Estimating the future burden of Long-COVID in Australia

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Terms of Reference Point 3 "Research into the potential and known effects, causes, risk factors, prevalence, management, and treatment of long-COVID and/or repeated COVID infections"

Summary

Australia faces a growing burden of chronic disease due to SARS-COV-2. This study will be developed in a more detailed format, but is presented here as early data to inform the parliamentary inquiry. Using a mathematical model, we estimated the age-specific burden of Long COVID in Australia to October 2023. The model does not consider re-infections, so is a minimal estimate. The model estimated that with a vaccine-only policy and no other efforts to mitigate transmission, almost all Australians will be infected at least once in the time window from January 2021 to August 2023. The total people with long-COVID by December 2023 is 1,323,482, with 43,910 of these being children 0.4 years of age. This does not include the burden of long-COVID caused by reinfections. Over 3% of the 0–4-year-old age group are estimated to never recover, while almost 1% of 5–19-year-old and over 6% for the population 20+ years old were estimated to never recover. The true burden will be higher than this, as reinfections will add to the burden of Long-COVID. A vaccine plus strategy, which includes increased access to testing, isolation, masks and safe indoor air, will mitigate the continued infection of Australians with SARS-COV-2 and help reduce the long-term burden of long-COVID. Models of long-COVID projections can be used to test the impact of infection prevention and control strategies on future burden of long-COVID.

Introduction

Long-COVID is a serious concern for the community, public health professionals and healthcare systems internationally, with rapidly accumulating evidence that SARS-COV-2 has effects on many organ systems beyond the acute infection (1-3). The term "long COVID" is defined by symptoms persisting beyond the acute infection, but the pathophysiology of these symptoms may range from respiratory, cardiac, neurocognitive to immunological or other causes.

Neurological symptoms (e.g. memory disturbances, weakness), possible cardiac disturbances (e.g. chest pain, increased heart rate) and respiratory symptoms (e.g. cough) are being reported at increased rates among individuals who have had a previous COVID-19 infection compared with those who have no previous reported infection (4). Additional symptoms include fatigue, shortness of breath, palpitations, anxiety, and depression with varying levels of persistence one month and up

until 12 months following initial infection (5-9). A greater level of severe illness during hospitalization for initial infection has shown to contribute to more extensively diminished pulmonary capacities and unusual chest imaging presentations (9). The prevalence of long-COVID is estimated to range from 15 – 30% in adults aged 18 – 64 years old, and between 26.6% - 45.4% in adults aged 65 years and over (5, 7-38). However, the data varies according to study and population size with some studies reporting long-COVID prevalence rates up to 80% among adults (5, 7-38).

A range of health effects, for varying lengths of time (weeks to months) after infection are being reported after COVID-19, with those reporting symptoms experiencing impairment of their ability to conduct normal day-to-day activities (1, 4). The use of vaccines is protective against development of long-COVID, but that protection may be around 15% (39). Research suggests that the incidence and severity of long-COVID may be influenced by the severity of the acute COVID-19 infection, variants of concern, vaccination status prior to infection, certain comorbidities, age, sex, reinfection, and antiviral treatment (2, 4, 10, 40, 41). Long-COVID is more common in adults, and in people who have suffered severe infection (42). However, it can also occur after mild infection and in children (6, 43, 44). For children it is unknown if the longer term sequalae of long-COVID and repeated infections will have long-lasting impacts on not only their health, education, and social development. The prevalence of long-COVID amongst children and adolescents between the ages of 0 and 18 varies between studies from 4 to 66% among survivors who were 4 or more weeks since initial infections (6, 19, 43, 45-57). Rates of long COVID increase among both children and adolescents and adults if they have been hospitalized in their initial infection, suggesting that more severe initial illness is associated with a greater risk of developing long-COVID (6, 58).

