

# Post-COVID-19 syndrome/condition or long COVID

## *Persistent illness after acute SARS-CoV-2 infection*

CPD 

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### Background

Approximately 10 million Australians have had confirmed SARS-CoV-2 infection. The waves of infection in the population have been succeeded by smaller waves of people affected by persistent illness following acute infection. Post-COVID-19 symptoms may extend for months following infection. There is a range of symptoms causing mild to debilitating impairment.

### Objective

This article summarises what is currently understood about the pathophysiology, risks factors, symptoms and how to approach both the assessment and care of people with post-COVID-19 sequelae.

### Discussion

Currently recommended is a person-centred approach from a multidisciplinary team, with general practitioners centrally coordinating care. As the understanding of post-acute COVID-19 is evolving, regularly updated or 'living guidelines' will be crucial for those affected to be provided with best care within the health system.

**IN 2020**, months after the first reported cases of SARS-CoV-2 infection, reports of persisting symptoms post acute infection emerged. People with lived experience called this 'long haul' or 'long COVID'. Consumers were instrumental in highlighting the issue to healthcare providers and policymakers.<sup>1</sup> Symptoms are now understood to be experienced by both adults and children who had either mild, moderate or severe COVID-19, with variation in the duration of symptoms and clinical history.<sup>2-4</sup> Names for persisting symptoms include post-COVID-19 condition or syndrome, post-acute COVID-19, post-acute sequelae of COVID-19, long COVID and long haul COVID.

In late 2021, the World Health Organization used a consensus process to define post-COVID-19 condition as: 'occurs(ing) in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually three months from the onset, with symptoms that last for at least two months and cannot be explained by an alternative diagnosis'.<sup>2</sup> This definition has been criticised by consumers as it leaves a gap between acute illness and recognition of health impacts, during which time a person needs care. The National Institute of Clinical Excellence in the UK categorises symptoms lasting

up to four weeks as acute COVID-19, while symptoms lasting 4-12 weeks are categorised as 'ongoing symptomatic COVID-19'; post-acute COVID-19 begins from 12 weeks.<sup>5</sup>

In this article, we will use the term post-COVID-19 condition, as contained in the Australian living guidelines developed by the National COVID-19 Clinical Evidence Taskforce (NCET), to describe the symptoms that develop during or after an infection consistent with SARS-CoV-2, continue for more than 12 weeks and are not explained by an alternative diagnosis. Post-COVID-19 condition usually presents with clusters of symptoms, often overlapping, that can fluctuate and change over time and 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.<sup>6</sup>

This article summarises what is understood about the pathophysiology, frequency of symptoms, factors associated with increased risk of disease and how to approach both the assessment and care of people with post-COVID-19 condition in Australia. We highlight current evidence-based guidelines from the broad recommendations of the NCET (<https://clinicalevidence.net.au/wp-content/uploads/>

FLOWCHART-11-CARE-OF-PEOPLE-AFTER-COVID-19.pdf),<sup>6</sup> general practice-specific guidance from The Royal Australian College of General Practitioners<sup>7</sup> and localised advice about investigation and referral from HealthPathways.<sup>8</sup>

### Pathophysiology

The pathophysiology of post-COVID-19 symptoms is likely to arise from virus-mediated damage at the time of acute infection and/or ongoing inflammation that may persist in the months following infection. A combination of viral persistence, microvascular injury, immune dysfunction and loss of the angiotensin converting enzyme-2 protective pathway results in damage to various organs, hypercoagulability and ongoing inflammation that persists for months after infection.<sup>3,9-11</sup> Thus, there is variability in presentation of symptoms and symptom duration in people with post-COVID-19 condition. Emerging evidence may distinguish phenotypes relating to symptom clusters and trajectories.

### Incidence and factors associated with post-COVID-19 condition

The estimations of the incidence of post-COVID-19 condition are complicated by studies with variable follow-up times, settings and symptoms surveyed. A recent large study in the UK of people treated in the community showed that approximately 3% of the population reported at least one symptom at four weeks post-acute infection, and of these, 83% had experienced symptoms for at least 12 weeks previously, 45% at least one year previously, and 22% at least two years previously.<sup>12</sup> A smaller Australian cohort found that 5% had persistent symptoms at three months.<sup>13</sup>

A recent model predicted up to 230,000 cases of post-COVID-19 condition in Australia.<sup>14</sup> It is important to note these estimates are from 2020 and 2021, when most COVID-19 cases were caused by alpha, beta, gamma or delta variants. Research into the effect of the omicron variants on the incidence

of post-COVID-19 condition in a highly vaccinated population suggests a lower rate of post-COVID-19 symptoms, with recent data from the UK showing that approximately 4–5% of people who were triple vaccinated reported at least one symptom at three months.<sup>15</sup>

Post-COVID-19 condition can occur in any person with past infection but is influenced by factors that increase or modify the risk (Box 1). For instance, in those with a history of admission to hospital, persistent symptoms are more common – between 50% and 89% have at least one symptom at two months.<sup>16</sup> Persistent illness is also likely to be more prevalent in populations that were disproportionately affected by the pandemic and perpetuate the health inequalities that characterised the waves of acute infection.<sup>17</sup> The factors in Box 1 are noted as ‘potential’ factors because the availability of more comprehensive well-controlled studies is still emerging.

