Rapid testing strategies for traced contacts: comparing quarantine, quarantine and testing, and repeat daily testing

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Summary

- Traced contacts of confirmed SARS-CoV-2 cases in the UK are currently asked to quarantine until 14 days have passed from their last exposure to the index case to avert onwards transmission of SARS-CoV-2.
- Here we assess the merit of using lateral flow antigen (LFA) tests to allow for a shorter quarantine period by testing at its end, or to replace quarantine altogether by testing daily upon tracing and isolating only when test-positive.
- We use an agent-based model of SARS-CoV-2 infection to simulate an exposed contact's contact tracing delay, incubation period, probability of becoming symptomatic, infectivity profile, and time-varying probability of detection with PCR and LFA.
- We find that testing on day 7 post-exposure with LFA may avert 46% (95% UI: 26, 64%) of onward transmission compared to 47% (95% UI: 30, 62%) with a 14-day post-exposure quarantine period with no testing, assuming a 3 day delay from testing of the index case to isolation of contacts, 50% of contacts fully adhering to quarantine, and 67% of contacts fully adhering to post-symptom or post-positive test isolation.

- If contacts are not required to quarantine, but instead undergo daily LFA tests for the 5 days after they are traced, 44% (95% UI: 23, 66%) of transmission may be prevented, accounting for current Test and Trace delays.
- Daily repeated lateral flow testing may allow for the requirement to quarantine to be removed with a small increase in transmission risk, which could itself be offset by increased participation and adherence to isolation. As LFA testing reportedly has high sensitivity at high viral loads, cases may be detected and isolated as soon as they become infectious, averting subsequent transmission.
- However, the amount of transmission averted from secondary infections is limited by the delay from testing of the index case to isolation of contacts, and by the proportion of contacts who adhere to quarantine and self-isolation. By comparison, the potential loss in programme effectiveness through switching from a policy of 14 day quarantine to 7 day quarantine with a subsequent LFA test, or daily LFA testing upon tracing, is small.

Introduction

In the UK, along with many other countries, contacts of SARS-CoV-2 cases are currently asked to quarantine for 14 days since their last contact with a case to avert pre- and asymptomatic onwards transmission. However, there is increasing evidence that many contacts of cases are unable to effectively quarantine for such a long period. The increasing availability of testing, particularly rapid, low-cost lateral flow tests, opens up the possibility of shorter periods of quarantine when combined with a negative test (a test and release strategy), or even the avoidance of quarantine entirely if it is replaced with daily testing. Both of these strategies have the potential to drastically reduce the quarantining of uninfected contacts, which could simultaneously improve adherence and reduce the economic and social damage associated with the current policy. This paper quantifies the impact of these strategies on the risk of transmission compared with quarantining individuals without a test.

Method

Here we adapt the individual-based, stochastic model in (1), supplemented with later data on the probability of detection by PCR over the course of infection from Hellewell & Russell et al. (2), to estimate the utility of two broad strategies to reduce onwards transmission from secondary infections. First, we consider quarantine-based strategies where traced

contacts must quarantine until *n* days since exposure, with or without a test on the final day. Secondly, we consider a daily-testing strategy, where contacts are not required to immediately quarantine, but instead must take a lateral-flow antigen test daily for *n* days after tracing, only isolating if any test is positive.

In the model, infected persons (both index cases and secondary cases) have an infectivity profile (3) with infectiousness peaking around symptom onset. We generate the exposure times of secondary cases according to this profile. We then assume that 1 day after symptom onset, index cases seek out and have a PCR test, at which point we assume that it takes 3 days to get a test result and trace contacts (based on a central estimate of 3.42 days from the latest NHS Test & Trace bulletin for the week 22-28 October 2020 (4)). We also investigate halved delays (1.5 days) and instant tracing (0 days) as a sensitivity analysis. We assume that index cases self-isolate from the point that they seek out and have a test, and therefore cannot generate secondary cases after this time.

