Covid-19 Modelling Aotearoa

Estimates of the effect and impact of different case isolation policies

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This memo was provided to the NZ Ministry of Health on **May 3rd, 2023** in response to a request for advice on April 21st, 2023. Here we present updated estimates of the effects of specific case isolation policies of interest: case isolation of 7 days with no test-to-release (current policy); case isolation of 5 days with no test-to-release; and case isolation of 5 days minimum with test-to-release, and either a 7 or 10 day maximum. Using these estimates we then calculate estimates of the impact on community transmission due to changing case isolation policies, and perform some sensitivity analyses on key unknown and uncertain parameters. This report should be read in conjunction with its partner report from CMA [1].

This version was finalised and published online on **August 16th 2023**, after minor edits following internal peer review. In this process a small coding error was identified - this did not change the findings, but some of the numbers in the tables have changed a small amount from the May 3rd version.

Key points from this report

- This report builds on previous work [2,3] to estimate both the individual level impact and the consequences for likely transmission increases/decreases for a range of case isolation scenarios, using updated parameter estimates from NZ case data [4] and recent scientific literature [7-15].
- The impact of the current isolation settings is difficult to estimate, but considering a range of assumptions produces estimates of between 10% to 25% reduction in transmission. This is broadly comparable with estimates from different modelling approaches used in previous analysis - e.g. [5].
- Changing from the current isolation settings to a policy with test-to-release (TTR) does not appreciably increase transmission and can offer a significant reduction in the burden of excess isolation, especially for asymptomatic cases or cases detected through periodic (e.g. workplace) testing.
- Reducing case isolation from 7 to 5 days, with no TTR, results in an increase in transmission, but much less than what would result from removing case isolation entirely.
- The relative changes in transmission calculated here can be used with models such as the CMA ODE model to estimate likely differences in the number of infections or hospitalisations following a change in isolation policy, e.g. [1, 5].

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Background

Case isolation is intended to reduce community transmission of infectious disease by reducing the number of interactions that infected individuals have during their infectious period. In particular, it aims to avoid interactions outside the dwelling after an infection is diagnosed. In order to estimate any differences in transmission for different isolation policies it is necessary to know both individual (time course of infection and isolation

period for a given diagnostic and isolation scenario) and population level parameters (estimated fraction of infections that are diagnosed/confirmed and which isolate).

The results presented in this memo use a simple model for transmission change (described in [1]) where differences in the number of hours infectious in the community for confirmed cases are used to estimate the relative impact of different case isolation policies on the effective reproduction number, *Rt*. These estimates can subsequently be used as an estimate of the change in growth rate in well-mixed contagion models such as the ODE model used by CMA [3,5].

The simple transmission change model described in [1] estimates the impact of changes in case isolation policies by calculating *r*, the relative change in the effective reproduction number due to isolation. Specifically, if *Rt* is the reproduction number without any isolation, then:

$$Rt^*=(1-r)Rt \qquad (1)$$

Where *Rt** is the reproduction number with the isolation policy. The quantity *r* is calculated using the equation:

$$r = p(1-q)[1-(T1+T2)/Ti] \qquad (2)$$

Where parameter definitions are given in **Table 1,** and the full derivation of this formula is given in [1]. In equation *(2)*, the term *p* is the proportion of all infections who test positive and follow the isolation policy, (*1-q*) is the fraction of onward infections that would happen outside the household if there was no isolation, and [*1-(T1+T2)/Ti*] is the proportion of the infectious period that is spent in isolation for the given isolation policy.

An important point to note is that we do not know *Rt* (what the instantaneous reproductive number would be if no one was isolating). However, using equation *(1)* we can calculate the relative change in growth rate due a change in isolation policies as:

$$Rt_{new}/\ Rt_{baseline} = (1-r_{new})/(1-r_{baseline}) \qquad (3)$$

where $Rt_{baseline}$ is the instantaneous transmission rate under the current (baseline) policy, e.g. 7 days isolation with no TTR, and Rt_{new} is what the transmission rate would change to under a 'new' isolation policy.

There are a number of simplifying assumptions made in this model (equations *(1)-(3)*) from [1], in particular the model assumes that:

- the degree of infectiousness is essentially constant throughout the infectious period;
- people are either 'isolating' or 'not isolating' and if they 'not isolating' they continue life as usual, with no change in their behaviour or contacts;

- the rate of non-household transmission events is constant through time, i.e. there are no saturation effects; and
- there is no change (increase or decrease) in the transmission rate within the household when someone is isolating.

Table 1: *Input parameters used in the relative transmission change model.*

p	The proportion of all infections who test positive and follow an isolation policy
q	The fraction of onward infections that would happen inside the household if there was no isolation
Ti	The mean total infectious period duration
T1	The mean period of time that a case is infectious for before testing positive and starting isolation
T2	The mean period of time that a case is still infectious after the end of their isolation

In this report we use NZ case data from MoH [4] alongside international literature (including [7-15]) to estimate metrics *Ti* and *T1*. We then use a stochastic simulation model for case isolation [1,2] to estimate *T2* (hours infectious after isolation) under different policy settings. Finally we use these values, in combination with plausible ranges for metrics *p* (fraction of infections that isolate) and *q* (ratio of onward infections inside vs outside the dwelling) to produce estimates of the relative change in *Rt** for changes in isolation policy. Because of the uncertainty in a number of these estimates and assumptions, we will also calculate how much the estimated change in *Rt** varies when these change.

A key assumption we will make in this work is that the only effect of an isolation policy is a change in *T2* - the mean period that a case is infectious for after their isolation period. That is, we will assume that there will be no change in the proportion of infections following the isolation guidance, or other behaviour such as how quickly cases would seek a test, test positive, or begin isolation.

It is extremely unlikely that a change in isolation policy would not result in a change in these other parameters however it is not possible to estimate in advance what the impact of a policy change might be on the magnitude or, for some parameters, even the direction of effect[1].

[1] For example, it can be argued that reducing isolation requirements could lead to an increase in the proportion of infected people isolating because the burden of isolation is lower. Alternatively, it can be argued that reducing isolation requirements will lead to a smaller proportion of people isolating because of a perception that isolation is less important.

Estimating input parameters

In the absence of an infection prevalence survey, or a representative longitudinal behavioural survey, the first two parameters in **Table 1** above are very difficult to estimate. In this work estimate plausible ranges and use these to give upper and lower bounds on our 'impact on transmission' estimates and treat them as scenarios.

