Quarantine and testing strategies in contact tracing for SARS-CoV-2: a modelling study

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Abstract

Background: In most countries, contacts of confirmed COVID-19 cases are asked to quarantine for 14 days following exposure to limit asymptomatic onward transmission. We assessed the merit of testing contacts to avert transmission as well as to replace or reduce the length of quarantine for uninfected contacts.

Methods: We used an agent-based model to simulate the viral load dynamics of exposed contacts, their probability of detection over time, and their potential for onwards transmission in different quarantine and testing strategies. We compare the performance of quarantine, quarantine and testing with polymerase chain reaction (PCR) or lateral flow antigen (LFA) tests, and daily LFA testing without quarantine, against the current 14 day quarantine strategy.

Findings: Assuming moderate levels of adherence to quarantine and self-isolation, self-isolation on symptom onset alone can prevent 37% (95% UI: 12%, 56%) of onward transmission potential from secondary cases. 14 days of post-exposure quarantine reduces transmission by 59% (95% UI: 28%, 79%). Quarantine with an LFA test 7 days after exposure or daily testing without quarantine for 5 days after tracing may avert a similar proportion (risk ratios of 0.88 (95% UI: 0.66, 1.11) and 0.88 (95% UI: 0.60, 1.43), respectively) compared to that of the 14 day quarantine, with greater benefit possible if individuals isolate more strictly after a positive test.

Interpretation: Testing may allow for a substantial reduction in the length of, or replacement of quarantine with a small excess in transmission risk. Decreasing test and trace delays and increasing adherence will further increase the effectiveness of these strategies.

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Introduction

In order to break transmission chains of SARS-CoV-2, testing of cases and the tracing and quarantine of their contacts has been employed as key non-pharmaceutical intervention (NPI) in many countries. This measure aims to prevent onward transmission from secondary infections (individuals infected by an index case). It has been employed successfully to prevent new outbreaks in countries such as South Korea without the need for "lockdown"-style measures. As of Autumn 2020, guidance in the United Kingdom is that traced individuals must self-isolate from the moment they are traced until 14 days have elapsed from their exposure to the index case. This 14 days represents the upper bound for the incubation period (1), when >95% of eventually-symptomatic persons will have developed symptoms and should subsequently enter a further period of self-isolation (10 days in the UK). However, there is growing evidence that many contacts of cases are unable to effectively quarantine for the entirety of this period, particularly for those not working from home or caring for an adult (2). The increasing availability of testing, particularly rapid, low-cost lateral flow tests (3,4), opens up the possibility of shorter periods of quarantine when combined with a negative test on exit (a test and release strategy), or even the avoidance of quarantine entirely if it is replaced with daily testing. If effective, both of these strategies have the potential to substantially reduce the burden of quarantine on uninfected contacts, which could simultaneously improve quarantine adherence and reduce the economic, personal, financial and social costs of the current policy.

Testing of traced contacts may result in the detection of incubating and asymptomatic cases, allowing for a reduction in the post-exposure quarantine period from 14 days. Key to this is the timing of testing, as testing contacts too early or too late in their infection may lead to false-negative results. Another crucial factor is the delays in testing and tracing, i.e, how long has passed since exposure of the index case to the isolation of their contacts, as approximately half of SARS-CoV-2 transmission occurs before the onset of symptoms (5). Additionally, there is evidence that the current 14 day quarantine period is poorly adhered to, with only 10.9% of contacts of cases reporting that they did not leave the house in the 14 days following exposure to the index case (6). It is possible that reducing this quarantine period may increase adherence and therefore avert more transmission overall.

To evaluate the effect of different quarantine and testing strategies on reducing onwards transmission from traced secondary infections, we used a stochastic, individual-based model, simulating an individual's exposure time, viral load trajectory, symptom onset, tracing and testing timings and other relevant epidemiological events. We vary: the required post-exposure quarantine period; the timing, number, and type of tests (whether that be the standard polymerase chain reaction (PCR) tests, or rapid lateral-flow antigen (LFA) tests). We also investigate the effect of reducing testing and tracing delays, as well as the impact of reduced adherence to quarantine. As an alternative to quarantine, we consider daily testing, upon being traced as a contact, and estimate the number of consecutive daily tests required prior to leaving isolation that would obtain a similar reduction in transmission to that achieved by quarantine.

Methods

Contact tracing model of infected individuals

The following model is specified in such a way as to focus on the cases' infectivity, rather than the number of additional cases generated, and, as such, is independent of the number of secondary or further cases generated.

For each individual in the model (index cases and secondary cases), we simulate a viral load trajectory of Ct (cycle threshold) values over the course of infection (Figure 1) using published data to inform our choice of parameters. Each curve is parameterised by a baseline Ct level, a peak Ct value, and an end time, representing a return to baseline. We assume a baseline Ct of 40 upon exposure (i.e, negative for SARS-CoV-2). The timing of the peak Ct is sampled from the incubation period (time from exposure to onset of symptoms) using the pooled log-normal distribution from a published meta-analysis (8). The peak Ct value is normally distributed with mean 22.3 and standard deviation of 4.2 (8) and the time of cessation of viral shedding, a return to baseline, is parameterised as normally distributed with mean 17 days after exposure and standard deviation of 0.94 days for symptomatics (9), with asymptomatics having a duration which is 40% shorter (10). The peak and end times are drawn, for each individual, in such a way that each individual is at the same quantile, q, in the cumulative densities of each distribution; this guarantees that the ordering of peak and end is maintained and that there are no rapid returns to baseline Ct after a slow transition to peak Ct. We then fit a cubic Hermite spline (11) to these three points for each individual, constraining the slope of the curve to be zero at each of them, to simulate viral load kinetics (in Ct) over the course of infection. We assume that an individual is infectious during the time period that their Ct value is less than 30. If an individual's Ct trajectory does not drop below 30, they are considered to never be infectious and therefore not relevant for transmission. We assume individuals are uniformly infectious during this period of Ct<30.

