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Briefing paper

Potential scale of Long COVID cases from the Omicron wave in Australia

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Introduction

Since the emergence of the Omicron variant on 26 November 2021, more than 1.5 million COVID-19 cases had been recorded by mid-January in Australia [1]. As Australia enters its third year battling COVID-19, case numbers in this latest wave have dwarfed those seen in earlier outbreaks in this country.

While the majority of patients recover from COVID-19, a proportion of patients continue to experience ill health post COVID infection [2]. Long COVID, also known as long-haul COVID, post-acute, PASC or chronic COVID [2, 3] is yet another facet of the COVID-19 pandemic that is likely to add more pressure to the healthcare system. Long COVID is clinically as defined as *"a condition that occurs in individuals with a history of probable or confirmed SARS CoV-2 infection, usually 3 months from the onset of COVID-19 with symptoms and that last for at least 2 months and cannot be explained by an alternative diagnosis"* by the World Health Organization [3]. This condition presents a wide array of symptoms that could affect a patient's daily functioning, work productivity, and overall quality of life [2, 4-7].

Recent studies shed insights into the diagnosis and treatment of Long COVID [8, 9]. A study in Australia found that Long COVID patients had persistent immunological dysfunction for at least 8 months post initial mild to moderate COVID infection [8]. Another study in the US reported four possible factors that increase the likelihood of developing long lasting effect of COVID such as high viral load, autoantibodies, Type 2 diabetes and Epstein-Barr [9]. Current treatment options for Long COVID are still based on symptom management and various potential treatments are still under investigation [10]. However, while not conclusive, a growing number of studies provide evidence that vaccination could provide a protective effect from Long COVID even in "breakthrough" COVID-19 infections [11-13].

Given the scale of COVID cases in Australia that have occurred in the midst of the Omicron outbreak [1], there is clearly potential for a large number of Long COVID cases to unfold in the coming months. In previous modelling (undertaken prior to Omicron), we explored the potential impact of Australia's National Reopening Plan on Long COVID cases, and predicted that Australia could potentially experience more than 50,000 Long COVID cases at week 5, 34,000 cases at week 12 and approximately 3,000 cases at week 52 upon international border reopening given a 70% vaccination rate and high seeding infection rate, while maintaining low public health and social measures and partial effectiveness of test, trace, isolate and quarantine program [14, 15]. The Omicron wave has already far surpassed the COVID infection case numbers originally modelled under the National Reopening Plan. Unfortunately, there is still no national data on the actual magnitude of Long COVID cases in Australia.

This study therefore provides an update of our earlier modelling of Long COVID cases, to reflect the emergence of Omicron in Australia and the very large number of COVID-19 infections experienced over the last two months. Our objective is to provide rapid, conservative estimates of the minimum number of Long COVID cases likely to eventuate in Australia over coming months.

Methods

The scale of Long COVID in Australia during the emergence of the Omicron COVID outbreak was modelled by multiplying the number of patients who survive the acute COVID infection by the probability of developing Long COVID, obtained from studies undertaken in New South Wales (Liu et al.) and the United Kingdom by the Office for National Statistics [15-17].

COVID-19 survivors

The number of COVID cases and COVID-19 mortality data from the period of 26 November 2021 to 16 January 2022 were acquired from publicly available sources [1, 18-20]. Only patients who survive COVID-19 infection were included in this analysis on the assumption that only COVID-19 survivors can potentially experience lingering effects of COVID-19.

The actual number of vaccinated and unvaccinated individuals who were infected with COVID-19 is often not publicly available. Thus, the number of COVID-19 cases was stratified by vaccination status using data from the NSW epidemiological report [21]. According to the NSW epidemiological report, a large proportion of fully vaccinated individuals were infected with COVID from the period of 26 November 2021 to 08 January 2022. 70.5% (267,381) of patients infected with COVID-19 were fully vaccinated, 9.7% (36,797) were either partially vaccinated or with no effective doses or not eligible and 19.8% (74,878) were under investigation[21]. Since 19.8% of the reported cases were under investigation, we distributed these cases in the same proportion as the ascertained cases. Similarly, the number of deaths was stratified by vaccination status using the same approach. Using this data, it was estimated that 87.9% COVID-19 infections had occurred in fully vaccinated individuals. This number was applied to the total number of COVID cases in NSW[19], Victoria [18] and Australia [1] from the period of 26 November 2021 to 16 January 2022. Table 1 shows the number of cases used in this model.

