This report was updated on 16/11/2020 to include a sensitivity analysis of the time-varying probability of detection curve for lateral flow tests.

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

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Summary

- Traced contacts 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 either reduce the duration of quarantine by testing at the end, or to replace quarantine altogether by testing daily upon tracing and isolating only when test-positive.
- We use an agent-based model to simulate an exposed contact's contact tracing delay, incubation period, probability to become symptomatic, infectivity profile, and time-varying PCR and LFA detection probability.
- We find that testing on day 7 post-exposure with LFA may avert 50% (95% UI: 31, 69%) of onward transmission compared to 53% (95% UI: 35, 68%) with a 14-day post-exposure quarantine period and no testing, assuming a 3 day delay from testing of the index case to isolation of contacts, 50% of contacts adhering to

quarantine, and 67% of contacts adhering to post-symptom or post-positive test isolation.

- Repeated lateral flow testing may allow for the requirement to quarantine to be removed, with a small increase in transmission risk, which may itself be offset by increased participation and adherence to isolation.
- If contacts are not required to quarantine, but instead are required to take daily LFA tests for the 3 days after they are traced, 43% (95% UI: 20, 64%) of transmission may be prevented. However if we consider a shorter window of detection than that of PCR tests, then the benefit of additional days of testing is increased, a strategy which may closely match the effectiveness of a quarantine and testing strategy (48% for 5 days of testing (95% UI: 28, 67%); 51% for 7 days of testing, 95% UI: 29, 72%).
- Lateral flow testing is only marginally less effective than PCR at averting onwards transmission from traced secondary infections despite a lower sensitivity, and may present a viable alternative due to logistical advantages.
- The amount of transmission averted from secondary infections is limited substantially 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 subsequent LFA test, or daily LFA testing upon tracing, is small.
- Key limitation: We use conservative assumptions on the test sensitivity of LFA. See Figure S5 for a sensitivity analysis of this assumption.

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: quarantine-based strategies, where traced contacts must quarantine until *n* days since exposure, with or without a test on the final day; or a daily-testing strategy, where contacts are not required to immediately quarantine, but instead must take a daily lateral-flow antigen test 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 scheduled end-of-quarantine test is 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 develop symptoms or test positive. 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. We provide a sensitivity analysis of 0% and 100% for each of these assumptions.

The probability of detecting an infection by PCR over time is given by sampling a posterior curve from the model in (2). To account for the lower sensitivity of PCR and LFA, we scale the PCR positivity curve by 0.739 (Figure S1A). This value is derived by integrating the PCR positivity curve from 5-10 days (the time around the peak detectability) and finding the value which, when multiplied by this area under the curve (0.622), matches the mean reported sensitivity of the LFA (46.0%, expert opinion reported to the UK Government's SPI-M expert advice body for infectious disease modelling on 18 October 2020). As a sensitivity analysis, we also consider an alternative 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 peak probability of infectivity, multiplied by 95% to reflect peak detectability by the Innova rapid antigen test at high viral loads (5). 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).

For each strategy, we simulate 1000 index cases, who generate 10 secondary infections (based on the upper limit of cases generated in superspreading events (7). 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