Once they are traced, contacts are then 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 tests (LFA) on the final day of quarantine. However, if the end-of-quarantine test is scheduled to occur prior to tracing, we assume that contacts are tested as soon as they are traced; hence, a 0 day quarantine with a test is equivalent to an immediate test and release strategy. In the daily testing strategy, contacts are required to take an LFA test each day for 1, 3, 5, 7 or 10 days after being traced, and are not required to quarantine or isolate unless they either develop symptoms or have at least one positive test. We then calculate the proportion of the infectivity profile a secondary case spends in isolation (i.e, averted transmission potential), from the point of tracing, to release, whether that be due to: the end of quarantine (with a negative test result if required); a subsequent 10 day isolation period if testing positive; or a 10 day isolation period from symptom onset (if eventually symptomatic). We assume that 50% of individuals adhere to their quarantine, which then increases to 67% for the 10 day isolation period after a positive test or after symptom onset (DHSC isolation compliance data, unpublished). We provide a sensitivity analysis of 0% and 100% for each of these assumptions on adherence to quarantine and isolation.

We consider a time-varying sensitivity curve for LFA, which is derived from scaling the infectivity profile (3) so that the probability of detection is equal to the probability of infectivity, multiplied by 95% to reflect peak detectability by the Innova rapid antigen test

(used in the Liverpool mass testing (MAST) pilot) at high viral loads (5). The probability of detecting an infection by PCR at a given point in the course of infection is given by sampling a posterior curve from the model of time-varying probability of detection in (3) (Figure S1A). We assume that the probability of detection by PCR after 30 days is 0. We assume asymptomatic infections make up 31% (95% CI 26%, 37%) of infected individuals (6), do not develop symptoms and hence do not self-isolate, but have the same probability of detection by each test as symptomatic cases (7).

For each strategy, we simulate 1000 index cases, who each generate 10 secondary infections (based on the upper limit of cases generated in superspreading events (8)). The onwards transmission potential of those secondary infections is then summarised by index case, and quantiles are then taken from those 1000 runs.

More detail on the methods may be found in (1).

