
Recommendations

1

Establish an independent expert advisory group that includes clinical and research experts in long COVID and consumers and/or carers with lived experience of long COVID to advise the health minister on the health, social and economic impacts of recurrent SARS-CoV-2 infections and long COVID.

2

Support international and national collaboration and networking activities to understand and improve the health, social and economic impacts of recurrent SARS-CoV-2 infections and long COVID.

3

Continue to fund the National Clinical Evidence Taskforce to identify, assess, and synthesise up-to-date evidence and convene clinical expertise to develop and sustain recommendations for the clinical care of long COVID in adult and paediatric populations in Australia.

4

Endorse and fund access to healthcare through a model of care that involves a tiered and integrated approach to care, as appropriate to the needs of patients and their carers and loved ones.

5

Invest in Australian research to understand the impact of recurrent SARS-CoV-2 infections and long COVID including prevalence and prognosis, pathological mechanisms, assessment and diagnosis, and prevention, treatment and models of care.

6

Convey a clear message to the public and to health care providers that prevention of COVID-19 is the most-effective method of preventing long term health issues resulting from SARS-CoV-2 infection.

7

Continue to invest in collaborative preventive activities to strengthen the message that prevention of COVID-19 is the most-effective method of preventing long term health issues resulting from SARS-CoV-2 infection.

Introduction

About the National Clinical Evidence Taskforce

The National Clinical Evidence Taskforce (henceforth referred to as the “Taskforce” or “NCET”) was established in early 2020 in response to the rapidly evolving SARS-CoV-2 scenario - at that point, a novel virus with unknown clinical impacts. The Taskforce aims to provide up to date, evidence-based guidance for Australian clinicians caring for people with COVID-19 (the Guidelines).

Since the beginning of the pandemic, the volume of COVID-19 publications has been unprecedented and overwhelming (Else, 2022). There is much inconsistency in the quality of the available research in general (Eysenbach et al., 2022), and also noted specifically in COVID-19 research (Zdravkovic et al., 2022). Clinicians desperately needed support to sift through the vast amounts of emerging research, to identify the reliable research, or fill the gaps where reliable research was lacking (based on best clinical practice), to ensure they were able to provide the best care for COVID-19 patients.

The Guidelines address clinical topics specific to managing COVID-19 and cover the full acute disease course across mild, moderate, severe and critical illness, and care after COVID-19. The Taskforce develops recommendations using the gold standard method for guideline development, GRADE (Grading of Recommendations, Assessment, Development and Evaluations) (BMJ 2022), and is one of the international leaders in developing living guidelines. Our model ensures that clinicians across Australia receive relevant, reliable advice in near real-time.

Taskforce recommendations are drafted by an expert clinical panel in conjunction with methodological experts. Drafted guidance is then approved by a Guidelines Leadership Group and a Steering Committee, and reviewed by a consumer panel. Altogether, these groups comprise over 250 representatives from 35 peak health professional bodies from across Australia. To date, the Taskforce has published > 100 updates of the guidelines with almost 200 recommendations.

References

- BMJ - British Medical Journal. What is GRADE? Accessed 16 Nov 2022. <https://bestpractice.bmj.com/info/toolkit/learn-ebm/what-is-grade/>
- Else H. How a torrent of COVID science changed research publishing - in seven charts. *Nature*. 2020 Dec;588(7839):553. doi: 10.1038/d41586-020-03564-y. <https://pubmed.ncbi.nlm.nih.gov/33328621/>
- Eysenbach G, Powell J, Kuss O, Sa ER. Empirical studies assessing the quality of health information for consumers on the world wide web: a systematic review. *JAMA*. 2002 May 22-29;287(20):2691-700. doi: 10.1001/jama.287.20.2691. <https://pubmed.ncbi.nlm.nih.gov/12020305/>
- Zdravkovic M, Berger-Estilita J, Zdravkovic B, et al.. Scientific quality of COVID-19 and SARS CoV-2 publications in the highest impact medical journals during the early phase of the pandemic: A case control study. *PLoS One*. 2020 Nov 5;15(11):e0241826. doi: 10.1371/journal.pone.0241826. Erratum in: *PLoS One*. 2021 Apr 8;16(4):e0250141. <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0241826>

Taskforce guidance on long COVID and repeated COVID-19 infections

Long COVID, which is also known as “post-COVID-19 condition”, “post-COVID-19 syndrome” or, “post-acute sequelae of SARS-CoV-2 infection” has been reported since April 2020. The Taskforce published the initial Australian guidance on long COVID in December 2020 and have published 6 major updates to the guidance since then. The Taskforce guidance on Care of People after COVID-19 primarily addresses the following clinical topics:

1

In patients with post-COVID-19 condition, which interventions are recommended to facilitate recovery?

A) Which rehabilitation strategies should be used to facilitate recovery for patients who have had COVID-19? What frequency, intensity and duration of treatment is recommended?

B) What psychosocial interventions are effective at alleviating stress or mental health symptoms of post COVID-19 condition? What frequency, intensity and duration of treatment is recommended?

C) What is the effect of the COVID-19 vaccination on symptoms of post-COVID-19?

2

In patients with acute COVID-19, which interventions are recommended to prevent or reduce severity of post-COVID-19 condition?

3

In patients where COVID-19 has impacted on a pre-existing comorbidity, which interventions are recommended to facilitate recovery?

In addition, the Guidelines provide the Australian case definition for long COVID, assessment criteria, and guidance on goals of care for patients and their carers or significant other(s).

