Protocol: An integrated epidemiologic and economic model to predict optimal future COVID-19 pandemic policy in Victoria, Australia

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Contents

1 INTRODUCTION

The COVID-19 pandemic is well into its third year, with ongoing high levels of SARS-CoV-2 transmission globally driving significant associated morbidity and mortality. This is due in part to the emergence of viral variants (such as the B.1.1.529, or Omicron, variants) that possess enhanced capacity for transmission and the ability to evade pre-existing immunity. Continued viral evolution is likely,[4] however in the current phase of the pandemic this is occurring against a complex backdrop of growing population immunity (from vaccination, natural infection, or both) and improved public health approaches to managing SARS-CoV-2 outbreaks and associated clinical disease.

At present there is tension between the desire of populations to 'return to normal' and the very real possibility of a both infectious and virulent SARS-CoV-2 variant emerging,[4] carrying with it the potential for further major social, economic and public health consequences if left to spread unchecked. Given Omicron causes less severe clinical disease than previous variants of concern such as Delta, some have suggested that the arrival of future variants is likely to be associated with a decreasing trend in virulence over time.[4] Unfortunately, however, this hope is not supported by the realities of SARS-CoV-2 evolution; the virulence of a variant largely arises independently of its ability to transmit or evade the immune response.[4,5]

It is increasingly clear that COVID-19-related policy decisions cannot be made based solely on the state of the pandemic today. The uncertainty inherent in attempting to predict the future, however, creates a challenge for policy makers. Without a framework to manage this uncertainty, it is impossible to assess what the optimal policy might be to manage the pandemic in the medium to long term. It is also critical that moving forward the benefits and costs of the growing array of intervention options available to respond to the pandemic are assessed and compared explicitly, rigorously and systematically (including cost effectiveness),[6] given that these interventions can have serious implications for travel, trade and migration, the economy, and the personal freedoms of citizens.

To reflect this, we aimed to determine which of 24 select policy packages was optimal, formed by combining two suppression strategy approaches (intensity of public health and social measures), provision or not of free respirators (e.g., N95 masks) to the public, and six scenarios of future vaccine schedules (current mRNA vaccines, and next-generation omicron-targeted or multivalent vaccines). To make future uncertainty tractable to analysis, we specified 64 scenarios of future SARS-CoV-2 variant

characteristics (low and high virulence, low and high innate infectiousness, low and high immune escape, and four dates of arrival). Our case study was the state of Victoria, Australia, over the 18 months from April 2022 to September 2023. These 1536 scenarios were simulated in an agent-based model (ABM) that also allowed for further uncertainty around parameters such as public compliance, background mask wearing, vaccine waning and joint vaccine- and natural infection-derived immunity. Outputs from the ABM were then analyzed using a net monetary benefit (NMB) approach which trades off health and cost impacts of policy decisions and facilitates the ranking of policy choices for a given valuation of health adjusted life years. We use both a health system perspective (i.e., costs incurred in the health system) and sensitivity analyses including estimated GDP losses (from lockdowns in particular). The results should be generalizable to other high-income countries with comparable health systems, levels of vaccination and previous SARS-CoV-2 infection.

2 METHODS

2.1 Agent-based model

Details regarding the ABM have been published elsewhere.[7] In brief, the model has a daily cycle length and contains 2,500 agents that are scaled up to represent the Victorian population (6.7 million people), with each agent moving in a two-dimensional space and creating opportunities for between-agent infection informed by model parameters than influence viral transmission (such as agent age and vaccination status; Supplementary Table 1). This model was previously calibrated to the first COVID-19 waves in Australia and New Zealand and has been used in the past to inform COVID-19 pandemic policy in Victoria.[8] For this study, the model was further calibrated to Victorian epidemic curves from April and May 2022.

Over a timeline of 18 months (April 2022 to September 2023), 1536 scenarios were run 400 times (100 iterations of separate draws of input parameters [e.g. random draw of mask effectiveness from its probability distribution], each run 4 times to dampen stochastic variation), to generate 100 averages of total SARS-CoV-2 infections, symptomatic infections, hospitalisations, intensive care unit (ICU) admissions, deaths and time in each stage of public health and social measures (PHSMs) for each scenario. In addition to these outputs, we also determined for every iteration of every scenario the loss of health adjusted life years (HALYs), COVID-19-related health expenditure, net future health expenditure beyond 2023, and projected GDP loss.

2.2 Modelled scenarios

2.2.1 Policy options

Suppression policy

Five incremental stages of PHSMs were specified (Supplementary Table 2). Stages sequentially have more restrictions up to Stage 5, which approximates a lockdown. The ABM cycles between these stages based on predicted pressure on health service infrastructure and two suppression strategy policy options – *barely* suppression and *loose* suppression – which aim to keep peak hospital occupancy less than 400 and 200 per million residents respectively (Supplementary Table 5). The behaviour of agents is also dynamic based on the 7-day average of new infections, to reflect the public modulating their interactions in response to infection incidence independent of government-imposed restrictions.

2.2.1.1 Respirator policy

Respirators (such as N95 masks) reduce infection risk in wearers by approximately 80%.[9] We modelled the maintenance of a stockpile of 10 respirators per person for the whole Victorian population aged 10 years and older, that are distributed for use at four-week intervals if in Stage 3 or higher.

2.2.1.2 Vaccination policy

Six potential future vaccine schedule scenarios were modelled. These included currently available mRNA vaccines in addition to scenarios of 'next-generation' vaccines either specifically targeting the Omicron variant or targeting several variants (Supplementary Table 6). At the beginning of the model agents were designated as double- and triple-vaccinated (no single-vaccinated agents were modelled) and/or previously infected to reflect age-specific rates in Victoria as of 1 April 2022. Pre-Omicron past infection was uncommon in Victoria and was ignored. The proportion of previously infected agents was double that of reported cases in Victoria to allow for under-notification.[10] Agent protection against infection, symptomatic disease, hospitalisation, ICU admission and death following vaccination, previous infection, or both (plus onward transmission if infected) was a dynamic continuously waning function of age, time since last vaccine dose or infection, the number and type of vaccine doses received, and the variant responsible for primary infection, based on an a previously published logistic regression model of vaccine effectiveness (Appendix).[11]

2.2.2 Variant scenarios

2.2.2.1 Timing of arrival

Four days of arrival of a new variant of concern were modelled – 91, 182, 273 and 364 days into the model run, approximating the beginning of July and October 2022, and January and April 2023.

2.2.2.2 Transmissibility

Intrinsic transmissibility of a new variant was parameterised with an R_0 of 11 (mean = 11, uniform range 10 to 12; similar to that for Omicron BA.2) or 14 (mean = 14, uniform range 13 to 15).

2.2.2.3 Virulence

New variants were characterized as either low virulence (approximating current Omicron) or high virulence. To set the low virulence infection fatality risk (IFR), we scaled age-specific IFRs associated with the ancestral variant[12] to approximate total deaths observed in Victoria from 1 April to 30 May 2022 (a period of Omicron predominance). This process was repeated using previously published age-specific hospital and ICU admission risks.[13] Previous estimates of the age-specific probability of symptomatic infection[14] were adjusted to achieve a $4^{0.25}$= 1.41 ratio difference between high and low virulence variants. We also assumed 4^{1}= 4, $4^{0.75}$= 2.83 and $4^{0.5}$= 2 ratio differences in IFR, risk of ICU admission, and risk of hospital admission between the low and high virulence variants (Appendix; i.e. approximating a shift in severity distribution, such that the IFR varies four-fold between the less and more virulent variant through to a 1.41 difference in symptomatic proportion). Length of hospital and ICU stay were also determined by variant virulence, based on Australian estimates from Delta and Omicron-dominant periods (Supplementary Table 7).[15]

2.2.2.4 Immune escape

The capacity of a new variant for immunological escape (either from vaccine- or natural infection-derived immunity) was defined as nil, moderate or high and was calculated using ORs applied to vaccine effectiveness (VE) and/or natural infection-derived immunity estimates (Supplementary Table 8, Supplementary Table 9). High immune escape equated to an OR of 0.5 applied to the VE or natural infection protection odds, and moderate escape an OR of 0.707 (i.e., $0.5^{\wedge 0.5}$). Each new variant was only allowed two levels of escape (nil or moderate, or moderate or high) dependent on its innate transmissibility (i.e., if the new variant had high innate transmissibility, then it would not require immune escape to have a survival advantage and was thus assigned nil or moderate escape).

2.3 Morbidity and mortality

2.3.1 Acute COVID-19

We quantified the morbidity associated with acute symptomatic COVID-19 by using existing disability rates (DRs) from the Global Burden of Disease (GBD) study to estimate four increasingly severe acute COVID-19 health states.[16] Morbidity was calculated separately for high and low virulence variant infections by altering the duration of illness, and length of hospital or ICU stay, based on data comparing Delta (high virulence) and Omicron (low virulence) symptomatic infection parameters[15,17] (Supplementary Table 13, Supplementary Table 14).

2.3.2 Long COVID

We calculated morbidity estimates individually for each major reported long COVID symptom as the product of its DR (estimated from GBD study disability weights), duration and prevalence among acute COVID-19 survivors.[18] Prevalence estimates were drawn from published risk differences between COVID-19 cases and controls.[19-22] Long COVID morbidity estimates were stratified by age, severity of acute infection, vaccination status, and variant virulence (Supplementary Table 17).

2.3.3 Future HALY loss from COVID-19 deaths

For each COVID-19 death during the 18-month intervention duration, we estimated future HALY loss (3% discount rate) assuming that people dying of COVID-19 are more likely to have comorbidities and be frail with 1.5 times the age-specific morbidity (10% SD ln scale, i.e. 95% UI 1.23 to 1.84) and twice the age-specific mortality rates (95% UI 1.64 to 2.43) compared to the general population (Supplementary Table 18).

2.4 Net monetary benefit analyses

To assess the optimal policy option, we used a NMB approach where 3% per annum discounted HALYs incremental to business-as-usual were monetised at Australian GDP per capita (US$50,000). Total net health expenditure was subtracted from these monetised HALYs to generate a NMB in each iteration of the model, with two perspectives considered – health system and health system plus GDP.

2.4.1 Acute COVID-19 expenditure

We applied unit costs for resource use to each agent in every iteration of the model depending on their infection and clinical outcome status. These included SARS-CoV-2 testing, medication, ambulatory care, and hospital and ICU costs (Supplementary Table 19, Supplementary Table 20).

2.4.2 Long COVID expenditure

We applied estimates of likely healthcare utilisation for those experiencing long COVID symptoms based on available international data and formal guidelines for healthcare professionals in Australia,[23,24] stratified by acute disease severity, variant virulence, and vaccination status of agents (Supplementary Table 23).

2.4.3 Intervention costs

Vaccines and respirators were assigned unit costs, in addition to fixed program expenditure (transportation, storage, vaccine administration, respirator distribution, and health promotion costs) depending on policy options active in each model iteration (Supplementary Table 24). Regarding vaccines, we assumed Omicron-targeted vaccines would be 1.25 times the unit price of current mRNA vaccines, and multivalent vaccines 1.5 times, with generous uncertainty intervals (10% SD on ln scale giving 95% UI of 1.03 to 1.52 and 1.23 to 1.82 respectively).

2.4.4 GDP loss due to PHSMs

Due to societal changes (e.g. work from home, increased IT use for business), we assume no GDP impacts in Stages 1 to 2. GDP loss from time in Stage 3 (working from home and social distancing strongly encouraged), Stage 4 (soft lock down) and Stage 5 (hard lockdown) in 2022 to 2023 are difficult to estimate, but surely less than those in 2020 due to societal change. Accordingly, we assumed wide uncertainty of 10% to 50% (uniform distribution) of the Australian-Government estimated GDP losses per week in 2020[25] for Stages 3, 4 and 5 (Supplementary Table 25).

2.5 Uncertainty and sensitivity analyses

Large uncertainties are already included in the above modelling through 64 scenarios about future variants and within all model runs uncertainty about most input parameters propagated through the Monte Carlo simulations to give uncertainty intervals about all outputs (total infections, hospitalisations, time in stages of PHSMs, net health expenditure, GDP losses and NMB).

Within each model iteration we determine which policy scenario is 'best' for each given selection of input parameter values – which when aggregated by the 100 iterations of each of the 1536 scenarios, and then aggregated again for the 24 policy options (i.e. assuming equal likelihood of each of the 64 future variant scenarios) gives the proportion of times each policy option was 'best' (e.g. using cost effectiveness acceptability curves).

To further aid understand of the impact of uncertainty, we additionally give heatmaps of key model outputs for all 1536 scenarios in Supplementary Figures. Accompanying these heatmaps, we estimate the ratio difference in hospitalisations, net health expenditure and NMB between key scenario attributes (e.g., levels of immune escape, innate infectiousness).

We also present tornado plots showing the variation in NMB (health system perspective only) and other outputs comparing the lowest quintile and highest quintile (i.e. approximating comparison of 10th and 90th percentiles) of selected key input parameters: a) initiating VE (i.e. the lowest and highest quintile of iterations for triple dose VE at 2 weeks against any Omicron infection (which is correlated with VE against hospitalisation and mortality)); b) initiating natural infection immunity (highest and lowest quintiles of protection from infection 2 weeks prior); c) waning (any/symptomatic VE, hosp/ICU/death VE, natural protection); d) mask effectiveness; f) infectiousness of asymptomatic cases relative to symptomatic cases; g) proportion of undetected symptomatic cases who self-report; h) infection hospitalisation risk for base Omicron (which is correlated with that for a more virulent variant); i) Infection fatality risk for base Omicron; j) HALY loss per infection aged 60 in base Omicron scenario (for values of morbidity loss from acute and long COVID and HALY loss from deaths summed, then ranked into quintiles of iterations – for acute COVID, long COVID and death); k) cost per unit of current generation mRNA vaccines; l) unit cost of Omicron targeted vaccines; m) unit cost of Multivalent vaccines; n) delivery and promotion costs of vaccination programs; o) per unit respirator costs; p) storage costs of respirators; q) health system expenditure per infection aged 60 in base Omicron scenario (i.e. summing costs of acute and long COVID, and future averted health system expenditure due to premature deaths, then ranking).

Finally, we undertook some specific sensitivity analyses for selected scenarios: running the ABM for 12 months only rather than 18; not allowing stages 4 and 5; setting initial vaccination coverage (2 doses) to 50% for < 5-year-olds, and 20 percentage points higher for less than 20-year-olds.

Appendix

3 AGENT-BASED MODEL (ABM)

3.1 ABM overview and input parameters

We used an agent-based model with 2500 agents and a daily cycle length. Each agent was given many attributes including age (in 10-year strata), essential worker status, and household. Depending on the scenario, agents were proportionately assigned vaccine, mask usage, and other characteristics. Using only 2500 agents, the model up- and down-scaled depending on the infection rate in the population, to keep between 40 to 120 agents (out of 2500) infected. During the scaling up and down, the impact on the total number of infected, vaccination, recovered, etc., people in a population the size of Victoria (6.7 million) was tallied and retained.

