

Research sheds new light on long COVID conditions

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Most people who get COVID-19 recover within a few weeks. But some

people—even those who had mild versions of the disease—have symptoms that last weeks or months after an initial COVID infection. These ongoing health problems, called post-COVID conditions (PCC), post-COVID-19 syndrome, long COVID-19, and post-acute sequelae of SARS COV-2 infection (PASC), can decrease quality of life for patients and increase the burden of disease on health systems. As more patients suffer from long COVID, it's increasingly important to define the symptoms associated with long COVID for effective diagnosis and treatment of the disease.

New research from physicians and researchers at Kaiser Permanente, the Mid-Atlantic Permanente Research Institute (MAPRI) and Johns Hopkins University identified 17 conditions associated with long COVID in order to better diagnose and treat the condition. The study, "Post-Acute Sequelae of SARS-CoV-2 with Clinical Condition Definitions and Comparison in a Matched Cohort," was published Oct. 12, 2022, in *Nature Communications*.

"Although there has been significant research done to determine a clinical definition of long COVID, the reality is that the disease may look very different from patient to patient," said lead author of the study Michael Horberg, MD, an infectious diseases physician and associate medical director at Kaiser Permanente, Mid-Atlantic Permanente Medical Group. "Our study set out to determine conditions that were most likely to be associated with long COVID."

The research looked at medical records of over 100,000 Kaiser Permanente Mid-Atlantic States' adult patients—over 30,000 who tested positive for COVID-19 and over 70,000 who tested negative for COVID-19—in 2020. The 17 conditions identified were:

- Other lower respiratory disease
- Diabetes

- Gastrointestinal disease
- Dizziness or vertigo
- Abdominal pain
- Nonspecific chest pain
- Mental health disorders
- Anxiety disorders
- Genitourinary symptoms
- Fatigue and malaise
- Cardiac dysrhythmias
- Nervous system disorders
- Respiratory failure
- Anosmia (loss of smell)
- Nausea and vomiting
- Fluid and electrolyte disorders
- Nutritional, endocrine and metabolic disorders

Researchers were most interested in conditions that developed in their patients within 30 days of a positive COVID-19 test and persisted for nearly four months post-test date, and conditions that developed in the 30-to-120-day period after a positive test. Key conditions included loss of smell, cardiac dysrhythmia, diabetes, genitourinary disorders, fatigue and chest pain.

Researchers used Kaiser Permanente's robust electronic [medical records](#) to categorize conditions into three distinct time intervals based on when a patient tested positive for COVID-19. By organizing the conditions by date of when a patient tests positive, researchers were able to effectively evaluate if the resulting symptoms were related to long COVID as opposed to being caused by a pre-existing health condition.

Additionally, by comparing COVID-19 positive patients to COVID-negative patients (the [control group](#)), researchers were able to tease out which symptoms appeared more often in the COVID-positive group,

which symptoms occurred more often in the COVID-negative group and which symptoms appeared at the same rate in both groups.

"One reason long COVID is difficult to identify is that many of its symptoms are similar to those of other diseases and conditions," Dr. Horberg said. "Some pre-existing conditions may have been present or worsened at the time of COVID-19 infection, but that doesn't mean it should be defined as long COVID."

"When we compared the COVID-positive population to the COVID-negative population, especially within and post the first 30 days of the positive test date, some of the predicted symptoms and conditions appeared less significant than we anticipated," said Eric Watson, MAPRI's director of research analytics and co-author of the study.

Overall, 16.5 % of COVID-positive patients within the study developed at least one long COVID-related condition within 120 days of a positive test. This finding is lower than national averages, which shows that [nearly 20% of American adults who've had COVID-19 report having long COVID symptoms](#) after the acute infection period.

Diabetes and long COVID

Researchers found that some patients may have developed diabetes after a COVID-19 infection. Over 780 patients received a new diagnosis of diabetes between 30 and 120 days after a positive COVID-19 test. Dr. Horberg said it is too early to determine if diabetes should be considered a condition associated with long COVID.

"It's possible that some [patients](#) were simply undiagnosed until they sought care for their COVID-19 infection, and that's why we saw such a jump in new diabetes diagnoses," Dr. Horberg said. "There needs to be more research on the relationship between diabetes and COVID-19"

before we can definitively say this is a long COVID condition."

Future research

Dr. Horberg and researchers are expanding their examination of conditions associated with long COVID in another study. The next phase of research will look at data from 2021 through 2022 and take a deeper dive into the relationship between diabetes and COVID-19, the effects of delta and omicron variants, the impact of vaccines and boosters, and the influence of widespread at-home testing.

"In contrast to 2020, in 2021, the U.S. underwent mass public vaccination, so we're very interested to see if vaccines reduced the incidence of long COVID. We're also interested to see if the newer variants had any effect on long-COVID symptomology," said Watson.

"This list will likely evolve as we conduct more research," Dr. Horberg said. "We are eager to continue to study long COVID in order to better diagnose and treat those who may be suffering months after a COVID-19 infection."

According to the Centers for Disease Control and Prevention (CDC), long COVID is more likely to impact people who have not been vaccinated against COVID-19. Boosters are recommended for everyone 12 and older and children 5 and older who received the Pfizer vaccine.

More information: Michael A. Horberg et al, Post-acute sequelae of SARS-CoV-2 with clinical condition definitions and comparison in a matched cohort, *Nature Communications* (2022). [DOI: 10.1038/s41467-022-33573-6](https://doi.org/10.1038/s41467-022-33573-6)

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