A preliminary assessment of the potential impact of the Omicron variant of SARS-CoV-2 in Aotearoa New Zealand

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Executive summary

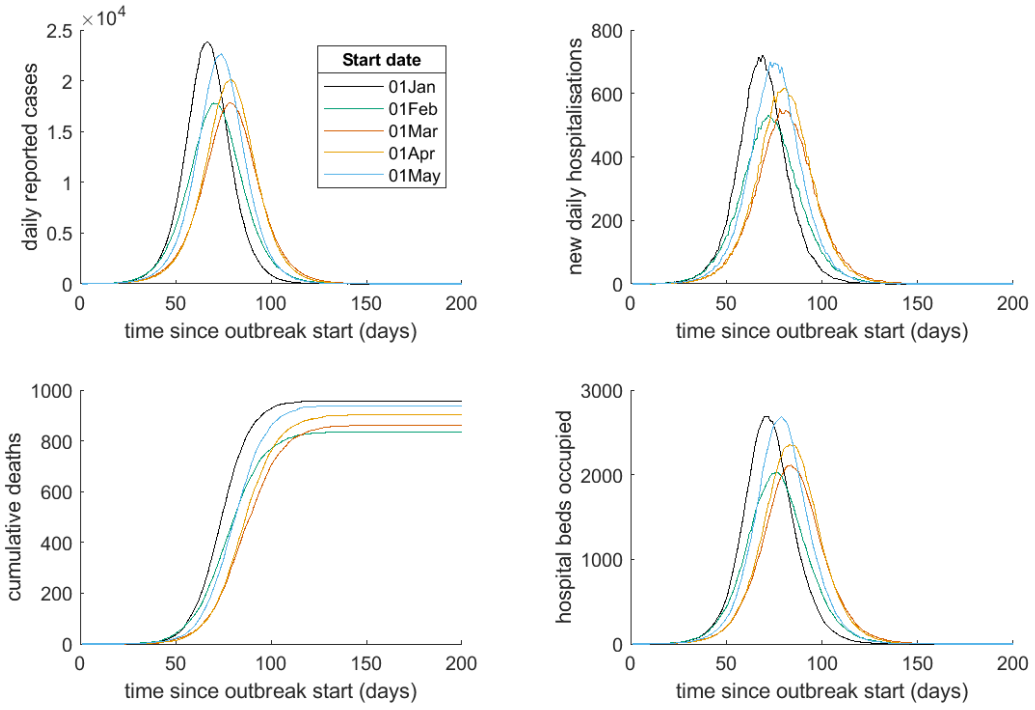
1. The results in this report are a preliminary assessment of the potential impact of Omicron in New Zealand and are subject to significant uncertainty. **This modelling was carried out before the detection of the Omicron outbreak on 23 January 2022.** Modelling will need to be updated once sufficient local data is available.
2. For an outbreak starting around 1 February, in scenarios where there is high booster uptake, peak hospital admissions range from 200 to 800 per day, and peak demand for hospital beds ranges from 800 to 3,300 depending on assumed transmission rates.
3. These numbers would put significant strain on hospital capacity. Thus, under these scenarios, public health measures may be necessary to flatten the curve and avoid overwhelming the healthcare system.
4. Due to the effects of waning immunity and the ongoing booster rollout, different groups will have different levels of risk at different times. Groups that are not yet eligible for the booster will be at elevated risk of severe illness.
5. In general, lower booster uptake leads to worse outcomes. Slowing an outbreak to allow time for more people to receive their booster doses is a strategy that could reduce the overall health burden.
6. However, the waning of immunity presents a danger that health outcomes in groups that were earliest to receive their booster become worse after a longer time period. Thus outbreaks that occur after significant waning of immunity can result in a higher overall health burden compared to outbreaks that occur during peak immunity. Maintaining high immunity levels across all groups will be important for future vaccination strategies.