Due to the sudden surge of COVID-19 infection in mid-December 2021, Australian COVID-19 testing centres and laboratories were overwhelmed and had exceeded their capacity leading to the recommendation of the use of Rapid Antigen test (RAT) as an alternative method for COVID-19 testing [22-24]. However, during this period, the supply of RAT was limited [25, 26] and many patients with a true COVID-19 infection may have gone untested and/or unreported. For this reason, the numbers noted in the publicly available data will clearly understate the real number of COVID-19 cases in the Australian community during this period. In the absence of clear estimates of the scale of this underreporting, we have not attempted to adjust our model to reflect this fact.

Rather than incorporating further epidemiological modelling of the likely future evolution of the current outbreak, we have used the following simplifying assumption in our analysis. We assume that the national outbreak peaked in mid-January 2022, and that approximately the same number of cases will be seen on the "way down" from this peak as were seen on the "way up". While simplistic, this assumption provides a conservative estimate; it is substantially more likely that plateauing (or indeed upticks) would add further to the eventual total number of cases, rather than the downslope proving to be substantially smaller than the upwards slope. We therefore justify this simplifying assumption by our stated objective of providing conservative, minimum estimates.

Table 1 COVID-19 Cases used in the analysis

Variable	Description	Cases	Source
ACTUAL 26 Nov – 16 Jan			
NSW COVID cases (vacc)	Outbreak from 26 November 2021 to 16 January 2022 (actual reported)	508,146	[19]
NSW Victorian COVID cases (unvacc)	Outbreak from 26 November 2021 to 16 January 2022 (actual reported)	69,906	[19]
Victoria COVID cases (vacc)	Outbreak from 26 November 2021 to 16 January 2022 (actual reported)	314,646	[18]
Victoria COVID cases (unvacc)	Outbreak from 26 November 2021 to 16 January 2022 (actual reported)	43,286	[18]
Australia COVID cases (vacc)	Outbreak from 26 November 2021 to 16 January 2022 (actual reported)	1,388,951	[1]
Australia COVID cases (unvacc)	Outbreak from 26 November 2021 to 16 January 2022 (actual reported)	191,080	[1]
DOUBLED			
NSW COVID cases (vacc)	Actual numbers - doubled	1,016,502	Assumption
NSW Victorian COVID cases (unvacc)	Actual numbers - doubled	139,842	Assumption
Victoria COVID cases (vacc)	Actual numbers - doubled	629,632	Assumption
Victoria COVID cases (unvacc)	Actual numbers - doubled	86,620	Assumption
Australia COVID cases (vacc)	Actual numbers - doubled	2,778,523	Assumption
Australia COVID cases (Unvacc)	Actual numbers - doubled	382,246	Assumption

Note: Vacc= Vaccinated, Unvacc= Unvaccinated, NSW=New South Wales

Probability of developing long COVID

Similar to our previous calculation of likely Long COVID cases in Australia upon international border reopening [14, 15], one source for the probability that patients will experience persistent symptoms after COVID-19 acute infection was obtained from the study undertaken in NSW by Liu et al [17]. However, in this current analysis, we have also used the most updated Long COVID prevalence estimates released by the ONS for the United Kingdom [16] on the 16th September 2021, which presented three approaches: Approach 1 presents the *"prevalence of any of the 12 symptoms such as fever, headache, muscle ache, weakness/tiredness, nausea/vomiting, abdominal pain, diarrhoea, sore throat, cough, shortness of* *breath, loss of taste, and loss of smell at a point in time after infection",* Approach 2 presents the "*prevalence of continuous symptoms after infection",* and Approach 3 presents the *"prevalence of self-reported long* COVID [16]. These latest ONS estimates were lower those released by ONS in April 2021 [16], which we had used in our earlier modelling. The estimates of Liu et al remain the most comprehensive study of Long COVID in an Australian cohort, but do not currently track patients for more than a few months. The most recent ONS estimates represent probably the largest and most robust study of Long COVID a very large population of confirmed COVID cases yet available worldwide. Therefore, results are presented for four sets of Long COVID prevalence:

