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Quantifying the impact of isolation period and the use of rapid antigen tests for confirmed COVID-19 cases

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EXECUTIVE SUMMARY

Isolating confirmed cases while infectious is an important way of reducing transmission of infectious diseases. Because the infectious period of most diseases varies between people, matching this period to an ideal isolation period is difficult. Doing so requires balancing the impact that isolation has on individuals and the community with the risk of avoidable onward infections if people are released from isolation while still infectious. Rapid antigen tests (RATs) have been suggested as a way to help identify cases who are still infectious and to better target isolation requirements. We extend the approach used by the UKHSA[1,2] to investigate the impact of different isolation periods and test-to-release conditions for SARS-CoV-2.

Our results suggest that introducing a test-to-release criterion, in conjunction with minimum and maximum isolation lengths, offers the opportunity to appreciably reduce the risk of onward transmission, while resulting in only minor increases in the average time spent in isolation. Adding a one (or two) test-to-release policy to Aotearoa New Zealand's current 7 day isolation policy (with a maximum isolation period of 10 days), is expected to lead to a reduction in the number of cases still infectious after release of 40% (or 60%), while the average isolation period will increase by only by 0.3 (or 0.6) days.

Alternatively, for a scenario with a minimum isolation period of only 5 days, but using a two test-to-release policy with a maximum isolation period of 10 days, results in an expected *decrease in risk*, relative to the current policy, as well as a *decrease in the overall time spent in isolation* for confirmed cases. This policy results in a 40% reduction in the number of cases infectious at release and hours infectious post-release. It is also expected to deliver a 8% decrease in the total hours spent in isolation for confirmed cases, but a 20% decrease in the total number of excess hours spent in isolation by cases that are no longer infectious.

The results above use a conservative 75% value for the assumed sensitivity of rapid antigen tests, and a short value for the assumed duration of mean infectious period. If the simulations are repeated with parameter values that use a higher rapid antigen test sensitivity and a longer mean infectious period — in line with recent literature — then we find that the benefits of test-to-release as part of an isolation regime are even greater.

1 Introduction

Isolating confirmed cases of an infectious disease is a fundamental public health tool that works to reduce onward transmission from those cases. In the initial period of the SARS-CoV-2 pandemic, many countries either required or recommended isolation periods of 10–14 days for confirmed infections, based on estimates of the infectious period for cases. This isolation period was grounded in literature which found that fewer than 5% of cases were estimated to still be infectious after 10 days, especially in the context of culturable virus[3–8].

Since the initial period of the pandemic, new, more transmissible variants of SARS-CoV-2, sometimes in conjunction with the relaxation of public health measures in some jurisdictions, have led to peaks in infection prevalence of close to 10%. In many cases, this resulted in pressure on supply chains, and the workforce, due to the large number isolating individuals. Many jurisdictions therefore looked for ways to shorten isolation periods for some or all cases, while attempting to retain the public health benefits of case isolation.

If individuals who are no longer infectious can be accurately identified and allowed to end their isolation period early, then there is the potential to reduce the disruption due to isolation requirements. However, if people are allowed to end their isolation period while still infectious, it is likely that they will go on to infect others in the community who will subsequently be expected to isolate, or simply unable to work, due to the symptoms of COVID-19. That is, a policy intending to *reduce* the total number of hours in isolation for a population by shortening isolation requirements can risk *increasing* the total hours in isolation for the population through increasing the number of onward cases.

It is therefore important that both the duration of an isolation period and the exit criteria from isolation are considered when trying to minimise the disruption due to isolation requirements (both the total number of isolation hours required for a population and, particularly, the number of excess hours of isolation for cases that are no longer infectious) while maximising the benefits of isolation from reduced future infections.

Policies that can reduce transmission, such as effective case isolation settings, offer the opportunity to reduce the total number of cases (and the corresponding total hours of case isolation) that occur, both during periods of stable case numbers and during any transmission 'waves'.

Mandated isolation periods and test-to-release policies play a particularly important role with respect to asymptomatic cases (or those with mild symptoms where cases may be tempted to classify themselves as "recovered" while still infectious). A review of literature by the Ministry of Health COVID-19 Directorate, based on international data for Omicron, suggests that for a population with a high rate of booster uptake, like Aotearoa, the expected proportion of asymptomatic *infections* is around 40%.[9] It is worth noting that the fraction of asymptomatic *confirmed* cases* will typically be lower than this, as asymptomatic infections are more likely to remain undetected

*When we refer to "confirmed cases" we typically mean cases that have tested positive on a rapid antigen test. Since late February 2022, these have accounted for the vast majority of confirmed infections of SARS-CoV-2 in Aotearoa New Zealand.

and to never be recorded as a confirmed case. Indeed, in data provided by the Ministry of Health, 73% of confirmed cases report a symptom onset date. A significant further fraction of cases will experience only mild symptoms, that will resolve before they stop being infectious.

1.1 Testing for SARS-CoV-2

A variety of different testing approaches are available for confirming an infection of SARS-CoV-2. Reverse transcription polymerase chain reaction (RT-PCR, or simply PCR) tests are highly sensitive but can yield a positive result for weeks after recovery, even when the person being tested is no longer infectious[10]. This is because SARS-CoV2 PCR tests amplify and detect both viable and non-viable RNA. The resulting high sensitivity of such tests is a valuable feature for confirmatory testing in the early stages of an infection when the amount of viral material in a sample is likely to be low, or if one wishes to detect even historic infections as part of a contact tracing process.

In contrast, rapid antigen tests (RATs) — also know as lateral flow tests — detect certain proteins in a configuration matching that of the live virus. RATs do not include any amplification steps, so only return a positive result when the initial sample contains a sufficiently large amount of virus protein that has not been denatured or degraded[11]. This means that the intensity of a result on a RAT correlates strongly with viral load[11–14], and hence such tests offer a good proxy for whether someone is likely to be infectious at the specific point in time when the test was carried out.

Rapid antigen tests can therefore play an important role in shortening isolation periods, because they are good at identifying when someone is likely to no longer be infectious (as measured by live viral culture) and can therefore be safely released from isolation[11–16].

1.2 Existing modelling and simulation studies

A number of earlier simulation studies have investigated the effect of different isolation periods combined with rapid antigen testing regimes for confirmed cases.

Peng *et al.*[17] modelled the viral load of individuals through time, following Larremore *et al.*[18] and found that for antigen tests with 80% sensitivity, requiring 2 negative RAT results for release made it possible to shorten the minimum isolation period to 10 days with no increased risk compared to a 14 day isolation period, and that a 5 day minimum with 2 negative tests to release would provide the same level of onward transmission risk as a 10 day isolation policy.

An study by Quilty *et al.*[19] used an agent based model to consider the onward transmission risk associated with the use of rapid antigen tests to shorten the isolation period for confirmed cases. the authors considered viral loads that varied through time, based on work by Kissler *et al.*[5], and found that the number of infectious days in the community could be reduced to almost zero by requiring at least 2 consecutive days of negative test results, with an isolation period as short as 3 days after the first positive test result.

Earlier work investigating the use of rapid antigen tests to reduce the period of quarantine for close contacts found that the rapid return of the result, combined with the high sensitivity during the infectious period, make rapid antigen tests an excellent tool for use during a quarantine period or for regular surveillance[18,20–22].

More recent work by Bays *et al.*[1,2] considered the use of rapid antigen tests for shortening the isolation period during the Omicron wave. They found that the requirement for 2 negative RAT results prior to ending isolation allowed for the minimum isolation period to be reduced to 6 days (release on day 7), with only a minimal increase in risk of onward transmission compared to a 10 day isolation period.

These studies used a range of approaches, often considered varying viral load and infectiousness through time, and reliably found that it was possible to reduce the minimum isolation period without increasing risk if rapid antigen tests were used as part of a test-to-release policy. Although these studies were all pre-Omicron, the value of the use of rapid antigen tests is that the policy will still provide a robust isolation policy even in light of emerging variants with longer or shorter incubation and infectiousness periods.