Evidence is now accruing that reinfection results in worse outcomes and may increase the risk of long-COVID. An online survey found that in those who had been reinfected, long-COVID symptoms became more severe in 80% of respondents after re-infection (40). Of those who had recovered from long-COVID, reinfection caused a resurgence of long-COVID in 60% of respondents (40). An increased number of vaccines may also be associated with lower long-COVID prevalence: those who were unvaccinated had the highest long-COVID prevalence at 41.8%, decreasing to 30% in those with 1 dose, then 17.4% in those with 2 doses and down to 16% in those with 3 doses (59). Australia has >95% two-dose vaccine coverage for people 16 years and over, 72.3% for a third dose and 42.1% for a fourth dose (60). Children 0-4 years are not recommended for vaccination unless severely immunosuppressed. Whilst vaccination with a fourth dose was recommended for those aged 65 and older, residents in aged care facilities, people over 16 years of age with severe immunocompromise and Aboriginal and Torres Strait Islander people aged 50 years and older in March 2022 (61), booster doses for those aged 16 to 64 were not recommended until July 2022 (62). A fifth dose was recommended for 30-49 years and 50+ years in November 2022 for aged care residents, people with chronic medical conditions and multiple comorbidities (63). Children aged 5-15 years are currently not recommended to have a booster beyond their primary course unless severely immunocompromised, have a disability or multiple health conditions, adolescents aged 16-17 years were recommended in October 2022, to have a booster 3 months after their primary course (64). Despite these recommendations, gaps remain between the number of people eligible for boosters and those who’ve received them and given the surge in COVID-19 variants of 2022 primary schedules and boosters are important in the arsenal to prevent severe disease and long-COVID.

Interestingly, numerous studies have found higher rates of long-COVID among female COVID-19 survivors (7, 9, 24). Pre-existing medical conditions have too been associated with an increased risk of long-COVID, including dyslipidemia, an increased body mass index and pre-existing lung disease such as asthma and COPD (2, 24). One study investigating symptoms at 6, 12 and 18-month intervals found 6% had not recovered and only 42% recovered partially (13). Such factors and their relationship with long-COVID are important to consider when treating COVID-19 patients, assessing vulnerability to long-COVID and tailoring interventions that may reduce susceptibility to long-COVID. Long-COVID is predicted to place an ongoing burden on health care providers and global health now and into the future, accompanied by societal and economic impacts (3, 65). In the UK, one in four employers report their workforce is affected by Long-COVID (66). Variations in estimates of Long-COVID reflect different definitions of long-COVID, different measurement, varying population age structure, and different rates of population vaccination (3). There remain gaps in knowledge regarding long-COVID, including the effects of long-COVID beyond 12 months after diagnosis (67). Projections of rates of long-COVID into the future are crucial to government, researchers, healthcare professionals, public health staff, economists and policy makers with the tools and knowledge to prepare for preventing, controlling, and treating long-COVID long-term.

Aim: To estimate the age-specific burden of Long-COVID in Australia over a 12-month period.

Methods

To assist public health and health department capacity building to manage the burden of long-COVID in Australia, we developed a modeling method to estimate the future burden of long-COVID in Australia. The model estimates the time for the entire population to be infected at least once from January 2021 and estimates the burden of long-COVID for the subsequent 12 months, factoring in rates of recovery from long-COVID. The model does not include reinfections, so is a minimal estimate. We assumed Australia would continue with a vaccine-only strategy, with minimal other mitigations.

Estimates of COVID-19 incidence in Australia based on notified data are not reliable due to decreased testing and lack of mandatory reporting of a positive RAT test, which would underestimate the incidence (68). There have been modelling studies to estimate the true number of new cases using different data such as hospitalization, testing and death rates (69).

We used the results from a serological survey using Australia blood donors in three different time points (70) for adults, and in a single time point for children (71) to estimate true infection rates. The first time point was between 23 February and 3 March 2022, the second time point was between 9-18 of June 2022 and the third time point was between 23 August and 2 September. The estimated proportion of the population with at least one COVID-19 infection in these three time points is shown in Table 1. For the age group 0-19, we only had the seroprevalence at a single time point, September. As such, we estimated the values for the two missed time points for children using relative changes in seropositivity adults (see Table 1).

