

## THE 1-2-3 OF LONG COVID: AN OVERVIEW FOR THE FAMILY PHYSICIAN

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### ABSTRACT

**Long COVID is a condition characterised by persistent symptoms following the acute phase of COVID-19. While the incidence and severity of long COVID has declined significantly over the course of the pandemic, a small proportion will continue to experience this. The pathophysiology of long COVID is not well understood, but reflecting the heterogeneity in individual experiences of this syndrome, there is likely to be a wide range of different causes. Long COVID is also a product of environmental and psychological factors. Diagnosing long COVID requires a careful assessment of the time course of symptoms in relation to SARS-CoV-2 infection and exclusion of alternative causes. Managing long COVID requires a holistic approach focused on supporting the patient through their recovery. There is no medication that has proven to be effective although SARS-CoV-2 vaccinations might help improve symptoms and will reduce the risk of re-infection.**

**Keywords: SARS-CoV-2; Long COVID; POTS; Chronic Fatigue Syndrome; Fibromyalgia**

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### INTRODUCTION

Long COVID is a condition characterised by symptoms that persist or develop over the three months following the acute phase of COVID-19.<sup>1,2</sup> While most people will recover from COVID-19 within a few days or weeks, some people experience lingering symptoms for months or years, which can significantly impact their daily life.

The reported incidence of long COVID varies widely based on the population, the study design, and the definition of long COVID.<sup>3-5</sup> It is clear, however, that both the incidence and severity of long COVID has declined significantly over the course of the pandemic. The emergence of the Omicron variant – more transmissible, but also less severe – coupled with infections now occurring among individuals who are not immunologically naïve (due to infection and/or

vaccination) means infection is now much more likely to result in a mild, self-contained illness.

The pathophysiology of long COVID is not well understood, but reflecting the heterogeneity in individual experiences of this syndrome, there is likely to be a wide range of different causes. Hypotheses that long COVID may be due to persistent viral replication or insertion of the virus into host genomes are not supported by the evidence. What underpins whether someone develops long COVID is the host immune response to SARS-CoV-2 infection.<sup>6</sup> In some individuals the immune response is dysfunctional and does not resolve as expected, with long-term consequences. Whether these consequences are primarily centred on the gut microbiome, vascular endothelium, innate, humoral, or cellular immunity remains controversial.<sup>7,8</sup>

Long COVID is also a product of environmental and psychological factors. The fear and anxiety associated with the pandemic affected many people's experience of SARS-CoV-2 infection.<sup>9</sup> The role of personality type, pre-existing depression, or anxiety in shaping whether someone develops long COVID is complex, and unfortunately open to misinterpretation. Furthermore, many individuals with long COVID develop mood disorders *because* of the symptoms and its impact on their life, along with the unfamiliar and frequently mysterious nature of the condition, the delays and difficulty with diagnosis, and the lack of certainty surrounding treatment approaches and time course.

While defining long COVID is challenging and has evolved over the course of the pandemic, some clinical presentations can be considered functionally distinct:

1. Persistent symptoms such as cough, rhinitis, or fatigue for more than a week or two after SARS-CoV-2 or any viral infection is not unusual. Compared with long COVID, these symptoms are more clearly related to the initial infection and will usually resolve or at least be improving over the subsequent weeks to months.
2. It is also expected that individuals who had a severe infection that resulted in pneumonia, hospital, or ICU admission may take many months to recover.<sup>10</sup> Severe infections typically occur in older adults with other medical conditions, frailty, and limited physical reserve. Recovery in this situation is likely to be protracted; in the most vulnerable people and severe infections, a return to pre-COVID health and functional capacity may not occur.
3. Among at-risk individuals, even a mild SARS-CoV-2 infection can cause a worsening of a pre-existing condition such as diabetes or result in medical complications including a cardiovascular event or stroke.<sup>11</sup> This usually happens during the acute illness,

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but it may trigger a chain of complications with long-term consequences and symptoms. In the literature, these medical complications are often described as Post-Acute Sequelae of SARS-CoV-2 infection (PASC), a term that is sometimes used interchangeably with long COVID.