- *Liu et al*: Long COVID estimate using the extrapolated NSW data
- *ONS Approach 1*: Long COVID estimate using the extrapolated ONS Approach 1 data
- *ONS Approach 2*: Long COVID estimate using the extrapolated ONS Approach 2 data
- *ONS Approach 3*: Long COVID estimate using the extrapolated ONS Approach 3 data

In using these estimates of Long COVID prevalence, readers should note that we are explicitly assuming that Omicron infections will prove to display the same likelihood of developing Long COVID as has been observed with previous variants. Data on the actual probability of Long COVID in people infected with Omicron are not yet available; but given the clear evidence that Long COVID frequently develops in people with "mild" initial infections, we feel this assumption is strongly defensible.

Since the ultimate duration of Long COVID is still unknown, datapoints were extrapolated up to two years by fitting an exponential decay curve using the actual ONS [16] and Liu et al [17] data points [27]. Table 2 shows the decay function constant and rate of decay that were used to extrapolate the data into two years.

Table 2 Decay function constant and rate of decay parameters

Source	**Constant**	**Power term**
Liu et al. (Baseline)	0.536	-0.169
Liu et al. (Lower limit)	0.559	-0.192
Liu et al. (Upper limit)	0.5121	-0.145
ONS App 1 (Baseline)	0.0997	-0.044
ONS App 1 (Lower limit)	0.0958	-0.046
ONS App 1 (Upper limit)	0.1043	-0.042
ONS App 2 (Baseline)	0.1799	-0.148
ONS App 2 (Lower limit)	0.1318	-0.16
ONS App 2 (Upper limit)	0.2501	-0.137
ONS App 3 (Baseline)	0.1444	-0.016
ONS App 3 (Lower limit)	0.1388	-0.016
ONS App 3 (Upper limit)	0.1508	-0.016

Note: Liu et al= New South Wales cohort [17], ONS= UK COVID confirmed cases [16]

Likely impact of vaccination in preventing Long COVID

The likely protective effect of COVID vaccines against Long COVID symptoms (in vaccinated patients experiencing "breakthrough" infections) were included in the analysis. Antonelli et al reported that patients who are fully vaccinated were less likely to experience Long COVID with an odds ratio of 0.51 (95% CI 0.32–0.82; p=0.0060)[11]. To incorporate the treatment effect of vaccines into long COVID, the odds ratio was converted to relative risk (RR) of 0.54 (95%CI: 0.35- 0.84) and was directly applied to the rates of vaccinated individuals [28, 29]. The relative risk ratio was expressed in percentage (%) using the following formula [30]

$$100 \times (1-RR) = \%$$

Therefore, in this analysis, COVID vaccine decreases the risk of Long COVID by 46% (RR=0.54), 16% (RR=0.84) and 65% (RR=0.35) as central, lower and upper limits respectively.

For partially and unvaccinated individuals, no treatment effects for vaccination were incorporated in the model. Sensitivity analysis was then conducted to examine the protective effect of vaccines against Long COVID by varying the levels using the lower and upper risk ratios of 0.35 and 0.84 [11].

Results

Table 3 presents the likely Long COVID cases for NSW, Victoria and Australia using double the actual cases. As there were more reported COVID infections in NSW, it is not surprising that there are more potential Long COVID cases in NSW compared to Victoria across all scenarios.