We can use estimates of the case ascertainment rate (*p*) from the CMA ODE Model[6] to give guidance for plausible estimates for the proportion of infections that become confirmed cases and follow an isolation policy. NZ case data, combined with simulations using the CMA Network Contagion Model can be used to estimate plausible bounds for the fraction of infections that occur within the dwelling vs other interaction contexts (*q*). Details for these estimates are given in the Appendix section: Estimates for community spread and infections isolating.

The period of time that cases are infectious in the community after isolation *(T2)* can be informed by previous reports from CMA e.g. [3]. However, estimates for the infectious period duration *(Ti)* and the period infectious in the community prior to isolation *(T1)* cannot be taken from this previous work because it made the simplifying assumption that the time of symptom onset is aligned with the beginning of the infectious period and that people began isolation on the day of symptom onset. The main impact this has is on the estimate of *T1*, but this assumption will also have an impact on the hours infectious in the community after isolation *(T2)* and potentially the overall infectious period *(Ti)*.

In this work we have used NZ case data and international literature to update our estimates for key disease progression and testing related parameters. There are a large number of uncertainties in the literature estimates but the NZ case data allows us to tighten the bounds on what combinations are possible. Details for these estimates are given in the Appendix section: Estimates for disease progression and testing parameters.

Combining these distributions produces estimates of *Ti* and *T1* to use in equation *(2),* and allows us to produce a new estimate for the time from t=0 to becoming infectious. Using our new estimate of the time from t=0 to becoming infectious, we re-run the stochastic simulations of case isolation [2]. All other parameters and simulation settings as as in [3], with the 'shorter' infectious period, and the 'higher RAT sensitivity' distribution parameters[2]. This produces a new estimate for *T2*.

[2] We choose to use the 'higher sensitivity RATs' estimate from [3], because what we are estimating here is the RAT sensitivity in those who have already tested positive. If one wanted to estimate the impact of lack of compliance with a TTR policy, then it would be best to explicitly calculate the combined impact, rather than using RAT sensitivity as a proxy for compliance. For example, you would estimate the proportion who would follow TTR, *p1*, combined with the *T2* for the TTR policy, to calculate the reduction *r1* due to that, and the proportion who would just isolate

Individual level risk results

We have produced updated estimates of the individual case consequences of different isolation policies. These simulations use the stochastic simulation method and code found at [2]. All parameters are the same as in the previous report[3] except for the updated estimates for time of becoming infectious relative to *t=0* (reference time on 'Day 0', the day of symptom onset). Additionally, the simulations have been adjusted to use the 'reference time' of 8am rather than 12 noon each day. The results are shown in **Table 2**. Although these results only apply for symptomatic cases who can 'backdate' their Day 0, data from NZ Ministry of Health [4] indicates that this is around 97% of all reported cases.

Table 2: *Estimated individual level impacts of different case isolation policies. Results are the mean and 95% intervals for the four different isolation policies.*

	Proportion still infectious across all cases	Hours infectious after release across all cases	Hours infectious after release for those released while still infectious	Hours excess isolation across all cases
7 days no TTR	19% [14%, 26%]	12 hrs [7.4, 19]	62 hrs [54, 71]	69 hrs [59, 80]
5 days no TTR	38% [30%, 45%]	25 hrs [18, 34]	67 hrs [58, 76]	35 hrs [29, 41]
5 min 7 max 1TTR	23% [16%, 29%]	13 hrs [8.2, 20]	58 hrs [50, 67]	44 hrs [38, 51]
5 min 10 max 1TTR	14% [9.4%, 18%]	6.7 hrs [3.9, 10]	49 hrs [41, 57]	50 hrs [45, 56]

Here we see that adding test-to-release (TTR) to an isolation policy can appreciably reduce the number of hours of excess isolation. Depending on the maximum isolation period associated with a TTR policy, the number of hours infectious in the community after isolation would increase by only a small amount or would even decrease (e.g. for min 5, max 10 days isolation with TTR). Whereas reducing the isolation period to 5 days without using a TTR policy would almost double the number released while still infectious and double the number of hours infectious in the community after release.

We find that the adjustments made to the start of the infectious period and the shift to 8am as the time of 'release' has shifted the estimates for the proportion released while still infectious to somewhere between the 'shorter' and 'longer' infectious period estimates from earlier work[1] (see also **Table A1**). This is as expected, as the 'shorter'

for 5 days and not test, *p2*, combined with the *T2* for 5 days no TTR, to calculate the reduction *r2* due to those people. And finally calculate *r=r1+r2*.

and 'longer' estimates in the earlier work were intended to capture some of the uncertainty in the time of becoming infectious relative to symptom onset (Day 0). See Discussion of earlier work and why we can't use the numbers from the earlier report directly for further details.

Changing the definition of 'Day Zero' for the isolation period

We were also asked to estimate the effect of changing the timing of 'Day 0' for the 'isolation clock' from the current policy of 'Day 0 = first day of symptoms' to a policy of 'Day 0 = day of first positive test'. Again, these estimates apply to the 97% of cases to date that reported symptoms in NZ MoH data. Based on international literature and NZ case data, starting isolation on the day of the first positive test would mean that a case's 'isolation clock' starts, on average, ~1.7 days later. However, estimating the impact of this is not as simple as just taking 1.7 days off the isolation period because those who test positive later are more likely to be those who also became infectious later, relative to symptom onset.

We cannot currently implement a change in the definition of the 'isolation clock' in the stochastic simulation code[2], which means that we cannot produce estimates of policy change impacts using this approach. However, for the policies with no test-to-release, we can simply sample from the distributions in Estimates for disease progression and testing parameters to estimate the proportion still infectious at release. This produces the estimate of the proportion of cases still infectious (at 8am) after a 5 or 7 day isolation period to be 22% (c.f. 38%) or 11% (c.f. 19%), respectively.

The proportion of cases still infectious at the end of the isolation period is substantially reduced when switching from the 'Day 0' starting at first symptoms to first positive test because of the later start time for the isolation period. This would have the consequence of producing more time spent in isolation, and longer 'excess isolation' if used without a test-to-release option.

An important caveat is that it is possible that the current policy incentivises cases to report symptoms before their first positive test so as to shorten their effective isolation period. Changing to 'Day 0 = day of first positive test' may incentivise earlier testing but also reduce symptom reporting. Without more controlled cohort studies, or more detailed follow up with a subset of reported cases, we would not know how change was affecting biases in the case data.