Input parameters had probability distributions from which values were drawn for each of the 100 iterations of the Monte Carlo analysis in the ABM. Key ABM input parameters are shown in Supplementary Table 1. All variables (except the last 'carefulness' parameter) were specified a priori and not subject to amendment in calibration. The 'carefulness' parameter is – we argue – theoretically justified, in that as the pandemic has evolved citizens are increasingly dynamically responding to infection rates. For example, staying at home to work and avoiding public transport when infection rates are high, and elderly people at most risk of severe illness being particularly cautious. The exact values of this parameter were set in calibration (see next section).

Within each iteration, there was an inner loop of four stochastic iterations; with just 2500 agents in the ABM, the stochastic uncertainty for the Victorian population of 6.7 million is likely overestimated. Under a normal distribution approximation the average output value (e.g. number of infections) over four stochastic runs will halve the standard deviation attributable to stochastic uncertainty ($1/\sqrt{4} = 0.5$).

Supplementary Table 1: Key agent-based model input parameters

Parameter	Estimate
Time post infection to being infectious, and increase in infectivity	The infectiousness on each day of the agent's infection is set to approximate data on Delta,[27] parameterised by agent-level draws for peak infectivity, time to peak infectivity, and illness duration. The infectivity of an agent on a given day is determined by linearly interpolating: - 10% of their peak infectivity on day 0, - their full peak infectivity at their time to peak infectivity, and - zero at the illness duration.

Parameter	Estimate
Time to peak infectivity (days, log-normal)	Per-agent log normal distribution: mean = 4.4, SD = 1.5[27]
Mean illness period	Normal distribution: Mean = 10.9, SD = 2 (time to peak infectivity[27] plus time from infected to end of infection [mean 6.5 days, SD 0.77])
Mean adherence with isolation of infected cases	Global beta distribution (beta 450.3, 23.7; mean = 95%, SD = 1%)
Infectiousness of asymptomatic cases vs symptomatic cases per contact	RR 0.58 (95% CI 0.34 to 0.99)[28] parameterised as a log normal distribution with median -0.545 and SD 0.270
Household size	Scaled beta distribution with median 3.0. Beta 2.2, 2.2 scaled to [1, 5] with draws rounded to nearest integer
Proportion of non-household contacts traced within the first three days, at a caseload of 5 per day.	0.9
Chance of an infected non-household contact of a known case becoming known through contact tracing, per day.	chance = 1 / (dailyCases * ((a* dailyCases ^0.92 - b) + 100)) dailyCases = known daily cases averaged over the last week. Solve for a and b with (dailyCases, chance) = (1, 0.729) and (5, 2.679). This traces 90% and 98% of contacts at a caseload of 5 and 1 per day respectively. The expected number of cases traced per day asymptotes at 100. (Note this parameter is less critical in current modelling in 2022-23 when society is 'living with the virus', as compared to 2020 and 2021 when Australia had a zero-COVID approach.)
Chance of an infected household contact of a known case becoming known, per day.	100%
Proportion of undetected symptomatic cases who spontaneously reported themselves	Beta 6,6
Time of undetected symptomatic cases spontaneous self-reporting	1-2 days after peak infectivity
Transmission multiplier of person who is complying with their isolation	0.33
Relative susceptibility to infection, by age (OR for infection given exposure)	0 – 9 years: 0.34 10-19: 0.67 20 – 59 years: 1 60-69: 1.23 ≥70 years: 1.47[29] Uncertainty on all values +/- 15% SD
Relative 'carefulness' against infection, by age (OR for infection given exposure)	0 – 9 years: 2.09 10 – 19 years: 1.34 20 – 49 years: 1 50 – 59 years: 0.84 60 – 69 years: 0.51 70 – 79 years: 0.24 80 – 89 years: 0.22 ≥90 years: 0.21

3.2 ABM calibration

Having set a priori variables in Supplementary Table 1, we calibrated the model to achieve R_0s of 10, 12, 13 and 15 in a situation with no vaccination, no previous infection, no contact trading, and public health and social measures. R_0s were found by introducing a single infected person into the naïve population and counting infections caused by case zero – 40000 times. The key variable to 'tune' was the base transmissibility of the virus, i.e., the probability of a single average interaction between an infected and susceptible infecting the susceptible. Spatial parameters were also tuned to allow for a range of transmissibilities to hit the required R_0s.

With R_0 calibrated, we then calibrated the PHSMs in Stage 2 to achieve, over an average of 1000 runs, 1.2 million infections in the 60 days following the 1st of April 2022. This corresponds to an average of 20,000 infections per day, which is twice the average daily reported cases in this period. Transmissibility was drawn uniformly from the range corresponding R_0s 10 and 12. To initiate the model, we used a separate model to initiate the joint infection and vaccination status of the 2500 agents to approximate the vaccination by age (and time since vaccination) as in Victoria on 1 April 2022, and a cumulative infection (twice that of reported cases allowing for under-registration) with variation by age as shown in Supplementary Table 2. Infections were randomly assigned to agents with less probability to those vaccinated (allowing for waning vaccine immunity over time using logistic odds of [11]).

Supplementary Table 2: Age, vaccination and cumulative infection of 2500 initiating agents

Age	Percentage distribution of population	% double vaccinated as of 1 April 2022	% triple vaccinated as of 1 April 2022	Cumulative infection as of 1 April 2022
0-4	5.7%			32.0%
5-11	8.7%	30.2%		34.5%
12-17	6.9%	95.6%	12.4%	45.6%
18-29	16.5%	87.1%	44.5%	48.8%
30-39	15.5%	93.8%	56.2%	40.3%
40-49	12.8%	96.4%	68.2%	34.7%
50-59	12.0%	96.4%	74.4%	25.7%
60-69	10.2%	97.1%	81.1%	17.2%
70+	11.6%	98.8%	88.1%	11.3%
All		*83.5%*	*53.1%*	*32.9%*

The PHSMs for Stage 2 were iteratively adjusted until the target of 1.2 million infections was achieved. The result is in Supplementary Table 4. In parallel, the 'carefulness' parameter in Supplementary Table 1 was adjusted to achieve the age distribution of infections occurring in April and May, as per Supplementary Table 3.

Supplementary Table 3: Calibration target of infections by age

Age	Target distribution of infections by age
00-09	12.50%
10-19	13.00%
20-29	14.10%
30-39	18.90%
40-49	15.30%
50-59	11.80%
60-69	7.80%
70-79	4.30%
80-89	1.80%
90+	0.60%

3.3 Modelled scenarios

3.3.1 Policy options

3.3.1.1 Suppression policy

Supplementary Table 4: Key input parameters by stage of public health and social measures

	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5
Proportion of people who try to avoid contact with others (excluding their household)[†*]	42%	58%	65%	75%	85%
Proportion of time spent trying to avoid contacts, for those that attempt to do so[†*]	55%	67%	73%	80%	90%
Proportion of workers attending work in person[†]	65%	44%	38%	25%	20%
Schools open (disable contact avoiding behaviour among students)	Yes	Yes	Yes	No	No
Proportion of people that wear masks outside the home[†]					
≥20-year-olds	25%	40%	60%	80%	90%
10- to 19-year-olds	16.7%	26.67%	40%	53.3%	60%
<10-year-olds	11.1%	17.78%	26.67%	35.6%	40%
Proportion of mask wearing that is with a respirator[#]					
No government supply	20%	20%	20%	20%	20%
Government supply policy	20%	20%	80%	80%	80%

Proportion of people that engage in super spreading behaviour each day (move to a random gathering location)[†]	4%	3.1%	2.2%	1.6%	1%
Underlying frequency of visiting a random nearby gather location each day (e.g., a supermarket)	14.28%	14.28%	14.28%	14.28%	14.28%
Radius for determining whether a gather location counts as nearby	8.8	6.7	6	5	3.6
Maximum distance moved by an agent each day	10	8.5	8	5	5

[†]ORs of 2, 4, 6 and 8are applied to the proportion of people that wear a mask, isolation compliance (Supplementary Table 1), proportion of people that avoid others, and proportion of time spent avoiding others for those aged50-60, 60-70, 70-80 and those aged ≥80 respectively. Reciprocals of these ORs are applied to daily chance of visiting a gather location, and daily chance of superspreading. Note agents ≥60 years old are excluded from the category of workers.

[*]In stages 1-3, the proportion of people who try to avoid contact with others and the proportion of time spent trying to avoid contacts for those attempting to do so are dynamic, based on the average number of infections over the last 7 days. Proportions are as written above if the 7-day average of infections is <5000.Proportion of people who try to avoid contacts and proportion of time spent avoiding increase to a maximum of 15% and 10%, respectively, at 32000 daily infections over the last seven days. The region between 5000 and 32000 is linearly interpolated.

[#]Only applies to those aged 10+.

Supplementary Table 5: Triggers for escalation and de-escalation of stages of public health and social measures, by suppression policy

Triggers for *barely* suppression	Escalation If average expected number of people in hospital 10-14 days into the future (inclusive) is: - >600 per million → Stage 5 - >400 per million → Stage 4 - >270 per million → Stage 3 - >180 per million → Stage 2 De-escalation If no de-escalation in last 7 days, and average expected number of people in hospital 10-14 days into the future is: - <450 → Stage 4 if in Stage 5 - <300 → Stage 3 if in stage 4 or 5 - <200 → Stage 2 if in Stage 3, 4 or 5 - <140 → Stage 1
Triggers for l*oose* suppression	Escalation: If average expected number of people in hospital 10-14 days into the future is: - >300 per million → Stage 5 - >200 per million → Stage 4 - >130 per million → Stage 3 - >90 per million → Stage 2 De-escalation: If no de-escalation in last 7 days, and average expected number of people in hospital 10-14 days into the future is: - <230 → Stage 4 if Stage 5 - <150 → Stage 3 if in stage 4 or 5 - <100 → Stage 2 if in Stage 3, 4 or 5 - <70 →Stage 1

3.3.1.2 Respirator policy

There is a paucity of high-quality evidence providing estimates of the degree of protection afforded by mask-wearing at the individual level in community settings for the transmission of SARS-CoV-2. A recent systematic review and meta-analysis[30] that examined the effectiveness of public health measures in reducing the incidence of COVID-19 reported a relative risk of infection of 0.47 (95% CI 0.29 to 0.75) associated with mask-wearing overall, based on six studies. The authors note, however, a high degree of heterogeneity between these studies and substantial risk of bias. In a World Health Organization-commissioned systematic review and meta-analysis published in 2020, protection afforded by wearing an N95 mask or "surgical or similar" mask was estimated at 95% (95% CI 34% to 100%) and 58% (95% CI 24% to 77%) respectively. This review, however, included literature regarding three betacoronaviruses (MERS-CoV, SARS-CoV and SARS-CoV-2) and studies in both healthcare and community-based settings,[31,32] limiting applicability to our model.

We elected to base our estimates of mask effectiveness on a recently published test-negative case-control study enrolling individuals receiving COVID-19 test results from February to December 2021 in California, USA, which provides estimated effect sizes for protection stratified by type of mask.[9] Estimates were adjusted for vaccination status, household income, race/ethnicity, age, sex, state region and county population density. The primary analysis assessed self-reported mask use in indoor public settings during the 14 days preceding testing between those receiving positive and negative SARS-CoV-2 test results and found adjusted odds of infection of 0.44 (95% CI 0.24 to 0.82) associated with always using any type of mask or respirator. Adjusted odds for infection associated with using cloth masks, surgical masks and respirators were 0.44 (95% CI 0.17 to 1.17), 0.34 (95% CI 0.13 to 0.90) and 0.17 (0.05 to 0.64) respectively. Assuming 5% of 'always' mask use was N95 masks, these reported estimates were adjusted to the following for use in our model:

- Cloth/surgical masks: odds ratio (OR) 0.468 (or -0.76 on ln scale, with SD 0.31)
- N95 respirators: OR 0.204 (or -1.59 on ln scale, with SD 0.65)

We specified 100% correlation on draws of mask effectiveness and assumed the same risk reduction in onward transmission if wearing a mask.

At the time of writing, masks were no longer mandated in most indoor settings in Victoria but were still recommended. Masks remained mandatory on public transport, in airports, on aircraft, in health care settings, and if a close contact of a COVID-19 case. These regulations, however, do not specify the type of mask that the public should use. We modelled the maintenance of a stockpile of 10 respirators per person for the whole Victorian population aged 10 years and older, that are distributed for use at four-week intervals (rotating masks on a five-day cycle with extra masks to cover for spoilage) if in Stage 3 or higher. In essence, this changes the proportion of people wearing respirators from 20% at baseline to 80% in these stages while the respirator policy is active.

3.3.1.3 Vaccination policy

Australia had a mixed rollout of mRNA- and viral vector-based vaccines for the primary series and predominantly mRNA-based vaccines for third and subsequent doses. In our model, we combined all currently available vaccines into one generic 'current generation' vaccine with effectiveness as outlined below. We then specified two types of 'next generation' vaccines to reflect expected advances in vaccination technology – (i) those that target the Omicron variant specifically and (ii) those that are

designed to be variant agnostic and confer broader spectrum protection against several variants. Examples of Omicron-targeted vaccines include mRNA-1273.529 (developed by Moderna). Examples of multivalent vaccines include the Spike Ferritin Nanoparticle (SpFN) vaccine developed by the Walter Reed Army Institute of Research and Vaxart's oral formulation VXA-CoV2-1, with VE against emerging variants expected to be superior to current-generation vaccines. We specified six hypothetical vaccination schedules as shown in Supplementary Table 6. These schedules were informed by current vaccination policy discussions in the Australian context, including debate regarding the need for a fourth vaccine dose for the general public or delaying this to await the arrival of next generation vaccines.

Supplementary Table 6: Six vaccination schedules treated as policy options

Scenario	Apr-Jun 2022	Jul-Sep 2022	Oct-Dec 2022	Jan-Mar 2023	Apr-Jun 2023	Jul-Sep 2023
a) Nil further						
b) Current generation (CG)		CG		CG		CG
c) CG, then omicron-targeted (OT)		CG		OT		OT
d) OT only			OT		OT	
e) CG then multivalent (M)		CG		M		M
f) Multivalent only			M		M	

Applies to ≥20-year-olds with triple dose coverage and <20-year-olds with double dose coverage on 1 April 2022. At each wave of vaccination, it is assumed that 80% of people (+/-10% SD, beta distribution) vaccinated in the last wave take up new offering. For example, 80% of ≥20-year-olds who start the model on 1 April 2022 already triple-vaccinated receive the next dose of the scheduled vaccine. ≥20-year-olds who had not received their third dose by 1 April 2022 do not receive any further vaccines. Vaccine rollout is even over three months (i.e., no difference by age for simplicity).

3.3.2 Future variant scenarios

There were 64 future variant scenarios, formed by cross-classifying timing of arrival [4 options], transmissibility [2; R_0 11 and 14], virulence [2; low (similar to Omicron) and high], immune escape [2 levels] and type of variant [2; antigenically Omicron-like and novel]. The following four sections address these, with the fourth section describing type of variant and immune escape (and immune escape in response to future vaccines is a function of type of variant).

3.3.2.1 Timing of arrival

We set four alternative dates for the arrival of a new variant into Victoria: the start of July 2022, October 2022, January 2023 or April 2023 (implemented in 91-day increments from 1 April 2022). This was implemented by a 2% chance of newly infected people spontaneously receiving the new variant applied to every infection event after the incursion date.