### Assessment

At present, there are no measures or tools that are recommended to confirm a diagnosis of post-COVID-19 condition.<sup>18</sup> Post-COVID-19 condition should be considered in the context of the individual and their medical history, comorbidities and exclusion of other causes of their presenting symptoms. Assessment should involve an initial detailed history and symptom-based examination where clinically indicated,<sup>7,11</sup> including:

- confirming that the person has had COVID-19 (by checking that they tested positive on a rapid antigen test or polymerase chain reaction test) or is likely to have had COVID-19 (by checking that they have had symptoms consistent with a SARS-CoV-2 infection and/or known contact with a positive case)
- assessing the symptoms in the context of intercurrent illness and pre-existing comorbidities (Table 1) to determine if they are likely to be a result of COVID-19
- discussing the impact of the symptoms on everyday functioning (eg exercise tolerance, work, activities of daily

living and mental wellbeing) and exploring the person’s concern about the symptoms

- assessing whether comorbid conditions and lifestyle factors are contributing to the presentation of the symptoms
- assessing for the presence of red flags requiring urgent assessment and referral – severe, new onset or worsening breathlessness or hypoxia; syncope; unexplained chest pain, palpitations or arrhythmias; delirium or focal neurological signs or symptoms; and, in children, multisystem inflammatory syndrome (MIS). MIS is characterised by ongoing fever plus more than one of the following symptoms: bloodshot eyes, skin rash, gastrointestinal symptoms including stomach pain, vomiting and diarrhoea or dizziness (signs of low blood pressure).

People with ongoing symptoms following acute COVID-19 need a considered and compassionate approach to their situation. Individuals might experience disbelief or minimisation of their symptoms by family, friends, employers or healthcare providers. They may hold fears that they have lasting impairment that can reduce their quality of life permanently.

It is important that the clinician confirms the person is no longer infectious before seeing them in person by taking

#### Box 1. Potential factors associated with increasing or modifying the risk of post-COVID-19 condition symptoms<sup>12,24-27</sup>

Potential factors increasing the risk of post-COVID-19 condition

- Middle age
- Female sex
- Increased severity of symptoms during the acute infection
- Increased number of symptoms during the acute infection
- Intensive care admission
- Pre-existing comorbidities

Factors modifying the risk of post-COVID-19 condition

- Vaccination with one or more vaccines

**Table 1. Symptoms described by people after COVID-19**<sup>3,4,6,16,18,28,29</sup>

<b>Respiratory symptoms</b>	<ul style="list-style-type: none"> <li>• Shortness of breath</li> <li>• Cough</li> </ul>
<b>Generalised symptoms</b>	<ul style="list-style-type: none"> <li>• Fatigue</li> <li>• Fever</li> <li>• Pain</li> </ul>
<b>Cardiovascular symptoms</b>	<ul style="list-style-type: none"> <li>• Chest tightness</li> <li>• Chest pain</li> <li>• Palpitations</li> </ul>
<b>Neurological symptoms</b>	<ul style="list-style-type: none"> <li>• Cognitive impairment ('brain fog', loss of concentration or memory issues)</li> <li>• Headache</li> <li>• Sleep disturbance</li> <li>• Peripheral neuropathy (pins and needles and numbness)</li> <li>• Dizziness</li> <li>• Delirium (in older populations)</li> <li>• Mobility impairment</li> <li>• Visual disturbance</li> </ul>
<b>Gastrointestinal symptoms</b>	<ul style="list-style-type: none"> <li>• Abdominal pain</li> <li>• Nausea and vomiting</li> <li>• Diarrhoea</li> <li>• Weight loss and reduced appetite</li> </ul>
<b>Musculoskeletal symptoms</b>	<ul style="list-style-type: none"> <li>• Joint pain</li> <li>• Muscle pain</li> </ul>
<b>Ear, nose and throat symptoms</b>	<ul style="list-style-type: none"> <li>• Tinnitus</li> <li>• Earache</li> <li>• Sore throat</li> <li>• Dizziness</li> <li>• Loss of taste and/or smell</li> <li>• Nasal congestion</li> </ul>
<b>Dermatological symptoms</b>	<ul style="list-style-type: none"> <li>• Skin rashes</li> <li>• Hair loss</li> </ul>
<b>Psychological/psychiatric symptoms</b>	<ul style="list-style-type: none"> <li>• Depression</li> <li>• Anxiety</li> <li>• Post-traumatic stress disorder</li> </ul>

a detailed history of the acute illness and following public health guidance. If face-to-face care begins at the time of the acute illness, appropriate personal protective equipment must be worn.<sup>19</sup>

Post-COVID-19 condition symptoms can manifest as ongoing complications from acute COVID-19, new symptoms following recovery of COVID-19 or decompensation of pre-existing medical conditions.

