Work Package 1: TTIQ

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Executive summary

Strategies to streamline and focus TTIQ responses as jurisdictions move into Phases B and C of the National Plan were identified through consultation with the Communicable Disease Network of Australia and the Australia Health Protection Principal Committee. This report examines the likely impacts of these modified TTIQ strategies on transmission potential in the context increasing caseloads, the Delta variant, and high vaccine coverage. Further, the report outlines requirements for real-time monitoring of the effectiveness of the entire TTIQ system to support ongoing adaptation of strategies to the epidemiological situation.

- Streamlined and focused test-trace-isolate-quarantine (TTIQ) processes (supported by PHSMs) will be required for future public health responses to remain effective.

  TTIQ is limited by case ascertainment. The fraction of infections displaying symptoms will decrease with increasing vaccination coverage, limiting opportunities for detection.

- Targeting a transmission potential (TP) at or around 1, as per the national strategy, will constrain community transmission. Accordingly, we evaluate TTIQ strategies by estimating the percentage change in TP.

  The impact of even minor changes in TP on the local epidemiology depends critically on how close TP is to the national strategic objective of maintaining a control threshold of 1. If TP at the population level is very close to 1, even a small increase can be sufficient to drive a change from decreasing to increasing epidemic activity, the consequences of which depend on caseloads.

Findings

- Testing on Day 1 of quarantine supports timely identification and isolation of downstream infections and is always the most important test to prioritise

- Case-initiated contact tracing supports timely quarantine in times of system stress

- Reducing quarantine requirements for vaccinated individuals from 14 days to 7 days has no discernible impact on the performance of the TTIQ system. Completely removing isolation and/or quarantine for vaccinated individuals is estimated to increase TP by 3–5%.

- Prioritising the most recently identified cases for contact tracing increases impact of the TTIQ response, as late case finding is associated with diminishing returns on TP reduction

Monitoring of TTIQ impact is required for situation assessment. We describe data requirements and a framework for real-time evaluation of TTIQ impact on transmission.

Random population prevalence surveys would provide gold standard evidence of the number and proportion of infections by vaccination and symptom status over time.

Overview and key question

Overview: Doherty Modelling has clearly identified the critical importance of maintaining optimal test, trace, isolate and quarantine (TTIQ) capability as defined in our previous work into the next phases of our transition to living with COVID-19. This second piece of work has undertaken quantitative risk assessment to inform CDNA and AHPPC consideration of the future requirements of public health responses and inform planning for public health workforce.

Previously, as part of Phase 1 of the National Plan Modelling, we estimated the effectiveness of TTIQ on reducing transmission potential from case data: times from infection to isolation of cases. These delays from infection to isolation are the outcomes of contact tracing which we directly translated into reductions in transmission potential.

To address the key questions in this next phase of work, we now model how different proposed strategies affect transmission potential, via impacts on contact tracing delays, isolation, and quarantine strategies. This requires understanding of component delays and processes within the TTIQ system and the likely impact of vaccination and alternate strategies on system effectiveness.

Key question: What are the most effective and sustainable strategies for TTIQ to manage COVID-19 as vaccination rates increase in Phase A then Phases B and C to achieve the aim of constrained community transmission and avoid lockdown requirement?

National Plan Phases B and C context

The aim of TTIQ is to detect and place cases into isolation as soon as possible. If cases are already in quarantine at the time of onset of infectiousness, the risk to the community is lowered.

In our analyses below, we consider cases detected in the community via testing of symptomatic individuals (passive detection) and via testing of close contacts identified through contact tracing (active detection). Other means of enhanced case finding such as routine asymptomatic screening of individuals in high-risk settings are not included in our analyses. Such strategies, focused on workforce continuity, have the potential to further reduce transmission by increasing the overall proportion of cases ascertained.

The potential impact of TTIQ on transmission is limited by case ascertainment – people with undetected infections are not placed into isolation and so both they and their infected contacts will continue to contribute to transmission. Detection of unlinked symptomatic infections in people presenting for testing (passive symptomatic detection) enables reinitialisation of contact tracing on these undetected chains of transmission. Given that COVID-19 vaccines reduce the probability of developing symptoms, we anticipate lower levels of passive symptomatic detection with increasing vaccination coverage, for similar surveillance effort.

Compared to the pre-vaccination and pre-Delta era, transmission is likely to be concentrated in different population groups and settings (*e.g.*, low coverage groups, schools), which may require different TTIQ strategies and related public health responses.

As we transition to Phases B and C, the objective of TTIQ responses will explicitly change from supporting a goal of 'no community transmission', to one of 'constrained community transmission, that is maintaining transmission potential (TP) around 1'. As a result, TTIQ strategies will need to adapt to higher caseloads. This change in strategy implies a different objective of TTIQ: to reduce transmission in support of overall health and societal goals, rather than the previous aim of minimising the probability of *any* cases being missed and not placed into isolation. Adaptation of measures will therefore likely include pivoting contact tracing procedures to focus on reducing the time infectious in the community for the majority of cases, rather than identifying all downstream and upstream contacts of each case (as previously). With this re-framing, the goal is to identify

strategies where similar reductions in transmission potential can be achieved with a lower per case burden on the contact tracing system.

Key modelling assumptions

The estimated effectiveness of different TTIQ strategies will be sensitive to assumptions about infectiousness and test sensitivity as functions of time since infection, the probability of developing symptoms, and the probability of seeking a test given symptoms, for vaccinated and unvaccinated individuals.

Key biological parameters:

- Infectiousness over time since infection (for vaccinated and unvaccinated)
- Test sensitivity over time since infection (for vaccinated and unvaccinated)
- Probability of developing symptoms for vaccinated and unvaccinated infections

Key behavioural parameters:

- Probability of seeking a test given symptoms (for vaccinated and unvaccinated)

Links to previous work: Estimating TTIQ performance from case data

Figure 1 displays SARS-CoV-2 infection progression over time and how passive and active case detection may each reduce the proportion of infectiousness in the community.

Timely identification and quarantine of contacts (active detection) cuts off a much greater proportion of community infectiousness compared to isolation of symptomatic individuals (passive detection). This is because even if individuals seek a test promptly after symptom onset, they have already contributed several exposure days to the community before they knew they were infected and infectious. However, both modes of detection are critical to the overall impact of TTIQ, since the contact tracing process is initiated by passively detected cases.

Figure 1 also indicates how reductions in the proportion of infectiousness in the community due to passive symptomatic case finding and active contact tracing can be measured from case data. For Phase 1 of the National Plan Modelling, we used times from infection to isolation of cases to estimate the effectiveness of TTIQ on reducing transmission potential. We estimated that periods of 'Optimal' TTIQ reduced transmission potential by 54% and 'Partial' TTIQ reduced transmission potential by 42% (Figure 2).

To address the key questions in this next phase of work, we now model how different proposed strategies affect delays from infection to isolation. This requires understanding of each of the component delays within the TTIQ system and the likely impact of alternate strategies based on vaccination status of cases and/or contacts on system effectiveness.

Component delays include the time from symptom onset to test, test to case notification, case notification to case interview, case interview to contact notification. Figure 3 illustrates the timing of key TTIQ actions, these component delays, and the impact of longer delays on the timeliness of identification and quarantine of contacts.

Figure 1: Schematic of SARS-CoV-2 infection progression (**A**) and two modes of case detection: testing of symptomatic individuals (passive detection, **B**) and testing of close contacts identified through contact tracing (active detection, **C**). We also illustrate two key intervals for estimating TTIQ effectiveness from case data: times from infection to isolation and times from symptom onset to isolation. Isolation times enable more accurate measurement of TTIQ effectiveness than routinely available detection/notification times. Isolation times are not yet available in the National Notifiable Disease Surveillance System (NNDSS). Note: Both the displayed shape of the infectiousness curve (orange) and reductions in transmission are for illustrative purposes only, they do not correspond to specific model parameters and their impacts on transmission.

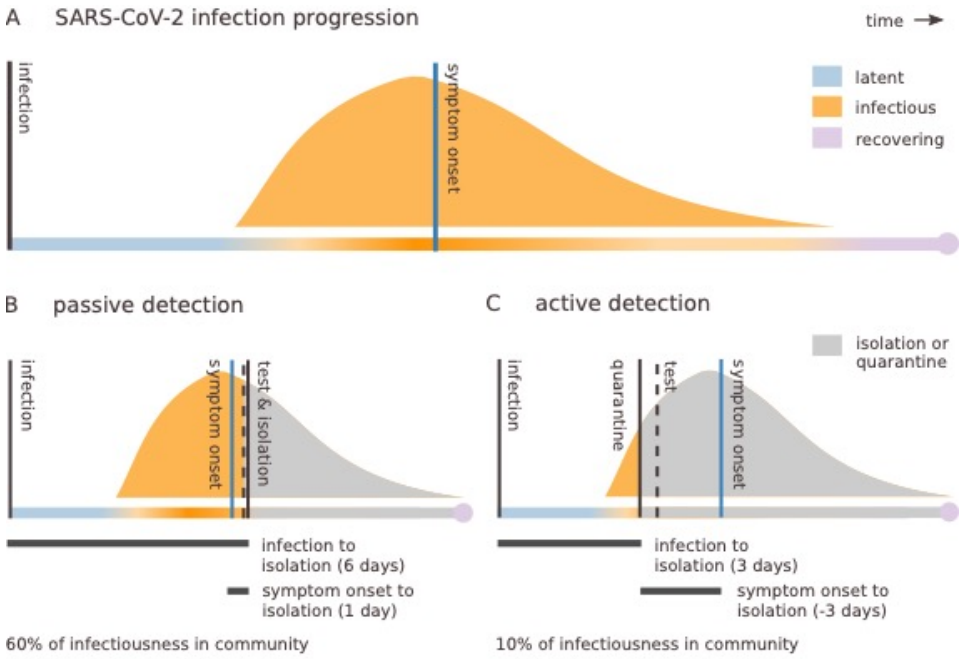


Figure 2: Percentage of cases isolated relative to time of infection for Optimal TTIQ (left) and Partial TTIQ (right) and corresponding reductions in transmission potential. Dashed vertical lines indicate the time of symptom onset.

