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## Long COVID: aiming for a consensus



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Published Online

May 4, 2022

[https://doi.org/10.1016/S2213-2600\(22\)00135-7](https://doi.org/10.1016/S2213-2600(22)00135-7)

For more on the **patient community perspective on COVID-19 recovery** see <https://patientresearchcovid19.com/research/report-1/>

The spectrum of signs and symptoms that can newly occur and persist for months to years after SARS-CoV-2 infection was initially named long COVID. This term was collectively created by the patient community in the spring of 2020,<sup>1</sup> and was later followed by other terms, such as post-COVID-19 condition, post-acute sequelae of SARS-CoV-2 infection, and post-COVID syndrome.<sup>2</sup> This condition can affect different organs and body systems, with a wide range of signs and symptoms reported. Given the magnitude of the sequelae of SARS-CoV-2 infection, it is essential to agree upon the nomenclature and definition to assess its incidence, subtypes, and severity. This process cannot be left to agencies, health-care providers, or researchers alone, but requires extensive consultation, notably including the people affected.

In early 2021, WHO established technical working groups to provide a clinical case definition for this condition and amplified the calls of patient groups for recognition, research, and rehabilitation. A rapidly increasing number of studies started to investigate the incidence and prevalence, features, and risk factors of the prolonged sequelae of SARS-CoV-2 infection, the underlying mechanisms, and case management approaches.<sup>3</sup>

There are concerns about differences in terminology, with some public health experts and policy makers avoiding the term long COVID. The use of different terms can raise worries, especially among those with lived experience of the condition who originally coined the term long COVID. Many issues have been raised by patient-researchers and other adopters of the term. One issue is epistemic injustice in medicine, including the poor recognition of patient-led expertise. Patient perspectives emphasise the tradition in medical history that those who first identify and describe a condition, name it. In the case of long COVID, it was people with lived experience of it who brought it to the world's attention and described it via a wide range of methods. The first publication on prolonged symptoms of COVID-19 was authored by patient-researchers with long COVID, later known as the Patient-Led Research Collaborative.<sup>4</sup> Another issue is that the severity, features, and urgency of long COVID—as highlighted by patients—are not fully addressed within the framework of other terms and definitions. Long COVID remains the patient-preferred term.<sup>1</sup>

Beyond the name, the condition has many definitions, in both research and clinical settings, with none of them universally agreed. Attempts were made to harmonise data collection, actively involving patient groups in the process, with tailored case-report forms developed by the International Severe Acute Respiratory and emerging Infection Consortium (ISARIC) and WHO. However, the outcomes and diagnostic criteria used vary widely, with no consensus on a minimum core set of outcomes and how to measure them.<sup>2</sup> Most published research uses persistent symptoms, measured at variable time points after an acute episode or proven infection, as a primary outcome,<sup>3</sup> and call this outcome one of the above-mentioned names, which is another source of heterogeneity. Analysis of the condition's development over time is crucial.

Various agencies have generated their own terms and definitions, including WHO (through an international Delphi consensus process<sup>5</sup>), the UK National Institute for Health and Care Excellence,<sup>6</sup> and the US Centers for Disease Control and Prevention (table).<sup>7</sup> Notably, long COVID is still widely used by researchers as a very broad term covering persistent signs and symptoms that continue or develop after acute SARS-CoV-2 infection for any period of time, whereas some other terms have much more stringent definitions.

This lack of harmonisation in terminology and definitions brings heterogeneity into research on long COVID phenotypes.<sup>8</sup> A recent analysis showed that clinical manifestations described in more than 80 cohorts 3 weeks or more after acute SARS-CoV-2 infection resulted in 287 unique clinical findings in accordance with the Human Phenotype Ontology, which is a widely used standard for exchange and analysis of phenotypic abnormalities in human disease.<sup>9</sup> It is difficult to accurately establish the time when acute COVID-19 ends, and data regarding the duration of long-term viral persistence are lacking, although long COVID is not necessarily caused by viral persistence. The health consequences of various SARS-CoV-2 variants are still unknown. With differing terms and definitions, the number of long COVID phenotypes might grow exponentially, confusing stakeholders and preventing development of effective interventions.