Using Liu et al's estimate, 166,190 (153,936 -179,746) and 102,940 (95,349 - 111,337) Long COVID cases were modelled from the 1,156,344 COVID cases in NSW and 716,252 cases in Victoria respectively at week five post COVID infection. Overall, Australia could potentially face 454,266 (420,770 - 491,322) Long COVID cases from the 3,160,769 total COVID cases at five weeks post-infection. However, Long COVID cases would rapidly decrease to at least 38,861 (NSW), 24,071 (Victoria) and 106,224 (Australia) at week 12. The exponential decay function fitted to Liu et al's data indicates that Long COVID case could drop to less than 550 Long COVID cases one year after acute infection.

Using the ONS data provides significantly different results. Under ONS Approach 1, at week 5 post-infection, 152,971 (145,414 - 161,781) Long COVID cases were calculated in Australia. Of these, more than 53,000 and 32,000 Long COVID cases would come from NSW and Victoria respectively. Potential Long COVID cases would decrease to 40,960 (38,397 - 43,926) for NSW, 25,371 (23,784 -27,208) for Victoria and 111,959 (104,955 - 120,067) for Australia by week 12. However, at 52 weeks post-acute infection, 19,086 (16,524 – 22,162) might still be experiencing any of the 12 symptoms.

For ONS Approach 2, 164,289 (112,768 - 243,262) patients would likely continue to report any of the 12 symptoms at week five in Australia, and around 41,000 and 25,000 could be seen in NSW and Victoria. Unlike the other ONS scenarios, fewer cases were calculated at week 12 with approximately 13,000 cases in NSW, 8,000 cases in Victoria and 36,000 cases across Australia. The exponential decay function as fitted to these data points predicts very few Long COVID cases by week 52 (154 cases).

Under ONS Approach 3, 257,583 (247,332 -269,326) patients were modelled as having "self-reported Long COVID" at week 5 in Australia, of which 94,235 (90,485 -98,531) and 58,370 (56,047 -61,031) were modelled for NSW and Victoria respectively. At week 12, at least 220,000 Long COVID cases were modelled in Australia and 80,000 in NSW and 50,000 in Victoria. This approach suggests that at least 115,000 Long COVID cases could still remain at week 52.

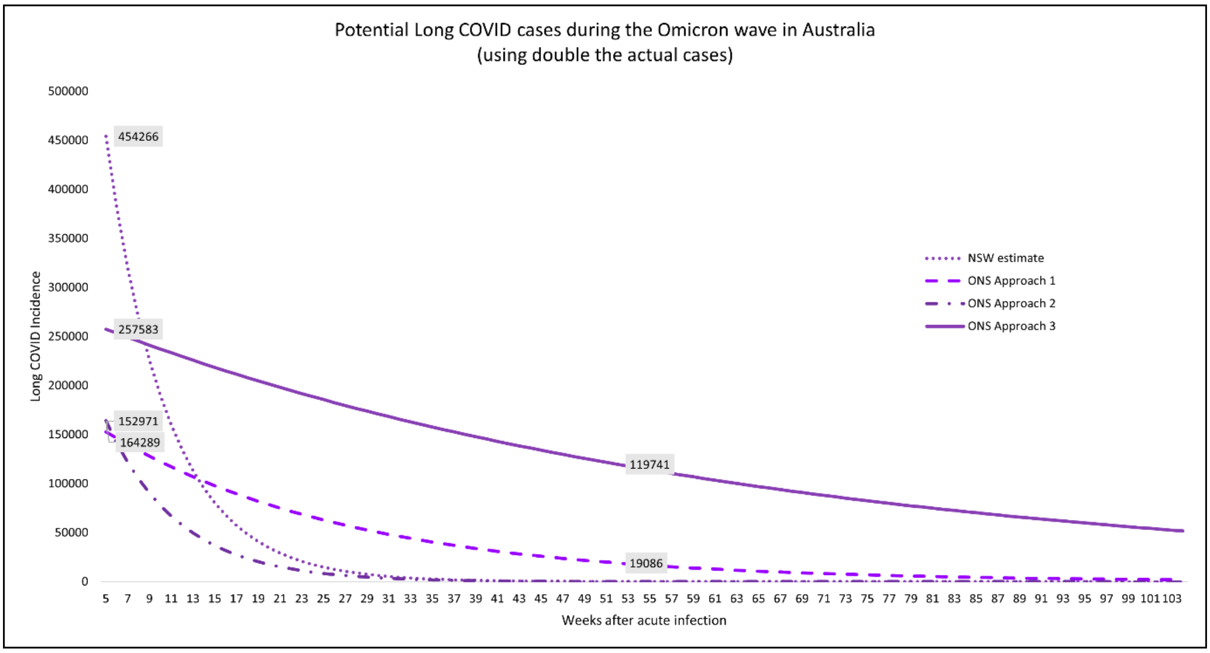
Table 3 Modelled Long COVID cases (Using cases doubled)

