Long COVID: understanding the neurological effects

The concept of so-called long COVID has gained prominence in recent months, with some patients reporting persistent neurological manifestations, from milder symptoms such as headaches, hyposmia, hypogeusia, and fatigue to more severe conditions including sleep disorders, pain, cognitive impairment, and (in very rare cases) Guillain-Barré syndrome. WHO updated their living guidance for the clinical management of COVID-19 in January, 2021, which now incorporates a new practice statement on caring for patients with persistent, new, or changing symptoms after suspected or confirmed COVID-19. The guidance notes that clinical characterisation of long COVID is inadequate and, therefore, further research on long-term sequelae is warranted.

Multiple initiatives to gather clinical neurological data about COVID-19, with the aims to aid management and to understand the long-term clinical manifestations of the disease, were launched last year. In April, 2020, the European Academy of Neurology (EAN) set up the EANcore NeuroCOVID-19 task force and began collating resources to help neurologists prepare for and manage this medical crisis. Almost 1 year on, the task force has accomplished some goals, including producing a consensus statement on the management of patients with neurological diseases and COVID-19. The EANcore NeuroCOVID-19 task force has also created the ENERGY registry to evaluate the prevalence of neurological manifestations in patients with confirmed COVID-19, the findings of which are expected to be published later in 2021. EAN has also established collaborations with several international organisations, including a formal collaboration with the Neurocritical Care Society in the USA.

Additionally in the USA, the National Institute of Neurological Disorders and Stroke (NINDS) is supporting several projects, including an initiative to track neurological symptoms, complications, and outcomes of COVID-19, to gain insights into how the disease affects the nervous system and to estimate the prevalence of these potentially rare complications. One of the NINDS-supported initiatives is the NeuroCOVID Project, which was launched on Jan 26, 2021, by researchers at NYU Langone Health. The project aims to build and maintain an 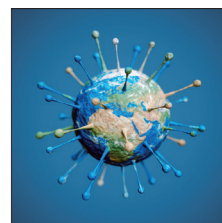international resource of deidentified clinical data and biospecimens. Recognising the scant understanding of the recovery process after SARS-CoV-2 infection, NINDS is also participating in the National Institutes of Health (NIH) Post-Acute Sequelae of SARS-CoV-2 Infection (PASC) Initiative. Research opportunities were announced by the PASC Initiative in February, 2021, and will provide grants for clinical recovery cohort studies, autopsy cohort studies, and studies based on real-world data, with the aim to identify risk factors for and biomarkers of adverse long-term outcomes and to understand pathophysiological mechanisms that could help in development of prevention strategies and novel treatments.

The EAN and NIH initiatives can be added to multiple additional projects that have been started worldwide. In May, 2020, the Environmental Neurology Specialty Group of the World Federation of Neurology (WFN) committed to curate research from national and international registries, making these data freely available on the WFN website. However, with so many registries available, the risk of duplication of data and variation in case definitions are potential complications. With much still unknown about the long-term effects of COVID-19, and many projects ongoing or being initiated, organisations need to work together. Approaches need to be standardised, and case definitions should be used consistently across studies. With the aim to refine guidelines for the management of patients with COVID-19 and characterise its long-term neurological manifestations, large-scale and multidisciplinary collaborations will be essential.

As the COVID-19 pandemic enters its second year, a notable achievement has been approval of SARS-CoV-2 vaccines. People with neurodegenerative diseases are at particular risk for a poorer outcome after SARS-CoV-2 infection, since pre-existing comorbidity and older age are risk factors. Vaccination strategies are prioritising older adults and people with comorbidities. However, despite expectations about vaccination heralding the return to normality, availability of vaccines is limited and many people are likely to remain unprotected for a long time to come. In the meantime, collaboration to improve our knowledge of COVID-19, including its long-term neurological manifestations, must continue to be a high priority. ■ *The Lancet Neurology*