Challenges to developing clinical guidance on long COVID

Long COVID is not a single condition

The Australian Guidelines developed by NCET define post-COVID-19 condition/syndrome ("long COVID") as, *"Signs and symptoms that develop during or after an infection consistent with COVID-19, continue for more than 12 weeks and are not explained by an alternative diagnosis. It usually presents with clusters of symptoms, often overlapping, which can fluctuate and change over time and can affect any system in the body. Post COVID-19 condition may be considered before 12 weeks while the possibility of an alternative underlying disease is also being assessed."*

1 This definition has been developed by national expert consensus and closely aligns with high quality international guidelines (Soriano 2021, NICE 2022). Symptoms of post-COVID-19 condition may be experienced by people who had mild, moderate or severe COVID-19, or in people who were infected with SARS-CoV-2 but did not progress to COVID-19. Symptoms of long COVID may be attributed to impairment in the structure and function of various and multiple organs (Crook et al. 2022). Some symptoms subside gradually with self-directed care alone, while other symptoms may require care from a health professional, and new symptoms may arise over time.

The term 'long COVID', whilst encompassing post-COVID-19 condition, refers also to sequelae beyond four weeks post initial infection based on the US Centers for Disease Control and Prevention (CDC) definition (CDC, 2022). It is important to recognise both terminologies as symptoms that arise in the days and weeks following acute COVID-19 can be debilitating for the patient and delaying treatment until 12 weeks may hamper recovery.

A better understanding of long COVID is required to determine its role in peoples' treatment needs; health screening requirements; psychosocial needs and risks of other adverse outcomes (including cardiovascular, neurological and immunological conditions).

Understanding the prevalence and burden of long COVID in Australia is hampered by inadequate recording of long COVID in clinical software.

2 Existing high quality Australian qualitative studies describe the physical, psychological, economic and social effects of long COVID on patients, their carers and significant others. However, it is not currently possible to obtain a reliable and accurate quantitative understanding of the health, social and economic impact of long COVID in Australia. International estimates of long COVID range between 5-50% (Ledford 2022).

This variation reflects non-standard case definitions internationally, sub-optimal study design such as self-reporting with inadequate controls and variations in coding software.

A recent Australian survey study reported that 29% of adults with confirmed or suspected COVID-19, reported ongoing symptoms more than 4 weeks after COVID-19 and almost 5% reported ongoing symptoms three months or more after COVID-19 (Biddle and Korda 2022). Given that 10 million cases of COVID have been reported in Australia, it can be estimated that 5% (~ 500,000) Australians have experienced or are currently experiencing, post-COVID condition (symptoms lasting 3 months or more).

Existing long COVID clinics have been able to generate crucial data about the prevalence of long COVID secondary care, including data about likely prognosis for people receiving clinical treatment for long COVID in secondary care, however, this data cannot be extrapolated outside this setting. At the same time there is no comparable data source describing the prevalence of long COVID seen in primary care. Without this information it is impossible to understand the true experience or impact of long COVID in Australia.

Staying up-to-date with a rapidly evolving and complex evidence base.

We currently know little about long COVID, however, research is emerging which will add to the growing body of evidence and help us to understand more about the condition and how it may be best managed.

3 Studies researching long COVID tend to be complex, and interpretation of the results requires high level appraisal and synthesis skills. Furthermore, understanding how individual study results contribute to the whole evidence-base requires broad knowledge of the topic. New research is likely to continue to emerge for the foreseeable future, and mechanisms need to be in place to support clinicians to ensure they are able to provide consistent, evidence-based practice.

References

- CDC - Centers for Disease Control and Prevention. Long COVID or Post-COVID Conditions. 1 Sept 2022. <https://www.cdc.gov/coronavirus/2019-ncov/long-term-effects/index.html>
- Crook H, Raza S, Nowell J, Young M, Edison P. Long covid-mechanisms, risk factors, and management. *BMJ*. 2021 Jul 26;374:n1648. doi: 10.1136/bmj.n1648. Erratum in: *BMJ*. 2021 Aug 3;374:n1944. <https://www.bmj.com/content/374/bmj.n1648.long>
- Datta SD, Talwar A, Lee JT. A proposed framework and timeline of the spectrum of disease due to SARS-CoV-2 infection: illness beyond acute infection and public health implications. *JAMA* 2020;324:2251-2. doi:10.1001/jama.2020.22717 <https://jamanetwork.com/journals/jama/fullarticle/2773338>
- Ledford H. How common is Long COVID? Why studies give different answers. *Nature News*. June 2022. <https://www.nature.com/articles/d41586-022-01702-2>
- National Institute for Health and Care Excellence. COVID-19 rapid guideline: managing the long-term effects of COVID-19. <https://app.magicapp.org/#/guideline/6744>
- Soriano JB, Murthy S, Marshall JC, Relan P, Diaz JV; WHO Clinical Case Definition Working Group on Post-COVID-19 Condition. A clinical case definition of post-COVID-19 condition by a Delphi consensus. *Lancet Infect Dis*. 2022 Apr;22(4):e102-e107. doi: 10.1016/S1473-3099(21)00703-9. Epub 2021 Dec 21. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8691845>

Responses to Inquiry themes

1

The patient experience in Australia of long COVID and/or repeated COVID infections, particularly diagnosis and treatment

Recommendations:

- Establish an independent expert advisory group that includes clinical and research experts in long COVID and consumers and/or carers with lived experience of long COVID to advise the health minister on the health, social and economic impacts of recurrent SARS-CoV-2 infections and long COVID.
- Endorse and fund access to healthcare through a model of care that involves a tiered and integrated approach to care, as appropriate to the needs of patients and their carers and loved one

Supporting evidence:

In late 2020, the Taskforce conducted two focus groups with consumers and carers who had experienced long COVID, asking specifically about their experiences of long COVID. In addition, we have continually sought verbal and written feedback from consumers on the Australian long COVID guidelines. Across these conversations, consumers have described key values that they have either experienced or found to be missing. These include (a) continuity of care and clear handover between health care providers; (b) advocacy from clinicians to facilitate access to appropriate care and (c) advocacy from clinicians to facilitate engagement with employment; (d) demonstrating respect for patients by acknowledging symptoms, patient needs and patient and carer expertise; and (e) consistency of clinical care. These findings are corroborated by Australian and international studies that demonstrate significant impacts on physical and mental health, functional outcomes and economic impact for people with long COVID as well as their careers (Hodgson 2021, Macpherson 2022, Hitch 2022 unpublished).