3.3.2.2 Transmissibility

The model is calibrated to produce R_0s of 11 (uniform distribution 10 to 12) for low virulence variants and 13 (uniform distribution 12 to 14) for high virulence variants.

3.3.2.3 Virulence

New variants were characterized as either high (approximating the Delta variant) or low (approximating Omicron) virulence. We first specified low virus virulence by calibrating 'best' international estimates to the Victorian Omicron wave experience. For the high virulence variant, we assumed 4^1= 4, $4^{0.75}$= 2.83, $4^{0.5}$= 2 and $4^{0.25}$= 1.41 ratio increases in the infection fatality risk (IFR), risk of ICU admission, risk of hospital admission, and risk of being symptomatic, respectively, compared to low virulence variants. The remainder of this section describes the specification and calibration of IFR, ICU and hospital admission per infection, and risk of being symptomatic.

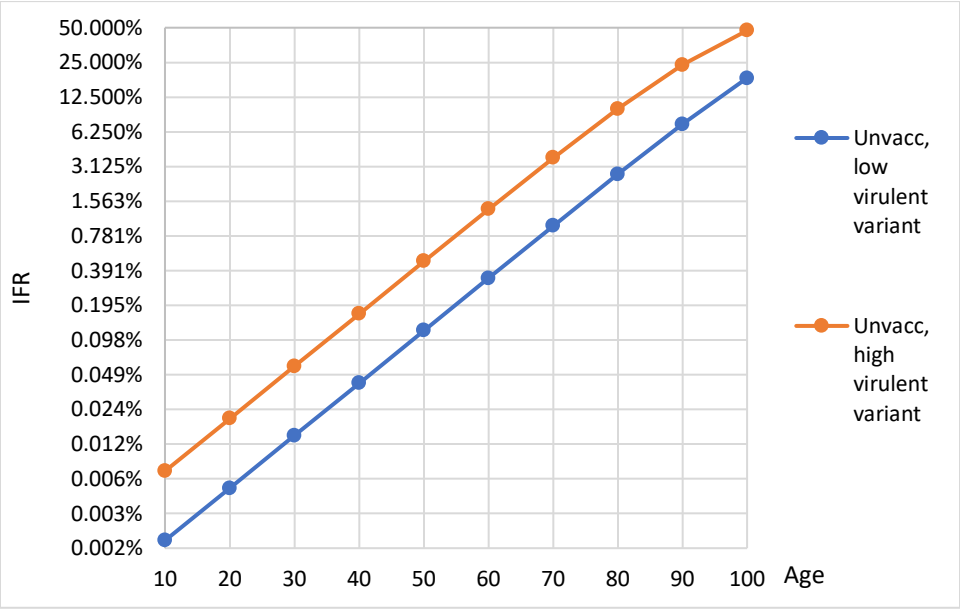
Infection fatality ratio

We fitted a logistic regression model to Institute for Health Metrics and Evaluation (IHME) estimates of age-specific IFRs (greater than 10 years of age) for the ancestral strain of SARS-CoV-2 (Table 1 of [12]). This gave a coefficient of 0.1049 for age (in years). We then used this age variation in the calibrated ABM applied to 60 days post 1 April in Victoria that included vaccination status and ongoing infection status of agents; an intercept or constant of -11.9861 for the equation predicting IFR among the unvaccinated output the number of deaths actually observed in Victoria during these 60 days when the model was generating 20,000 infections per day (see calibration section). The equation is shown below, as well as that similarly set as a constant IFR among the unvaccinated for <10 year olds. The equation for the high virulence variant simply had ln(4) = 1.3863 added (i.e. to achieve four-fold higher IFRs for the more virulent variant.

- Current Omicron and low virulence new variant
    - ≥10 years: logit(IFR) = 0.1049*age – 11.9861 (SD = 0.205)
    - <10 years: logit (IFR) = -11.6051 (SD = 0.269)
- High virulence new variant
    - ≥10 years: logit(IFR) = 0.1049*age – 10.5999 (SD = 0.205)
    - <10 years: logit(IFR) = -10.2189 (SD = 0.269)

The resultant IFRs for unvaccinated and previously uninfected people, for the low and high virulent variant, are shown in Supplementary Figure 1. (The IFRs are extensively modified according to vaccination and infectious status (with waning) for each agent in the actual modelling.)

Supplementary Figure 1: IFRs used in modelling, for unvaccinated and previously uninfected, for low and high virulent variants.



ICU admission risk

To obtain the age-dependent probability of ICU admission given infection, we use the age gradient published by Knock et. al. for ancestral SARS-CoV-2.[13] For those aged ≥30 years the probability of ICU admission given infection increases approximately linearly by age on a logarithmic scale, described by the equation logit(ICU | inf) = 0.1293*age – 12.866. Risks in Knock et al of ICU admission given infection on the logarithmic scale for those aged 0 to 9 years and 10 to 29 years were -9.2629 and -10.4237 respectively. ICU risk beyond 80 years was set as that for an 80-year-old. We then reduced ICU admission risk for those aged 80-89 years by 25% and those aged ≥90 years by an additional 75% to reflect a lower likelihood of ICU admission in older age despite clinically severe disease.

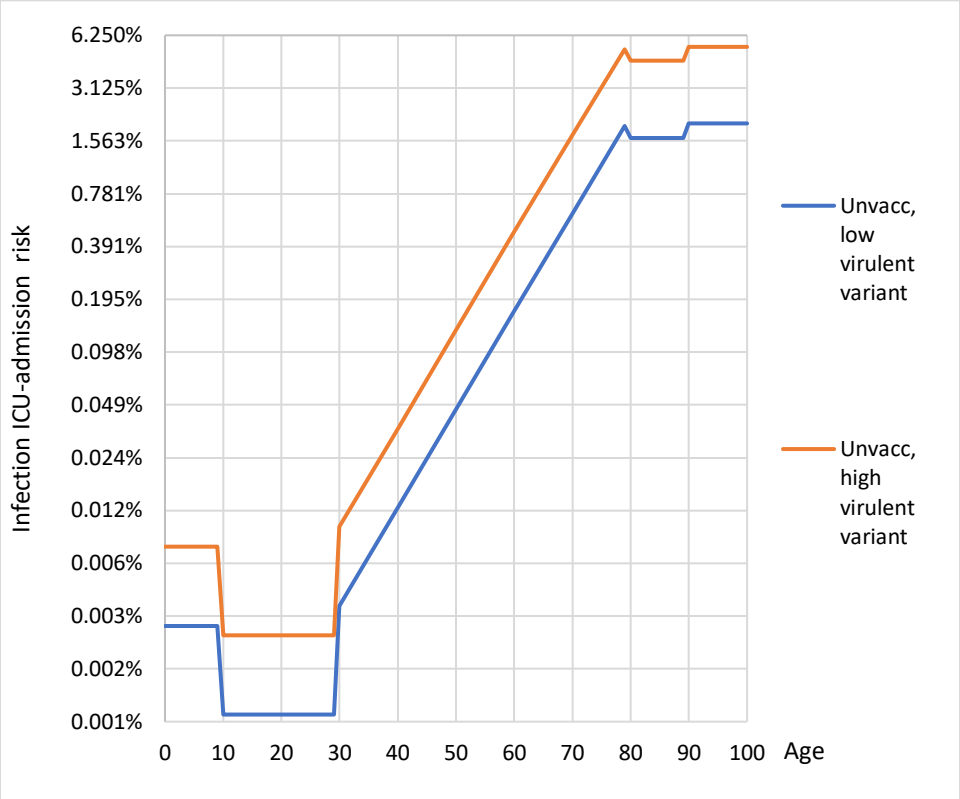
These estimates were then adjusted during calibration (similarly to that above for IFR) for a low-virulence variant (approximating Omicron) to achieve the number of COVID-19-related ICU admissions in Victoria from 1 April to 30 May 2022 (on a background of vaccination and infection rates approximating

that in Victoria during this period). We then applied a $4^{0.75}$= 2.83 ratio difference in ICU admission risk between the low and high virulence variants to give the following:

- Current Omicron and low-virulence new variant
    - ≥90 years: logit(ICU | inf) = 0.129*age – 13.386 – (0.481+1.386) – 0.266 (SD = 0.1)
    - 80-89 years: logit(ICU |inf) = 0.129*age – 13.386 – (0.481 + 0.288) – 0.266 (SD = 0.1)
    - 30-79 years: logit(ICU | inf) = 0.129*age – 13.386 – 0.481 – 0.266 (SD = 0.1)
    - 10-29 years: logit(ICU | inf) = -10.943 – 0.481 – 0.266 (SD = 0.1)
    - <10 years: logit(ICU | inf) = -9.783 – 0.481 – 0.266 (SD = 0.1)
- High-virulence new variant
    - ≥90 years: logit(ICU | inf) = 0.129*age – 12.346 – (0.481+1.386) – 0.266 (SD = 0.1)
    - 80-89 years: logit(ICU |inf) = 0.129*age – 12.346 – (0.481 + 0.288) – 0.266 (SD = 0.1)
    - 30-79 years: logit(ICU | inf) = 0.129*age – 12.346 – 0.481 – 0.266 (SD = 0.1)
    - 10-29 years: logit(ICU | inf) = -9.904 – 0.481 – 0.266 (SD = 0.1)
    - <10 years: logit(ICU | inf) = -8.743 – 0.481 – 0.266 (SD = 0.1)

The resultant infection ICU-admission risks for unvaccinated and previously uninfected people, for the low and high virulent variant, are shown in Supplementary Figure 2. (The risks are modified according to vaccination and infectious status (with waning) for each agent in the actual modelling.)

Supplementary Figure 2: Infection ICU-admission risks used in modelling, for unvaccinated and previously uninfected, for low and high virulent variants.



Hospitalisation risk

To obtain the age-dependent probability of hospitalization given infection, age-variation is also based on those published by Knock et. al.[13] For individuals aged ≥30 years, the Knock et al probability of hospitalization given infection increases approximately linearly by age on a logarithmic scale, described by the equation logit(hosp | inf) = 0.0997*age – 8.9113. For people younger than 30 years the risk of hospitalization given infection is not linear on the logarithmic scale and as such averages of point estimates were used (-6.0308 for those aged 0 to 9 years and -7.1235 for those aged 10 to 29 years).

These estimates were then calibrated for a low-virulence variant (approximating Omicron, and as above for IFR and ICU) to achieve the number of COVID-19-related hospital admissions in Victoria from 1 April to 30 May 2022. We applied a $4^{0.5}$= 2 ratio difference in hospitalisation risk between the low and high virulence variants to give the following:

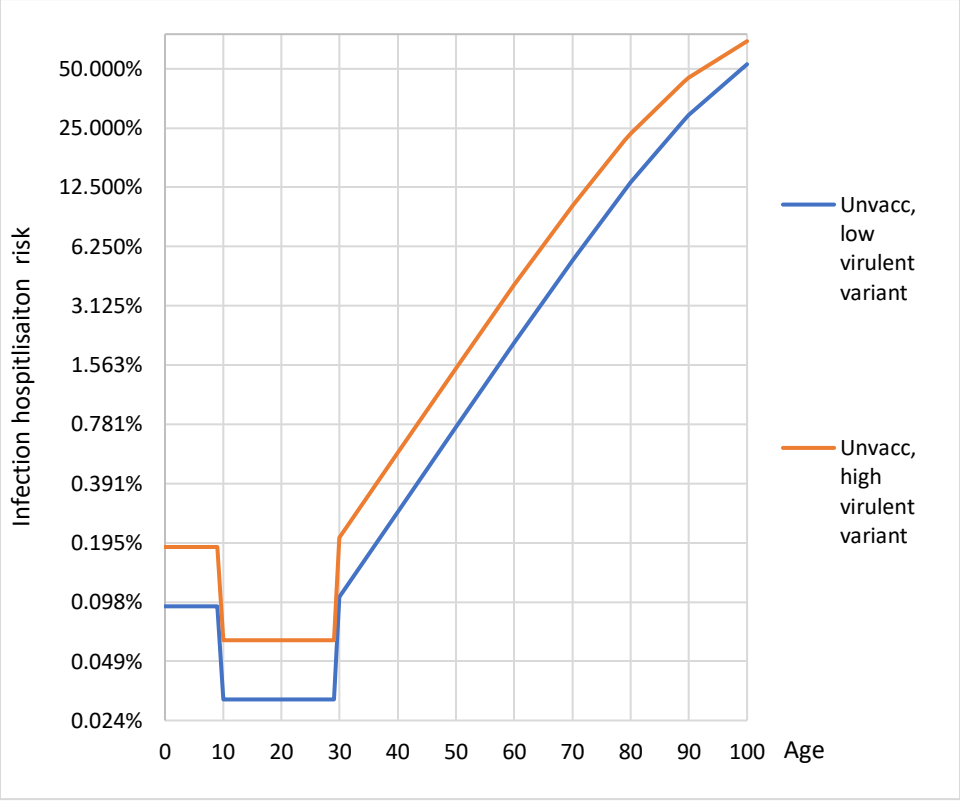
- Current Omicron and low-virulence new variant

- ≥30 years: logit(hosp | inf) = 0.0997*age – 9.258 – 0.601 (SD = 0.1), capped at risk for an 80-year-old (i.e. constant hospitalisation risk for those aged 80 years and older)
- 10-29 years: logit(hosp | inf) = -7.470 – 0.601 (SD = 0.1)
- <10 years: logit(hosp | inf) = -6.377 – 0.601 (SD = 0.1)

- High-virulence new variant
  - ≥30 years: logit(hosp | inf) = 0.0997.age – 8.5647 – 0.601 (SD = 0.1), capped at risk for an 80-year-old
  - 10-29 years: logit(hosp | inf) = -6.777 – 0.601 (SD = 0.1)
  - <10 years: logit(hosp | inf) = -5.684 – 0.601 (SD = 0.1)

The resultant infection hospitalisation risks for unvaccinated and previously uninfected people, for the low and high virulent variant, are shown in Supplementary Figure 3. (The risks are modified according to vaccination and infectious status (with waning) for each agent in the actual modelling.)

Supplementary Figure 3: Infection hositalisation risks used in modelling, for unvaccinated and previously uninfected, for low and high virulent variants.