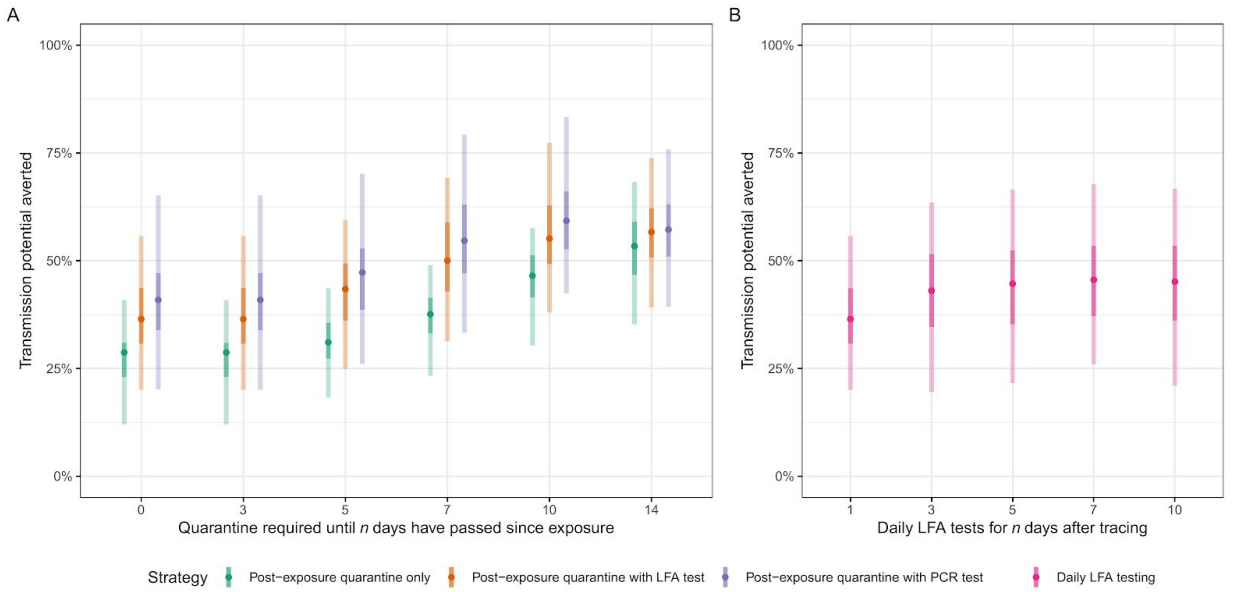

Figure 1: **Transmission potential averted** (integral of infectivity curve over time spent in quarantine or isolation) for each strategy, with quarantine-based strategies (quarantine required from time of tracing until *n* days have passed since exposure, either with or without a test on the final day) 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 an 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 38% (95% UI: 23 49%), and a 14 day post-exposure quarantine period would avert 53% (95% UI: 35, 68%). 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. PCR and LFA averting a comparable amount of transmission. Immediate testing upon tracing with lateral-flow antigen tests may avert 36% of overall transmission (95% UI: 20, 56%) whereas PCR may avert 41% (95% UI: 20, 65%), 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, this increases to 50% (95% UI: 31, 69%) and 57% (95% UI: 39, 74%) respectively for LFA, and 55% (95% UI: 33, 79%) and 57% (95% UI: 39, 76%) respectively for PCR.

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 43% (95% UI: 20, 64%) of transmission with 3 tests (FIgure 1B), with little benefit to requiring additional tests (5, 7 and 10 daily tests averting a median 45%, 46% and 45% respectively).

Sensitivity analysis of lateral flow antigen detection curve

If the LFA detection curve is assumed to be equal to the infectivity profile multiplied by 95%, rather than the PCR curve multiplied by 0.739 (i.e, a shorter window of detection for antigen tests) (Figure S4), the benefit of a greater number of days of testing tests is increased, with 5 and 7 days of testing averting 48% (95% UI: 28, 67%) and 51% (95% UI: 27, 71%) respectively, with additional tests beyond 7 gaining greater benefit if Test & Trace delays are shortened (Figure S5).

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 60% (95% UI: 40, 76%) (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, 77% (95% UI: 72, 81%) 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 3 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 unnecessarily, with a small increase in transmission risk. However, for our baseline assumptions of 3 days from the index case getting tested to contacts being traced, 50% adherence to quarantine and 67% adherence to symptomatic self-isolation or post-positive test self-isolation, we found that the current 14-day quarantine is limited to averting 53% of onwards transmission on average. This is due to the potential for transmission prior to tracing (due to test and trace delays), after release from quarantine (due to a false negative test result) or a failure to isolate upon developing symptoms. As such, making efforts to reduce the delay to isolation of traced contacts, and ensuring that contacts adhere to quarantine and isolation, may counteract the additional risk introduced by reducing or eliminating the quarantine requirement through testing of contacts. 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 (8). Shorter quarantine periods may also be easier to adhere to due to lower potential for fatigue.

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, so in this analysis we have scaled the PCR probability of detection over time curve by 0.739 to match the reported sensitivity of LFA tests. It may be the case that LFA testing is less sensitive in the tail of the curve than PCR due to faster clearance of antigen. As such, we consider a sensitivity analysis using the infectivity profile as the detection probability for LFA, reducing the detection probability later in an individual's infection (Figure S4); this leads to more days of daily testing averting greater amounts of transmission, as there are more opportunities for a test to detect cases during this short window (Figure S5). Hence, a strategy of 5 or 7 days may be more appropriate. We also consider repeat tests to be fully independent, which may not account for heterogeneity in viral load by individual. Further research linking viral load and detectability by lateral flow antigen tests is required to improve these assumptions.