A key limitation of these previous studies is that they did not consider the possibility of rapid antigen tests returning a positive result *after* an individual was no longer infectious, as has been found when comparing rapid antigen results to viral culture[14,15]. By not accounting for the potential lag between the end of an individual's infectious period and the time at which they would be likely to return a negative test result on a RAT, past studies will tend to over estimate the benefit in the reduction of excess hours of isolation that could be achieved through the use of RATs for a test-to-release policy.

In this report we look at the latest evidence from literature on infectious period and RAT sensitivity and specificity, including effects such as the lag between end of infectious period and returning a negative results on a RAT. We use these estimates to parameterise stochastic simulations to estimate the impact on onward transmission risk and excess isolation for a range of isolation policies.

2 Background

2.1 NZ Context

The isolation period in Aotearoa New Zealand for SARS-COV-2 was set to 14 days for the majority of the COVID pandemic. This was based on literature estimates that fewer than 1% of cases will still be infectious after 14 days[3–8]. This policy was in line with the Elimination strategy pursued from early 2020 to late 2021, and the associated potential for significant consequences in terms of onward spread if someone was released into the community while still infectious. When the number of confirmed cases was low, there was also a proportionately lower impact from a 14 day isolation period. In response to the arrival of Omicron in Aotearoa, and the expected large number of total population isolation days resulting from a 14 day isolation period combined with expected high case numbers, the isolation period was initially shortened to 10 days, and subsequently to 7 days as part of Aotearoa New Zealand's Omicron response. In Aotearoa New Zealand, day zero of the isolation period is defined as the day symptoms began or the first positive test result, whichever came first.

Most estimates in the literature for the proportion of cases still infectious after 7 days range between 10-30%[2,23–25]. More recent studies have found that 8 days after symptom onset half of all cases are still infectious (as measure by live viral culture)[26]. Consequently, Aotearoa's use of an

isolation period of 7 days, with no test-to-release procedure, means that there will be an appreciable fraction of people who are released from isolation while still infectious.

2.2 International Context

A number of countries have introduced a 'test to release' policy in order to shorten the minimum isolation period, including the UK, USA, and Singapore. Such policies are often combined with other measures such as requirements or expectations for people who have been recently released from isolation requirements to take additional 'precautions', to mitigate any residual risk due to false negatives. These 'precautions' include limiting the risk of onward transmission through indoor masking when outside the home, and avoiding environments with people who have a higher risk of severe outcomes from COVID-19, including childcare, aged care, and healthcare settings.

Using RATs to allow early release from isolation, if symptoms have resolved, was introduced by the UK in January 2022. This decision was based on modelling[1,2] that found that, under a so-called 'test-to-release' policy, the minimum isolation period could be shortened to 6 days (release on day 7) with almost the same risk of releasing people while infectious as a 9 day isolation period (release on day 10) with no testing. This prior modelling found that under the test-to-release policy, most people (79%) would only need to isolate for the 6 day period, while the remainder who were still infectious after 6 days would likely test positive on a RAT between days 7 and 9, and would therefore be required to isolate for a maximum of 9 days.

In the US, in response to a wave of Omicron cases, in January 2022 the CDC reduced the minimum isolation period for all cases from 10 days to 5 days. However, they also clearly acknowledged that many people would also still be infectious after a 5 day isolation period. As part of this, they recommended that people should use a rapid antigen test to inform their choice to end isolation after day 5[27], and recommended people take transmission reduction steps for the full 10 days of the original isolation period. These measures included the use of well-fitted masks when around others and avoiding high-risk settings including nursing homes, schools, healthcare facilities. For healthcare workers in the US, the isolation policy for confirmed cases remains as test-to-release after 7 days isolation in general, though this 7 day minimum can be shortened for critical workers.[28]

Singapore uses a minimum isolation period of 72 hours after a positive COVID test, regardless of the time of symptom onset, and requires either a negative RAT result or 7 days for vaccinated individuals (14 days if unvaccinated) to end isolation. The use of a positive test to start an individual's isolation period ensures that the 'clock' for the isolation period has started at a time of high viral load and is roughly comparable to a minimum isolation period of 5–6 days and a maximum isolation period of 9-10 days, since it often takes 1–2 days after the start of the infectious period for a rapid antigen test to turn positive[14,25,29], and can take 2–3 days after symptom onset for the infectious period to start (as measured by first positive PCR result)[26].

2.3 RAT sensitivity and specificity

The wide spread use of rapid antigen tests, combined with the wide spread nature of SARS-CoV-2 infections means that there is now extensive data on the performance of RATs with respect to their sensitivity and specificity over the time course of infection. Although the lack of an amplification

process means that RATs are lower sensitivity than PCR, in general, they are still highly sensitive during the period when individuals are most infections (have highest viral load). A mean sensitivity of 75% can be taken as a robust lower bound for RATs, with most studies finding sensitivities of over 90–95% during peak viral load[11–14,30–35]. Poor sampling technique can, of course, lead to a lower observed sensitivity for RATs, or for that matter, many other self-administered tests.

Similarly, when a SARS-CoV-2 rapid antigen test returns a positive result it is highly predictive of a a SARS-CoV-2 infection. That is, the likelihood of false positives from RATs is very low. An important point to note is that the lower sensitivity estimates for RATs have been from studies which compared to PCR results, but did not take into account the possibility of false negatives on PCR tests. More reliable studies that are either in very low prevalence settings, or which account for PCR sensitivity, produces estimates of RAT specificity that range from 99.5% to 100%.[11,16,31,36–40]

While RATs will typically be slower than PCR to detect infection in the very first days of infection[14,15,29], they are particularly informative for indicating the presence of live virus and hence the progresion of an individual's infectious period.[12–14] That is, after initial case confirmation, a positive result on a RAT is a good proxy for an individual being infectious.

The observed sensitivity of RATs can vary from individual to individual. This can be due to a number of factors including differences in sampling technique with self-administered RATs and differences in the nature of an individual's infection; that is, variation in where viral material is concentrated. This variation of observed sensitivity between individuals can be captured in simulations by making RAT sensitivity in the simulation a parameter that varies for each individual.

Individuals may still test positive on a RAT for a short period after the end of their infectious period, as measured by live viral culture. This lag is on the order of one day for most people but can be up to 2–3 days in rare cases[14,15]. In contrast, individuals can continue to test positive via PCR test for a week or more after the end of the period when it is possible to culture live virus.

3 Method

We follow the approach of Bays and colleagues[1,2], but extend it to allow for a lag of 1–2 days at the end of the infectious period before a RAT would become negative[14,15], and use the latest evidence for the infectious period distribution for Omicron.

Key model assumptions:

- The start of an individual's isolation clock is defined as day 0. This is the earlier of when they first develop symptoms or first return a positive test result. We assume that the period between day 0 and when an individual's infectious period begins is modelled by a parameter drawn from a Normal distribution for each individual, centered around zero, with a small standard deviation i.e. that day 0 is the same day as the start of the infectious period.

- The length of the infectious period for each individual is drawn from a Gamma distribution. The shape and scale parameters for this distribution are fixed for each realisation, and determined by fitting to literature. See Table 2 and Figure 1 for selected values, and Appendix for

details of the fit to literature.

- There is a lag between when someone becomes infectious and when RATs could return a positive result[14,15,29]. For the purposes of this study, this is assumed to be shorter than the minimum isolation period considered here, because, by definition, someone would need to have returned a positive test result before being considered a confirmed case, and being subject to these isolation rules.

- There is an offset between the time when the infectious period ends and the time when an individual would no longer return a positive RAT result. After this offset time, RATs are assumed to always return a negative result (100% specificity). The value for the offset is drawn for each individual from a distribution which comes from fitting to the data in[14] and has a mean of 1-2 days. This mean value is also consistent with the findings in[15] for the offset in timing between viral culture and antigen test results.