Results

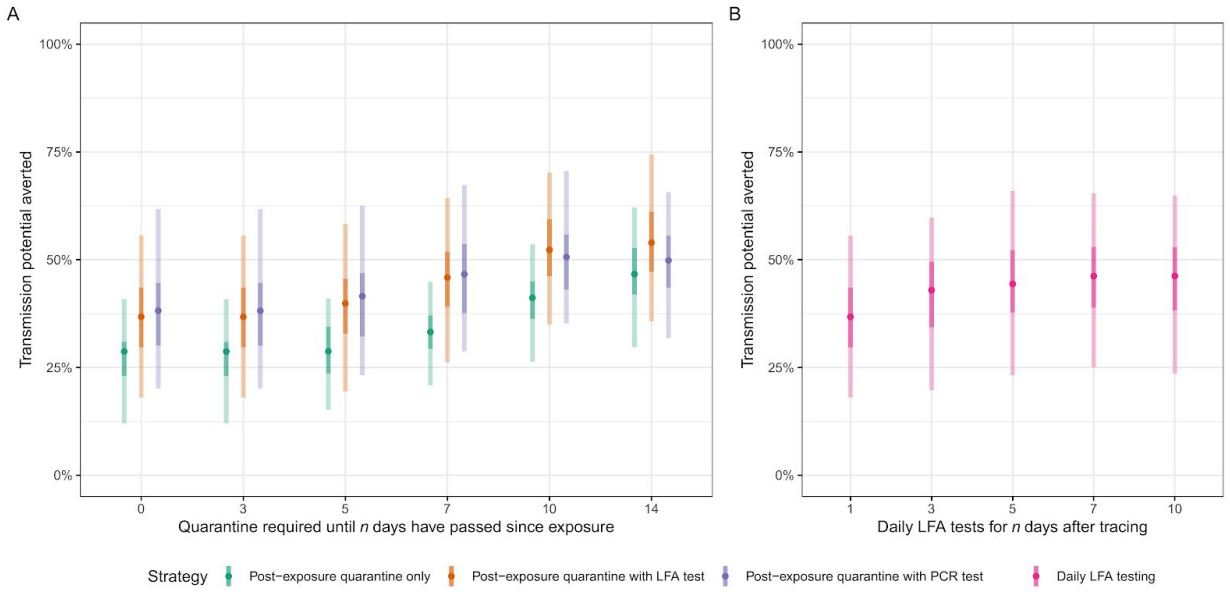

Figure 1: **Transmission potential averted** (integral of infectivity curve over time spent in quarantine or isolation) for each strategy, with quarantine-based strategies (quarantine required from time of tracing until *n* days have passed since exposure, either with or without a test on the final day) 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 adherence assumed to be 50% prior to symptom onset or a positive test result, where adherence is assumed to increase to 67%. The delay from index case's positive test until the tracing of secondary cases is assumed to be 3 days (current average) (4). Time-varying values of sensitivity of LFA given by

scaling the corresponding PCR value by 0.739. Central bars indicate the median amount of transmission potential averted for a given strategy, with 95% and 50% uncertainty intervals indicated by light and dark shaded bars, respectively. Here PCR tests (purple) are shown on the day of sampling, however the return of a result would take 1-2 days, and hence some additional transmission would be averted while awaiting a test result. For other assumptions of symptomatic self-isolation rates, and test and trace delays, see Figure S2 and S3.

Quarantine-based strategies

With a 3 day delay from an index case getting tested to contacts being traced, no testing for traced contacts, and relying only upon 67% of eventually-symptomatic contacts isolating for a further 10 days upon symptom onset, we estimate that 29% (95% UI: 12, 41%) of overall transmission would be averted from secondary infections when taking a weighted average of symptomatic and asymptomatic transmission potential (Figure 1A). Requiring a 7 day post-exposure quarantine period would avert 33% (95% UI: 21, 45%), and a 14 day post-exposure quarantine period would avert 47% (95% UI: 30, 62%). Introducing testing for traced contacts at the end of the specified quarantine period (or upon tracing if the quarantine period is shorter than the delay to isolation) acts to detect and isolate infectious persons earlier in their infectious period, averting additional transmission (Figure 1A); however, the benefit of this diminishes with longer quarantine periods. Immediate testing upon tracing with lateral-flow antigen tests may avert 37% of overall transmission (95% UI: 18, 56%) whereas PCR may avert 38% (95% UI: 20, 62%), however additional transmission may be averted due to the additional 2 days (on average (4)) in quarantine waiting for the PCR test result. At 7 and 14 days of quarantine, inclusion of LFA is estimated to avert 46% (95% UI: 26, 64%) and 54% (95% UI: 36, 74%) of transmission, and use of PCR is estimated to avert 47% (95% UI: 29, 67%) and 50% (95% UI: 32, 66%) of transmission.

Daily testing strategies

Requiring contacts to take a series of daily tests after being traced, with isolation required only upon a positive test, may avert 44% (95% UI: 23, 66%) of transmission with 5 tests (FIgure 1B), with diminishing returns when requiring additional tests (7 and 10 daily tests both averting a median 46% respectively).

Sensitivity analysis of Test & Trace delays and adherence

Substantial reductions in onwards transmission can be made by decreasing Test & Trace delays, as well as increasing adherence to quarantine and isolation (Figure S2, Figure S3). Keeping all other variables constant, halving the delay from an index case being tested to

contacts being traced from 3 to 1.5 days could increase the overall transmission potential averted with a 14 day post-exposure quarantine period to 54% (95% UI: 35, 68%) (Figure S2) due to a greater proportion of the infectivity profile being spent in quarantine. If 100% of contacts adhere to quarantine as well as self-isolate upon a positive test or developing symptoms, 68% (95% UI: 59, 75%) may be averted at 14 days (Figure S3).