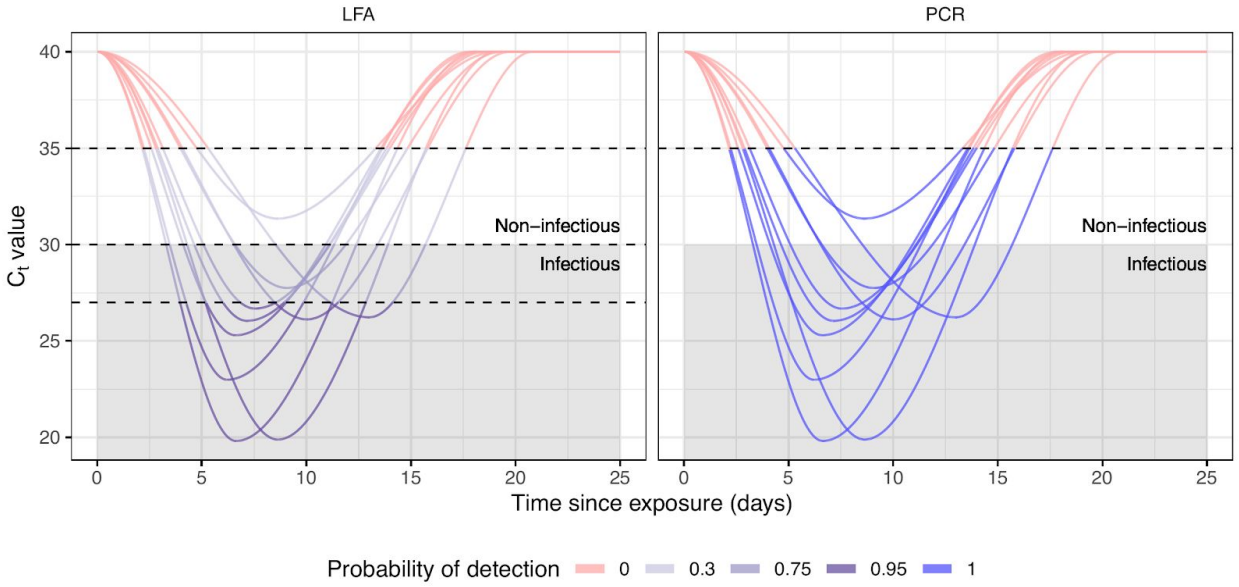

Figure 1 - Simulated Ct curves for ten individuals infected with SARS-CoV-2. Dashed lines represent thresholds for detection probabilities (8) and the shaded region, with boundary at Ct=30, indicates the time during which individuals are considered infectious; note that one of the ten individuals never reaches Ct=30 and thus, while detectable by PCR, and detectable with probability 0.3 for LFA during $t \in (5, 13)$, is not infectious.

We simulate index cases as individuals who become exposed, then infectious, at which point they begin exposing their contacts and generating secondary cases. Once the index cases develop symptoms, they begin a period of self-isolation where they are unable to generate additional secondary cases. We assume that 1 day after symptom onset, they seek out and have a PCR test which is returned positive, which begins the process of contact tracing. Based on the latest NHS Test and Trace (T&T) data, we assume that it takes a delay of 3 days from the sample being taken to contacts being instructed to quarantine (12). To investigate the effect of faster contact tracing (e.g through rapid testing and app-based tracing (13)), we consider halved delays (1.5 days) and instant T&T (0 days) as a sensitivity analysis.

Quarantine and testing strategies

We assume all contacts are successfully identified and traced and, that once traced, are subject to one of several strategies designed to avert onwards transmission. In the quarantine-based strategy, we investigate quarantine durations of 0, 3 ,5, 7, 10 and 14 days post exposure to the index case, with either no testing, or testing with PCR or lateral-flow antigen (LFA) tests on the final day of the specified quarantine period (in order to highlight the effect of said test at end of quarantine). However, if the end-of-quarantine test is scheduled to occur prior to the time of the secondary case's tracing, we assume that they are tested as soon as they are traced; hence, a 0 day quarantine with a test will be equivalent to an immediate test and release strategy. In the daily testing strategy, contacts are required to take an LFA test every day for 1, 3, 5, 7, 10 or 14 days after they are traced and are not required to quarantine unless they either develop symptoms or test positive. Those secondary cases displaying symptoms at any point post-exposure, or testing positive at any time, will then isolate until 10 days have passed since onset of symptoms (14). Given that asymptomatic secondary cases never develop symptoms, they will only self-isolate if they test positive. We sample the proportion of secondary infections which are asymptomatic from a Beta distribution which has a median of 31% and 95% CI of 24%, 38% (15) (Table 1). Further details on the model parameters are provided in Table 1.

The probability of detecting an infected and possibly infectious individual depends on their Ct value at the time of testing, and is drawn from their individual Ct trajectory (Figure 1). For PCR, we assume that the probability of detection is 100% for Ct below 35 and 0% above 35. For LFA, we assume that the probability of detection is 95% for Ct below 27, 75% for Ct between 27 and 30, 30% for Ct between 30 and 35, and 0% above 35, based on the results of the Innova rapid antigen test evaluation (4). To simulate more conservative estimates of test sensitivity, as a sensitivity analysis we reduce these LFA probabilities by 33% to reflect the average sensitivity observed in the Liverpool Mass Testing Pilot (16).

As a moderate baseline, we assume 50% of individuals adhere to quarantine and 67% adhere to self-isolation guidelines. To investigate the impact of increased or reduced adherence to quarantine and self-isolation on the effectiveness of the programme, we consider adherences of 100% and 0% for post-tracing quarantine, and 100% and 0% for self-isolation upon a positive test or symptom onset. We assume adherence as a binary

adhering/not-adhering variable for each individual by sampling from a Bernoulli distribution with the probability given by the proportion adhering.

Table 1 - Values of parameters in simulation of cases' infection histories and PCR testing. *Parameters are location and scale for log-Normal distribution, not summary statistics of observed incubation period.

Model parameter	Description	Value	Source
Incubation period (days)	Time from exposure to onset of symptoms.	Log-normal(1.63, 0.5) Median: 5.1 days IQR: (3.9, 6.7) days 95%: (2.3, 11.5) days	(7)
Infectious period	Time for which $C_t < 30$	Symptomatics: Mean: 7.56 days SD: 1.54 days Asymptomatics: Mean: 4.32 days SD: 1.09 days	Derived
Asymptomatic fraction of secondary cases, α	Proportion of infections which are asymptomatic.	Beta(51, 115) Median: 0.31 IQR: (0.28, 0.33) 95%: (0.24, 0.38)	Derived from quantile matching 95% PI (15)

Transmission potential

For each secondary case we consider the infectious period as the period of time when their Ct values are less than 30. We then calculate the amount of the infectious period which is spent in quarantine, or in self-isolation due to the onset of symptoms or following a positive test as transmission potential averted. Assuming that the majority of SARS-CoV-2 transmission is driven by superspreading events (17), we report the uncertainty associated with the average secondary transmission potential averted per super spreading event by simulating 1000 index cases with 10 secondary cases. We calculate the median and inner 50% and 95% ranges for the sum of the secondary cases' infectious periods spent in quarantine or self-isolation divided by the sum of secondary cases' infectious periods if there were no quarantine or self-isolation requirements. As the model considers averting this transmission rather than focusing on the generation of additional cases, the average amount of infectivity in secondary cases averted by quarantine and/or testing is independent of the number of additional cases generated, and the choice of the number of secondary cases affects the width of the uncertainty intervals (here we consider a reasonable upper bound on secondary cases based on superspreading, as mentioned, in an attempt to faithfully characterise real-world uncertainty). We also calculate the risk ratio of transmission averted by the given strategy compared to the baseline scenario (a 14 day quarantine period with no testing, 3 days from testing of the index case to tracing, 50% adherence to quarantine and 67% adherence to self-isolation).