- In the period when test results from RATs can return a positive result (between the above two offsets) they are assumed to return a positive result with a probability that does not vary through time. This test sensitivity is drawn from a distribution with a mean of 75%, but with a long (lower sensitivity) tail. This is likely to be a pessimistic estimate of test sensitivity, as literature which compares viral culture to RAT results finds test sensitivities of 90-95%. We consider the results from modelling using a higher test sensitivity in the Appendix.

- The test sensitivity is drawn once for each individual, and is then fixed for that whole realisation. This is based on discussions with public health clinicians, in order to capture the observed correlation between test results for individuals. This correlation could be attributed to test taking technique of individuals, as well as individual differences in overall viral loads and in viral antigen concentrations in the sample site (nasal for most RATs).

Case data for Aotearoa[41] during the Omicron outbreak shows that people do not return an initial positive RAT result until on average 2 days after symptom onset. That is, day 0 of their isolation period is about 2 days before the date that they first test positive. This dataset also indicates that 73% of confirmed cases have a symptom onset date recorded, which suggests that we are capturing data for most symptomatic cases. Furthermore, only 1% of cases have a recorded symptom onset after their first positive test result. Because the survey that asks about symptom onset timing is often filled out within 1-2 days of the first reported positive test result, the 28% without a symptom onset is an upper bound on the asymptomatic proportion of cases, as some could have had symptom onset after they filled out the survey. For the purposes of this modelling work, although we do not explicitly consider symptoms, we are effectively assuming that, for symptomatic cases, symptom onset coincides with the start of the infectious period.

The selected parameter values are given in Table 1.

3.1 Infectious period estimates

We consider two scenarios for the distribution of infection duration for individuals. In the first of these, individuals in the model have an infectious period drawn from a Gamma distribution with

Parameter	Distribution	Sampling
Infectious period	Gamma(shape=IPD_shape, scale=IPD_scale)	Per individual
Start of isolation period relative to start of infectious period	Normal(mean=0, sd=0.3) Truncated at min=-3 max=3	Per individual
RAT sensitivity	Weibull(8, 0.8) Truncated at min=0 max=1	Per individual
Time no longer able to test positive relative to end of infectious period	Normal(mean=1.10, sd=1.36)	Per individual

Table 1. Parameter values for the distributions in the model. Values are drawn independently for each individual.

shape = 2.62 (se=0.33) and scale = 1.88 (sd=0.23). This produces a distribution with a median infectious period of 4.3 days and a mean infectious period of 4.9 days. These parameter values are selected by fitting a Gamma distribution to data estimating infectiousness over time from international literature using a range of study approaches; the standard deviations associated with the fitted means are chosen to match those used in previous similar work[1,2]. Estimates of the standard deviations based on fitting estimates tend to be broader. For more details, see Appendix. Figure 1 shows the resulting estimate for the infectious period distributions for this 'shorter' infectious period.

Recent literature has suggested that using symptom onset to start the isolation period may start the isolation 'clock' before the infectious period has begun (as measured by first PCR result, or viral culture). In order to investigate the potential impact of this, we also consider a 'longer' infectious period distribution, by fitting to "Culture negative after first PCR or symptom onset" data from Boucau et al.[26]. The best fit (Figure 1, 'longer') was found with infectious period drawn from a Gamma distribution with shape = 3.71 (se=0.37) and scale = 2.11 (se=0.20). This produces a distribution with a median infectious period of 7.1 days and a mean infectious period of 7.8 days.

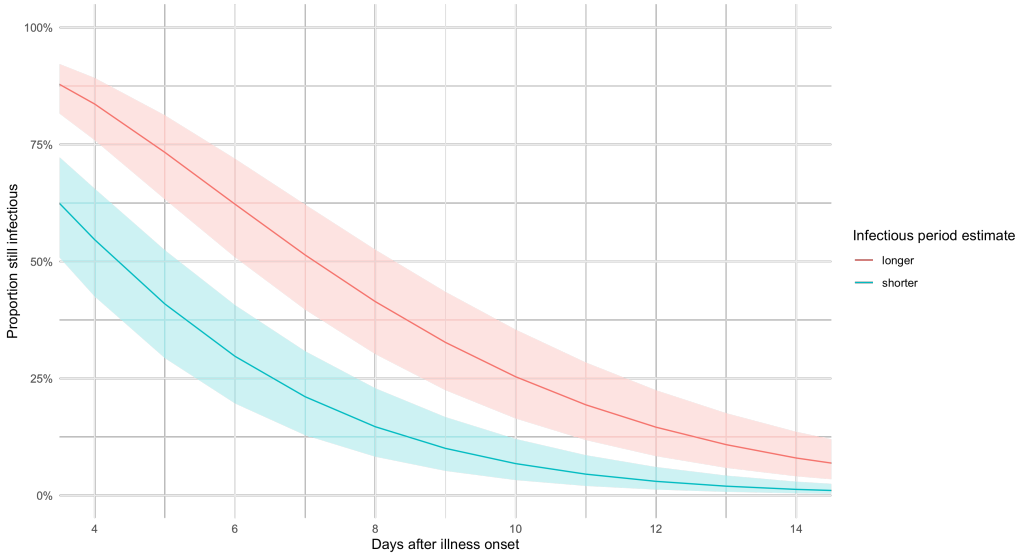

Figure 1. The mean and 95% confidence intervals for the proportion of people still infectious on a given day after the **shorter** and **longer** infectious periods.

Parameter	Distribution	Sampling
IPD_shape (shorter)	Normal(mean=2.62, sd=0.1) Truncated at min=0 max=100	Per realisation
IPD_scale (shorter)	Normal distribution(mean=1.88, sd=0.1) Truncated at min=0 max=100	Per realisation
IPD_shape (longer)	Normal(mean=3.71, sd=0.1) Truncated at min=0 max=100	Per realisation
IPD_scale (longer)	Normal distribution(mean=2.11, sd=0.1) Truncated at min=0 max=100	Per realisation

Table 2. Parameter values for the **shorter** and **longer** infectious period distribution estimates. These values are fixed for each realisation. See Appendix for more details.

3.2 Implementation of policies

In order to investigate the impact of different potential isolation policies we specify isolation settings using three parameters. The first parameter is the maximum isolation period. After this time all individuals are released from isolation, regardless of whether or not they are still infectious. For a maximum isolation period of 10 days, all individuals would be released on, or before, day 11. Under a test-to-release policy, we also specify the earliest possible release day and the number of negative tests required for release. If only one negative test is required for early release, this test will first occur on the earliest possible release day. If the test result is negative, then the individual is released immediately. Otherwise, they remain in isolation and attempt to release, via returning a negative test, for each subsequent day. If an individual reaches the maximum isolation period they are released regardless of status.

If two consecutive negative tests are required for early release, the first test occurs the day before the earliest possible release day. For example if two tests are required and the earliest release from isolation is day 8, then we first test on day 7. An example of the test and release timing possibilities for a minimum period of 7 days and a maximum of 10 days is shown in Table 3.

Day 7	Day 8	Day 9	Day 10	Day 11
(-)	(-) release early			
(+)	(-)	(-) release early		
(-)	(+)	(-)	(-) release early	
(+)	(+)	(-)	(-) release early	
No RATs				Release as usual

Table 3. Examples of when people would be released with different test results for the policy settings: 2 tests required, earliest release=day 8, maximum isolation period=10 days (release on day 11).

Following these assumptions, we simulate a population of infected individuals and calculate the following metrics:

- the fraction of individuals who are released while still infectious;
- the amount of time people spend in the community post-isolation while still infectious (both

as a population level statistic and as a statistic that only considers the subset of people who were released while infectious);

- the average number of hours that confirmed cases spend in isolation;
- and the amount of time people spend in isolation unnecessarily, beyond the end of their infectious period (as a population level statistic).