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Supplementary appendix

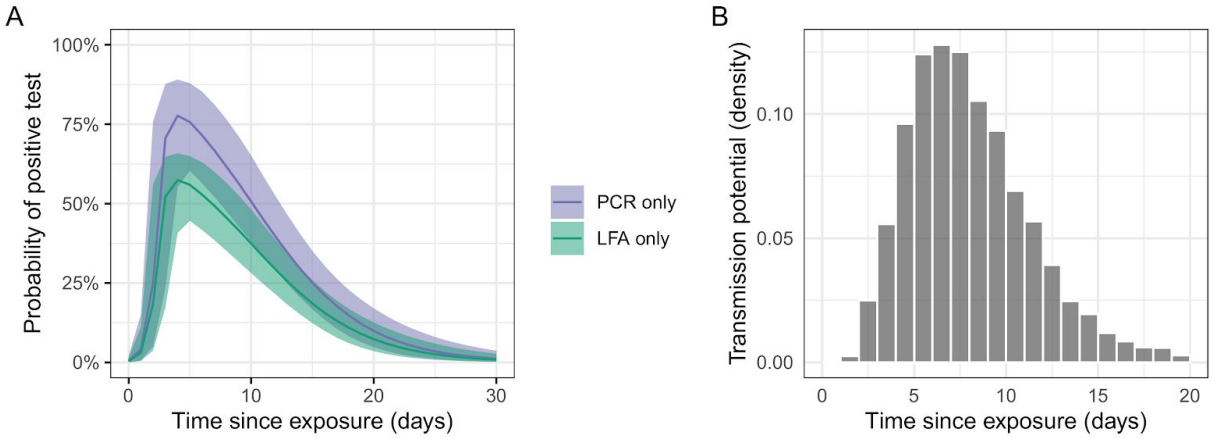

Figure S1 - Positive test detection rate and transmission potential of SARS-CoV-2 infected individuals. A: Posterior medians and 95% credible intervals for probability of a positive test for an individual infected with SARS-CoV-2 as a function of the length of time since infecting exposure event for PCR, and the inferred detection curve for LFA using a scaling factor of 0.739. B: Transmission potential of persons infected with SARS-CoV-2, generated from the incubation period from McAloon et al. (2020) (9) and infectivity profile from He et al. (2020) (3). Sampled sum of log-normally distributed onset of symptoms, with location parameter 1.63 and scale parameter 0.41, and Gamma-distributed infectivity from onset, with shape 97.19, rate 3.71, and shifted by 25.62 days.