Results

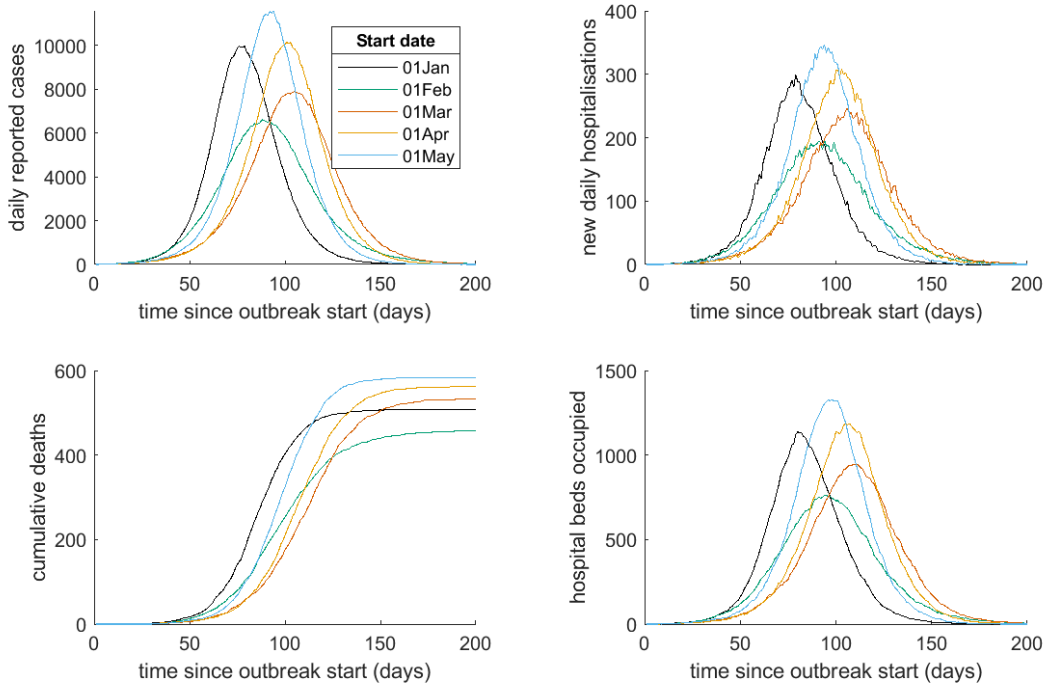
The results below show median simulated outbreaks starting on 1 January, 1 February, 1 March, 1 April or 1 May 2022 and assuming 90% booster uptake among those eligible. Results are shown for a baseline scenario and also under scenarios with lower/higher rates of transmission (see next page). The low, baseline and high scenarios are approximately consistent with outcomes from the Omicron wave to date in South Australia, London, and New York respectively.

Note the timing of the peak is relative to the first seed infections rather than the first detected cases, and is sensitive to stochasticity in the early stages of the outbreak (e.g. superspreading events). More reliable estimates of peak size and timing will require a period of data on community transmission of Omicron in New Zealand.

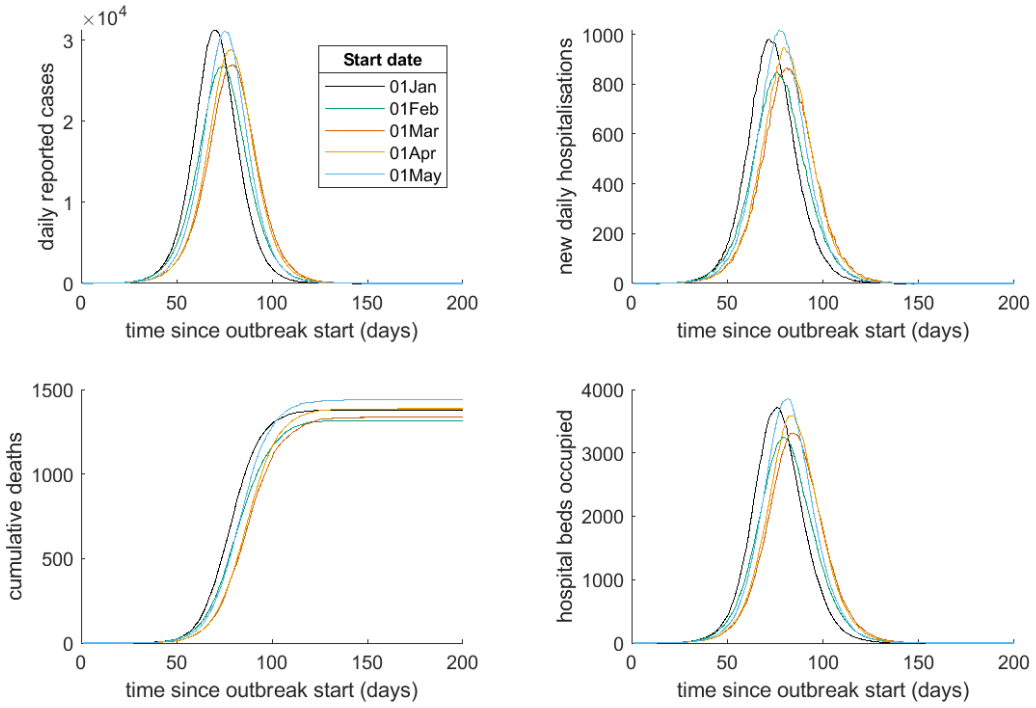
Baseline scenario (comparable with London)



Low transmission scenario (comparable with South Australia)



High transmission scenario (comparable with New York)



Note the different y-axis scales in different scenarios.