Discussion

The current UK policy of quarantine for 14 days after exposure to an index case infected with SARS-CoV-2, while conceptually effective at averting transmission, may be poorly adhered to and is a substantial burden for uninfected contacts. Using a stochastic, individual-based model, we find that shorter quarantines of 7 or 10 days with a rapid antigen or PCR test on the final day may avert a comparable amount of onwards transmission to that of the current 14-day quarantine. Alternatively, repeat testing of contacts with 5 or more days of rapid antigen tests with individuals isolating only upon symptom onset or a positive test may eliminate the time spent in quarantine, with a small increase in transmission risk. However, for our baseline assumptions we found that the current 14-day quarantine is limited to averting 47% of onwards transmission on average. This is due to the potential for transmission prior to tracing (due to test and trace delays) or a failure to isolate upon developing symptoms. As such, making efforts to reduce the delay to isolation of traced contacts through improving test and trace, remains essential to reducing transmission (Figure S2). Additionally, ensuring that contacts adhere to quarantine and isolation when positive has the potential to counteract the increase in transmission associated with reducing or eliminating quarantine. These measures in themselves may increase participation rates, as adherence to isolation by known (i.e, symptomatic or test-positive) SARS-CoV-2 cases is reportedly higher than that of quarantining contacts of unknown case status (9). Shorter quarantine periods may also be easier to adhere to due to lower financial and social costs.

There are several limitations to this analysis. Here we model only infected persons, and hence do not monitor negative outcomes of mass testing which may occur, such as false positives. However, the Innova antigen test is reported to be highly specific (5), and as such, 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. An LFA-specific probability of detection over time is not yet available in the published literature, so in this analysis we assume that the probability of

detection scales with that of viral load, and hence infectivity, which has been reported as a symmetric curve centred around symptom onset in an analysis of infector-infectee pairs (3). The implication of this assumption is that the sensitivity of LFA testing is comparable to PCR early in the course of infection, peaking at peak infectiousness, then decreasing rapidly as virus (and hence antigen) is cleared from the body (10). PCR however will continue to detect non-viable viral RNA for up to several weeks after the infection has been cleared. As such, detecting and isolating cases at this late stage will have little impact on transmission. It then follows that the utility of repeat testing to avert transmission depends on having sufficient sensitivity early in the course of infection when an exposed individual has high viral load and hence is highly infectious, as lateral-flow antigen tests are reported to have (5). To improve these assumptions, additional longitudinal studies should be conducted to determine the viral load and the probability of detection by PCR and LFA over the course of infection - assessing heterogeneity in different individuals by age and other factors if possible - with focus being the critical pre-symptomatic infectious period.

Repeated testing with lateral-flow tests for 5 or more days, with contacts isolating only upon a positive test, may be able to avert a similar amount of transmission to that of the current 14 day post-exposure quarantine period. However, delays in testing index cases and tracing contacts as well as low levels of adherence to quarantine and self-isolation severely limit the effectiveness of any test and trace programme. Reducing the financial and social costs of quarantine through shorter durations or replacement with daily testing may go some way to alleviating these limiting factors.