To estimate the proportion of the population living with long-COVID-19 symptoms over time, we used an adjusted SIR model (Figure 1), where the S compartment represents people that have never

had COVID-19 in 2022. To inform this compartment we used the age specific population for Australia in 2020-2021 (5). The I compartment represents the people that had covid at least once in 2022, and this compartment and the rate of people passing from S to I, have been estimated by interpolating the three values from the serosurvey surveillance results over time in 2022. For Table 2, to estimate the age specific proportion of people suffering from long-COVID symptoms, we have collected data on the prevalence of long-COVID derived from studies focusing on children, adolescents, and adults (5, 57). If the specific article compared cases with controls, prevalence was calculated to identify the difference (cases minus controls). This method was used for the symptoms for up to 3 months. For symptoms up to 12 months, we used the estimated percentage of those who have no recovery at 12 months and subtracted this from the prevalence (13).

Figure 1 shows the SIR model diagram used.

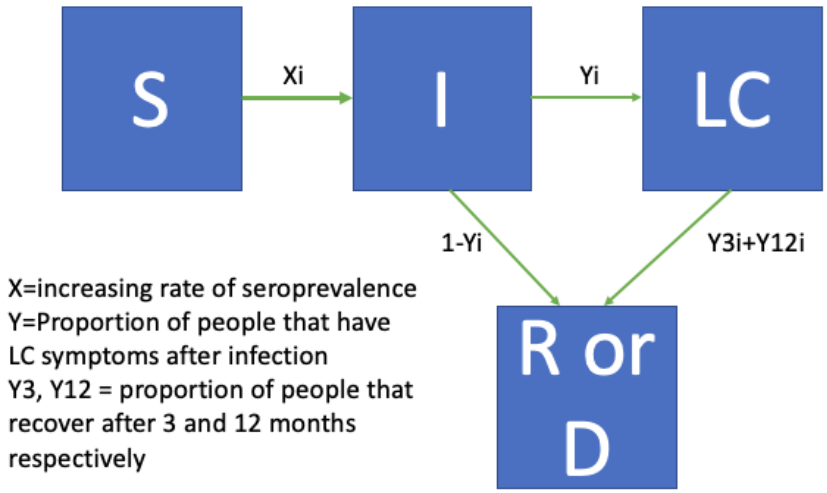

Figure 1: SIR model diagram with susceptible (S), infected (I), with long COVID symptoms (LC) and recovered or dead (R or D), while every compartment is age specific following i=1,...,9 age groups and the time t is in months.

***Table 1: Data used for the estimation of increase in seropositivity over time in months* (70, 71).**

Age group	March 2022	June 2022	September 2022
0-19	15.8%	45%	64%
20-29	27.2%	61.7%	79.7%
30-39	21.7%	52.6%	72.5%
40-49	16.1%	47.5%	68.3%
50-59	11.9%	38.9%	63%
60-69	8.3%	30.2%	49.2%

70+	6.4%	25.7%	41.6%
All	17%	46.2%	65.2%

Table 2: Age specific rates of Long-COVID for at 3 months and 12 months

Age groups	Symptoms up to 3 months	Symptoms up to 12 months
0-4	12.8% (57)	6.144% (13, 57)
5-9	4.4% (57)	2.112% (13, 57)
10-19	4.7% (57)	2.256% (13, 57)
20-59	20.8% (5)	9.984% (5, 13)
60+	26.9% (5)	12.912% (5, 13)

Results

Figure 2 shows the projection by age group of the proportion of people will have COVID-19 at least once up to August 2023. The model estimated that almost all Australians will be infected at least once in the time window from January 2021 to August 2023. As shown in Figure 2, the seroprevalence in older age groups (60+) increases at a slower rate than younger age groups in accordance with less contacts in those age groups.