Symptomatic infection risk

Estimates regarding the probability of being symptomatic given infection with SARS-CoV-2 were based on those from a meta-analysis using data through to April 2021.[14] These were then multiplied $2^{0.25}$ and $0.5^{0.25}$ to obtain estimates of the probably of symptomatic disease given infection on an OR scale for a more or less virulence variant respectively, to give the following (converted back to a percentage scale; uncertainty +/-10% SD for all values):

- Current Omicron and low-virulence new variant
    - ≥60 years: Pr(symptomatic | inf) = 0.774
    - 20-59 years: Pr(symptomatic | inf) = 0.640
    - <20 years: Pr(symptomatic | inf) = 0.490
- High-virulence new variant
    - ≥60 years: Pr(symptomatic | inf) = 0.829
    - 20-59 years: Pr(symptomatic | inf) = 0.716
    - <20 years: Pr(symptomatic | inf) = 0.576

Length of hospital and ICU stay

Variant virulence impacted length of hospital and ICU stay are shown in Supplementary Table 7, with estimates based on those for New South Wales, Australia, during periods of Delta and Omicron predominance:[15]

Supplementary Table 7: Mean (and 95% confidence interval) length of stay associated with low and high virulence SARS-CoV-2 variants

	Age (years)	Omicron/low virulence variant	High virulence variant
Hospital LOS	≤39	2.05 (1.80 to 2.30)	3.60 (3.48 to 3.81)
	40-69	2.92 (2.50 to 3.67)	5.78 (5.59 to 5.99)
	≥70	6.02 (4.91 to 7.01)	12.31 (11.75 to 12.95)
ICU LOS	≤39	3.93 (2.58 to 5.68)	7.50 (6.99 to 8.33)
	40-69	4.30 (3.29 to 5.72)	9.44 (8.81 to 10.07)
	≥70	4.36 (3.40 to 5.57)	8.94 (7.80 to 9.91)

LOS: length of stay. Uncertainty around these values parameterised in the model using a normal draw with a standard deviation based on the width of the reported 95% confidence interval, divided by 3.92

3.3.2.4 Immune escape

SARS-CoV-2 is under strong evolutionary pressure to develop mutations that afford it the ability to escape pre-existing immunity, either obtained through vaccination or previous infection.[4] We reflected this in our model via ORs applied to agent immune protection at any given point in time (either vaccine- or natural infection-derived; see below for details regarding calculation of protection). For the Omicron variant, both next-generation Omicron-targeted and pan-SARS-CoV-2 vaccines are assumed to 'boost' VE by an OR of 2. That is, we assume that a next-generation pan-SARS-CoV-2 vaccine incorporates the benefits of a next-generation Omicron-targeted vaccine. For new variants that have the same innate transmissibility as Omicron, they must possess some capacity for immune escape to become the dominant circulating strain. As such, we model moderate and large immune escape capacity using the ORs in Supplementary Table 6. For new variants that have higher innate infectiousness, no immune escape is required to have a survival advantage. Hence, we model nil and moderate immune escape for these variants using the ORs in Supplementary Table 8. Immune escape also applies to immunity following natural infection as shown in Supplementary Table 9.

Supplementary Table 8: Immune escape odds ratios for vaccines cross-classified by variants in the model

		Current generation double dose	Current generation 3+ doses	Next-gen Omicron-targeted 1+ doses	Next-gen multivalent 1+ doses
	Current Omicron (BA.2)	1 (ref)†	1 (ref)‡	*2*	*2*
New variants with same innate infectiousness as Omicron BA.2 (i.e. R0 = 11, range 10 to 12)	Omicron-like variant	*0.707, 0.5*	*0.707, 0.5*	*1.414, 1*	*1.414, 1*
	Novel variant	*0.707, 0.5*	*0.707, 0.5*	*1, 0.707*	*1.414, 1*
New variants with higher innate infectiousness than Omicron BA.2 (i.e. R0 = 14, range 13 to 15)	Omicron-like variant	*1, 0.707*	*1, 0.707*	*2, 1.414*	*2, 1.414*
	Novel variant	*1, 0.707*	*1, 0.707*	*1.414, 1*	*2, 1.414*

†Reference for the current generation double dose column

‡Reference for the current generation triple dose, next-generation omicron-targeted and next-generation multivalent columns

These ORs apply at any point in time, with waning post last dose also in effect. All italicized ORs are drawn from a range of 0.841 to 1.189 of their stated values, with 100% correlation, (including the OR of 2 for next-generation vaccines for current Omicron), uniformly on the log OR scale. For each combination of vaccine and variant, 2 levels of possible immune escape are modelled.

Supplementary Table 9: Immune escape odds ratios for natural protection following primary infection cross-classified by variants in the model

		Previous infection with Omicron	Previous infection with new variant
	Current Omicron (BA.2)	1 (ref)	*1, 1*
New variants with same innate infectiousness as Omicron BA.2 (i.e. R0 = 11, range 10 to 12)	Omicron-like variant	*0.707, 0.5*	*1, 1*
	Novel variant	*0.707, 0.5*	*1, 1*
New variants with higher innate infectiousness than Omicron BA.2 (i.e. R0 = 14, range 13 to 15)	Omicron-like variant	*1, 0.707*	*1, 1*
	Novel variant	*1, 0.707*	*1, 1*

These ORs apply at any point in time, with waning post last dose also in effect. All italicized ORs are drawn uniformly from a range of 0.841 to 1.189 of their stated values, with 100% correlation, uniformly on the log OR scale. For each combination of vaccine and variant, 2 levels of possible immune escape are modelled.

3.4 Vaccine effectiveness and protection against reinfection

Supplementary Table 10: Double-dose and triple dose vaccine completion rates and proportion previously infected among agents at model outset (1 April 2022)

Age (years)	Double dose completed	Triple dose completed	Previously infected
0-4	0%	0%	32%

5-11	30.18%	0%	34.53%
12-17	95.58%	12.43%	45.64%
18-29	87.09%	44.46%	48.79%
30-39	93.84%	56.20%	40.27%
40-49	96.37%	68.23%	34.67%
50-59	96.42%	74.44%	25.66%
60-69	97.08%	81.14%	17.24%
≥70	98.81%	88.09%	11.28%

3.4.1 Vaccine effectiveness

The effectiveness of COVID-19 vaccines peaks soon after receipt of a full vaccination course and wanes in a non-linear fashion thereafter.[33-35] To dynamically model waning of vaccine-derived immunity for the outcomes of symptomatic infection and hospitalisation from COVID-19, we developed a log-odds system of equations that has been published elsewhere[11] building on data regarding VE published by the UK Health Security Agency (UKHSA).[33,36] In summary, a random effects logistic regression model with a separate class for each combination of vaccine course and outcome was fitted to the UKHSA data, excluding observations within 2 weeks since last vaccine dose (given peak immunity would still have been developing) and weighted by the inverse variance as follows:

$$logit(VE) = \alpha + \beta_1 Hosp + \beta_2 Triple + \beta_3 Month + \beta_4 Hosp * Month + \beta_5 Triple * Month$$

where:

VE is vaccine effectiveness;

α is the intercept, or the logit of the VE for the reference case (VE against symptomatic illness two weeks after double dose vaccine);

Hosp is a dummy variable for hospitalisation versus symptomatic illness;

Triple is a dummy variable for triple versus double vaccine course;

Month represents months (continuous) since last vaccine dose minus 0.5 (i.e., 'centered' on two weeks post the last vaccine dose to aid interpretation of model coefficients);

*Hosp*Month* is an interaction term of hospitalisation and month (i.e., how VE wanes differently on the ln odds scale for protection against hospitalisation as compared to protection against symptomatic illness); and

*Triple*Month* is an interaction term of triple and month.

For models including interaction terms of *hosp*triple*month* and *triple*hosp* these coefficients had non-significant p values, and the differences in deviance statistics between these models and that without these interaction terms were trivial and non-significant. As such they were not retained in the final model.

The UKHSA data used to develop the random effects logistic regression model described above does not include VE estimates stratified by age. However, there is evidence that VE varies by age.[34] To alter the regression equation to reflect this, we focused on estimates at 10-14 weeks post-vaccination. Using data from a study reporting VE against the Delta variant stratified by age group (≥16 years, 16-39 years, 40-64 years, ≥65 years) and vaccine type (ChAdOx1-S or BNT162b2)[34] we specified the following:

- The VE OR for ≥65-year-olds compared to <65-year-olds for BNT162b2 VE against symptomatic disease was 0.77 (at 10-14 weeks after receipt of a second dose).
- The VE OR for ≥65-year-olds compared to <65-year-olds for BNT162b2 VE against hospitalization was 0.36 (at 10-14 weeks after receipt of a second dose).
- The proportion of symptomatic cases in the <65-year-old group was 94%, and the proportion of hospitalisations in the <65-year-old group was 70.2%.

To fit these data, the above logistic regression model was re-estimated to preserve VE at 3 months post-vaccination, by solving for a new intercept. Further adjustments were then made to generate coefficients split by 3 age strata; <60 years, 60-69 years, and ≥70 years (to fit the 10-year age strata specified in our ABM).

Next, we extended the above logistic regression model to account for the outcomes of any infection (including asymptomatic infection), ICU admission and death. The UKHSA reports VE (all vaccines combined) for mortality against the Omicron variant for those aged ≥50 years to be 95% at 2+ weeks following receipt of a third dose.[37] By combining this estimate with their reported OR for symptomatic disease 2+ weeks after 3 doses for the same age group (0.41) and the associated 95% confidence intervals we drew 5000 estimates of the odds VE of mortality v. symptomatic disease, the median of which was used to estimate a coefficient for the outcome of death in the overall VE logistic regression equation. Whilst these input data were for ≥50-year-olds who were triple-dose vaccinated, given we do

not allow for interactions of age with severity and triple dose with severity we could use estimates at any age to estimate the 'independent' or 'main' effect for VE protection against death.

Limited data is available to inform estimates of VE against any infection with the Omicron variant (i.e., asymptomatic and symptomatic infection combined). As such, data from the UK Vaccine Effectiveness Expert Panel[37] were used to estimate the odds ratio for VE for all infections compared to the VE for symptomatic infection at 3 months (for BNT162b2 and mRNA-1273) and obtain the coefficient for any infection. Specifically, for each of the four combinations of BNT162b2 and mRNA-1273, for two and three doses:

- the values reported in Table 3 of the UKHSA Week 13 Report (VE as a percentage with a range both for any infection and symptomatic infection) were converted to logit(VE) with mean = ln odds of central VE, and SD = range/3.92 (approximating the 95% uncertainty interval).
- 5000 draws on the ln odds scale were taken of each of 'any infection' and 'symptomatic infection', with 0.5 correlation between the two values.
- The median and 2.5th and 97.5th percentiles of the ln odds VE were determined.

The final coefficient for any infection was the average of the four ln odds VE values (-0.78), and the final SD (on the ln odds scale) was the average of the SD (assumed as 97.5th percentile – 2.5th percentile, divided by 3.92; 0.27). For the outcome of ICU admission, the coefficient was estimated as the mid-point between the coefficients for hospitalization and death, with the same standard deviation as that for death. The final VE equation utilized in the ABM was therefore defined as follows:

$$logit(VE) = \alpha + \beta_0 Age + \beta_1 Severity_j + \beta_2 Triple + \beta_3 Month + \beta_4 Severity * Month + \beta_5 Triple * Month$$

where:

α is the intercept or the logit of the VE for the reference case (<60 years old, two doses of vaccine, against symptomatic infection, 2 weeks after the last dose);

Age is a categorical variable of ≥70 years, 60-69 years, or <60 years (ref);

Severity is categorical value of any infection, symptomatic infection (ref), hospitalisation, ICU admission or death;

Triple is a dummy variable for triple versus double vaccine course;

Month represents months (continuous) since last vaccine dose minus 0.5 (i.e., 'centered' on two weeks post the last vaccine dose to aid interpretation of model coefficients);

*Severity*Month* is an interaction term of severity and month; and

*Triple*Month* is an interaction term of triple and month.

Actual coefficient values this VE system are shown in Supplementary Table 11. Footnotes to the table describe how values were sampled for each draw (then taken into the 100 iterations of each scenario in the ABM). Note we assumed that waning (on the log odds scale) was the same for any and symptomatic infection, and the same for hospitalisation, ICU and death. We also assumed that peak effectiveness and waning for a third dose vaccine applied also to any subsequent vaccine doses.[38,39] As of 1 April 2022, Omicron BA.2 was assumed to be responsible for all SARS-CoV-2 infections in Victoria – estimates of the effectiveness of vaccines against BA.1 appear to continue to apply for BA.2 and as such estimated VE was not adjusted in response to this.[37,40] See Supplementary Figure 4 for an example of VE estimates against the Omicron variant for <60-year-olds following a third vaccine dose.

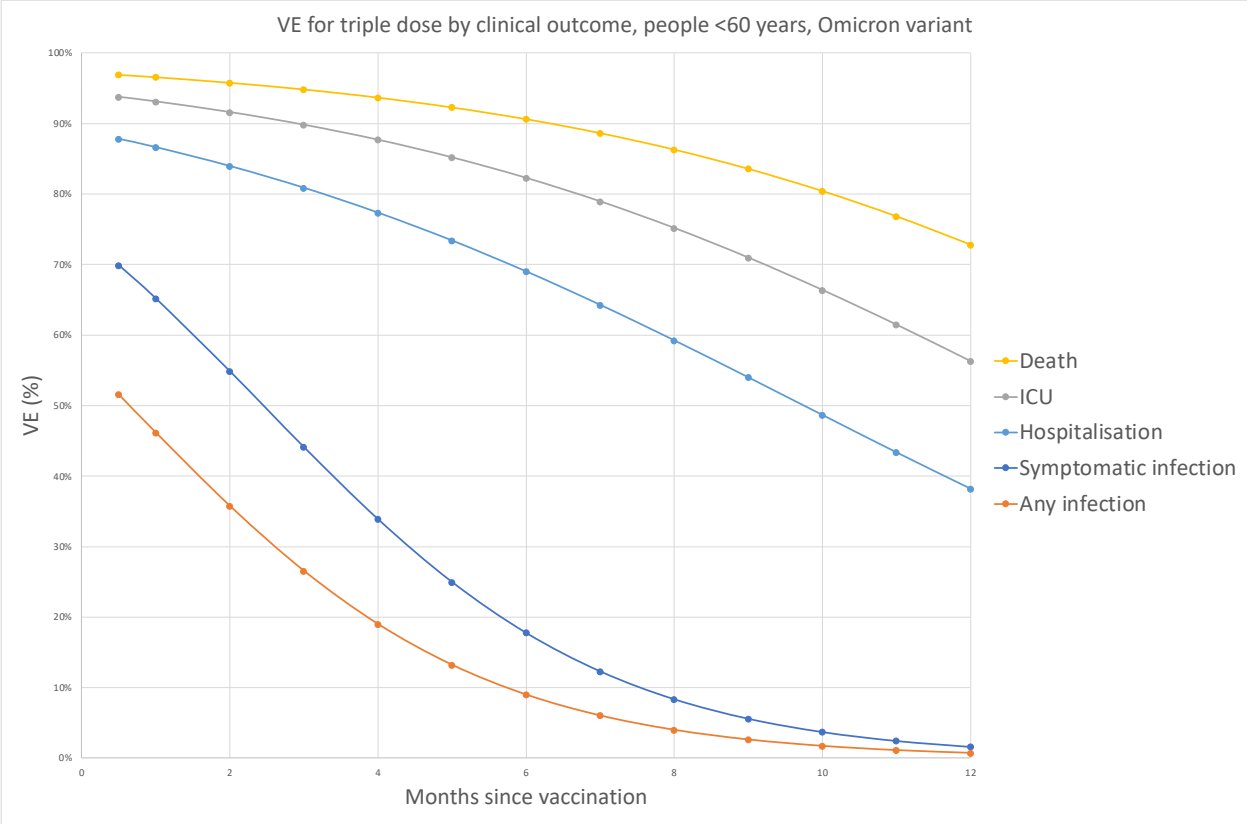
Supplementary Table 11: Vaccine effectiveness log odds equation coefficients for the Omicron variant

Coefficients	**Central**	**SD**	**Odds (%)**	**95% UI odds**
Intercept†	0.75	0.12	2.27 (68.0%)	1.67 to 2.70
			OR	**95% UI**
Age ≥70 years£	-0.26	0.12	0.77	0.61 to 0.98
Age 60-69 years‡	-0.13	0.061	0.88	0.78 to 0.99
Age <60 years (ref)	0	N/A	N/A	N/A
Severity_Any‡	-0.78	0.27	0.46	0.27 to 0.77
Severity_Sympt (ref)	0	N/A	N/A	N/A
Severity_Hosp†	1.13	0.26	3.11	1.87 to 5.16
Severity_ICU‡	1.87	0.37	6.47	13.14 to 13.40
Severity_Death‡	2.60	0.37	13.46	6.52 to 27.80
≥3Doses†	0.092	0.14	1.10	0.83 to 1.45
2 Doses (ref)	0	N/A	N/A	N/A
Month (continuous, centered on 0.5 months after last dose)†	-0.64	0.029	0.53	0.50 to 0.56
Months*Severity_Any	0	N/A	N/A	N/A
Months*Severity_Sympt (ref)	0	N/A	N/A	N/A
Months*Severity_Hosp †	0.22	0.095	1.24	1.03 to 1.50
Months*Severity_ICU	0.22	0.095	1.24	1.03 to 1.50
Months*Severity_Death	0.22	0.095	1.24	1.03 to 1.50
Months*≥3Doses †	0.21	0.033	1.23	1.16 to 1.32

†Drawn from covariance matrix accompanying regression model on UKHSA data.