Long COVID sits in a different space from the above presentations, where the cause is not explicable or attributable to any other condition. It is more likely to affect a younger and otherwise healthy population and is more common among women. Except for individuals with symptoms similar to Postural Orthostatic Tachycardia Syndrome (POTS) – see below – it is also typically not associated with objective abnormal findings on examination or a thorough medical workup.

## SYMPTOMS OF LONG COVID

Long COVID encompasses a wide array of symptoms.<sup>12</sup> These symptoms vary considerably between individuals in frequency and severity, making diagnosis and management challenging. The time course, onset, and apparent triggers for these symptoms may be variable over the course of the illness and even from day-to-day.

### Respiratory Symptoms

- Persistent cough
- Shortness of breath
- Chest pain

### Cardiovascular Symptoms

- Palpitations
- Chest tightness
- Elevated heart rate

### Neurological Symptoms

- Brain fog
- Headaches
- Dizziness
- Sleep disruption
- Smell/taste disturbances

### Gastrointestinal Symptoms

- Diarrhoea
- Nausea
- Abdominal pain

### Dermatological Symptoms

- Rashes
- Hair loss

### General Symptoms

- Fatigue and malaise
- Joint pain
- Muscle aches

### Psychological Symptoms

- Anxiety
- Depression
- Mood swings

## LONG COVID, CHRONIC FATIGUE SYNDROME (CFS), FIBROMYALGIA, AND POTS

The clinical features of long COVID, Chronic Fatigue Syndrome (CFS), and fibromyalgia share some overlapping characteristics, including:

- Severe fatigue and post-exertional malaise
- Cognitive impairments, often referred to as “brain fog”
- Muscle and joint pain
- Sleep disturbances
- Significant impact on daily functioning and quality of life

Long COVID follows a COVID-19 infection, whereas the triggers for CFS and fibromyalgia are unclear, and may include various factors, including bacterial or viral infections. Whether there are shared pathophysiological mechanisms is unknown.

The Fukuda criteria can be used to assist clinicians with a diagnosis CFS.<sup>13</sup> Tools such as the modified COVID-19 Yorkshire Rehabilitation Scale (C19-YRS) and the Post-COVID-19 Functional Status (PCFS) scale are useful for describing and assessing the symptom burden in long COVID but no similar diagnostic criteria has been widely accepted.<sup>14,15</sup>

Postural Orthostatic Tachycardia Syndrome (POTS) and Idiopathic Tachycardia Syndrome (ITS) are complex, multisystem conditions that were described prior to the COVID pandemic and as an uncommon consequence of a viral infection.<sup>16</sup> Characteristic symptoms include sustained tachycardia on standing up or minimal exertion. This is often associated with fatigue, post-exertional malaise, “brain fog”, and anxiety. The pathophysiology of POTS is not known and has been proposed to be due to autonomic dysfunction or an autoimmune disease.

## DIAGNOSIS OF LONG COVID

Diagnosing Long COVID requires a careful assessment of the time course of symptoms in relation to SARS-CoV-2 infection, and exclusion of alternative causes. A non-judgemental, sympathetic approach is important to help build a relationship with the patient.

Patients may present with a long history of symptoms and investigations conducted by other healthcare providers, and may have preconceived notions about the cause, triggers, and treatments of long COVID. These are often derived from their own experience, advice from family, friends, and support groups of fellow sufferers, and the wealth of (mis) information online.

For most patients, the first steps are to:

- Collect a detailed medical history, including any previous COVID-19 infections and vaccinations
- Evaluate the range of symptoms, their onset and

duration, and effect they have on the patient's ability to do their usual activities – work, leisure, physical exertion

- Conduct a thorough physical examination to screen for any physical signs

The role of diagnostic tests is largely to screen and rule out other medical conditions that might explain the symptoms; it is expected that these will be normal in most patients with long COVID. There is no specific diagnostic test for long COVID. Relevant investigations may include:

- Full Blood Count (FBC)
- Inflammatory Markers: C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)
- Liver and Kidney Function Tests
- Thyroid Function Tests
- Electrocardiogram (ECG)
- Chest X-ray

Most patients do not require referral to a specialist clinic, except when presenting with a POTS-like diagnosis when a cardiology assessment and investigations such as a 24-hour Holter monitor, echocardiogram, and autonomic testing should be considered.

