Data sources/assumptions informing a Bayesian network to assess chances of having long COVID six months post-infection in Australia

Model inputs	Data sources, assumptions, rationale (references)
Risk of symptomatic infection	Risk of symptomatic infection was set to 1.0 to ensure risk estimates within the model pertain to a scenario in which one is already symptomatically infected.
Vaccine effectiveness against hospitalisation and ICU admission	Data on vaccine effectiveness against hospitalisation and ICU admission were drawn from the UK Government's Vaccine Surveillance Report Week 14 2023[1]. Incomplete vaccination (one dose only) was assumed to be ineffective. When data were presented in smaller time categories than presented in the model, data were averaged to received estimated particular to the model time-points. Data pertaining to the fourth dose were presented as relative to protection from a third dose received 25-39 weeks ago; calculations using the provided estimate of 52.6% were made to achieve an estimate of unrelative vaccine effectiveness. Insufficient data were available at the time of model development to include possible effects of ongoing medical conditions on vaccine effectiveness. See Supplementary Table 1.
Drug treatment	The model assumes you receive no treatment, except in the bars showing 'Chance if you get antiviral drug treatment during the first week of infection'. This option assumes an equal likelihood of receiving molnupiravir (within first five days of testing), metformin (1500mg immediate release taken over six days) within 7 days of symptom onset, metformin (1500mg immediate release taken over six days) within three days of symptom onset, or nirmatrelvir (Paxlovid) (within first five days of testing). See Supplementary Table 2.
Hospitalisation	To achieve estimates of case numbers for symptomatic COVID-19 cases from omicron variants requiring hospitalisation within Australia, and to keep separate the effects of vaccination, data on unvaccinated, hospitalised cases between 26/11/21 and 05/02/22 were drawn from the New South Wales (NSW) COVID-19 Surveillance Reports[2]. These proportions were then applied to the Australian population, assuming an equal proportion of hospitalisations throughout Australia as in NSW. Data were manipulated to provide estimates for age categories displayed within the model. As data were taken from population estimates, the effect of number of ongoing medical conditions on hospitalisation risk is assumed to be integrated. Data on effects of repeat infection on hospitalisation risk were drawn from published research using the US Department of Veterans Affairs national healthcare databases[3]; the model thus operates under the assumption that these data may apply more broadly to the Australian population. Data on effects of each treatment option on reducing the risk of hospitalisation from COVID-19 were drawn from published literature[3–6]. See Supplementary Table 3.
ICU admission	To achieve estimates of case numbers for symptomatic COVID-19 cases from omicron variants requiring ICU admission within Australia, and to keep separate the effects of vaccination, data on unvaccinated, ICU-admitted cases between 26/11/21 and 05/02/22 were drawn from the New South Wales (NSW) COVID-19 Surveillance Reports[2]. These proportions were then applied to the Australian population, assuming an equal proportion of ICU admissions throughout Australia as in NSW. Data were manipulated to provide estimates for age categories displayed within the model. As data were taken from population estimates, the effect of comorbidity number on ICU admission risk is assumed to be integrated. Data on effects of repeat infection on ICU admission risk were drawn from published research using the US Department of Veterans Affairs national healthcare databases[3]; the model thus operates

	under the assumption that these data may apply more broadly to the Australian population. This assumption is justified and conservative based on results from other published literature[7]. Data on effects of each treatment option on reducing the risk of ICU admission from COVID-19 were drawn from published literature[4–6]. See Supplementary Table 3.
Vaccine effectiveness against death if infected	Data on vaccine effectiveness against death were drawn from the UK Government's Vaccine Surveillance Reports Weeks 5, 14, and 24, 2023[1,8,9]. Incomplete vaccination (one dose only) was assumed to be ineffective. When data were presented in smaller time categories than presented in the model, data were averaged to received estimated particular to the model time-points. Insufficient data were available at the time of model development to include possible effects of number of ongoing medical conditions on vaccine effectiveness. See Supplementary Table 1.
Die from COVID-19	To achieve estimates of case numbers for symptomatic COVID-19 cases from omicron variants ending in mortality within Australia, and to keep separate the effects of vaccination, data on unvaccinated, COVID-19 fatalities between 26/11/21 and 05/02/22 were drawn from the New South Wales (NSW) COVID-19 Surveillance Reports[2]. These proportions were then applied to the Australian population, assuming an equal proportion of deaths throughout Australia as in NSW. Data were manipulated to provide estimates for age categories displayed within the model. As data were taken from population estimates, the effect of number of ongoing medical conditions on mortality risk is assumed to be integrated. Data on effects of repeat infection on mortality risk were drawn from published research using the US Department of Veterans Affairs national healthcare databases[3]; the model thus operates under the assumption that these data may apply more broadly to the Australian population. Data on effects of each treatment option on reducing the risk of death from COVID-19 were drawn from published literature[4–6]. Data pertaining to metformin were on reducing risk of hospitalisation or death; it has been assumed this data is acceptable to use as the protection of the treatment again death alone may be estimated to be higher. See Supplementary Table 3.
Long COVID outcomes	Data on the effects of vaccination status[10], infection number[3], hospitalisation status, age, sex, and number of comorbidities[11] on six-month risks of long COVID outcomes affecting different organ systems were drawn from three published studies performed by Ziyad Al-Aly et al. using the US Department of Veterans Affairs national healthcare databases. Use of these three studies in combination allowed for seamless integration of these many effects on risk and negated the need to make assumptions to achieve estimates for the chosen model timepoint, as all studies reported risks at six months post-infection. However, this data is limited by describing a skewed population of 90% men with an average age of 61 years – consequently, the model relies on the assumption that these estimates are applicable to the broader population. Data on effects of each treatment option on reducing the risk of long COVID were drawn from published literature[4–6]. See Supplementary Table 4.