Complications from acute COVID-19 include:

- extra-pulmonary medical complications of COVID-19 (eg deep vein thrombosis, pulmonary embolism, pulmonary fibrosis or scarring)
- myocarditis (cardiac muscle inflammation).

Syndromes that can manifest following acute COVID-19 include:

- post-intensive care syndrome (PICS)

- PICS refers to one or more of the following symptoms that people experience following care in an intensive care unit: anxiety, depression, cognitive impairment, memory loss, muscle weakness, dysphagia and reduced quality of life<sup>18,20</sup>
- multisystem inflammatory syndrome
  - in some people, both adults and children, symptoms corresponding to multisystem inflammatory syndrome have been reported<sup>21</sup>
- post-COVID-19 lung conditions including pulmonary fibrosis or scarring
- cardiovascular dysautonomia such as postural orthostatic tachycardia syndrome
- new and/or co-incident medical conditions
- destabilisation or exacerbation of pre-existing medical conditions.

### Examination

A comprehensive physical examination should be conducted, including baseline observations (pulse rate, blood pressure, body mass index, oxygen saturation and urine analysis) and comparison with historical measurements where available.<sup>8</sup> Examination should be directed by reported symptoms or a history suggestive of severe complications including severe pneumonia, acute coronary syndrome, stroke or pulmonary embolism or other comorbid conditions or syndromes.

If the patient has normal oxygen saturation, breathlessness and pulmonary embolus is not considered a likely differential diagnosis, a standardised desaturation test (one-minute sit-to-stand test and the 40-step test) can be used to evaluate potential exertional deoxygenation.<sup>22,23</sup>

Specific examination for general muscle strength, balance and nutritional status may be considered.

If new cognitive symptoms are reported, a screening tool for cognitive function can be used to assess at baseline.

### Investigations to consider in a person with persistent symptoms

Investigations should be directed by the history and physical examination. The

investigations advised by HealthPathways are listed in Box 2.<sup>8</sup> They should be compared with past results where available and in the context of history of hospitalisation follow-up recommended post discharge.

## Management

At present there is no evidence for specific interventions for post-COVID-19 condition. The approach to management of common presentations comes from consensus recommendations, with supporting practice points and evidence from rehabilitation in similar diseases.<sup>6</sup> Management approaches currently involve pulmonary or neurorehabilitation and psychological support, with ongoing studies investigating these and other treatment options.

General practitioners and primary health teams are well placed to coordinate person-centred care along with the person's carer or significant support. The following is a general summary of the consensus-based recommendations within the national guidelines.<sup>6,7</sup>

- Provide education, support and regular review of rehabilitation goals
- Begin rehabilitation as early as possible, include a multidisciplinary team and arrange regular review and reassessment to assess function and new symptoms.
- If red flags or serious complications are identified, arrange an emergency assessment or urgent opinion from a specialised service.
- For all presentations, optimise the management of comorbidities and monitor and manage lifestyle factors (eg smoking, nutrition, sleep, alcohol use and physical activity).
- Develop a management plan with the person addressing their main symptoms, problems or risk factors and access issues in determining location for further treatment or rehabilitation (eg home-based, telehealth or face-to-face options).
  - Fatigue: use a physical rehabilitation plan involving consultation with allied health professionals for cautious initiation and pacing of activity or movement.

- Disturbance of smell and taste: consider smell and taste retraining.
- Respiratory symptoms: advise breathing retraining to improve symptoms of dyspnoea.
- People with post-COVID-19 condition may be referred to a team including but not limited to physiotherapists, occupational therapists, exercise physiologists, speech pathologists, dietitians, psychologists, rehabilitation physicians and/or geriatricians. Use local and regional protocols or health pathways to determine the optimal referral action.
- Work with the individual to support return to pre-injury work or education. People should be encouraged to follow official guidance for vaccination, but explain that it is not known if vaccines have any effect on ongoing symptomatic COVID-19 or post-COVID-19 condition. Vaccination post infection has been shown to provide additional protection against reinfection when compared with natural immunity alone.<sup>19</sup>

Rehabilitation services can be accessed through community health, rehabilitation programs or post-COVID-19 clinics, where available. Chronic disease planning, mental healthcare or other enhanced care plans may facilitate increased access to multidisciplinary care. Additional support may be required for frail or elderly people,

people from Aboriginal or Torres Strait Islander communities and culturally and linguistically diverse communities.