Results detail

start date	infections	cases	hosp	peakBeds	deaths	maxPrev10	maxAvgCas7	daysToPeakCases
LOW TRANSMISSION (S Australia) - 90% of eligible get boosted								
1Jan	1,611,000	413,800	12,200	1,100	510	8%	9,900	76
1Feb	1,500,000	386,400	11,500	800	460	5%	6,600	88
1Mar	1,676,000	432,800	13,200	1,000	530	6%	7,900	105
1Apr	1,818,000	470,100	14,300	1,200	560	8%	10,100	101
1May	1,902,000	491,700	15,000	1,400	590	9%	11,500	94
LOW TRANSMISSION (S Australia) - 70% of eligible get boosted								
1Jan	1,846,000	475,200	14,700	1,500	610	10%	12,500	76
1Feb	1,732,000	447,000	13,800	1,200	560	8%	9,800	80
1Mar	1,804,000	467,300	14,700	1,300	580	8%	10,100	89
1Apr	1,947,000	504,100	15,800	1,500	620	9%	12,000	91
1May	2,032,000	526,300	16,500	1,600	650	10%	13,500	84
MEDIUM TRANSMISSION (London) - 90% of eligible get boosted								
1Jan	2,660,000	681,700	21,400	2,700	960	19%	23,400	67
1Feb	2,439,000	626,000	19,300	2,100	840	14%	17,700	70
1Mar	2,474,000	637,900	20,200	2,100	850	14%	17,600	79
1Apr	2,609,000	673,900	21,600	2,400	900	16%	19,800	79
1May	2,729,000	705,000	22,600	2,700	940	18%	22,300	74
MEDIUM TRANSMISSION (London) - 70% of eligible get boosted								
1Jan	2,812,000	723,100	23,700	3,100	1,040	21%	25,700	66
1Feb	2,646,000	680,200	21,900	2,600	950	17%	21,300	67
1Mar	2,637,000	681,400	22,200	2,600	950	17%	21,000	74
1Apr	2,724,000	704,400	23,300	2,800	990	18%	22,400	72
1May	2,833,000	732,500	24,200	3,000	1,030	20%	24,600	70
HIGH TRANSMISSION (New York) - 90% of eligible get boosted								
1Jan	3,479,000	887,600	29,700	3,700	1,390	25%	30,800	70
1Feb	3,359,000	857,900	28,400	3,300	1,330	21%	26,500	74
1Mar	3,368,000	863,500	29,300	3,400	1,330	21%	26,600	79
1Apr	3,463,000	888,600	30,600	3,600	1,390	23%	28,400	79
1May	3,560,000	913,700	31,600	3,900	1,450	25%	30,600	75
HIGH TRANSMISSION (New York) - 70% of eligible get boosted								
1Jan	3,595,000	919,500	32,300	4,200	1,540	27%	33,000	69
1Feb	3,500,000	895,600	31,000	3,800	1,450	24%	29,800	71
1Mar	3,480,000	893,800	31,400	3,800	1,460	24%	29,500	74
1Apr	3,537,000	909,800	32,200	4,000	1,460	25%	30,600	73
1May	3,628,000	931,800	33,000	4,200	1,510	26%	32,600	72

Columns show: date first cases are seeded; total number of infections during the simulation; total number of reported cases during the simulation; total number of hospitalised cases during the simulations; peak number of hospital beds occupied; total number of deaths during the simulation; peak infection prevalence (number of new infections in a 10-day period); peak 7-day average daily reported cases, and number of days from the first infection to the peak number of daily cases.

International benchmarking

	Peak infection prevalence	**Peak daily cases per mil. (7d avg)**	**Peak hospital occupancy per mil.**	**% pop. fully vaxxed [boosted] 01/01/22**	**Stringency index 7/01/22**
Model 1 Feb outbreak: low R	5%	1,300	150		
Model 1 Feb outbreak: medium R	14%	3,500	400		
Model 1 Feb outbreak: high R	21%	5,200	640		
NSW		4,800	350	79% [15%]	
VIC		4,800	180	79% [14%]	
QLD		3,300	170	71% [14%]	
South Australia		2,200	170	75% [15%]	
London	9%	3,200	500	70% [44%]	
England	7%	2,800	300	70% [51%]	48.5
Scotland	6%	3,000	300	73% [55%]	
New York		4,400	700	74%	
France		5,200	420 [rising 24/01]	73% [33%]	72.2
Denmark		6,000	140 [rising 24/01]	78% [48%]	35.2
Portugal		4,500	200 [rising 24/01]	90% [29%]	42.6
Ireland		4,800	220	77% [46%]	52.8

Model outputs are for the low, medium and high transmission scenarios with 90% eventual uptake of booster doses. Data for Australian states is from https://covidlive.com.au; data for UK is from https://coronavirus.data.gov.uk and the Office for National Statistics https://www.ons.gov.uk; data for New York is from Johns Hopkins https://coronavirus.jhu.edu; data for other countries is from Our World in Data https://ourworldindata.org/coronavirus. Vaccination rates are as at 1 January 2022, except for booster rates in Australian states which are for 10 January 2022 (the earliest data available). The Oxford stringency index is a composite measure based on nine response indicators including school closures, workplace closures, and travel bans, rescaled to a value from 0 to 100 (100 = strictest) https://ourworldindata.org/covid-stringency-index.

Additional scenarios and sensitivity analysis

The table below compares the baseline scenario with alternative scenarios where there is no booster coverage, and with an alternative estimate of vaccine effectiveness parameters (1). With no booster coverage, all outcomes are significantly worse (note the model likely underestimates the amount of severe illness in scenarios with no booster and a late outbreak start as we do not model any further waning more than 20 weeks after the second dose). The alternative vaccine effectiveness estimates also result in worse outcomes than the baseline scenario, though the pattern with respect to time of outbreak seeding remains consistent.