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Supplementary appendix

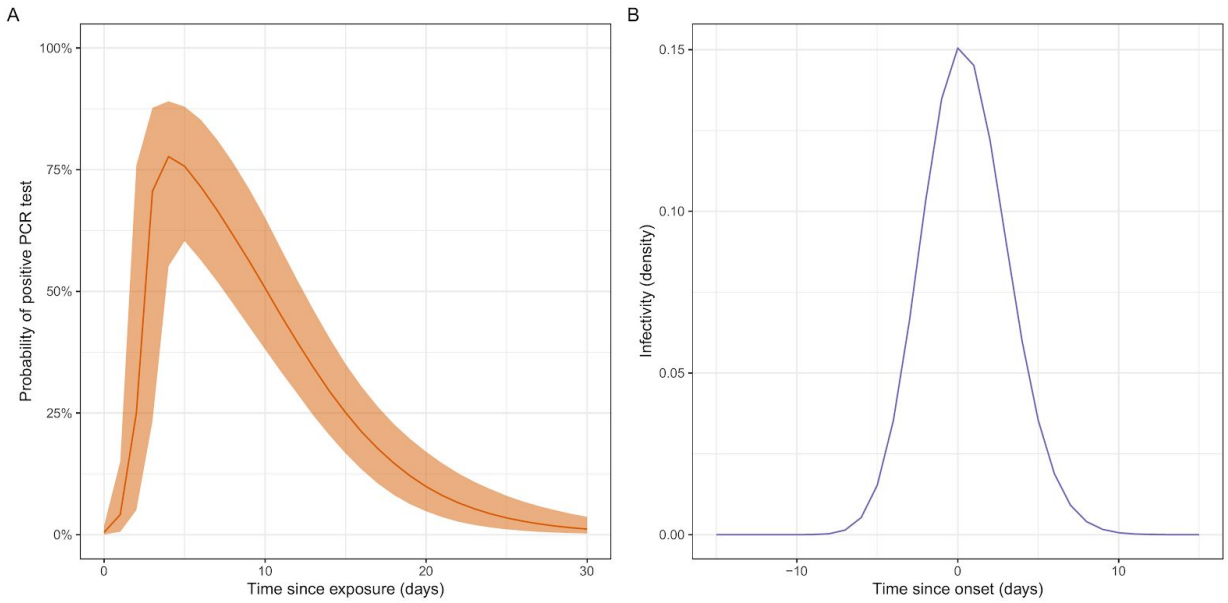

Figure S1 - Positive test detection rate and transmission potential of SARS-CoV-2 infected individuals. A: Posterior medians and 95% credible intervals for probability of a positive test for an individual infected with SARS-CoV-2 as a function of the length of time since infecting exposure event for PCR(2). B: Infectivity profile from He et al. (2020) (3). Gamma-distributed from onset, with shape 97.19, rate 3.71, and shifted by 25.62 days.