The model was coded in R 4.0.3 and the entire code required to reproduce this analysis is available at https://github.com/cmmid/pcr_test_trace.

Role of funding source

The funders of this study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

All authors had full access to all of the data and the final responsibility to submit for publication.

Results

Effect of quarantine on transmission from secondary cases

Relying only on 67% of eventually-symptomatic persons self-isolating upon developing symptoms, 37% (95% UI: 12%, 56%) of transmission may be averted from secondary infections, a risk ratio (RR) of 0.68 (95% UI: 0.22, 0.95) compared to the baseline scenario (a 14 day quarantine period with no testing, 3 days from testing of the index case to tracing, 50% adherence to quarantine and 67% adherence to self-isolation). By tracing contacts and instructing them to self-isolate for a period of time after their last exposure to the index case, additional transmission may be averted from asymptomatic and pre-symptomatic secondary cases (Figure 2A). The amount of transmission averted rises to 46% (95% UI: 16%, 63%), RR: 0.81 (95% UI: 0.49, 0.99) at 7 days post-exposure, 54% (95% UI: 24%, 71%) RR: 0.92 (95% UI: 0.72, 1.00) at 10 days post-exposure and 59% (95% UI: 28%, 79%) at 14 days post-exposure.

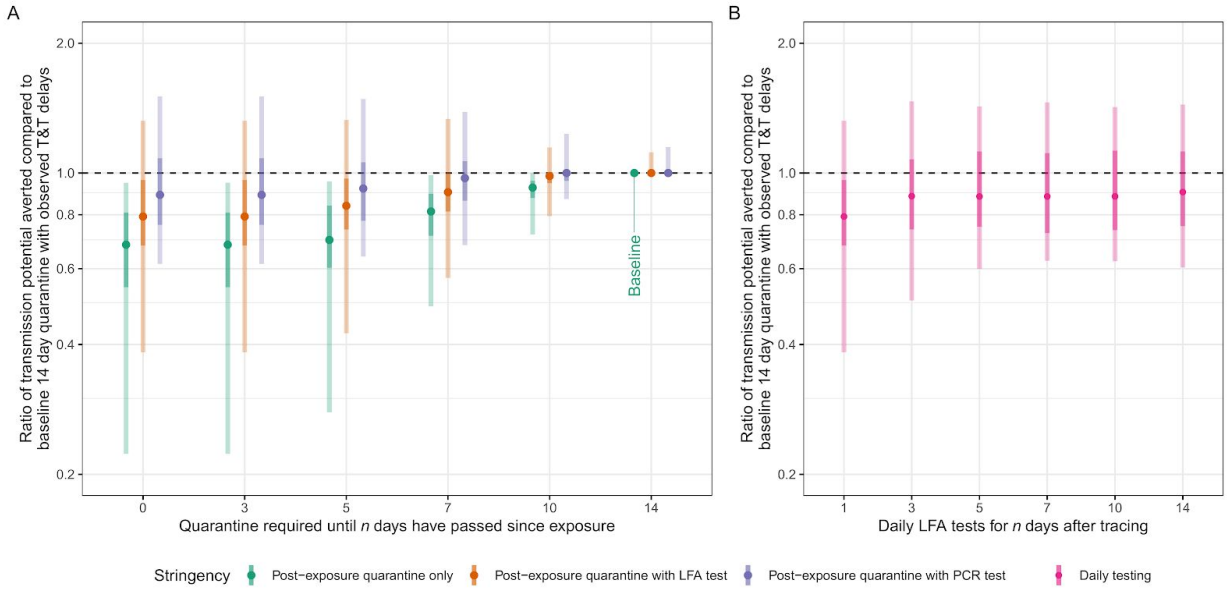

Figure 2: **Ratio of transmission potential averted** (sum of days of secondary cases' infectious periods spent in quarantine or self-isolation / sum of days of secondary cases' infectious periods) for each strategy vs the baseline of 14 days quarantine with no testing, with quarantine-based strategies (quarantine required from time of tracing until *n* days have passed since exposure, either with or without a test on the final day) in **A** and daily testing strategies (daily lateral-flow antigen tests without quarantine for *n* days from

tracing, isolating only upon a positive test result) in **B**. Quarantine and self-isolation adherence assumed to be 50% and 67%, respectively. The delay from index case's positive test until the tracing of secondary cases is assumed to be 3 days (current average) (18). Central bars indicate the median ratio for a given strategy, with 95% and 50% uncertainty intervals indicated by light and dark shaded bars, respectively.

Effect of testing at the end of quarantine

The amount of transmission potential averted can be increased if LFA or PCR testing is conducted on the final day of quarantine (or upon tracing, if the specified quarantine period ends before a case is traced). The introduction of an immediate test is estimated to avert 49% (95% UI: 24%, 68%) of transmission with an LFA test (RR: 0.79 (95% UI: 0.38, 1.32)) and 53% (95% UI: 24%, 79%) of transmission with an PCR test (RR: 0.89 (95% UI: 0.62, 1.51)) (Figure 2A). However, the greater time spent in quarantine waiting for a PCR test result may avert additional transmission, though these delays may not be desirable features of a T&T system. Shorter quarantines with a test may avert a similar amount of transmission to that of the current 14 day quarantine (7 days with LFA test: 50% (95% UI: 28%, 77%); 10 days with LFA test: 56% (95% UI: 32%, 81%); 7 days with PCR test: 54% (95% UI: 31%, 81%); 10 days with PCR test: 56% (95% UI: 33%, 81%). As the quarantine period increases in length, the relative contribution of a test is lessened, as the majority of the infectious period is spent in quarantine. With 14 days of mandatory quarantine, 59% (95% UI: 33%, 79%) of transmission is averted with no testing, and 59% (95% UI: 33%, 82%), RR: 1.00 (95% UI: 1.00, 1.04)) with either a PCR or LFA test (Figure 2A). While no shorter quarantine strategy with testing may exceed the median amount averted by the 14 day quarantine period, all PCR testing strategies evaluated avert equivalent amounts of transmission within the 50% uncertainty bounds.

Effect of daily rapid testing after tracing

If traced contacts are required to take a daily LFA test for n days after tracing instead of entering quarantine, 5 days of testing may avert 50% (95% UI: 23%, 81%, RR: 0.88 (95% UI: 0.60, 1.43)) of transmission, with additional days of testing averting a similar amount (Figure 2B).

