In brief

Long COVID

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Question

What is the evidence on the prevalence, presentation and management of long-COVID?

Background

• The World Health Organization defines long COVID (or ‘post COVID-19 condition’, ‘post-acute sequelae of COVID infection’ (PASC)) as an illness that occurs in people who have a history of probable or confirmed SARS-CoV-2 infection; usually within three months from the illness onset, with symptoms and effects that last for at least two months. The symptoms and effects of long COVID cannot be explained by an alternative diagnosis.1, 2

• The definition of long COVID and the approaches to estimating prevalence vary considerably across studies.1 Researchers have called for consensus in definitions.2

• Many studies have weak designs – many are cross-sectional, rely on self-reported symptoms for enrolment and subsequent self-reported outcomes or often do not have a control group.3

Summary

Prevalence

• Estimates of long COVID prevalence vary. More recent, large and rigorous studies report between 3.7% and 20.0% of people will develop long COVID after acute infection.1, 4-8

• Prevalence estimates may be linked to study rigour (with a meta-analysis finding that higher study quality was associated with lower prevalence).9

• Studies suggest lower prevalence of long COVID following infection with Omicron (4.5%) than with Delta (10.8%), especially among double vaccinated individuals and irrespective of time elapsed between infection and most recent vaccination.7, 10 In triple vaccinated individuals, the prevalence was similar for Delta (5.0%), Omicron BA.1 (4.5%) and Omicron BA.2 (4.2%) infections.10

• In children, COVID-19 infection (pre-Omicron) was associated with an increased risk of reporting at least one symptom lasting more than two months than controls (absolute risk difference: 12.8% for 0-3 years; 4.4% for 4-11 years; 4.7% for 12-14 years).11 Other studies (pre-Omicron) estimate a prevalence of around 1.7% for long COVID symptoms in non-hospitalised children at three months post-infection.12, 13

Symptoms

• Symptoms may:
  - range from mild to severe
  - be singular or multiple
  - be continuous or episodic
  - be chronic sequelae of acute COVID-19 disease (such as loss of smell or cough)14, 15
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- Include fatigue, shortness of breath or difficulty breathing, memory, concentration or sleep problems, persistent cough, chest pain, trouble speaking, muscle aches, loss of smell or taste, depression or anxiety and fever.
- Predominantly include mood symptoms, fatigue and sleep disorders for children.

- Numerous studies have proposed subtypes or phenotypes of long COVID, however, their conclusions differ considerably and as yet there is no international consensus.
- There are a number of chronic sequelae of severe acute COVID-19 disease that will lead to persistent impairment and may result in chronic disease:
  - Pulmonary fibrosis secondary to acute lung injury (pre-print)
  - Myocarditis which may lead to persistent cardiac dysfunction
  - Pulmonary thromboemboli
  - Diabetes
  - Cardiovascular and cerebrovascular disease.

Risk and protective factors
- Risk factors for long COVID may include: number of initial COVID-19 symptoms; certain comorbidities, such as hypertension, diabetes, obesity and asthma; and certain demographic factors, such as being older and living in more deprived areas.
- A more severe initial COVID-19 infection may be associated with persistent illness, however, the available studies are low quality. People admitted for acute infection have been noted to recover slower from long COVID symptoms than those with a milder acute illness.
- According to most studies, women are more likely to develop long COVID than men.
- Protective factors for long COVID include vaccination and young age.

Mechanisms
- Little is known about the underlying cause of long COVID, as per most post-acute infection syndromes. Other respiratory illnesses, such as influenza, have also been associated with persistent symptoms of a similar nature.
- The mechanisms for ongoing symptoms are proposed to be due to viral persistence, persistent immune activation or autoimmunity, however, these are not proven hypotheses.

Diagnosis and assessment
- In a clinical setting, there is no definitive test for long COVID. Diagnosis is based on ruling out other similar conditions.
- A growing range of assessments, such as brain imaging or plasma samples to identify persistent SARS-CoV-2 viral reservoirs, may act as a useful biomarkers of long COVID.
- Differential diagnosis is critical, since the clusters of symptoms associated with long COVID can overlap with other post-acute infection syndromes, such as post intensive care syndrome.
- A Delphi consensus study has recently confirmed a core outcome set to be suggested for use in clinical practice and research. A patient-reported outcome measure for long COVID has recently been developed and proposed.
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- Guidelines advocate for a holistic, person-centred approach to diagnosis, including a comprehensive clinical history and an examination that involves assessing physical, cognitive, psychological and psychiatric symptoms, as well as functional abilities.\(^4^7\), \(^5^1\)

Management
- Regarding management of long COVID, high quality, evidence-based guidelines are not yet available.\(^6^0\)
- Recent available guidelines recommend:
  - A medically-led, multidisciplinary approach\(^6^1\)
  - Clinicians work with the person (and their family or carers) to develop a personalised rehabilitation and management plan\(^4^7\)
  - Patients be given advice and information on self-management\(^4^7\)
  - Symptom management in primary care or referral to specialised care as required.\(^5^1\)
  - Relevant local guidelines should inform onward referral for anxiety and mood disorders or other psychiatric symptoms.\(^4^7\)
  - A graded and individualised approach to exercise.\(^6^2\), \(^6^3\) High level evidence on the role of exercise and its impact on post-exertional malaise is scant, even in conditions such as chronic fatigue or myalgic encephalitis.\(^6^4\), \(^6^5\)

Method
To inform this brief, PubMed and Google Scholar searches were conducted using terms related to long COVID, on 01 August 2022.

References
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In brief documents are not an exhaustive list of publications but aim to provide an overview of what is already known about a specific topic. This brief has not been peer-reviewed and should not be a substitute for individual clinical judgement, nor is it an endorsed position of NSW Health.


Evidence checks are archived a year after the date of publication