

Response to the House Standing Committee on Health, Aged Care and Sport inquiry into long COVID and repeated COVID infections, November 2022

The Australian Academy of Health and Medical Sciences (AAHMS) and the Australian Academy of Science (AAS) welcome the opportunity to respond to the Standing Committee on Health, Aged Care and Sport's Inquiry into Long COVID and Repeated COVID Infections. The AAS and AAHMS are Learned Academies that provide independent, authoritative, and influential scientific advice to government. We have amongst our Fellows some of Australia's leading experts in a range of scientific and health matters, including researchers, health professionals and individuals working in industry.

The Academies were at the forefront of the Australian COVID response. In the first year of the COVID pandemic, both AAHMS and the AAS prepared timely reports based on specific questions raised by the Australian Government through the Rapid Research Information Forum.¹ These peer-reviewed reports briefly synthesised available information at the start of the pandemic on a variety of questions asked for by the Australian Government

Given our expertise, our responses focus on the Terms of Reference that relate most closely to research, innovation, and evidence-based care. This response has been developed based on input from our Fellows and other experts. We received most input on current issues associated with long COVID, to which the majority of our comments are addressed.

Key Messages

- Preventing COVID-19 infections remains the best way of preventing long COVID.
- Evidence on long COVID and repeated infections is still evolving. Decisions need to be made based on emerging evidence and it is crucial that we continue this research to inform future decision making.
- Based on current evidence, the individual burden of long COVID is most commonly associated with neurocognitive difficulties ("brain fog") and fatigue.
- The World Health Organisation (WHO) case definition for long COVID emphasises that these symptoms should be "unexplained by an alternative diagnosis" (e.g. fatigue 'explained' by cardiac failure) and will "generally have an impact on everyday functioning".
- Considering physical, mental, psycho-social, economic and occupational impacts, there is currently limited understanding of the burden and experiences of those suffering from repeated COVID-19 infections.
- As Australia's path through the COVID-19 pandemic was different from that of most other countries due to early lockdowns until vaccination rates were high, our experience of long COVID may be different. There is a strong case for progressing targeted research specifically within the Australian community.

- A national coordinated effort is needed to collect and utilise appropriate data relating to long COVID and repeated infections, to build a more complete picture of prevalence and the associated impacts in Australia.
- Patients experiencing long COVID report that they have not always felt understood and supported by the health system.
- Australia can improve access to healthcare for patients experiencing long COVID and develop better and clearer care pathways within the health system. Well-defined and consistent guidelines, along with adequate resources, are needed to assist healthcare professionals to identify, diagnose and manage the different manifestations, trajectories and impacts, direct or indirect, of long COVID.
- Overall, a health system in which research and innovation are embedded as core functions will be best equipped to understand and address ongoing challenges arising from the COVID pandemic, including long COVID and repeated infections.

Introduction

The COVID-19 pandemic has had dramatic effects on Australia and worldwide.

As communities adopt their 'new normal', there are ongoing impacts that must be addressed, including the effects of long COVID and repeated COVID infections. There is still considerable uncertainty surrounding the best approaches to diagnosis, treatment and prevention of long COVID, as well as the prevalence and impacts of repeated infections.²⁻⁵ Disease prevalence is the proportion of a population that a particular disease or condition at a specified point in time. Without understanding the true impact of long COVID and repeated infections, we cannot adequately and proportionately support those experiencing long term complications.

The WHO defines long COVID as at least one persisting symptom three months post-infection.⁶ There are more than 200 known symptoms associated with long COVID and 12 core outcomes, which is relatively high for a single condition.^{7,8} A core outcome set is a group of standardised outcomes relating to a particular condition that should be reported in all clinical trials focussing on that condition. Researchers use them to measure and compare clinical outcomes across multiple studies.⁹ For long COVID, some core outcomes include mental and physical function, cardiovascular function and pain.⁸ Risk factors associated with a higher likelihood of developing long COVID include female sex, increasing age and increasing body mass index.¹⁰

There are limited active studies of long COVID in Australia, and most evidence currently comes from overseas. However, there is significant heterogeneity in overseas literature.¹¹ Current studies on long COVID often examine considerably different groups, which vary for instance in hospitalisation status, average cohort age, follow-up methods and symptom assessment tools. Without the same conditions being used by studies in differing contexts, it is hard to ensure that conclusions made are translatable to the Australian context.