[‡]Correlated 1.0 with the value in this domain drawn from covariance matrix accompanying regression model on UKHSA data. E.g., if the value drawn for Severity_Hosp was at the 63%ile of its distribution, then all other values for Severity_Any, Severity_ICU and Severity_Death are allocated the 63%ile of their distribution.
[£]The value for age was drawn independently but correlated 1.0 for ≥ 70 years and 60-69 years.

Supplementary Figure 4: Estimated vaccine effectiveness against the Omicron variant by month following a third vaccine dose, age <60 years



3.4.2 Protection from reinfection

Current evidence suggests that previous natural infection provides considerable protection against reinfection with SARS-CoV-2.[41,42] For the purposes of our model, we extracted protection from reinfection at approximately 6 months post-infection from a large population-level observational study conducted in Denmark in 2020[43] which was comparable to estimates from other studies (e.g. [44-48]). Given these estimates were derived from the first and second large outbreaks of COVID-19 in Denmark, prior to the widespread emergence of SARS-CoV-2 variants of concern, we assumed they therefore approximated the protection against reinfection with the *same* variant as the initial infection (for example, reinfection with the Omicron variant following a primary Omicron infection). This study reported estimates by age, which we recalculated by the three age groups used in our model. Note the log odds of protection from natural infection by age varies more than for VE (Supplementary Table 12).

For seasonal coronaviruses that cause upper respiratory tract infections in humans, infection-derived protective immunity wanes allowing for reinfection within approximately 12 months.[49] Studies specifically investigating the duration of protection following infection with SARS-CoV-2 are relatively scarce. In the aforementioned Danish study of the protection afforded by natural SARS-CoV-2 infection,[43] no evidence of a decrease in immunity between 3-6 months and ≥7 months post-infection was detected. Similarly, a total population cohort study from Sweden reported high and stable levels of protection against infection and hospitalisation over time following primary infection.[42] However, more recent data from Israel[50,51] reports increasing adjusted rates of infection over time for those previously infected, from 10.5 infections per 100,000 days at risk at 4-6 months post-infection to 30.2 infections per 100,000 days at risk by ≥12 months. In addition, recent data from the UK provides further evidence for the existence of waning of natural immunity.[52] Among unvaccinated individuals, adjusted protection against reinfection up to 1 year following primary infection was 86%; this dropped to 69% >1 year after primary infection.

Therefore, we modelled immunity and waning following natural infection by assuming an OR for waning per month of 0.825 (halfway between the waning of immunity for symptomatic infection following the third dose of a vaccine and no waning in the VE waning system described above). This approximates the relative change in natural protection as reported in the aforementioned Israeli study between 4 and 12 months following primary infection.[51] This parameter is genuinely very uncertain, so we specified a SD of 40% of its value on the log odds scale, giving a 95% uncertainty interval for the OR of monthly waning of 0.71 to 0.96 (much wider in relative terms than that for waning VE). These estimates for protection against reinfection (i.e., any infection) were then adjusted proportionally based on the VE system outlined above to also obtain reinfection protection estimates for symptomatic infection, hospitalisation, ICU admission, and death (Supplementary Table 12). Note these apply to unvaccinated individuals. See Supplementary Figure 5 for an example of reinfection protection estimates following primary infection for <60-year-olds.

Supplementary Table 12: Natural protection log odds equation coefficients for reinfection with the same variant as the primary infection

Coefficients	Central	SD	Odds (%)	95% UI odds
Intercept	2.56	0.25†	12.94 (92.8%)	(7.92 to 21.12)
			OR	**95% UI**
Age ≥70 years‡	-1.62	0.45†	0.20	(0.08 to 0.48)
Age 60-69 years‡	-0.55	0.25†	0.58	(0.35 to 0.94)

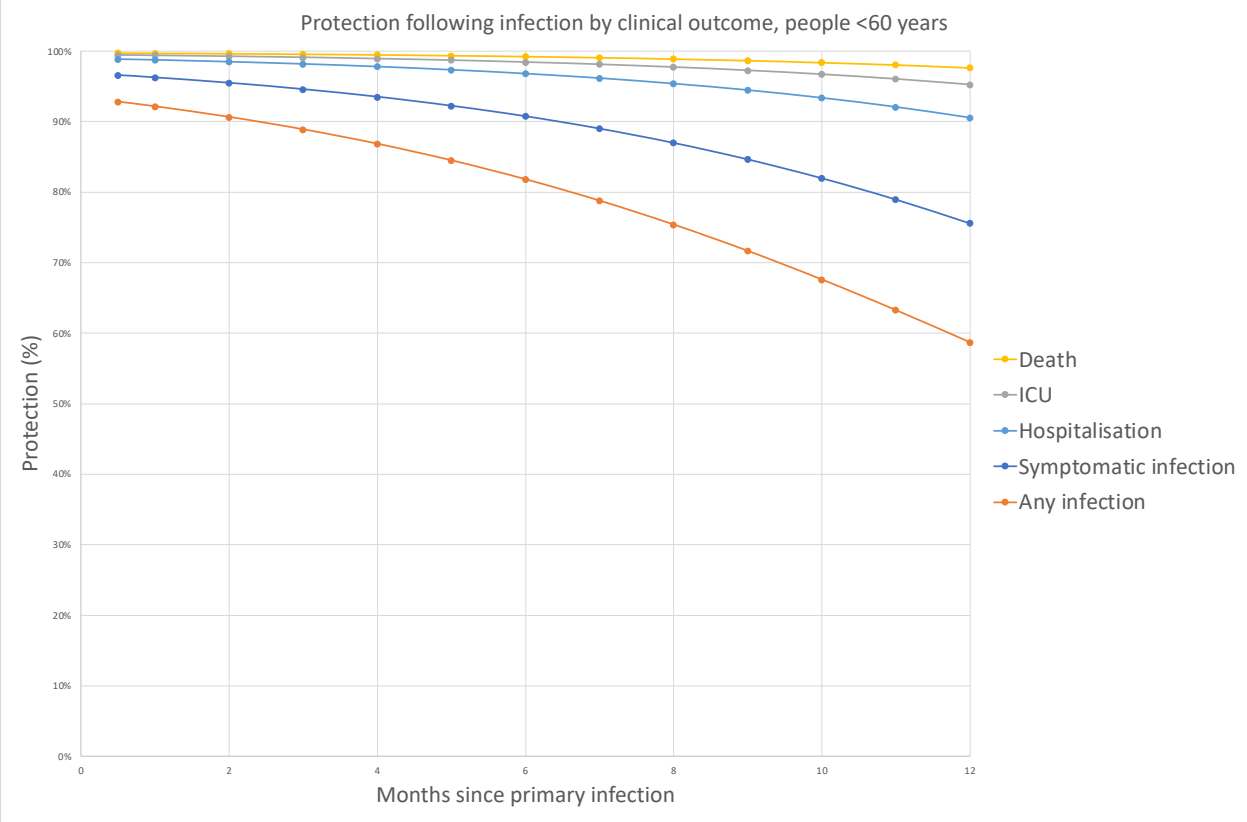
Age <60 years (ref)	0	N/A	N/A	N/A
Severity_Any (ref)	0	N/A	N/A	N/A
Severity_Sympt‡	0.78	0.30	2.18	(1.21 to 3.93)
Severity_Hosp‡	1.91	0.26	6.75	(4.06 to 11.24)
Severity_ICU‡	2.65	0.37	14.15	(6.85 to 29.23)
Severity_Death‡	3.38	0.37	29.37	(14.22 to 60.65)
Month (continuous)^	-0.192	0.077	0.83	(0.71 to 0.96)

†SD approximated from CI about VE in [53].

‡Correlated 1.0 with other values drawn in this domain.

^This coefficient was fixed at half the waning of triple and more doses of vaccine. The uncertainty is high here, so we simply set the SD at 40% of the central estimate.

Supplementary Figure 5: Estimated protection against any reinfection by month since primary infection, age <60 years, unvaccinated



3.4.3 Hybrid immunity

Immunity provided by the combination of vaccination and natural infection (hybrid immunity) has been quantified by, for example, two studies conducted in Israel[54,55] a large population-level study in Sweden,[42] and a study in Qatar.[56] In both Israeli studies, protection against reinfection was assessed among previously infected individuals either receiving a single dose of the BNT162b2 mRNA vaccine or

remaining unvaccinated. In both, the hazard ratio for reinfection among individuals both infected and subsequently vaccinated was 0.18 compared to those previously infected and unvaccinated. In the study from Sweden, hybrid immunity was found to provide additional protection above natural immunity for both reinfection and hospitalisation risk.[42] The kinetics of hybrid immunity are complex however, owing to variability in terms of timing of infection and vaccination (and the time elapsed between these two sensitizing events) in addition to consideration of dominant circulating variants, for example, and several potential sources of bias in estimates.[42] We therefore assumed the two types of immunity act independently on a relative scale, with total protection for an individual agent calculated as 1 – (1 – VE)*(1 – protection from primary infection).

3.4.4 The effect of immunity on onward transmission

Data quantifying the effect of immunity (either from vaccination or previous infection) on ongoing transmission if one becomes infected is scarce. Guided by evidence of reduced transmission for Omicron following vaccination in Danish households[57] and evidence that this reduced transmission does wane over time[58] we assumed that the reduction in ability to transmit the virus if infected following vaccination or previous infection follows the same function as VE and/or natural protection against any infection (and wanes accordingly).

3.5 Morbidity and mortality estimates

3.5.1 Acute COVID-19

We estimated the number of asymptomatic, non-hospitalised symptomatic, hospitalised symptomatic, and ICU-admitted cases for the quantification of acute COVID-19 morbidity and health expenditure, and deaths for the quantification of HALYs lost due to death from COVID-19. We measured morbidity impacts using disability rates (DR), according to the severity of acute infection (cases managed in the community, being either mild or moderate, and cases requiring hospitalisation, either managed in ward only or additionally including ICU admission) using estimates from the Global Burden of Disease (GBD) study.[16] For ICU admissions, the DR was based on the GBD disability weight (DW) for 'severe chronic obstructive pulmonary disease (COPD) and other respiratory infections', to reflect acute respiratory distress syndrome (ARDS). The GBD does not have an estimate for ARDS directly – the estimate used here is the GBD's most severe rating for respiratory infections.[16] We assumed that survivors return to their baseline health status (DR = 0) following a specified recovery period as described below. This does

not apply to those who go on to develop symptoms of long COVID – morbidity associated with long COVID was quantified separately.

Estimates are presented separately for high virulence variant infections (using data relating to the Delta variant), and low virulence variant infections (using data relating to the Omicron variant). The duration of symptoms for the purpose of morbidity calculations changes for low virulence variant infections compared to a high virulence variant, however the DWs applied are the same for both. The duration of symptoms for low virulence variants and high virulence variants was obtained from a large ongoing UK-based study, comparing acute illness parameters for Omicron vs. Delta infections.[17] In this study, the duration of symptomatic infection was not stratified by hospitalisation status – as such, estimates relating to cases managed in the community are for those with infection of duration 21 days or less.[17] For duration of symptoms for hospitalised patient sub-groups, the length of stay defined in Supplementary Table 5 are applied (including either hospital stay only, or hospital stay + ICU stay).

Morbidity loss for the four categories of symptomatic SARS-CoV-2 infection with a high-virulence variant (Supplementary Table 13) was calculated as follows:

- Morbidity for symptomatic, but not hospitalised, infections were split evenly as 50% moderate infection, with a DR of 0.051 (95% CI 0.032-0.074), and 50% mild infection, with a DR of 0.006 (95% CI 0.002-0.012), both with a mean duration of 8.89 days (95% CI 8.61-9.17).[59]
- Morbidity for hospitalised patients not requiring ICU admission assumes a period of 1 week prior to hospitalisation with moderate acute infection, with a DR of 0.051 (95% CI 0.032-0.074), followed by a duration of hospital stay varying by age (as per Supplementary Table 7), all with a DR of 0.133 (95% CI 0.088-0.190) for severe acute infection. A duration of 1-week post-hospitalisation for return to baseline health was applied, with a DR reducing linearly to zero from the severe acute infection DR.
- Morbidity for hospitalised patients requiring ICU admission assumes a period of 1 week prior to hospitalisation with moderate acute infection, with a DR of 0.051 (95% CI 0.032-0.074), followed by a duration of stay in hospital (on a general ward) varying by age (as per Supplementary Table 7), all with a DR of 0.133 (95% CI 0.088-0.190) for severe acute infection. This is followed by duration of stay in ICU as per Supplementary Table 7, all with a DR of 0.408 (95% CI 0.273-0.556) to approximate ARDS. A duration of 2 weeks for return to baseline health was applied, with a DR reducing linearly to zero from the ARDS DR.

Morbidity loss for the four categories of symptomatic SARS-CoV-2 infection by a low-virulence variant (Supplementary Table 14) was calculated as follows:

- The proportion of mild/moderate symptomatic, but not-hospitalised, infections were altered compared to high-virulence variant infections: 28% have moderate infection, with a DR of 0.051 (95% CI 0.032-0.074), and 72% have mild infection, with a DR of 0.006 (95% CI 0.002-0.012), both with duration of 6.87 days (95% CI 6.58-7.16). The proportion with mild vs. moderate severity of infection was estimated from the aforementioned UK-based study, which found the odds of 'classic' acute COVID-19 symptoms were reduced by 44% for Omicron compared to Delta infections.[17]
- Morbidity for hospitalised patients not requiring ICU assumes a period of 1 week prior to hospitalisation with moderate acute infection, applying a DR of 0.051 (95% CI 0.032-0.074), followed by a duration of stay varying by age as per Supplementary Table 7, all with DR of 0.133 (95% CI 0.088-0.190) for severe acute infection. A duration of 1-week post-hospitalisation for return to baseline health was applied, with a DR reducing linearly to zero from the severe acute infection DW.
- Morbidity for hospitalised patients requiring ICU admission assumes a period of 1 week prior to hospitalisation with moderate acute infection, with a DR of 0.051 (95% CI 0.032-0.074), followed by a duration of stay in hospital (on a general ward) varying by age as per Supplementary Table 7, all with DR of 0.133 (95% CI 0.088-0.190) for severe acute infection. This is followed by duration of stay in ICU as per Supplementary Table 7, all with DR of 0.408 (95% CI 0.273-0.556). A duration of 2 weeks for a post-hospitalisation for return to baseline health was applied, with the DW reducing linearly to zero from the ARDS DR.

