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.

obvious, but probably not just a matter of using the sequence of the most recent variant of concern.

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Charting a course for the management of long COVID


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It is difficult to think beyond the immediate crisis, when wave after wave of the COVID-19 pandemic has repeatedly overwhelmed health systems and resulted in high rates of mortality and severe disruption to normal life. However, the recognition of a syndrome of prolonged, multisystem disability in survivors of COVID-19[1–3]—commonly referred to as long COVID or the post-COVID-19 condition—has made obtaining knowledge of its pathogenesis, prognosis, and management an important competing priority. A comprehensive, coordinated global research strategy for the post-acute sequelae of COVID-19, rather than a piecemeal approach, is clearly required, although difficult to achieve in the midst of a pandemic.

For this reason, the Position Paper from the UK-based International COVID-19 Airways Diseases Group in *The Lancet Respiratory Medicine*,[4] presenting research priorities for the long-term effects of COVID-19 in the context of airways disease, is to be welcomed. The consensus recommendations, which are both broad and insightful, will inform future research efforts.

The highest-ranked research priorities, identified by the group using the Child Health and Nutrition Research Initiative (CHNRI) prioritisation method, include investigation of whether prognostic scores and clinical or radiological features at hospital admission predict post-discharge morbidity in groups of patients with and without pre-existing airways disease. This strategy allows targeted follow-up and management of patients who are at risk of greatest morbidity from long COVID within overstretched health-care systems, where resourcing will inevitably be constrained. This priority is based in part on evidence that, for long COVID, there is a risk gradient that increases according to the severity of the acute SARS-CoV-2 infection.[2] However, evaluation of prediction scores in those not admitted to hospital will also be important, as long COVID can also occur in both adults and children who have had mild acute SARS-CoV-2 infection.[2,3] Indeed, the greatest total burden of disease from long COVID is likely to occur in the vast majority of those with SARS-CoV-2 infection who are not admitted to hospital.

The broad focus on comparisons of patients with and without pre-existing airways disease is sound, as many of the pulmonary and extrapulmonary symptoms of long COVID and airways disease are shared. Similarly, the recommendation to extend assessments of the effects of long COVID to extrapulmonary organs is warranted, because although acute SARS-CoV-2 infection primarily affects the lungs, COVID-19 is a multisystem disease,

and long COVID is likewise associated with multi-organ impairment.[1–3] The extent of extrapulmonary involvement is illustrated on MRI, with abnormalities frequently observed not only in the lungs, but also in the heart, kidneys, liver, and brain of patients with COVID-19 2–3 months after disease onset compared with matched controls.[5] Extensive multiorgan involvement is not restricted to those recovering from severe COVID-19. In a study of a young low-risk population with ongoing symptoms, about two-thirds of individuals had MRI evidence of impairment in one or more organs 4 months after initial symptoms of SARS-CoV-2 infection.[6]

From a clinical perspective, high-dimensional characterisation of long COVID in patients who have survived for at least 30 days after SARS-CoV-2 infection has enabled identification of incident sequelae beyond the respiratory system, including nervous system disorders, neurocognitive and mental health disorders, metabolic disorders, cardiovascular disorders, gastrointestinal disorders, malaise, fatigue, musculoskeletal pain, and anaemia.[2] There was also increased incident use of several therapeutic agents for airways disease such as bronchodilators, anti-asthmatic agents (eg, anti-inflammatories by inhalation), and glucocorticoids, as well as β blockers, analgesic medications (both opioid and non-opioid drugs), and antidepressant, anxiolytic, and oral hypoglycaemic agents.

It will be interesting to observe whether substantive differences emerge between patients with pre-existing asthma or chronic obstructive pulmonary disease (COPD) in the presentation and severity of long COVID. In patients with COPD, SARS-CoV-2 infection is known to result in an increased risk of hospital admission and death, whereas those with asthma are probably not at increased risk.[7] Furthermore, there is now evidence that inhaled corticosteroids might reduce progression and shorten recovery time in COVID-19, and it will be intriguing to find out whether this benefit extends to long COVID.[8]

The COVID-19 pandemic has disproportionately affected vulnerable populations such as ethnic minorities, migrant workers, women and gender-diverse communities, and those with lower socioeconomic status.[9] The multiple risk factors intersect to exacerbate existing inequities, compounded by the structural racism present within many health and support systems, highlighted at the international level by the inequitable distribution of and access to vaccines and therapeutics. The burden of long COVID is likely to follow this trend, making research into preventing and tackling inequity in the diagnosis and management of long COVID a priority, as recommended in the Position Paper.[4]

Most of the research priorities identified would involve observational rather than intervention studies. The recommendations for intervention studies of different rehabilitation and nutritional programmes are important, and these programmes might require innovative approaches as their provision is likely to be severely affected by health systems struggling to provide health care.

Moving forward from the Position Paper, serious consideration also needs to be given to undertaking randomised controlled trials of pharmacological, psychological, and lifestyle interventions to prevent and treat the many pulmonary and extrapulmonary manifestations of long COVID. In considering such interventions, it is important to recognise that within the syndrome of long COVID, there are likely to be numerous disorders with both overlapping and separate clinical manifestations,[1–3] and a one-size-fits-all management approach is unlikely to be adequate. Rather, a personalised medicine approach, in which specific disorders are identified and managed, is probably required. For example, disabling breathlessness in a patient with airways disease who has survived SARS-CoV-2 infection might have numerous causes beyond asthma and COPD, such as bronchiectasis, pulmonary fibrosis, venous thromboembolic disease, cardiovascular disorders, neuropsychiatric complications, poor nutritional status, and physical deconditioning. This treatable traits approach, similar to that recommended in airways disease,[10] should be the focus of randomised controlled trials to guide clinical practice in long COVID. However, to be used in clinical practice, this approach will require novel algorithms that integrate symptom and prediction scores with the investigation and treatment of underlying causes. In this way, we could obtain the evidence required to chart a course for the management of long COVID.

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