Estimates for asymptomatic cases

We were also asked to consider the impact of case isolation on asymptomatic cases. Data from NZ MoH suggests that under 3% of reported cases are asymptomatic. See Appendix section Asymptomatic proportion of cases for details. Without symptoms to initiate test seeking, asymptomatic cases will typically be detected later in their infectious

period, likely as a consequence of being a contact of a confirmed case or through periodic testing (e.g. workplace testing), and thus will, on average, stop being infectious earlier in the isolation period than symptomatic cases.

Here we split the analysis into consideration of those who are testing because they are household contacts, and those who are doing weekly surveillance testing e.g. for workforce testing.

Asymptomatic household cases: If household contacts of a confirmed case test positive but are asymptomatic at the time of testing then 'Day 0' of their isolation period is the same as the date of their first positive test and the results above for 'Day 0 = day of first positive test' would be a reasonable approximation. This corresponds to 22% and 11% of cases being still infectious at the end of isolation for a 5 and 7 day isolation period respectively.

Asymptomatic cases discovered through regular testing: Running a simple sampling approach to approximate random weekly testing (e.g. testing in the workplace), using the infectious period duration and RAT lag periods used in [3] and assuming 100% RAT sensitivity during the 'could test positive period', we find:

- 62% of infections are detected
- Cases are detected much further through their infectious period (mean of 3.7 days).
- Infections that are detected have a bias towards those that are infectious for longer (mean of 6.3 days infectious for detected infections)

Fitting a Weibull function to the time of positive test relative to becoming infectious we find that *Weibull[shape=1.91,scale=4.12]* is a reasonable fit. Using this for the t_iso_entry_dist for the stochastic simulations[2] we find that the proportion of asymptomatic cases still infectious at the end of a 5 day and 7 day isolation period are 9.8% and 4.5% respectively. These cases experience much longer durations of excess isolation, but the use of test-to-release can help to allow these asymptomatic cases who are recovered to leave isolation sooner. **Table 3** presents these estimates for the four different isolation policies. For these cases, far fewer are released while infectious (compared to cases discovered through symptomatic seeking or household contacts). However, it is important to note that those who are released while still infectious can still be infectious for a number of days due to the variability in infectious period and in the timing of the positive test during their infectious period.

Table 3: *Individual level impacts of different case isolation scenarios for asymptomatic cases discovered through regular or random testing (not linked to being a contact of a confirmed case). Such cases are typically detected later in their infectious period and hence experience longer periods of excess isolation, in the absence of TTR.*

	Proportion still infectious at release	Hours infectious after release across all cases	Hours infectious after release for those released while still infectious	Hours excess isolation across all cases
7 days no TTR	4.5% [2.5%, 7.1%]	2.6 hrs [1.2, 4.6]	57 hrs [50, 65]	165 hrs [151, 178]
5 days no TTR	9.8% [6.3%, 14%]	5.9 hrs [3.3, 9.5]	60 hrs [52, 68]	120 hrs [107, 132]
5 min 7 max 1TTR	5.6% [3.4%, 8.4%]	3.0 hrs [1.5, 5.0]	53 hrs [45, 60]	122 hrs [111, 133]
5 min 10 max 1TTR	3.3% [1.9%, 5.0%]	1.5 hrs [0.70, 2.5]	44 hrs [37, 51]	124 hrs [114, 135]

Likely impact of isolation policy changes on transmission

Effect of changing isolation policy from our current isolation policy (7 days no TTR)

We sample from the distributions for the time from symptom onset to start of the infectious period and the lag from infectiousness to testing positive on a RAT to estimate *T1* (29 hours); the mean of the infectious period duration distribution to estimate *Ti* (118 hours); and use the results for time infectious after release in **Table 2** to estimate *T2* for equation *(2)*.

We assume 20% and 50% for the lower and upper bounds on the proportion of transmission that happens within the household (*q*). We use a range of different estimates for the proportion of all *infections* testing positive and following the isolation policy (*p*). See Appendix section Estimates for community spread and infections isolating for details.

The resulting estimates for the change in transmission (Rt^*) are shown in **Table 4**. All estimates are relative to the status quo isolation policy, which is 7 days isolation, backdated to the day of first symptoms, and with no test-to-release.

***Table 4**: Estimates of the relative change in transmission (Rt*) compared to the current policy (7 days no TTR) for different proportions of infections being detected and following the policy, p.*

Isolation policy	Proportion of all infections testing positive and following the isolation policy (p) for q=[0.2,0.5]		
	Best guess p=0.33	Lower p=0.25	Higher p=0.4
5 days no TTR	2.1% (q=0.5) to 3.6% (q=0.2)	1.5% to 2.6%	2.6% to 4.5%
5 min 7 max 1TTR	0.19% (q=0.5) to 0.32% (q=0.2)	0.14% to 0.23%	0.23% to 0.40%
5 min 10 max 1TTR	-0.86% (q=0.5) to -1.5% (q=0.2)	-0.63% to -1.1%	-1.1% to -1.9%
No isolation	12% (q=0.5) to 21% (q=0.2)	8.9% to 15%	15% to 26%

Estimates of the impact of the current isolation policy (7 days no TTR) - sensitivity to behaviour and disease parameter assumptions.

In order to assess the sensitivity of the results above to a range of assumptions, and where parameter choices were uncertain, we calculated the impact of changing these assumptions. The main impact of these changes is to change the estimated baseline value for the estimated impact that the current isolation policy is having. Once estimates of the current policy are calculated, the subsequent relative changes in impact for different isolation policies (5 days no TTR, 5 min 7 max 1TTR, 5 min 10 max 1 TTR) are not substantially different from those in **Table 4**. However the estimate of the impact that case isolation is having at all, compared to no isolation, does change substantially.

Table 5 presents estimates which show how much our estimate for the effect that the current isolation policy (*7 days no TTR*) is having changes under a range of different assumptions about behaviour and uncertain parameters. When this number is larger than the 'best guess' then this means that the current case isolation behaviour is having a larger impact on reducing transmission, and vice-versa.