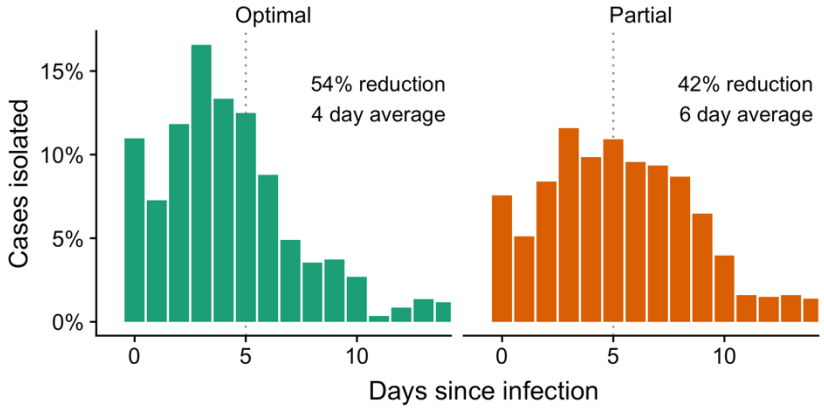
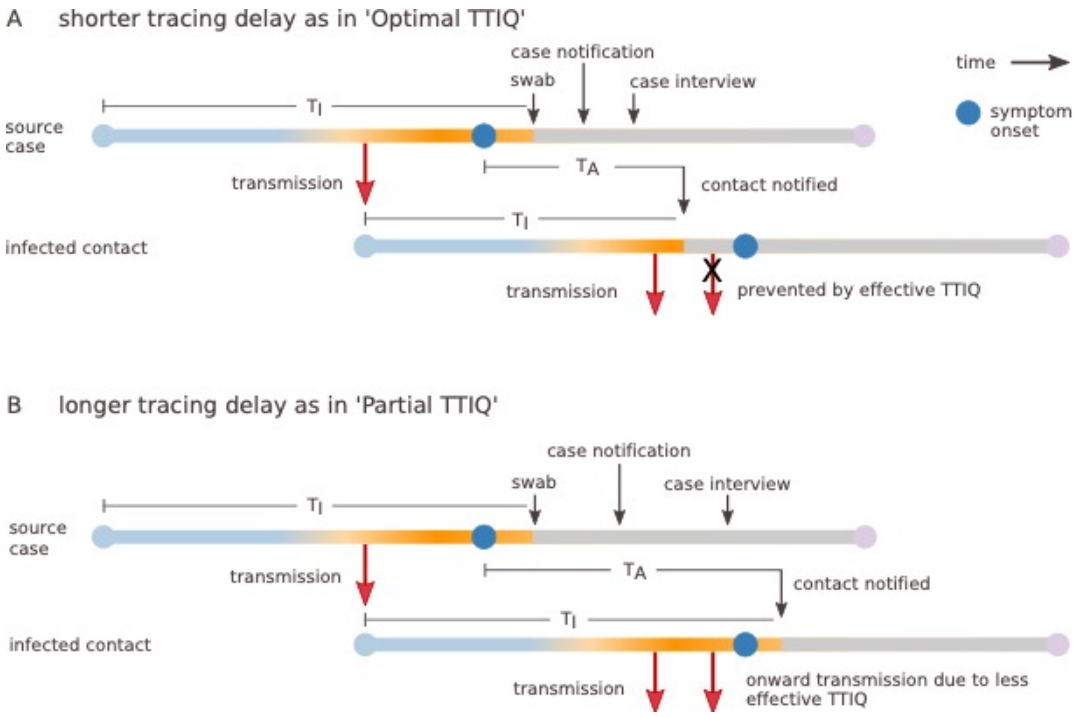


Figure 3: Representation of infection progression for a passively detected case (source case) and an infected contact, with the timings of key TTIQ actions indicated. TTIQ aims to reduce the time from infection to isolation (I_A). Longer tracing delays (T_A) result in longer times to quarantine/isolation and a greater proportion of infectiousness in the community (orange) compared to when delays are short. Further, when delays are long, isolation times of traced contacts are no faster than via passive detection (provided infected contacts develop symptoms).



Case ascertainment in Phases B and C

Detection of infections is central to the impact of TTIQ on transmission. The earlier a case is detected and isolated, the smaller the fraction of infectiousness in the community.

If a case is not detected at all, not only do they spend their entire infectious period in the community, but their infected contacts cannot be detected by downstream contact tracing, and so will be found later (through passive symptomatic detection), if at all.

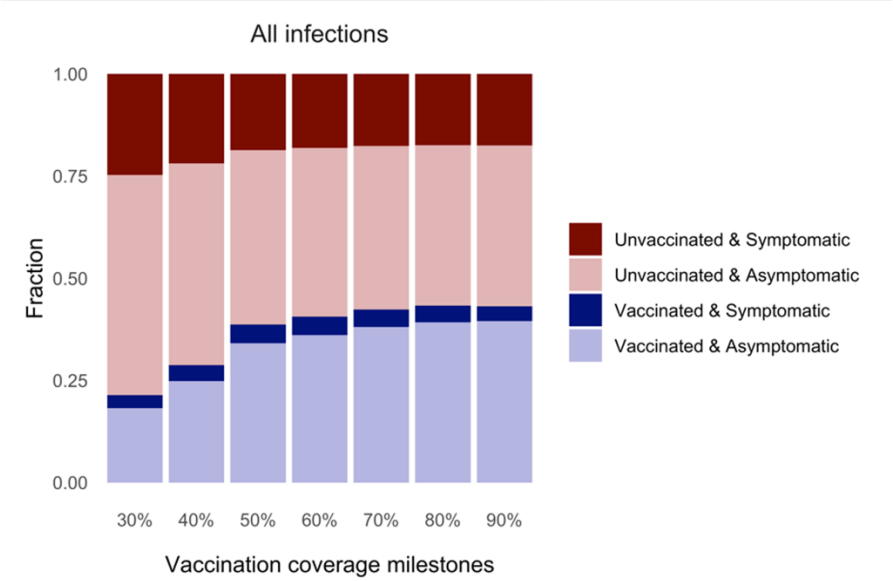
When an otherwise-unlinked infected individual develops symptoms and presents for testing (passive symptomatic detection), they enable public health units to isolate the case and re-start chains of contact tracing, placing more infected people in isolation more quickly. If the fraction of cases ascertained drops, fewer cases are placed into isolation and the TTIQ effect is lessened.

The fraction of cases ascertained by passive symptomatic detection is likely to reduce as Australia moves to higher population vaccination coverage in Phases B and C of the National Plan. COVID-19 vaccines reduce the probability of developing symptoms given infection. Higher rates of vaccination in adults than children will also result in infections being concentrated in children, who have a lower probability of developing symptoms than adults, with or without vaccination. We might therefore expect lower levels of passive symptomatic detection with increasing vaccination coverage, for similar surveillance effort.

Figure 4 displays the expected breakdown of all infections by vaccination and symptom status on the dates Australia crosses milestones of the proportion of the 16+ population fully vaccinated. This is calculated from Australia-wide vaccination coverages by age, vaccine type, and dose, and estimates of age- and location-structured population mixing and age-differences in susceptibility, contagiousness, and the probability of developing symptoms (as per Davies et al 2020 and updated susceptibility estimates). As vaccination coverage increases, the fraction of all infections that are vaccinated increases, and the fraction with symptoms (and therefore detectable by symptomatic screening) decreases.

While Figure 4 displays the split by vaccination and symptom status of all infections, differences in the probability of detection by vaccination and symptom status – driven by properties of the TTIQ system as well as behavioural choices – will result in a different fraction among cases.

Figure 4: Panel A shows the estimated proportion of asymptomatic and symptomatic **infections** stratified by vaccination status for different levels of vaccination coverage across all ages (Australia-wide coverage as per Australian Immunisation Registry (AIR) data and Quantium modelling).



Section 1: TTIQ strategies for evaluation

Table 1 outlines key TTIQ strategies for evaluation as identified through the consultation process undertaken with members of the Office of Health Protection, CDNA and AHPPC.

Table 1: TTIQ strategies for evaluation, expressed as modelling questions, targeting each component of the TTIQ system. The model framework used to address each question is also indicated. PCC = primary close contact. SCC = secondary close contact. TP = transmission potential.

TTIQ component	Modelling question	Model framework
Testing	A. What is the impact of no longer testing vaccinated symptomatic individuals?	Dynamic model
	B. What is the optimal testing schedule for quarantine of PCCs?	Quarantine model
Case interviews (trace)	C. What is the impact of case interview prioritisation based on risk and delays?	TP framework
	D. What is the impact of only contact tracing unvaccinated cases?	Dynamic model
Contact notification (trace)	E. What is the impact of case-initiated contact notification?	TP framework
Isolation	F. What is the impact of shortened isolation for vaccinated cases?	Dynamic model
PCC quarantine	G. What is the impact of no or shortened quarantine for vaccinated PCCs?	Dynamic model

Section 2: Predicted impact of proposed TTIQ strategies on transmission potential

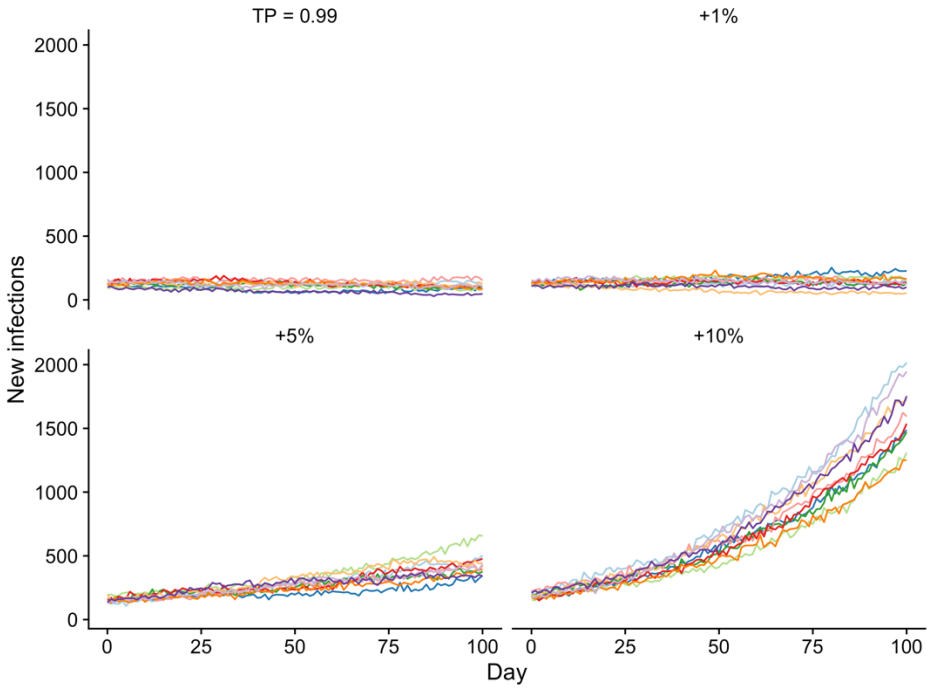
Evaluation and epidemiological context

We evaluate proposed TTIQ strategies by computing a change in transmission potential (TP) under each strategy compared to a reference strategy. The change in TP is reported as either a percentage change or multiplier depending upon the question under consideration.

