Severely stressful events worsen symptoms of long COVID

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The death of a loved one, financial or food insecurity, or a newly developed disability were some of the strongest predictors of whether a patient hospitalized for COVID-19 would experience symptoms of long

COVID a year later, a new study finds.

Led by researchers from NYU Grossman School of Medicine, the study found that adult patients with such "major life stressors"—present in more than 50% of those followed—were at least twice as likely to struggle with depression, brain fog, fatigue, sleep problems, and other long-term COVID-19 symptoms, say the study authors.

Published online this week in the *Journal of the Neurological Sciences (JNS)*, the analysis also confirmed the contribution of traditional factors to greater long COVID risk as shown by past studies—older age, disability level to start with, and a more severe initial case of COVID-19.

"Our study is unique in that it explores the impact of life stressors—along with demographic trends and neurological events—as predictors of long-term cognitive and functional disabilities that affected quality of life in a large population," says lead study author Jennifer A. Frontera, MD, professor in the Department of Neurology at NYU Langone Health. "Therapies that lessen the trauma of the most stress-inducing life events need to be a central part of treatment for long COVID, with more research needed to validate the best approaches."

The research used standard telephone survey tools in the field—the modified Rankin Scale (mRS), the Barthel Index, the Montreal Cognitive Assessment (t-MoCA), and the NIH/PROMIS Neurological Quality Of Life (NeuroQoL) batteries—to measure level of daily function, clear thinking (cognition), anxiety, depression, fatigue and sleep quality. The team attempted follow-up with each of 790 patients six months and a year after COVID-19 hospitalization within NYU Langone Health between March 10, 2020 and May 20, 2020.

Of these surviving patients, 451 (57%) completed 6-month and/or

12-month follow-up, and of them, 17% died between discharge and 12-month follow-up and 51% reported significant life stressors at 12-months.

In analyses that compared factors against each other for their contribution to worse outcomes, life stressors including [financial insecurity](link), [food insecurity](link), death of a close contact, and new disability were the strongest independent predictors of prolonged COVID-19 symptoms. These same stressors also best predicted worse functional status, depression, fatigue, sleep scores, and reduced ability to participate in activities of daily living such as feeding, dressing, and bathing.

Gender was also a contributor, as past studies have found that women are more susceptible in general to—for instance—autoimmune diseases that could have an impact on outcomes. Additionally, undiagnosed mood disorders may have been unmasked by pandemic-related stressors.

Neurological long COVID may include more than one condition

A second study led by Frontera and colleagues, and published online September 29, 2022, in *PLOS ONE*, found that patients diagnosed as having long COVID neurological problems can be divided into three symptom groups.

Because there is no current biological definition of long COVID, many studies lump disparate symptoms into what is currently a blanket diagnosis, and without an assessment of clinical relevance, says Frontera. The resulting vagueness has made it "difficult to assess treatment strategies."

For the *PLOS ONE* study, the research team collected data on symptoms, treatments received, and outcomes for 12 months after hospitalization

with COVID-19, with treatment success measured again by standard metrics (modified Rankin Scale, Barthel Index, NIH NeuroQoL). The three newly identified disease groups were:

- Cluster 1: Few symptoms (most commonly headache) in patients who received few therapeutic interventions
- Cluster 2: Many symptoms, including anxiety and depression, in patients who received several treatments, including antidepressants to psychological therapy
- Cluster 3: Primarily pulmonary symptoms such as shortness of breath. Many patients also complained of headache and cognitive symptoms, and mostly received physical therapy.

The most severely affected patients (symptom Cluster 2) had higher rates of disability, worse measures of anxiety, depression, fatigue and sleep disorders. The most severely affected patients had higher rates of disability, worse measures of anxiety, depression, fatigue and sleep disorders. All patients whose treatment included psychiatric therapies reported symptom improvement, compared to 97% who received primarily physical or occupational therapy, and 83% who received few interventions.

The Brookings Institution estimated in August 2022 that roughly 16 million working-age Americans (aged 18 to 65) have long COVID, out of whom 2 to 4 million are out of work due to long COVID.

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