Table 5: *Estimates of the decrease in transmission due to the current policy compared to no isolation, for the current isolation policy (7 days, no TTR) under a range of alternative assumptions where parameter uncertainty exists.*

Alternative assumptions	Proportion of all infections testing positive and following the isolation policy (p) for q=[0.2,0.5]		
	Best guess p=0.33	Lower p=0.25	Higher p=0.4
Best guess for *T1, Ti*, and *T2*	11% to 17%	8.1% to 13%	13% to 21%
Isolating after symptoms, before testing positive	15% to 23%	11% to 18%	18% to 28%
Decreased infectiousness at beginning and end[3]	14% to 22%	10% to 17%	17% to 26%
Infectiousness begins at symptom onset[4]	9.6% to 15%	7.2% to 12%	12% to 19%
'Longer infectious period'[5]	11% to 18%	8.5% to 14%	14% to 22%

From these results we find that if symptomatic cases are isolating (at least partially) before testing positive, or if there is lower infectiousness at the beginning and end of the infectious period, then the current isolation behaviour is having a larger impact on reducing transmission than in the 'best guess' estimates. This means that the impact of removing or changing case isolation would result in greater transmission increases than those in **Table 4.** If the onset of infectiousness, on average, begins closer to symptom onset than we estimated, this would mean that isolation is missing slightly less of the infectious period, and the overall impact that case isolation is having is slightly less. However, this would be more than counteracted by the effect of the assumptions about isolating when symptomatic, and infectiousness being lower at the beginning and end. Finally, if we assume that there is a 'longer infectious period', we estimate that isolation is having a slightly larger impact on reducing transmission. This is somewhat counterintuitive because we know from earlier results [3] that a longer infectious period leads to more cases released while still infectious (and a larger *T2*). However, in order to be consistent with the data from studies which found that the end of the infectious

[3] We halve *T1* and *T2* but keep the value of *Ti* the same, to account for the beginning and end of the infectious period being less infectious than the middle of an individual's infectious period.
[4] Here *T1* increases to the 1.7 days in NZ case data, and *T2* decreases to the 8.9hrs in the earlier report [3].
[5] Using *T2* from the 'longer infectious period' results in [3], with *T1*=12hrs, and *Ti*=6.3 days.

period was later relative to symptom onset, and studies that measure the overall infectious period duration, we have estimated that the infectious period *(Ti)* would be increased, but also that the time infectious relative symptom onset would also need to be later, and thus *T1* is decreased. Our specific estimates then result in a decrease in the value of *(T1+T2)/Ti* in equation *(2)*. However, this is very dependent on the balance of disease parameters including symptom onset and test sensitivity relative to the infectious period, and the length and variability of the infectious period.

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Appendix

Discussion of earlier work and why we can't use the numbers from earlier reports directly

In earlier work [3] we produced estimates of the impact of different case isolation policies on individual case measures (**Table A1**) . In this report, we made the simplifying assumption that the isolation clock day 0 was the same as the 'start of the infectious period'[6]. Since we use 'day of symptom onset' as 'day 0' in Aotearoa NZ, the 'infectious period' measure we used in the previous work was technically the 'time of symptom onset to the end of infectiousness' rather than the 'start of the infectiousness to the end of infectiousness".

Table A1: Estimates from the earlier report [3] for the policies of 5 or 7 days isolation, with no test-to-release

	'Short' time from symptom onset to end of infectiousness		**'Long'** time from symptom onset to end of infectiousness	
Isolation period, no TTR	**5 days**	**7 days**	**5 days**	**7 days**
Percent of cases infectious at release	30% [22%, 37%]	15% [9.7%, 20%]	62% [55%, 69%]	41% [33%, 50%]
Average hours infectious post-release	19 hrs [12, 27]	8.9 hrs [5.1, 14]	62 hrs [47, 77]	37 hrs [25, 50]
Average hours infectious post-release for those who are infectious at release	64 hrs [56, 73]	60 hrs [52, 68]	98 hrs [85, 112]	88 hrs [76, 101]
Average hours excess isolation	45 hrs [38, 53]	83 hrs [73, 94]	17 hrs [13, 22]	41 hrs [32, 49]

Although there is reasonable evidence that the mean infectious period is ~5 days [7], there is some evidence that the time from symptom onset to the end of the infectious period could be longer - up to 8 days [8], because symptom onset is not the same as the start of the infectious period.

[6] Technically, we assumed that the difference between noon on the day of symptom onset and the onset of infectiousness was normally distributed with a mean of 0 and a small standard deviation

In earlier work we accounted for this by presenting results for two different 'infectious period' durations[7] to give upper and lower limits on the estimates for the different case isolation policies. Results are shown in **Table A1**. However, in the current report, a crucial parameter that affects the impact on overall transmission is the time someone is infectious for before testing positive and starting their isolation. Because there is some evidence [9,10] that the mean onset of infectiousness is after symptom onset, we cannot just use the time of testing positive relative to symptom onset from NZ case data [4].

Additionally, we know that there will be a strong correlation between the timing of testing positive and the timing of becoming infectious, as RATs detect infectious virus. This means that those who test positive early, are most likely to have become infectious early, and conversely, those who test positive later are more likely to have become infectious later.

Finally, another caveat in the previous modelling was that it estimated the proportion infectious at noon on the day of release. Although this would align well with literature (where the daily testing would be spread throughout the day depending on experimental procedures) it is less likely to be applicable to people going to work/school on the 'day of release' from isolation. Because of this, in this report we update the parameter estimates to use 8am as the time of testing (or release from isolation) in the stochastic simulations [2].

NZ case data details

Since March 2022, in NZ the first time a person reports a positive RAT result (in a 30 day period), they are sent a follow up text message within the next 24hrs with a link to fill in a survey. This survey asks a number of questions including whether they have symptoms and if so, when they began. It also asks about their household contacts. For some people there is also follow up via phone call or other means to attempt to fill in this data, but the majority come from the automated survey

Asymptomatic proportion of cases

Data we have from NITC between 25th Feb 2022 and 4th Sep 2022:

- For known 'first cases in a household' (827,521 cases) the data shows that 99.9% responded to either the survey or a follow up phone call, and of all cases, 97.8% have a symptom onset date recorded and 2.1% had no symptoms - at least by the time of the survey or phone call.
- For all cases (1,697,759 cases), 76% (1,293,192) have responded to the survey or a phone call, and of that subset, 97% have a symptom onset date recorded

[7] A 'Short' period with a mean of ~5 days and a 'Long' period with a mean of ~8 days

(1,255,175) and 2.9% (38,017) did not have symptoms by the time of filling out the survey.

- Taking the *complement* of the 'first case' dataset, we find that for the 51% of cases (870,238) which are not known to be a 'first case in the household', we have symptom presence/absence data for 51% (448,146) of them. And of these, 4.6% (20,492) had responded and had no symptoms.

