THE LANCET
Microbe

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Kennedy-Shaffer L, Baym M, Hanage WP. Perfect as the enemy of good: tracing transmissions with low-sensitivity tests to mitigate SARS-CoV-2 outbreaks. *Lancet Microbe* 2021; published online March 12. https://doi.org/10.1016/S2666-5247(21)00004-5.

***Appendix to*:**
Perfect as the enemy of the good: tracing transmissions with low-sensitivity tests to mitigate SARS-CoV-2 outbreaks
Lancet Microbe

Lee Kennedy-Shaffer, PhD[1,2,3], Michael Baym, PhD[4], and William P. Hanage, PhD[1,2]

[1] Center for Communicable Disease Dynamics, Harvard T. H. Chan School of Public Health, Boston, MA
[2] Department of Epidemiology, Harvard T. H. Chan School of Public Health, Boston, MA
[3] Department of Mathematics and Statistics, Vassar College, Poughkeepsie, NY
[4] Department of Biomedical Informatics, Harvard Medical School, Boston, MA

Corresponding Author: Dr. Lee Kennedy-Shaffer; email: Lkennedyshaffer@vassar.edu; tel: 717.497.5336
Address: Dr. Lee Kennedy-Shaffer, Box 226, Vassar College, 124 Raymond Avenue, Poughkeepsie, NY, 12604-0226

Effectiveness of Transmission Tracing

We assume the test has perfect specificity, sensitivity of $a \times 100\%$, and that the test results of any two individuals are independent conditional on their true infection status (that is, there are no strain effects that would cause two people infected by the same source to be more likely to both incorrectly test negative).

The value of the transmission tracing strategy depends on two key points: that an individual who has transmitted to at least one contact is more likely to have transmitted to more contacts than an individual not known to have transmitted at least once; and that a low-sensitivity test has a high probability of identifying a group of infected contacts who are all tested.

The first point relies on the negative binomial distribution of secondary cases. The expected number of infected contacts of an individual is $E[Z] = R_0$. We can reparameterise the negative binomial distribution by letting $p = \frac{R_0/k}{1+R_0/k}$.[21] The expected number of infected contacts of an individual given that they have infected at least one individual is: $E[Z|Z \geq 1] = \frac{R_0}{1-P[Z=0]} = \frac{R_0}{1-(1-p)^k}$. When $E[Z|Z \geq 1] - R_0 > 1$, the probability of any other contact of an index individual known to have infected at least one contact is higher than the probability of any contact of an index individual not known to have infected any contacts.

The second point relies on the independence of test results among secondary cases. If this condition holds, then the probability of at least one positive test among n infected individuals is given by: $P[\geq 1\, positive\ test\ among\ n\ infected\ individuals] = 1 - (1-a)^n$. Even for low sensitivity values, this probability increases quickly as n increases.

More concretely, we can calculate the expected number of secondary cases isolated/quarantined under strategies A, B, and C. The expected number of secondary cases per index case isolated by transmission tracing (strategy A) is:

$$
\begin{aligned}
E[Z_A] = &\sum_{n=0}^{\infty} n \binom{n+k-1}{n} (1-p)^k p^n \left(1-(1-a)^n\right) \\
&= E[Z] - \sum_{n=0}^{\infty} n \binom{n+k-1}{n} (1-p)^k \big(p(1-a)\big)^n \\
&= R_0 - \left(\frac{1-p}{1-p+ap}\right)^k \frac{p(1-a)k}{1-p+ap} \\
&= R_0 \left(1-(1-a)\left(1+\frac{aR_0}{k}\right)^{-(1+k)}\right).
\end{aligned}
$$

The expected number of secondary cases per index case quarantined by quarantining all contacts (strategy B) is $E[Z_B] = R_0$. The expected number of secondary cases per index case who test positive (and are thus isolated under strategy C) is:

$E[Z_C] = R_0 P[positive\ test|infected] = aR_0$.

Cost of Transmission Tracing

We use the proportion of index cases whose contacts are isolated as a proxy for the cost (in terms of number of people isolated and resources spent on epidemiologic measures for isolated individuals) of the strategy. For strategy B, the proportion quarantined is 1. For strategy C, this proportion is less relevant as individuals are isolated based on their own test results rather than based on the source of their potential infection. For transmission tracing (strategy A), the probability that an index case's contacts will be isolated is given by:

$$P[isolated] = P[Z = n]P[\geq 1\ positive\ test\ among\ n\ infected\ individuals]$$

$$= \sum_{n=0}^{\infty} n \binom{n+k-1}{n} (1-p)^k p^n (1-(1-a)^n)$$

$$= 1 - \sum_{n=0}^{\infty} \binom{n+k-1}{n} (1-p)^k \left(p(1-a)\right)^n$$

$$= 1 - \left(\frac{1-p}{1-p+ap}\right)^k = 1 - \left(1 + \frac{aR_0}{k}\right)^{-k}.$$

This cost can be measured in different ways in different settings: the economic cost of quarantine and isolation of individuals, the social and individual burden of the stress of quarantine and isolation, and the effect of unnecessary quarantine and isolation on perception of and compliance with current and future public health efforts.