

# The Significance of the Increased Incidence of New Onset Seizures and Epilepsy After a COVID-19 Infection

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With over 600 million people infected worldwide,<sup>1</sup> including 95 million<sup>2</sup> in the United States as of September 2022, the lasting health consequences of the coronavirus disease 2019 (COVID-19) pandemic must be examined. Research has already highlighted several short-term and long-term neurologic consequences of COVID-19, including fatigue, headache, memory impairment, and other neurologic sequelae.<sup>3,4</sup> With such a wide-reaching effect, there is a need to continue investigating the development of neurologic outcomes among individuals who were infected with COVID-19 to prepare the neurology workforce for a potential increase in patients and proactively identify opportunities to improve health outcomes.

In this issue of *Neurology*®, Taquet et al.<sup>5</sup> used data from a network of linked electronic health records (EHRs), which includes over 81 million patients, to examine the incidence of new onset epilepsy and seizures in the 6 months after COVID-19 diagnosis. The authors found that the overall incidence of new onset seizures was 0.81%, and the incidence of new onset epilepsy was 0.30%. Although these are relatively low overall, the authors found that when matched to comparable patients, those who had COVID-19 had a significantly higher incidence of both seizures and epilepsy. Critically, the authors found that, relative to influenza, the incidence of epilepsy was higher among those patients with COVID-19 who were not hospitalized, underscoring the potential for neurologic sequelae in even mild cases of COVID-19. These findings are particularly strong given the use of a large network of EHR data, totaling 81 million patients to identify 2 matched cohorts of 152,754 patients each who had been diagnosed with COVID-19 or influenza, respectively, and the consideration to match to a comparable disease of influenza.

The findings from this study have immediate implications for clinical practice for both generalists and neurologists. First, it is important to consider whether, among those patients with COVID-19, there are other risk factors that may increase the risk of seizures or epilepsy. Furthermore, although the incidence of new onset seizures and epilepsy after COVID infection was low, in view of the large number of people worldwide who have been infected with COVID-19 the neurology workforce should be prepared for a potential increase in the number of patients with seizures and epilepsy.

This study had some limitations that are worth noting. First, the limited 6-month follow-up means that longer-term risk for seizure and epilepsy, as well as the persistence of seizures and potential antiseizure medication resistance, was not captured. Given the several reports highlighting the cardiovascular<sup>6</sup> and stroke<sup>7</sup> risks that result from COVID-19, we must examine whether there will be an increased prevalence of epilepsy that results from stroke, which commonly manifests after more than 6 months.<sup>8</sup> These findings were strengthened by their use of a large and geographically diverse data set. However, the use of these large databases precludes more detailed characterization of patients, including their seizure types, other clinical factors, and outcomes. The authors were not able to address the influence of COVID-19 vaccination status or SARS-CoV-2 variant infection on the incidence of seizures and epilepsy in these cohorts. It would be important for future studies to examine whether there are more

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specific phenotypes of acute COVID-19 (e.g., neurologic involvement) that were associated with a greater risk of seizures or epilepsy and the influence of other factors (e.g., comorbidities, social determinants of health, environmental exposures) on risk and outcomes. Finally, this study was unable to determine whether the incidence of new onset seizures and epilepsy in the comparator group, after influenza infection, was different to that of the baseline risk of the general community. If it was also increased, then the impact of COVID-19 infection could be even greater than the hazard ratio of 1.55 and 1.87 for seizures and epilepsy, respectively, reported in this study.

Finally, it is critical to consider how the findings from Taquet et al.<sup>5</sup> indicate the potential for increasing the existing disparities in epilepsy prevalence. Minoritized (i.e., non-White) and lower socioeconomic populations have up to 2 times the risk of COVID-19 infection.<sup>9</sup> Therefore, the implications of the findings from Taquet et al.<sup>5</sup> for an increase in the incidence of seizures and epilepsy may disproportionately affect these already disadvantaged communities. Furthermore, the elevated relative incidence of seizures and epilepsy after COVID-19 was found to be even greater in children than adults, and so this may even further exacerbate the already disproportionate impact of childhood seizures and epilepsy in developing countries.<sup>10</sup> Overall, Taquet et al.<sup>5</sup> provided us with important new knowledge about the implications of the COVID-19 pandemic to increase the incidence of new onset epilepsy and seizures, knowledge that should be operationalized to improve care and outcomes for these patients.

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