This suggests that, for that time period (when there were household contact quarantine restrictions, more workplace testing, and stronger pre-event testing guidelines) around 3% of cases were asymptomatic, or developed symptoms more than a day or so after testing positive (depending on how long it took to fill out the survey, we don't have that information).

By looking at the split between 'first cases' and 'not first cases' we see evidence that the slight majority of asymptomatic cases were found due to testing in household contacts (4.6% of non-first cases who filled out the survey). However 2% of 'first cases in a household' were asymptomatic, which suggests that there was still a reasonable amount of asymptomatic testing going on e.g. workplace testing, testing due to close (non-household) contacts testing positive, and testing before high-risk events or visiting vulnerable individuals.

We do not have data for the proportion of cases that filled out the survey who were asymptomatic for the more recent time periods, but due to the reduced emphasis on testing and removal of household contact quarantine, it is likely to be lower than during the Feb to Sept period last year.

How quickly do people test positive and start isolation

We have data for when people tested positive relative to their symptom onset. For the most recent period (September 2022 to February 2023), shown in **Figure A1**, the median of 1 day after symptom onset, and a mean of ~1.7 days. This mean > median is expected from the 'long tailed' shape of the distribution and is partly driven by some very long delays (over 10 days after symptom onset) in reported case data.

For the period February 2022 to September 2022, we found that for all cases the time until the first positive test was slightly longer; they tested positive a mean of 1.9 days after symptom onset. For this time period, we also have information about which cases were 'first cases' in the household, and we compared the timing of testing positive for 'first cases' to 'not first cases' in **Figure A2**. We see that more 'not first cases' are being detected sooner than 'first cases' which supports our assumption that 'not first cases' are household contacts who have increased testing rates compared to the general population. Comparing the mean time for these two plots produces a higher mean for 'Not first' cases (1.9 days c.f. 1.8days) but this is driven by the large number of cases with

symptom onset more than 14 days prior to a test result. This 'effect' disappears in more recent data (**Figure A1**) and is likely related to teething issues with the introduction of RATs and the PCR delays in February and March 2022.

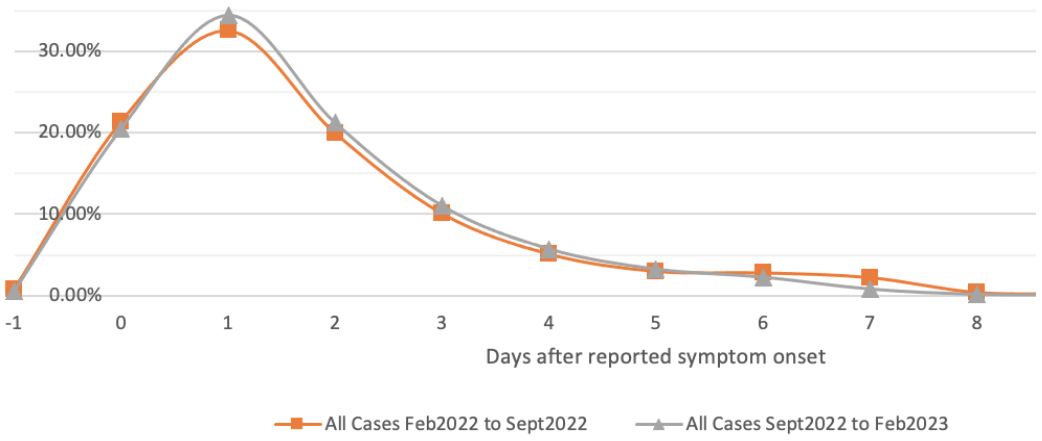

Figure A1: *Day of first positive test relative to symptom onset for all reported cases comparing the period [Feb 2022 - Sep 2022] (orange) to the period [Sep 2022 - Feb 2023] (grey).*

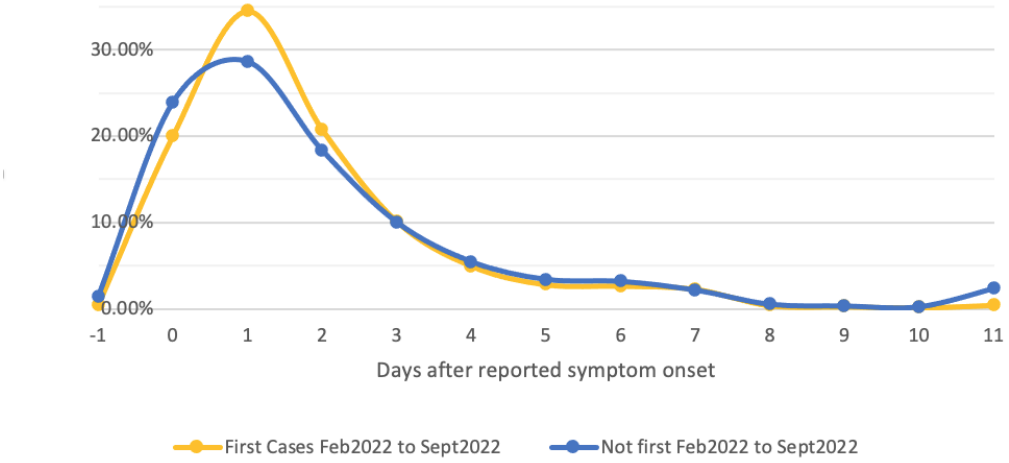

Figure A2: *Day of first positive test relative to symptom onset for reported cases between Feb 2022 - Sep 2022, split by whether they are 'first case in a household' (yellow) or 'not the first case in a household'.*

Estimates for community spread and infections isolating

Proportion of infections that would occur within the household (q)

From NZ case data [4] in the period between 25th February 2022 and 4th September 2022, 49% of reported cases were defined as 'first case in household'. In the remaining 51%, 51% (~25% of all cases) responding to the survey and so we know they are not 'first cases', and 49% (~24% of all cases) didn't respond to the survey so we don't know if they were 'first cases' or household contacts. This suggests that, for the February 2022 to

September 2022 period, around 25-50% of transmission occurred within the household (and 50-75% occurred in the community).

If household contacts who tested positive were less likely to report their test results - as they were already isolating, and in contact with health services due to the first case in their household - the data would be biased towards overestimating community transmission. However, we also know that in that period in 2022 there was much less spread in the community relative to households, with higher case reporting and case isolation, household contact quarantine rules, and more community transmission reduction measures in place (e.g. masking and ventilation). This means that the amount of spread within the household (vs in the community) in a completely uncontrolled scenario would be lower than the above data estimates.