Some parallels in the use of terminology can be drawn between long COVID and post-intensive care syndrome (PICS), which is a complex and multidimensional problem defined as “new or worsening impairments in physical, cognitive, or mental health status arising after critical illness and persisting beyond acute care hospitalisation”.<sup>10</sup> Although long COVID can develop after acute illness of any severity and PICS is associated with recent critical illness, both are highly heterogeneous conditions. The term PICS, created by an international multidisciplinary

group (including patient representatives) convened by the Society of Critical Care Medicine, was developed to increase awareness of long-term sequelae after critical illness among all relevant stakeholders. The patient-made origin of long COVID can also serve a similar role, being an overarching term covering broad sequelae and disease processes from acute infection. Other terms have much more rigid definitions, explicitly outlining symptom duration, and can be incorporated within the long COVID umbrella term.

	Developed or proposed	Definition	Suggested website references
Long COVID*	Patients and people with lived experience; patient-researchers	Can be broadly defined as signs, symptoms, and sequelae that continue or develop after acute COVID-19 or SARS-CoV-2 infection for any period of time; are generally multisystemic; might present with a relapsing–remitting pattern and a progression or worsening over time, with the possibility of severe and life-threatening events even months or years after infection	<a href="https://www.sciencedirect.com/science/article/pii/S0277953620306456?via%3Dihub">https://www.sciencedirect.com/science/article/pii/S0277953620306456?via%3Dihub</a>
Persistent symptoms or COVID-19 consequences	Commonly used research term	Persistent signs and symptoms that continue or develop after acute COVID-19 for any period of time	<a href="https://www.sciencedirect.com/science/article/pii/S0163445321005557">https://www.sciencedirect.com/science/article/pii/S0163445321005557</a> ; <a href="https://gh.bmj.com/content/6/9/e005427.long">https://gh.bmj.com/content/6/9/e005427.long</a>
Post-COVID-19 condition	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 that last for at least 2 months and cannot be explained by an alternative diagnosis; common symptoms include fatigue, shortness of breath, and cognitive dysfunction, and generally have an impact on everyday functioning; symptoms might be new onset after initial recovery from an acute COVID-19 episode or persist from the initial illness; symptoms might also fluctuate or relapse over time; a separate definition might be applicable for children	<a href="https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00703-9/fulltext">https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00703-9/fulltext</a>
Ongoing symptomatic COVID-19	NICE†	Signs and symptoms of COVID-19 from 4 weeks up to 12 weeks	<a href="https://www.nice.org.uk/guidance/ng188/resources/covid19-rapid-guideline-managing-the-longterm-effects-of-covid19-pdf-51035515742">https://www.nice.org.uk/guidance/ng188/resources/covid19-rapid-guideline-managing-the-longterm-effects-of-covid19-pdf-51035515742</a>
Post-COVID-19 syndrome	NICE†	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; it usually presents with clusters of symptoms, often overlapping, which can fluctuate and change over time and can affect any system in the body; post-COVID-19 syndrome might be considered before 12 weeks while the possibility of an alternative underlying disease is also being assessed	<a href="https://www.nice.org.uk/guidance/ng188/resources/covid19-rapid-guideline-managing-the-longterm-effects-of-covid19-pdf-51035515742">https://www.nice.org.uk/guidance/ng188/resources/covid19-rapid-guideline-managing-the-longterm-effects-of-covid19-pdf-51035515742</a>
Post-COVID conditions	US Centers for Disease Control and Prevention	An umbrella term for the wide range of physical and mental health consequences experienced by some patients that are present four or more weeks after SARS-CoV-2 infection, including by patients who had initial mild or asymptomatic acute infection	<a href="https://www.cdc.gov/coronavirus/2019-ncov/long-term-effects/index.html">https://www.cdc.gov/coronavirus/2019-ncov/long-term-effects/index.html</a>
Post-acute sequelae of SARS CoV-2 infection*	US National Institutes of Health	Persistent or new symptoms after COVID-19 infection; the definition will be revised in an iterative manner based on existing data, medical literature, and feedback from patient representatives, patients, and the scientific community; updated definitions might be used to implement a strategy to modify deeper phenotyping	<a href="https://recovercovid.org/docs/RECOVER-Adult-Protocol_02-02-2022.pdf">https://recovercovid.org/docs/RECOVER-Adult-Protocol_02-02-2022.pdf</a>