The overall morbidity for each clinical infection category was calculated as the sum of the symptom severity-specific DR multiplied by the symptom duration (in years). Note these are not additive.

Supplementary Table 13: Disability rate distribution and duration by SARS-CoV-2 category, high virulence variant

Category	Symptom severity (health state)	Duration in days, mean (95% CI)	Disability Rate[†], mean (95% CI)
Admitted to ICU	Moderate acute infection	7	0.051 (0.032-0.074)
	Severe acute infection (ward)	Supplementary Table 7	0·133 (0·088–0·190)
	In-ICU (COPD for ARDS)	Supplementary Table 7	0.408 (0.273-0.556)
	Return to baseline health	14	Linearly to 0 from ARDS DR
	Moderate acute infection	7	0.051 (0.032-0.074)

Admitted to hospital, no ICU	Severe acute infection (ward)	Supplementary Table 7	0.133 (0·088–0·190)
	Return to baseline health	7	Linearly to 0 from severe acute infection DW
Symptomatic, not admitted	50% Moderate acute infection	8.89 (8.61-9.17)	0.051 (0.032-0.074)
	50% Mild acute infection	8.89 (8.61-9.17)	0·006 (0·002–0·012)

†Disability Rate applied based on DWs for equivalent health states from [16]

Supplementary Table 14: Disability rate distribution and duration by SARS-CoV-2 category, low virulence variant

Category	Symptom severity (health state)	Duration in days, mean (95% CI)	Disability Rate†, mean (95% CI)
Admitted to ICU	Moderate acute infection	7	0.051 (0.032-0.074)
	Severe acute infection (ward)	Supplementary Table 7	0·133 (0·088–0·190)
	In-ICU (COPD for ARDS)	Supplementary Table 7	0.408 (0.273-0.556)
	Return to baseline health	14	Linearly to 0 from ARDS DW
Admitted to hospital, no ICU	Moderate acute infection	7	0.051 (0.032-0.074)
	Severe acute infection (ward)	Supplementary Table 7	0.133 (0·088–0·190)
	Return to baseline health	7	Linearly to 0 from severe acute infection DW
Symptomatic, not admitted	28% Moderate acute infection	6.87 (6.58-7.16)	0.051 (0.032-0.074)
	72% Mild acute infection	6.87 (6.58-7.16)	0·006 (0·002–0·012)

†Disability Rate applied based on DWs for equivalent health states from [16]

Given the above, the following HALY loss was applied to each agent based on their clinical outcome category[1]:

- Current Omicron and low-virulence new variant:
    - For an infected, asymptomatic agent: 0
    - For an infected, symptomatic agent: 0.000350087671
    - For a hospitalised agent: 0.000978082 + ((length of hospital stay in days/365)*0.133) + 0.001275342
    - For an ICU admitted agent: 0.000978082 + ((length of hospital stay in days/365)*0.133) + ((length of ICU stay in days/365)*0.408) + 0.007824658
- High-virulence new variant:

[1] The 95% confidence intervals about disability rates all approximate a SD of about 20% of the mean. Thus, for sums of such figures, the SD as a % of the total is also 20%.

- For an infected, asymptomatic agent: 0
- For an infected, symptomatic agent: 0.000694150685
- For a hospitalised agent: 0.000978082 + ((length of hospital stay in days/365)*0.133) + 0.001275342
- For an ICU admitted agent: 0.000978082 + ((length of hospital stay in days/365)*0.133) + ((length of ICU stay in days/365)*0.408) + 0.007824658

3.5.2 Long COVID

Ongoing symptoms following acute SARS-CoV-2 infection can be grouped into two phases: the 'acute post-COVID symptoms' or 'ongoing symptomatic' phase (up to 12 weeks post-infection) and 'long COVID' phase (≥12 weeks post-infection).[60,61] Long COVID, formally termed 'Post-Acute Sequelae of SARS-CoV-2' and defined in ICD-10 classification as 'Post-COVID-19 Condition', describes the persistence and/or emergence of a heterogeneous group of physical and cognitive symptoms following acute SARS-CoV-2 infection.[61,62] The exact mechanisms and symptom profile of long COVID are yet to be fully understood. Comparisons have been made with chronic fatigue syndrome, as fatigue, muscle weakness, and concentration difficulty (or 'brain fog') have been some of the most reported symptoms.[63,64] However, other notable sequelae unique to long COVID include an impaired sense of taste (dysgeusia)/smell (dysosmia) and shortness of breath (dyspnoea).[65]

For the purpose of this model a bottom-up approach was utilized to estimate long COVID morbidity, calculating a morbidity estimate individually for each major long COVID symptom as the product of its disability rate, duration and prevalence among acute COVID-19 survivors. The disability rate for each symptom has been estimated from the GBD study DWs.[16] Some long COVID symptoms do not have direct health states for which DWs exist – in these cases best estimates have been determined from related health states. For example, the DWs of other sensory conditions (mild hearing loss and mild visual impairment) have been used as proxies for the DWs of dysosmia and dysgeusia (the full list of DWs applied are presented in Supplementary Table 16).

Symptom prevalence estimates were drawn from risk differences between COVID-19 cases and COVID-negative controls from published large international studies. Four variables were identified from the available literature with which to stratify long COVID estimates: age (adult vs. child), severity of acute infection (approximated for this model as hospitalised vs. community cases), vaccination (at least 2

doses vs. less than 2, with waning not considered), and SARS-CoV-2 variant (high vs. low virulence variant). The 'base cases' for which prevalence estimates were available in the literature are adults/children infected with a pre-Omicron variant of SARS-CoV-2 (i.e. 'high virulence' group), who are not vaccinated at the time of infection.

Symptom prevalence was drawn from four studies:

- A case-control study by Vedel Sørensen et. al. conducted in Denmark: used to obtain prevalence of physical long COVID symptoms, for adult patients diagnosed with acute COVID-19 6-12 months previously, compared to PCR-negative/seronegative controls, separately for individuals hospitalised vs. non-hospitalised during the acute disease period.[19]
- A case-control study by Caspersen et. al. based in Norway: used to obtain prevalence of cognitive long COVID symptoms for adult patients either 1-6 or 11-12 months post-infection. Patients were stratified into 'mild' vs. 'moderate/severe' cases, with moderate cases including those not hospitalised – weighting was therefore applied to the prevalence estimates for these groups to achieve the risk ratio (RR) for any long COVID symptoms between hospitalised and non-hospitalised patients found by Vedel Sørensen et al. (RR=2) and approximate the prevalence of symptoms for previously hospitalised vs. non-hospitalised groups.[19,20]
- A multi-country case-control study by Magnúsdóttir et. al.: used to obtain the prevalence of psychological long COVID symptoms (insomnia, anxiety and depression), stratified by hospitalised vs. community adult cases. Insomnia occurred at a greater prevalence for cases compared to controls for hospitalised and non-hospitalised groups, however, anxiety and depression only occurred more frequently in hospitalised cases compared to controls (not for community cases vs. controls).[21]
- A systematic review by Behnood et. al.: used to obtain prevalence estimates for children (age 0-17), for whom there is estimated to be a much lower risk of ongoing symptoms.[66] The meta-analysis from this review combined data from 5 large, controlled studies undertaken in children. Sub-groups by hospitalisation/severity are not considered for children, given the lower risk of hospitalisation compared to adults.

Base case prevalence estimates were then adjusted to account for vaccination, and low virulence variants of SARS-CoV-2. The prevalence of each symptom is multiplied by an OR of 0.55 for those who were vaccinated (both adults and children), given findings from large population-based studies by

Antonelli et. al. and the Office for National Statistics in the UK, indicating reduced odds of long COVID symptoms for those vaccinated, compared to those unvaccinated.[67,68] Separately, the prevalence of each symptom was multiplied by an OR of 0.25, based on findings from a recent UK-based case-control study showing a reduced odds of any ongoing symptoms at least 4 weeks post-infection for Omicron variant infections compared to Delta variant infections.[69] It is assumed that this reduced symptom prevalence will continue into the long COVID period at least 12 weeks post infection.

A multivariate method was applied to account for the joint probability of having two long COVID symptoms, by multiplying the prevalence of each combination of two symptoms, then using multiplicative adjustment to combine DWs for such comorbidity.[70] The probability of having three or more symptoms was assumed to be low, and therefore only the joint probability of two symptoms was included. The following formulae are used for multiplicative adjustment:

$$Combined\ prevalence = Frequency_{Symptom\ A} \times Frequency_{Symptom\ B}$$

$$Combined\ DW = 1 - (1 - DW_{Symptom\ A}) \times (1 - DW_{Symptom\ B})$$

The duration of each symptom was estimated based on a recent analysis by Wulf Hanson et. al., which found a median duration of long COVID symptoms across 10 cohort studies of 3.99 months (interquartile range [IQR] 3.84-4.20) for community cases, and 8.84 months (IQR 8.10-9.78) for previously hospitalised cases.[71] For community cases, a linear decline in the DW applied at onset to full health at 8 months (DR = 0) was applied. For previously hospitalised cases, the given DW was applied to 6 months post infection, followed by a linear decline to 12 months (DR = 0). Exceptions to this were psychological symptoms, for which a shorter duration has been documented – for these symptoms, a linear decline in the DW from onset to 6 months post-infection was applied for both sub-groups.[72] Additionally, as symptoms in children resolve in a much shorter time frame compared to adults, a time frame of 3 months post-infection was applied for long COVID symptoms in children, followed by immediate return to full health (DR = 0).[73,74] Each time frame applied excludes the duration of acute infection, but includes the ongoing symptomatic phase in addition to the long COVID period.[60] No difference in duration is applied for low vs. high virulence variants, given the lack of data available to inform this. Duration and prevalence estimates for each symptom, across relevant patient sub-groups, are shown in Supplementary Table 15.

Supplementary Table 15: Long COVID symptom prevalence and duration estimates

Symptom	Prevalence[†]		Duration
Adults community cases			
	High virulence	**Low virulence**	
Dysosmia	10.4%	2.6%	Linear decline from onset (1-week post-infection) to 8 months
Dysgeusia	8.2%	2.1%	Linear decline from onset (1-week post-infection) to 8 months
Fatigue	7.8%	2.0%	Linear decline from onset (1-week post-infection) to 8 months
Dyspnoea	4.2%	1.1%	Linear decline from onset (1-week post-infection) to 8 months
Chest pain	1.8%	0.5%	Linear decline from onset (1-week post-infection) to 8 months
Muscle weakness	4.1%	1.0%	Linear decline from onset (1-week post-infection) to 8 months
Dizziness	2.3%	0.6%	Linear decline from onset (1-week post-infection) to 8 months
Muscle/joint pain	3.2%	0.8%	Linear decline from onset (1-week post-infection) to 8 months
Headache	3.0%	0.8%	Linear decline from onset (1-week post-infection) to 8 months
Numb limbs	3.2%	0.8%	Linear decline from onset (1-week post-infection) to 8 months
Concentration difficulty[*]	7.6%	1.9%	Linear decline from onset (1-week post-infection) to 8 months
Memory impairment[*]	5.5%	1.4%	Linear decline from onset (1-week post-infection) to 8 months
Insomnia	5.3%	1.3%	Linear decline from onset (1-week post-infection) to 8 months
Adult hospitalised cases[#]			
Dysosmia	7.0%		6 months from onset (4 weeks post-infection), followed by linear decline to 12 months
Dysgeusia	6.9%		6 months from onset (4 weeks post-infection), followed by linear decline to 12 months
Fatigue	13.1%		6 months from onset (4 weeks post-infection), followed by linear decline to 12 months
Dyspnoea	10.3%		6 months from onset (4 weeks post-infection), followed by linear decline to 12 months
Chest pain	4.1%		6 months from onset (4 weeks post-infection), followed by linear decline to 12 months
Muscle weakness	11.3%		6 months from onset (4 weeks post-infection), followed by linear decline to 12 months

Dizziness	4.8%		6 months from onset (4 weeks post-infection), followed by linear decline to 12 months
Muscle/joint pain	6.3%		6 months from onset (4 weeks post-infection), followed by linear decline to 12 months
Headache	4.3%		6 months from onset (4 weeks post-infection), followed by linear decline to 12 months
Numb limbs	7.0%		6 months from onset (4 weeks post-infection), followed by linear decline to 12 months
Concentration difficulty*	10.9%		6 months from onset (4 weeks post-infection), followed by linear decline to 12 months
Memory impairment*	14.3%		6 months from onset (4 weeks post-infection), followed by linear decline to 12 months
Insomnia	19.4%		Linear decline from onset (4-weeks post-infection) to 6 months
Anxiety	11.8%		Linear decline from onset (4-weeks post-infection) to 6 months
Depression	23.2%		Linear decline from onset (4-weeks post-infection) to 6 months
Children			
	High virulence	**Low virulence**	
Dysosmia	8.0%	2.0%	3 months from onset (1-week post-infection)
Headache	5.0%	1.3%	3 months from onset (1-week post-infection)
Eye soreness	2.0%	0.5%	3 months from onset (1-week post-infection)
Sore throat	2.0%	0.5%	3 months from onset (1-week post-infection)
Cognitive difficulties	3.0%	0.8%	3 months from onset (1-week post-infection)

Prevalence estimates presented are for unvaccinated sub-groups – each estimate is multiplied by OR=0.55 to achieve prevalence for vaccinated groups.

[†]Prevalence measured as a risk difference between cases and controls.