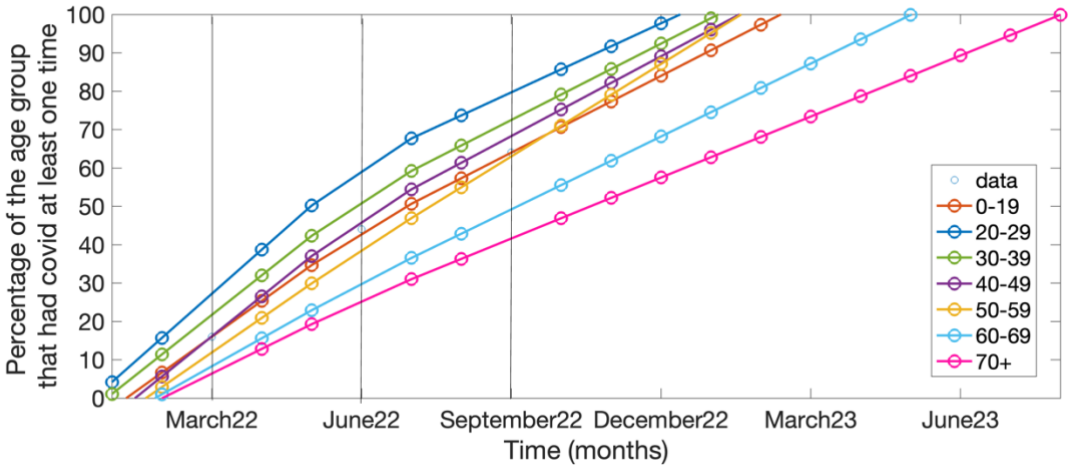

Figure 2: Estimation of age-specific seroprevalence over time, using the values over time listed in Table 1.

Figure 3 shows the monthly number of people suffering from long-COVID symptoms in each month from January 2022 until August 2023 with a peak and then waning which reflects recovery of a proportion of people from Long-COVID. However, the data only included people that got infected in the time window from January 2022 to January-August 2023 depending on age-groups (See Figure 2).

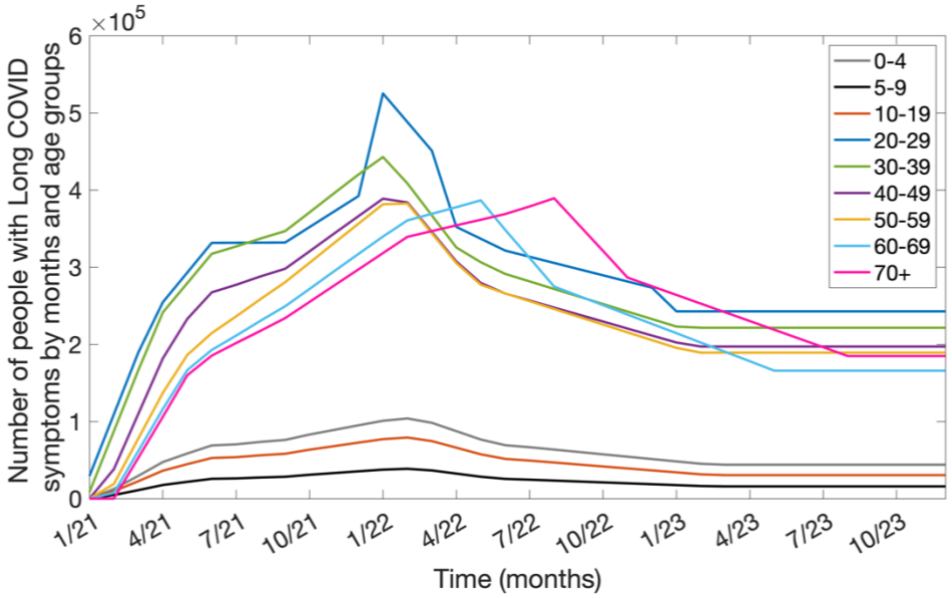

Figure 3: Number of people with long-COVID symptoms arising from infections between January 2022 and August 2023.

Table 3 shows the monthly estimated number of people with long-COVID in three age groups - 0-4 years (mostly unvaccinated), 5-19 years (partially vaccinated) and 20+ (mostly vaccinated). The total people with long-COVID by December 2023 is 1,323,482, with 43,910 of these being children 0.4 years of age. This does not include the burden of long-COVID caused by reinfections. Over 3% of the 0–4-year-old age group are estimated to never recover, while almost 1% of 5–19-year-old and over 6% for the population 20+ years old were estimated to never recover.