The epidemiological impact of a change in TP depends strongly on the epidemiological context. The national strategy is to target a transmission potential at or around 1. Near this critical threshold, strategies that marginally increase the TP (by just a few percent) may drive a change from decreasing to increasing epidemic activity. In consequence, strategies need to be considered carefully as they may (ultimately) prompt the need for other measures, including the requirement for increased PHSMs. These considerations emphasise the need for monitoring of TTIQ impact on TP as part of routine epidemic assessment (see Section 3).

Figure 5 illustrates this concept by simulating timeseries of daily infections from our dynamic transmission model under a scenario when small increases in TP can have a strong effect. With a baseline TP of 0.99 epidemic activity is slowly declining. While an increase of 1% has a minor but noticeable effect, increases of 5% and 10% lead to escalating epidemics.

Figure 5: Example simulations of epidemic curves with modest increases in TP, but with an initial TP just below the control threshold of 1.



Modelling approaches and assumptions

To address the questions outlined in Table 1, we use three different modelling approaches. Each model contains features required for addressing a specific question. However, the following biological and behavioural assumptions were employed across all models:

- Probability of seeking a test given symptoms is 0.5.
- 31% of all infections are symptomatic (see Figure 4 above)
- Relative infectiousness of asymptomatics is 0.5.
- Probability that an infected individual is identified as a PCC via downstream manual contact tracing is 0.95.

Vaccine efficacies in the transmission potential framework and dynamic transmission model (against infection, symptomatic disease, and onward transmission) are taken to be the mid-points between the two-dose efficacies for Pfizer and AstraZeneca. The probabilistic quarantine model uses slightly more conservative VEs against onward transmission (0.4) and against infection (0.72).

Transmission potential framework with delays

A stochastic simulation model is used to represent the relationship between contact tracing delays, symptomatic detection, and times from infection to isolation in continuous chains of contact tracing. Sampling from distributions of contact tracing times, this model generates distributions of time from infection to isolation, which can be used to calculate expected reductions in transmission potential, as per figures 1 and 2. See Appendix for details.

Dynamic transmission model

An individual-based infection simulation model is used to simulate TTIQ processes in scenarios where ascertainment may be low (chains of transmission undetected). This model considers the vaccination and symptom status of cases (and therefore the ability to transmit and be detected), but without reduction of transmission due to infection-acquired immunity:

- Cases found by either downstream contact tracing from their source case or testing of symptomatic individuals, following the same process as the transmission potential model (supplementary figure 1).
- All cases are fully isolated when found (*i.e.*, assumes perfect compliance).
- Neither upstream contact tracing nor asymptomatic screening are in effect. With the above parameterization, and baseline TTIQ strategies in place, 38% of all infections are ascertained.
- Baseline isolation and quarantine are assumed to be 14 days from date of swab and date of identification as a case and PCC, respectively. We note that while the COVID-19 Series of National Guidelines (SoNG) recommends a 14-day isolation period for cases, multiple jurisdictions employ a 10-day isolation period.

Unless otherwise stated all analyses assume:

- National vaccination coverage (across all eligible age-groups) as predicted at the date Australia exceeds the threshold of 80% of the 16+ population fully vaccinated. As those aged 12-15 are eligible for the vaccine, the national coverage achieved and used in simulations accounts for current and predicted coverage in that age group.
- Contact tracing delay distributions are as estimated during the 'Optimal' period from NSW case data (directly provided by NSW Health).

In this model, the ratio of TPs (our key reporting metric) is insensitive to the underlying epidemic trajectory (growing or declining). Accordingly, an initial number of infections and the pre-vaccination reproduction number were calibrated for each analysis to ensure the ratio of TPs between strategy scenarios was reliably estimated.

Probabilistic quarantine model

Described in section 2B.

Testing

A. What is the impact of no longer testing vaccinated symptomatic individuals?

To evaluate the impact of no longer testing vaccinated symptomatic individuals via passive detection (*i.e.*, individuals who have not been identified as a PCC), we use the dynamic transmission model.

Note that symptomatic vaccinated individuals who are PCCs of known cases are still tested and their contacts are traced.

We evaluate the impact of this strategy on *transmission potential*. However, testing of symptomatic vaccinated individuals supports other epidemiological and public health priorities including detection of immune evading variants of concern and monitoring of vaccine effectiveness. These other epidemic surveillance objectives are not captured by our analysis.

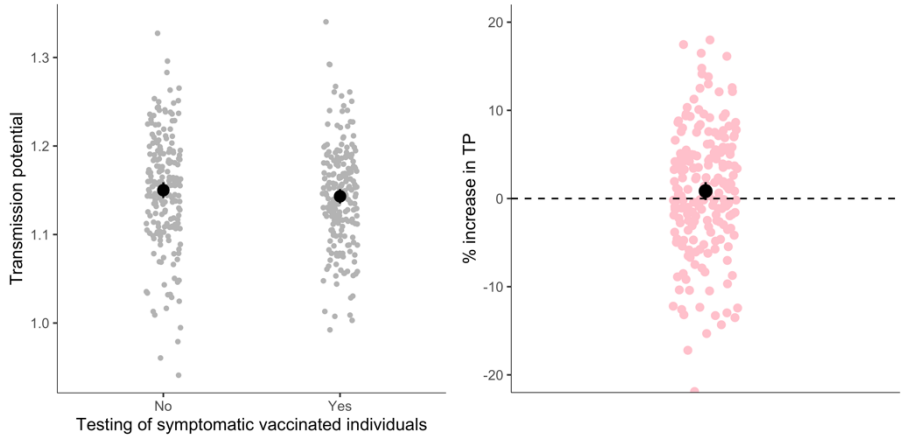
We compute the percentage change in TP between two scenarios:

- 50% of *vaccinated* symptomatic infections are detected via passive screening.
- 0% of *vaccinated* symptomatic infections are detected via passive screening.

In both scenarios, 50% of *unvaccinated* symptomatic infections are detected via passive screening. Asymptomatic infections irrespective of vaccination status can only be identified via contact tracing.

The model is calibrated to a population vaccination coverage corresponding to the 80% national coverage milestone and a pre-vaccination TP of 5.5.

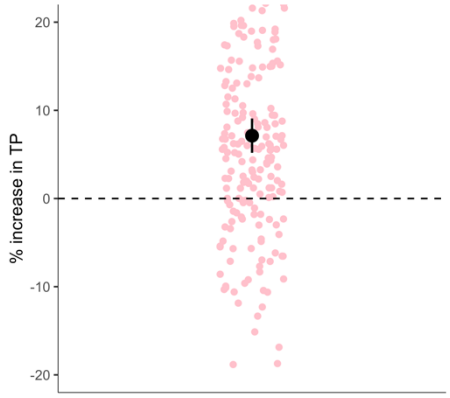
Figure 6: Left: Estimated transmission potential for each of 200 model simulations (grey dots) assuming testing and no testing of symptomatic infected individuals via syndromic surveillance (black dots and lines = mean ± 2SE). **Right:** Percentage increase in TP for randomly paired simulations (pink dots). Black dots and lines show the mean estimated increase in TP of 0.84% (± SE 0.51%). Simulations were initialised with 100 infections, population vaccination coverage corresponding to the 80% national coverage milestone and a pre-vaccination TP of 5.5. Transmission potentials were calculated from a time-average of secondary infections from each infection between days 20 and 50 of each simulation.



Our analysis shows a marginal increase in transmission potential as a consequence of this strategy. Symptomatic infected individuals make up a small proportion of all infections (Figure 6) and are less infectious compared to unvaccinated symptomatic infections.

While this result is unsurprising in terms of anticipated impact of the strategy on whole-of-population transmission dynamics, in certain sub-populations the impact may be different. In Figure 7 we consider a sub-population with high vaccination coverage (90%), a high symptomatic fraction of infections (60%), and a high probability of seeking a test given symptoms (80%), such as a retirement village or township with a particular demographic profile. In this scenario, not testing symptomatic vaccinated individuals results in an increase in TP of approximately 7%. As illustrated in Figure 5, such an increase may drive a change from decreasing to increasing epidemic activity.

Figure 7: Percentage increase in TP for 200 paired simulations (pink dots). Black dots and lines show the mean estimated increase in TP of 7.13% increase (± SE 0.97). All simulations were initialised with 1000 infections and assume 80% of symptomatic individuals present for a testing, 60% of all infections are symptomatic, 90% of the entire population are fully vaccinated, and a pre-vaccination reproduction number of 5.0. Transmission potentials were calculated between days 10 and 300 of each simulation.



B. What is the optimal testing schedule for quarantine of primary close contacts?

Quarantining and testing of primary close contacts (PCCs) aims to reduce transmission in two ways:

- By directly preventing onward transmission from infected PCCs
- By enabling timely tracing of the contacts of infected PCCs

We use a probabilistic model to determine optimal testing schedules for quarantine of primary close contacts that meets both objectives. Accordingly, we measure the impact of each quarantine testing strategy by calculating the average number of infections arising from those infected by the PCCs (herein "IPq").

The model incorporates the following features:

- Infected PCCs can infect others (in the community or household) prior to being identified and placed in quarantine.
- Infected PCCs in quarantine can only infect their household members.
- PCCs not identified through the testing schedule (or if there are no tests) continue to be able to infect household members and are released into the community while potentially still infectious.
- The time taken to identify and isolate the PCC (and thus those they infect) will depend on the current performance of the TTIQ system (e.g., optimal or partial delays).

All analyses make the following assumptions:

- 85% vaccination coverage in 12+ ages which maps to 72% population-level coverage.
- PCCs are assumed to be vaccinated in proportion to the population coverage. This results in approximately 20% of infected PCCs being vaccinated.
- We induce a correlation between the vaccination status of the PCC and their household members. This means that unvaccinated PCCs (who are more likely to transmit the infection) are more likely to have unvaccinated household members (who are more susceptible to infection). We assume household members of a PCC have a 90% chance of having the same vaccination status as the PCC.

- The pre-quarantine, pre-vaccination TP is assumed to be 5. Number of secondary cases are simulated from a Negative Binomial distribution with mean TP, and over-dispersion parameter (k=) 0.2.

We investigate optimal test timing for different quarantine durations (7-day or 14-day) and numbers of tests (1, 2, or 3). Tests may be conducted on any day from day 1 of quarantine through to the final day of quarantine inclusive. The first test must be conducted no later than on day 5 if conducting more than one test and tests must be separated by at least one day.

Figure 8: Estimated IPq for testing strategies where one test is conducted during the 7- or 14-day quarantine period, assuming 'Optimal' delays. The black dot indicates the testing strategy with the lowest IPq, *i.e.*, the optimal strategy in terms of transmission reduction.