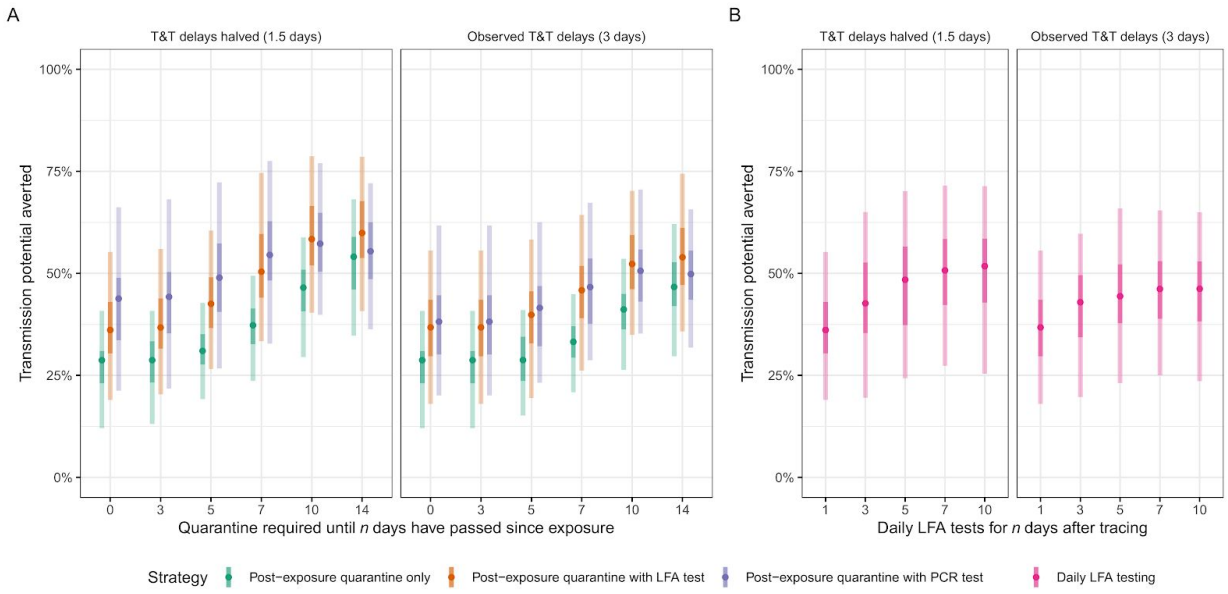

Figure S2: Sensitivity analysis with halved Test & Trace delays. **Transmission potential averted** (integral of infectivity curve over time spent in quarantine or isolation) for each strategy, with quarantine-based strategies (quarantine required from time of tracing until *n* days have passed since 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**, for. Quarantine adherence assumed to be 50% prior to symptom onset or a positive test result, where adherence is assumed to increase to 67%. The delay from index case's positive test until the tracing of secondary cases is assumed to be 3 days (current average), with halved delays shown for comparison (4). Time-varying values of sensitivity of LFA given by scaling the corresponding PCR value by 0.739. Central bars indicate the median amount of transmission potential averted for a given strategy, with 95% and 50% uncertainty intervals indicated by light and dark shaded bars, respectively. Here PCR tests (purple) are shown on the day of sampling, however the return of a result would take 1-2 days, and hence some additional transmission would be averted while awaiting a test result.

