Estimating detection of infection among household gathering attendees based on one-off pre-gathering lateral flow tests

Adam Kucharski, Tim Russell, Joel Hellewell, on behalf of CMMID COVID-19 working group
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Summary

- Using estimates for lateral flow test sensitivity at different points post-infection based on HCW data (assuming LFT returns a positive if Ct ≤ 27), we explored the probability that infection would be detected during a one-off LFT among attendees before different size gatherings.

- Under conservative assumptions, we estimated that a one-off LFT pre-gathering (with any detected infections self-isolating) could lead to a 23% reduction in expected secondary transmission in the first generation of an outbreak during a gathering, and a 32% reduction if onset of symptoms or LFT positivity is used to identify infections (Figure 3). This limited effectiveness arises because the individuals who are most likely to generate future transmission are also the ones earliest in their infectious period, and hence harder to detect by LFT (Figure 1).

- We estimated that individuals who test negative alongside all of their household members are much less likely to be false negatives, because of the correlation in risk within households (Figure 4). The joint information obtained from testing whole households is particularly valuable in the later stages of an outbreak, e.g. after a household has been together for the equivalent of multiple generations of infection. Testing of whole households before measures are relaxed could therefore provide more confidence of household infection status than unlinked testing of individuals.

Methods & Results

Probability of detection by lateral flow test at given point post-infection

We used Ct data from repeat PCR testing of healthcare workers in the SAFER study (Houlihan et al, 2020), with infections confirmed by paired serology, to estimate the probability of detection by PCR and lateral flow test (LFT), assuming here that LFT will detect infections with Ct ≤ 27 (Hellewell et al, 2020). Figure 1 shows the relative probabilities of testing positive over time since infection, as well as an estimate of the median onwards infectiousness to come in future, assuming that the LFT curve reflects the distribution of infectiousness over the period of infection. We assume the test has high specificity.

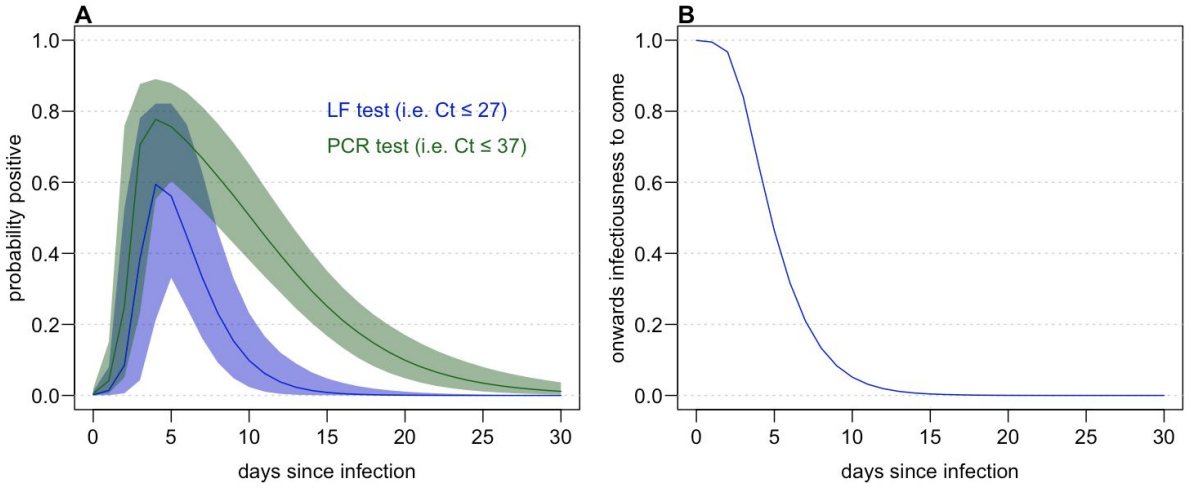

Figure 1: Detection and infectiousness over time. A) Estimated probability of testing by PCR (defined as Ct ≤ 27) and LFT (Ct ≤ 27) based on data from SAFER study. Median and 95% credible intervals shown. B) Estimated onwards infectiousness to come, based on the cumulative LFT distribution over in (A), normalised so equal to 1 at t=0.