It is also important to note that Australia's COVID pandemic experience has been quite different from that of many other countries. Australia maintained relatively low infection rates before vaccination was available and then experienced relatively high rates of vaccination, although booster vaccination rates have slowed as public health measures have

relaxed. Australia is also a high-income country with a public healthcare system, meaning our population had better access to healthcare during the pandemic than other countries.

Given this contrast, international evidence may have limited value when used to determine the most appropriate responses in Australia. It would be more effective and appropriate to develop policy based on evidence directly from within the Australian community.

Q3. Research into the potential and known effects, causes, risk factors, prevalence, management, and treatment of long COVID and/or repeated COVID infections in Australia

Australia's health and medical research and innovation sector has played a vital role in tackling the pandemic.¹² This sector will remain crucial to Australia's ongoing understanding of and response to long COVID and repeated infections.

At present, the evidence base required to guide decisions surrounding long COVID and repeated infections is inadequate. At a foundational level, we are yet to understand the immunopathogenesis of long COVID (i.e. the underlying disease mechanisms which are causing this heterogeneous condition). There are several possible explanations, two or more of which may co-exist: long COVID could be (1) due to remnants of the virus persisting in an individual's system; (2) an autoimmune phenomenon where the body makes immune cells and/or antibodies that react against certain of its own tissues; (3) a result of an excessive immune cell or inflammatory response to the infection; or (4) effects of the body trying to repair itself after experiencing a COVID-19 infection. By determining the cause(s) of long COVID, we can better develop specific diagnostic tests, evidence-based approaches and guidelines for individually tailored decision-making regarding treatments, rehabilitation and symptom management.

Some examples of current gaps in our knowledge, or where we have only a partial understanding, include:

- Immunopathogenesis (and pathology) of long COVID
 - Underlying mechanisms of long COVID
 - Markers at a biological level that help identify the presence of the disease and assist in diagnosing the condition
 - Impact of vaccination and variant on prevalence, severity, recovery and developing long COVID
- Epidemiology
 - Prevalence of long COVID and incidence of repeat infections
 - Impact on individuals and their daily functioning
 - Length of average recovery time
 - Impact on neurocognitive (brain) and social skills development (specifically in children and young people)
 - Quality of life of those experiencing these conditions
 - Prevention of long COVID and repeated infections beyond reducing the risk of exposure (e.g. mask wearing) and disease through vaccination
 - Risk factors for repeated infections beyond exposure to the virus
 - Severity of second and third infections compared with initial infection

- Influence of SARS-CoV-2 variants and vaccination status/antiviral treatments/other measures on prevalence and presentation of long COVID
- Potential impacts of long COVID on individuals experiencing comorbidities
- Health system management
 - Clinical and community service requirements to support patients with long COVID and repeated infections (which will be addressed further in the 'Health system impacts' section below).
 - Quality of care being received by long COVID patients in different settings
 - Different care settings across Australia and the difference between those who have interacted only with a general practitioner (GP) compared to being hospitalised for both initial COVID infection and long COVID
 - Impacts of long COVID and repeated infections on the health system and other sectors
 - Additional care considerations for vulnerable communities, such as aged care residents and children
- Treatment and recovery
 - Appropriate effective treatments
 - Validated short term management strategies to alleviate the burden of lingering symptoms

Given that long COVID is a relatively new disease, there will naturally be some gaps in our understanding. However, it is important that these gaps are addressed as quickly as possible.