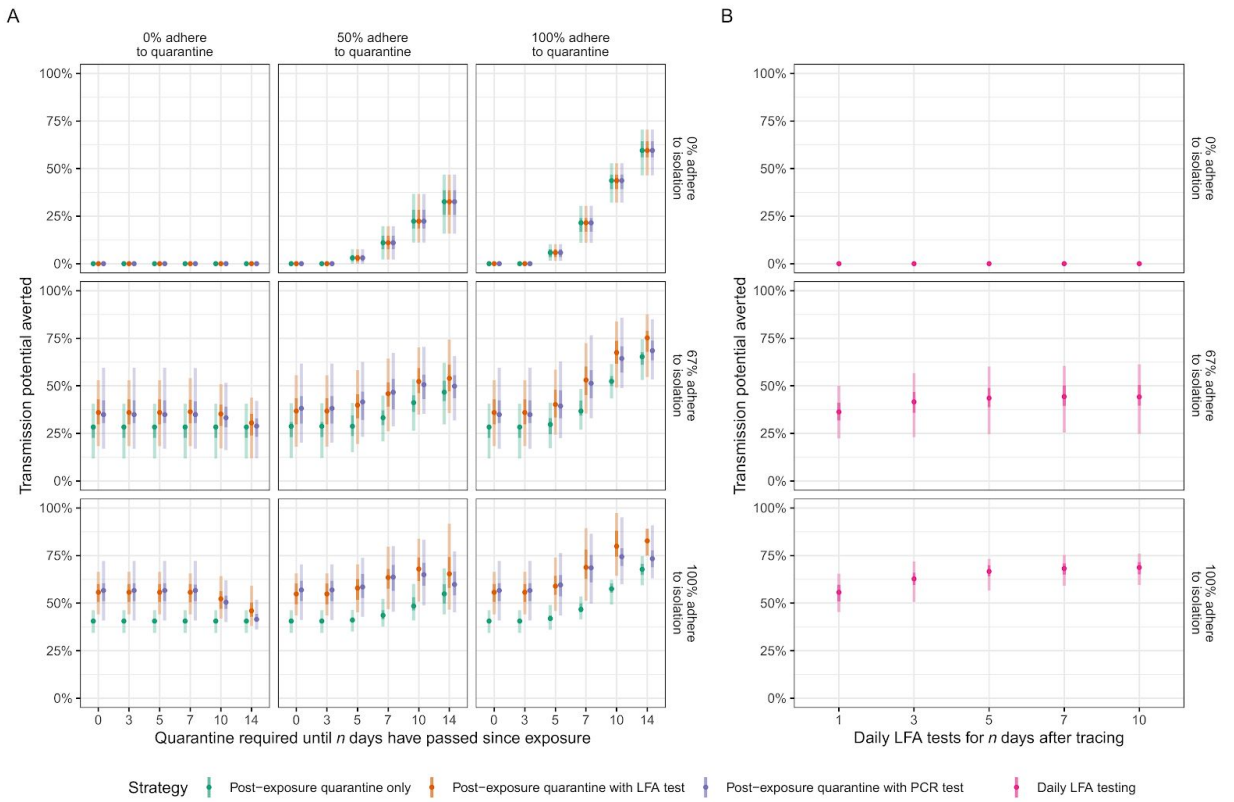

Figure S3: Sensitivity analysis of adherence to quarantine and isolation. **Transmission potential averted** (integral of infectivity curve over time spent in quarantine or isolation) for each strategy, with quarantine-based strategies (quarantine required from time of tracing until *n* days have passed 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 adherence refers to adherence to the quarantine required prior to symptom onset or a positive test result; Isolation adherence refers to the period after this. The delay from index case's positive test until the tracing of secondary cases is assumed to be 3 days (current average) (4). Time-varying values of sensitivity of LFA given by scaling the corresponding PCR value by 0.739. Central bars indicate the median amount of transmission potential averted for a given strategy, with 95% and 50% uncertainty intervals indicated by light and dark shaded bars, respectively. Here PCR tests (purple) are shown on the day of sampling, however the return of a result would take 1-2 days, and hence some additional transmission would be averted while awaiting a test result.

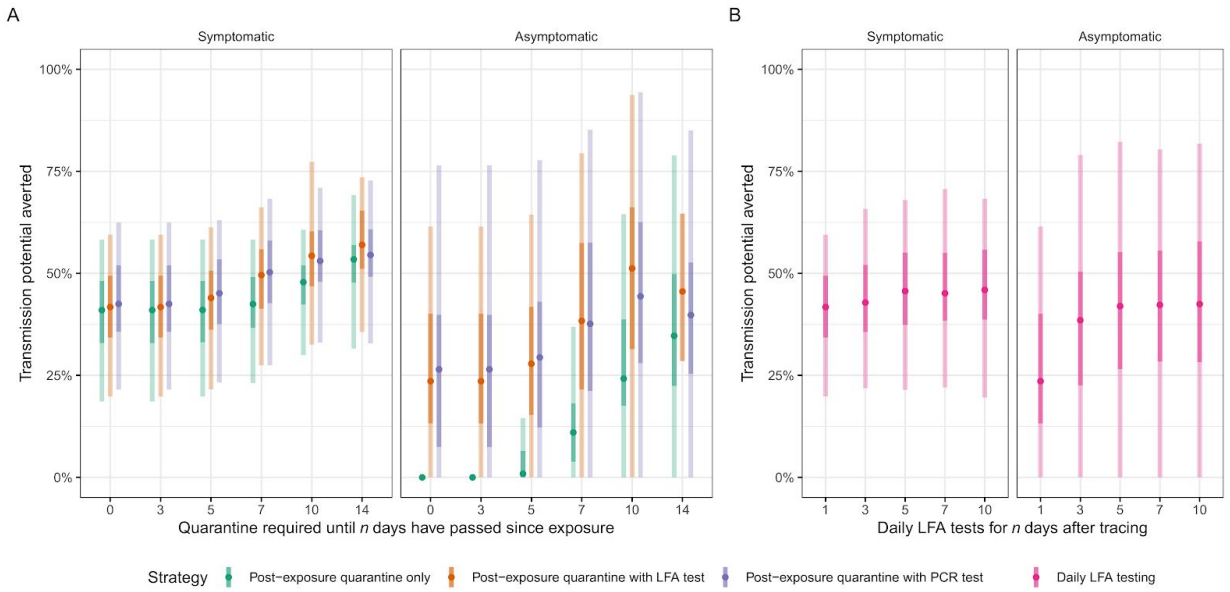

Figure S3: Sensitivity analysis of infection type (symptomatic vs asymptomatic). **Transmission potential averted** (integral of infectivity curve over time spent in quarantine or isolation) for each strategy, with quarantine-based strategies (quarantine required from time of tracing until *n* days have 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 adherence refers to adherence to the quarantine required prior to symptom onset or a positive test result; Isolation adherence refers to the period after this. The delay from index case's positive test until the tracing of secondary cases is assumed to be 3 days (current average) (4). Time-varying values of sensitivity of LFA given by scaling the corresponding PCR value by 0.739. Central bars indicate the median amount of transmission potential averted for a given strategy, with 95% and 50% uncertainty intervals indicated by light and dark shaded bars, respectively. Here PCR tests (purple) are shown on the day of sampling, however the return of a result would take 1-2 days, and hence some additional transmission would be averted while awaiting a test result.