NSW	NSW			VIC			Australia		
Lui et al									
Weeks	**Central**	**LL**	**UL**	**Central**	**LL**	**UL**	**Central**	**LL**	**UL**
5	166,190	153,936	179,746	102,940	95,349	111,337	454,266	420,770	491,322
12	49,246	38,861	62,991	30,503	24,071	39,017	134,609	106,224	172,180
52	56	18	187	35	11	116	154	49	512
ONS Approach 1									
5	55,963	53,199	59,186	34,664	32,952	36,661	152,971	145,414	161,781
12	40,960	38,397	43,926	25,371	23,784	27,208	111,959	104,955	120,067
52	6,983	6,045	8,108	4,325	3,744	5,022	19,086	16,524	22,162
ONS Approach 2									
5	60,104	41,256	88,996	37,229	25,554	55,125	164,289	112,768	243,262
12	21,103	13,360	33,592	13,072	8,275	20,807	57,684	36,517	91,820
52	56	22	139	35	14	86	154	60	379
ONS Approach 3									
5	94,235	90,485	98,531	58,370	56,047	61,031	257,583	247,332	269,326
12	84,008	80,675	87,825	52,035	49,971	54,400	229,629	220,518	240,063
52	43,807	42,088	45,773	27,134	26,070	28,352	119,741	115,044	125,116

Note: NSW= New South Wales, LL= Lower limit, UL= Upper Limit, ONS=Office for the National Statistics

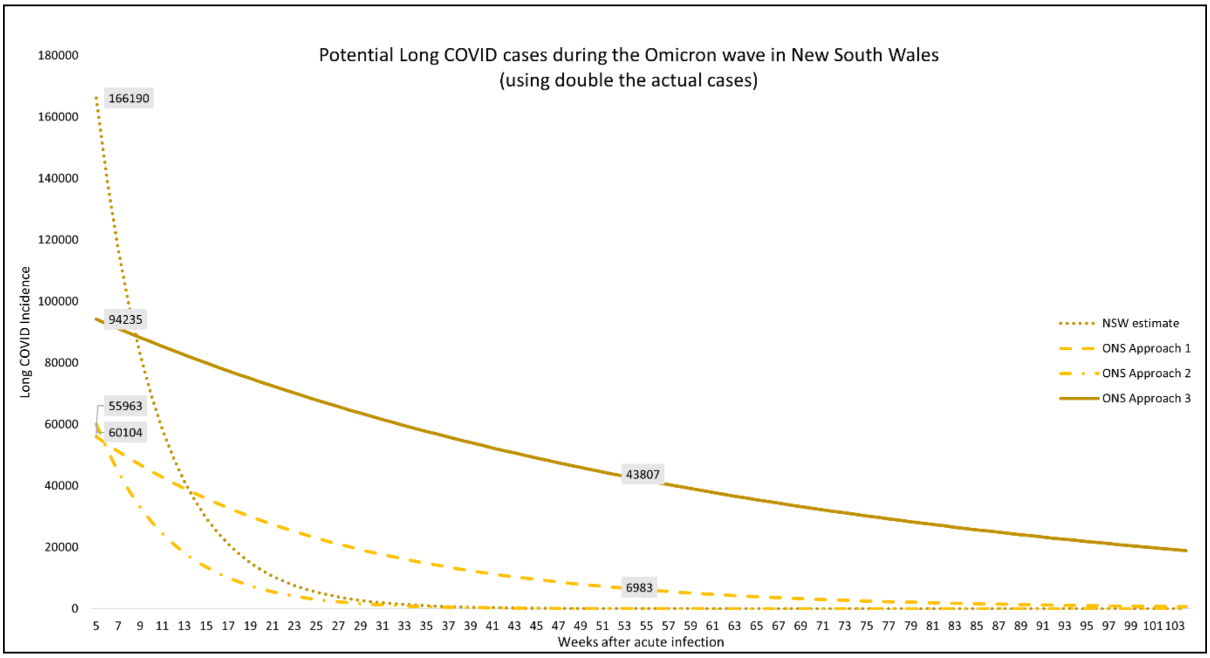
Figures 1, 2 and 3 present the potential Long COVID cases over time, using the assumed exponential decay functions.