From CMA Network Contagion Model simulations of a scenario with no prior immunity, and where there are good testing rates, case isolation and household quarantine requirements, and strong transmission reduction measures in the community, we find that around half of infections occur within the household. This acts as a sense check of the NZ case data, and as an upper estimate, as the transmission reduction measures simulated all act to reduce spread in the community. **For the calculations in this report, we use 20-50% as the plausible range for *q*[8].**

Proportion of infections that would test positive and follow isolation policy (*p*)

In the absence of any kind of empirical estimates of infection numbers, the case ascertainment rate (CAR) is highly uncertain. Our best estimate is that CAR is 35%, based on ODE model estimates from fitting to reported cases, hospital admissions, and estimated IHR. This is consistent with ESR wastewater estimates. Peak was ~45% in March last year, with lower ascertainment now driven mainly by lower testing/reporting in younger age groups. If some confirmed cases don't report their result but still isolate, then this estimate should be higher for the Rt estimate calculation, but if some cases that report don't strictly isolate, then this estimate should be lower for the Rt* estimate calculation. **We use 33% as a 'best guess', and 25% and 40% as lower and higher estimates for *p*[9].**

[8] The ODE team in report [4] have used q=30% and q=60% as their plausible estimate for q with the stated aim to be on the conservative side (produce a higher increase in Rt* estimate).

[9] The ODE team in report [4] have used p=33% and p=50% with the stated aim to be on the conservative side (produce a higher increase in Rt* estimate).

Estimates for disease progression and testing parameters

Summary

Following a review of international literature we have produced a set of estimates for the necessary parameter distributions, that are 1) consistent with the international literature and 2) consistent with NZ case data[4]. Our estimates are:

- Cases become infectious, on average, 0.5 days after symptom onset but with 25% of cases becoming infectious before symptom onset.
  t_infectious_from_symptom_onset=*Normal[mean=0.5, 0.7]*.
- Cases are infectious for a mean duration of 4.9 days
  t_infectious_duration=*Gamma[shape=2.62, scale=1.88]*.
- Lag in RATs returning an initial positive result with an average of 1 day relative to onset of infectiousness
  t_positive_from_infectious=*Gamma[shape=1.25, scale=0.8]*
- Lag in RATs returning a negative result of an average of 1.2 days after the resolution of infectiousness
  t_negative_from_not_infectious=*Normal[mean=1.1, 1.36]*.

For checking against literature and NZ case data, when we combine these distributions they produce the following results:

- The earliest cases could test positive on a RAT is a mean of 1.4 days after symptom onset.
- Cases stop being infectious, on average, 5.6 days after symptom onset[10].
- Cases would start testing negative on a RAT, on average, 7.2 days after symptom onset.

Compared to international case data for the end of RAT positivity and the end of the infectious period based on viral culture, relative to symptom onset, these are reasonable estimates [7-15]. If anything, the infectious duration estimates are on the shorter side, but because our stochastic model does not include consideration of the decrease in infectiousness near the end of the infectious period, we have chosen to bias our estimates to shorter infectious period duration to partially compensate for that.

Looking at NZ case data from Sept 2022 to Feb 2023 (details in section NZ case data details), reported cases test positive on average 1.7 days after symptom onset. This implies that, given the estimates above for first testing positive on a RAT, accounting for any lag in returning an initial positive RAT results, cases in NZ must be testing positive quite quickly. We use an exponential distribution for the time from when someone could test positive until they would, and find that an average delay in test taking of 6 hours matches the mean and median of the NZ case data best, but that the distributions are slightly different. See section t_first_positive_test for more details and discussion.

[10] This is longer than in earlier work[1] because of the change in the start of the infectious period relative to symptom onset (Day 0).

Our comparisons to international literature and to NZ case data allow us to conclude that the estimates we have developed are plausible and consistent with the available data. However, if there was evidence for a longer delay in test seeking in NZ, then the estimates for the lag for RATs after the beginning of the infectious period or the estimate for the time of becoming infectious relative to symptom onset (or both) would need to be adjusted to be slightly shorter.

Estimating *T1*

From the estimated distributions, and some assumptions about test seeking delay, we can produce an estimate of *T1* (the time infectious before starting to isolate). The section t_first_positive_test describes in more detail how we have generated a distribution of when people test positive relative to symptom onset. We cannot use the NZ case data directly because we need an estimate of when each case became infectious and this is not independent of when they would test positive.

Using the estimates for **t_infectious** and **t_first_positive_test** that we developed in t_first_positive_test we can calculate when people test positive relative to becoming infectious:

T1 (if isolating after positive test) = t_first_positive_test - t_infectious

Where '-' or '+' indicates the linear combination (convolution) of independent distributions. This produces a distribution with a mean of 29 hours that people are infectious for before testing positive.

We can also estimate what *T1* would be if people isolated from when they first developed symptoms, instead of just when they first tested positive. To do this we calculate the time infectious before symptom onset:

T1 (if isolating from first symptoms) = t_symptoms - t_infectious

This produces a distribution with a mean of only 2.3 hours infectious before isolation, which shows how much benefit there is if people can stay home when sick.

Estimating *Ti*

For *Ti* we use the mean of **t_infectious_duration** which is 118 hours.

Estimating *T2*

In order to calculate *T2* we use the stochastic simulation package [2]. We use all the same parameters as in the previous report[1], except for **t_iso_entry_dist** (the distribution of the time between the *t=0*[11] and the start of the infectious period for each case). In

[11] Note: *t=0* is explicitly defined as the reference time (in this case we assume 8am) on the day of symptom onset, as that is the day that the isolation clock begins (Day 0) in New Zealand.

order to calculate this we first assume that symptom onset is uniformly distributed throughout the day, and define t=0 as 8am on the day of symptom onset:

$$t\_symptom\_onset = Uniform[-0.3333, 0.6667]$$

We can then calculate the time of becoming infectious relative to t=0 using:

$$t\_iso\_entry = t\_symptom\_onset + t\_infectious\_from\_symptom\_onset$$

Where '+' indicates the linear combination (convolution) of independent distributions. We then fit a normal distribution to the resulting t_iso_entry distribution and find the best fit to be a normal distribution with parameters:

$$t\_iso\_entry\_dist = Normal[mean = 0.67,\ sd = 0.76]$$

This distribution is then used in stochastic simulations[2] and the results from these are used to estimate *T2* for different isolation policies.