Successfully tackling long COVID demands a rapid and coordinated research effort to better target the condition. Currently there are only six registered clinical trials addressing long COVID in Australia, four of which are trialling an intervention (correct as of 28 October 2022).¹³ Areas of research and innovation that warrant further development include:

- Studying the pathophysiological basis of long COVID.
- Gathering data to improve our understanding of patient experiences including lingering symptoms from COVID infections, the duration of impacts and the recovery process, which must include a control group or groups to be meaningful.
- Optimising current preventative strategies for COVID-19, such as considering routine vaccine schedules.
- Investigating treatments, symptom management and recovery options through randomised-controlled trials (RCTs) for those experiencing long COVID.
- Discovering new treatment options for long COVID.
- Linking COVID registries with social and demographic factors, such as occupation, geographical location, socioeconomic status and cultural background to monitor the potential unequal distribution of long COVID in our community.
- Utilising qualitative methods to collect data on patients' lived experiences, thoughts and feelings as well as the experience of health professionals in managing the everyday impacts of the COVID-19 pandemic.
- Incorporating co-design methodology in research development, involving all stakeholders including those affected directly and indirectly (e.g. family members) as well as consumer representatives.

We welcome all efforts by Australian governments to work with health professionals, researchers, industry and those living with long COVID as it is critical to learn more about this condition to make informed and appropriate system level decisions. A more complete evidence base will assist policy makers to take actions that improve ongoing management, therapies, and rehabilitation as well as alleviate broader societal impacts. Until then, health and medical researchers, health professionals and patients are relying on research and information from various sources which may not be suited to an Australian context.

Q4. 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

It has been reported that some people experiencing long COVID do not feel they have been adequately understood and supported, which has led to patients feeling stigmatised, isolated and sometimes even dismissed by health professionals.^{14,15} The AAHMS' recent report underscored the desire for patients, consumers, families and carers to be involved in their health journeys.¹² The current lack of information for long COVID patients limits their potential to receive proactive and comprehensive care. It is also important that the health sector can engage in dialogue with other sectors so that resources are readily available for all to understand and support long Covid.

Health professionals do not have enough information to fully understand the condition, how to identify it and how to manage or refer their patients.¹⁶

There is a concern among some experts that the impact of long COVID will be different between various groups in our community. At present, there needs to be more evidence to draw clear conclusions about this aspect of long COVID. We urge the Government to consider these potential knowledge gaps and underlying impacts on at-risk groups:

- **The impacts of different long COVID experiences on quality of life** – the definition of long COVID remains broad, meaning patients may have a range of experiences. Although, anecdotally, fatigue and brain fog are the most commonly reported symptoms, they are not necessarily associated with as large an impact on daily function as respiratory or cardiovascular symptoms (reported less commonly). Additionally, some patients experience episodic disability, meaning that those symptoms causing a significant burden are not continuously present.
- **The impacts of long COVID on families and carers** – a key group that will be impacted by long COVID is the families and carers of patients. Many symptoms associated with long COVID can affect an individual's ability to complete tasks, work, interact and focus. Families and carers will likely assume a significant level of caring responsibility and additional household tasks to compensate for this loss in daily functioning. This is likely to place a considerable burden on families and carers, whether the condition is medically recognised or not.

- **The potential mental health and neurological impacts of long COVID** – these are relevant to all people with long COVID, but researchers believe that children and adolescents may be more susceptible – even among those with no history of mental illness or developmental delay. We need to ensure their experiences are understood, physical symptoms addressed, and if they have lost a level of daily function, the psychological impacts are adequately acknowledged and managed.
- **The impact of long COVID, and the COVID-19 pandemic more broadly, on those of low socioeconomic status (SES)** – low SES communities have been continually disadvantaged throughout the COVID-19 pandemic in Australia.¹⁷ A study of patients in England found that persisting symptoms post-COVID infection placed a higher burden on those living in low SES areas and on those with lower incomes.¹⁸ It has not yet been possible to explore whether this is the case in Australia due to limited studies considering SES as a factor in COVID-19 recovery. Governments need to consider how to deliver ongoing support for long COVID patients and repeated infections equitably across Australia – and to collect data to inform such decision-making.