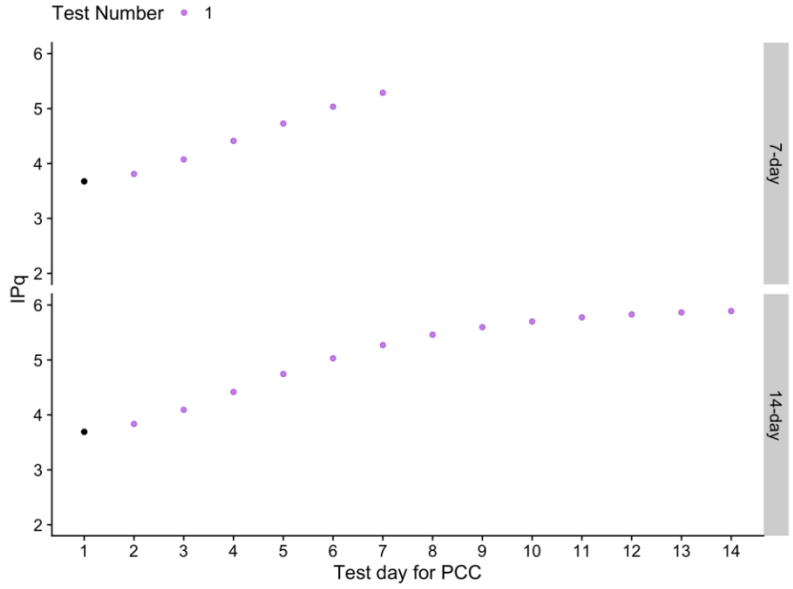


Figure 9: Estimated IPq for testing strategies where two tests are conducted during the 7- or 14-day quarantine period, assuming 'Optimal' delays. Each pair of purple (test 1) and green (test 2) dots, joined by a horizontal line, represent a single testing strategy. The paired black dots indicate the testing strategy with the lowest IPq, *i.e.*, the optimal strategy in terms of transmission reduction.

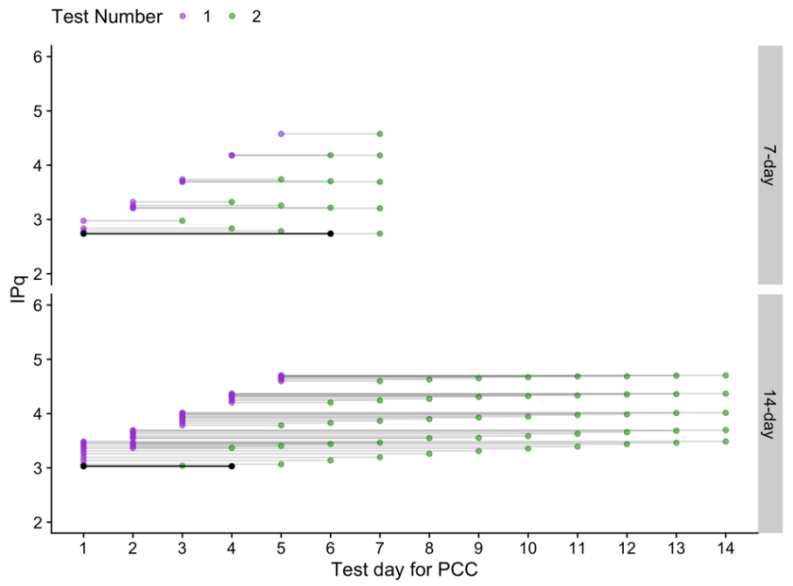


Figure 10: Estimated IPq for testing strategies where three tests are conducted during a 14-day quarantine period, assuming 'Optimal' delays. Each triple of purple (test 1), green (test 2) and orange (test 3) dots, joined by a horizontal line, represent a single testing strategy. The trio of black dots indicate the testing strategy with the lowest IPq, *i.e.*, the optimal strategy in terms of transmission reduction.

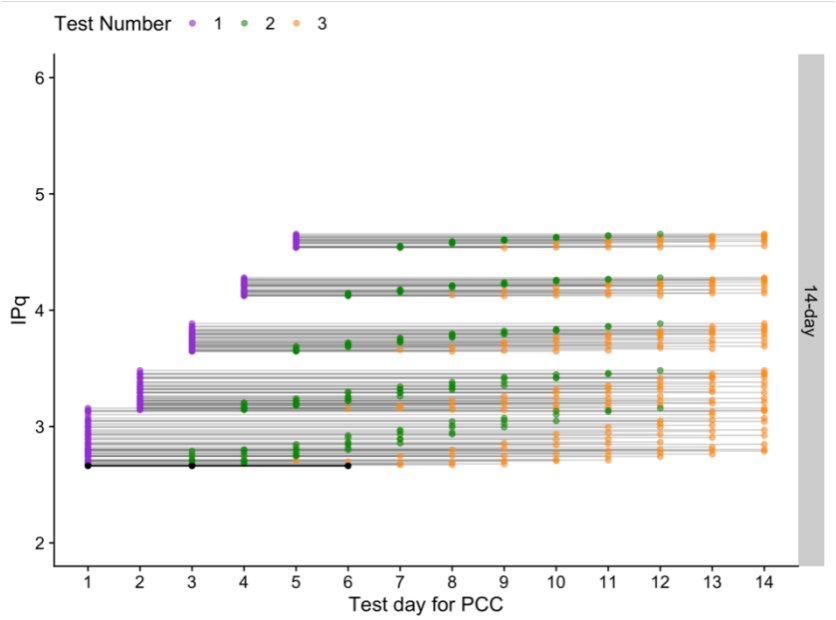


Table 2: Optimal testing strategies for each of 1–3 tests, under 7- and 14-day quarantine, for 'Optimal', NSW current case-initiated, and 'Partial' contact tracing delays.

		Delay distribution		
Quarantine duration (days)	Number of tests	Optimal	Partial	NSW case Initiated
14	3	(1,3,6)	(1,3,10)	(1,3,8)
14	2	(1,4)	(1,4)	(1,4)
14	1	(1)	(1)	(1)
7	2	(1,6)	(1,7)	(1,6)
7	1	(1)	(1)	(1)

Figures 8–10 and Table 2 demonstrate the importance of testing on Day 1 of quarantine. A day 1 test is included in the optimal strategy for all explored quarantine durations and testing schedules. This is because early identification of PCCs that are infected is important for timely identification and isolation of the individuals that they have infected.

Under a 7-day quarantine strategy, a later second test is preferred (e.g., 1, 6), to increase the chance of identifying cases prior to release from quarantine. Under a 14-day quarantine strategy, two early tests are optimal to increase the chance of early identification of infected PCCs and their contacts.

Figures 9 and 10 show that for strategies with 2 or 3 tests, several testing strategies perform similarly well to the optimal testing strategy (i.e., there is some flexibility in testing day). In Table 3 we present a range of testing days for each test that correspond to no more than a 2% loss in strategy performance.

Table 3: Range of testing days for each test that correspond to no more than a 2% loss in strategy performance.

		Delay distribution		
Quarantine duration (days)	Number of tests	Optimal	Partial	NSW Case Initiated
14	3	1, 3–4, 5–11	1, 3–12, 5–14	1, 3–4, 5–12
14	2	1, 3–5	1, 3–14	1, 3–5
14	1	1	1	1
7	2	1, 5–7	1, 3–7	1, 5–7
7	1	1	1	1

When TTIQ system performance is consistent with 'Partial' delays (i.e., PCCs are identified later than under 'Optimal' or current NSW case-initiated delays), in addition to testing on Day 1, testing on nearly any other day is sufficient, resulting in a minimal loss of performance.

Figure 11: Performance of optimal testing strategies (as per Table 1) under each of the 'Optimal', 'Partial', and NSW current case-initiated delays, for 7- and 14-day quarantine.

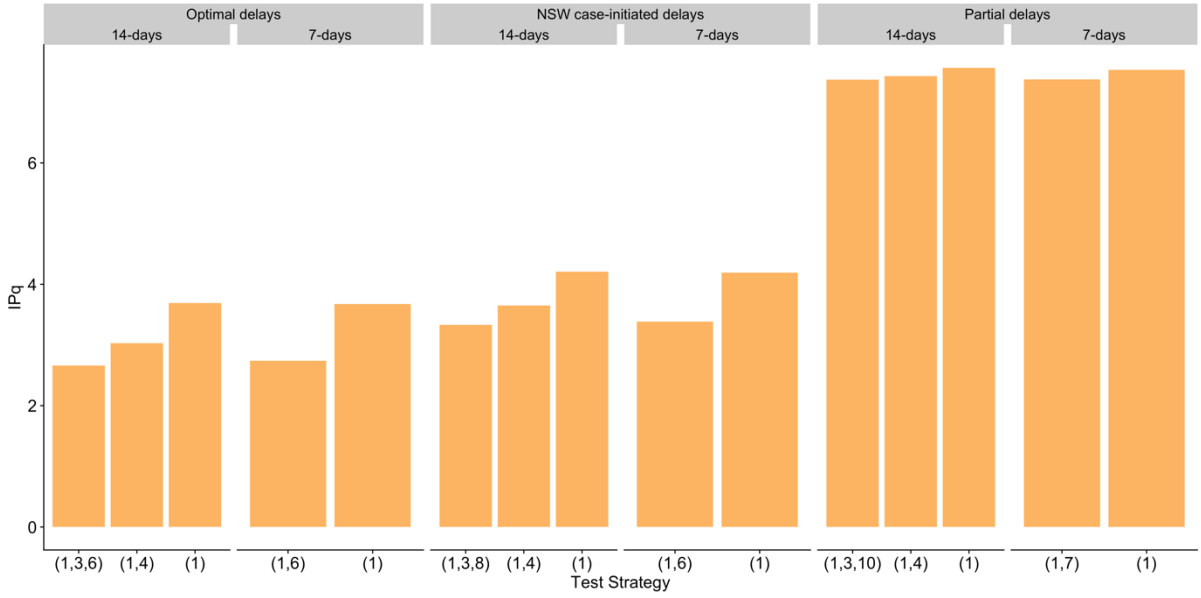


Figure 11 shows that the reduction in transmission achieved by conducting additional optimally timed tests is smaller than the loss of system performance due to increased delays (*e.g.*, from 'Optimal' to 'Partial'). It may therefore be favourable to perform fewer tests for quarantining PCCs if that supports improvements to system performance through a reduction in the time to identify and isolate cases.

In Figure 12, in the context of optimal testing strategies, we explore the impact of differential strategies for quarantine of vaccinated and unvaccinated PCCs on system performance. These results have relevance to Question G.

