"Long COVID"

Living Evidence Summary

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Queensland
Government

Contents

Terminology

"Long COVID" is one term used to describe the protracted resolution of COVID-19 symptoms. Other names for the condition include "post-acute sequelae of COVID-19" (PASC), "post-COVID-19 condition" (PCC), and "post-COVID-19 syndrome" (PCS).

Definitions of Long COVID

Definitions vary across studies and agencies

There is no settled definition of Long COVID. When reviewing any Long COVID study or report, it is important to check which definition is used. The use of different definitions across different studies affects our understanding of Long COVID and its prevalence. Key differences between definitions include:

- The time period post-infection: some may consider ongoing health issues 4 weeks after COVID-19 to be "Long COVID", and others may use 12 weeks after diagnosis.
- The number and type of symptoms. Some will consider one ongoing symptom to be Long COVID, others will require multiple symptoms to meet the definition. Some include the onset of new symptoms that arise in the period up to "long COVID", others exclude them.
- The functional impact. Some do not consider whether symptoms have an impact on daily function. As a result, a mild lingering occasional dry cough risks being considered of equal impact with fatigue severe enough to inhibit a return to work.
- The patient profile. Some reports do not adequately describe the types of patients in a study. They may include post-intensive care patients, with a risk that these patients have a "post intensive care syndrome" rather than Long COVID, or not define whether the patients are exclusively made up of hospitalised or non-hospitalised groups.

Examples of different Long COVID definitions

a) World Health Organisation (WHO)

Post COVID-19 condition occurs in individuals with a history of probable or confirmed SARS CoV-2 infection, **usually 3 months** from the onset of COVID-19 with symptoms, and that last for at least 2 months, and **cannot be explained by an alternative diagnosis**. See WHO.

b) National Institute for Health and Care Excellence (NICE) (UK)

The NICE rapid guideline definition is – after the WHO – frequently cited and uses the following clinical case definitions to identify and diagnose the long-term effects of COVID-19:

- **Acute COVID-19**
  Signs and symptoms of COVID 19 for **up to 4 weeks**.
- **Ongoing symptomatic COVID-19**
  Signs and symptoms of COVID 19 from **4 weeks up to 12 weeks**.
- **Post-COVID-19 syndrome**
  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**.

c)   Office of National Statistics (UK)

Symptoms continuing **for more than four weeks** after the first suspected coronavirus (COVID-19) infection that were not explained by something else. See ONS summary.

d)   Centre for Disease Control (CDC) (US)

Post-COVID conditions are a wide range of new, returning, or ongoing health problems that people experience after first being infected with the virus that causes COVID-19. Most people with COVID-19 get better within a few days to a few weeks after infection, **so at least four weeks after infection** is the start of when post-COVID conditions could first be identified. See CDC Summary.

What causes Long COVID?

The mechanisms that lead to Long COVID are still poorly understood. This is also the case for other post-viral syndromes. In August 2023, the US Centre for Disease Control (CDC) reported that "[Long COVID] *symptoms are not unique to COVID-19 or post-COVID conditions*". A good example of the challenges in understanding post-acute infection syndromes is linked here.

There remains no single biomarker for those experiencing Long COVID. Many hypotheses on the cause of Long COVID have been proposed. They include:

- viral persistence
- unrepaired tissue damage
- persistent immune activation
- autoimmunity
- impaired oxygen delivery due to micro-clotting
- disruption of cellular energy metabolism
- alterations in gut microbiome
- microvascular dysregulation
- vasculo-proliferative processes initiated by prior hypoxia

In addition, it has been suggested that the involvement of psychological mechanisms in Long COVID needs consideration.

Some speculate that Long COVID is not a unique phenomenon. Its broad symptomatology, multi-system impacts and lack of a single pathophysiological explanation draws parallels with other post-viral syndromes and post-pandemic experiences.

This has resulted in calls for more research that compares COVID-19 to other respiratory viral illnesses in order to understand if it is a unique illness.