We estimate these for a number of different isolation and testing strategies. To obtain uncertainty estimates, we run 1000 realisations of each scenario with 500,000 confirmed cases per scenario.

3.3 Code availability

Simulation code used to produce the results in this paper is available within the *Julia* package *MitigatingIsolationAndQuarantine.jl*[42] and is licensed under a CC-BY 4.0 International License. Instructions on how to install *Julia*, *MitigatingIsolationAndQuarantine.jl* and tutorials on how to run the case isolation simulation can be found in the package's documentation.

4 Results

We calculate the proportion of confirmed cases that are released while still infectious; the population average duration of time infectious in the community for confirmed cases after their release; the population average duration of time spent in isolation while not infectious (excess isolation); and the average time spent in isolation across all confirmed cases. All metrics reported here are mean values from the 1,000 realisations, with intervals given as 2.5% and 97.5% quantiles of the values returned by each realisation. This effectively creates 95% simulation -based confidence intervals for the metrics of interest.

4.1 Results with the shorter infectious period estimate

We consider policies with maximum isolation periods of either 7 and 10 days, and look at the impact of changes to the minimum required isolation period, in conjunction with different test-to-release requirements. In Figure 2 we show the impact these different policies have on the proportion of confirmed cases infectious at release, and in Figure 3 we convert this into a measure of the average number of hours infectious in the community after release.

Table 4 presents estimates for the proportion of cases who would still be infectious at time of release, along with the average time spent in isolation for different policies.

In Table 5 we look into how much time, on average (across all confirmed cases) would be spent infectious in the community after release, and compare that against the average number of hours spent in isolation after a case is no longer infectious.

For the current policy of a 7 day isolation period and no test to release, we estimate that around 14.6% of cases are released while still infectious, for the shorter estimates of infectious period. This results in a average of 8.9 hours infectious in the community across all confirmed cases (Table 5). The absence of test to release in the current policy means that a number of cases stop being infectious before the end of their 7 day isolation period. This results in a average of 83 hours of

Minimum isolation (days)	Maximum isolation (days)	Tests to release	Proportion of cases released while infectious	Average days spent in isolation*	Description
5	5	0	29.7% [22.4%, 37.2%]	5.5	5 days only
5	7	1	20.8% [15.4%, 26.9%]	6.1	TTR, min 5 days, max 7 days
		2	16.8% [11.7%, 22.7%]	6.4	
5	10	1	17.5% [12.4%, 22.9%]	6.2	TTR, min 5 days, max 10 days
		2	9.1% [6.1%, 12.2%]	6.9	
7	**7**	**0**	**14.6% [9.7%, 20.1%]**	**7.5**	**Current policy**
7	10	1	9.3% [6.1%, 13.2%]	7.8	TTR, min 7 days, max 10 days
		2	6.2% [3.7%, 9.1%]	8.1	
10	**10**	**0**	**4.7% [2.5%, 7.2%]**	**10.5**	**Phase 2 policy**

Table 4. Proportion of cases released while still infectious and estimated extra time spent in isolation beyond the minimum for test to release policies, for the **shorter** infectious period. Minimum and maximum isolation periods refer to the days in isolation. i.e. a minimum isolation period of 5 days means release on day 6, at the earliest. *here we assume that for a 7 day isolation period, there are 7.5 days spent in isolation on average, due to the definition of day 0. Bold entries correspond to case isolation policies that are currently, or were previously, implemented in Aotearoa.

Minimum isolation (days)	Maximum isolation (days)	Tests to release	Average hours of infectiousness after release**	Average hours of excess isolation**
5	5	0	19.3 [12.4, 27.1]	45.2 [37.9, 53.4]
5	7	1	12.4 [7.9, 18.1]	50.9 [44.0, 57.9]
		2	10.1 [6.0, 15.1]	57 [49.7, 64.2]
5	10	1	10.1 [6.2, 14.9]	53.3 [46.2, 61.0]
		2	5.0 [2.9, 7.5]	65.6 [60.3, 71.3]
7	**7**	**0**	**8.9 [5.1, 13.5]**	**83.2 [72.8, 94.3]**
7	10	1	5.2 [3.0, 8.1]	86.7 [77.1, 96.3]
		2	3.4 [1.7, 5.6]	92.3 [83.1, 101.6]
0	**10**	**10**	**2.7 [1.3, 4.6]**	**148.4 [135.3, 162.1]**

Table 5. Number of hours of infectiousness after release, and the average number of hours of 'excess' isolation, for the **shorter** infectious period. **these metrics are calculated across all confirmed cases - i.e. divided by the total 500,000 confirmed cases. Bold entries correspond to case isolation policies that are currently, or were previously, implemented in Aotearoa.

isolation while not infectious, across all confirmed cases (for the 14% released while infectious, their 'excess hours of isolation' is set to zero).

In contrast, a policy such as an isolation period for a minimum of 5 days and a maximum of 10, with release from isolation possible between days 5 and 10 following a negative test or tests

can offer a significant reduction in the numbers of hours of excess isolation with either a decrease (2 tests to release) or a small increase (1 test to release) in the proportion of cases released while infectious and hours infectious in the community.

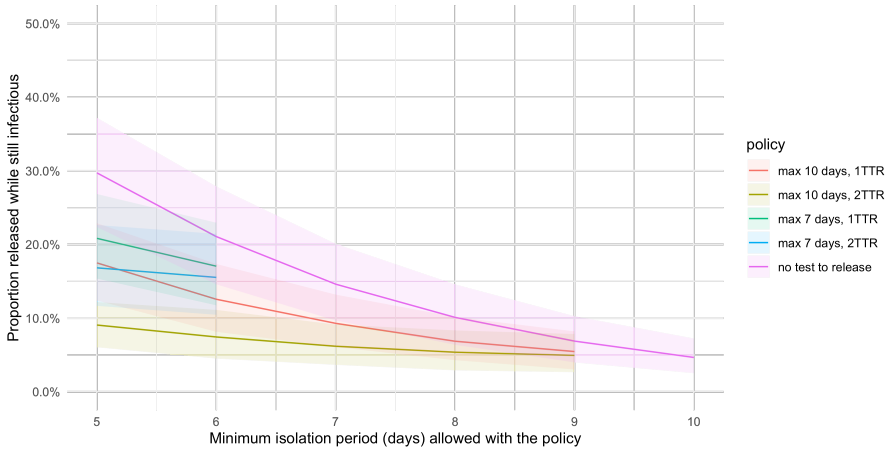

Figure 2. Proportion of cases released while still infectious for each testing and minimum isolation period policy for the **shorter** infectious period distribution. Policies include: no test to release, with test-to-release and with a maximum isolation period of 10 days (release on day 11), and with test to release and with a maximum isolation period of 7 days (release on day 8).

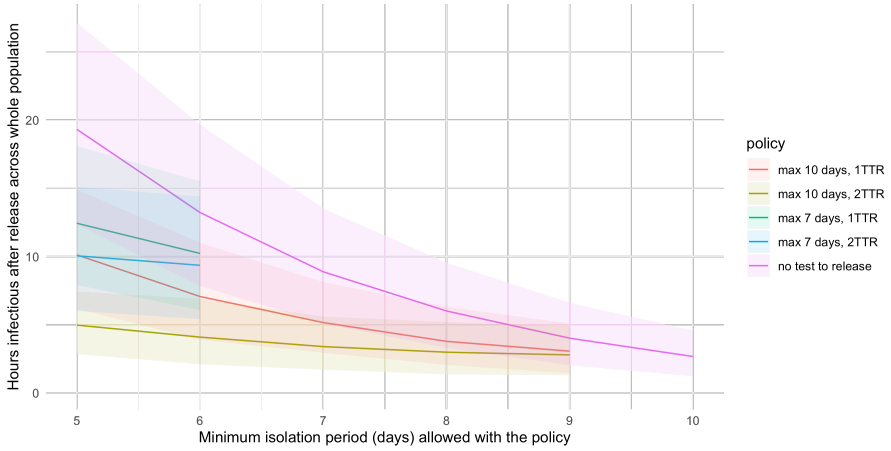

Figure 3. Average hours infectious in the community after release across all confirmed cases for different policy choices, with a **shorter** infectious period.