Probability at least one infection given negative results

Throughout this report, we use 'infected' to mean anyone who is currently infected and is infectious or will be in future (i.e. not people who would still test PCR positive but be very unlikely to transmit to others). We assume that a proportion q of the population is currently infected and assume infected attendees are equally likely to be in the first fifteen days of infection (i.e. the period during which there is still some onwards infectiousness in Figure 1B; this assumption implies epidemic incidence is currently flat).

The probability there is at least one infected person at a gathering is a simple function of prevalence and gathering size: $P(\textit{at least one infected}) = 1-(1-q)^n$

The probability there is at least one infected person at a gathering given all attendees test negative in a one-off LFT is as follows:

$$P(\textit{at least one infected} \mid \textit{all test negative}) = 1 - P(\textit{not infected} \mid \textit{test negative})^n$$

where

$$P(\textit{not infected} \mid \textit{test negative}) = \frac{P(\textit{not infected})}{P(\textit{infected})P(\textit{test negative} \mid \textit{infected}) + P(\textit{not infected})} = \frac{1-q}{q\,P(\textit{test negative} \mid \textit{infected}) + (1-q)}$$

and

$$P(test\ negative \mid infected) = \sum_{i=0}^{15} P(test\ negative \mid on\ day\ i\ of\ infection)\, P(on\ day\ i\ of\ infection)$$

and

$$P(on\ day\ i\ of\ infection) = 1/16$$

The above equation gives the results in Figure 2. The apparently limited impact of a one-off LFT test on reducing the probability at least one infection is present is largely the result of inclusion of the whole infectious period in the analysis. Specifically, an attendee who is late in their infection when tested may not be detected. However, such individuals may also be unlikely to transmit substantially in future (Figure 1A). Hence, we need to consider onwards infectiousness as well as just whether someone is currently infected. We do this in the next section.

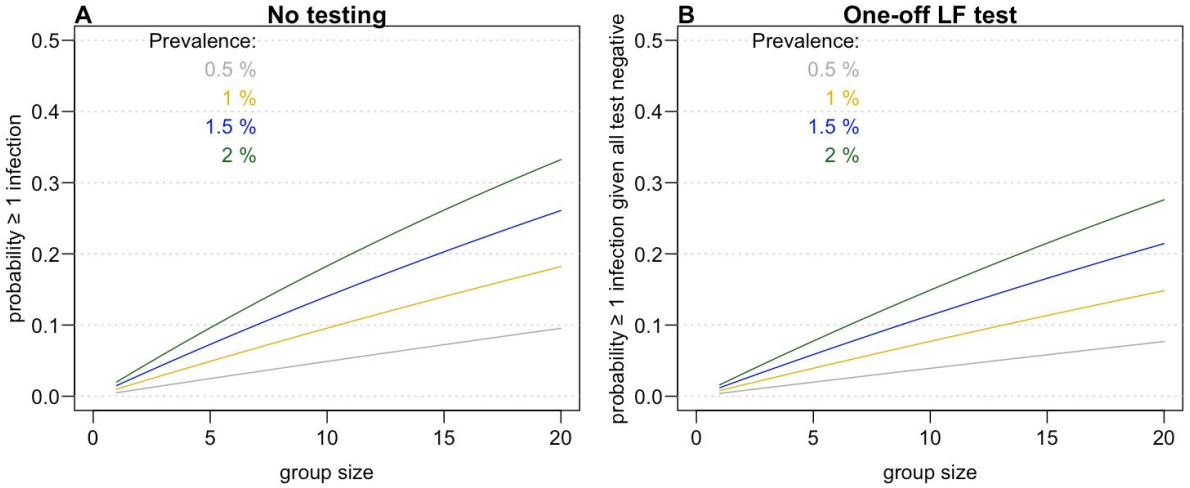

Figure 2: Probability that at least one attendee is infected, for different levels of background prevalence, with: A) no testing pre-gathering; B) a one-off LFT.