Reducing tracing delays

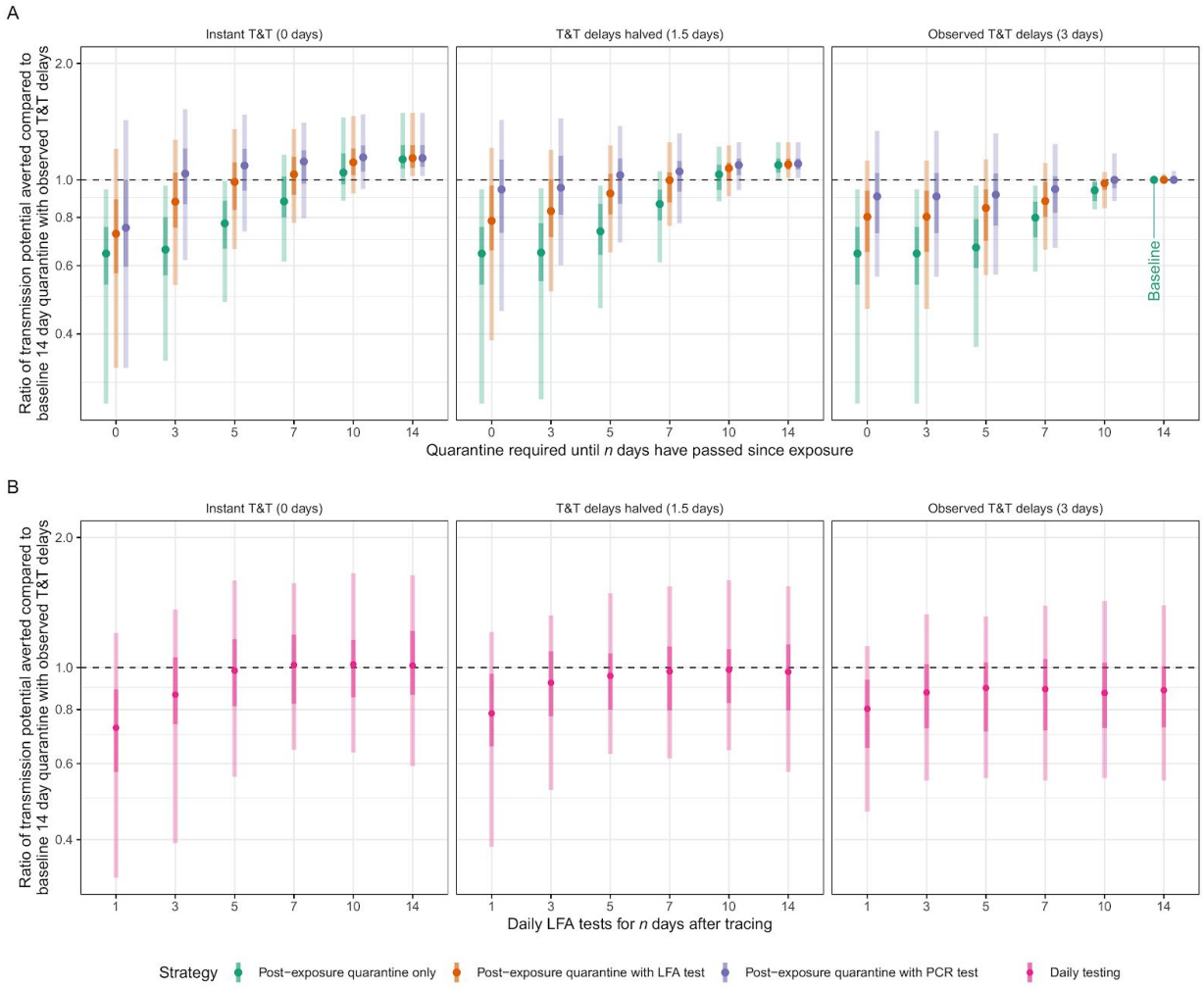

Figure 3: **Ratio of transmission potential averted with reduced test and trace delays** (sum of days of secondary cases' infectious periods spent in quarantine or self-isolation/ sum of days of secondary cases' infectious periods) for each strategy vs the baseline of 14 days quarantine with no testing, with quarantine-based strategies (quarantine required from time of tracing until *n* days have passed since exposure, either with or without a test on the final day) in **A** and daily testing strategies (daily lateral-flow antigen tests without quarantine for *n* days from tracing, isolating only upon a positive test result) in **B**. Quarantine and self-isolation adherence assumed to be 50% and 67%, respectively. The delay from index case's positive test until the tracing of secondary cases is assumed to be 3 days (current average (12)) in the baseline scenario, with halved and eliminated delays investigated. Central bars indicate the median ratio for a given strategy, with 95% and 50% uncertainty intervals indicated by light and dark shaded bars, respectively.

If test and trace delays (i.e, the time from the index case having a test to the tracing of their contacts) can be reduced, shorter quarantines may become more viable, as the proportion of the infectious period spent in the community prior to tracing decreases (Figure 3A). The effect of daily testing strategies also may exceed the effect of the current 14 day strategy if test and trace delays can be reduced to 0 (i.e, app-based contact tracing following a positive rapid test); however, as secondary infections will be traced earlier in their infection when

viral loads are lower, the likelihood of false negatives increases, and additional days of testing (i.e 7 to 10 days) may be required (Figure 3B).