> In 2023, the British Medical Journal published Queensland Health's research that compared impacts three months after COVID-19 with those following influenza.
>
> It found no difference between the rates of ongoing symptoms and functional impairment after COVID-19 and influenza.

Incidence and Prevalence

Ascertaining incidence and prevalence is a major challenge

In 2023, a detailed critique of long COVID research was published to widespread media attention. It described a range of flaws in the methodologies of most research into Long COVID. According to the authors, this has meant that many widely-reported scientific publications overestimate prevalence.

When reviewing an estimate of prevalence, it is essential to consider the below:

- The use of different Long COVID definitions. For example, people who have symptoms after 4 weeks may be counted under the CDC's definition, but they may have recovered by 12 weeks and so would not be counted under the WHO's definition.
- The study should have a control or comparator group. A comparison is important because many symptoms also occur in the COVID-free population (although given the extent of COVID infections, this is complicated) as well as after other illnesses like influenza.
- The study should look at whether Long COVID symptoms existed in people prior to SARS-CoV-2 infection, and/or look at symptoms across a random sample of the population. This is because these symptoms are not unique to COVID-19.
- When the study occurred (eg. the year), and the different variants at that time. The risk of Long COVID has steadily reduced from the original strain to the Omicron variant.
- The population's COVID experience or naivety (eg. the US had significant exposure to multiple variants, whereas Australia was primarily exposed to Omicron).
- The patient profile. A study where all the COVID patients were in intensive care units or in hospital is likely to show a higher prevalence of long COVID than a random sample.
- The population's vaccination status at that time, given vaccination reduces Long COVID risk. The participants may have been unvaccinated (highest risk), partially vaccinated, or fully vaccinated (lower risk). There is also a risk of waning immunity after vaccination.
- The risk of sampling bias, which occurs when some members of the population have a higher probability of being included than others. For example, self-enrolment in a study or self-reporting of symptoms is generally associated with higher prevalence. This is because people with ongoing symptoms may be more motivated to participate.

Prevalence in Australia

Given these confounders, prevalence estimates from overseas studies are generally not relevant to the Australian context. The RACGP noted that overseas estimates are likely to overstate the prevalence in Australia.

Queensland Health's submission to the parliamentary inquiry into Long COVID and repeated infections stated that the prevalence in Queensland is low. NSW Health's submission cited an Australian Long COVID study (see its supplementary material) and said

> *"recent Victorian estimates for a highly vaccinated population during the Omicron wave suggested 2% of hospitalised and 0.09% of non-hospitalised adults develop Long COVID".*

Risk factors

Evidence on risk factors is highly varied, and this is likely to be attributable to the generally poor quality of Long COVID research. The Australian Institute of Health and Welfare's (AIHW) literature review noted growing evidence supporting the below as risk factors:

- severity of acute disease
- age, most common in middle-aged adults
- female sex, and
- pre-existing comorbidities, including obesity.

This is supported by a large systematic review released in March 2023, which added smoking as an additional risk factor.

The AIHW's literature review also noted that

> *"many of the studies… use populations that come into contact with health services, and therefore capture more severe cases. It is also unclear whether different risk factors are associated with different sets of symptoms".*

Protection and Prevention

Two large studies have shown vaccination offers protection against Long COVID. In a Swedish study, vaccination reduced the risk of Long COVID by 21% with one dose, 59% with two doses, and 73% with three doses. In a study of more than 10 million vaccinated and 10 million unvaccinated people from the UK, Spain and Estonia, one vaccination reduced the risk of Long COVID by 48% to 59%.

An Israeli study found that people with two vaccinations were no more likely to report typical symptoms than people who never had COVID-19.

Note that these three studies all featured primarily pre-Omicron cases of COVID-19.

Studies have shown antiviral treatment following a COVID-19 infection with nirmatrelvir (paxlovid) or molnupiravir (lagevrio) is associated with reduced risk of Long COVID. Treatment with monoclonal antibodies after infection may also reduce the risk, although not to the same extent as prior vaccination.