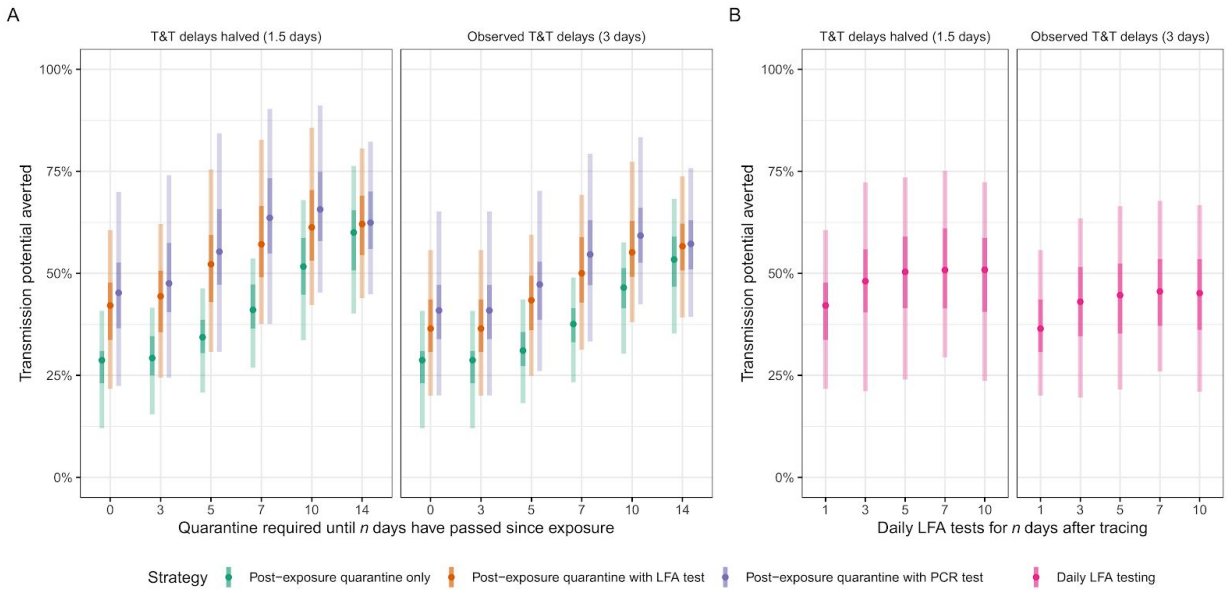

Figure S2: Sensitivity analysis with halved Test & Trace delays. **Transmission potential averted** (integral of infectivity curve over time spent in quarantine or isolation) for each strategy, with quarantine-based strategies (quarantine required from time of tracing until *n* days have passed since 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.

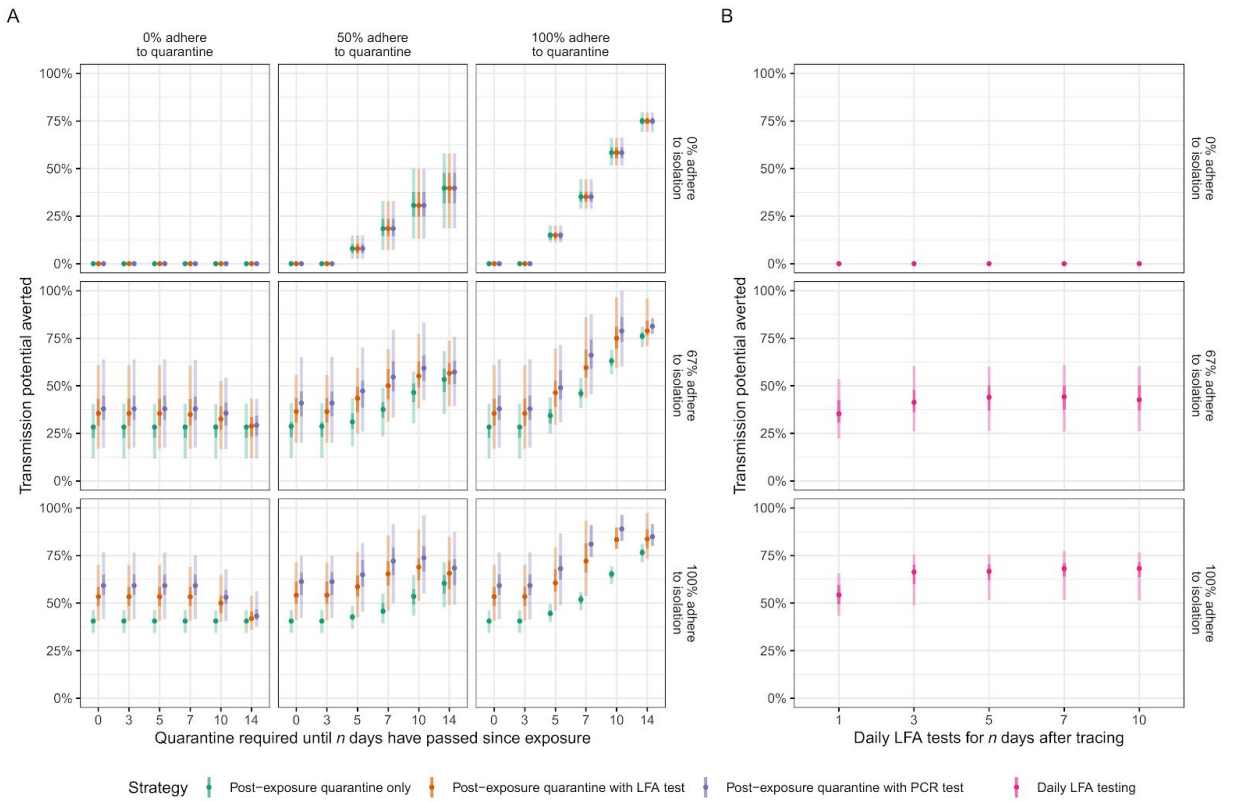

Figure S3: Sensitivity analysis of adherence to quarantine and isolation. **Transmission potential averted** (integral of infectivity curve over time spent in quarantine or isolation) for each strategy, with quarantine-based strategies (quarantine required from time of tracing until *n* days have passed 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.