Increasing adherence to quarantine and self-isolation

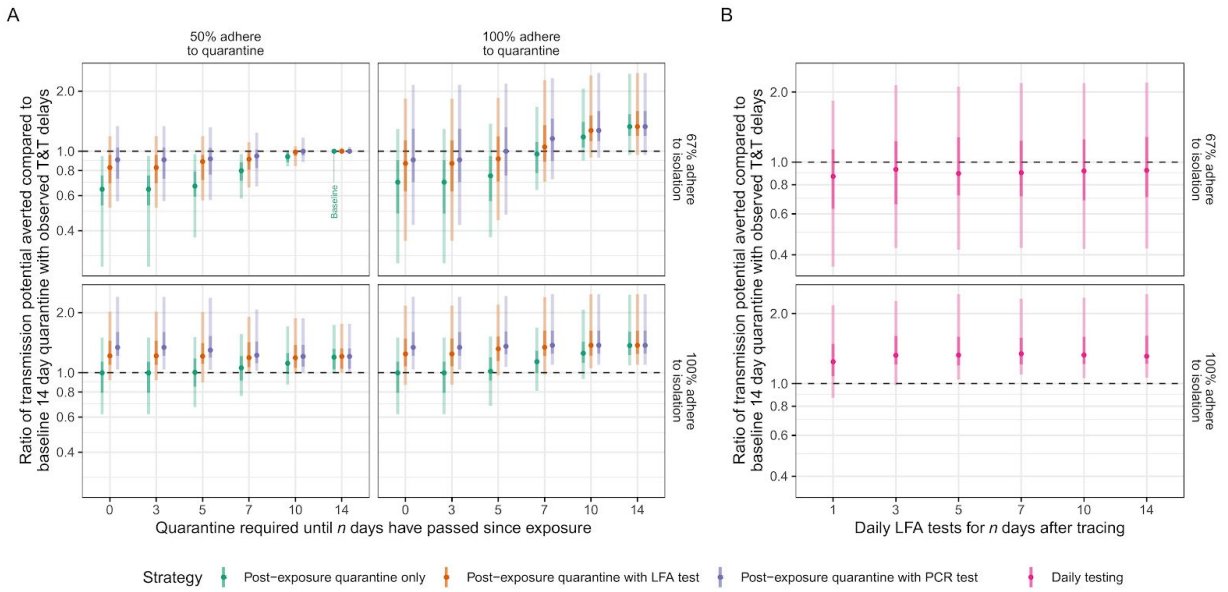

Figure 4: **Ratio of transmission potential averted with increased adherence to self-isolation and quarantine** (sum of days of secondary cases' infectious periods spent in quarantine or self-isolation/ sum of days of secondary cases' infectious periods) for each strategy vs the baseline of 14 days quarantine with no testing, with quarantine-based strategies (quarantine required from time of tracing until *n* days have passed since exposure, either with or without a test on the final day) in **A** and daily testing strategies (daily lateral-flow antigen tests without quarantine for *n* days from tracing, isolating only upon a positive test result) in **B**. Quarantine and self-isolation adherence assumed to be 50% and 67%, respectively, in the baseline scenario, with 100% explored in both. The delay from index case's positive test until the tracing of secondary cases is assumed to be 3 days (current average) (12). Central bars indicate the median ratio for a given strategy, with 95% and 50% uncertainty intervals indicated by light and dark shaded bars, respectively.

If rates of adherence to quarantine and self-isolation can be boosted, substantial increases in effect over that of the baseline 14 day quarantine policy may be achieved, assuming that in the baseline scenario, 50% of individuals adhere to quarantine and 67% of individuals adhere to post-symptom or post-positive test self-isolation (Figure 4). For example, if individuals adhere perfectly to self-isolation upon a positive test in a daily testing scenario, 5 days of testing with LFA after tracing may avert 80% (95% UI: 66%, 89%) of transmission (RR: 1.33 (95% UI: 1.04, 2.42)).

Discussion

Using a model combining SARS-CoV-2 viral load dynamics with a range of possible quarantine and testing strategies for contact tracing, we estimate the recommended 14 days of quarantine following last exposure from a confirmed case can prevent 59% (95% UI: 28%, 79%) of onward transmission from secondary cases, assuming 50% adherence to quarantine and a total delay of 3 days from the index case having a test to the tracing of their

contacts. Assuming the same level of adherence for quarantine and 67% adherence to self-isolation upon symptom onset or a positive test, a lateral flow antigen (LFA) test 7 days after exposure with quarantine from tracing until testing or alternatively daily testing with LFA tests for 5 days after tracing may avert a similar proportion to that of the 14 day quarantine (risk ratios of 0.88 (95% UI: 0.66, 1.11) and 0.88 (95% UI: 0.60, 1.43), respectively), potentially allowing for the reduction of or removal of the quarantine requirement for traced contacts. In strategies requiring quarantine, the additional benefit of testing diminishes with longer quarantine durations, as infectious persons spend a greater proportion of their infectious period in quarantine, and have a higher probability of developing symptoms (if ever-symptomatic) and self-isolating. PCR testing performs better than LFA testing (by averting a greater amount of transmission), however PCR testing may be limited by the requirement to process samples in a laboratory, a process which has inherent delays (24 hours minimum) and logistical limitations (transporting of samples, requirement for skilled staff). Further work on COVID-19 quarantine adherence is required in order to understand how quarantined individuals behave, and whether isolation of cases and suspected cases in hotels or hospitals may be considered to prevent onward transmission.

We find that the effectiveness of contact tracing can be limited by low adherence to quarantine and isolation. It is possible that some of the factors inhibiting adherence to the current 14 day quarantine period are 1) difficulty in completing fully due to social and financial burdens, and 2) low perception of the risk to others given an unknown case status (19). As such, reducing the duration of quarantine and increasing the use of tests to compensate may raise adherence through making it easier to complete a full term, and by making cases aware that they may be infectious. Investigating this assumption in our modelling, we find that raised adherence increases the benefit of both short quarantines with testing (at the end of quarantine) and daily testing, beyond that of the current 14 day quarantine period. As well as the boost in adherence which may arise through these strategies, effort should be made to increase adherence through other methods, such as increasing trust in government and public health advice; producing clear guidance on the specified contact tracing protocol; increasing the perceived importance of quarantine in reducing transmission; building strong local and social support networks; and increasing the level of income support and provision of other supplies (19).

We find that the ability of any contact tracing programme to minimise the transmission potential of secondary cases is limited substantially by the delays from the testing of index cases to the tracing of their contacts, as secondary cases may have been transmitting for a number of days in the community during the time the contact tracing is taking place. If these delays can be reduced through the adoption of rapid testing, rapid app-based contact tracing (13), or both, a greater overall proportion of transmission may be averted; for example, 68% (95% UI: 38%, 86%) of transmission may be averted from secondary cases if cases can be notified as soon as a case is tested (assuming the same baseline assumptions for adherence). As such, great emphasis should be put on monitoring and reducing the time taken to reach secondary cases.

This study has several limitations. In this analysis, we have focused on the potential for quarantine and testing to reduce the transmission potential of traced secondary infections and have not evaluated the number, and cost, of tests which may be required, nor the possibility of false positives which despite the high specificity of PCR and LFA, may arise in mass testing of asymptomatic individuals. However, in the context of contact tracing where prevalence of SARS-CoV-2 among contacts of confirmed cases is likely to be higher than the general public, this is unlikely to lead to a low positive predictive value. Due to a lack of currently available data, we have assumed that index cases seek out and take a PCR test one day after the onset of symptoms. We do not consider

other aspects of the test and trace system which may result in poor outcomes, such as the fraction of index cases that do not engage with the service (20), variation in the number of cases generated by each index case (21), or the proportion of secondary cases missed by tracers (22). Additionally, we do not consider the quarantine and/or testing of the contacts of contacts (i.e household members) who test positive, which may constitute a substantial additional effect. For our assumptions of adherence to quarantine and self-isolation, we selected static, moderate values of the proportion of contacts who adhere to each. It is probable that adherence varies, for example, waning with the duration of quarantine. However in the absence of suitable data on the functional form of such changes in adherence, we take a parsimonious approach to modelling adherence.

One of the simplifying assumptions we have made is that the Ct curve is a reasonable proxy for both probability of detection by testing (under both PCR and LFA) and potential for transmission. Alternative parameterisations of transmission potential are possible (23,24) but unresolved challenges in comparing testing approaches with the transmission potential based on a combination of an incubation period (7) and infectivity relative to onset of symptoms (25) include the need to convert from PCR sensitivity curves (26,27) to LFA in such a way that the timing and height of the two curves are matched meaningfully. A more complete picture of daily testing would require mapping a curve of viral load to one of test sensitivity and one of infectivity.

We have demonstrated that quarantine with a test on day 7 post exposure, or 5 days of lateral flow antigen tests, could reduce the transmission potential from secondary cases notified through contact tracing to similar levels to that of a 14 day quarantine without testing. However, factoring in structural issues in contact tracing such as testing and tracing delays and poor adherence of traced cases greatly reduces the ability of quarantine and testing to reduce onwards transmission, and addressing these should be a focus of policy.