Since 2021, the National Centre for Infectious Diseases (NCID) has operated a multi-disciplinary long COVID clinic. This clinic is operated by infectious diseases with support from various specialities including rehabilitation medicine, cardiology, and neurology as required.

## MANAGEMENT OF LONG COVID

Managing long COVID requires a holistic approach focused on supporting the patient through their recovery. There is no medication that is proven to be effective; anti-virals are not indicated as treatment, though they might help with prevention<sup>17</sup>; systemic corticosteroids and other medication with a significant risk of side effects should be avoided.

Understanding why a patient has decided to seek medical attention is important, so that treatment is tailored to their specific symptoms and needs. Some patients might simply require reassurance that their symptoms are likely to improve, and that there is no serious underlying condition, while for others regular follow-ups to monitor progress and adjust treatment plans is helpful. Approaches may also include:

- Symptom management: Address specific symptoms with appropriate treatments, such as bronchodilators for respiratory symptoms or pain relievers for musculoskeletal pain.
- Exercise: Gradual, supervised exercise programmes to improve physical fitness without exacerbating symptoms.
- Mental Health Support: Provide psychological support and counselling to address anxiety, depression, and other mental health issues.

- Lifestyle Modifications: Encourage patients to adopt healthy lifestyle practices, including a balanced diet, regular exercise as tolerated, and adequate sleep.
- Patient Education: Educate patients about long COVID, its symptoms, and management strategies to empower them in their recovery journey.

Advising patients on how to manage fatigue is important. This may include helping patients to recognise limitations in their “body battery”, strategies such as prioritising the most important tasks in a day, and avoiding “boom and bust” in energy levels.

SARS-CoV-2 vaccination can improve long COVID symptoms in some individuals through unclear mechanisms. The risk of long COVID is highest with first SARS-CoV-2 infection, but reducing the risk of re-infection through booster vaccination is prudent.

## CONCLUSION

Long COVID is a complex and multifaceted condition that has affected a significant number of COVID-19 survivors worldwide. Understanding its symptoms, diagnosis, and management is crucial for providing effective care and improving patient outcomes. As research continues to uncover the mechanisms underlying long COVID, healthcare providers must adapt their models of care delivery to meet the needs of affected individuals. By adopting a comprehensive and multidisciplinary approach, we can better support patients on their journey to recovery and mitigate the long-term impact of this condition.

## DECLARATIONS

The author declares honoraria/speaker fees from AstraZeneca, Gilead, Moderna, Pfizer, Sanofi unrelated to this article.

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## LEARNING POINTS

- **Long COVID is a condition characterised by persistent symptoms following the acute phase of COVID-19. While most people will recover from COVID-19 within a few days or weeks, some people experience lingering symptoms for months or years, which can significantly impact their daily life.**
  - **The clinical features of long COVID, Chronic Fatigue Syndrome (CFS), and fibromyalgia share some overlapping characteristics, including severe fatigue and post-exertional malaise, cognitive impairments, often referred to as “brain fog”, significant impacts on daily functioning and quality of life.**
  - **The modified COVID-19 Yorkshire Rehabilitation Scale (C19-YRS) and the Post-COVID-19 Functional Status (PCFS) scale are useful for describing and assessing the symptom burden in long COVID but no diagnostic criteria has been widely accepted.**
  - **The role of diagnostic tests is largely to screen and rule out other medical conditions that might explain the symptoms; it is expected that these will be normal in most patients with long COVID. There is no specific diagnostic test for long COVID.**
  - **Managing long COVID requires a holistic approach focused on supporting the patient through their recovery. There is no medication that has been proven to be effective. Treatment is tailored to specific symptoms and needs. Some patients might simply require reassurance, while for others regular follow-ups to monitor progress and adjust treatment plans is helpful.**
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