Figure 12: Evaluation of 7-day quarantine for vaccinated PCCs under 'Optimal' (left) and 'Partial' (right) delays. The reference strategy where both vaccinated and unvaccinated PCCs quarantine for 14 days (left bar in each facet) is compared to two strategies in which vaccinated PCCs quarantine for 7 days. In the first, optimal scheduled testing is present for vaccinated PCCs (middle bar). In the second, there is no scheduled testing (right bar). Under both strategies, unvaccinated PCCs quarantine for 14 days. Where testing is implemented, the optimal strategy for the corresponding delay distribution and quarantine duration is implemented as per Table 1 (*e.g.*, (1,3,6) for 14-day quarantine with 'Optimal' delays, and (1,3,10) with 'Partial' delays).

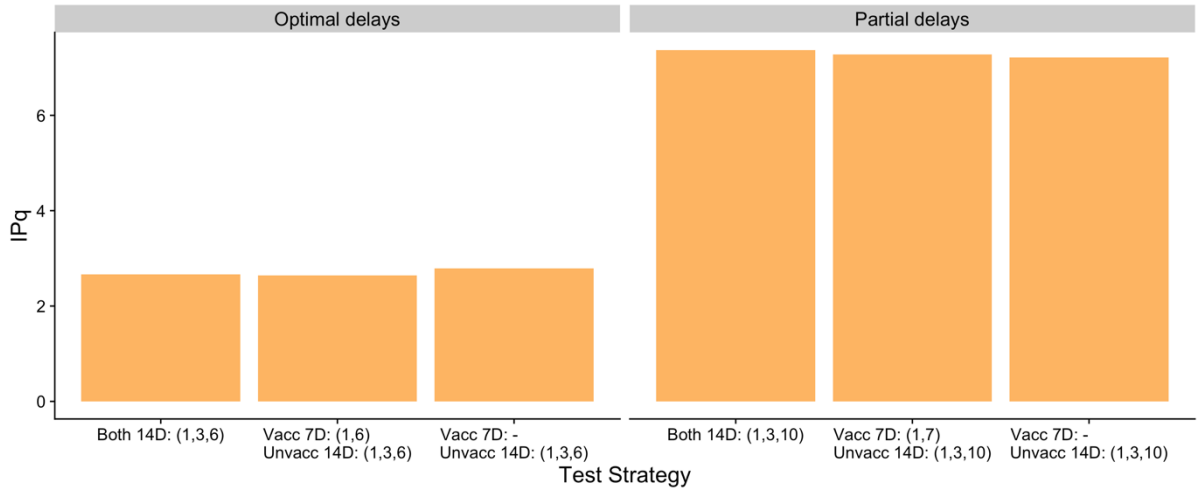


Figure 12 shows that reducing quarantine duration from 14 to 7 days for vaccinated PCCs has no discernible impact on the performance of the TTIQ system. Furthermore, not testing vaccinated PCCs during a 7-day quarantine period has minimal impact on performance. These results follow from the high chance that infections are detectable within the first 7-day period, and that vaccinated PCCs are less likely to acquire infection and, if infected, are less infectious.

Note however that further reductions in quarantine duration for vaccinated PCCs may result in increases in overall transmission, as explored below in Question G.

Tracing

C. What is the impact of case interview prioritisation based on risk and delays?

When the TTIQ system is under stress due to high caseloads, it may no longer be possible for public health units to complete all case interviews on the same day as case notification.

We explore the impact of different strategies for case interview prioritisation by using outputs from a queuing model within the TP framework model.

Queuing model

- Each day a random number of cases (drawn from a time-homogeneous Poisson distribution) are added to the interview queue and a fixed number of cases in the queue are interviewed.
- Cases may be prioritised for interview according to the time since test swab and/or vaccination status.
- Any cases not interviewed within 5 days of notification are removed from the queue (*i.e.*, never interviewed).
- Independent of capacity, we assume that 20% of cases cannot be interviewed on their date of notification due to a range of reasons such as missing contact details or out-of-hours notification.

We examine the impact of four different case interview prioritisation strategies:

1. No prioritisation (*i.e.*, random)
2. Prioritise the most recently swabbed cases
3. Prioritise unvaccinated cases and then the most recently swabbed cases
4. Prioritise the most recently swabbed cases and then unvaccinated cases

We explored these strategies under three different case interview capacities (20%, 50%, 80%). This capacity corresponds to the proportion of average daily incoming cases that the public health unit can interview.

Note that at 100% capacity, the model would assume 80% of cases are interviewed on the date of notification and 20% on the following day. Since some observed times from notification to interview during the 'optimal' TTIQ period in NSW were longer than 1 day (Figure 15, top middle panel), at 100% capacity the model would predict a higher effect than the optimal TTIQ. This is because the model only assesses the impact of prioritisation and does not consider the potential for longer delays for other reasons. We suggest that the TTIQ effect at 80% capacity can be broadly interpreted as representative of the optimal TTIQ scenario, and reductions in TTIQ effect at lower capacities considered relative to that benchmark.

Figure 13: Estimated reduction in transmission potential under four case interview prioritisation strategies: 1) No prioritisation ("Random"). 2) Prioritise the most recently swabbed cases ("New cases"). 3) Prioritise unvaccinated cases and then the most recently swabbed cases ("Unvaccinated then new cases"). 4) Prioritise the most recently swabbed cases then unvaccinated cases ("New cases then unvaccinated"). Results are plotted for three different case interview capacities (20%, 50% and 80%).

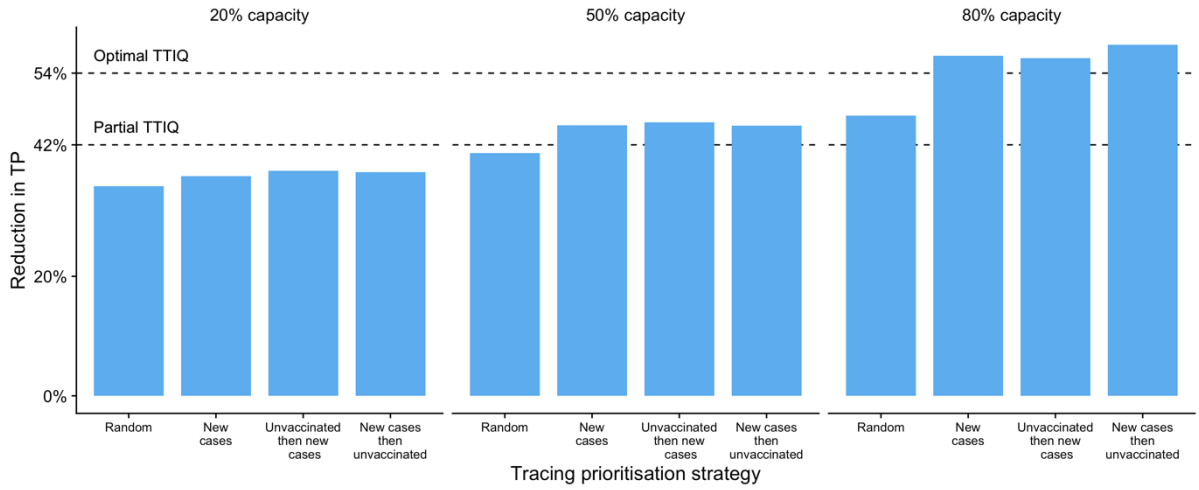


Figure 13 shows that prioritising interviews of the most recently swabbed cases yields the greatest gains in transmission reduction, regardless of contact tracing capacity.

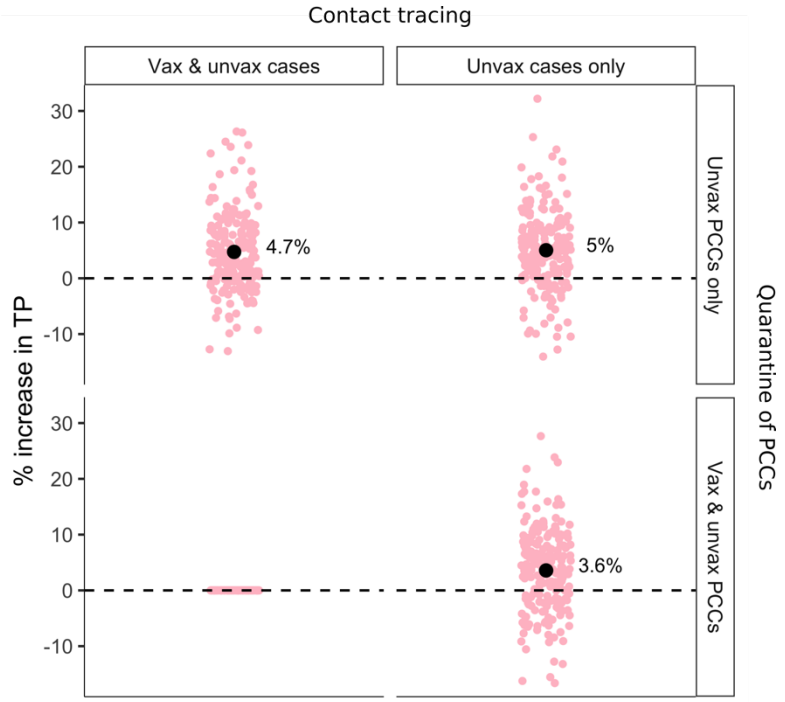
D. What is the impact of only tracing contacts of unvaccinated cases?
G. What is the impact of no or shortened quarantine for vaccinated primary close contacts?

We address questions D and G together, using the dynamic transmission model. We consider a reference strategy where contact tracing of both vaccinated and unvaccinated cases occurs and both vaccinated and unvaccinated PCCs of those cases are placed into quarantine (Figure 14, bottom left).

We then estimate the percentage change in transmission potential between this reference strategy and the following three strategies:

- Contact tracing of both vaccinated and unvaccinated cases is performed, and only unvaccinated PCCs are placed into quarantine (Figure 14, top left)
- Only contact tracing of unvaccinated cases is performed, and both unvaccinated and vaccinated PCCs are placed into quarantine (Figure 14, bottom right)
- Only contact tracing of unvaccinated cases is performed, and only unvaccinated PCCs are placed into quarantine (Figure 14, top right).

Figure 14: Mean percentage change in TP estimated for three TTIQ strategies compared to a reference strategy (black dots) across 200 paired simulations (pink dots). **Bottom left (reference):** Contact tracing of both vaccinated and unvaccinated cases occurs and both vaccinated and unvaccinated PCCs quarantine. **Top left:** Contact tracing of both vaccinated and unvaccinated cases is performed, and only unvaccinated PCCs quarantine. **Bottom right:** Only contact tracing of unvaccinated cases is performed, and both unvaccinated and vaccinated PCCs quarantine. **Top right:** Only contact tracing of unvaccinated cases is performed, and only unvaccinated PCCs quarantine. Simulations were initialised with 100 infections, population vaccination coverage corresponding to the 80% national coverage milestone and a pre-vaccination reproduction number of 5.5. Transmission potentials were calculated between days 20 and 50 of each simulation.