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References

1. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. N Engl J Med. 2020 26;382(13):1199–207.
2. Wright L, Steptoe A, Fancourt D. What predicts adherence to COVID-19 government guidelines? Longitudinal analyses of 51,000 UK adults [Internet]. Epidemiology; 2020 Oct [cited 2020 Nov 25]. Available from: http://medrxiv.org/lookup/doi/10.1101/2020.10.19.20215376
3. World Health Organization. Antigen-detection in the diagnosis of SARS-CoV-2 infection using rapid immunoassays [Internet]. [cited 2020 Nov 11]. Available from: https://www.who.int/publications-detail-redirect/antigen-detection-in-the-diagnosis-of-sars-cov-2infection-using-rapid-immunoassays
4. University of Oxford. Oxford University and PHE confirm high-sensitivity of Lateral Flow Tests following extensive clinical evaluation | University of Oxford [Internet]. [cited 2020 Nov 15]. Available from: https://www.ox.ac.uk/news/2020-11-11-oxford-university-and-phe-confirm-high-sensitivity-lateral-flow-tests-following
5. Ashcroft P, Huisman JS, Lehtinen S, Bouman JA, Althaus CL, Regoes RR, et al. COVID-19 infectivity profile correction. Swiss Med Wkly [Internet]. 2020 Aug 5 [cited 2020 Sep 11];150(3132). Available from: https://smw.ch/article/doi/smw.2020.20336
6. Smith LE, Potts HWW, Amlot R, Fear NT, Michie S, Rubin J. Adherence to the test, trace and isolate system: results from a time series of 21 nationally representative surveys in the UK (the COVID-19 Rapid Survey of Adherence to Interventions and Responses [CORSAIR] study) [Internet]. Public and Global Health; 2020 Sep [cited 2020 Sep 30]. Available from: http://medrxiv.org/lookup/doi/10.1101/2020.09.15.20191957
7. McAloon C, Collins Á, Hunt K, Barber A, Byrne AW, Butler F, et al. Incubation period of COVID-19: a rapid systematic review and meta-analysis of observational research. BMJ Open. 2020 Aug;10(8):e039652.
8. Kissler SM, Fauver JR, Mack C, Olesen SW, Tai C, Kalinich CC, et al. SARS-CoV-2 viral dynamics in

acute infections. medRxiv. :36.
9. Cevik M, Tate M, Lloyd O, Maraolo AE, Schafers J, Ho A. SARS-CoV-2, SARS-CoV, and MERS-CoV viral load dynamics, duration of viral shedding, and infectiousness: a systematic review and meta-analysis. Lancet Microbe. 2020 Nov;S2666524720301725.
10. Viral dynamics of SARS-CoV-2 infection and the predictive value of repeat testing | medRxiv [Internet]. [cited 2020 Nov 24]. Available from: https://www.medrxiv.org/content/10.1101/2020.10.21.20217042v1
11. Dougherty RL, Edelman AS, Hyman JM. Nonnegativity-, monotonicity-, or convexity-preserving cubic and quintic Hermite interpolation. Math Comput. 1989 May 1;52(186):471–471.
12. NHS Test and Trace (England) and coronavirus testing (UK) statistics: 12 November to 18 November [Internet]. GOV.UK. [cited 2020 Dec 2]. Available from: https://www.gov.uk/government/publications/nhs-test-and-trace-england-and-coronavirus-testing-uk-statistics-12-november-to-18-november
13. Kretzschmar ME, Rozhnova G, Bootsma MCJ, van Boven M, van de Wijgert JHHM, Bonten MJM. Impact of delays on effectiveness of contact tracing strategies for COVID-19: a modelling study. Lancet Public Health. 2020 Jul;S2468266720301572.
14. UK Government. How long to self-isolate [Internet]. National Health Service; 2020 Aug. (Coronavirus (COVID-19)). Available from: https://www.nhs.uk/conditions/coronavirus-covid-19/self-isolation-and-treatment/how-long-to-self-isolate/
15. Buitrago-Garcia DC, Egli-Gany D, Counotte MJ, Hossmann S, Imeri H, Ipekci AM, et al. Asymptomatic SARS-CoV-2 infections: a living systematic review and meta-analysis [Internet]. Epidemiology; 2020 Apr [cited 2020 Aug 5]. Available from: http://medrxiv.org/lookup/doi/10.1101/2020.04.25.20079103
16. HM Government. Community testing: a guide for local delivery. 2020 Nov p. 34.
17. Adam DC, Wu P, Wong JY, Lau EHY, Tsang TK, Cauchemez S, et al. Clustering and superspreading potential of SARS-CoV-2 infections in Hong Kong. Nat Med. 2020 Sep 17;1–6.
18. NHS Test and Trace (England) and coronavirus testing (UK) statistics: 22 October to 28 October [Internet]. GOV.UK. [cited 2020 Nov 10]. Available from: https://www.gov.uk/government/publications/nhs-test-and-trace-england-and-coronavirus-testing-uk-statistics-22-october-to-28-october
19. Webster RK, Brooks SK, Smith LE, Woodland L, Wessely S, Rubin GJ. How to improve adherence with quarantine: rapid review of the evidence. Public Health. 2020 May;182:163–9.
20. O'Dowd A. Covid-19: UK test and trace system still missing 80% target for reaching contacts. BMJ. 2020 Jul 17;m2875.
21. Endo A, Centre for the Mathematical Modelling of Infectious Diseases COVID-19 Working Group, Abbott S, Kucharski AJ, Funk S. Estimating the overdispersion in COVID-19 transmission using outbreak sizes outside China. Wellcome Open Res. 2020 Apr 9;5:67.
22. 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 Jun 23;jech-2020-214051.
23. Quilty BJ, Clifford S, Flasche S, Kucharski AJ, CMMID COVID-19 Working Group, Edmunds WJ. Quarantine and testing strategies in contact tracing for SARS-CoV-2 [Internet]. medRxiv; 2020 Aug [cited 2020 Oct 20]. Available from: http://medrxiv.org/lookup/doi/10.1101/2020.08.21.20177808
24. Clifford S, Quilty BJ, Russell TW, Liu Y, Chan Y-WD, Pearson CAB, et al. Strategies to reduce the risk of SARS-CoV-2 re-introduction from international travellers [Internet]. medRxiv; 2020 Jul [cited 2020 Aug 3]. Available from: http://medrxiv.org/lookup/doi/10.1101/2020.07.24.20161281
25. He X, Lau EHY, Wu P, Deng X, Wang J, Hao X, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. Nat Med. 2020 May;26(5):672–5.
26. Kucirka LM, Lauer SA, Laeyendecker O, Boon D, Lessler J. Variation in False-Negative Rate of Reverse

