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Understanding the burden of post-covid-19 condition

A complex picture is emerging, along with urgent priorities for future research

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Covid-19 cases and deaths have decreased globally,[1] yet, the long term consequences of infection, including post-covid-19 condition (often known as long covid), are still being managed. Most people who have covid-19 recover soon after the acute phase of the disease but others experience persistent health problems for months or longer, and these problems can impact quality of life and ability to work.[2-6] Understanding the trajectory of symptom burden and recovery from post-covid-19 condition is crucial for policy making, treatment decisions, and care coordination.

Early studies reported widely varying estimates of post-covid-19 condition prevalence and symptom trajectories, mainly due to differences in sample representativeness and survey designs. As commented on by previous work,[2 3 6] research has been limited by: data sources not representative of the general infected population because much covid data are based on patients admitted to hospital; scarcity of information on symptom trajectory because population level studies rarely survey a comprehensive set of symptoms or the change in their severity; absence of a comparable covid-free control group because some symptoms might result from existing conditions or seasonal illness; and recall bias because the experience that respondents are asked to recollect can easily date back to months, or even years, ago.

The linked article in *The BMJ* by Tala Ballouz and colleagues (doi:10.1136/bmj-2022-074425) makes an important contribution to the study of post-covid-19 condition by addressing many of these limitations.[7] The analyses are based on a population based, prospective, longitudinal cohort of unvaccinated individuals who contracted a SARS-CoV-2 infection between 6 August 2020 and 19 January 2021 and who were compared with individuals who had not had the virus, all from canton of Zurich, Switzerland. The survey collected information on 23 potential symptoms of post-covid-19 condition, their severity, and their perceived relevance to covid-19, which were assessed over 24 months. For symptoms that were hard to measure, such as fatigue, dyspnea, depression, and stress, a scale based assessment was adopted.

Ballouz and colleagues found that recovery after infection did not occur in 23% of individuals at six months, in 19% at 12 months, and in 17% at 24 months.[7] The proportions of people still experiencing symptoms perceived to be related to covid-19 at the three timepoints were similar but slightly higher, decreasing from 29% at six months, to 20% at 12 months, and to 18% at 24 months. These findings are consistent with previous studies with similar time frames,[3 6] and extend our knowledge of post-covid-19 condition to two years after infection. Importantly, compared with people who did not have an infection, those with covid-19 had excess risks for both physical problems (eg, altered taste or smell, malaise after exertion, fatigue, and dyspnea) and mental health issues (eg, reduced concentration and anxiety) at month six.

Most patients with persistent covid symptoms after infection recovered between six months and 12 months, but those who did not recover seemed to develop chronic health problems and had very little improvement after month 12. People who were symptomatic at all follow-ups or reported worsened symptoms were more likely to be older and to have pre-existing health problems.

This new study identifies remaining uncertainties and indicates where future research is needed.[7] Post-covid-19 condition may induce a wide variety of symptoms, each with independent courses and complex inter-relationships. The study did not aim to evaluate all possible symptoms but surveying for more in future studies might show a more complete picture of the experience of post-covid-19 condition. Another recent *The BMJ* article[3] provides a good example. The authors examined 30 postacute covid symptoms and identified 13 combinations of symptom clusters, including patterns of cluster co-occurrence. The most prevalent symptom cluster observed was fatigue, which frequently co-occurred with neurocognitive impairment and chest symptoms.

An important limitation of Ballouz and colleagues' study was its focus on only wild type SARS-CoV-2 in an unvaccinated population. Empirical evidence accounting for vaccination status and later virus strains is emerging. For example, another study[8] found that vaccinated individuals with breakthrough infections had a significantly lower risk of persistent dyspnea and hair loss 30-90 days after infection when compared with unvaccinated individuals. Additionally, the risks of developing post-covid-19 condition were not significantly different among people who had an infection with wild type, alpha, or delta variants.

Post-covid-19 condition remains a global public health crisis. The design of future treatments, clinical trials, and policy interventions will depend on robust studies based on high quality population level data. Further studies focusing on more recent phases of the pandemic, and accounting for complexities (eg, more virus strains, vaccination statuses, and reinfections), will be particularly valuable. Additionally, in view of the complexity of symptom trajectories and the unique disease burden experienced by each individual patient with

post-covid-19 condition, patients should be more closely involved in the design and conduct of these studies going forward.

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