Our analysis shows that ceasing contact tracing for vaccinated cases will increase the TP by approximately 3–4% (bottom right). Similarly, removal of quarantine requirements for vaccinated PCCs will also increase the TP, by an estimated 4–5% (top row).

The increase in TP when vaccinated PPCs are not quarantined contrasts with the finding that a reduced quarantine duration for vaccinated PCCs of 7-days results in minimal additional risk (Question B). This result follows from the fact that a much higher proportion of infected individuals become infectious within the first 7-day period since infection compared to the second 7-day period.

As described at the beginning of this report, with a national plan seeking to constrain community transmission by targeting a transmission potential around 1, a small percentage increase *may* have a significant epidemiological impact. Accordingly, whether or not adjustments to TTIQ processes based on vaccination status (driving a change in the TP) could be considered will depend upon evaluation of the epidemiological context and the expected resultant transmission potential.

E. What is the impact of case-initiated contact notification?

During the NSW outbreak of the Delta variant, seeded in mid-June 2021, NSW Health implemented a policy of case-initiated contact notification to reduce delays associated with high case numbers. This strategy involves instructing confirmed cases to self-identify their primary close contacts and ask them to get tested and quarantine.

We use the TP framework model to consider the likely impact of this approach on transmission potential, given some assumptions about compliance and the proportion of contacts that can be ascertained by this means (see Appendix for details). Empirical and modelled distributions for each scenario and contact tracing delay are shown in Figure 15

We validate our simulations by relating them to available data on timeliness of case isolation from NSW over various time periods. These data were provided by NSW Health.

NSW scenarios

We applied our model to consider three scenarios for NSW:

- *optimal* – the period from July 2020–February 2021 representing 'optimal' TTIQ in the National Plan Modelling report, without case-initiated contact tracing
- *current without case-initiated* – a four-week period commencing August 15 2021, without case-initiated contact tracing,
- *current with case-initiated* – as for current, but with an assumption that 80% of infected contacts are immediately identified by the case.

During the 'current with case-initiated' scenario, we assumed that 80% of close contacts were readily identifiable by the case (e.g., household contacts). This high proportion reflects the fact that stay-at-home restrictions during this period will minimise the number of social contacts and concentrate infected contacts in household and essential workplace settings where contacts are fewer and more easily identifiable. We would expect the fraction of cases found by case-initiated contact tracing to be less under less stringent restrictions.

Results and interpretation

The left most panel of Figure 16 shows that our model can re-produce the TP reduction calculated from observed distributions of times from infection to isolation ('optimal TTIQ' estimated for Phase 1 of the National Plan Modelling, 54% reduction).

The middle panel shows that with a high level of case-initiated contact tracing, current contact tracing delays in NSW can still achieve similar reductions in transmission potential as for the 'partial TTIQ' (42% reduction) estimated for Phase 1 of the National Plan Modelling.

The right most panel shows that the current contact tracing delays in NSW (mid-August to mid-September 2021) would be predicted to result in a much smaller reduction in TP if case-initiated contact tracing (or other strategies to reduce times to isolation) were not in place.

Figure 17 displays estimates of times from infection to isolation from case data. The right most panel (NSW current, mid-August to mid-September 2021) suggests that our model predictions of TP reduction for the case-initiated contact tracing scenario broadly align with estimates from case data in NSW. Both our predictions and the estimates from case data are close to the 'partial TTIQ' benchmark.

Figure 15: Modelled distributions of various delays in the contact tracing process as estimated from NSW data provided by NSW Health (dots = data). These distributions are used as inputs in our model of TTIQ impact on transmission potential (TP). Time from swab to notification and notification to interview are informed by NSW data from July 2020 to February 2021 ('optimal', row 1) and from mid-August to mid-September 2021 ('current without case-initiated', row 2). 'Other delays' is calibrated to match the overall distribution of delays from infection to isolation for the 'optimal' period and has a mean delay of one day. This represents all other delays in the contact tracing process that we are not yet to estimate from data. For example, the time from interview to contact notification and the time from contact notification to isolation. 'current with case-initiated' (row 3) assumes the same delays as for 'current without case-initiated' except that 80% of notification to interview delays are set to zero. This represents a high proportion of contacts being immediately advised by the case to isolate (*e.g.*, household contacts).

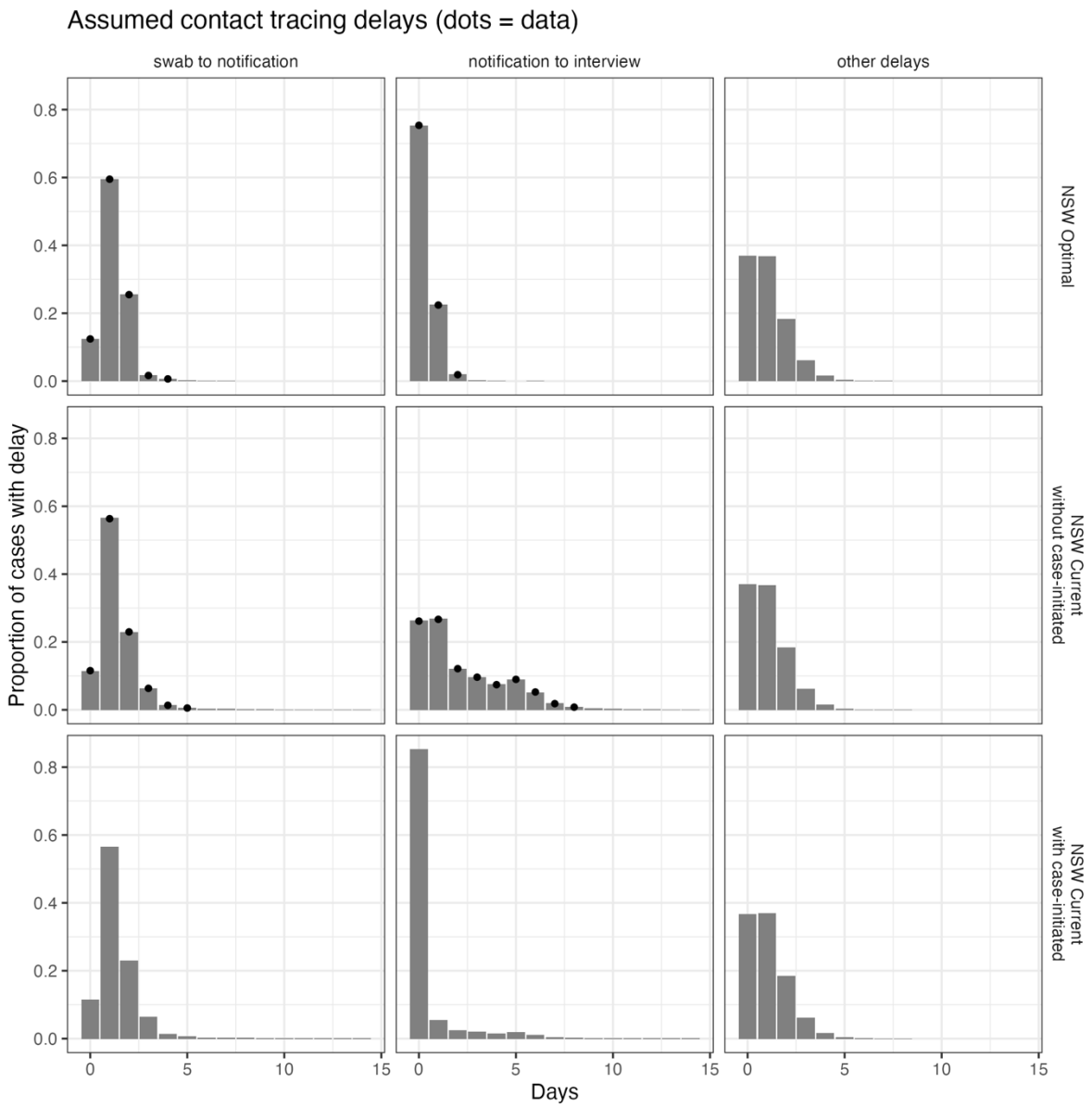

Assumed contact tracing delays (dots = data)
swab to notification
notification to interview
other delays
NSW Optimal
NSW Current without case-initiated
NSW Current with case-initiated
Proportion of cases with delay
0.0
0.2
0.4
0.6
0.8
0
5
10
15
Days

Figure 16: Distribution of delays from infection to isolation, and the resulting % reduction in transmission potential, **predicted by our model** under three delay scenarios (as outlined in Figure 15). Dashed vertical lines indicate the time of symptom onset.

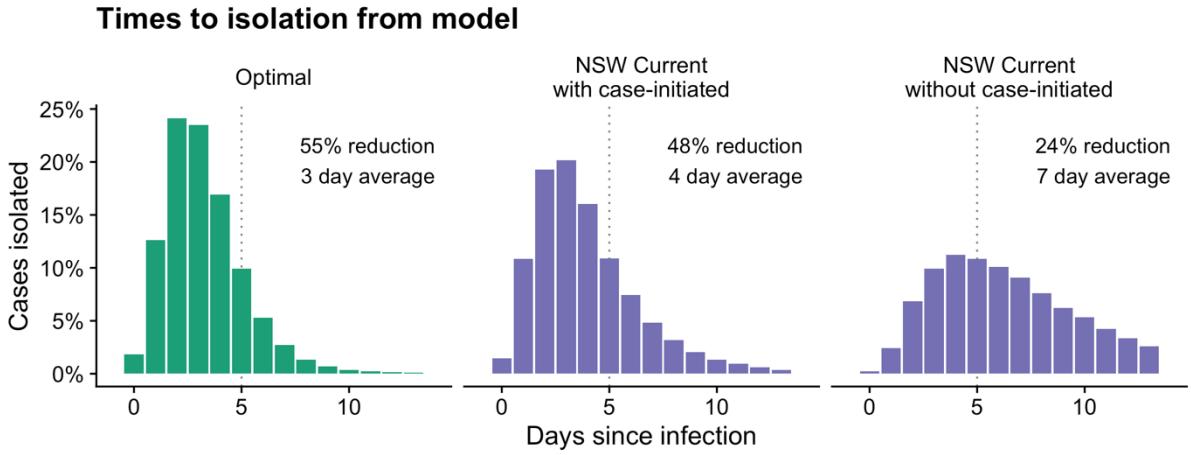
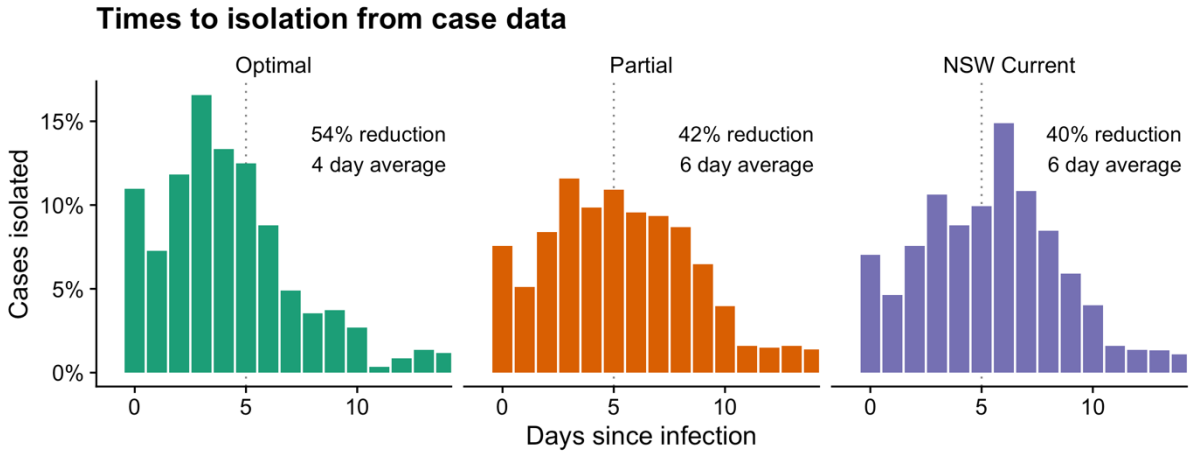