General consensus remains that the "*best way of protecting people from long COVID is to protect against COVID-19 itself*". This includes adopting healthy behaviours and being up-to-date with vaccination.

Is reinfection a risk or protective factor?

The UK's Office of National Statistics reported in February 2023 "*there was no evidence of differences in the relative risk of reporting new-onset long COVID after a second COVID-19 infection*". Other evidence emerging in 2023 (pre-print) suggests the risks of Long COVID following reinfection are significantly reduced across all symptom domains at both 28 days and 90 days after reinfection. Notwithstanding this, it would be prudent to see further evidence on reinfection and Long COVID.

Symptoms

The WHO says there are now over 200 symptoms associated with Long COVID in the literature. The most common scenario is non-specific multisystem post-viral symptoms. The RACGP's advice to GPs describes the following:

- fatigue
- dyspnoea
- joint pain
- chest pain
- cough
- change in sense of smell or taste
- cognitive disturbances
- hoarse voice

Less common symptoms include:

- insomnia
- low-grade fevers
- headaches
- neurocognitive difficulties
- myalgia and weakness
- gastrointestinal symptoms
- rash
- depression.

It should be noted that the above list was compiled before the arrival of the Omicron variant. More recent information shows that symptoms are changing with newer COVID variants and sub-variants.

According to the ONS, fatigue continued to be the most common symptom reported by individuals with Long COVID (72% of those with self-reported Long COVID), followed by concentration issues (51%) and shortness of breath (48%).

Urgent need for better research on symptoms

A widely reported overview of Long COVID's effects on the body is linked here. However, caution should be exercised when reading this review because it cites numerous studies that do not have adequate controls and are often low quality (eg. using self-reported conditions).

A critique of this article in the RACGP's newsletter is here.

Further research is needed into impacts on the body, and it is essential that these studies use comparator groups like influenza and similar viral illnesses.

Functional Impacts

Investigations into Long COVID infrequently consider the functional impact and rarely compare pre-COVID functional levels with post-COVID levels. Evidence of functional impact should also be compared with functional impact arising from other viral illnesses.

The risk of not considering functional impact is that mild ongoing symptoms (for example, a lingering night-time dry cough) may be conflated with impacts severe enough to inhibit a return to pre-COVID levels of daily activity and work.

Queensland Health conducted research into ongoing symptoms and functional impairment three months after infection by COVID-19 or influenza. The results were published in the British Medical Journal in August 2023. It found there was no difference in the rates of ongoing symptoms or functional impairment between people who had COVID-19 or influenza.

Labour Market Impact

Australian estimates of labour market impact have been based on models from overseas (for example, this model from Deakin University). This risks overstating the impact from where earlier variants affected unvaccinated / partially vaccinated populations.

On 5 December 2022, the UK's Office of National Statistics noted "*Long COVID is unlikely to be the sole driver of increasing levels of inactivity in the UK labour market during the COVID-19 pandemic. Following a period of stable inactivity rates, the number of working-age adults who are inactive mainly because of ill-health has been rising since 2019… This was before the arrival of COVID-19 in the UK*".

Diagnosis

There are no definitive tests for Long COVID. It has been described as a diagnosis of exclusion requiring the elimination of other potential explanations. The US Department of Health and Human Services noted "*no laboratory test can distinguish it from other causes*".

To complicate diagnosis, it has been noted that "*commonly reported post-acute COVID-19 symptoms are not specific to COVID-19 and are commonly reported regardless of infection status, for a variety of reasons*".

Coupled with the lack of a definitive diagnosis, there is a higher risk of diagnosing Long COVID where other factors may offer an equally justifiable explanation (eg. poor post-pandemic mental health, deconditioning due to inactivity, temporal associations like age-related hair loss). A useful example of this risk is found here.