4.1.1 Detailed results showing how policies play out daily

For a specific policy, we can then look at the breakdown of infectious vs non-infectious cases released on each day after the minimum isolation period. In Figure 4 we show results for an isolation policy with a minimum isolation period of 5 days and a maximum of 10 days, combined with a single test to release. This is for the '*shorter*' estimate of the infectious period distribution, and for the conservative 75% test sensitivity estimate.

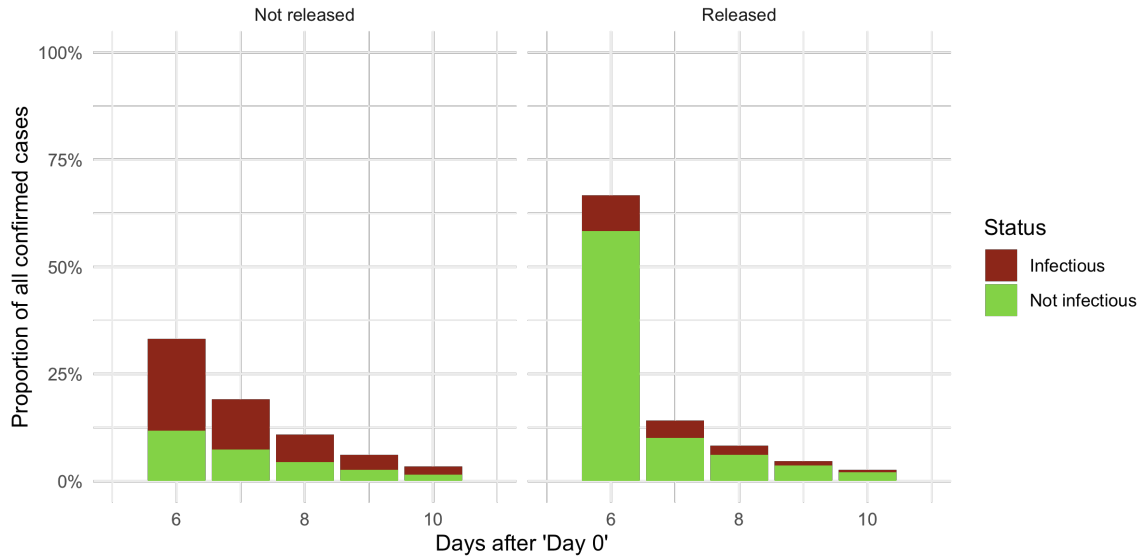

Figure 4. Results for an isolation policy with a 5 day minimum isolation period and 10 day maximum, combined with a one-test test-to-release criterion. This shows the proportion of cases released (left) or not released (right) each day, colour-coded whether they were still infectious or not. Here we see that the majority of people who are not released early and must continue to isolate **(left plot)**, are still infectious (brown bars a larger than green bars). Similarly, of those released early **(right plot)** the majority are not infectious (green bars are larger than brown bars). Not shown is that on day 11 around 3.5% of cases will be released (after the maximum 10 day isolation period) of whom 40% will be still infectious.

In Figure 4 we see that on day 6:

- 59% of cases are released and not infectious (correctly identified as non-infectious and released);
- 12% of cases remain in isolation despite not being infectious due to the lag of RATs relative to live viral culture (misidentified as infectious and not released);
- 8% of cases are released even though they are still infectious due to a false negative test (misidentified as non-infectious and released); and
- 21% of cases are still infectious and still in isolation because they tested positive (correctly identified as infectious and not released).

On days 7–10, around half of those remaining in isolation are released each day, and the remaining 3.5% still in isolation after 10 days are released then. During days 7–10, we can see from Figure 4 that of those not released (lefthand plot), the majority are still infectious – the brown bars are larger than the green bars. In contrast, during days 7–10, the majority of those released (Fig-

ure 4 righthand plot) are no longer infectious – the green bars are much larger than the brown bars. This shows that, even with a conservative estimate of RAT sensitivity, and allowing for a lag period at the end of the infectious period, a test to release policy is effective at targeting the burden of isolation to those who are most likely to still be infectious, while allowing those who are not to leave isolation earlier.

We can use the results on who gets released or not (positive or negative test result) each day, and whether they are still infectious or not, to calculate the positive and negative predictive value of RATs through time. For the 5 day minimum, 10 day maximum, 1 test to release policy, we find:

- For those who test positive on a RAT, at day 6, 65% are still infectious, this gradually decreases to 55% by day 10.
- For those who test negative on a RAT on day 6, 13% are still infectious and it is a false negative.
- For those who stay in isolation longer than the minimum due to positive test(s) and then test negative on days 7–10 and are released, 20-30% are still infectious, with the proportion decreasing through time.

These findings are conserved over different policy options, for example, for a 7 day minimum, 10 day maximum, 1 test to release policy, we find:

- For those who test positive on a RAT, at day 8, 59% are still infectious, this gradually decreases to 55% by day 10.
- For those who test negative on a RAT on day 8, only 5% are still infectious and it is a false negative. This is lower than the day 6 results above due to a greater proportion of people not being infectious anymore at this stage compared to on day 6, thus lowering the pre-test probability.
- For those who stay in isolation longer than the minimum due to positive test(s) and then test negative on days 7–10 and are released, 20–25% are still infectious (decreasing through time).

In context of their use for ending a period of isolation, the positive predictive value (PPV) of RATS is not dependent on the test sensitivity, but only on the assumed distribution of the offset between the end of the infectious period and when a RAT would turn negative. For those who are kept in isolation after they are no longer infectious due to a 'false positive', they will almost always only need to isolate for an extra day, and the policy is still well targeted.

For the negative predictive value (NPV) of RATs, the situation is a bit more complicated. On the first possible day of release, the NPV depends on: the proportion of people assumed to still be infectious at that point (pre-test probability), the assumed test sensitivity, and the proportion of cases who we assume who start testing negative before their infectious period ends.

The majority of people are released on the first possible day in our simulations, which means that the biggest risk of releasing people while still infectious occurs on that first day. However, due to the majority of people being recovered by then, this first day is also the day where the negative

predictive value is highest. For a 5 day minimum, the NPV is 87% on day 6, and for a 7 day minimum, the NPV increases to 95% – even with the conservative assumption of a 75% test sensitivity. The fact that the NPV decreases as the minimum isolation period decreases, illustratues the fact that, with test-to-release, as the minimum isolation period is reduced, the value of a policy that requires two consecutive negative tests to release increases.

For the period after the first possible day of release, and before the maximum isolation period, the NPV is strongly driven by the assumed test sensitivity, and the proportion of cases who we assume who start testing negative before their infectious period ends. The values we use in this work are deliberately conservative, but highlight the importance of having public health guidance that recommends that precautions are taken up until day 10.

4.2 Results with the longer infectious period estimate

Here we produce all the same plots and tables as above, but for simulations using the longer infectious period distribution from[26].

In Figure 5 we can see that the longer infectious period estimate significantly increases the proportion of cases that are still infectious at release, for all isolation policies. For the current isolation policy, the longer estimate of infectious period corresponds to 41.4% [33.2%, 49.8%] of (symptomatic) confirmed cases being still infectious at the end of the 7 day isolation period.