start date	infections	cases	hosp	peakBeds	deaths	maxPrev10	maxAvgCas7
BASELINE SCENARIO - 90% of eligible get boosted							
1Jan	2,659,966	681,689	21,370	2,706	955	19%	23,403
1Feb	2,439,369	625,972	19,301	2,061	839	14%	17,655
1Mar	2,474,163	637,912	20,175	2,128	852	14%	17,601
1Apr	2,609,408	673,915	21,576	2,380	903	16%	19,848
1May	2,729,050	704,968	22,646	2,704	941	18%	22,296
NO BOOSTERS							
1Jan	3,241,735	841,393	31,615	4,504	1,433	26%	33,024
1Feb	3,287,706	852,115	31,373	4,630	1,379	28%	34,799
1Mar	3,229,454	839,296	30,644	4,568	1,317	28%	34,549
1Apr	3,164,354	823,749	30,018	4,424	1,292	27%	33,708
1May	3,194,354	830,743	30,193	4,436	1,298	27%	33,930
LOW VE - 90% of eligible get boosted							
1Jan	3,148,212	780,545	31,298	4,782	2,351	28%	32,884
1Feb	2,736,182	668,639	25,059	3,074	1,983	18%	21,998
1Mar	2,759,097	674,698	25,949	3,086	2,091	18%	21,338
1Apr	2,897,914	712,094	27,898	3,494	2,274	20%	23,827
1May	3,020,582	744,716	29,617	3,933	2,414	22%	26,788

Model assumptions

We use an age-structured stochastic model for transmission of SARS-CoV-2. This model has previously been used to describe the Delta outbreak that started from a border-related source in 2021. With a time-varying control function fitted to data on new daily cases, the model can provide a reasonably good fit to cases, hospitalisation and deaths using parameter values for the Delta variant (2). Here we modify key parameter values to reflect the characteristics of the Omicron variant, as described below, and model the effects of waning immunity over time. For a complete model specification, see Technical Appendix.

Vaccine coverage

Vaccine coverage by 5-year age band is as per data on 17 January 2022, with the additional assumption that everyone who had received their first dose by 17 January receives their second dose five weeks later. This means that approximately 91% of over-12-year olds are double-vaccinated. Note that model vaccine coverage may be lower than official Ministry of Health statistics because we used the StatsNZ estimated resident population (ERP) as population denominators, rather than the health service utilisation (HSU) population, which is typically smaller. At the time of writing, adults become eligible for the booster dose 120 days after receiving their second dose and we assume that either 70% or 90% of adults receive their third dose two weeks after becoming eligible. Vaccination of 5-11-year-olds began on 17 January 2022, with an eight-week interval between the first and second dose. As a simple model of the effects of vaccinating this age group, we assume that there is a 75% uptake over an eight-week period.

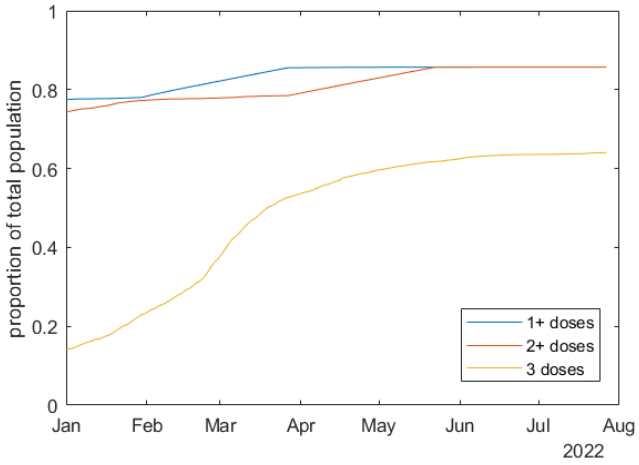


Figure 1. Modelled proportion of the total population who have received at least one dose, at least two doses, and three doses (under the assumption that 90% of those eligible get a booster dose), plotted by date the immunity takes effect, which is assumed to be 14 days after the vaccine is received.

Vaccine effectiveness

Vaccine effectiveness of the Pfizer/BioNTech mRNA vaccine is characterised by three parameters: reduction in risk of infection, risk of hospitalisation, and risk of death. Effectiveness is assumed to wane with time since most recent dose (Table 1) according to estimates by UKHSA (3). In addition, we assume that effectiveness against infection is the same as effectiveness against symptoms (which is supported by UK data from routine testing of healthcare workers (3)), but that there is no additional reduction in transmission for breakthrough infections. This is an optimistic assumption as regards infection prevention, but a pessimistic assumption as regards breakthrough transmission. We assume that effectiveness against death is halfway between effectiveness against hospitalisation and 100%, as vaccines tend to provide better protection against more severe outcomes. These assumptions are broadly consistent with the range of vaccine effectiveness values used by UK SPI-MO modelling groups (4-6). Some of these parameter values are investigated in sensitivity analysis.

Vaccine effectiveness	Dose 2 2-5 wks	5-10 wks	10-15 wks	15+ wks	Dose 3 2-5 wks	5-10 wks	10-15 wks	15+ wks
Infection	62%	55%	40%	28%	64%	57%	47%	40%
Hospitalisation	83%	80%	75%	72%	92%	88%	83%	79%
Death	92%	90%	88%	86%	96%	94%	92%	90%

Table 1. Assumed vaccine effectiveness parameters for Omicron by time since receiving dose 2 or dose 3 of the Pfizer/BioNTech mRNA vaccine (3, 6).