Supplementary Table 1. Vaccine effectiveness against hospitalisation and ICU admission or death in those infected with SARS-CoV-2

Vaccine dose and timing	Vaccine effectiveness against	
	Hospitalisation & ICU admission[1]	**Death if infected**
None	0%	0%
1st		
3 weeks ago	0%	0%
2nd		
2 weeks – 5 months ago	71.24%	63.06% [8]
6–11 months ago	54.4%	47.9% [8]
12+ months ago	35.5%	49.7% [8]
3rd		
2 weeks – 5 months ago	69.5%	79.44% [1]
6–11 months ago	52.35%	62.38% [1]
12+ months ago	52.3%	56.9% [1]
4th		
2–4 weeks ago	83.53%	80.9% [1]
5–9 weeks ago	78.95%	79.5% [1]
10–14 weeks ago	71.48%	71.2% [1]
15+ weeks ago	63.7%	68.2% [1]

Supplementary Table 2. Effect of drug treatment during the first week of acute SARS-CoV-2 infection on the relative risk of having long COVID symptoms six months post-infection

Drug treatment	Relative risk of		
	Post-acute sequelae of COVID-19	**Hospitalisation or ICU admission**	**Death**
None	1.0	1.0	1.0
Molnupiravir[4]	0.86	0.86	0.62
Metformin within 7 days of onset	0.59 [5]	0.42 [5]	0.47 [12]
Metformin within 3 days of onset	0.37 [5]	0.42 [5]	0.47 [12]
Nirmatrelvir[6]	0.74	0.76	0.53

Supplementary Table 3. Hospitalisations, ICU admissions and deaths from COVID-19 in the unvaccinated population of NSW during the omicron wave, 26/11/21–05/02/22[2]

Age group	Cases	Hospitalisations (proportion of cases)	ICU admissions (proportion of cases)	Deaths (proportion of cases)
18-60	77,433	451 (0.58%)	48 (0.06%)	13 (0.02%)
61-70	6693	146 (2.17%)	25 (0.37%)	21 (0.31%)
71+	4726	397 (8.40%)	38 (0.81%)	165 (3.49%

Supplementary Table 4. Long COVID outcome example calculation

Effect	Example: Six-month risk of cardiovascular long COVID for an unvaccinated female aged 65 years living with 4+	Risk

	comorbidities who is hospitalised while experiencing COVID-19 for the second time, and received metformin within 7 days of symptom onset	
Vaccination status[10]	Of 1000 symptomatic COVID-19 cases in unvaccinated persons, 102.52 are estimated to suffer from cardiovascular symptoms of long COVID six months post-infection. Risk = 0.10252	102.52 / 1000 = 0.1025
Infection number[3]	Those experiencing their second symptomatic SARS-CoV-2 infection have a hazard ratio of 2.1 for experiencing cardiovascular symptoms of long COVID six months post-infection. Risk = 0.10252*2.1	0.1025 * 2.1 = 0.2153
Hospitalisation or ICU status and Age[11]	Of 1000 hospitalised COVID-19 cases, 98.31 are estimated to suffer from cardiovascular symptoms of long COVID six months post-infection. This increases to 102.85 in those aged 61-70. The hazard ratio for this age range therefore equals 1.046 in comparison to the hazard ratio of 1 for the total hospitalised population.	0.2153 * 1.046 = 0.2252
Sex[11]	For hospitalised females, the six-month hazard ratio for suffering from cardiovascular symptoms of long COVID equals 0.904.	0.2252 * 0.904 = 0.2036
Number of ongoing medical conditions[11]	For hospitalised patients with four or more comorbidities, the six-month hazard ratio for suffering from cardiovascular symptoms of long COVID equals 1.391.	0.2036 * 1.391 = 0.2832
Drug treatment[5]	As this patient is high-risk due to living with multiple ongoing medical conditions, she is treated with metformin within seven days of symptom onset, reducing her relative risk to 0.59.	0.2832 * 0.59 = 0.1671

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