Figure 17: Distribution of delays from infection to isolation, and the resulting % reduction in transmission potential, **estimated from case data** under three delay scenarios (as outlined in Figure 15). 'Optimal' is times from infection to isolation from NSW case data between July 2020 and January 2021, provided by NSW Health. The distribution of times from infection to isolation for 'Partial' and 'NSW Current' are extrapolated from 'Optimal' based on delays from symptom onset to notification measured for VIC on 4 August 2020 (Partial) and for NSW on August 15 2021 (NSW Current). Dashed vertical lines indicate the time of symptom onset.



Isolation and quarantine

F. What is the impact of shortened isolation for vaccinated cases?

To evaluate the impact of shortened isolation from 14 to 7 days for vaccinated cases, we use the dynamic transmission model.

We compute the percentage change in TP between two scenarios:

- Unvaccinated and vaccinated cases isolate for 14 days
- Unvaccinated cases isolate for 14 days and vaccinated cases isolate for 7 days.

Figure 19: Left: Estimated transmission potential (TP) from each of 200 model simulations (grey dots) assuming 14-day and 7-day day isolation for vaccinated cases (black dots and lines = mean ± 2SE). **Right:** Percentage increase in TP for paired simulations (pink dots). Black dots and lines show the mean estimated increase in TP of 1.21% (± SE 0.622)**.** Simulations were initialised with 100 infections, population vaccination coverage corresponding to the 80% national coverage milestone and a pre-vaccination reproduction number of 5.5. Transmission potentials were calculated between days 20 and 50 of each simulation.

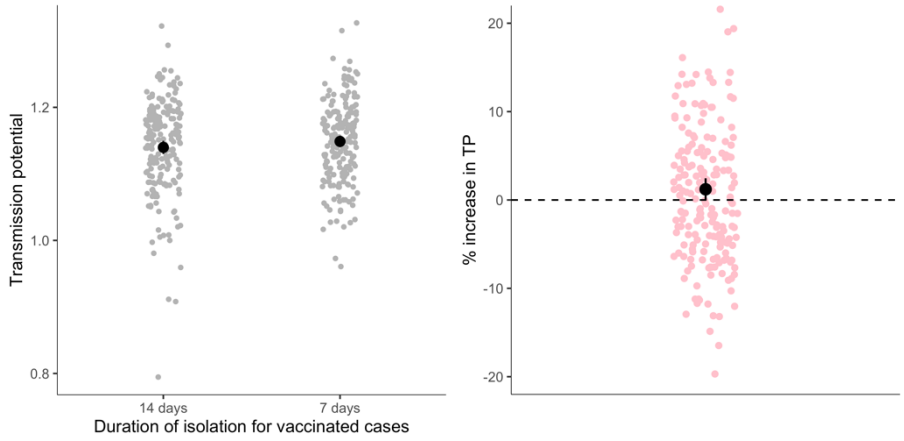


Figure 19 shows a marginal increase in transmission potential as a consequence of shortened isolation from 14 to 7 days for vaccinated cases. This result follows from the high fraction of all infectiousness that occurs in the days around symptom onset.

G. What is the impact of no or shortened quarantine for vaccinated primary close contacts?

Addressed under Question D.

Section 3: Monitoring TTIQ performance

TTIQ is an interdependent system that relies on public health capabilities, community participation, response objectives, and the status of the epidemic. Monitoring the effectiveness of TTIQ at reducing transmission is required to understand the reasons for changes in transmission rates (as measured by the reproduction number) and to anticipate the need for other localised measures, such as PHSM, to maintain a target level of outbreak control.

A monitoring system needs to meet two objectives:

- Measure the overall performance of the TTIQ system
- Measure components of the TTIQ system to enable identification of the source(s) of lowered system performance (if relevant)

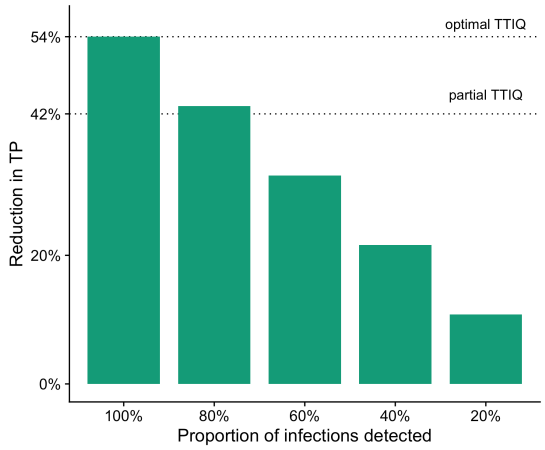
Overall indicator of TTIQ system performance

The principal indicator of TTIQ system performance at controlling outbreaks is the percentage reduction in transmission potential due to TTIQ. This depends on both how quickly cases are found and isolated (Figure 1), and what proportion of infections are detected.

To date in Australia, TTIQ responses have included extensive contact tracing and epidemiological investigation, with the aim of identifying all infections in chains of transmission. This has included strategies such as upstream contact tracing and asymptomatic screening. Consequently, ascertainment of infections has so far been very high. The percentage reduction in transmission potential is approximately proportional to the fraction of infections detected. For example, if only

half of infected people are detected, only half of infections can have any onward transmissions averted due to isolation (Figure 20)

Figure 20: Change in the TTIQ effect (reduction in TP) as ascertainment decreases.



The main overall indicator is the TTIQ effect: the percentage reduction in transmission potential due to TTIQ (Figure 21, panel 1). The TTIQ effect is itself the product of two components (Figure 21, panel 2): the TTIQ effect for *detected* infections (*i.e.*, cases) and the fraction of infections ascertained (case ascertainment). In turn, these indicators can be inferred, using epidemiological knowledge and models, from component indicators and case data (Figure 21, panel 3).

Estimating the TTIQ effect

TTIQ effect for cases

TTIQ reduces transmission through the detection and isolation of cases. The earlier a case is detected and isolated, the smaller the fraction of infectiousness in the community.

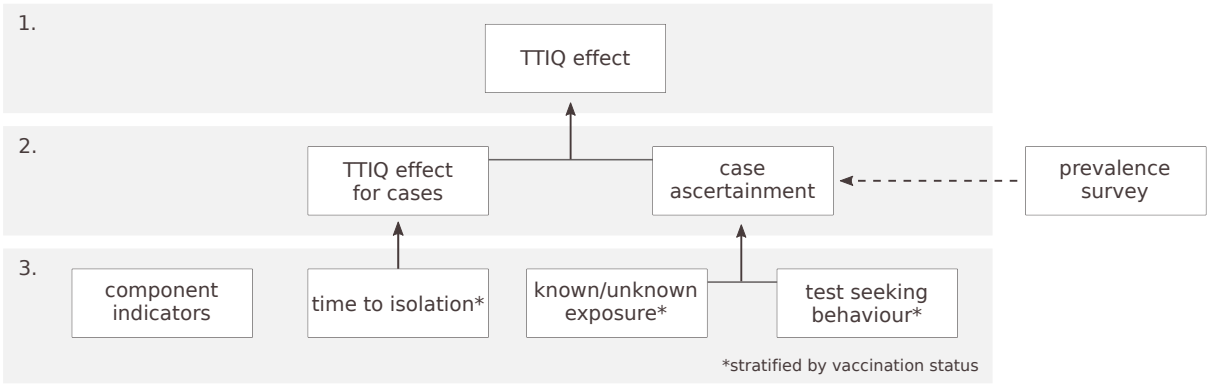
We have a developed a method that uses times from symptom onset to isolation of cases (Figure 1, panel 3) to estimate the percentage reduction in transmission potential for detected infections due to TTIQ.

Case ascertainment

To understand the overall impact of TTIQ on transmission, we need to estimate the fraction of infections which are undetected (and thus unlikely to isolate). To accurately estimate the level of case ascertainment requires temporal information on the prevalence of infection in the community. The UK has been undertaking random population screening of 150,000 people (approximately 0.2% of the population) regardless of symptoms each fortnight throughout the pandemic. This prevalence survey has provided an objective assessment of the total number of both asymptomatic and symptomatic infections over the course of their epidemic by age group and region. These observations are now differentiated by vaccination status, enabling estimation of vaccine effectiveness.

It may be possible to infer the fraction of infections ascertained over time using a model fitted to data on the proportion of cases with known versus unknown exposure at the time of test and other test seeking behaviours, stratified by vaccination status (Figure 21, panel 3). Estimates from such a model would be uncertain and would need to be validated, motivating the need for future consideration of prevalence surveys in Australia.

Figure 21: Elements required to estimate the TTIQ effect (percentage reduction in transmission potential due to TTIQ).



Data requirements for estimating the TTIQ effect

TTIQ effect for cases:

- Date of symptom onset for each case (NNDSS) to compute times from infection to isolation
- Date last in the community for each case (NNDSS) to compute times from infection to isolation
- Vaccination status of each case (NNDSS) because vaccination reduces the probability of onward transmission in infected vaccine recipients.
- Place of acquisition (NNDSS) for each case to determine whether the case has arisen from the local epidemic or was infected overseas/interstate.