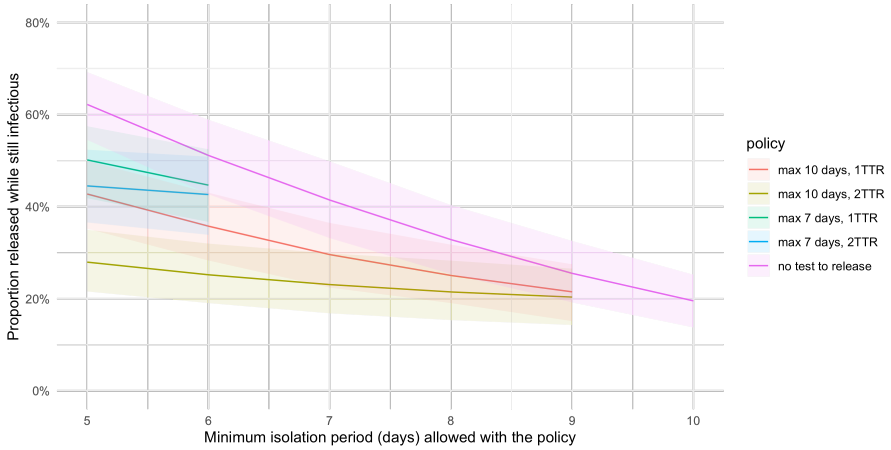

Figure 5. Proportion of cases released while still infectious for each testing and minimum isolation period policy with the **longer** infectious period from[26].Policies include: no test to release, with test-to-release and with a maximum isolation period of 10 days (release on day 11), and with test to release and with a maximum isolation period of 7 days (release on day 8).

In Table 6 we see that adding a test to release policy substantially reduces the proportion of confirmed cases who are still infectious at release. The average hours infectious in the community across all confirmed cases decreases from 36.6 hours (current policy) to 23.6 hours for one test to release (minimum of 7 days isolation, maximum of 10), and to 18 hours with two tests to release (min 7 days, max 10) - see Table 7 and Figure 6.

For the longer estimate of the infectious period, reducing the minimum isolation period below 7 days becomes more risky because so many cases are still infectious after 5 days. However, if a

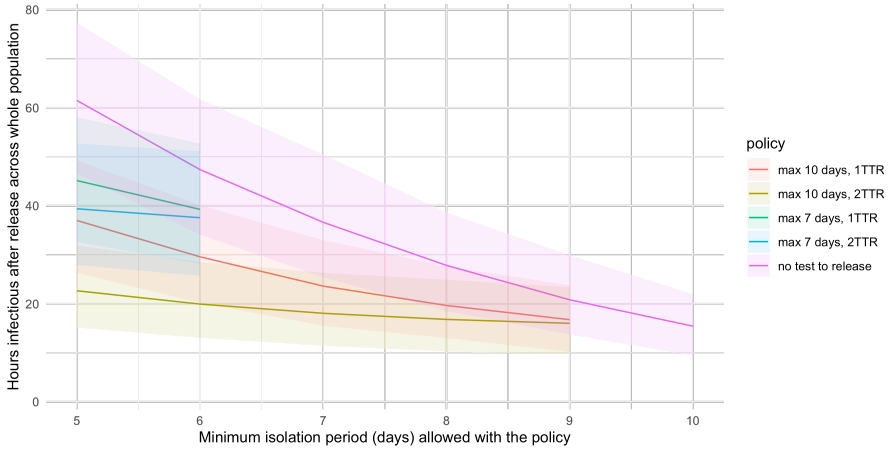

Figure 6. Average hours infectious in the community after release across all confirmed cases for different policy choices, with a **longer** infectious period.

shorter minimum isolation period of 5 days is complemented with 1 test-to-release and a 10 day maximum isolation period, then it is possible to reduce the excess hours in isolation (27.2 hours, relative to 40.7 hours for the current policy) with no appreciable increase in the number of hours infectious in the community (37 hours c.f. 36.6 hours).

Alternatively, a two test to release policy (5 day minimum, 10 day maximum) results in a decrease in risk compared to current policy (22.6 hours infectious in the community c.f. 36.6 hours) with no significant increase for the excess hours spent in isolation (41 hours c.f. 40.7 hours) — see Table 7.

Minimum isolation (days)	Maximum isolation (days)	Tests to release	Proportion of cases released while infectious	Average days spent in isolation*	Description
5	5	0	62.2% [54.5%, 69.2%]	5.5	5 days only
5	7	1	50.2% [41.8%, 57.5%]	6.4	TTR, min 5 days, max 7 days
		2	44.5% [36.6%, 52.4%]	6.9	
5	10	1	42.8% [35.2%, 50.0%]	6.9	TTR, min 5 days, max 10 days
		2	28.0% [21.6%, 35.0%]	8.1	
7	**7**	**0**	**41.4% [33.2%, 49.8%]**	**7.5**	**Current policy**
7	10	1	29.6% [22.4%, 36.5%]	8.3	TTR, min 7 days, max 10 days
		2	23.1% [16.8%, 29.9%]	8.9	
10	**10**	**0**	**19.5% [13.8%, 25.2%]**	**10.5**	**Phase 2 policy**

Table 6. Proportion of cases released while still infectious for the **longer** infectious period from Boucau et al. and estimated extra time spent in isolation beyond the minimum for test to release policies. Minimum and maximum isolation periods refer to the days in isolation. i.e. a minimum isolation period of 5 days means release on day 6, at the earliest. *here we assume that for a 7 day isolation period, there are 7.5 days spent in isolation on average, due to the definition of day 0. Bold entries correspond to case isolation policies that are currently, or were previously, implemented in Aotearoa.

Minimum isolation (days)	Maximum isolation (days)	Tests to release	Average hours of infectiousness after release**	Average hours of excess isolation**
5	5	0	61.5 [46.6, 77.4]	17.4 [13.3, 22.1]
5	7	1	45.1 [32.6, 58.1]	23.0 [18.5, 28.5]
		2	39.4 [27.9, 52.7]	28.2 [23.0, 34.1]
5	10	1	37.0 [26.3, 49.3]	27.2 [22.4, 32.4]
		2	22.6 [15.1, 31.9]	41 [35.3, 46.8]
7	**7**	**0**	**36.6 [25.4, 50.4]**	**40.7 [32.3, 49.4]**
7	10	1	23.6 [15.5, 33.0]	47.4 [39.8, 56.2]
		2	18 [11.4, 26.3]	54.8 [39.8, 63.4]
10	**10**	**0**	**15.4 [9.4, 21.9]**	**91.5 [79.8, 105.1]**

Table 7. Number of hours of infectiousness after release, and the average number of hours of 'excess' isolation, for the **longer** infectious period. **these metrics are calculated across all confirmed cases - i.e. divided by the total 500,000 confirmed cases. Bold entries correspond to case isolation policies that are currently, or were previously, implemented in Aotearoa.

5 Discussion of results and limitations

We have considered three key components of case isolation policy in this paper: when to 'start the clock' of an isolation period; releasing cases based on negative results from rapid antigen tests ('test-to-release'); and the consequences of various minimum and maximum periods of isolation periods under test-to-release and non-testing regimes. We have investigated how each of these components impacts the proportion, and duration, of confirmed cases that are still infectious at time of release from isolation, as well as the proportion, and duration, that remain in isolation when they are no longer infectious. We also note there are some additional considerations which, while they are relevant for policy considerations, are out of the scope of the modelling for this paper.

5.1 Definition of day zero significantly impacts the proportion of cases released while still infectious

Aotearoa New Zealand's current definition of the beginning of the isolation period (day zero) is the earlier of when symptoms first occur, or first positive test result. Based on Ministry of Health data[41], over 72% of confirmed cases report a symptom onset date that was before their positive test result[†].

