STAT: Risk of "brain fog" persists up to 2 years after COVID infection, study shows 20 BY ELIZABETH COONEY / AUGUST 17, 2022

Risk of 'brain fog' and other conditions persists up to two years after Covid infection

Among the many worrying consequences of Covid-19, neuropsychiatric conditions rank high. A <u>year ago</u> researchers from Oxford University reported that 1 in 3 patients experienced mood disorders, strokes, or dementia six months after Covid infection. Now the same group is back with a longer-term analysis of 1.25 million Covid patient records, including what they believe is the first large-scale look at children and at new variants.

Their news is both bad and good.

Up to two years after Covid-19 infection, the risk of developing conditions such as psychosis, dementia, "brain fog," and seizures is still higher than after other respiratory infections, the researchers report in their <u>study</u> published Wednesday in the Lancet Psychiatry. But while anxiety and depression are more common soon after a Covid-19 diagnosis, the mood disorders are transient, becoming no more likely after the two months than following similar infections such as flu.

Children were not more likely to be diagnosed with anxiety or depression, right away or up to two years after Covid, and their risk of brain fog subsided over two years. But they were still more likely than children recovering from other respiratory infections to have seizures and psychotic disorders. Overall, the likelihood of all these diagnoses was lower in children than in adults.

On variants, the risk of neuropsychiatric diagnoses rose, from 10% higher for anxiety to 38% for brain fog — after the Delta variant emerged than after the alpha version. Similar risks continued with Omicron, even though that variant has milder effects during the acute phase of infection.

"What these data show in this very large cohort retrospectively analyzed is that the mood disorders and anxiety problems that are really, really prevalent in long Covid tended to resolve in a matter of months, which is great news for patients with long Covid who are not used to suffering in those ways," Wes Ely, a critical care physician at Vanderbilt University Medical Center and associate director for research for the VA Tennessee Valley Geriatric Research and Education Clinical Center, told STAT. He was not involved in the Oxford studies.

"The other finding of this fascinating investigation is that the cognitive problems, the neurocognitive deficits that make people have brain fog, do not resolve so quickly," he said. "Clinically, in my own practice and in our long Covid clinic, this is exactly what we're seeing: that the acquired dementia that these patients get tends to be lasting and very problematic."

To reach their conclusions, the Oxford team combed through data on 14 neurological and psychiatric diagnoses entered into electronic health records in the TriNetX network, mostly from the U.S., over a two-year period. For a control group, the 1.25 million Covid patients were matched with an equal number of patients with any other respiratory infection and no history of Covid. Compared with the people in the control group:

Adults under 65 with a history of Covid infection up to two years previously had a higher risk of cognitive deficit, better known as brain fog (640 vs. 550 cases per 10,000 people), and muscle disease (44 vs. 32 cases per 10,000 people).

Adults 65 and over who had Covid over the same time span had more diagnoses of brain fog (1,540 vs. 1,230 per 10,000 people), dementia (450 vs. 330 per 10,000 people), and psychotic disorder (85 vs. 60 per 10,000 people).

Children who had Covid were more likely to have seizures (260 vs. 130 cases per 10,000 children) and psychotic disorders (18 vs. 6 per 10,000 children).

Max Taquet, National Institute for Health and Care Research academic clinical fellow in psychiatry at Oxford and a study co-author, stressed that the elevated risk for seizures and psychotic disorders in children was still low. "It's important to keep in mind the absolute numbers are often very small, much smaller than in adults," he said on a call with reporters.

Taquet made the same point about adults. "I think it's very clear that this is not a tsunami of new dementia cases," he said. "Equally, I think it's hard to ignore it, given the severity of the consequences of dementia diagnoses. A 1.2% increase in the population in absolute terms and compared to in other previous infections is hard to ignore."

Paul Harrison, professor of psychiatry at Oxford and a study co-author, said these numbers were still important. "Certainly for some conditions, there appears to be a nontrivial and persisting greater risk of these diagnoses being made," he said on the call with reporters. "And for some of those diagnoses, it's highly likely that those people are going to need medical attention."

While waiting for the mechanisms of long Covid — and any potential treatments — to be understood, "What's important for me as a physician is that we know that we can have long-term outcomes in very severe persistent and disabling, neuropsychiatric disorders," some of which can be treated, Teodor Postolache, professor of psychiatry at the University of Maryland School of Medicine, said.

An editorial published with the paper sounds a note of caution on psychiatric diagnoses.

"Dementia has an insidious onset, and the cohort is likely to have had some participants with undiagnosed or subclinical cases at baseline," Jonathan Rogers and Glyn Lewis of University College London write. "Although concerning, the findings regarding psychosis and dementia need replication in a cohort in which there is more thorough ascertainment of case status."

Electronic health records have limitations in how well they reveal complicated neuropsychiatric conditions — which might mean they are underreported, another long Covid researcher said. "I can tell you for a fact that it is really difficult to express in medical records, particularly if you're busy doing a lot of them, all the nuances that sort of go along with the neurocognitive issues," Steven Deeks, a professor of medicine at University of California, San Francisco, told STAT. "This stuff can be subtle. This is only picking up very blunt stuff. At the end of the day, it provides additional proof that long Covid is real, that some people can have profound symptoms, and that they can persist for a couple of years."

Rachel Sumner, a senior research fellow at Cardiff Metropolitan University, called the study results "alarming" while Covid continues to spread. "The finding of complex and potentially severe psychiatric and neurological fallout of Covid infection adds yet more weight and concern to the impact of repeated infections that will occur should the virus continue to be allowed to spread to re-infect with little to no control," she said in a statement.

The study didn't explore the causes of the neuropsychiatric illnesses, but Vanderbilt's Ely said the prevalence it reports lines up with emerging research on different parts of the brain being affected by the SARS-CoV-2 virus, corresponding to mood disorders and to cognitive impairment. And he's worried about what comes next.

"This paper ... fits the narrative both of clinically what I see in practice, but also the actual brain science that we're coming up against," he said. As for cognitive impairment, he said, "This is something that is very hard for people to cope with because they can't go back to work. They have to retire early, and they desperately need answers."