Secondary infections reduced by one-off LFT

To calculate the expected secondary infections that would be generated from initially infectious attendees, we first calculate the total person's worth of infectiousness-to-come present among n attendees, denoted E(infectiousness). We can think of this as the proportion of n that would be expected to contribute infectiousness to the gathering:

$$E(infectiousness) = q\,[\sum_{i=0}^{15} P(on\ day\ i\ of\ infection) f(i)]\, n$$

where $f(i)$ is the onward infectiousness function shown in Figure 1B. Next, we use this to calculate the number of secondary infections per initial case at the gathering (analogous to a within-household reproduction number):

$$E(secondary\ infections) = SAR_{HH}\ SI = SAR_{HH}(1-q)\, n\, E(infectiousness)$$

Where SAR_{HH} is the household secondary attack rate, assumed to be 35% (based on Bernal et al, 2020 in UK and Grijalva et al, 2020 in the US). In the scenario where one-off LFTs are

used, we estimate the infectiousness that results accounting for the infections that are missed (i.e. any positives isolate and do not attend gathering):

$$E(infectiousness) = q\,[\sum_{i=0}^{15} P(test\ negative \mid on\ day\ i\ of\ infection)\,P(on\ day\ i\ of\ infection) f(i)]\,n$$

We also consider a scenario where one-off LFTs are used, and anyone who is infected and has had symptom onset also self isolates and does not attend the gathering

$$E(infectiousness) = q\,[\sum_{i=0}^{15} P(test\ negative \mid on\ day\ i\ of\ infection)\,P(on\ day\ i\ of\ infection\ \&\ no\ symptoms\ yet) f(i)]\,n$$

where, assuming 30% of infections are asymptomatic and similar transmission profile between asymptomatic, presymptomatic and symptomatic groups, we obtain:

$$P(on\ day\ i\ of\ infection\ \&\ no\ symptoms\ yet) = [0.7\,P(no\ symptoms\ by\ day\ i) + 0.3] P(on\ day\ i\ of\ infection)$$

The results are shown in Figure 3. A one-off LFT gives an estimated 23% reduction in secondary infections compared to no testing, and if symptoms are used alongside LFT to detect infections pre-gathering, it is estimated to result in a 32% reduction. (Note: as we are assuming asymptomatic transmission is same as symptomatic, the actual reduction may be even higher).

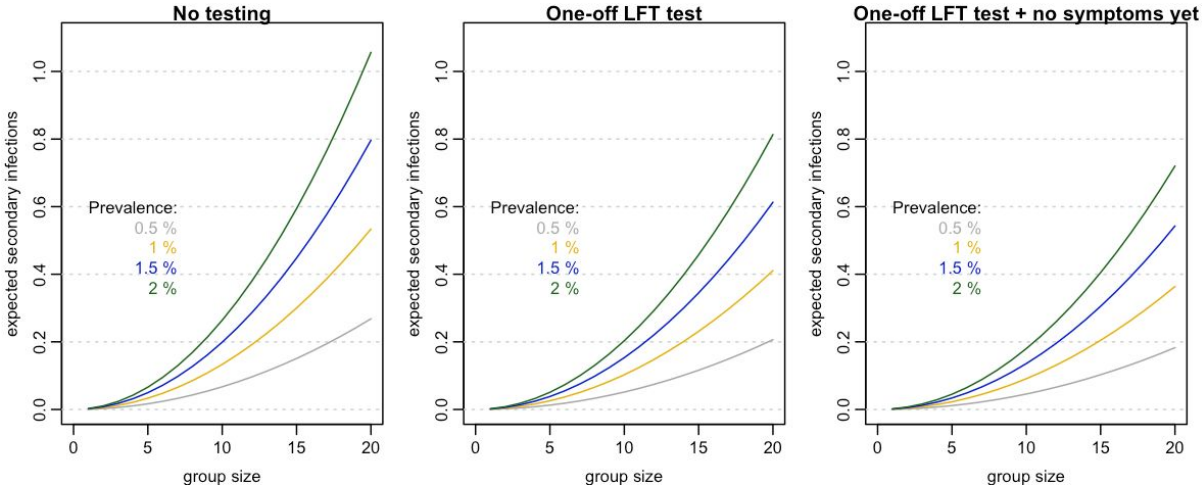

Figure 3: Expected secondary infections generated by initially infectious attendees at a multi-day gathering with: A) no testing in place; B) a one-off LFT test immediately before gathering; C) a one-off LFT test and confirmation that nobody is yet symptomatic immediately before gathering.