In Australia, patients may be referred directly to rehabilitation following severe or critical COVID, where they are likely to receive high quality multidisciplinary care. However, for those who had mild or moderate COVID, access to diagnosis and treatment of long COVID can be more complicated. In our study, consumers who have a high level of health literacy, are located in close proximity to health care services and who have established therapeutic relationships with clinicians who themselves are receptive and informed about long COVID describe access to care optimistically. This experience was, unfortunately, described infrequently. Consumers with less positive experiences described clinician disbelief of their symptoms, clinician inability to provide or coordinate care, ensuing impacts on daily living, employment, and mental and social well-being, and the additional burden of being responsible with directing their own care pathway whilst dealing with the sometimes debilitating symptoms of long COVID. Long COVID is a complex and variable condition

and patients with long COVID and their carers have substantially different needs depending on the condition, ability to access care, and ability of the healthcare system, provider or team to provide this care.

Decisions about health system approaches to provide care should be informed by an expert advisory group that includes clinical and research experts in long COVID and consumers and/or carers with lived experience of long COVID. Members may be selected following a nomination and application process.

A tiered and connected model of care involving primary care, allied healthcare providers and specialist physicians would enable clinicians to facilitate optimal and patient-centred clinical care options for patients and their carers.

References

- Hodgson, C.L., Higgins, A.M., Bailey, M.J. et al. The impact of COVID-19 critical illness on new disability, functional outcomes and return to work at 6 months: a prospective cohort study. *Crit Care* 25, 382 (2021). <https://doi.org/10.1186/s13054-021-03794-0>
- Macpherson K, Cooper K, Harbour J, et al. Experiences of living with long COVID and of accessing healthcare services: a qualitative systematic review. *BMJ Open* 2022;12:e050979. doi: 10.1136/bmjopen-2021-050979 <https://bmjopen.bmj.com/content/12/1/e050979.info>

Recommendations:

- Continue to fund NCET to identify, assess, and synthesise up-to-date evidence and convene clinical expertise to develop and sustain recommendations for the clinical care of long COVID in adult and paediatric populations in Australia.
- Endorse and fund access to healthcare through a model of care that involves a tiered and integrated approach to care, as appropriate to the needs of patients and their carers and loved ones.

Supporting evidence:

COVID-19 appears to impact a plethora of body systems which may result in long lasting organ damage (Ayoubkhani et al. 2021). In addition, SARS-CoV-2 infection can lead to ongoing inflammation and damage to the immune system (Phetsouphanh 2022). For patients who are re-infected by SARS-CoV-2, there is evidence emerging which suggests a cumulative effect of infections on the body (Al-Aly et al. 2022, Bowe et al. 2022). These varying, and potentially cumulative, underlying pathologies result in the large range of symptoms and symptom profiles that patients with long COVID describe.

Clinicians and health systems are however tasked with providing clinical care for individual patients, as appropriate to their needs, circumstance and setting. This is a challenging task, especially for clinicians who may have no direct experience in providing this care and require trustworthy education, resources and systems to either provide this care themselves or facilitate multidisciplinary care, where appropriate.

The Taskforce recommends three solutions to assist clinicians and healthcare services to provide optimal care to patients with long COVID and repeated COVID-19 infections:

A

Continue to fund NCET to identify, assess, and synthesise up-to-date evidence and convene clinical expertise to develop and sustain recommendations for the clinical care of long COVID in adult and paediatric populations in Australia.

At present, ClinicalTrials.gov lists 190 studies underway focused on long COVID (NIH 2022) and in the past 12 months there were more than 4000 studies on long COVID published (PubMed 2022). It is not possible for a clinician to evaluate this quantity of data alone.

B

Endorse and support a model of care delivery that involves a tiered approach to providing clinical care.

Most patients with long COVID will not require specialist care. Many of these patients will be able to self-manage their clinical care. However others, will require clinical care from a general practitioner, and others still will require more intensive multi-disciplinary care involving the primary care team plus allied health and a variety of specialists such as rehabilitation specialists, occupational therapists, psychologists, psychiatrists, respiratory physicians, sleep specialists, dieticians, physiotherapists and others. At present, there is no clear pathway for patients and their care team to determine the most appropriate setting of care and how to facilitate transition between these settings.

C

Continue to invest in research that explores the experience of and effectiveness of treatments for long COVID in Australia so that this can inform clinical care and health services for long COVID. International research will provide valuable information, however, local research will produce specific data relevant to our population and healthcare services.