Assessment and Management

A summary of tools to support assessment and management is in the appendix. The Australian National COVID-19 Clinical Evidence Taskforce provides guidance on assessment of people for Long COVID. Two tools valuable in the identification of Long COVID conditions are:

1. The Post COVID Functional Scale (PCFS). This is a short, validated self assessment enabling people to identify the degree of impact on a short scale. The PCFS can also be used to ascertain if respondents had pre-COVID functional impacts. For those who have a moderate or greater impact, many services then direct people to the validated Post-Covid-19 Yorkshire Rehabilitation Screen (below).

2. The Post-Covid-19 Yorkshire Rehabilitation Screen (C19-YRS). This validated tool enables the identification of the different domains of impact, with the respondent rating the degree of impact on a 0-10 scale (or 0-3 in the modified C19-YRSm version).

Once the impacted domains are ascertained and rated, the user can be triaged into self-management or more comprehensive support where required.

Self Management

There are a range of valuable tools to assist patients with self-management of Long COVID. They include:

- Queensland Health's advice on recovering from COVID-19 and long COVID (PDF)
- Queensland Health's steps to recovery after COVID-19 (PDF), including a link to a daily symptom diary
- Queensland Health's guidance on breathing exercises and physical activity (PDF) to aid recovery
- WHO's Support for Rehabilitation: Self Management after COVID-19-related illness. This is used in a number of Australian Long COVID clinics (eg. Nepean Hospital, RPA, Tasmania). It is a pdf where consumers take themselves to the relevant sections within the document for rehab programs.
- RACGP's Patient Resource: Managing Post-COVID-19 Symptoms. Its format is also a pdf requiring consumers to find the correct section of a pdf for their rehabilitation.

Clinician Management

Given the broad spectrum of potential Long COVID symptoms, the management of Long COVID patients is centred on the management of each person's symptoms. Options include:

- NSW ACI's model of care for the management of Long COVID patients.
- The NSW ACI's Clinical practice guide for assessment and management of adults with post-acute sequelae of COVID-19 (as management tool). The ACI has also published a model of care to guide acute care clinicians in the post-acute phase which is valuable prior to the post-COVID condition phase.
- The RACGP's Caring for Patients with Post-COVID-19 Conditions provides an excellent summary of management options and pathways (see p8-9, Box 3: Management of Common Symptoms).

Further guidance is available from the:

- [Australian National COVID-19 Clinical Evidence Taskforce](#)
- [National Institute for Health and Care Excellence (NICE)](#)

Getting better after COVID-19

At the population level, almost everyone will fully recover after COVID-19 within a week or two. For those whose symptoms linger, it is very rare that these symptoms do not resolve. **As a result, Long COVID must be framed around** *recovery*.

For those whose recovery is protracted, the time to recovery is difficult to predict owing to the normal variability in a person's response to an illness. There remains a paucity of studies examining the impact of the Omicron variant in vaccinated populations.

In the US, the Centre for Disease Control [published data in August 2023](#) that looked at the impact of Long COVID on those who had tested positive one year ago. The study found:

"Persistence of any symptom prevalence at 12 months was not statistically significantly different between the COVID test-positive and COVID test-negative participant groups".

Risks to Recovery

Many studies are poorly designed and overestimate the threat of Long COVID, [as shown in this review](#). It noted that the findings of high quality Long COVID research are reassuring, yet they are not consistent with the scenarios generally reported in the media. Ongoing exposure to negative messaging about Long COVID and "worst-case" scenarios that are portrayed across the media have been acknowledged as a health risk. [One report](#) noted the pandemic created "*a 'perfect storm' for the development of persistent physical symptoms,*" which contributed to

- *predisposing factors* (eg. psychological distress, stress, anxiety, depression, inactivity, social isolation, adverse media exposure).
- *precipitating factors* (eg. acute COVID-19 symptoms).
- *perpetuating factors* (eg. beliefs of a serious prolonged illness conveyed by the terms "Long COVID" and "long-hauler", and medical and media portrayal of serious consequences and prolonged recovery).