Transcriptase Polymerase Chain Reaction–Based SARS-CoV-2 Tests by Time Since Exposure. Ann Intern Med. 2020 May 13;M20-1495.
27. Hellewell J, Russell TW, The SAFER Investigators and Field Study Team, The Crick COVID-19 Consortium, CMMID COVID-19 working group, Beale R, et al. Estimating effectiveness of frequent PCR testing at different intervals for detection of SARS-CoV-2 infections [Internet]. Centre for Mathematical Modelling of Infectious Diseases, London School of Hygiene and Tropical Medicine; Available from: https://cmmid.github.io/topics/covid19/pcr-positivity-over-time.html

Supplementary appendix

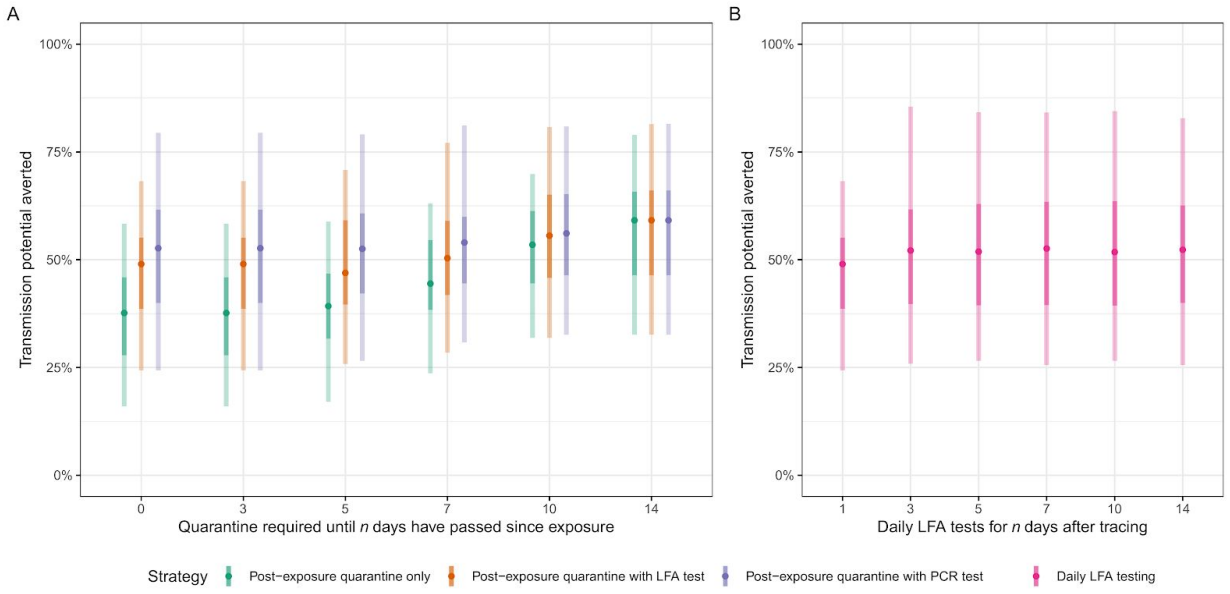

Figure S1: **Transmission potential averted** (sum of days of secondary cases' infectious periods spent in quarantine or self-isolation/ sum of days of secondary cases' infectious periods) for each strategy with quarantine-based strategies (quarantine required from time of tracing until *n* days have passed since exposure, either with or without a test on the final day) in **A** and daily testing strategies (daily lateral-flow antigen tests without quarantine for *n* days from tracing, isolating only upon a positive test result) in **B**. Quarantine and self-isolation adherence assumed to be 50% and 67%, respectively. The delay from index case's positive test until the tracing of secondary cases is assumed to be 3 days (current average) (12). Central bars indicate the median ratio for a given strategy, with 95% and 50% uncertainty intervals indicated by light and dark shaded bars, respectively.

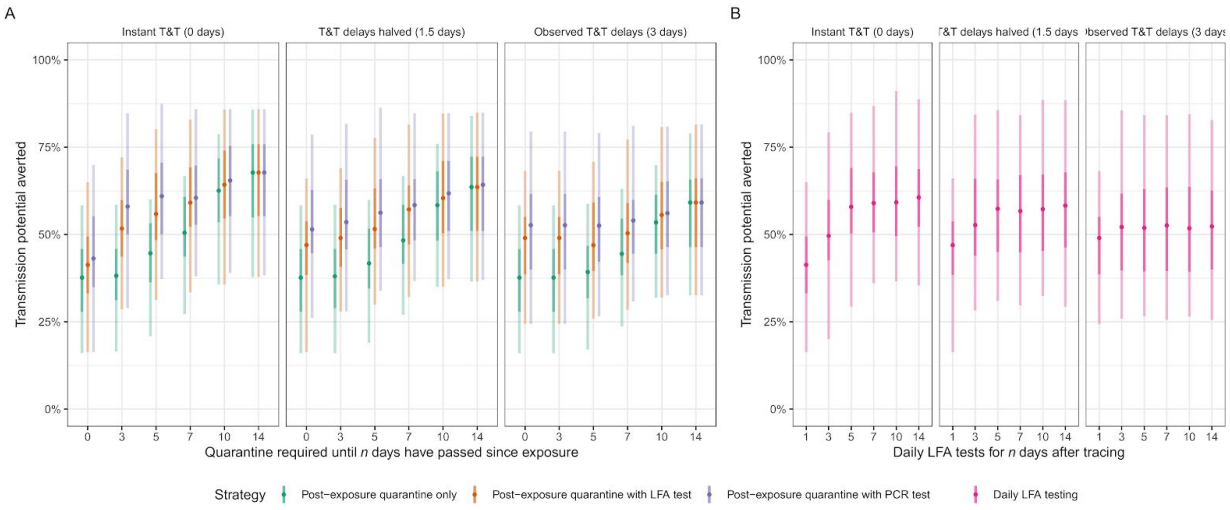

Figure S2: **Transmission potential averted with reduced test and trace delays** (sum of days of secondary cases' infectious periods spent in quarantine or self-isolation/ sum of days of secondary cases' infectious periods) for each strategy with quarantine-based strategies (quarantine required from time of tracing until *n* days have passed since exposure, either with or without a test on the final day) in **A** and daily testing strategies (daily lateral-flow antigen tests without quarantine for *n* days from tracing, isolating only upon a positive test result) in **B**. Quarantine and self-isolation adherence assumed to be 50% and 67%, respectively. The delay from index case's positive test until the tracing of secondary cases is assumed to be 3 days (current average (12)), with sensitivity analysis with halved delays or instant Test & Trace. Central bars indicate the median ratio for a given strategy, with 95% and 50% uncertainty intervals indicated by light and dark shaded bars, respectively.