## Discussion

People affected by post-COVID-19 condition and their general practitioners are faced by challenges in defining a best-practice approach to this new condition in the absence of evidence for specific interventions. People with post-COVID-19 condition need compassionate and considerate care, meeting their needs for investigation, rehabilitation and specialised care. The prognosis for post-COVID-19 condition is uncertain, but like for other complex conditions, early rehabilitation and person-centred care are likely to be beneficial.

Care is best coordinated with a multidisciplinary approach including appropriate allied health services, psychological support and referral. As evidence emerges about the management strategies for post-COVID-19 condition, it will be important to establish which disease patterns or subtypes are amenable to each strategy.

Knowledge about post-COVID-19 condition will inevitably increase in the next few years. The NCET continues to review the evidence and work with 'living' guideline groups around the world to provide evidence that is continuously

### Box 2. Investigations to consider in a person with post-COVID-19 condition<sup>5,30</sup>

Decisions about blood tests should be guided by the person's symptoms. If clinically indicated, offer blood tests, which may include a full blood count, kidney and liver function tests, C-reactive protein, ferritin, B-type natriuretic peptide (BNP), HbA1c and thyroid function tests. Evidence-based recommendation (EBR)

If appropriate, offer an exercise tolerance test suited to the person's ability (for example, the 1-minute sit-to-stand test). During the exercise test, record level of breathlessness, heart rate and oxygen saturation. Follow an appropriate protocol to carry out the test safely. EBR

For people with postural symptoms, for example palpitations or dizziness on standing, carry out lying and standing blood pressure and heart rate recordings (3-minute active stand test for orthostatic hypotension, or 10 minutes if you suspect postural tachycardia syndrome, or other forms of orthostatic intolerance). Consensus-based recommendation

Offer a chest X-ray by 12 weeks after acute COVID-19 only if the person has continuing respiratory symptoms and it is clinically indicated. Chest X-ray appearances alone should not determine the need for referral for further care. EBR

*Reproduced from National Institute for Health and Care Excellence, COVID-19 rapid guideline: Managing the long-term effects of COVID-19, London, UK: NICE, 2020. Available at [www.guidelines.co.uk/infection/nice-long-covid-guideline/455728.article](http://www.guidelines.co.uk/infection/nice-long-covid-guideline/455728.article) [Accessed 14 October 2022].*

updated and can inform guideline development for healthcare providers in Australia.

## Resources

Resources for primary care:

- National COVID-19 Clinical Evidence Taskforce flow chart – Care of people after COVID-19 (updated regularly), <https://clinicalevidence.net.au/wp-content/uploads/FLOWCHART-11-CARE-OF-PEOPLE-AFTER-COVID-19.pdf>
- The Royal Australian College of General Practitioners – Caring for patients with post-COVID-19 conditions, [www.racgp.org.au/clinical-resources/covid-19-resources/clinical-care/caring-for-patients-with-post-covid-19-conditions/introduction](http://www.racgp.org.au/clinical-resources/covid-19-resources/clinical-care/caring-for-patients-with-post-covid-19-conditions/introduction)

Information for patients:

- The Royal Australian College of General Practitioners – Patient resource: Managing common post-COVID-19 symptoms at home, [www.racgp.org.au/clinical-resources/covid-19-resources/patient-resources/patient-resource-managing-post-covid-19-symptoms/introduction](http://www.racgp.org.au/clinical-resources/covid-19-resources/patient-resources/patient-resource-managing-post-covid-19-symptoms/introduction)

There are peer support groups that have formed, but no peak body exists yet in Australia for people with persistent symptoms.

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Primary and Chronic Care Panel, which develops recommendations on post-COVID-19. SC is Methods Chair of this panel. MM received research funding for a data linkage project in Queensland for patients diagnosed with COVID-19 in 2020–2021 and research funding to investigate prevention of conversion of gestational diabetes to type 2 diabetes. MM receives consulting fees from The Royal Australian College of General Practitioners (RACGP), Department of Health, National Prescribing Service, Gold Coast Primary Health Network and Victoria University. MM is Chair of RACGP Expert Committee for Quality Care and member of various committees, Chair of Practice Incentives Program Quality Improvement Data Governance Committee for the Department of Health, and contributor to the Australian Health Policy Collaboration of Victoria University. SC is employed by the National COVID-19 Clinical Evidence Taskforce. Funding: None.

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