Table 3: Number of people with long-COVID symptoms by months and three age groups, 0-4 (unvaccinated), 5-19 (partially vaccinated) and 20+ (mostly vaccinated).

2021	**0-4**	**5-19**	**20+**	**2022**	**0-4**	**5-19**	**20+**	**2023**	**0-4**	**5-19**	**20+**
January	0	0	36950	**January**	100870	77706	2546140	**January**	48240	35253	1326470
February	12550	9671	277370	**February**	103910	79906	2500220	**February**	45160	32737	1291860
March	29600	22806	693810	**March**	98250	75357	2314740	**March**	43910	31722	1277270
April	47400	36518	1091020	**April**	87450	66835	2067630	**April**	43910	31722	1262680
May	58490	45057	1381720	**May**	76600	58276	1957760	**May**	43910	31722	1247850
June	68920	53094	1581600	**June**	69230	52380	1844160	**June**	43910	31722	1247850
July	70350	54191	1669310	**July**	66600	50240	1752640	**July**	43910	31722	1247850
August	73550	56662	1761070	**August**	63570	47761	1659870	**August**	43910	31722	1247850
September	76070	58602	1848780	**September**	60480	45244	1597880	**September**	43910	31722	1247850
October	83070	63994	1994810	**October**	57400	42728	1535890	**October**	43910	31722	1247850
November	89010	68567	2142620	**November**	54360	40249	1473130	**November**	43910	31722	1247850

December	95030	73209	2288660	**December**	51280	37732	1411150	**December**	43910	31722	1247850

Discussion

Australia faces a growing burden of chronic disease due to SARS-COV-2. This study will be developed in a more detailed format, including economic projections for Australia, but is presented here as early data to inform the parliamentary inquiry.

Vaccinating children 0-4 years should be considered based on the modelled outcomes for this age group in Australia, and the higher incidence of long-COVID in this age group compared to older children (57). The higher incidence of Long-COVID among the youngest children in Denmark may reflect this age group being unvaccinated.

Proactive booster policies should also be considered to ensure wider access to 3rd and 4th doses. Despite concerns about original antigenic sin, no clinical trial shows that boosters reduce protection. In fact, they increase protection (72).

In this study we found that cumulative infections over 12-18 months can result in a very high proportion of people living with long-COVID. Over 3% of the 0–4-year-old age group are estimated to never recover, while almost 1% were estimated to never recover in the 5–19-year-old age group and over 6% for the population 20+ years old.

This study has some limitations. To identify the prevalence of long-COVID in children, adolescents, and adults we selected large scale studies with community-based selection of participants, and ensured estimates were based on largely vaccinated population (5, 57). The prevalence rates are based on countries where population studies were conducted, including the United States of America and Denmark. Each country had differing COVID-19 rates and population vaccination rates when compared with Australia (73). However, given the robustness of the studies and comparable economic and life expectancies between the countries, we believe that these prevalence rates are generalisable for an Australian population (74). Data from an Australian survey suggested 29% of people suffer long COVID, but we used lower and more conservative estimates. We did not consider re-infection in the model, so the results presented are a minimal estimate. We also did not consider the impact of a new variant of concern with greater immune evasion.

Similar to other modelling studies done in Australia, our results suggest that hundreds of thousands of people across the country will have long-COVID (75). Modeling from the Institute for Health Transformation at Deakin University predicted between 80, 000 and 325, 000 people will experience Long-COVID for at least 12 weeks, with as many as 170, 000 still experiencing long-COVID symptoms up to 12 months post infection (75). Our findings suggest that in October 2023, over 1 million people could be experiencing long-COVID symptoms.

A vaccine plus strategy, which includes increased access to testing, isolation, masks and safe indoor air, will mitigate the continued infection of Australians with SARS-COV-2 and help reduce the long-term burden of long-COVID.

Models of long-COVID projections can be used to test the impact of infection prevention and control strategies on future burden of long-COVID. We will continue to develop this work.

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