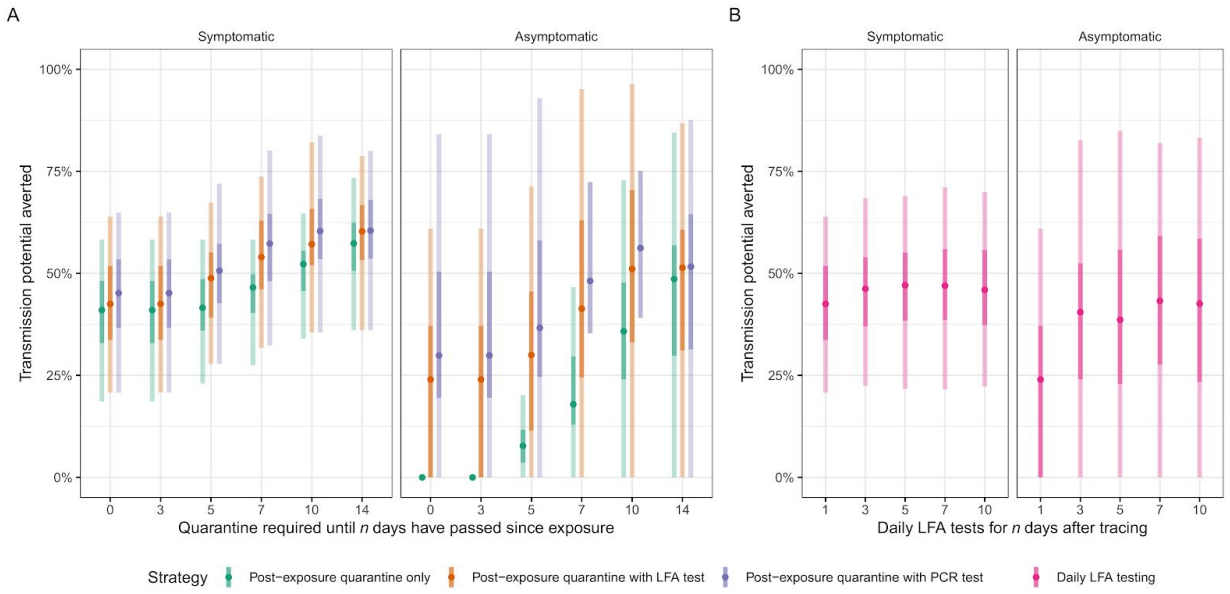

Figure S3: Sensitivity analysis of infection type (symptomatic vs asymptomatic). **Transmission potential averted** (integral of infectivity curve over time spent in quarantine or isolation) for each strategy, with quarantine-based strategies (quarantine required from time of tracing until *n* days have 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.