References

- Al-Aly, Z., Bowe, B. & Xie, Y. Long COVID after breakthrough SARS-CoV-2 infection. *Nat Med* 28, 1461–1467 (2022). <https://doi.org/10.1038/s41591-022-01840-0>
- Ayoubkhani D, Khunti K, Nafilyan V, et al. Post-covid syndrome in individuals admitted to hospital with covid-19: retrospective cohort study *BMJ* 2021; 372 :n693 doi:10.1136/bmj.n693 <https://www.bmj.com/content/372/bmj.n693>
- Bowe, B., Xie, Y. & Al-Aly, Z. Acute and postacute sequelae associated with SARS-CoV-2 reinfection. *Nat Med* (2022). <https://doi.org/10.1038/s41591-022-02051-3>
- NIH - National Institutes of Health. US National Library of Medicine. ClinicalTrials.gov. Accessed 28 Oct 2022 <https://clinicaltrials.gov/ct2/results?cond=%22long+covid%22&term=&cntry=&state=&city=&dist=>
- Phetsouphanh, C., Darley, D.R., Wilson, D.B. et al. Immunological dysfunction persists for 8 months following initial mild-to-moderate SARS-CoV-2 infection. *Nat Immunol* 23, 210–216 (2022). <https://doi.org/10.1038/s41590-021-01113-x>
- PubMed (search function). Accessed 28 Oct 2022. https://pubmed.ncbi.nlm.nih.gov/?term=%22Long+COVID%22+OR+%22Post-COVID%22+OR+%22Post+COVID%22&filter=date-searchy_1&sort=date

Recommendations

- Invest in Australian research to understand the impact of recurrent SARS-CoV-2 infections and long COVID including prevalence and prognosis, pathological mechanisms, assessment and diagnosis, and prevention, treatment and models of care.
- Continue to fund NCET to identify, assess, and synthesise up-to-date evidence and convene clinical expertise to develop and sustain recommendations for the clinical care of long COVID in adult and paediatric populations in Australia.

Supporting evidence

Long COVID is poorly understood (Biddle and Korda 2022; Dryden et al. 2022; Erinoso et al. 2022), with a significant lack of clarity around the available data and subsequent implications for clinical care. This current situation could be said to parallel our situation in early 2020 for acute COVID – where clinical guidance was urgently needed for a topic for which there was limited evidence and research was underway. Research is ongoing with a long pipeline of studies in progress, which will add to the growing body of knowledge and improve our understanding of the overall impact of long COVID.

The volume and reach of the research shows that the scientific community feels there are many areas to explore and highlights the current lack of understanding of this condition. As more long COVID research becomes available, there will be a need to review emerging research and update long COVID guidance more, to ensure Australians are provided the best care based on the most up-to-date evidence.

Overseas, much funding has been invested into long COVID research, with the United Kingdom allocating over £50 million (over \$89 million Australian dollars) (NIHR 2022), and the United States of America planning to spend US\$1.15 billion (over \$1.5 billion Australian dollars) (Subbaraman 2022). Collaborative Australian research into long COVID could prove valuable as it would provide specific data relevant to our population and healthcare services, and enable decisions to be based on local context and patient needs. Additionally, there is a need to keep abreast of emerging international research into long COVID to ensure management of this condition in Australia is adhering to best available evidence.

Long COVID topics are being researched across the globe, including the prevalence of long COVID, characteristics of long COVID, direct impacts (e.g. on central nervous system and lungs, musculoskeletal pain), the lived experience of long COVID, some research focusing specifically in the impact of long COVID in paediatric populations, and a range of interventions (drug treatments, rehabilitation, even digital interventions). See Appendix 1 for further details and links.

Australian research on long COVID and reinfection following SARS-CoV-2 infection has been crucial to understanding the experience of long COVID by patients, carers and health care workers. Programs such as the ADAPT study (Phetsouphanh 2021) have helped to describe the prevalence of long COVID in Australia and contribute to understanding the biological mechanisms that drive long COVID symptoms. Similarly, qualitative research with consumers and carers has helped to describe the experiences of care amongst people with long COVID. Finally, these research groups along with many others have established interdisciplinary translational study groups to share their learnings spanning basic laboratory science, clinical research, epidemiology, health services research, health economics and clinical guideline development. The Victorian Post-Acute COVID Study group for example has been operating un-funded since 2021. This multidisciplinary group has enabled efficient translation of research into clinical practice and policy but is at risk of dissolution without ongoing funding support.

While much can be learned from international research, it is necessary to conduct Australian studies for a few reasons: 1) the Australian context differs somewhat to other countries as the majority of infections were Omicron in a highly vaccinated population, and 2) to understand the patient and health care system needs in Australia and translate research findings into Australian clinical practice. For instance, some of Australia's strongest estimates of long COVID (Angeles et al. 2022) for decision-making has been based, necessarily, on international data, because Australian data is lacking (PREPRINT Howe et al. 2022).

Since the general understanding of the long COVID condition remains somewhat equivocal at this point in time, the impact on deferring treatment, reduced health screening, postponed elective surgery, and increased risks of other outcomes (including cardiovascular, neurological and immunological conditions) is also unclear.

References

- Angeles, M.R., Wannan Arachchige Dona, S., Nguyen, H. et al. Modelling the potential acute and post-acute burden of COVID-19 under the Australian border re-opening plan. *BMC Public Health* 22, 757 (2022). <https://doi.org/10.1186/s12889-022-13169-x>
- Howe S, Szanyi J, Blakely T. The health impact of long COVID during the 2021-2022 Omicron wave in Australia: a quantitative burden of disease study. medRxiv 2022.08.01.22278219; doi: <https://doi.org/10.1101/2022.08.01.22278219> PREPRINT
- NIHR - National Institute for Health and Care Research. Researching long COVID. Accessed 28 Oct 2022. <https://www.nihr.ac.uk/covid-19/researching-the-long-term-impact.htm#:~:text=Research%20into%20long%20COVID.in%20long%20COVID%20research%20projects>
- Phetsouphanh, C., Darley, D.R., Wilson, D.B. et al. Immunological dysfunction persists for 8 months following initial mild-to-moderate SARS-CoV-2 infection. *Nat Immunol* 23, 210–216 (2022). <https://doi.org/10.1038/s41590-021-01113-x>
- Subbaraman N. US health agency will invest \$1 billion to investigate 'long COVID'. *Nature*. 2021 Mar;591(7850):356. doi: 10.1038/d41586-021-00586-y. <https://www.nature.com/articles/d41586-021-00586-y>

The health, social, educational and economic impacts in Australia on individuals who develop long COVID and/or have repeated COVID infections, their families, and the broader community, including for groups that face a greater risk of serious illness due to factors such as age, existing health conditions, disability and background.