Basic reproduction number and generation interval

There is significant uncertainty about the relative contribution of intrinsic transmissibility (as measured by R_0), generation time, and immune evasion to Omicron's transmission advantage over Delta. Here we investigate a baseline scenario in which the reproduction number excluding the effects of immunity (R_{EI}) is $R_{EI} = 2.6$ and the mean generation time ($\acute{g}$) is $\acute{g} = 3.3$ days (7, 8). The assumed reproduction number includes the effects of moderate public health measures, such as those required at the red setting of the Covid Protection Framework, but assume there is no strict lockdown. Immunity in the population from vaccination and from prior infection reduce the effective reproduction number below the assumed value of R_{EI}. We also consider a high transmission ($R_{EI} = 3.4$, $\acute{g} = 5.05$ days) and a low transmission scenario ($R_{EI} = 2.2$, $\acute{g} = 2.7$ days) (9, 10). We do not attempt to model individual public health interventions or restrictions and other combinations of R_{EI} and $\acute{g}$ are possible. We focus on these scenarios as they provide a range of plausible outcomes with case doubling times that are approximately consistent with international observations. Note that the low transmission scenario would likely require an effective public health response to reduce transmission.

Disease severity

The assumed risk of hospitalisation and death in five-year age bands for infections in unvaccinated people is shown in Table 2. The risk of hospitalisation is based on the estimates of (11), adjusted as in our previous model by an odds ratio of 2.26 for the Delta variant (12), and additionally adjusted by a hazard ratio of 0.33 reflecting lower intrinsic severity of Omicron relative to Delta (13, 14). The risk of death is based on estimates of (11) adjusted by a hazard ratio of 0.3 for Omicron. (14) found that the risk of death for Omicron cases was 0.19 times the risk of death for Delta cases. However, they did not have sufficient data to adjust this estimate for other covariates. Not controlling for vaccination status and prior infection means this may be an underestimate of the relative risk because Omicron cases are more likely to be breakthrough infections, which tend to be milder. We therefore use a larger hazard ratio of 0.3. Note that these hazard ratios describe the intrinsic severity of Omicron relative to Delta. The realised severity is the product of intrinsic severity with vaccine effectiveness against infection and hospitalisation, and the age and vaccination status of the subpopulation that becomes infected. The reduction in realised severity relative to Delta is a model output and may be more than, similar to, or less than the reduction in intrinsic severity (15). We assume that the average length of hospital stay for Omicron is four days (16), which is shorter than estimates for the Delta variant.

Age band (years)															
0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75+
Proportion of infections causing hospitalisation (%)															
0.31	0.31	0.13	0.20	0.29	0.42	0.61	0.90	1.27	1.87	2.77	3.90	5.65	7.94	11.1	19.9
Proportion of infections causing death (%)															
0.0004	0.0004	0.0004	0.0008	0.002	0.003	0.006	0.011	0.023	0.045	0.087	0.168	0.331	0.635	1.22	4.27

Table 2. Hospitalisation and death rates for unvaccinated infected people in five-year age bands.

Other simplifying assumptions

- We do not consider the effects of a concurrent outbreak of the Delta variant.
- Immunity from infections that may have occurred prior to the start of the simulated time period is ignored. This assumption is not likely to have a large effect on model results given that, at the time of writing, New Zealand has had approximately 12,000 confirmed community cases of Covid-19, which is around 0.25% of the total population.
- Differences in the effectiveness of the AstraZeneca vaccine relative to the Pfizer vaccine are ignored. This is expected to have a negligible effect on population-level outcomes as the number of AstraZeneca vaccines given in New Zealand is very small.
- Infection with the Omicron variant is assumed to provide complete protection against re-infection with Omicron for the remainder of the simulation.
- Vaccine effectiveness and waning for people who have had one vaccine dose is ignored. This affects a relatively small part of the population.
- The effects of seasonality are not included in the model.
- Simulations are initialised with 500 seed infections introduced over a one-week time period. This models some initial undetected community transmission and means that model outputs are restricted to seeding events that lead to established community transmission and exclude those that go stochastically extinct. Key model outputs are not highly sensitive to the number of seed infections, though it will affect the timing of the peak.

Key limitations and uncertainties

- Estimates of vaccine effectiveness against symptomatic disease and against hospitalisation are based on estimates from UK data (3). However, vaccine effectiveness against infection and transmission are less certain. We have assumed that the observed prevention of symptomatic Covid-19 is due to infection prevention. However, if overall reduction in transmission is lower than this, our results for the number of cases could be significant underestimates.
- We have assumed that vaccine effectiveness against death is higher than vaccine effectiveness against hospitalisation. This is consistent with observed patterns that vaccines tend to be more effective against more severe health outcomes than against milder outcomes. However, if vaccine effectiveness

against death is closer to vaccine effectiveness against hospitalisation, the number of deaths could be up to double our estimates.

