

Long COVID

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A new study published in *the Lancet's EClinicalMedicine* has found that patients who experience long COVID report more than 200 symptoms across ten organ systems. The study, which is the most extensive international study to date on long COVID, also found that for the majority of respondents (>91%), the time to recovery exceeded 35 weeks (8 months) ([1]).

Accumulating evidence confirms the presence of persistent multiorgan symptoms and complications beyond the initial period of acute infection and illness with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) ([2],[3]). Symptoms of long-lasting COVID-19 sequelae and complications, termed long COVID by patients ([4]), have been reported worldwide yet relatively little is known about the underlying aetiology, symptom makeup and severity, expected clinical course, impact on daily functioning, and return to baseline health.

For the current study, researchers connected to patients through the Body Politic online COVID-19 support group. A web-based survey was conducted comprising 257 questions designed to characterise the symptom profile and time course in patients with confirmed or suspected long COVID over seven months, along with the impact on daily life, work, and return to health ([1]).

Data were collected from September 6, 2020, to November 25, 2020. Researchers analysed responses from 3,762 participants with confirmed (diagnostic/antibody positive; 1,020) or suspected (diagnostic/antibody-negative or untested; 2,742) COVID-19, from 56 countries, with illness lasting over 28 days and onset before June 2020.

The majority of respondents were women (78.9%), white (85.3%), residing in the United States, and aged 30 to 60 years (33.7%). More than half of respondents (56.7%) did not seek hospital-based care and 34.9% visited an ER or urgent care clinic but were not admitted to a hospital. 8.43% of respondents were hospitalised.

Key findings of the survey are summarised below.

Symptom duration

- The probability of symptoms lasting beyond 35 weeks was 91.8%.
- Of the 3,762 respondents, 3,608 (96%) reported symptoms beyond 90 days, 2,454 (65%) experienced symptoms for at least 180 days (six months), and only 233 (6%) had recovered by 7 months.
- In those who recovered in less than 90 days, the average number of symptoms (11.4 out of 66 symptoms that were measured over time) peaked at week two, and for those who did not recover in 90 days, the average number of symptoms (17.2) peaked at month two.
- Respondents with symptoms for over six months experienced an average of 13.8 symptoms in month 7.

Symptom prevalence

- Almost all participants (99.7%) experienced systemic symptoms and 100% of participants experienced head, ears, eyes, nose, throat (HEENT) symptoms.
- Musculoskeletal, cardiovascular, gastrointestinal, pulmonary, and neuropsychiatric symptoms were prevalent in >85% of participants.
- Participants experienced an average of 55.9 symptoms across an average of 9.1 organ systems during their illness.
- The top three symptoms experienced were fatigue, post-exertional malaise (PEM), and brain fog and cognitive dysfunction, experienced by 98.3%, 89% and 85.1% of participants, respectively.
- The top three most debilitating symptoms listed by patients were fatigue (n>2,652), breathing issues (n>2,242) and cognitive dysfunction (n>1,274).

Recovery, return to baseline.

- Relapses were primarily triggered by exercise, physical or mental activity, and stress. At the time of the survey, 86.7% of unrecovered respondents were experiencing fatigue compared to 44.7% of recovered respondents.
- A total of 2,454 (65.2%) respondents were experiencing symptoms for at least six months. For this group, the top remaining symptoms after 6 months were a combination of systemic and neurological symptoms, including fatigue (80%), PEM (73.3%), cognitive dysfunction (58.4%), sensorimotor symptoms (55.7%), headaches (53.6%), and memory issues (51%).
- 1,700 respondents (45.2%) required a reduced work schedule compared to pre-illness, and an additional 839 (22.3%) were not working at the time of the survey due to illness.
- 30%-50% of respondents were experiencing the following symptoms after six months: insomnia, heart palpitations, muscle aches, shortness of breath, dizziness and balance issues, sleep and language issues, joint pain, tachycardia, and other sleep issues.

These data indicate that post-acute SARS-CoV-2 infection, or long COVID, is a multifaceted syndrome affecting several organs, with significant impacts on morbidity, mortality, and quality of life. Furthermore, long COVID has overlapping similarities with myalgic encephalomyelitis /chronic fatigue syndrome (ME/CFS), which is a severe multisystemic disease characterised by the hallmark symptom of PEM ([5],[6],[7]).

