Australian Government
National Health and Medical Research Council

NHMRC

National COVID-19 Health and Research Advisory Committee*

Date of report: 30 July 2021

Advice 22: The implications of immunisation for long COVID

Focus

The Chief Medical Officer has requested a review of the evidence on the implications of immunisation for long COVID. Specifically the review seeks to answer the following questions:

- For individuals with long COVID, do the symptoms ease/get better after vaccination?
- For individuals who contract COVID-19 after vaccination, do they get long COVID?

This report was developed under the guidance of National COVID-19 Health and Research Advisory Committee (NCHRAC) members: Professor Alison Venn and Mr Daniel Zou.

This report reflects the evidence as of 8 July 2021 and may need further review as more evidence is available.

Key findings

- Preliminary findings suggest that vaccination of those who experience long COVID can occur without adverse impact. There is insufficient evidence available to support a conclusion that symptoms of long COVID ease after vaccination.
- Some individuals who contract COVID-19 after their first vaccination report symptoms that persist beyond 28 days, but there is insufficient evidence available to determine whether the risk of long COVID differs among individuals who are infected post-vaccination, compared with unvaccinated individuals.

Background

Long COVID is defined as both physical (respiratory and non-respiratory) and mental health effects that occur:

- For community cases: after the post-infectious period; that is, approximately 10–14 days after infection with SARS-CoV-2.
- For hospitalised cases: post-acute hospitalisation.

* NHMRC is providing secretariat and project support for the Committee, which was established to provide advice to the Commonwealth Chief Medical Officer on Australia's health response to the COVID-19 pandemic. The Committee is not established under the NHMRC Act and does not advise the NHMRC CEO.

Long COVID is also referred to as long-term sequelae of COVID-19, Long Haul COVID, Post COVID, Post-Acute Sequelae of COVID-19 (PASC) and Post-Acute COVID-19 Symptoms (PACS). For the purposes of this document the term 'long COVID' will be used.

Symptoms of long COVID are varied and numerous and research is underway identifying all symptoms associated with long COVID. Detailed advice on the evidence regarding long-term sequelae of COVID-19 has previously been provided in NCHRAC Advice 12.

Out of scope:

- Examination of long COVID symptoms connected to different strains of SARS-CoV-2.

Evaluation of the evidence

A search of PubMed on 1 July 2021, using the terms: long-term sequelae, vaccination, SARS-CoV-2, long-COVID and COVID-19 with a search date of 1 December 2020 to 1 July 2021 revealed 61 publications. But, the research aims of these publications did not align with the scope of the review and were excluded.

A search of MedRxiv on 6 July 2021, using the terms: long-term sequelae, vaccination, SARS-CoV-2, long-COVID and COVID-19 with a search date of 1 December 2020 to 6 July 2021 revealed 69 publications. The research aims for 57 of these publications did not meet the scope of the review and were not analysed further. Of the remaining 12 publications, 10 did not consider vaccination and its implications on long COVID.

The remaining two pre-print publications were in scope, and are summarised as follows:

1. A small prospective observational study that assessed the change in quality of life and symptoms of long COVID after vaccination.[1]
    - When compared to matched unvaccinated participants, those who had received a vaccine had a small overall improvement in long COVID symptoms (5.6% vaccinated vs 14.2% unvaccinated) and increase in symptom resolution (23.2% vaccinated vs 15.4% unvaccinated) (p=0.035). No difference in response was identified between Pfizer and AstraZeneca vaccines.
    - The study aimed to address vaccine hesitancy amongst individuals with long COVID; as such the primary conclusion was that vaccination is not associated with a worsening of long COVID symptoms, quality of life or mental wellbeing.
2. A community-based nested case-control study with 4000+ participants that used data from the COVID Symptom Study to: describe the individual factors associated with SARS-CoV-2 infection that occur at least 14 days post first vaccination; and assess the illness duration, severity and symptom profile in individuals with SARS-CoV-2 infection after first vaccination compared to unvaccinated individuals with SARS-CoV-2 infection.[2]
    - Vaccinated individuals were found to be less likely than unvaccinated individuals to have multiple (ie >5) symptoms in the first week of illness, or to present to hospital, and were more likely to be asymptomatic.
    - Overall there was no significant difference in symptoms lasting >28 days.

A search of the grey literature revealed the following studies completed or underway:

- A survey by the LongCovidSOS advocacy group examined the impact of different vaccines across 14 common long COVID symptoms.[3] Nine hundred participants completed an online survey of their self-reported symptoms. Statistical analysis from the survey revealed 56.7% of participants reported an overall improvement in symptoms, 18.7% reported a deterioration, and 24.6% remained unchanged.
- A team from Yale University will study the effect of vaccination on people with long COVID. This work will build upon results from an unpublished survey conducted by an advocacy group where about 40% of people reported mild to full resolution of their long COVID symptoms after vaccination.[4]

In addition, the National Institutes of Health (NIH) has launched a research initiative on long COVID, which aims to identify the causes of long COVID, develop ways to treat individuals who do not fully recover, and ultimately prevent the disorder.[5] It is not clear whether the NIH study will include a consideration of the effects of vaccination on long COVID.

Conclusions

Vaccines for COVID-19 emerged for use in December 2020, as such only a small amount of research has occurred on this issue. It is too early to provide robust advice on the relationship between long COVID symptoms and vaccination for COVID-19. Larger well-designed studies are required.

Other considerations

In the course of developing this advice, NCHRAC identified the following considerations that were out of scope for this advice, but are important and related considerations:

- That evidence is emerging on the "real world" incidence and risk factors for SARS-CoV-2 infection in vaccinated individuals.

References

Note: Research papers shared before peer review are identified as pre-prints in this reference list. Accordingly, they should be interpreted with caution.

[1] DT Arnold, A Milne, E Samms, L Stadon, NA Maskell, FW Hamilton. Are vaccines safe in patients with Long COVID? A prospective observational study. doi: https://doi.org/10.1101/2021.03.11.21253225 **[Pre-print]**

[2] Michela Antonelli, Rose S Penfold, Jordi Merino, Carole H Sudre, Erika Molteni, Sarah Berry, Liane S Canas, Mark S Graham, Kerstin Klaser, Marc Modat, Benjamin Murray, Eric Kerfoot, Liyuan Chen, Jie Deng, Marc F Österdahl, Nathan J Cheetham, David Drew, Long Nguyen, Joan Capdevila Pujol, Christina Hu, Somesh Selvachandran, Lorenzo Polidori, Anna May, Jonathan Wolf, Andrew T Chan, Alexander Hammers, Emma L Duncan, Tim D Spector, Sebastien Ourselin, Claire J Steves. Post-vaccination SARS-CoV-2 infection: risk factors and illness profile in a prospective, observational community-based case-control study. doi: https://doi.org/10.1101/2021.05.24.21257738 **[Pre-print]**

[3] Ondine Serwood, W David Strain, Jeremy Rossman. The impact of COVID vaccination on symptoms of Long COVID. An international survey of 900 people with lived experience. https://www.longcovidsos.org

[4] https://news.yale.edu/2021/05/10/study-probes-vaccines-effects-people-long-covid

[5] www.nih.gov/about-nih/who-we-are/nih-director/statements/nih-launches-new-initiative-study-long-covid