been encountered as the pandemic continues. For example, user uptake and retention with digital tracing apps (in multiple nations), and the distinction between complex versus non-complex cases in NHS test and trace in contacts of test positive individuals being successfully identified and reached.

Figures & Tables

Table 1: As Figure S2 uses d=0.5, should the assumed values for d listed be expanded to "0.1, 0.2, 0.5"?

Table 2: I believe there is scope for an accompanying figure to visualise, for a given value of the overdispersion parameter, how the mean number of transmission from a primary case and the tail probabilities vary with the reproduction number.

Figure 2 caption title: It may be beneficial to add the study definition of tracing effectiveness into the caption title (e.g. "The estimated proportion of generation-3 (G3) cases averted by forward and backward contact tracing"). This would match the style used in the Figure 3 caption title.

Figure 2 caption, L4: Add the notation *c* in the sentence "Colours represent..." The subsequent description of *c* (L5-6) can then be removed.

Figure 2 caption, L5: Replace "successful" with "successfully".

Figure 3 caption: The sentence "*R*, the reproduction number" duplicates the preceding sentence and may be removed.

Is the work clearly and accurately presented and does it cite the current literature? $\ensuremath{\mathsf{Yes}}$

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others? $\ensuremath{\mathsf{Yes}}$

If applicable, is the statistical analysis and its interpretation appropriate? $\ensuremath{\mathsf{Yes}}$

Are all the source data underlying the results available to ensure full reproducibility? $\ensuremath{\mathsf{Yes}}$

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Mathematical epidemiology; infectious disease modelling.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.