Details for fitting specific distribution estimates

t_infectious_from_symptom_onset

Although the day of symptom onset is often recorded, especially relative to the time when viral culture stopped being positive (end of infectious period), we found that symptom onset relative to the start of the infectious period is not often directly measured. This is because it would require testing in advance of a positive test result.

In Hay et al [10] who looked at the delays from detection (via PCR) to symptom onset in an NBA cohort with regular PCR testing. For those with frequent testing (early detection) they found there was a distribution in the delay from PCR positive to symptom onset that was vaguely 'Normal' looking, with median ~ 1 day, mean ~0.8 days (Appendix 1 - Figure 5 [10]). However, we know from other literature that PCR tests are often positive before the start of the infectious period (as measured by viral culture) by about a day [9,12], so the actual time of infectiousness relative to symptom onset may be closer to zero. The shape of the distribution for this data gave us confidence that for some people it would be before and some after, and that using a Normal distribution for the time someone would become infectious relative to symptom onset was reasonable.

The only estimates we could find which directly compared viral culture becoming positive with the day of symptom onset was Hakki et al. [9]. They found that only ~20% of cases were shedding infectious virus when swabbed on the day of symptom onset, despite 50% being PCR (viral RNA) positive on the day of symptom onset. In order to estimate the distribution we needed to account for the fact that in the experiment, symptom onset could be anytime throughout a day, and swabbing for viral culture only occurred once each day. In order to compare to the data we assume that t=0 is noon on the day of symptom onset, and that symptom onset could have occurred anytime during that day:

$$t\_symptom\_onset = Uniform[-0.5, 0.5]$$

$$day\_symptom\_onset = 0$$

We then assume that there is some (unobserved) time that someone becomes infectious relative to symptom onset to calculate:

$$t\_infectious\_start = t\_symptom\_onset + t\_infectious\_from\_symptom\_onset$$

Where '+' indicates the linear combination (convolution) of independent distributions. Based on [10] the shape of the time from symptom onset to PCR positivity was normally distributed, so we make the assumption that:

$$t\_infectious\_from\_symptom\_onset = Normal[mean, sd]$$

Finally, in order Hakki et al. [9] they only 'observe' whether someone is infectious or not once a day. We assume that this observation time is also at noon for convenience, and thus each individual we can calculate the day that the viral culture test would first be positive:

$$day\_first\_positive\_viral\_culture = ceiling(t\_infectious\_from\_symptom\_onset)$$

We found the best fit to the data in [9] using the distribution $Normal[mean=0.5, sd=0.7]$ for the time from symptom onset to infectiousness onset. This gives us the result that about 23% would be infectious according to viral culture at midday on the day of symptom onset, and 75% by noon the day after symptom onset.

t_positive_from_infectious and t_negative_from_not_infectious

t_positive_from_infectious is fit to literature from a challenge study [11] and a study with a cohort doing daily testing[9], where they had both RAT and viral culture results. There are many distributions that could match the observed data for t_positive_from_infectious but for this work we assume that the small number of positive RAT results before viral culture is positive (~5%) are false negatives on the viral culture. With t_positive_from_infectious>=0 we find that a Gamma distribution with a mean of 1 day is the best fit (shape=1.25, scale=0.8), but there is considerable uncertainty in this estimate. A plot showing how our estimates compare to literature is shown in **Figure A3**.

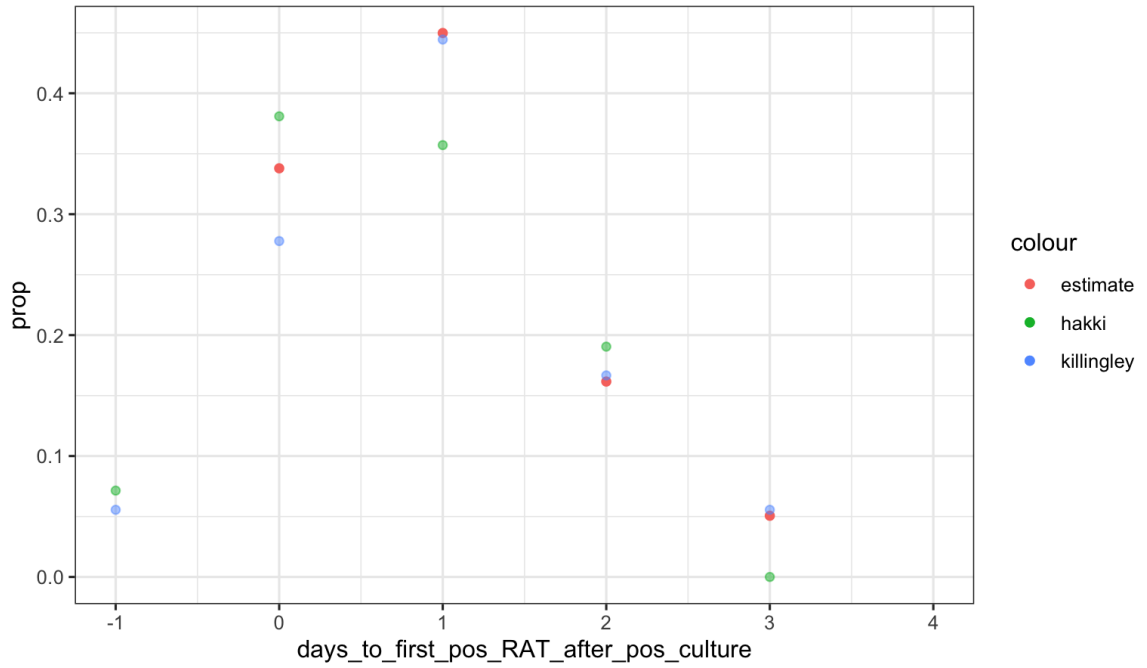

Figure A3: *Day of first positive RAT result relative to first positive viral culture in Hakki et al. [9], Killingley et al. [11], and the estimate produced from our selected distributions.*

t_negative_from_not_infectious is fit to literature from the challenge study [11]. Here we allow for a RAT to turn negative before the end of the infectious period, and fit to a Normal distribution. The best fit for this is ***Normal[mean=1.1, sd=1.36]***[12].

These are the same distributions used in the previous report[3].

t_infectious_duration

Literature that measured infectiousness (viral culture) and included distributions that used 'time of symptom onset' as t=0 produced estimates of the proportion still infectious on day 7 of 20-50%, and the median times from symptom onset to last positive viral cultures ranging between 4 and 9 days [7-9,12-15].