NICE=National Institute for Health and Care Excellence (UK). \*We are unaware of any agreed definition for the term at the time of writing. †NICE also states that: “In addition to the clinical case definitions, the term ‘long COVID’ is commonly used to describe signs and symptoms that continue or develop after acute COVID-19. It includes both ongoing symptomatic COVID-19 (from 4 to 12 weeks) and post-COVID-19 syndrome (12 weeks or more).”<sup>6</sup>

**Table: Commonly used terminology in the research of COVID-19 sequelae**

With millions affected by COVID-19, the large number developing long COVID has major detrimental effects on people, society, and public health, including long-term follow-up, support, and lost productivity. There is an urgent need for unification of terminology for the sequelae of SARS-CoV-2 infection. Different terms may be used, but only if they are well defined and help ensure that research is directed towards and translated into interventional trials to improve the outcomes of people with long COVID. It is essential to bring together clinicians, researchers, patients, carers, funders, and policy makers to harmonise terminology. This is to help advance the field via improved harmonisation and comparability, while allowing for adjustment and flexibility in view of new discoveries.

DM reports grants from the British Embassy in Moscow, UKRI/NIHR, and the Russian Foundation for basic research funding projects related to COVID-19 and long COVID. DM is also a co-chair of the ISARIC Global Paediatric long COVID working group and member of the ISARIC working group on long-term follow-up in adults as well as co-lead of the PC-COS and PC-COS paediatric projects aiming to define the core outcome set for long COVID. DMN is a co-lead of the PC-COS project aiming to define the core outcome set for long COVID. EP reports being a Long Covid Kids Champion (an unpaid, volunteer role aimed at facilitating the recognition of long Covid in paediatric patients) for the charity Long Covid Kids. All other authors declare no competing interests.

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## E-cigarette company tactics in sports advertising

Published Online  
 May 11, 2022  
[https://doi.org/10.1016/S2213-2600\(22\)00166-7](https://doi.org/10.1016/S2213-2600(22)00166-7)

John Bunyan coined the phrase "The Captain of all these the men of death" and applied it to consumption (ie, tuberculosis); Sir William Osler subsequently applied the phrase ("Captain of the men of death") to pneumonia in the pre-antibiotic era; but both diseases gave way to tobacco-related lung disease, which now has the unanswerable claim on that title. Eventually, the pioneering work of Sir Richard Doll and many others was recognised, demonstrating the toll of premature death caused by the tobacco industry, but only after many decades of harm. Despite an industry campaign of disinformation supported by physicians lauding the virtues of smoking, legislation to restrict smoking in public and ban advertising was passed and resulted in many demonstrable health benefits. The sight of a tobacco advertisement in a public place or a tobacco-

sponsored sporting event today would be shocking, and it seemed attitudes towards tobacco and public health were improved and heading in the right direction.

However, the tobacco industry now promotes vaping. Other than in the UK, the uniform response of learned societies and governments to vaping has been one of ineluctable opposition. Robust position papers, including from the American and European Academies of Pediatrics, the European Respiratory Society, the American Thoracic Society, and the International Federation of Respiratory Societies, all warn of the dangers of electronic nicotine delivery systems (ENDS). All of these groups acknowledge the evidence that the acute toxicity from ENDS is greater than that of tobacco.<sup>1</sup> There is ongoing documentation of cases of ENDS acute lung injury in children and younger people.<sup>2</sup> As of Jan 8, 2020, 244 suspected adverse