Governments should consider strategies for engaging and supporting those living with long COVID. Based on the constellation of symptoms that long COVID patients may experience, those with “mild brain fog” will need a different care and referral pathway and ongoing management strategy than those with a predominant cardiorespiratory disease. Distinguishing these care pathways can inform and enhance our approach to care while improving patients’ experience of interacting with the health system. As an extension of this approach, the Government should aim to ensure that long COVID considerations are made within welfare and disability schemes to adequately support the diverse range of long COVID presentations.¹⁶

We also note the potential impacts of long COVID on Australia’s research and innovation community and its capacity to inform the response to these issues. The university research workforce comprises roughly 45% of Australia’s research workforce and has a high proportion of casual and fixed term workers who may not have access to adequate financial and/or career support if they experience long COVID.¹⁹ This poses risks to Australia’s pipeline of researchers, potentially weakening Australia’s intellectual and technological capability. It also threatens the research community’s ability to conduct research targeted towards Australia’s unique circumstances.

Furthermore, the pandemic has delayed efforts to improve diversity and inclusion. For example, women in the STEM workforce are under-represented as a whole and in senior and therefore more secure roles.²⁰ Consequently, disruption to the research pipeline may also threaten strategic aims to diversify Australia’s research workforce.²¹

Q5. 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

During the pandemic, we have seen Australia's health system work closely with research and innovation groups to rapidly build our understanding of the novel coronavirus, SARS-CoV-2, and then to translate that understanding efficiently into practice for treatment and prevention. This provides an important demonstration of how Australia is best equipped to generate and respond to local relevant evidence, and therefore to deliver cutting edge, cost-effective care when we embed research and innovation as core functions of the health system. This approach needs to be applied to long COVID, and indeed to other health challenges. The Australian Academy of Health and Medical Sciences has recently published a report setting out a plan for how Australia can build such a system, making the best use of existing resources in the health system and will ensure we are better placed to tackle future pandemics.¹²

Long COVID is still a very new condition, and we have yet to understand its pathogenesis. In time we may be able to attribute other explanations to the condition and its symptoms. Post-viral syndromes are a phenomenon following many common viral infections, such as Epstein-Barr virus infection (which causes glandular fever) and Ross River Fever, as well as historical pandemics such as SARS from the early 2000s and the 1918-1919 influenza pandemic.²² It is unsurprising that similar post-viral conditions would persist following COVID-19 infections. The current WHO long COVID definition encompasses many symptoms beyond those attributed to post-viral syndromes.⁶ Some long COVID experiences could transpire due to injury from the COVID-19 infection itself, such as end-organ complications. Studies have also suggested that immunocompromised patients are more likely to experience prolonged, or chronic, COVID infection and they will have particular needs that should be considered in healthcare and other support provided.²³

Given the potentially chronic nature of long COVID, these alternative explanations and the variety of patient experiences, a multi-pronged strategy will best support the health system in caring for those experiencing all post-viral syndromes and assisting long COVID patients in their recovery.

A network of long COVID clinics has been established, predominantly located in capital cities. Although more of these facilities are required to treat complex cases of long COVID, it is unlikely that these clinics alone will be sufficient to care for all affected Australians.¹⁶ Their concentration in urban areas creates inequitable access to care for those in regional, rural and remote areas. Realistically, most long COVID care will be provided at the primary and community level and so we must ensure that considerations are made to best support this requirement.¹²

Diagnosis of exclusion

Some long COVID symptoms are also associated with other conditions, such as post-intensive care syndrome, which can develop after hospitalisation. It is important to exclude

alternative explanations such as these when diagnosing long COVID.^{24,25} This is crucial to enabling health professionals to determine the most appropriate treatments and management approaches.

By using structured clinical assessments and laboratory investigations for conditions or disease that may be confused with long COVID, health professionals can exclude other conditions, characterise key symptoms and understand the associated functional impact. This would require our health system to support increased and standardised screening and a workforce with the knowledge and capacity to undertake these assessments.

General practice

The Government has identified general practice as a priority service provider, and we encourage policymakers to consider the impact long COVID and repeated infections could have on general practice workloads, as well as the role that GPs will play in diagnosing and treating those experiencing long COVID.²⁶

Most cases of long COVID are not likely to require hospitalisation and will be predominantly treated through primary care. GPs, nurse practitioners and other health professionals need to be adequately equipped to understand and acknowledge patient experiences, identify the condition in its various presentations and refer selected cases to appropriate specialists.