Probability negative given negative test and HH negative

Because household attack rates are higher than for many other settings, infections within households will be correlated, which means multiple negative tests should provide more confidence in a single test result than it would if that test were considered in isolation. We calculate the probability that a person is not infected given they and their household (of size n) test negative as follows:

$$P(not\ infected \mid all\ test\ negative) = \frac{P(not\ infected)}{P(infected)P(all\ test\ negative \mid infected) + P(not\ infected)} = \frac{1-q}{q\,P(test\ negative \mid infected) + (1-q)}$$

where

$$P(\text{all test negative} \mid \text{infected}) = P(\text{test negative} \mid \text{infected})\, P(\text{test negative} \mid \text{infected})^{E(\text{infections in HH})}$$

and

$E(\text{infections in HH}) = (n-1)\, SAR_{HH}$ in the 'early outbreak' scenario (i.e. first generation of infection only), or

$E(\text{infections in HH}) = \text{mean outbreak size in Reed Frost model (minus initial infection)}$ in the 'late outbreak' scenario (i.e. final household outbreak size minus initial infection).

and, as before,

$$P(\text{test negative} \mid \text{infected}) = \sum_{i=0}^{15} P(\text{test negative} \mid \text{on day } i \text{ of infection})\, P(\text{on day } i \text{ of infection})$$

The results are shown in Figure 4, illustrating that accounting for household correlation in infection risk can substantially reduce the probability of a false negative, particularly in larger households that have been mixing for a while (i.e. are more likely to be in the later stages of any outbreak).

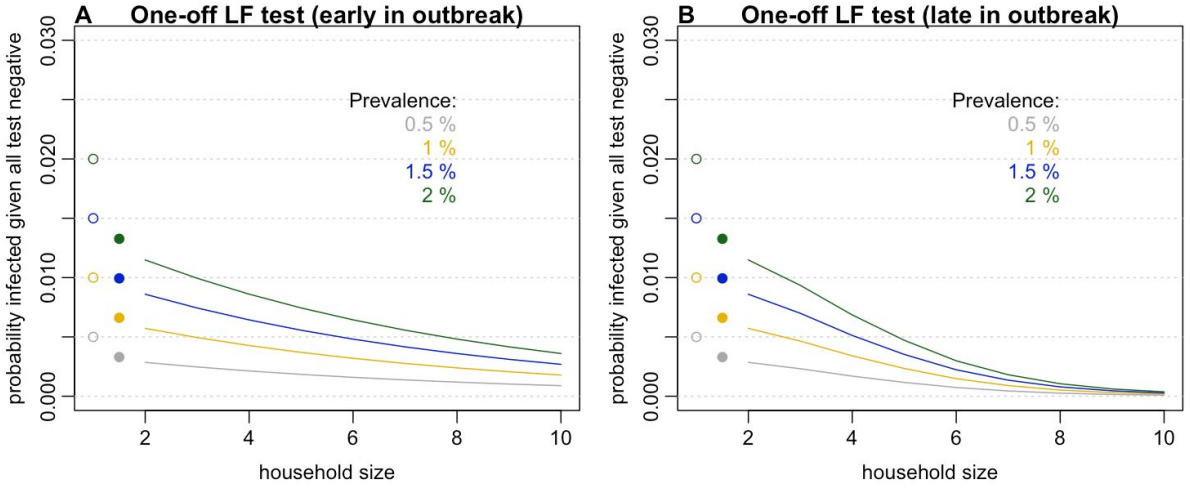

Figure 4: Probability that a single individual is infected given this person and all of their household tests negative by LFT, for different background levels of prevalence. For context, hollow circles show probability infected without testing (i.e. equal to prevalence); solid points show probability if just the individual is tested. A) Testing early in a household outbreak (i.e. when only one generation of infection has occurred); B) Testing late in a household outbreak, when the expected outbreak size in a Reed-Frost model has been reached.