Figure 1 Potential Long COVID cases in Australia



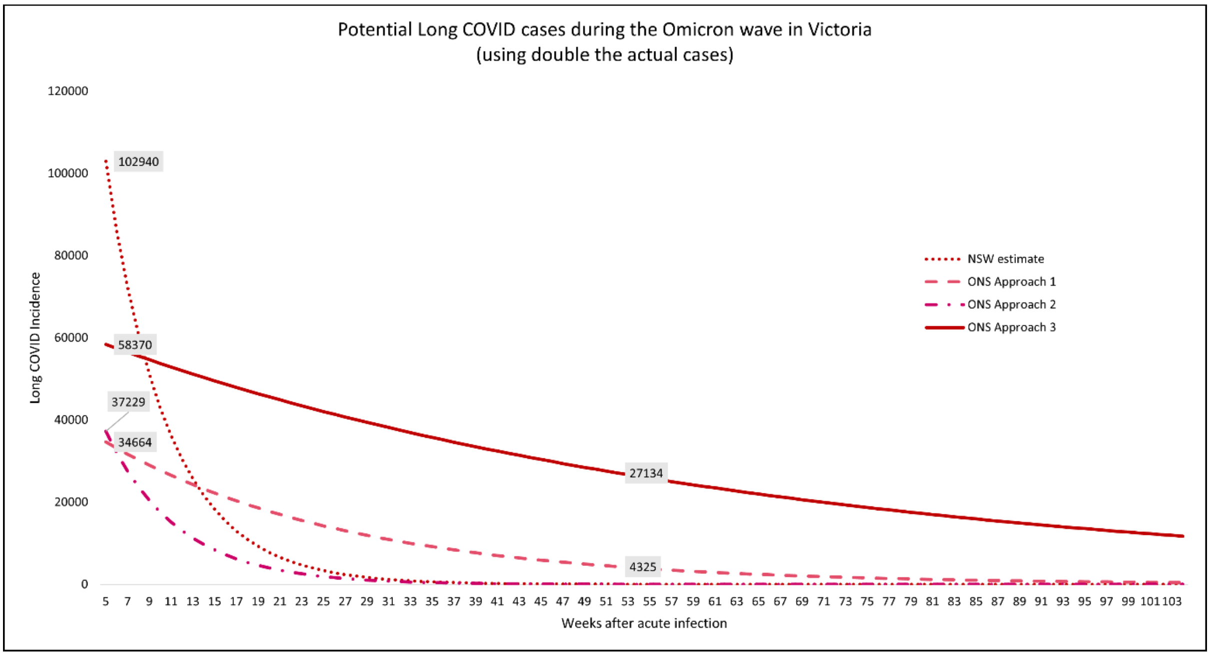
Note: numbers refer to central estimates