Recommendation:

- Establish an independent expert advisory group that includes clinical and research experts in long COVID and consumers and/or carers with lived experience of long COVID to advise the health minister on the health, social and economic impacts of recurrent SARS-CoV-2 infections and long COVID.
- Invest in Australian research to understand the impact of recurrent SARS-CoV-2 infections and long COVID including prevalence and prognosis, pathological mechanisms, assessment and diagnosis, and prevention, treatment and models of care.

Supporting evidence

Given we currently have limited understanding of the various impacts of long COVID, it is not entirely clear what health, social, educational and economic impacts may be on individuals in Australia who develop long COVID and/or have repeated COVID infections, their families, and the broader community (including for groups that face a greater risk of serious illness due to factors such as age, existing health conditions, disability and ethnic background). Estimates of the prevalence of long COVID are challenging, with results from international prevalence studies ranging widely, (5 - 50% (Ledford 2022)) and even then it is not clear if this percentage is per total COVID-19 infections or per total population. A recent Australian survey study suggests that long COVID affects 29% of adults with confirmed or suspected COVID-19, leading to an estimated almost 5% (~ 1 million*) of adult Australians having experienced, or are currently experiencing, long COVID, with symptoms lasting 3 months or more (Biddle and Korda 2022).

Current epidemiological studies also indicate that long COVID is disproportionately reported in women and that re-infections are disproportionately reported by young people, people from low-earning households and healthcare workers (Thompson et al. 2022). These groups make up a significant part of the labour workforce so en masse impacts on these groups are likely to have notable downstream effects on workplaces and society.

It is likely that an illness such as COVID-19 will have disproportionate effects on people in socially and financially disadvantaged groups (de Leeuw et al. 2022). Surveillance of effects of care needs to look closely Aboriginal and Torres Strait Islander Peoples, Culturally and Linguistically Diverse (CALD) communities, LGBTIQ+, people with serious mental illness, as well as other relevant groups and early

involvement and appropriate representation of people from these groups should be considered for relevant expert committees.

The anticipated volume of the burden of long COVID will depend on the prevalence of the condition. Long COVID follows a SARS-CoV-2 infection, and the impact of SARS-CoV-2 infections (based on available evidence) appears to be cumulative (Al-Aly et al. 2022, Bowe et al. 2022) - i.e. the health prognosis becomes poorer with each additional infection. Thus, aiming towards limiting the number of SARS-CoV-2 infections is a logical way to minimise the potential (and somewhat unknown - at this stage) impact of long COVID and repeated SARS-CoV2 infections. Despite a highly vaccinated population, however, a recent Australian study estimated that long COVID caused 74% of the overall years lived with disability from SARS-CoV-2 infections in the BA.1/BA.2 wave (Howe 2022).

Discussions around long COVID tend to focus on adults, however the potential impact of long COVID on the paediatric population is also being considered in research (Haddad et al. 2022; Lopez-Leon et al. 2022; Zimmerman et al. 2022). It would be prudent to monitor emerging evidence around the potential impacts of long COVID on the paediatric population, who may have to live with outcomes for a longer period of time, with potential ramifications for their health, quality of life, along with associated impacts on the healthcare system and social and economic flow-on effects. As we anticipate the health, social and economic impacts of recurrent SARS-CoV-2 infections and long COVID will evolve, it is necessary to establish an independent expert advisory group that can inform the Health Minister on these changes and to provide advice to the minister about potential solutions.

Decisions about long COVID in Australia, however, need both international and Australian data. Many of the epidemiological characteristics, such as prevalence, and the impacts of these in Australia will only be possible if data on long COVID is captured accurately across all settings of care.

* based on an assumption of approximately 20 million Australian adults (over 18 years), and the findings from Biddle and Korda 2022.

