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Editorial On the new post COVID-19 condition[☆] Sobre la nueva condición post COVID-19 Joan B. Soriano,^{a,b,c,*} Julio Ancochea^{a,b}

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Coronavirus disease 2019 (COVID-19) is still far from over¹. At the end of spring 2020, when the first wave of cases began to be controlled, something unusual was observed: some COVID-19 patients still had symptoms weeks after the initial infection had passed. They reported symptoms that included fatigue, dyspnea, chest pain, palpitations, gastrointestinal symptoms, mental confusion, anxiety, and depression, and more than 150 other possible associated symptoms² that persisted for weeks or months. This was surprising, because some patients who had less severe disease initially and were treated only in primary care or remained practically asymptomatic during acute infection, were eventually among the most sick³. The terminology for this phenomenon varies (Table 1). The WHO currently recommends calling it a "post-COVID-19 condition", as this name does not attribute causality or duration, and there are already specific ICD-10 (U09) and ICD-11 (RA02) codes to identify it⁴. Beyond the name, a universal definition agreed by consensus with societies, organisms, and patients, is necessary⁵.

Estimates of how many people develop post-COVID-19 condition vary. Curiously, it seems to affect more middle-aged adults than elderly people, but so far no one knows for certain why it occurs or who is most likely to be affected, and with more than 126 million cases of COVID-19 to date worldwide, the number of people at risk is increasing⁶. Many post-COVID-19 patients, individually or jointly in associations such as SOSCOVID, Persistent COVID-19 Collective Madrid, and others, report that their primary care doctors (and pulmonologists) initially ruled out and ignored their symptoms, thus aggravating their suffering⁷. This phenomenon also occurs in children, to their parents' despair. Multidisciplinary clinics to treat these patients have now sprung up in hospitals and clinics in the United Kingdom and Italy⁸.

SARS-CoV-2 is not the first virus to cause lasting symptoms or new associated syndromes⁹. Previous epidemic viral outbreaks such as Zika, chikungunya, SARS, and MERS, and before them, the 1918 flu (wrongly called the Spanish flu) left many people weakened for months, sometimes years. In these patients, the virus is

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no longer live or active, but they present persistent symptoms. In terms of causative mechanisms, we have some possible suspects.

Excess inflammation: this is the primary candidate, as abnormally high levels of inflammation are seen in many patients.

Autoimmune response: raised levels of autoantibodies have been found in patients with post-COVID-19 condition. And certain autoimmune diseases, such as lupus and rheumatoid arthritis, commonly cause fatigue and digestive problems.

Nervous system problems: dysautonomy, which refers to the deregulation of the autonomic nervous system, affects blood flow, including to the brain, and can cause fatigue, headaches, mental confusion, and exercise intolerance.

Blood clots and vascular damage: many patients with elevated Ddimer blood levels improve with the administration of prophylactic anti-coagulation. Autopsies of people who died of COVID-19 have revealed widespread clots.

This brings us to the question of how these patients should be treated. Many need to be seen by various specialists, from respiratory medicine experts to cardiologists, gastroenterologists, and of course, primary care physicians^{10–12}. After magnetic resonance imaging, tomography, blood analyses, and other tests have been performed, the goal of treatment must be to identify underlying problems, control symptoms, and improve functional capacity.

The post-COVID-19 condition is a new challenge¹³, caused by a new virus. New studies will soon provide some answers. Meanwhile, the best way to protect yourself is . . . avoid infection. If you contract COVID-19, be sure to take enough time to recover before returning to your normal activity. We know from Zika, chikungunya, SARS, and MERS, and from patients with chronic fatigue syndrome (now called systemic exercise intolerance disease) that putting on too much pressure on sufferers can cause recurrence and a slower than expected recovery. The good news is that after 6 months a gradual improvement is seen in most series of patients, including those who were admitted to the ICU¹⁴. Paraphrasing George Bizet's Carmen (1845): "Prends garde de faire un faux pas!!" – "Watch out . . . for the post-COVID-19 condition!"



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Table 1

Repository of suggested names for post-COVID-19 condition.

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| Late sequelae of COVID-19 | CDC website [Accessed 29 March 2021] Available from: |
| | https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/late-sequelae.html |
| Long covid | Mahase E. <i>BMJ</i> . 2020 July 14;370:m2815 |
| Long COVID | Perego E, et al. Wellcome Open Research 2020;5:224; Editorial. The Royal Society |
| LONG COVID | Nature Editorial [Let patients help define long-lasting COVID symptoms] 8 October 2020; Long COVID Forum 9–10 December |
| | 2020 from ISARIC/GLOPIDR/LONG COVID Support; Lancet Editorial [Facing up to long COVID] 12 December 2020; |
| Long-haul COVID | Nath A. Long-Haul COVID. Neurology. 2020 September 29;95(13):559–560.; Scientific American (By Carolyn Barber on |
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| Post-COVID syndrome | NHS-National Health Service (UK) [Accessed 29 Mar 2021] Available from: |
| | https://www.england.nhs.uk/coronavirus/post-covid-syndrome-long-covid/ |
| Post-acute COVID-19 | Several papers in: BMJ, Eur J Phys Rehabil Med, Eur J Intern Med |
| Post-acute sequelae of | Subbaraman N. US health agency will invest \$1 billion to investigate 'long COVID' Nature. 2021;591:356. DOI: |
| SARS-CoV-2 infection | https://doi.org/10.1038/d41586-021-00586-y |
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