- Deaths are a particularly uncertain model output because there is currently limited direct data on vaccine effectiveness against death and the risk of death for the Omicron variant.
- We have assumed that vaccine effectiveness is the same in all age groups. There is some preliminary evidence that the effectiveness of the Pfizer vaccine against symptomatic disease caused by Omicron wanes faster in over 65-year-olds than in younger groups (17). Although vaccine effectiveness against hospitalisation was still high, if waning results in an increasing number of infections in older age groups, our results for the total number of hospitalisation and deaths could be underestimates.
- Evidence about the severity of Omicron relative to Delta is still accumulating and estimates of hospitalisation and death rates are subject to uncertainty.
- In New Zealand's 2021 Delta outbreak, the proportion of cases hospitalised exceeded model predictions. This could be because the outbreak was concentrated in relatively high-risk groups. If this pattern is repeated in an Omicron outbreak, our results for hospitalisations could be underestimates.
- The generation interval of Omicron is a key model parameter that is uncertain at present. We have considered scenarios that range from a relatively high R number and generation interval that is similar to the original strain of SARS-CoV-2 to a smaller R number and generation interval that is significantly shorter (7, 10). However, other combinations of R and generation time are possible. If the rate of spread is significantly different from these scenarios, our results could be underestimates or overestimates.
- The model does not take into account a stringent policy response such as lockdown, nor any behavioural changes that may arise dynamically as a result of the epidemic. If such measures have a substantial impact on transmission, this would be expected to flatten the curve of cases, hospitalisations and deaths. There could also be a long tail or a second wave following the initial peak if mixing drops and then increases again as normal behaviour resumes.
- In addition to uncertainties around key epidemiological characteristics of the Omicron variant, the results in this report are made in the absence of any data on transmission of Omicron in New Zealand. The date of introduction of Omicron into the New Zealand community and the vaccine coverage that will have been achieved at that time are unknown. These results should therefore be treated as highly preliminary estimates of potential outcomes, and the relative effect of the booster rollout. The model will need to be updated to reflect conditions and observed case growth rates when Omicron begins to spread in New Zealand.
- The prevalence of Delta in New Zealand is very low at present. However, if the number of Delta cases increases greatly at the same time as an Omicron wave, this could significantly add to the health burden of the epidemic. It would also complicate situational awareness given the large number of anticipated cases, limited sequencing coverage and differential risks of clinical outcomes for the two variants. It is possible that Delta could account for a low proportion of cases but a higher proportion of healthcare demand.

- The model investigates how the dynamics of waning immunity and ongoing vaccination interact to affect key outcomes for Omicron outbreaks starting at different times. However, the model ignores other variables that may also affect outcomes, such as higher transmission rates and higher non-Covid demand on the healthcare system during winter months.
- The model includes waning of vaccine-induced immunity up to around six months after the most recent dose. The model does not include waning of immunity following infection. This means that the model is not suitable for investigating the long-term dynamics of the epidemic and transition to endemicity.
- The timing of the peak is subject to variability in how long it takes for transmission to become established.
- The model ignores important sources of heterogeneity in the New Zealand population that could affect rates of transmission, peak number of cases, and clinical outcomes. Model results show the national picture but this is likely to be unevenly distributed across the population. Communities with low vaccination rates, high comorbidity rates, poorly served by healthcare systems, or other risk factors are likely to be disproportionately affected. Māori and Pasifika are at higher risk from an Omicron outbreak: Māori and Pasifika have higher risk of severe illness if infected with previous variants of SARS-CoV-2 (18) and bore a disproportionate health burden in the recent Delta outbreak.
- The model assumes a relatively stable proportion of infections are reported as cases and does not take into account the effects of limited testing capacity. If testing capacity is exceeded, reported case numbers may cease to be a useful reflection of the true incidence of Covid-19.
- Parameters are based primarily on estimates from studies where the BA.1 lineage of the Omicron variant was dominant. The BA.2 lineage is growing faster than BA.1 in several countries and may have a transmissibility advantage, though preliminary estimates are that vaccine effectiveness is similar to BA.1 (19).
- Results show the median from model simulations. Because the number of infections is large, the difference between independent realisations of the stochastic model are relatively small. We therefore do not report percentile ranges of simulation because the greater source of uncertainty comes from parameter uncertainty and potential model misspecification.

Technical appendix: model specification

We model transmission of SARS-CoV-2 using a stochastic age-structured branching process model (20). Infected individuals are categorised as either clinical or subclinical, with the clinical fraction p_{clin} increasing with age (see Table S1). Subclinical individuals are assumed to be $\tau = 50\%$ as infectious as clinical individuals (21-23). Clinical individuals are assigned a symptom onset time which is gamma distributed with shape parameter 5.8 (24). In the absence of interventions, we assume generation times for the Delta variant of SARS-CoV-2 are drawn from a Weibull distribution with shape parameter 2.8 (9). Different values for the mean generation time are investigated and for simplicity the mean incubation period is assumed to be proportional to the mean generation time.

Test-trace-isolate-quarantine system model

We assume that the probability of detection for all infected individuals with clinical symptoms is $p_{test} = 0.2$, and detection occurs with an exponentially distributed delay from onset with mean 4 days. Although using an exponential distribution is a simplifying assumption, the coefficient of variation of the exponential distribution ($CV = 1$) is similar to the coefficient of variation of observed data from the August 2021 outbreak on the time from symptom onset to reporting for cases designated as "sought healthcare" in EpiSurv ($CV = 1.025$). The shape of the distribution is also approximately consistent with onset to reporting times from the August 2020 outbreak. Furthermore, we note that, for a given overall effect of TTIQ on R_{eff}, model results are not highly sensitive to the shape of the assumed onset to detection distribution. Subclinical individuals do not get tested, although may be detected via contact tracing (see next paragraph).