References

- Al-Aly, Z., Bowe, B. & Xie, Y. Long COVID after breakthrough SARS-CoV-2 infection. *Nat Med* 28, 1461–1467 (2022).
<https://doi.org/10.1038/s41591-022-01840-0> <https://www.nature.com/articles/s41591-022-01840-0>
- Biddle N and Korda R. The experience of COVID-19 in Australia, including long-COVID – Evidence from the COVID-19 Impact Monitoring Survey Series, August 2022. 12 Oct 2022.
https://csrcm.cass.anu.edu.au/sites/default/files/docs/2022/10/The_experience_of_COVID-19_in_Australia_-_For_web.pdf
- Bowe, B., Xie, Y. & Al-Aly, Z. Acute and postacute sequelae associated with SARS-CoV-2 reinfection. *Nat Med* (2022).
<https://doi.org/10.1038/s41591-022-02051-3>
- de Leeuw E, Yashadhana A, Hitch D. Long COVID: sustained and multiplied disadvantage. *Med J Aust.* 2022 Mar 21;216(5):222-224. doi: 10.5694/mja2.51435. Epub 2022 Mar 6. PMID: 35249215; PMCID: PMC9115005.
<https://pubmed.ncbi.nlm.nih.gov/35249215/>
- Haddad A, et al. Long COVID symptoms in exposed and infected children, adolescents and their parents one year after SARS-CoV-2 infection: A prospective observational cohort study. *EBioMedicine.* 2022 Oct;84:104245. doi: 10.1016/j.ebiom.2022.104245. Epub 2022 Sep 22.
<https://www.sciencedirect.com/science/article/pii/S2352396422004273>
- Howe S, Szanyi J, Blakely T. The health impact of long COVID during the 2021-2022 Omicron wave in Australia: a quantitative burden of disease study. medRxiv 2022.08.01.22278219; doi:<https://doi.org/10.1101/2022.08.01.22278219>
- Ledford H. How common is long COVID? Why studies give different answers. *Nature.* 2022 Jun;606(7916):852-853. doi: 10.1038/d41586-022-01702-2.
<https://www.nature.com/articles/d41586-022-01702-2>
- Lopez-Leon, S., Wegman-Ostrosky, T., Ayuzo del Valle, N.C. et al. Long-COVID in children and adolescents: a systematic review and meta-analyses. *Sci Rep* 12, 9950 (2022).
<https://doi.org/10.1038/s41598-022-13495-5>
<https://www.nature.com/articles/s41598-022-13495-5>
- Thompson EJ, Williams DM, Walker AJ, et al. Long COVID burden and risk factors in 10 UK longitudinal studies and electronic health records. *Nat Commun.* 2022 Jun 28;13(1):3528. doi: 10.1038/s41467-022-30836-0.
<https://www.nature.com/articles/s41467-022-30836-0>

The impact of long COVID and/or repeated COVID infections on Australia’s overall health system, particularly in relation to deferred treatment, reduced health screening, postponed elective surgery, and increased risk of various conditions including cardiovascular, neurological and immunological conditions in the general population

Recommendations:

- Establish an independent expert advisory group that includes clinical and research experts in long COVID and consumers and/or carers with lived experience of long COVID to advise the health minister on the health, social and economic impacts of recurrent SARS-CoV-2 infections and long COVID.
- Invest in Australian research to understand the impact of recurrent SARS-CoV-2 infections and long COVID including prevalence and prognosis, pathological mechanisms, assessment and diagnosis, and prevention, treatment and models of care.
- Convey a clear message to the public and to health care providers that prevention of COVID-19 is the most-effective method of preventing long term health issues resulting from SARS-CoV-2 infection.
- Continue to invest in collaborative preventive activities to strengthen the message that prevention of COVID-19 is the most-effective method of preventing long term health issues resulting from SARS-CoV-2 infection (e.g. vaccination - including boosters where appropriate, use of masks in crowded indoor scenarios, hand washing, cough/sneeze etiquette, staying home when sick, isolating until symptoms resolve).

Supporting evidence

Note: SARS-CoV-2 relates to the virus and the infection, while COVID-19 refers to the disease [first recorded in 2019] caused by the SARS-CoV-2 virus. Some people may experience asymptomatic SARS-CoV-2 infections, and not progress to COVID-19, yet some research suggests asymptomatic infections may still carry the risk of developing long COVID (Malkova 2022). “Repeated SARS-CoV-2 infections” and “long COVID” are related, but distinct, concepts and we currently lack clarity about both topics.

A

Repeated SARS-CoV-2 infections

While our understanding remains limited, some research suggests that the impact of repeated SARS-CoV-2 infections could lead to long term health consequences. One large United States (US) cohort study found increased risk of death and other disorders (cardiovascular, coagulation and haematologic, gastrointestinal, kidney, mental health, metabolic, musculoskeletal and neurologic disorders) related to breakthrough SARS-CoV-2 infections (infections after vaccination) 6 months after infection suggesting that vaccination alone may not optimally reduce long-term health consequences of SARS-CoV-2 infection and that the impact of repeated infections may be cumulative. (Al-Aly et al. 2022)

B

Long COVID

There is much uncertainty around long COVID. The potential impacts of long COVID are likely to be larger if there are more (including repeat), SARS-CoV-2 infections for a few reasons, including:

- The likelihood of people developing long COVID outcomes increases with more SARS-CoV-2 transmission,
- The long-term health impacts of repeated SARS-CoV-2 infections may be cumulative, and
- An increase in the volume of long COVID patients potentially requiring healthcare intervention may place additional pressure on an already strained healthcare system struggling with issues, including staffing shortages.

The more infections there are, the increased likelihood of long COVID outcomes, and worse long COVID outcomes are likely with repeated infections, worsening with each successive infection. Additionally, the potential for the emergence of immune evasive variants exists while SARS-CoV-2 continues to circulate, which may increase the risk of SARS-CoV-2 transmission and increase the total number of infections.

C

Long term impact

Due to limited understanding of the long COVID condition, there exists a huge clinical knowledge and treatment gaps. There exists a potential for long COVID to lead to longer term health issues that could impact all Australians, with potentially serious implications for our healthcare workers, healthcare system (RACGP 2022) which may potentially indirectly contribute to social and economic impacts (O'Brien 2022; Cutler 2022).

D

Protection against long COVID

Hybrid immunity (the combined impact of vaccination with a history of SARS-CoV-2 infection) appears to provide additional protection than vaccination or infection alone (Hui 2022; Zar et al. 2022). For Australia, with extremely high vaccine coverage, this means that the general population are in a strong position in terms of overall immune protection against SARS-CoV-2. However, as at the end of Oct 2022 we continue to record over 30,000 SARS-CoV-2 infections weekly (Aus. Gov. 2022) and we continue to identify further long COVID cases (ABC RN 2022). This ongoing occurrence of SARS-CoV-2 infections and long COVID cases demonstrates an ongoing need for continued clinical and public vigilance to prevent SARS-CoV-2 infections and long COVID.