In our modelling, we assume that the timing of symptom onset matches the start of the infectious period for cases. There is increasing evidence that using symptom onset, rather than the first positive test result, as the day zero of any isolation period will lead to a longer observed duration until cases are no longer infectious, as measured by longer time before viral culture[15,26], or rapid antigen tests[43,44] turns negative. This means that the 'shorter' infectious period results presented here could under-estimate both the proportion of cases who are released while will infectious, and

[†]of the remaining 28%, 17% have no symptom onset date recorded, and less than 1% have a symptom onset date after their positive test was reported

the time 'infectious in the community after release'.

In order to account for this, we also calculated results for a 'longer' infectious period that we fit to the 'time to culture negative after symptom onset' from[26]. We use this longer infectious period as a proxy for an early entry to isolation (e.g. if day zero is day of symptom onset and this preceeds day of first positive test result). In this case we find that the risk of onward transmission from confirmed cases with the current isolation policy is much higher, and that the value of using a test-to-release policy is even greater than for the shorter estimated infectious period, with most policies reducing the risk of onward transmission relative to the current policy.

For asymptomatic cases, the isolation period clock will always start on the day that cases first test positive. This means that, even with regular testing, asymptomatic cases are likely to be 1–2 days through their infectious period before their isolation clock starts. Using a test-to-release policy for these cases has even greater potential benefits in terms of reducing excess hours of isolation, while preventing onward transmission from those who are still infectious.

A number of studies[19] and countries (e.g. Singapore), use the first positive test result to start the isolation clock. As well as being a reliable measure of the start of the infectious period, this has the additional advantage that this approach is robust to changes in the beginning of the infectious period relative to symptom onset. However, there may be disadvantages in terms of individual's perceived value of isolating when symptoms first appear, if these days do not get counted towards their isolation period. This could risk increasing transmission during the initial period of infection, between the start of the infectious period and when a rapid antigen test would turn positive.

5.2 Accuracy of RATs during the infectious period enables test to release policies, reducing excess isolation

To be confident that a test-to-release policy is safe and effective, there must be confidence in the sensitivity of the test used. The literature we have referenced shows RATs to be a suitably accurate test of whether a confirmed case is still infectious or not.

Simulations using a RAT sensitivity distribution based off conservative values in literature showed that a policy with an isolation period of a minimum of 5 days and a maximum of 10, with release possible between days 5 and 10 following 2 negative tests, resulted in a decrease in the proportion of cases released while infectious compared to the current policy, in addition to a significant reduction in the number of hours of excess isolation.

The high sensitivity and specificity of RATs enables test-to-release policies to be considered without increased risk of increased community transmission, and with the hope that such regimes will increase availability of people in the workforce. However, while test-to-release may enable cases to return to work before their maximum isolation period is complete, in reality they may not be physically well enough to do so. People with ongoing acute symptoms will need to isolate longer than the minimum period, regardless of any test result. This is not captured in our modelling. This would require information about symptom duration relative to infectious period in order to estimate the proportion of cases who would still have symptoms each day.

Evidence we could find suggested that symptoms were not a good predictor of infectiousness timing, and that symptoms may resolve before the end of infectiousness[44]. Currently in New Zealand, some critical health workers are able to return to work after a minimum isolation period, after two subsequent days of negative tests. However the Minister for COVID-19 Response has publicly noted that often workers are still too unwell to work and there has not been much utilisation of the allowance[45]. Consequently, although a test-to-release policy for ending case isolation may provide a way to safely end isolation for cases, the practicality of ending isolation may not always follow. This will be particularly true in situations where the person ending isolation may be one of the first infections in a household and may be required to care for family members who have subsequently become cases during their isolation period. Clinical recovery from COVID-19 may take longer than the infectious duration: since adequate rest is required to support a sustained recovery from a COVID-19 infection, attempting to reduce isolation periods beyond a certain point could increase, rather than decrease, aggregate absenteeism and illness.

5.3 Additional considerations and limitations of this modelling

- This modelling does not consider the effect of an isolation policy that includes a period after the isolation period where people are not strictly isolating but are told to take 'precautions' e.g. they are required to wear masks when indoors and avoid high risk settings[‡] (similar to the CDC and Australian government advice). This would act to reduce the risk of onward transmission in the days following release when people might still be infectious. Although difficult to parameterise, estimates of such effects can be calculated using an individual based contagion model for onward transmission, such as the Network Contagion Model developed by COVID-19 Modelling Aotearoa.

- This modelling does not consider the effect of any isolation policy on people's willingness to test or their adherence to isolation rules. It is possible that lengthy isolation periods may discourage some people from testing or from reporting their test result. However, test-to-release policies mitigate against this to some extent by generally enabling shorter isolation periods for the majority of cases, and only requiring longer isolation periods for people who continue to test positive.

- When estimating the probability of onward transmission from a case, it is important to consider infectiousness through time. Not all hours 'infectious in the community' are equal. In general, the further through an infectious period someone is (after their peak infectiousness) the less risk of onward transmission there is. This points to the value of reducing the impact of false negatives if the minimum isolation period is shortened below 7 days, through requiring two tests instead of just one. In general, the shorter you make the minimum isolation period, the more consecutive negative tests you need to require to increase confidence that the people you are releasing are not infectious.

- We do not separate out symptomatic and asymptomatic cases in our analysis. Asymptomatic infections have been found to have a lower test sensitivity[11]. However, the observed

[‡]both in terms of avoiding high transmission risk settings, as well as avoiding contact with people with high health risks

sensitivity findings can be explained partly by the lack of symptoms meaning that the timing of these tests often misses the infectious period. In this work we are only considering confirmed cases, who have, by definition, tested positive on a RAT, and so their infection must be detectable by RATs. The estimates for RAT sensitivity used in this modelling are highly cautious, with respect to literature estimates, hence are unlikely to be overestimating RAT sensitivity for asymptomatic cases. Additionally, one study of healthcare workers suggested a potentially shorter infectious period[43] due to an observed reduction in RAT positivity for asymptomatic individuals returning to work from day 5. However, this result could be explained by the fact that these individuals would have started their 'clock' (day 0) later[26].

- We do not consider whether there are differences in the infectious period for children, as we could not find evidence on this. There is limited evidence of a shorter serial interval if the infector is a child[46], but this is possibly due to their later symptom onset relative to infectious period, due to more children being unvaccinated, rather than a difference in infectious period duration. Using RATs to determine the required duration of isolation would reduce unnecessary isolation for children who recover sooner.

- An important consideration in recommending test to release is the potential risk of increased interactions associated with false negatives. That is, if people assume a negative test means they are definitely not infectious, as discussed in[1]. However, recent literature points to very high sensitivity of RATs (90–95%) during the infectious period, and so this is a small risk. Furthermore, with the existing policy the NZ govt says 'you're good to go' on day 8, and so the risk of some cases having false negatives would need to be greater than the current risk of no test results at all.

- It is important to note that shortening or removing isolation requirements does not solve the workforce disruption issues, because so many cases are too unwell to work, even if they are legally allowed to. In workforces and countries where legally required isolation periods have been shortened[45] or removed[47,48], the impact of COVID-19 on the workforce has continued to be substantial. For cases who are experiencing noticeable symptoms, a policy of continuing to isolate until after symptoms have resolved, independent of specified minimum isolation periods and test results, is still important from both a public health and an individual health perspective.

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Appendix

A Fitting infectious period distributions to literature

In this section we show the two different fitted infectious period Gamma distributions used for the results in this report, alongside values from literature, and describe the source of the estimates.

To fit the *shorter* infectious period distribution (Figure 7), we use data on 'days from first positive PCR test' until viral culture is negative from NIID[25] and Boucau *et al.*[26], and we use data on 'days after illness onset' until the CT value on a PCR test would no longer be below 30 from Hay et al.[23]. The best fit is obtained for shape=2.61 (standard error=0.33), and scale=1.88 (standard error=0.23).