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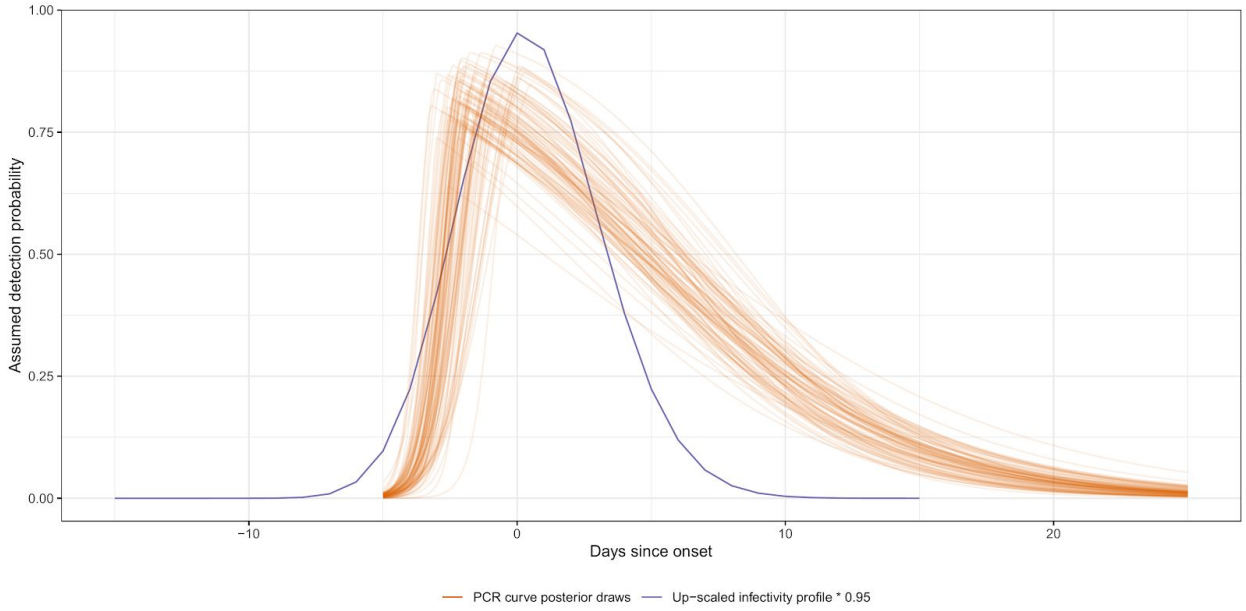

Figure S4: Sensitivity analysis of the probability of detection curve. Purple curve derived from scaling the infectivity profile (3) so that the probability of detection is equal to the peak probability of infectivity, multiplied by 95% to reflect peak detectability by the Innova rapid antigen test at high viral loads (5).

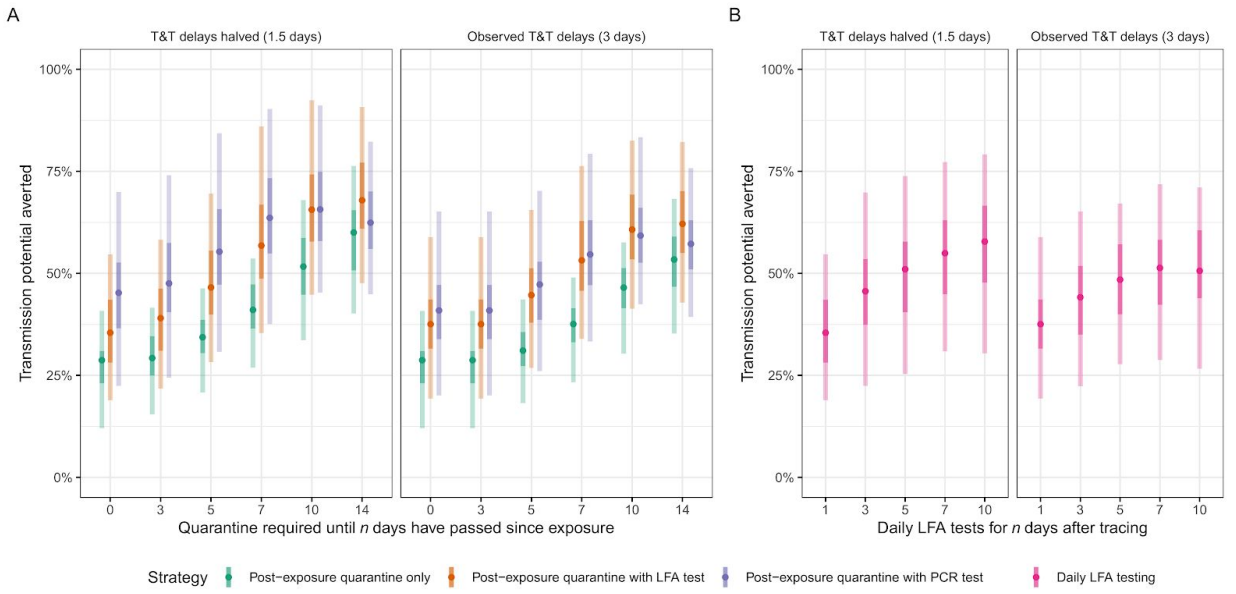

Figure S5: Sensitivity analysis with up-scaled infectivity profile multiplied by 95% as the probability of detection over time for lateral-flow antigen tests. **Transmission potential averted** (integral of infectivity curve over time spent in quarantine or isolation) for each strategy, with quarantine-based 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

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