!

Of additional concern, while the SARS-CoV-2 virus continues to circulate, there remains the risk of emergent immune evasive variants - an unknown variable which could throw current COVID-19 and long COVID planning off kilter, and may lead to an unexpected increase in SARS-CoV-2 cases.

!

Evidence has demonstrated the effectiveness of COVID-19 vaccines, social distancing, and appropriate mask use to decrease the impact of the SARS-CoV-2 virus. (Trauer 2021)

With the shift away from mandated mask use and regular reporting of COVID-19 cases, and the recent removal of the requirement for isolation following confirmed infection, people may have the highly inaccurate impression that COVID-19 is “over”. There is a lack of messaging that potential health risks related to COVID-19 continue to be relevant and that vaccines, mask use in crowded indoor spaces, testing and isolation are still a valuable way to decrease the transmission of SARS-CoV-2, and mitigate the impact of long COVID.

References

- ABC Radio National. Long COVID cases on the rise in Australia. Aired 13 Oct 2022. <https://www.abc.net.au/radionational/programs/breakfast/long-covid-cases-on-the-rise-in-australia/101528514>
- Al-Aly, Z., Bowe, B. & Xie, Y. Long COVID after breakthrough SARS-CoV-2 infection. *Nat Med* 28, 1461–1467 (2022). <https://doi.org/10.1038/s41591-022-01840-0>
- Aus. Gov. Dept. of Health. Coronavirus (COVID-19) case numbers and statistics. Accessed 28 Oct 2022. <https://www.health.gov.au/health-alerts/covid-19/case-numbers-and-statistics>
- Cutler DM. The Costs of Long COVID. *JAMA Health Forum*. 2022;3(5):e221809. doi:10.1001/jamahealthforum.2022.1809 <https://jamanetwork.com/journals/jama-health-forum/fullarticle/2792505>
- Hui DS. Hybrid immunity and strategies for COVID-19 vaccination. *Lancet Infect Dis*. 2022 Sep 21:S1473-3099(22)00640-5. doi: 10.1016/S1473-3099(22)00640-5. Epub ahead of print.
- Malkova A, Kudryavtsev I, Starshinova A, et al.. Post COVID-19 Syndrome in Patients with Asymptomatic/Mild Form. *Pathogens*. 2021 Oct 30;10(11):1408. doi: 10.3390/pathogens10111408.
- O'Brien E. Bloomberg - Politics Economics. 10 Oct 2022. <https://www.bloomberg.com/news/articles/2022-09-10/long-covid-costs-australia-economy-3-6-billion-a-year-report>
- RACGP. 'Large potential burden': Long COVID warning for GPs. 24 Jun 2022. <https://www1.racgp.org.au/newsgp/clinical/large-potential-burden-long-covid-warning-for-gps>
- Trauer JM, Lydeamore MJ, Dalton GW, Pilcher D, Meehan MT, McBryde ES, Cheng AC, Sutton B, Ragonnet R. Understanding how Victoria, Australia gained control of its second COVID-19 wave. *Nat Commun*. 2021 Nov 1;12(1):6266. doi: 10.1038/s41467-021-26558-4. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8560916/>
- Zar HJ, MacGinty R, Workman L, et al. Natural and hybrid immunity following four COVID-19 waves: A prospective cohort study of mothers in South Africa. *EclinicalMedicine*. 2022 Sep 17;53:101655. doi: 10.1016/j.eclinm.2022.101655.

Best practice responses regarding the prevention, diagnosis and treatment of long COVID and/or repeated COVID infections, both in Australia and internationally

Recommendations:

- Continue to fund NCET to identify, assess, and synthesise up-to-date evidence and convene clinical expertise to develop and sustain recommendations for the clinical care of long COVID in adult and paediatric populations in Australia.
- Support international and national collaboration and networking activities to understand and improve the health, social and economic impacts of recurrent SARS-CoV-2 infections and long COVID.
- Endorse and fund access to healthcare through a model of care that involves a tiered and integrated approach to care, as appropriate to the needs of patients and their carers and loved ones.

Supporting evidence

A

Prevention

Given our limited understanding of long COVID, the best practice would be to prevent long COVID, by limiting exposure to the SARS-CoV-2 virus. This is challenging given the Omicron variant is considered one of the most infectious viruses known (RACGP 2022). However, we know that adhering to vaccine recommendations and limiting exposure (through physical distancing and use of appropriate masks) work (Talic et al. 2022), and that testing and isolation (where possible) can reduce potential transmission (Kucharski et al. 2022).

Since 2020, the Taskforce has been gathering and synthesising data to inform best practices clinical care for the treatment of long COVID (NCET 2022). Our approach involves daily searches for evidence, appraisal of this evidence and development of recommendations for clinical care using the GRADE methodology. The Guidelines are approved by the NHMRC (National Health and Medical Research Council) and endorsed by 35 health care organisations across Australia.

B**Diagnosis**

At present there is no established definitive test for long COVID. To avoid adding burden to the person, limit investigations to those that are necessary for determining care. General practitioners are well placed to undertake initial investigations and diagnosis of long COVID, including determining if symptoms are related to or exacerbated by comorbid conditions. In some instances, patients may require additional assessment by more than one specialist to exclude other conditions contributing to their symptoms. A tiered model of care (similar to that used for COVID-19) could be employed across the healthcare system, notably coordinated within primary care, to avoid unnecessary burden on the patient and health system and to guide patient-centred and appropriate clinical care.