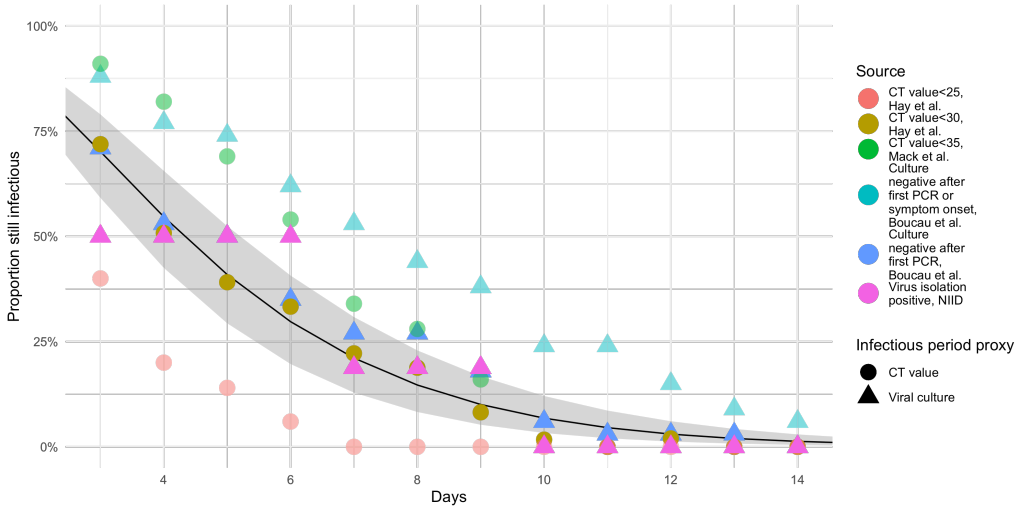

Figure 7. The black curve and grey bands show the mean and 95% confidence intervals for the proportion of people still infectious on a given day after the **shorter** infectious period began for the fitted parameters. Coloured circles (CT value data) and triangles (viral culture data) show how these selected parameter values line up with data from references. The literature values that we fit to are "CT value <30, Hay et al."[23], "Culture negative after first PCR, Boucau et al."[26], and "Virus isolation positive, NIID"[25]. Note: we also show values from "CT value<25 Hay et al."[23], "CT value<35, Mack et al."[24], and "Culture negative after first PCR or symptom onset, Boucau et al."[26], but we do not fit to this data.

For the *longer* infectious period distribution, we fit to just the 'time from the earlier of symptom onset or first positive PCR' in Boucau *et al.*[26], in Figure 8. In Boucau *et al.*[26], the appearance of symptoms before the infectious period begins is one of the suggested explanations for the longer 'time to culture negative' times (median 8 days c.f 5–6 days) when using the earlier of symptom onset or positive PCR as day 0. To capture this we could have attempted to fit to a combination of the 'infectious period' distribution parameters and the 'Start of isolation period relative to start of infectious period' distribution parameters. However, we found that a reasonable fit was achieved using just the infectious period distribution. This allowed for fewer free parameters in the fit, whilst not affecting the simulation outputs, as we do not consider test-to-release policies with testing that begins earlier than day 5. The best fit is obtained for shape=3.71 (standard error=0.37), and scale=2.11 (standard error=0.20).

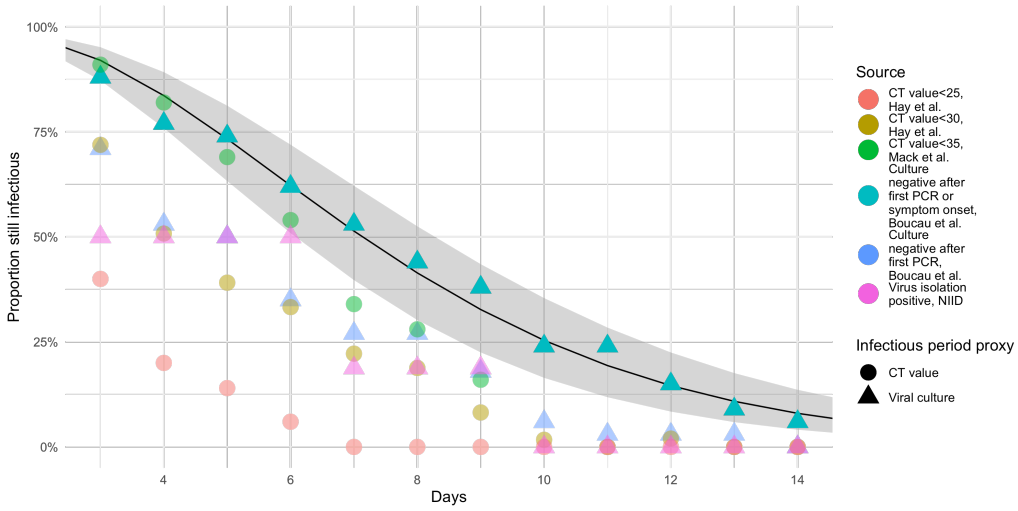

Figure 8. The black curve and grey bands show the mean and 95% confidence intervals for the proportion of people still infectious on a given day after the **longer** infectious period began for the fitted parameters. Teal triangles show how these selected parameter values line up with data from "Culture negative after first PCR or symptom onset, Boucau et al."[26]

B Considering higher RAT sensitivity in confirmed cases

For the results presented in the main body of the report, we assumed a test sensitivity distribution with a mean of 75%. This is highly conservative, when comparing to viral culture, or to CT values below 25 or 30 on PCR tests. In these cases estimates for the sensitivity of RATs increases to 90–95%[11–14,30–35].

Additionally, because confirmed cases have overwhelmingly been identified through testing positive on a RAT, the expected sensitivity for this subset is even higher. After initially testing positive, the sensitivity of subsequent tests to detect infectiousness is very high. This is because by testing positive on a RAT these cases must have had a high enough viral load, good sampling technique, and viral antigens produced in the sampling site.

We have re-run the simulations for the 'shorter' infectious period distribution with a mean test sensitivity during the infectious period of 95% (Weibull distribution with scale=40, and shape=0.96, truncated to the range [0,1]). Figure 9 shows that with this higher RAT sensitivity value, the effectiveness of a test to release policy in terms of avoiding infectious hours in the community is even stronger. In particular, using 2 tests to release allows the minimum isolation period to be substantially reduced with almost no increase in risk of onward transmission. Furthermore, with these parameter values, using just one test to release is now closer to the effectiveness of using two tests, when compared to the 75% sensitivity results in Figure 3.

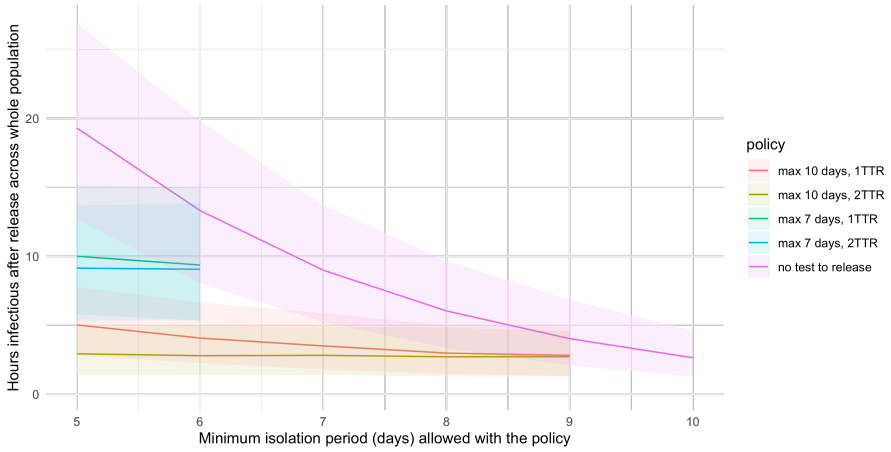

Figure 9. Average hours infectious in the community after release across all confirmed cases for different policy choices, with a **shorter** infectious period, but assuming 95% test sensitivity during the infectious period.