Patients also need the best quality information to navigate the health system. The UK has adopted a leading model of care for long COVID supported by an investment of roughly £224 million.²⁷ This has included a range of long COVID clinics, specialist hubs for children and young people, increased education for general practice, the development of a recovery website (which has 10.8 million users), and a self-guided rehabilitation platform (used by 2,200 patients).²⁸ These resources could be adapted to the Australian context as part of a holistic approach to managing long COVID and repeated infections.

Additional service requirements

Patients with long COVID will need access to a range of healthcare services. For instance, rehabilitative physiotherapy is successfully used for screening, managing and treating conditions with similar cardiovascular and respiratory symptoms and has also been used to assist long COVID patients.²⁹

The approach is different from that required for rehabilitation of fatigue syndromes. In long COVID patients with these fatigue related conditions, traditional cardiovascular and respiratory rehabilitative methods may trigger or worsen symptoms. Ongoing clinical research investigations should consider which rehabilitative methods are most appropriate for long COVID patients.

It is also important to note that the ongoing impacts of the pandemic relate not only to long COVID and repeated infections, but to the knock-on impacts of lockdowns, isolation, loss of income, domestic violence, education and many other issues stemming from the pandemic. There are concerns around the longer-term impacts on mental health and health inequities, and it is crucial that clinical services are available and equipped to support this aspect of pandemic recovery.

Q6. Best practice responses regarding the prevention, diagnosis and treatment of long COVID and/or repeated COVID infections, both in Australia and internationally

Long COVID is a very new health condition with a limited evidence base. International guidelines are emerging to support the clinical management of COVID-19, long COVID and repeated infections, including most prominently from the WHO.⁶

It should not be assumed that international clinical management guidelines will perfectly integrate into the Australian context, nor that they will be appropriate for our population: indeed, it is unlikely to be the case. Any guidelines adopted in the Australian health system should be developed in collaboration with our health professionals, researchers and those with lived experience.

Prevention

Preventing SARS-CoV-2 infection, including repeated infections, remains the best way of preventing long COVID, especially since its causes are not clear, and hence should remain a priority for the Government.³⁰ Methods of prevention have remained consistent throughout the pandemic, including social distancing, hygiene measures, mask-wearing and later, vaccination.³¹ Many of these public health measures have recently been relaxed for the general population and it is unclear how this will impact on long COVID and the occurrence of repeated infections. Modelling may assist research in this area and help guide the Australian response.

Vaccination reduces the likelihood of developing long COVID.³² Although Australia has reached high levels of vaccination against COVID-19 with a primary vaccine course, these rates have slowed, with only 72.2% of those over 16 years old receiving a third dose of the vaccine, compared with 97.2% receiving their first dose (correct as of 19 October 2022).³³ In addition, of those aged 5-15 years old, only 86.2% of those who received a first vaccine dose have also received a second dose. A continuing focus on ensuring optimal vaccination levels against COVID-19 and appropriately applying bivalent vaccines is an essential component of any response to long COVID.

Risk communication

A recurring theme from our discussions with researchers and clinicians was the need for better risk communication about long COVID and its prevention. Although it is understood that there will be concern among those experiencing persistent symptoms, and that this might also prompt vaccine uptake, there needs to be an increased effort to reduce the fear and anxiety surrounding the condition by promoting accurate information and effective management strategies. All communication efforts should take into account those who are culturally and linguistically diverse and be available in formats so as not to exclude people living with a disability.

This briefing has been informed by contributions from Fellows of the Australian Academy of Health and Medical Sciences and the Australian Academy of Science as well as other experts in fields including immunology, pathology, mental health, infectious diseases, population and



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public health, respiratory health and physiotherapy. We are grateful for their valuable contributions.

For questions about this submission, or to arrange a consultation with Fellows of the Academies, please contact Lanika Mylvaganam (policy@aaahms.org) at Australian Academy of Health and Medical Sciences or Chris Anderson (chris.anderson@science.org.au) at the Australian Academy of Science.

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