C**Management**

The Taskforce guidelines recommend that due to the broad range of symptoms and signs following acute COVID-19, a biopsychosocial approach to care, within the local context, is important. The primary health care team is well placed to coordinate person centred care and should remain a central point in the care team along with the person's carer or significant other. Best practice would include a multidisciplinary team. This could be accessed through general practice, community health, rehabilitation programs or post-COVID-19 clinics, where these are available.

Whilst NCET aims to provide evidence-based recommendations, until recently, there has been sparse evidence that could be used to inform evidence-based recommendations specifically for the management of long COVID. In the absence of high-quality evidence, NCET develops expert-consensus based recommendations that are developed by a panel comprising many specialties across primary, secondary and tertiary care. These recommendations are also informed by learnings from international health systems through bi-monthly liaison with key international guideline development groups including the World Health Organization, National Institute for Health and Care Excellence, Public Health Agency of Canada and Danish Health Authority.

The evidence to inform treatment, however, is beginning to emerge with over 20 randomised controlled trials currently describing the effectiveness of rehabilitation interventions on long COVID. These, and future studies, will be continually reviewed by NCET to develop evidence-based recommendations for the clinical care of people with long COVID.

References

- NCET. Australian Guidelines for the clinical care of people with COVID-19. <https://app.magicapp.org/#/guideline/6689>
- Kucharski AJ, Klepac P, Conlan AJK et al.. Effectiveness of isolation, testing, contact tracing, and physical distancing on reducing transmission of SARS-CoV-2 in different settings: a mathematical modelling study. *Lancet Infect Dis.* 2020 Oct;20(10):1151-1160. doi: 10.1016/S1473-3099(20)30457-6. Epub 2020 Jun 16. [https://www.thelancet.com/article/S1473-3099\(20\)30457-6/fulltext](https://www.thelancet.com/article/S1473-3099(20)30457-6/fulltext)
- Talic S, Shah S, Wild H, et al.. Effectiveness of public health measures in reducing the incidence of covid-19, SARS-CoV-2 transmission, and covid-19 mortality: systematic review and meta-analysis. *BMJ.* 2021 Nov 17;375:e068302. doi: 10.1136/bmj-2021-068302. Erratum in: *BMJ.* 2021 Dec 3;375:n2997. <https://www.bmj.com/content/375/bmj-2021-068302>
- RACGP. 2 Mar 2022. How does Omicron compare with Delta?
<https://www1.racgp.org.au/newsgp/clinical/how-does-omicron-compare-with-delta>

Appendix 1: Ongoing long COVID research

Listed below are some examples of the many registered long COVID studies (NIH, 2022):

Paediatric

- Long COVID Kids DK - Investigating Long-term Covid-19, conducted by Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark.
(<https://clinicaltrials.gov/ct2/show/NCT04786353?cond=Long+COVID&draw=7&rank=55>)
- Long term influence of pediatric long COVID Syndrome, conducted by National Taiwan University Children Hospital Pediatric Neurology Department, Taipei, Taiwan
(<https://clinicaltrials.gov/ct2/show/NCT05566392?cond=Long+COVID&draw=2&rank=7>)

General

- Health-related Quality of Life and Long COVID (OpenPROMPT), conducted by London School of Hygiene and Tropical Medicine, London, United Kingdom.
(<https://clinicaltrials.gov/ct2/show/NCT05552612?cond=Long+COVID&draw=2&rank=2>)
- Exploring the characteristics of long COVID, conducted by University Hospital Zurich Zurich, Switzerland
(<https://clinicaltrials.gov/ct2/show/NCT04793269?cond=Long+COVID&draw=2&rank=3>)
- Long term effects of SARS-CoV-2 on the central nervous system and one year follow-up of long COVID patients, conducted by CHU Brugmann, Brussels, Belgium
(<https://clinicaltrials.gov/ct2/show/NCT05492292?cond=Long+COVID&draw=3&rank=14>)
- Developing an Integrative, Recovery-Based, Post-Acute COVID-19 Syndrome (PACS) Psychotherapeutic Intervention, conducted by James J. Peters VA Medical Center, Bronx, NY, United States.
<https://clinicaltrials.gov/ct2/show/NCT05453201?cond=Long+COVID&draw=5&rank=40>
- "Long COVID-19" on the Human Brain, conducted by Centre for Addiction and Mental Health, Toronto, Ontario, Canada.
<https://clinicaltrials.gov/ct2/show/NCT05433324?cond=Long+COVID&draw=5&rank=31>

Many studies focus on long COVID intervention options, including drug treatments, rehabilitation and other options, such as digital health interventions:

- Pulmonary rehabilitation
- Impact of Monoclonal Antibody Treatment on Post-Acute COVID-19 Syndrome
- Long-term COVID and Rehabilitation
- Effects of Sodium Pyruvate Nasal Spray in COVID-19 Long Haulers.
- CArdiac REhabilitation for Building Exertional heArt Rate for Chronotropic Incompetence in Long COVID-19
- Digital Health Intervention Based on Artificial Intelligence to Support the Personalized Recovery of Long COVID Patients Affected by Fatigue (AIDA)
- See list of related research:

<https://clinicaltrials.gov/ct2/results?cond=Long+COVID&term=&cntry=&state=&city=&dist=>

Reference

NIH - National Institutes of Health. US National Library of Medicine. ClinicalTrials.gov. Accessed 28 Oct 2022

<https://clinicaltrials.gov/ct2/results?cond=%22long+covid%22&term=&cntry=&state=&city=&dist=>