Figure 2 Potential Long COVID cases in New South Wales



Note: numbers refer to central estimates

Figure 3 Potential Long COVID cases in Victoria



Note: numbers refer to central estimates

Sensitivity analysis

Table 4 shows the results of the sensitivity analysis when levels of vaccine effectiveness in avoiding Long COVID are varied. Changing the parameter of vaccine efficacy against Long COVID would change the results of each scenario. If the vaccine had a protective effect of 65% against Long COVID, the number of Long COVID cases would be lower than under our central estimate. For example, under ONS Approach 3, Long COVID cases in Australia would decrease from 257,583 to 185,475 at week 5. Conversely, if the vaccine offered a protective effect of only 16%, more Long COVID cases would be expected. For instance, under ONS Approach 3, self-reported Long COVID cases at week 5 would increase from 257,583 to 364,572 cases.

Table 4 Results of the sensitivity analysis on vaccine impact on Long COVID

	NSW			**VIC**			**Australia**		
Liu et al									
Weeks	**Central**	**65%**	**16%**	**Central**	**65%**	**16%**	**Central**	**65%**	**16%**
5	166,190	120,406	232,181	102,940	74,581	143,815	454,266	329,119	634,648
12	49,246	35,333	70,245	30,503	21,885	43,510	134,609	96,579	192,008
52	56	40	81	35	25	50	154	110	221
ONS Approach 1									
5	55,963	40,174	79,736	34,664	24,884	49,389	152,971	109,811	217,951
12	40,960	29,369	58,508	25,371	18,191	36,240	111,959	80,277	159,926

52	6,983	4,994	10,031	4,325	3,093	6,213	19,086	13,650	27,419
ONS Approach 2									
5	60,104	43,160	85,574	37,229	26,734	53,006	164,289	117,974	233,911
12	21,103	15,109	30,246	13,072	9,359	18,734	57,684	41,298	82,674
52	56	40	81	35	25	50	154	110	222
ONS Approach 3									
5	94,235	67,855	133,376	58,370	42,030	82,615	257,583	185,475	364,572
12	84,008	60,440	119,115	52,035	37,437	73,781	229,629	165,209	325,590
52	43,807	31,417	62,544	27,134	19,460	38,741	119,741	85,876	170,960

Note: Central estimates assume a 46% vaccine protective effect, NSW= New South Wales, VIC= Victoria, ONS=Office for the National Statistics

Limitations

Similar to our previous model, this current study is subject to several limitations [14, 15]. The actual COVID-19 cases used in this study are most likely understated as most of the testing sites during this period were overwhelmed with the sudden surge of COVID cases, and RAT tests were unavailable due to limited supply [22-26]. The ultimate number of COVID-19 infections in the present outbreak cannot yet be known, and we have therefore relied on a simplifying assumption of the eventual total being roughly twice the number at our assumed "peak" (16th January 2022). The true ultimate number of COVID-19 infections, both reported and unreported may, of course, differ substantially from our assumed total. However, it is very unlikely that the true total would ultimately be smaller than that used in this modelling, thus giving reasonable confidence in our presentation of these estimates as conservative, lower bounds. Secondly, the total national number of fully vaccinated individuals in Australia that were infected with COVID-19 was not publicly available. Therefore, the number of full vaccinated COVID related infections was calculated using figures obtained from the NSW epidemiological report [21]. The current modelling did not stratify the cases per gender or by age group. However, publicly available information only provides aggregated data with no stratification of age and gender.

As noted, in the absence of other data, this study has assumed that the probability of developing Long COVID after Omicron infection will be similar to that seen with other variants. Our longer term (e.g. 52 weeks and beyond) estimates of Long COVID numbers are heavily influenced by the decay function used. For example, our 52 week estimates for "Liu et al" and "ONS Approach 2" generate only a handful of Long COVID cases at one year, numbers which are not credible given evidence from other sources. The larger 52-week estimates generated by ONS Approach 1 and 3 reflect the lower decay constants generated by the underlying data in these approaches. ONS itself notes that Approach 3 is most consistent with the approach it has used in its population-based "Prevalence of ongoing symptoms following coronavirus" survey [16], which has consistently indicated that hundreds of thousands of UK residents are likely to still display Long COVID symptoms a year or more after infection. Finally, this study has not estimated the potential longer health impacts of COVID (organ damage and permanent disability) that are beyond the scope of current definitions of "Long COVID".