In addition to symptom-triggered testing, we assume that a proportion $p_{trace} = 0.25$ of contacts (whether clinical or subclinical) of a confirmed case are identified via contact tracing and quarantined with a mean of 3 days from confirmation of the index case. The relatively low value of $p_{trace} = 0.25$ reflects a system that primarily involves quarantine of household contacts as opposed to active case finding and contact tracing by public health units. This is reasonable for a fast-spreading epidemic wave generating large numbers of daily cases.

We use quarantine to refer to pre-symptomatic or asymptomatic individuals identified via contact tracing who have not yet returned a positive test result, and isolation to refer either to contacts who have developed symptoms or to confirmed cases. We assume quarantine reduces transmission by 50% and isolation reduces transmission by 80%.

Vaccine effectiveness and coverage

Vaccine effectiveness is characterised by five parameters: effectiveness against infection (e_I), effectiveness against symptomatic disease in breakthrough infections (e_S); reduction in transmission in breakthrough infections (e_T), effectiveness against hospitalisation in breakthrough infections (e_D), and effectiveness against mortality in breakthrough infections (e_M). In the absence of separate estimates of different vaccine effectiveness parameters for Omicron, we assume $e_S = e_T = 0$ and model prevention of symptomatic disease entirely through the parameter e_I.

To model the effects of waning over time, vaccine effectiveness parameters are further categorised into compartments based on the time since the most recent dose: e_{Id}, e_{Dd}, e_{Md} represent vaccine effectiveness for people in "dose category" d, which may be: 0 doses, 1 doses, 2 doses (< 5 weeks ago), 2 doses (5-10 weeks ago), 2 doses (> 15 weeks ago), 3 doses (< 5 weeks ago), 3 doses (5-10 weeks ago), 3 doses (10-15 weeks ago), 3 doses (>15 weeks ago).

The proportion of each age group in each dose category at time t is based on Ministry of Health data for the number of people who received their first, second or third dose of the vaccine by age and date. Population denominators for each age band are taken to be the estimated resident population (ERP) according to StatsNZ (Table S1). Note that model vaccine coverage may be lower than official Ministry of Health statistics because the latter use the health service utilisation (HSU) population, which is typically smaller than the ERP, as denominators. To model the delay in the immune response to vaccination, all vaccine doses are assumed to take effect 14 days after being administered.

Age-structured transmission model

Transmission between age groups is described by a next generation matrix, whose (i, j) element is defined to be the expected number of secondary infections in age group i caused by an infected individual in age group j in the absence of control measures and given a fully susceptible population:

$$NGM_{ij} = U\left(p_{clin,j} + \tau\left(1 - p_{clin,j}\right)\right) u_i M_{ji}$$

where u_i is the relative susceptibility to infection of age group i, M is a contact matrix describing mixing rates between and within age groups (25), U is a constant representing the intrinsic transmissibility of the virus. The basic reproduction number R_0 is equal to the dominant eigenvalue of the next generation matrix, denoted $\rho(NGM)$. The value of U is chosen so that $\rho(NGM)$ is equal to the assumed value of R_0 (see Table S1).

The number of people in age group $j$and dose category d who are infected by clinical individual $l$between time $t$and $t + \delta t$ is a Poisson distributed random variable with mean:

$$\lambda_{l,jd}(t) = Y_l C(t) F_l(t) \left(\int_t^{t+\delta t} w\left(s - t_{inf,l}\right) ds\right) NGM^{clin}_{j,a_l} \left(1 - e_{Td_l}\right)\left(1 - e_{Id}\right) s_{jd}(t)$$

where:

- $Y_l$is a gamma distributed random variable with mean 1 and variance $1/k$ representing individual heterogeneity in transmission. We set $k = 0.5$ which represents a moderate level of over-dispersion and is consistent with estimates for SARS-CoV-2 transmission patterns (26, 27).
- $C(t)$ is a time-varying control parameter that is fitted to data (see below).

- $F_l(t)$ represents the effect of quarantine or isolation on the transmission rate of individual l at time t, and is equal to 1 if individual l is not in quarantine/isolation at time t, equal to $c_{quar} = 0.5$ if individual l is in quarantine, and equal to $c_{isol} = 0$ if individual l is in isolation.
- $w(\tau)$ is the probability density function of the assumed generation time distribution and $t_{inf,l}$ is the time individual l was infected.
- $NGM^{clin}_{j,a_l} = Uu_j M_{a_l,j}$ is the next generation matrix for clinical individuals and a_l is the age group of individual l.
- d_l is individual l's dose category at the time they became infected.
- $s_{jd}(t)$ is the fraction of age group j that is has not previously been infected and is in dose category d at time t.

The expression for $\lambda_{l,j}(t)$ above is multiplied by τ if individual l is subclinical. Note that the factor Y_l means that, in the absence of control measures, the total number of people infected by a randomly selected individual has a negative binomial distribution with mean R_0 and variance $R_0(1 + R_0/k)$ (28).