**Community and hospitalised sub-group prevalence estimates achieved through weighting of estimates for mild and severe sub-groups from [75]*

[#]No difference in prevalence applied for low vs. high virulence variant infections, for the hospitalised patient sub-group

Supplementary Table 16: Long COVID symptom disability weight estimates

Symptom	Disability Rate[†] (95% CI)	Health state and justification
Adults		
Dysosmia	0.01 (0.004-0.020)	Health state: hearing loss, mild & presbyopia. Assumed to be equivalent to mild impairment of other senses.
Dysgeusia	0.01 (0.004-0.020)	Health state: hearing loss, mild & presbyopia Assumed to be equivalent to mild impairment of other senses.
Fatigue	0.051 (0.036-0.062)*	Health state: infectious disease, post-acute consequences (adjusted down for depression and pain). No reasonable estimate exists for fatigue in the 2019 GBD study, however reasonable estimates exist for muscle/joint

		pain, and depression. Therefore, the DW applied in the present study for depression and muscle/joint pain were subtracted from 'infectious disease, post-acute consequences' DW (DW = 0.219 [95% CI 0.148-0.308]), which is characterised by weakness/tiredness, depression and body pain.
Dyspnoea	0.019 (0.011-0.033)	Health state: chronic obstructive pulmonary disease (COPD) and other chronic respiratory problems, mild.
Chest pain	0.011 (0.005-0.021)	Health state: abdominopelvic problem, mild. Assumed to be equivalent to gastroesophageal reflux disease (GERD).
Muscle weakness	0.004 (0.001-0.008)	Health state: anaemia, mild. Mild anaemia is characterised by feeling slightly weak/tired.
Dizziness	0.032 (0.021-0.046)*	Health state: vertigo (adjusted to estimate 'mild' vertigo health state). Assumed that dizziness is mild form of vertigo – as there is no 'mild' vertigo DW, 'vertigo' DW (DW=0.113 (95% CI: 0.074-0.158)) was multiplied by 0.29 (average ratio of mild/moderate DWs across all outcomes with mild, moderate, and severe ratings in the GBD study 2019).
Muscle/joint pain	0.023 (0.013-0.037)	Health state: musculoskeletal problems, lower limbs, mild.
Headache	0.037 (0.022-0.057)	Health state: headache, tension-type.
Numb/tingling limbs	0.023 (0.013-0.037)	Health state: musculoskeletal problems, lower limbs, mild.
Concentration difficulty	0.069 (0.046-0.099)	Health state: dementia, mild.
Memory impairment	0.069 (0.046-0.099)	Health state: dementia, mild.
Insomnia	0.03 (0.018-0.046)	Health state: anxiety disorder, mild. Anxiety disorder is characterised by difficulty sleeping and concentrating.
Anxiety	0.03 (0.018-0.046)	Health state: anxiety disorder, mild.
Depression	0.145 (0.099-0.209)	Health state: major depressive disorder, mild.
Children		
Dysosmia	0.01 (0.004-0.020)	Health state: hearing loss, mild & presbyopia. Assumed to be equivalent to mild impairment of other senses.
Headache	0.037 (0.022-0.057)	Health state: headache, tension-type.
Eye soreness	0.011 (0.005-0.02)	Health state: presbyopia. No health state for eye pain exists the 2019 GBD study, therefore estimated from presbyopia (characterised by mild near vision loss).
Sore throat	0.006 (0.002-0.012)	Health state: infectious disease, acute episode, mild. Assumed to be equivalent to mild upper respiratory infection.
Cognitive difficulty	0.045 (0.028-0.066)	Health state: attention deficit hyperactivity disorder (ADHD).

		ADHD is characterised by difficulty with concentration and memory.

†Disability Rate applied based on DWs for health states from [16]
*DW not directly taken from GBD study. Weight and 95% CI estimated by adjusting existing weights

Overall long COVID morbidity estimates were calculated for each sub-group, by adding the morbidity contributions for each individual symptom and joint symptom combinations. These are presented in Supplementary Table 17. They are applied to the ABM output for the relevant group of symptomatic acute COVID-19 survivors – both asymptomatic infections and second/any subsequent infections are excluded. Uncertainty is assumed to be high; therefore, a SD of +/- 30% is applied to each estimate.

Supplementary Table 17: Long COVID morbidity estimates

Population group		**Unvaccinated (95% UI)**	**Vaccinated (95% UI)**
High virulence variant, symptomatic			
Adults	Non-hospitalised	0.0075 (0.0031-0.0119)	0.0038 (0.0016-0.0060)
	Hospitalised	0.0442 (0.0182-0.0701)	0.0186 (0.0077-0.0296)
Children*		0.0010 (0.0004-0.0016)	0.0006 (0.0002-0.0009)
Low virulence variant, symptomatic			
Adults	Non-hospitalised	0.0017 (0.0007-0.0026)	0.0009 (0.0004-0.0014)
	Hospitalised	0.0442 (0.0182-0.0701)	0.0186 (0.0077-0.0296)
Children *		0.0003 (0.0001-0.0004)	0.0001 (0.00006-0.0002)

95% UI produced using +/-30% standard deviation.
OR of 0.25 applied to prevalence estimates from high-virulent variant cases to approximate prevalence of long COVID symptoms among low virulence variant cases.
OR of 0.55 applied to prevalence estimates from unvaccinated (<2 doses) cases to approximate prevalence of long COVID symptoms among vaccinated cases.
*Parameterised as ≤18 years in the model

3.5.3 Longer term consequences of SARS-CoV-2 infection

In addition to the long COVID symptoms described above, SARS-CoV-2 infection has been associated with an increased risk of cardiovascular outcomes including myocarditis, stroke, arrhythmias, and acute coronary disease, as well as other sequelae including Type 2 Diabetes Mellitus and acute kidney injury. This risk has been identified particularly in those hospitalised during their acute infection.[76] It is currently unknown whether the risk of chronic outcomes will reduce over time as is assumed for the above discussed long COVID symptoms, or whether such damage confers a lifetime increase in risk. Therefore, this risk has not been included in this model.

3.5.4 Future HALYs lost for COVID-19 deaths

For each COVID-19 death during the 18-month intervention duration, we estimate their future HALY loss (3% discount rate) as follows:

- All-cause mortality rates by sex and age for Australia for 2019 were sourced from GHDx. An ongoing 2% per annum fall in mortality rates (uniform by sex and age) was assumed. On average, people dying of COVID-19 have more comorbidities and are frailer than people not dying of COVID-19. Therefore, we assumed the counterfactual future all-cause mortality rates for people dying of COVID-19 (had they not died of COVID-19) would have been twice that of the general population. Given this is uncertain, we assumed a 10% SD about the 2.0 rate ratio (i.e., 95% UI 1.64 to 2.43).
- All-cause morbidity rates by sex and age were calculated as the GHDx 2019 YLDs for each sex by age group, divided by the population size in 2019, to generate a proportion of quality of life lost (also called prevalent YLDs, or pYLDs). These were assumed constant into the future by sex and age as all-cause morbidity rates by sex and age have been stable over time in the GBD. Just as people who die of COVID-19 have higher counterfactual mortality rates into the future if they had not died (above), the same applies for morbidity. We used our experience with the NZ Burden of Disease study that separately estimates Maori and non-Maori morbidity, where for an all-cause mortality rate ratio of two the all-cause morbidity ratio is approximately 1.5. Accordingly, we assumed the pYLD rate for those dying of COVID-19 into the future (had they counterfactually not died) would have been 1.5 times higher (95% UI 1.23 to 1.82).

The ABM has agents stratified by ten-year age group. Accordingly, we estimated the future HALY loss for decedents aged 5, 15, …, 95 and 105 years old. Estimates are shown in Supplementary Table 18, with standard deviations across Monte Carlo simulated values using the above uncertainties. The model does not distinguish sexes, so we generated an average HALY loss by age, each with uncertainty expressed as SD as a percentage of the HALY loss estimate.

Total HALY loss for each COVID-19 policy scenario was the sum of acute COVID-19 morbidity, long COVID-19 morbidity, and future HALY losses from COVID-19 deaths.

Supplementary Table 18: HALY losses (3% discount rate) for each COVID death, by sex and age

	Females			Males			Combined (average of males and females)	
Age group	*Average HALY loss*	*SD HALY loss*	*SD as % of Average*	*Average HALY loss*	*SD HALY loss*	*SD as % of Average*	*Average HALY loss*	*Average SD as % of HALY loss*
0-9 yrs	23.94	0.55	2.40%	24.28	0.48	2.00%	24.11	2.20%
10-19 yrs	21.89	0.65	3.00%	22.23	0.56	2.50%	22.06	2.75%
20-29 yrs	19.86	0.7	3.60%	20.06	0.6	3.00%	19.96	3.30%
30-39 yrs	17.7	0.7	4.00%	17.62	0.61	3.50%	17.66	3.75%
40-49 yrs	15.04	0.68	4.60%	14.6	0.61	4.10%	14.82	4.35%
50-59 yrs	11.82	0.64	5.50%	11	0.57	5.20%	11.41	5.35%
60-69 yrs	8.17	0.56	6.80%	7.2	0.5	6.90%	7.685	6.85%
70-79 yrs	4.54	0.41	9.10%	3.82	0.36	9.40%	4.18	9.25%
80-89 yrs	1.78	0.23	13.10%	1.52	0.2	13.00%	1.65	13.05%
90-99 yrs	0.48	0.1	20.90%	0.5	0.09	18.20%	0.49	19.55%
100-109 yrs	0.29	0.07	24.50%	0.33	0.07	19.80%	0.31	22.15%

100% correlation on uncertainty between age groups

4 COSTS

4.1.1 Testing costs

In Victoria currently, approximately one third of cases are detected with PCR and two thirds detected with rapid antigen testing (RAT). We included costs for PCR tests based on a reported PCR test positivity rate of approximately 20%. Given we assume 50% case ascertainment (i.e., the number of infections output in our model is double the number of cases that would be notified in Victoria) we applied the cost of 0.83 PCR tests (0.5*0.33*5) to each infection. The current RAT positivity rate in Victoria is unknown, given only positive RAT results are reported. As such we assumed a 10% RAT positivity rate and applied the cost of 3.33 RAT kits (0.5*0.66*10) to each infection. Unit costs for PCR and RAT testing were estimated at $42.50 (+/- 10%) (MBS item 69479) and $7.60 (median wholesale price as reported by the Australian Competition and Consumer Commission, with +/- 10% uncertainty applied) respectively.

4.1.2 Acute COVID-19 morbidity expenditure

We estimated acute COVID-19-related health expenditure using an ingredients approach. For each clinical patient subgroup, we estimated the expected patient pathway through the health system and calculated total health expenditure by first estimating resource use required for a typical patient (e.g., hospital or outpatient visits, or drugs) and then multiplying by unit costs for each of the specified resources based on model outputs. For ICU-admitted patients, we added the cost of their ICU stay onto the cost of a hospital stay.

Supplementary Table 19 shows resource use assumptions. The SARS-CoV-2 pandemic is expected to add additional costs to hospital operations, adjusting for complexity of patients and added infection control requirements including the need for isolation of patients, fitting of personal protective equipment, and enhanced cleaning regimens. As a result, inpatient and ICU hospital costs have been scaled up by 20% to account for these additional costs. We expect that this loading will be a moderate estimate, and likely underestimate the true hospital costs during a pandemic.

Supplementary Table 19: Resource use assumptions by SARS-CoV-2 category

Patient Subgroup	Resource	Explanation
Treated in ICU (note for these patients, resources from a non-	GP visit	Assume all patients will have 2 GP consultations (in addition to those applied for non-ICU hospitalisation), for example as part of post-discharge follow-up

ICU hospitalisation stay are also added)	ER visit	Captured in non-ICU hospitalisation, no additional cost applied
	ICU	Daily cost of ICU admission multiplied by length of ICU stay (see Supplementary Table 5)
	Inpatient (non-ICU)	Added as per costs for non-ICU hospitalisation below
	Pandemic loading	All hospital costs have 20% loading for pandemic†
Hospitalised	GP visit	Assume all patients will have 2 GP consultations prior to hospital admission
	ER visit	Base fee charged for presenting to an ER
	Inpatient	Cost of inpatient day multiplied by length of stay (see Supplementary Table 5)
	Pandemic loading	All hospital costs have 20% pandemic loading†
	Readmission	Approximately 10% of hospitalised patients are readmitted.[77] As such, hospitalisation costs are multiplied by 1.1.
Symptomatic	GP Visit	Assume half of all patients attend a GP appointment during their illness
	Paracetamol	Assume all patients will purchase 1 packet of paracetamol for symptomatic treatment
Asymptomatic	No resources	N/A

†https://revcycleintelligence.com/news/how-much-will-the-covid-19-pandemic-cost-hospitals; accessed 5 May 2020
ER: emergency Room, ICU: intensive care unit, LOS: length of stay, GP: general practitioner

Unit costs for each resource are shown in Supplementary Table 20.

Supplementary Table 20: Unit costs for healthcare resource use (2022 AUD)

Resource and cost (2022 AUD)	Source	Detail
Paracetamol $6.80	PBS item 10582Y (100 units, 500mg)	For symptomatic treatment of mild illness
GP visit $39.10	MBS item 23. Level B General consultation	
ER visit for dyspnoea $907.68	Data from NHCDC Report Round 2014 (Financial year 2019-20).[78]	Adjusted to 2022 cost
Inpatient day $1644.06	Data from H1N1 outbreak using AR-DRG code.	Total cost of inpatient day post ICU. Also assumed for all non-ICU patients. Adjusted to 2022 cost.
ICU day $6710.86	Micro-costed from H1N1 outbreak.	Total cost per day admitted to ICU. Allied health and overheads included. Adjusted to 2022 cost.

PBS: pharmaceutical benefits scheme, MBS: medicare benefits schedule, AR-DRG: Australian-refined diagnostic related groups, ICU: intensive care unit. All costs have +/- 10% uncertainty on log normal distribution applied.

Given the above, the following costs were applied for acute COVID-19-related health expenditure (note these costs are additive, unlike the morbidity calculations above):

- For an infected, asymptomatic agent: no additional costs
- For an infected, symptomatic agent: add 0.5*[GP visit cost] and 1*[paracetamol cost]
- If an agent is hospitalised (*in addition* to symptomatic agent costs):

- Add 1.5*[GP visit cost] and 1.2*[ER visit cost]
- Add length of hospital stay (days)*[cost of inpatient hospital bed per day]*1.1*1.2

- If an agent is admitted to ICU (*in addition* to hospitalised agent costs):
  - Add 2*[GP visit cost]
  - Add length of ICU stay (days)*[cost of ICU bed per day]*1.2

4.1.3 Long COVID morbidity expenditure

Few observational studies of long COVID occurrence, in Australia or internationally, have included thorough data collection of healthcare utilisation following acute COVID-19 infection. Additionally, clinical data on healthcare use relating to long COVID is not currently collected in Australia – the ICD-10 code assigned for long COVID is yet to have associated published hospital data. Therefore, in order to estimate the healthcare costs associated with long COVID, we applied expert estimates on the likely healthcare use for those experiencing long COVID symptoms, based on available international data and formal guidelines for healthcare professionals in Australia provided by the Royal Australian College for General Practitioners (RACGP) and the National COVID-19 Clinical Evidence Taskforce.[23,24] An additional informal expert knowledge elicitation was also conducted with General Practitioners (GPs) to confer information obtained from the former sources. Supplementary Table 21 shows the resources applied to each sub-group; unit costs are indicated in Supplementary Table 22. For estimates specific to particular long COVID symptoms, costs are assigned to proportions of symptomatic acute COVID-19 survivors with the relevant long-COVID-19 symptom (see 'Long COVID morbidity' section above for methodology).[19,75]

The following treatment items are considered:

- GP attendance: current guidelines indicate that long COVID is predominantly managed in the primary care setting, though few evidence-based management options currently exist.[24] In a survey of COVID-19 survivors 6-months post-acute illness (pre-Omicron, unvaccinated cohort) in Zurich, Switzerland, Menges et al. found that 63% of previously hospitalised adults, and 29% adult community cases, had at least 1 GP consult related to COVID-19 following the acute illness period.[79] The estimate for hospitalised adults is multiplied by 1.5 to include GP use in the second 6 months (reflecting the estimated duration of long COVID for this sub-group).
- Specialist attendance: a survey of symptomatic COVID-19 survivors (pre-Omicron, unvaccinated cohort) attending a post-COVID assessment clinic in London found that 18% were referred on to

specialist management, most commonly to a cardiologist, neurologist or ENT specialist.[80] Therefore, 18% of those who attend a GP at least once, are assumed to go on to see a specialist (single consult).

