

Long COVID data tracks fatigue, symptoms by variant

February 20 2023



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The latest published study from INSPIRE provides important new insight into how lingering symptoms differ by virus variant and more specific data about persistent fatigue—the symptom most associated

with what has become known as "long COVID."

"Given the evolving pathogenic properties of COVID variants, we need to better elucidate the difference in long-term symptoms between variants to help patients, clinicians, researchers, and policy advisors plan for longer-term impacts of COVID-19," said Dr. Michael Gottlieb, a RUSH emergency medicine physician and lead author of "Severe Fatigue and Persistent Symptoms at Three Months Following SARS-CoV-2 Infections During the Pre-Delta, Delta, and Omicron Time Periods: A Multicenter Prospective Cohort Study." The paper was published in *Clinical Infectious Diseases*.

INSPIRE is a Centers for Disease Control and Prevention-funded collaboration of eight [academic medical centers](#) seeking to better understand the long-term effects of COVID. Nearly 6,000 participants—including a comparative group who visited [health care facilities](#) with COVID-like symptoms but tested negative for the virus—have been self-reporting symptom data into a secure, online registry through a series of surveys. INSPIRE stands for Innovative Support for Patients with SARS-CoV-2 Infections Registry.

This is unlike most long COVID studies that rely predominantly on information from hospital [electronic health records](#) from initial visit and typically brief follow-up visit observations from providers.

This study focused on how participant-reported symptoms and [persistent fatigue](#) differed by virus variant periods. Among the COVID-positive group, significant differences in symptoms were reported at three months depending upon the variant period. For example, cases reported during pre-delta had a higher rate of fever, chills, loss of taste and smell, chest pains, shortness of breath, nausea, vomiting, diarrhea, and muscle and joint aches compared with cases reported during delta and omicron variant periods.

The study also reinforced the importance of vaccination. After accounting for vaccination status of participants, both the number of symptoms and fatigue severity after COVID no longer differed across the variant periods.

Deeper insight into fatigue severity, COVID's impact

A deeper and more quantifiable understanding of the severe fatigue is an especially important objective of the research. Since fatigue can vary from mild to debilitating and present with an array of symptoms, surveys and reporting tools were specifically designed to quantify fatigue severity. Because participants have been followed since the start of their illness, researchers are better able to understand what participants are actually experiencing rather than only relying on the often brief notes in medical records.

"While a number of studies have looked at fatigue, our data sought to explore it in greater detail," Gottlieb noted. "We looked at both the severity and types of fatigue symptoms that patients have been experiencing so that patients, clinicians, researchers, and public health experts can better understand what to expect."

While participants who were COVID-negative did report symptoms at three months, there were no observed differences in reported symptoms among these participants across the [variant](#) time periods. But researchers did identify a higher rate of prolonged fatigue in the COVID-negative group compared with the COVID-positive group.

While the reason for this finding is not fully apparent, the authors suggest this may reflect recognition of longer-term fatigue from other infectious conditions prompting these participants to get testing. Infectious disease experts have long observed lingering [fatigue](#) in some patients after recovering from a viral illness.

"Even if the ultimate risk of long COVID, as symptoms evolve over time, is not great, the numbers of affected patients will be dramatic—even a small percentage of 100 million-plus COVID infections in the U.S. will be huge and have major impacts on health care needs and financing," said co-author Dr. Robert Weinstein, an infectious disease specialist at Rush University Medical Center.

RUSH researchers stress the importance of continuing to track symptoms over time, especially via data that better reflects patient's lived experiences, as the lessons and science evolve.

"For clinicians, we hope the results help them better understand the disease so they can better advise and improve treatment for these patients," Gottlieb says. "For policymakers, we hope the results will help them better plan how to use our public health resources. And, for patients, we want to reassure them that they are not alone—a lot of people are going through this."

More information: Michael Gottlieb et al, Severe Fatigue and Persistent Symptoms at Three Months Following SARS-CoV-2 Infections During the Pre-Delta, Delta, and Omicron Time Periods: A Multicenter Prospective Cohort Study, *Clinical Infectious Diseases* (2023). [DOI: 10.1093/cid/ciad045](https://doi.org/10.1093/cid/ciad045)

Provided by Rush University Medical Center

Citation: Long COVID data tracks fatigue, symptoms by variant (2023, February 20) retrieved 8 April 2023 from <https://medicalxpress.com/news/2023-02-covid-tracks-fatigue-symptoms-variant.html>

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