At each daily time step, the susceptible compartment $s_{jd}(t)$ are depleted according to the number of new infections that occurred in that compartment. Prior infection is assumed to provide complete immunity against re-infection for the duration of the simulation. In addition, a proportion of $s_{jd}(t)$ moves to $s_{j,d+1}(t)$ according to the number of people who move to next dose category that day, either because of the time elapsed since the previous dose or receiving an additional dose.

Under this formulation, all vaccinated individuals have their probability of infection given exposure reduced by $e_{I,d}$. This is known as a leaky vaccine model as opposed to an all-or-nothing vaccine model, where a proportion e_I of vaccinated individuals are completely immunised and a proportion $1 - e_{I,d}$ are completely susceptible (29). Reality may be somewhere between these idealised models (i.e. there may be some individual heterogeneity in the level of protection provided by the vaccine but not as extreme as all-or-nothing). The all-or-nothing and the leaky vaccine model behave similarly when the proportion of the population with immunity from prior infection is relatively small. Waning of immunity from prior infection is ignored.

Hospitalisation and fatality model

We consider a simplified model for clinical pathways. More detailed models based on estimates of ICU admission risk and length of stay in ward, ICU and stepdown care could be overlaid onto simulation outputs for the number of infections, stratified by vaccination status and age, based on international studies or as more data from the current outbreak becomes available. Clinical individuals in age group i and dose category d at the time of infection are assumed to require hospitalisation with probability $\left(1 - e_{D,d}\right)/\left(1 - e_{S,d}\right) p_{hosp,i}/p_{clin,i}$, where $p_{hosp,i}$ is the infection to hospitalisation ratio for unvaccinated people in age group i (see Table S1). The time between symptom onset and hospitalisation is assumed to be exponentially distributed with mean 5 days (this assumption affects the timing but not the number of hospital admissions). The length of hospital stay is assumed to be exponentially distributed with mean t_{LOS} (the assumed value of t_{LOS} affects the number of hospital beds occupied at

any one time but not the total number of hospital admissions). Hospitalised cases in age group i die with probability $(1 - e_{M,d})/(1 - e_{D,d})\, IF\, R_i/p_{hosp,i}$ where IFR_i is the infection fatality ratio for unvaccinated cases in age group i (see Table S1). For simplicity, the date of death is assumed to be the same as the date of hospital discharge. In reality, the average time from hospital admission to death is longer (this assumption means that deaths will be more lagged relative to cases in reality than in the model but does not affect the total number of deaths).

Parameter	Value
(a) Baseline scenario	
Reproduction number excluding effects of immunity	$R_{EI} = 2.6$
Incubation period	Mean 3.6 days, s.d. 1.5 days
Generation interval	Mean 3.3 days, s.d. 1.3 days
(b) *Low transmission scenario*	
Reproduction number excluding effects of immunity	$R_{EI} = 2.2$
Incubation period	Mean 2.9 days, s.d. 1.2 days
Generation interval	Mean 2.7 days, s.d. 1.0 days
(a) *High transmission scenario*	
Reproduction number excluding effects of immunity	$R_{EI} = 3.4$
Incubation period	Mean 5.5 days, s.d. 2.3 days
Generation interval	Mean 5.0 days, s.d. 1.9 days
Relative infectiousness of subclinical individuals	$\tau = 0.5$
Heterogeneity in individual reproduction number	$k = 0.5$
Probability of detection for clinical individuals	$p_{test} = 0.2$
Probability of a contact of a confirmed case being traced	$p_{trace} = 0.25$
Time from symptom onset to test result	Mean 4.0 days, s.d. 4.0 days
Time from confirmation of case to quarantine of contacts	Mean 3.0 days, s.d. 1.7 days
Time form symptom onset to hospital admission	Mean 5.0 days, s.d. 5.0 days
Length of hospital stay	Mean 4.0 days, s.d. 4.0 days

Age-specific parameters

Age (yrs)	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75+
Pr(clinical) (%)	54.4	55.5	57.7	59.9	62.0	64.0	65.9	67.7	69.5	71.2	72.7	74.2	75.5	76.8	78.0	80.1
Susceptibility*	0.46	0.46	0.45	0.56	0.80	0.93	0.97	0.98	0.94	0.93	0.94	0.97	1.00	0.98	0.90	0.86
Popn (1000s)	306	327	335	315	337	378	380	338	311	328	329	326	295	251	217	339

Table S1. Other parameter values used in the model. *Susceptibility for age group i is stated relative to susceptibility for age 60-64 years. Age-dependent rates of clinical disease are based on (30).

Vaccine effectiveness	Dose 2				Dose 3			
	2-5 wks	5-10 wks	10-15 wks	15+ wks	2-5 wks	5-10 wks	10-15 wks	15+ wks
Infection	37%	24%	18%	14%	58%	43%	35%	28%
Transmission in breakthroughs	12%	6%	4%	3%	26%	16%	11%	8%
Symptoms	43%	29%	23%	17%	64%	49%	41%	33%
Hospitalisation	79%	67%	59%	51%	91%	83%	77%	71%
Death	78%	66%	58%	50%	90%	82%	76%	70%

Table S2. Alternative vaccine effectiveness parameters taken from (1) investigated in sensitivity analysis.

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