Level of case ascertainment:

- Estimates of the prevalence of infection (TBD)
- Probability of seeking a test given symptoms consistent with COVID-19 for vaccinated and unvaccinated individuals in the general population (national behavioural surveys and Flutracking)
- Vaccination status of each case (NNDSS) because:
    - Vaccination reduces the probability of developing symptoms given infection
    - Vaccination likely modifies the probability of seeking a test given symptoms
- Known versus unknown exposure at time of test for all cases (TBD)
- Place of acquisition (NNDSS) for each case to determine whether the case has arisen from the local epidemic or was infected overseas/interstate.

Component performance indicators of the TTIQ system (Figure 21, panel 3)

- Time from when test is taken to public health notification for positive cases
- Time from public health notification to when a case is interviewed (where case interviews are occurring) by public health authorities

There are other delays in the system that matter, but routine collection of data to inform indicators may not be practical. For example, while recording the times from case interview to notification of their contacts (where notification is occurring through public health authorities) would be valuable, it is our understanding that data for cases and their contacts are not easily integrated into existing surveillance reporting systems.

Overall assessment and benchmarking

The TTIQ system performance indicator (the "TTIQ effect") provides an estimate of the percentage reduction in TP due to TTIQ, which can be compared to that estimated for 'optimal' and 'partial' TTIQ periods as per the National Plan Modelling August 2021. Furthermore, when considered in the epidemiological context (alongside other epidemic monitoring components), an assessment of whether this effect is sufficient to achieve a target level of control can be made. Critical thresholds for the TTIQ effect should depend on the status of the epidemic as measured by other indicators (*e.g.*, TP and the effective reproduction number).

Without advance knowledge of the precise combination of TTIQ strategies in place, it is not possible to determine thresholds for component indicators that will flag a substantial reduction in the TTIQ effect. Since TTIQ strategies may be adapted to scale TTIQ system capacity to caseloads, direct monitoring of the TTIQ effect will be a more reliable indicator of whole-of-system performance. In the situation where TTIQ is not performing at a required level, changes in the component performance indicators provide insight into areas of possible lowered system performance, thereby supporting system adjustment.

Appendix

Transmission potential modelling framework with delays

Overview

Our previous estimates of the impact of TTIQ on transmission potential (TP), used in Phase 1 of the National Plan Modelling, were calculated from the observed distribution of times from infection to isolation for all cases (Figure 2). Shorter times from infection to isolation mean that more opportunity for transmission is averted and transmission is reduced (Figure 3).

This piece of work uses a recursive simulation model to link different TTIQ strategies to probability distributions of times from infection to isolation, enabling us to compute the TP reduction expected under proposed TTIQ strategies. This model accounts for two modes to detect each case: active detection by downstream contact tracing from the case's infector, and passive detection by the case developing symptoms and seeking a test (Supplementary Figure 1).

For each detection mode, there is a probability that the case is missed. There is therefore a fraction of cases that will be missed altogether, spending their full duration of infectiousness in the community. Where a case would have been detected and isolated by both active and passive detection modes, the case is isolated via whichever leads to earliest detection. Note that retrospective detection of cases via upstream contact tracing is not explicitly considered in this model.

We translate these distributions and parameter assumptions into a distribution of times from infection to isolation via a numerical simulation. For each simulated case, there is a probability that they would be detected by each mode, and if detected, the time from infection to isolation is sampled at random from a probability distribution of times to isolation.

For passive detection, the overall probability of detection depends on the probability that an infected person will develop symptoms, and the probability that a symptomatic person will seek a test. The distribution of times to detection if passively detected is represented by a lognormal distribution with median of 5 days and 50% density interval 3.6-7 days (parameters log(5) and 0.5).

For active detection, the distribution of times to isolation is given by: the time from infection of the source case to infection of the contact (generation interval); the time from infection to isolation for the source case; and a random sample from the distribution of times from isolation of the source

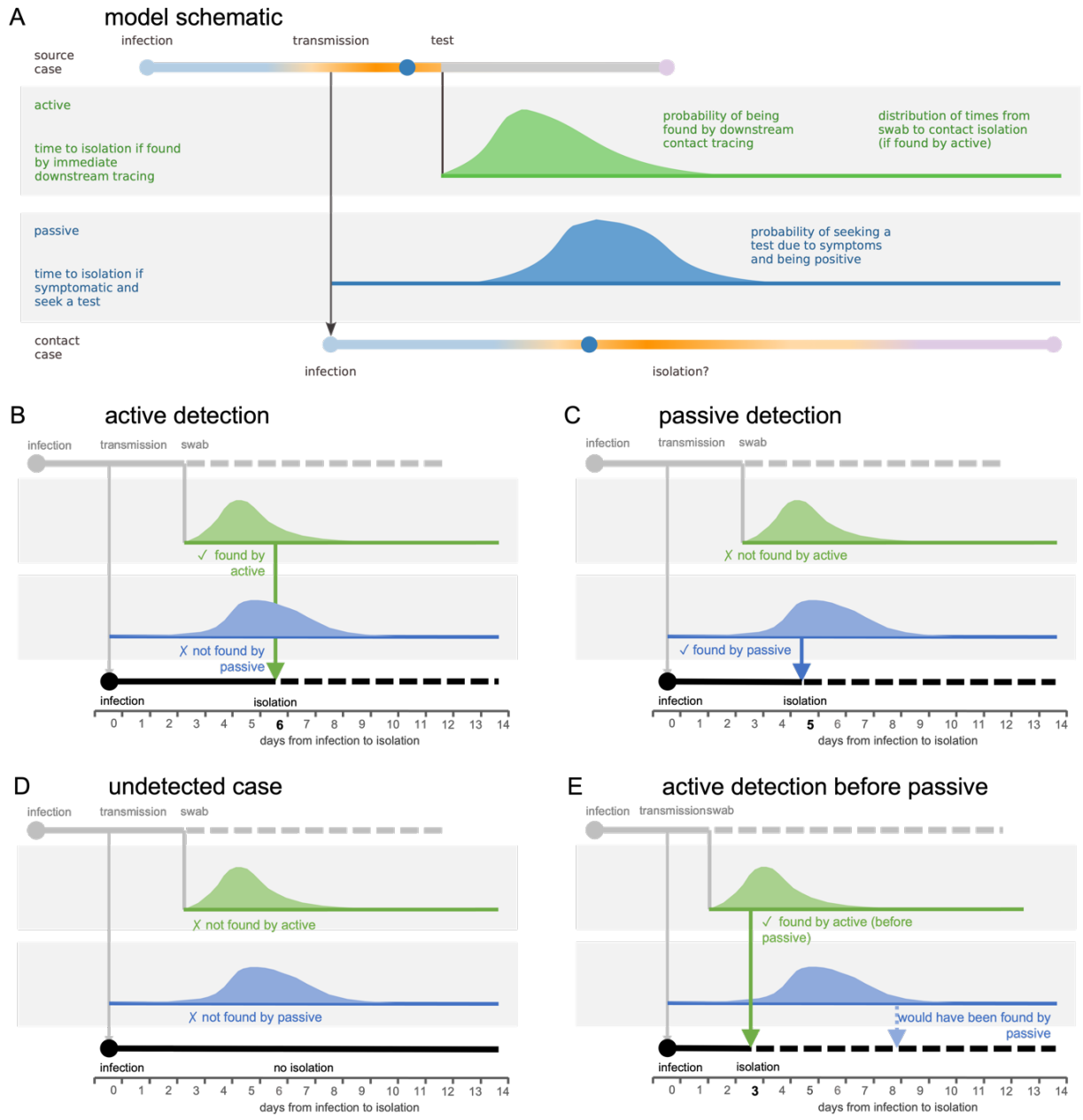
case to isolation of the infected contact (the contact tracing delay). The latter of these is comprised of several different component distributions, including the time from swab to case notification, the time from case notification to case interview, and the times from interview to contact notification and contact swab.

The times from infection to isolation (and therefore the time to onward transmission, which must be before isolation) of the source case also depend on the contact tracing delays and probabilities of detection. We jointly sample the source case times to isolation and times to onward transmission by simulating long chains of transmission via a recursive sampling algorithm (a Gibbs sampler) whereby each infected contact becomes the source for the next infected contact. This yields a distribution of times from infection to isolation for cases from which the reduction in transmission potential can be calculated. The calculation of transmission potential incorporates an assumption about the 'leakiness' of isolation, with a default assumption that when cases are instructed to isolate, they are then completely unable to infect others.

Within this modelling framework, we can investigate the likely impacts of various proposed TTIQ strategies by tweaking parameters and distributions to represent the implementation of those strategies. For example:

- case-initiated contact tracing can be represented by shortening the times from source notification to contact notification;
- prioritisation algorithms can be represented by modifying times from source notification to interview; and
- differences in prioritisation (and therefore contact tracing delays) of vaccinated cases can be modulated by adjusting the lower contribution to transmission of vaccinated infected cases.

Supplementary Figure 1: Illustration of model of active (ascertainment through contact tracing) and passive (symptomatic case finding) detection of each case. **A**) calculation of detection probabilities and times to detection by both modes. **B-E**) Examples of four possible outcomes for a single simulation of detection or non-detection via the two modes. For a given scenario of TTIQ strategies, we generate multiple simulations (each of which may be detected by either process or neither) to build a distribution of times from infection to isolation, from which the reduction in transmission potential can be calculated.



Modelling case-initiated contact tracing

We model scenarios of TTIQ with and without case-initiated contact tracing by modifying the overall contact tracing delay: the distribution of times from source case isolation to infected contact isolation.

We model the contact tracing delay as the sum of three other types of delay (Figure 15): the time from swab to notification, the time from notification to the infected contact being identified (via interview or by the case), and the aggregate of all 'other' delays. These other delays might include the time from source case isolation to swab, and the time from source case interview to the infected contact being instructed to isolate.

For scenarios without case-initiated contact tracing, we estimate the distributions of times from swab to case notification and from case notification to case interview from NSW data. We use a modelled distribution for 'other' delays with mean and variance of one day since we are not able to estimate these directly from the data.

For scenarios with case-initiated contact tracing, we use the same delays for times from swab to notification of the source case, and the 'other' delays, but we modify the times from source case notification to interview so that some fraction of these delays (those infected contacts that are identified by cases) are always set to zero, and the remainder are sampled from the estimated distribution of times (some of which are also zero). This reflects an assumption that instructions to notify contacts are sent to cases immediately, and that the case is immediately able to identify close contacts. It is assumed that the time taken from this point to instruct contacts to isolate is the same as for manual contact tracing, and this is included in the same distribution of 'other' delays.

Note also that this model assumes that in the absence of a formal case-initiated contact tracing policy, infected contacts do not isolate until after being identified by a case interview. However, cases may inform household members and other close contacts of their positive result, and these contacts may choose to self-isolate. The predominance of such self-directed isolation behaviour will likely be difficult to estimate from data, since recorded dates of isolation could represent the date when contacts are instructed to isolate, the date when they began isolating, or the last day in the community, but not all three dates.