Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

the world would like to see. As countries discharge their responsibility to protect vulnerable individuals in their populations, they must ensure adequate supply to other countries. Global policy must weigh the risks of adopting booster doses ad libitum across the world at this stage of the pandemic.

I declare no competing interests.

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Global surveillance, research, and collaboration needed to improve understanding and management of long COVID

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The scale of chronic ill health and disability after COVID-19 has been described as the next big global health challenge.[1] Prevalence estimates of a post-COVID-19 condition, long COVID, or post-acute sequelae of SARS-CoV-2 vary according to definition, methodology, and population. A recent systematic review reported persistent symptoms at 3–6 months in a median of 57% (range 13–92) of hospitalised patients (six studies) and 26% (2–62) of non-hospitalised patients (ten studies).[2] This study and other reviews identified few studies from low-income settings,[3] but with more than 245 million SARS-CoV-2 infections reported globally,[4] millions of people are likely to already be experiencing long-term illness. While COVID-19 vaccines have reduced the risk of severe COVID-19 and death, continued high rates of SARS-CoV-2 infection will lead to further disability, having a huge impact on individuals, their families, health services, and society.

Patients coined the unifying term long COVID,[5] but there is not yet a health professional consensus definition or nomenclature. In October, 2021, WHO used a Delphi method to develop a clinical definition of post-COVID-19 condition as a range of symptoms occurring 3 or more months after probable or confirmed SARS-CoV-2 infection that last for at least 2 months, cannot be explained by an alternative diagnosis, generally have an impact on daily functioning, and may fluctuate or relapse over time.[6] A separate definition is recommended for children.[6] Other definitions use different time frames and terminology,[7,8] but remain difficult to apply in research and clinical management.

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Long COVID has many characteristic symptoms, including post-exertional symptom exacerbation, severe fatigue, breathlessness, tachycardia, cognitive deficits, and dysautonomia.[9,10] However, the absence of specific diagnostic criteria means that clinicians and patients must live with substantial uncertainty, with the risk that people will be either overinvestigated and overtreated or not receive adequate support.[11]

A hidden epidemic of long COVID is possible given the challenges in access to care and uncertainty about diagnostic criteria—factors that will differ in their importance between low-income and high-income settings.[12] Patients report not being taken seriously by medical practitioners or refused referral to long COVID services.[5,13] These services remain limited and where they exist vary in scope, quality, and access to some therapeutic options. In the absence of diagnostic tests, long COVID is partly a diagnosis of exclusion, creating challenges for patients and carers. Previous diagnoses of exclusion, such as chronic fatigue syndrome, fibromyalgia, and irritable bowel syndrome, are now better defined than in the past, meaning patients are more able to obtain acknowledgment, treatment, sick pay, or insurance.[14]

Data from high-income countries suggest that ongoing symptoms after acute COVID-19 can occur irrespective of initial disease severity and are more prevalent in women, middle-aged and older adults, people with pre-existing health conditions, and those admitted to hospital with acute COVID-19,[15] although the latter might also reflect post-intensive care syndrome.[16] However, the pathophysiology of long COVID remains poorly understood with different mechanisms probably explaining the heterogeneous symptoms, including viral persistence, autoimmunity due to molecular mimicry, aberrant T-cell and humoral responses, and micro-thrombi.[17] Understanding the mechanisms and natural history of long COVID will inform diagnostic and therapeutic strategies, building on experience of other post-viral syndromes—eg, careful pacing in rehabilitation to avoid post-exertional symptom exacerbation. To date no antiviral or immunomodulatory drug has proven effective for the treatment of long COVID in trials. Some preliminary reports suggest COVID-19 vaccination might improve symptoms in some people,[18,19] supporting the notion of a possible role for persistent viral reservoirs, circulating virus fragments, or both in long COVID.[19]

The COVID-19 pandemic has shown the power and necessity of large-scale, multicentre, adaptive platform trials and applying these approaches to long COVID will help accelerate development of an evidence base for disease management. Importantly, these trials will need to include centres across various settings with different resource availabilities, such as in WHO's Solidarity and the Recovery and REMAP-CAP treatment trials. In the short term, it might be prudent to evaluate therapies for specific symptoms, such as cognitive dysfunction, breathlessness, and fatigue, rather than pursuing a single treatment for such a broadly defined syndrome, although patients would clearly welcome an effective general treatment.

Ideally, patients with this complex disease process which affects multiple systems should be assessed by a medical generalist with access to diagnostic tools and relevant multidisciplinary teams, but globally decentralised community services will be more sustainable in a COVID-19-endemic world. Robin Gorna and colleagues, writing as individuals with lived experience of long COVID, advise that "psychological aspects of disease should be managed as part of the recovery process, but not seen as the primary treatment focus for all".[13] As with most chronic disease, a holistic approach and individualised rehabilitation plan will be crucial. Reliable online and other resources are needed to ensure that clinicians, researchers, and patients can keep up to date with the latest evidence on long COVID in a rapidly evolving field. Yet these resources will be beyond what is available in many health systems, particularly in low-income and middle-income countries (LMICs).

COVID-19 has exacerbated existing inequities and created new vulnerabilities, especially in low-resource settings, and long COVID is amplifying these disparities.[20] Countries with limited resources and already overwhelmed health systems are unlikely to be able to provide specific services for long COVID, which will therefore remain hidden. Surveillance of this emerging public health threat must be a priority globally, and we support the need for national registers, with chronic cases reported alongside infections, hospitalisations, and deaths. Large-scale multinational partnerships, including LMIC

For the **WHO Solidarity trial** see https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments

For the **Recovery trial** see https://www.recoverytrial.net/

For the **REMAP-CAP trial** see https://www.remapcap.org/

researchers, patients, and funding, are needed to evaluate evidence-based diagnostics and therapeutics and assure affordability, applicability, and adaptability to different health-care systems, including in resource-limited contexts.[21] Such collaborative efforts should lead to greater understanding of disease mechanisms and treatments for long COVID, improving lived experience of the millions of people with this condition around the world.

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