[This report](#) argued that the negative public health messaging has induced fear of Long COVID in the population, including from constant messaging about its disabling symptoms and theorizing irreversible tissue damage as its cause. This has increased risks of the "nocebo effect" and functional somatic symptom disorders. Nocebo effects are "*powerful, pervasive and common in clinical practice*". They occur when the expectation of a negative future outcome causes that very physiologic negative outcome to occur. Negative messaging may also cause hyper-attentiveness to symptoms that further delays recovery.

The report says health leaders and the media should provide accurate (and therefore reassuring) information about Long COVID, without unduly exaggerated claims that perpetuate fear. It should include noting that Long COVID is usually not due to irreversible tissue or organ damage, and that a full recovery is the most likely outcome.

Further reading

Click on the links below for further information.

- Queensland Health's [website on Long COVID for the public](#)
- Queensland Health's [website on Long COVID for clinicians](#)
- Queensland Health's [research into Long COVID, published in the British Medical Journal](#)
- Queensland Health's [submission to the Australian Government's parliamentary inquiry into Long COVID and repeated infections](#)
- Australian Government Department of Health and Aged Care's [website on Long COVID](#)
- NSW Health's [website on Long COVID](#)
- NSW ACI Living Evidence Summary (PASC/Long COVID): https://aci.health.nsw.gov.au/covid-19/critical-intelligence-unit/post-acute-sequelae
- Australia's National COVID-19 Clinical Evidence Taskforce's [FAQs for COVID-19](#) (select drop-down for "Post-COVID-19")
- [Medscape's Long COVID resource page](#)
- [Long covid | New Scientist](#) (September 2023)
- [The Ongoing Risk Of Long COVID - Gideon M-K: Health Nerd (substack.com)](#) (September 2023)
- [Why the hypothesis of psychological mechanisms in long COVID is worth considering (nih.gov)](#) (January 2023)
- [Helen Salisbury: Unexplained symptoms aren't always long covid | The BMJ](#) (March 2023)
- [Healthy Lifestyle Linked to Lower Risk of Long COVID (medscape.com)](#) (February 2023)

Appendix: Management Tools

1. Self-Management Tools:

   a. Qld Health's advice on recovering from COVID-19 and long COVID (PDF)

   b. Qld Health's steps to recovery after COVID-19 (PDF), including a link to a daily symptom diary

   c. Qld Health's guidance on breathing exercises and physical activity (PDF) to aid recovery

   d. WHO: Support for rehabilitation: self-management after COVIC-19-related illness (dpf)

   e. RACGP's Patient Resource: Managing Post-COVID-19 Symptoms (PDF).

   f. The UK RCOT's Recovering from COVID-19: Post viral-fatigue and conserving energy - RCOT (online).

   g. Long COVID Physio's online portal (navigation by symptom).

   h. NHS's Long COVID Rehabilitation Booklet (PDF).

   i. NHS's "Your COVID Recovery" page with good, easily navigable self management (click links at "Your Road to Recovery" tile): I have or may have long COVID | Your COVID Recovery

2. GP first review: Post COVID Functional Scale. Patients self-identify the levels of functional limitations. If PCFS was used as an online screening tool:

   a. Grade 0 – no functional limitations: No further action (ie does not have Long COVID);

   b. Grade 1 - negligible functional limitations: optional self-management (see 3);

   c. Grade 2 – slight functional limitations: encourage self-management (see 3);

   d. Grade 3 – moderate functional limitations: GP review (see 2);

   e. Grade 4 – severe functional limitations (unable to self care): urgent GP review (see 2).

3. GP review: C19-YRS (Yorkshire Screening Tool). identify specific symptom domains for either self-management (see 3), further clinical investigation, or referral for specialist support.

4. GP Management tools:

   a. NSW ACI's model of care for the management of Long COVID patients.

   b. NSW ACI's Clinical practice guide for assessment and management of adults with post-acute sequelae of COVID-19 (as management tool). The ACI has also published a model of care to guide acute care clinicians in the post-acute phase which is valuable prior to the post-COVID condition phase.

   c. RACGP's Caring for patients with post-COVID-19 conditions