Discussion

Overall, this study has attempted to provide conservative estimates of the likely scale of Long COVID resulting from the emergence of the Omicron variant in Australia. It attempts to account for the likely protective effects of high levels of vaccination in the Australian population against Long COVID, while recognising that uncertainty remains on this effect.

Our findings suggest that Australia is likely to see some hundreds of thousands of people who will experience ongoing COVID symptoms for 5 or more weeks after their initial infection. Depending on how effective vaccines ultimately prove in preventing Long COVID developing in people with Omicron infections, Australia is likely to see between 80,000 and 325,000 people who will grapple with Long COVID symptoms for at least 12 weeks. One year on from their initial infection, as few as 14,000 or as many as 170,000 Australians might still be experiencing Long COVID symptoms. As noted, our analysis has sought at all times to take a conservative approach and to reflect uncertainties.

Especially amongst patients who experience Long COVID for several months or longer, these numbers are likely to translate into presentations for health care, as well as representing a significant burden of ill-health, social and economic distress for the individuals concerned, their families and communities.

Implications for health services

This study provides insights on the likely magnitude of Long COVID cases in Australia for the coming months which could potentially cause a significant burden to healthcare systems; our upper estimates are large enough to potentially have measurable adverse economic impacts through reduced ability to participate in the workforce and increased needs for healthcare and economic support. In fact, more studies are now reporting that Long COVID is having a considerable effect on patients' quality of life and is a major contributor to productivity losses [7, 31-33]. A study in Sweden following patients infected with COVID documented that taking sick leave is a common occurrence amongst Long COVID patients [32]. Therefore, Australian State and Federal Governments should be prepared to deal with the challenges of Long COVID across multiple sectors, and the quality of life and the productivity of people living with Long COVID may depend heavily on the Australian health system's response to Long COVID.

In 2021, we made a number of recommendations for actions necessary to prepare health care services and systems for the potential impacts of Long COVID, including the establishment of a national centre of excellence to oversee treatment guidelines, education and dissemination; establishment of care coordination centres at state and territory level to mobilise public and private sector resources to provide cost-effective, high quality care and rehabilitation in the community for people with Long COVID; and ensuring that Medicare Safety Net measures do not fail people with Long COVID and land them with large out-of-pocket bills for their ongoing care. These recommendations are still valid. However, the scale and rapidity of the Omicron wave now makes a number of other actions a matter of very considerable urgency:

1. Establishing large scale, national (and nationally consistent) measurement and surveillance of Long COVID, including large national surveys, based on the experience of the UK ONS, to be run by the Australian Bureau of Statistics and/or the Australian Institute of Health and Welfare. The overwhelming of testing capacity in this wave means that earlier preferences for surveillance based on data linkage by health care systems are no longer tenable.
2. Immediate surveillance and measurement of COVID infections and Long COVID symptoms amongst health care and aged care workers, to provide estimates on the extent to which Long COVID will further degrade and constrain health and aged care system capacity in coming months.
3. Given the limited access to both PCR and RAT testing experienced during the peak of the Omicron wave, the amendment of all clinical and treatment guidelines for Long COVID to drop any requirement for a positive test result, and instead to allow for presumptive / suspected / self-reported COVID-19 infection as sufficient grounds for inclusion.
4. The urgent establishment of a national Long COVID Care and Support Taskforce, with representation from health, disability and economic sectors, to provide a rapid whole of government review and response to Long COVID in all relevant dimensions of health care, disability / welfare benefits, employment and financing, to coordinate Commonwealth and State and Territory agencies and actions.

The clock is already ticking on Long COVID in Australia, but we are still flying blind as to its true extent and impact. These actions need to be undertaken in a matter of weeks, not months or years, if the most negative impacts of Long COVID are to be anticipated and mitigated.

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