- ER attendance: ER attendance is calculated specifically for those experiencing dyspnoea or chest pain – these groups are assumed to present to ER once throughout the disease course.
- Medication: medication use is estimated based on RACGP guidelines and informal expert elicitation with GPs. Short-acting beta-agonists (Salbutamol), or corticosteroids (Budesonide), are applied for patients with ongoing dyspnoea.[23] Paracetamol is applied for those with headache and muscle/joint pain.[23]
- Diagnostics: routine testing is advised by RACGP to rule out other causes of symptoms, e.g., anaemia. Therefore, for those with fatigue, routine blood testing including iron studies, a full blood examination, electrolytes and thyroid function tests are ordered. It is assumed that any diagnostic tests required for those with ongoing dyspnoea/chest pain (e.g., chest x-ray or ECG as per RACGP guidelines) occur at ER presentation, so are not separately included to avoid double costing. Other symptoms are judged as being too infrequent to consider any other specific testing.

Magnusson et al. conducted a large study in Norway on healthcare use in children in the period 5-12 weeks post-COVID infection.[81] No significant difference was found in healthcare utilisation between cases and COVID-negative controls during this period. This is in keeping with the relatively low morbidity impact of long COVID estimated for children compared to adults. Therefore, costs for children are not considered.

The proportions indicated in Supplementary Table 21 are calculated and applied for each sub-group of initially symptomatic acute COVID-19 survivors. For symptom-specific costs, proportions reflect long COVID symptom frequencies calculated for each patient sub-group (see long COVID morbidity section above for methodology). GP and specialist attendance proportions applied from the aforementioned literature are multiplied by an OR of 0.55 and separately by an OR of 0.25 to reflect use in vaccinated sub-groups and for low virulence variant infections (e.g., Omicron), respectively (in line with long COVID morbidity estimates).[67-69]

Supplementary Table 21*: Resource use assumptions for COVID-19 survivors by SARS-CoV-2 category*

Patient subgroup	Treatment item	Source

Community (acute infection) adult cases	GP visit	20% acute COVID-19 community cases have 1-2 visits, 7% 3-5 visits, 1% 6 visits.[79] For vaccinated groups, proportions are multiplied by an OR of 0.55. For low virulence variant groups, proportions are multiplied by an OR of 0.25.
	Specialist visit	18% who see GP (above) are referred to specialist.[82] Assume single visit. For vaccinated groups, proportions are multiplied by an OR of 0.55. For low virulence variant groups, proportions are multiplied by an OR of 0.25.
	ER visit	Assume those with dyspnoea and those with chest pain present to ER once. Standard ER presentation cost for asthma (to represent dyspnoea) and chest pain, are applied.
	Medication (budesonide, salbutamol)	Assume patients with dyspnoea are prescribed either salbutamol or budesonide (50/50 split) (single prescription with 5 repeats, equating to approximately 6 months use).
	Medication (paracetamol)	Assume patients with muscle/joint pain and headache purchase 1 packet of paracetamol.
	Diagnostics	Iron studies for those with fatigue to rule out anaemia, per RACGP guidelines.[23] Routine testing of FBC, Electrolytes and TFTs also included for this group.
Hospitalised (acute infection) adult cases	GP visit	During first 6 months, 44% 1-2 visits, 12% 3-5 visits, 5% 6 visits.[79] Proportions halved in the second 6 months, to reflect longer duration of symptoms compared to non-hospitalised patients. For vaccinated groups, proportions are multiplied by an OR of 0.55.
	Specialist visit	18% who see GP are referred to specialist.[82] Assume single visit.
	ER visit	Assume those with dyspnoea and those with chest pain present to ER once. Standard ER presentation cost for asthma (to represent dyspnoea) and chest pain, are applied.
	Diagnostics	Iron studies for those with fatigue to rule out anaemia, per RACGP guidelines. Also include routine FBC, Electrolyte and TFT testing.
	Medication (budesonide, salbutamol)	Assume patients with dyspnoea are prescribed either salbutamol or budesonide (50/50 split) (single prescription with 5 repeats, equating to approximately 6 months use). Proportions halved in the second 6 months, to reflect longer duration of symptoms compared to non-hospitalised patients.
	Medication (paracetamol)	Assume patients with muscle/joint pain and headache purchase 1 packet of paracetamol.

GP: general practitioner; ER: emergency room; FBC: full blood count; TFT: thyroid function tests.

Supplementary Table 22: Unit costs for long COVID healthcare resource use by COVID-19 survivors

Resource and cost (2022 AUD)	Source	Detail
ER visits ER visit for chest pain $998.97 (plus $199.79 for 20% pandemic loading) ER visit for dyspnoea $907.68 (plus $181.54 for 20% pandemic loading)	Data from NHCDC Report Round 2014 (Financial year 2019-20).[78]	Average cost per ER presentation, using AECC codes for chest pain and asthma (complexity level B for each). Adjusted to 2022 value.
Medication Budesonide (dyspnoea) $40.13 Salbutamol (dyspnea) $26.30 Paracetamol (headache/muscle/joint pain) $6.80	 PBS item 2065Q (500μg/2mL inhalation solution, 30 x 2mL ampoules).[83] PBS item 8288F (100μg/actuation inhalation, 200 actuations).[84] PBS item 10582Y (500mg tablets, 100 units).[85]	 PBS fee for budesonide with 5 repeats. PBS fee for salbutamol with 5 repeats. PBS fee for paracetamol with 1 repeat.
GP consultation $39.10	MBS item 23. Level B General consultation.[86]	MBS fee for standard attendance by General practitioners.
Specialist consultation $76.80	MBS item 104. Initial referred consultation.[87]	MBS fee for standard initial attendance by specialist practitioner.
Pathology testing Iron studies $27.70 TFT $29.60 FBE (including FBC) $14.45 Electrolytes $13.35	 MBS item 66596.[88]MBS item 66719.[89] MBS item 65070.[90] MBS item 66509.[91]	MBS fees for pathology testing items.

ER: emergency room; NHCDC: national hospital cost data collection; AECC: Australian emergency care classification; PBS: pharmaceutical benefits scheme; GP: general practitioner; MBS: Medicare benefits schedule; TFT: thyroid function tests; FBE: full blood examination; FBC: full blood count

The total cost for each patient sub-category is presented in Supplementary Table 23. Each overall cost is applied to the relevant sub-group of all previously symptomatic acute COVID-19 survivors.

Supplementary Table 23: Cost per patient category

Population group		Unvaccinated (95% UI)	Vaccinated (95% UI)
High virulence variant symptomatic			
Adults	Non-hospitalised	$95.29 (39.26-151.32)	$52.98 (21.83-84.14)
	Hospitalised	$269.76 (111.14-428.37)	$148.37 (61.13-235.60)
Low virulence variant symptomatic			
Adults	Non-hospitalised	$24.08 (9.92-38.24)	$13.25 (5.46-21.03)
	Hospitalised	$269.76 (111.14-428.37)	$148.37 (61.13-235.60)

UI applied using +/- 30%, in line with uncertainty applied for long COVID morbidity estimates. Costs apply to adults (≥18 years).

4.1.4 Intervention costs

Supplementary Table 24: Vaccine and respirator costs (2022 AUD)

	Item	Price	SD	Source
Vaccination variable costs	Current mRNA vaccine (per dose)	$35	10%	Financial Times
	Omicron-specific vaccine (per dose)*	$44	10%	Estimated 1.25 times the cost of current generation mRNA vaccine
	Multivalent vaccine (per dose)*	$52.50	10%	Estimated 1.5 times the cost of current generation mRNA vaccine
	Vaccine transport (per dose)	$1	10%	Estimate
	Personnel, consumables, waste management (per dose)	$30	10%	Estimated from relevant MBS items for GP administration of vaccines or rebate for pharmacy administration
	Overheads (per dose)	$1	10%	Estimate
Vaccination fixed costs	Promotion and advertising (per month (30.333 days))	$615,000	20%	Estimated from Australian Government Department of Finance report on COVID-19 vaccination campaign advertising spending 2020-2021 financial year, scaled to Victorian population and one month, updated to 2022 cost and rounded to nearest $5,000
Respirators variable costs	Respirator costs (per person, per round, i.e., 10 masks)	$14.70	10%	Commercial price for N95 masks in Australia
	Distribution cost (per person, per round)	$2.73	10%	Assumed 20% of the cost of vaccine administration cost and 2.2 persons

				aged ≥10 years in each household collecting respirators
	Overheads (per person, per round)	$0.09	10%	Assumed 20% of that for vaccination program and 2.2 persons aged ≥10 years in each household collecting respirators
Respirators fixed costs	Promotion and advertising (per month (30.333 days))	$460,000	20%	Estimated from Australian Government Department of Finance report on general COVID-19 health campaign advertising spending 2020-2021 financial year, scaled to Victorian population and one month, updated to 2022 cost and rounded to nearest $5,000
	Mask storage over 18 months (full stockpile)	$295,000	20%	6,400 respirators per pallet, commercial price for storage $4.50 per pallet per week, 10 respirators per person per round, approximately 586,250 ≥10-year-olds in Victoria. Rounded to nearest $5,000

*Omicron-specific and multivalent vaccine dose costs 100% correlated

Regarding fixed costs for vaccines, three months of promotion and advertising is conducted per vaccination rollout event (i.e., with each subsequent dose that becomes available). For respirators, promotion and advertising continues for the duration spent in stages 3 and above, and the storage cost of the stockpile applies once (on 1 April 2022) whenever the mask policy option is active in the model.

4.1.5 GDP costs of stages of PHSMs

We updated previously published estimates of GDP loss due to government-imposed pandemic control interventions[25] to estimate the current economic impact of time spent in various stages of PHSMs. Due to societal changes since the beginning of the pandemic (such as adaptations to facilitate remote working) we assumed no GDP impacts in stages 1 and 2. GDP loss in stages 3 – 5 in 2022 and 2023 are difficult to estimate, but given societal change we assumed wide uncertainty of 10% to 50% (uniform

distribution) of the GDP losses per week estimated in 2020. GDP losses per stage were thus estimated by the following:

Supplementary Table 25: GDP loss by stage of PHSMs (per week)

Stage	GDP loss per week in stage (AUD billions, Victoria only)
1	$0
2	$0
3	10% to 50% (uniform distribution) of $0.725
4	10% to 50% (uniform distribution) of $1.275
5	10% to 50% (uniform distribution) of $2.61

4.1.6 Unrelated disease costs

Consistent with recommended practice in cost effectiveness analyses we included 'unrelated disease costs' in the economic evaluation. This means that in addition to including the health expenditure on SARS-CoV-2 cases as above, future knock-on changes in health system expenditure are also included. This means that if someone dies due to a SARS-CoV-2 infection, their reduced health expenditure in the future is included (leading to a potentially net negative expenditure depending on the balance of costs, age and discount rate).

We estimated these future health expenditure savings for each COVID-19 death in the 18-month intervention duration, using an approach similar to that above for future HALY losses (Supplementary Table 18). Specifically, we used lifetables with sex and age-specific all-cause mortality rates (double that of the general population due to people dying of COVID-19 having more co-morbidities and frailty) to estimate remaining life years. For each expected remaining life-year, 1.5 times (due to greater comorbidities) the sex and age-specific expected annual health expenditure according to AIHW estimates[8] was allocated.

We assumed variable health expenditure was 90%, allowing 10% for fixed costs in running services. AIHW estimates capture 62.7% of total health expenditure, therefore we multiplied all age by sex empirical estimates by a factor of 90/62.7 to generate the estimated predicted Australian variable health expenditure per capita, by age and sex. Next, we inflation adjusted these expenditures to 2022 AUD using Australian CPI adjustment factors. Finally, we also generated USD values using OECD purchasing power parity (https://data.oecd.org/price/inflation-cpi.htm; 2021 PPP used as 2022 not available at time).

Males and females are not distinguished separately in the ABM. So also shown in the Supplementary Table 26 are the average by sex, which is used in the modelling. Noting the SD about the sex specific estimates, we set the SD as 15% of the age-specific estimate (normal distribution).

Supplementary Table 26: Future averted health expenditure for each COVID-19 death (3% discount rate; Aus $ 2020), by sex and age

	Females			Males			Combined (average of males and females)	
Age group	*Expected value, Aus$ CPI adj to 2022*	*Expected value, US$ OECD PPP adj*	*SD in Monte Carlo uncertainty analyses as % of expected*	*Expected value, Aus$ CPI adj to 2022*	*Expected value, US$ OECD PPP adj*	*SD in Monte Carlo uncertainty analyses as % of expected*	*Expected value, Aus$ CPI adj to 2022*	*Expected value, US$ OECD PPP adj*
0-9 yrs	$79,825	$54,526	15.90%	$97,190	$66,387	12.40%	$88,508	$60,457
10-19 yrs	$90,913	$62,099	15.70%	$77,596	$53,003	12.10%	$84,255	$57,551
20-29 yrs	$158,112	$108,000	15.70%	$79,192	$54,093	12.30%	$118,652	$81,047
30-39 yrs	$215,990	$147,534	15.00%	$99,970	$68,285	11.70%	$157,980	$107,910
40-49 yrs	$175,489	$119,869	14.00%	$128,337	$87,662	11.10%	$151,913	$103,766
50-59 yrs	$180,501	$123,293	13.60%	$160,764	$109,811	11.00%	$170,633	$116,552
60-69 yrs	$193,058	$131,870	13.90%	$191,507	$130,811	11.20%	$192,283	$131,341
70-79 yrs	$188,429	$128,708	14.40%	$188,763	$128,936	11.50%	$188,596	$128,822
80-89 yrs	$123,066	$84,061	14.70%	$130,017	$88,810	11.70%	$126,542	$86,436
90-99 yrs	$56,881	$38,853	14.30%	$67,573	$46,157	11.60%	$62,227	$42,505
100-109 yrs	$43,017	$29,383	13.00%	$53,564	$36,587	10.60%	$48,291	$32,985

100% correlation on uncertainty between age groups

5 NET MONETARY BENEFIT ANALYSES

We estimated the monetary benefit (NMB)[92] for each of the 100 runs:

$$NMB_{ijk} = \left(HALYs_{ik} \times WTP_j\right) - Cost_{ik}$$

Where:

- i indexes the 100 iterations
- j indexes the WTP
- k indexes the four policy scenarios
- and Cost is the net health expenditure for the health system perspective analyses, and from the societal perspective adds GDP costs to health system costs.

Within each iteration i and WTP j, the policy scenario with the highest NMB is selected. Across all 100 iterations, each policy response k will have a probability of having the highest NMB, and the policy option with the highest probability is deemed 'optimal' at that WTP. Finally, these outputs can be shown as cost effectiveness acceptability curves.

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