Survivors of previous coronavirus infections, including the SARS epidemic of 2003 and the Middle East respiratory syndrome (MERS) outbreak of 2012, have demonstrated a similar collection of persistent symptoms, reinforcing concern for clinically significant sequelae of COVID-19. For example, a 2011 study found SARS survivors had persistent fatigue, muscle pain, depression, disrupted sleep, and were unable to work 13-36 months after infection ([8]). In addition, a 2009 study revealed that 40% of people recovering from SARS still had chronic fatigue symptoms 3.5 years after diagnosis ([9]).

The aetiology of long COVID is not fully understood. However, known risk factors include female sex, older age, presence of co-morbidities, and presence of more than five symptoms in the acute stage of illness ([10]). Symptoms most commonly associated with long COVID include fatigue, headache, dyspnea, hoarse voice and myalgia ([11]).

The exact mechanisms behind the persistence of symptoms are yet to be identified but potentially include the sequelae of organ damage, the varying extent of organ damage and varying recovery time of each organ system, the persistence of chronic inflammation or immune response/autoantibody generation, and possible persistence of the virus in the body ([12]).

The current study has several limitations, including the retrospective design, which could impact the reliability of symptom prevalence estimates. Furthermore, most respondents were not hospitalised; therefore, the severity of illness that the survey captured may not represent the average long COVID patient.

However, given that almost 30% of COVID patients are believed to have symptoms 12 weeks after a positive diagnosis ([13]), there is an urgent need for further research to understand the pathophysiology of long COVID and to develop effective treatments. The current study reinforces the need for a multi-disciplinary approach for long COVID patients, including evaluation, symptomatic treatment, and psychological and social support.

References

- 1 Davis HE, Assaf GS, McCorkell L, Wei H, Low RJ, Re'em Y, Redfield S, Austin JP, Akrami A. Characterizing long COVID in an international cohort: 7 months of symptoms and their impact. Available at SSRN 3820561. 2021 Apr 6.
- 2 Sykes DL, Holdsworth L, Jawad N, Gunasekera P, Morice AH, Crooks MG. Post-COVID-19 symptom burden: what is long-COVID and how should we manage it?. *Lung*. 2021 Apr;199(2):113-9.
- 3 Venkatesan P. NICE guideline on long COVID. *The Lancet Respiratory Medicine*. 2021 Feb 1;9(2):129.
- 4 Callard F, Perego E. How and why patients made Long Covid. *Social Science & Medicine*. 2021 Jan 1;268:113426.
- 5 Décary S, Gaboury I, Poirier S, Garcia C, Simpson S, Bull M, Brown D, Daigle F. Humility and acceptance: working within our limits with long covid and myalgic encephalomyelitis/chronic fatigue syndrome.
- 6 Wong TL, Weitzer DJ. Long COVID and myalgic encephalomyelitis/chronic fatigue syndrome (me/cfs)—a systemic review and comparison of clinical presentation and symptomatology. *Medicina*. 2021 May;57(5):418.
- 7 Poenaru S, Abdallah SJ, Corrales-Medina V, Cowan J. COVID-19 and post-infectious myalgic encephalomyelitis/chronic fatigue syndrome: a narrative review. *Therapeutic Advances in Infectious Disease*. 2021 Apr;8:20499361211009385.
- 8 Moldofsky H, Patcai J. Chronic widespread musculoskeletal pain, fatigue, depression and disordered sleep in chronic post-SARS syndrome; a case-controlled study. *BMC neurology*. 2011 Dec;11(1):1-7.
- 9 Lam MH, Wing YK, Yu MW, Leung CM, Ma RC, Kong AP, So WY, Fong SY, Lam SP. Mental morbidities and chronic fatigue in severe acute respiratory syndrome survivors: long-term follow-up. *Archives of internal medicine*. 2009 Dec 14;169(22):2142-7.
- 10 Nabavi Nikki Long covid: how to define it and how to manage it. *BMJ*. 2020;370
- 11 Sudre CH, Murray B, Varsavsky T, Graham MS, Penfold RS, Bowyer RC, Pujol JC, Klaser K, Antonelli M, Canas LS, Molteni E. Attributes and predictors of long COVID. *Nature medicine*. 2021 Apr;27(4):626-31.
- 12 Raveendran AV, Jayadevan R, Sashidharan S. Long COVID: An overview. *Diabetes Metab Syndr*. 2021 May-Jun;15(3):869-875.
- 13 Whitaker M, Elliott J, Chadeau-Hyam M, Riley S, Darzi A, Cooke G, Ward H, Elliott P. Persistent symptoms following SARS-CoV-2 infection in a random community sample of 508,707 people. *medRxiv*. 2021 Jan 1.