Recent meta-analyses find duration of viral shedding (infectiousness) just over 5 days[7,14]. This is consistent with the infectious duration estimates from the earlier report [3]. Combining this with the above estimate for t_infectious_from_symptom_onset, produces the distribution from symptom onset to the end of infectiousness given by the convolution:

t_infectious_from_symptom_onset + t_infectious_duration

Which produces a distribution where cases stop being infectious, on average, 5.6 days after symptom onset, 27% are still infectious at noon on day 7. This is consistent with the

[12] Technically the best fit was ***Normal[mean=1.09, sd=1.29]*** but we use the values in the main text to match those used in the previous report [3].

data in the literature for the proportion still infectious [7-9,12-15]. Combining this with t_negative_from_not_infectious gives the estimate that cases would start testing negative on a RAT, on average, 7.2 days after symptom onset. With 41% still testing positive on a RAT at noon on day 7. Although this is in line with some literature, we note that there is considerable variability in this measure. In particular, some studies have found that the proportion still testing positive on a RAT on day 7 is closer to 70-80% [15], even though they are not positive on viral culture. If this was the case the distribution for t_negative_from_not_infectious may be an underestimate. We would need data from a test-to-release policy or similar to determine whether these values are reasonable for the NZ (and Omicron) context.

t_first_positive_test

For this we set noon on the day of symptom onset as t=0.

First we assume that someone develops symptoms at anytime on Day 0 using a uniform distribution

$$t\_symptoms = Uniform[-0.5,0.5]$$

Then we use t_infectious_from_symptom_onset and t_positive_from_infectious to determine the time (relative to noon on Day 0) that someone would first be able to test positive:

$$t\_infectious = t\_symptoms + t\_infectious\_from\_symptom\_onset$$

$$t\_positive = t\_infectious + t\_positive\_from\_infectious$$

We then estimate when someone would first test positive by considering that they would only test if they had symptoms, and that there would be some (exponentially distributed) delay after being able to test positive:

$$t\_first\_positive\_test = max(t\_symptoms, t\_positive) + Exp(test\_seeking\_delay)$$

Where we adjust test_seeking_delay until we match the median and mean of the NZ case data. We then filter out any test times that are impossible by removing any individuals who would have stopped being infectious and not be testing positive anymore

$$t\_first\_positive\_test > t\_negative$$

where

$$t\_negative = t\_infectious + t\_infectious\_duration + t\_negative\_from\_not\_infectious$$

This removes about 5% of individuals. We then translate these into daily counts:

$$day\_first\_positive\_test = round(t\_first\_positive\_test)$$

This requires test_seeking_delay=4 which is a mean delay of 6hrs. This produces a distribution of a mean of 1.7 days and a median day of testing positive of 2 days after symptom onset. Although the mean and medians match NZ case data, comparing the distributions through time, in **Figure A4** we see that there are some discrepancies.

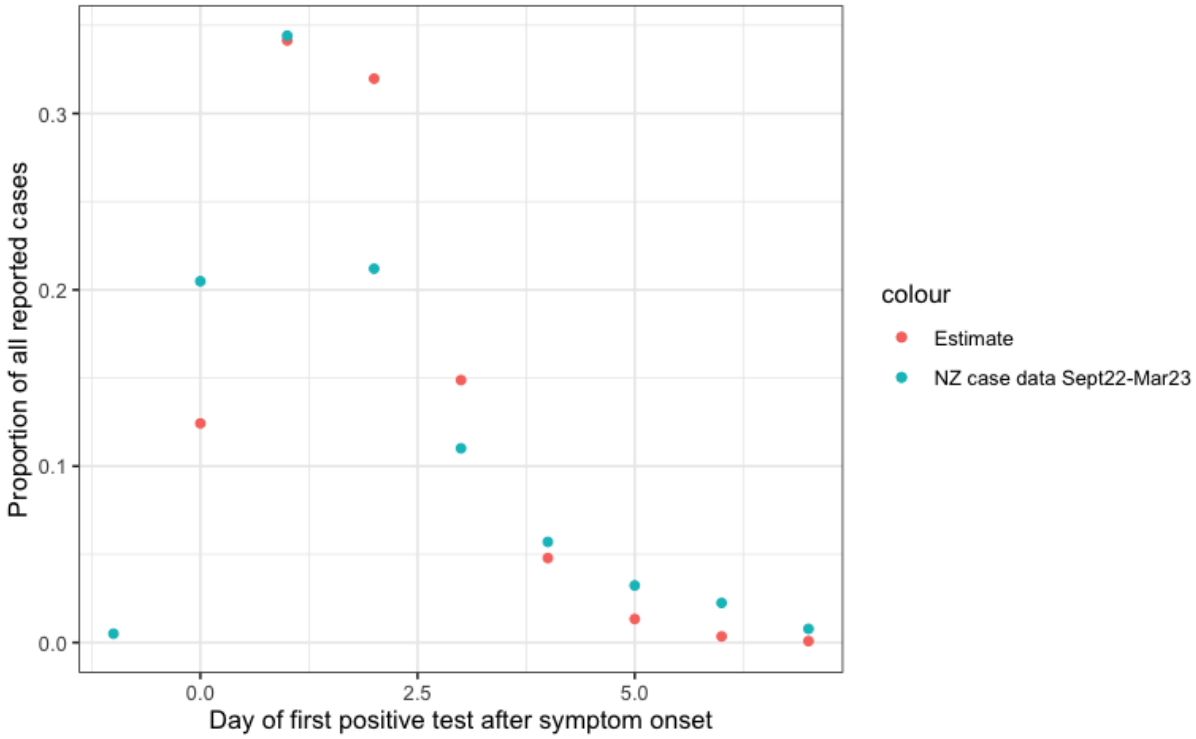

Figure A4: *Proportion of cases testing positive for the first time for each number of days after the day of first reported symptoms. Plotted for NZ case data, and for the distributions selected for this report. The means and medians match, but the real case data is more peaked around Day 1 and has a longer tail (more in Days 5+).*

In particular, this approximation underestimates the number that test positive on Day 0 and overestimates Day 2 and 3. It also doesn't capture the longer tail seen in the NZ case data. This is partly a consequence of the simplifying assumption of an exponential distribution in test delay from the latter of symptom onset and time able to test positive. It doesn't capture the behavioural factors around repeated tests for those who test negative on the first test they take after symptom onset, which are likely to occur periodically (daily?) after symptom onset, rather than some period after the unobservable 't_positive'.