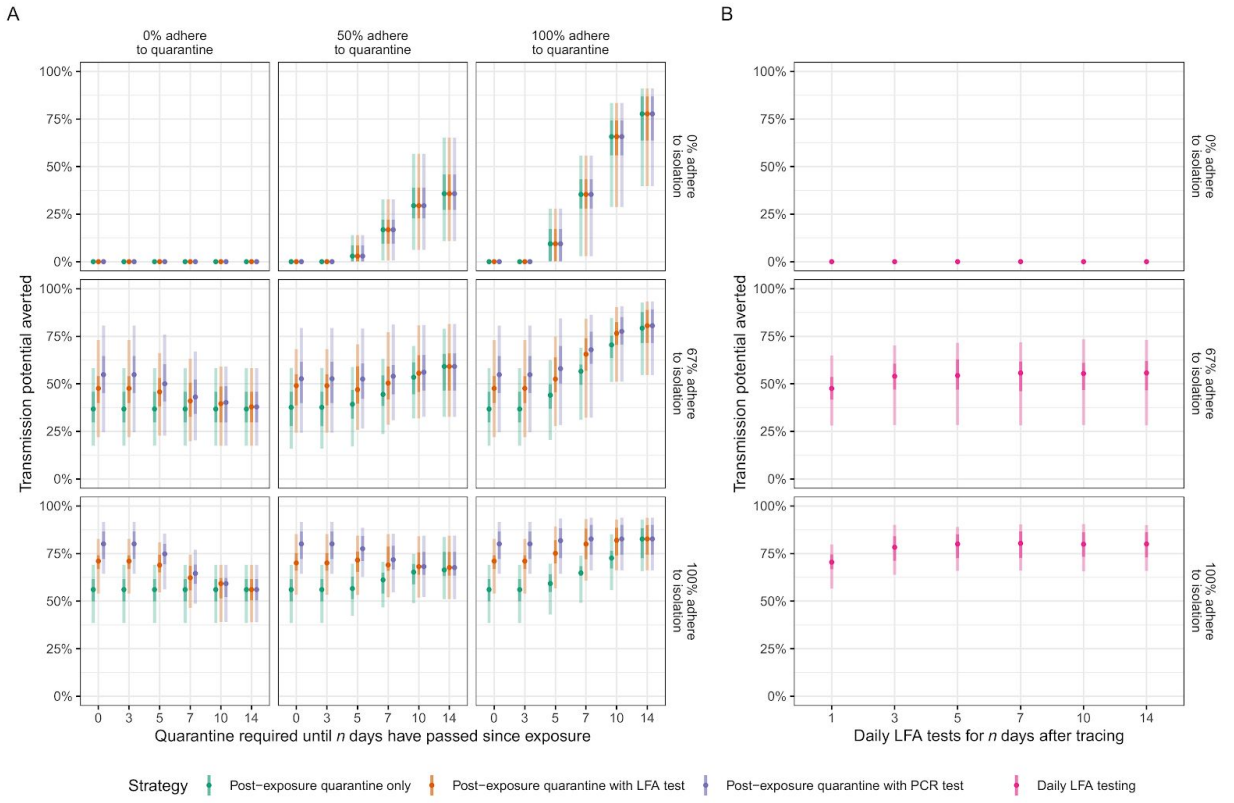

Figure S3: **Transmission potential averted with reduced or increased adherence** (sum of days of secondary cases' infectious periods spent in quarantine or self-isolation/ sum of days of secondary cases' infectious periods) for each strategy with quarantine-based strategies (quarantine required from time of tracing until *n* days have passed since exposure, either with or without a test on the final day) in **A** and daily testing strategies (daily lateral-flow antigen tests without quarantine for *n* days from tracing, isolating only upon a positive test result) in **B**. Quarantine and self-isolation adherence assumed to be 50% and 67%, respectively in the base case, with sensitivity analysis values of 0% and 100% for each. The delay from index case's positive test until the tracing of secondary cases is assumed to be 3 days (current average) (12). Central bars indicate the median ratio for a given strategy, with 95% and 50% uncertainty intervals indicated by light and dark shaded bars, respectively.

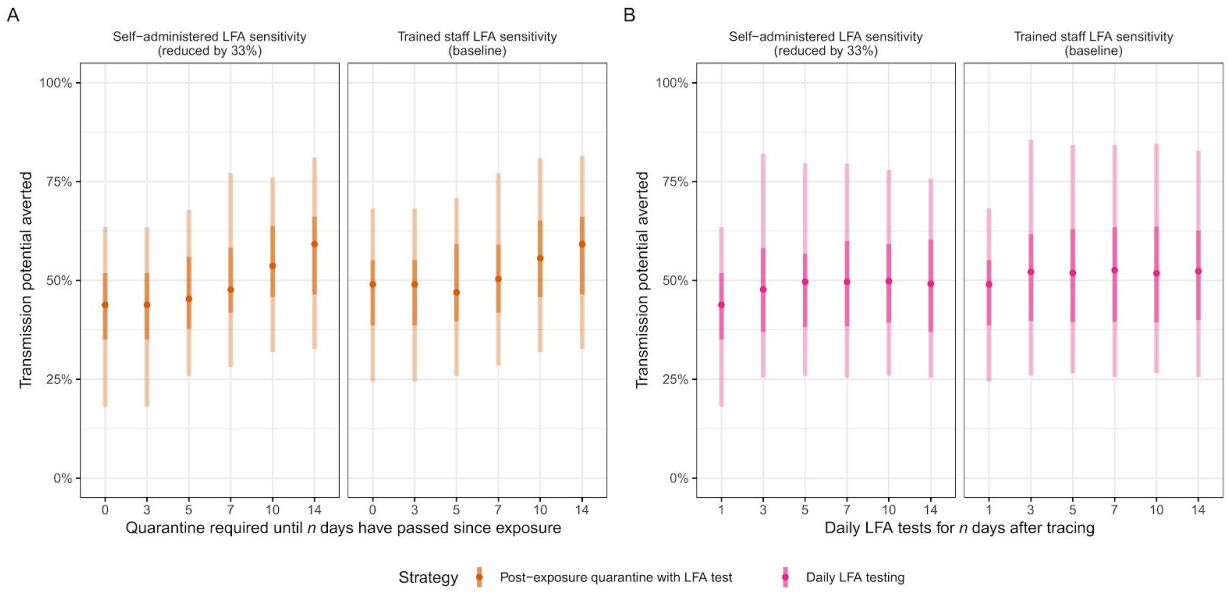

Figure S4: **Transmission potential averted assuming lower sensitivities of LFA when tests are self-administered** (sum of days of secondary cases' infectious periods spent in quarantine or self-isolation/ sum of days of secondary cases' infectious periods) for each strategy with quarantine-based strategies (quarantine required from time of tracing until *n* days have passed since exposure, either with or without a test on the final day) in **A** and daily testing strategies (daily lateral-flow antigen tests without quarantine for *n* days from tracing, isolating only upon a positive test result) in **B**. Quarantine and self-isolation adherence assumed to be 50% and 67%, respectively. The delay from index case's positive test until the tracing of secondary cases is assumed to be 3 days (current average) (12). Central bars indicate the median ratio for a given strategy, with 95% and 50% uncertainty intervals indicated by light and dark shaded bars, respectively.