Study determines most common long COVID symptoms in children and teens

August 21 2024

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A research team led by the National Institutes of Health's RECOVER Initiative and supported by its Clinical Science Core (CSC) at NYU Langone Health, has designed a new way to identify which school-age

children and adolescents most likely have long COVID.

Solely for the purpose of further study and not for use in clinical diagnoses, the team's new measure (index) identifies children and teens with the highest chances of having long COVID.

The research index is based on long-term symptoms that were more common among children with a history of a COVID-19 infection when compared to those who had no history of infection. Importantly, the study does not exclude any symptom from being part of long COVID.

Published online on August 21, in the *Journal of the American Medical Association*, the study index used combinations of symptoms distinct for each age group—10 symptoms in school-age children and eight in adolescents—to indicate the likely presence of long COVID.

Children and teens were found to experience prolonged symptoms after infection with the virus that causes COVID-19, SARS-CoV-2, in almost every organ system, with most having symptoms affecting more than one system.

A clear pattern of symptom differences was seen between school-age children (6 to 11 years) and adolescents (12 to 17 years), underscoring the need for studies like RECOVER that track long COVID over time as children develop.

In both children and adolescents identified as likely having long COVID, there was a group of patients with a large number of symptoms occurring together (as in adults), as well as a cluster dominated by fatigue and pain symptoms. School-age children had a distinct cluster with neuropsychological effects (trouble with memory or focusing) and sleep impacts, and another with stomach symptoms.

Adolescents had a specific cluster that experienced change in or loss of taste or smell, which was not found in school-age children.

"Our research index is a first step toward a tool that could someday be used to identify long COVID in children and adolescents—a widely understudied group—but it will likely change and expand as we learn more, and is not intended to be used as a clinical tool today," said corresponding study author Rachel Gross, MD, associate professor in the Departments of Pediatrics and Population Health at NYU Langone.

"While this provisional measurement tool may be used for ongoing research, we recognize that any one symptom, including those not in the index, may be sufficient to indicate the presence of long COVID in any given child," added Gross, who is also director of pediatric research for the RECOVER CSC at NYU Langone.

"We also found an association between the study index and overall health, physical health, and quality of life, highlighting the significant impact long COVID has on children and adolescents," added co-senior study author Melissa Stockwell, MD MPH, division chief of Child and Adolescent Health and the Felice K. Shea Professor of Pediatrics at Columbia University Irving Medical Center. Dr. Stockwell is also chair of the RECOVER Pediatric Coordinating Committee.

About 65 million people worldwide are living with long COVID, with impacts on global health expected to last for decades. The NIH's Researching COVID to Enhance Recovery (RECOVER) Initiative aims to fill gaps as a comprehensive study of the condition. As the RECOVER CSC, NYU Langone integrates research activities of about 200 clinical sites around the country and has enrolled nearly 30,000 participants in its observational cohort study.

As part of the RECOVER Pediatric Observational Cohort Study

(RECOVER-Pediatrics), the current study included 751 SAR-CoV-2 infected and 147 uninfected school-age children, along with 3,109 infected and 1,369 uninfected adolescents at more than 60 health care institutions across the United States.

"Most research to understand long COVID to date has focused on adults, with less known about this complex condition in children," said co-first study author Tanayott Thaweethai, Ph.D., instructor in medicine at Harvard Medical School and lead biostatistician for the RECOVER Data Resource Core at Massachusetts General Hospital.

"This work describes the first data-driven approach to revealing symptom patterns among school-age children and adolescents, which are both distinct from those seen in adults. We hope this leads to a better understanding of long COVID in pediatric populations."

Further study

RECOVER-Pediatrics is structured to enroll about 15,000 children between birth and 25 years old, as well as their parents or caregivers. These children either had a history of infection with COVID or did not. For children between 6 and 17 years old, caregivers were asked whether the children had experienced any of 75 prolonged, commonly occurring candidate symptoms.

The original symptoms list was then narrowed to include only those present in at least 5% of children or adolescents who had a history of a COVID infection. The study authors then used a series of statistical techniques to determine the odds of a person having each long-lasting symptom, comparing those who had been previously infected versus not ever infected.

Among the 5,376 study participants, the researchers found 18 symptoms

in school-age children and 17 in adolescents were the most common in those with a history of COVID infection compared to those without, with 14 overlapping symptoms between the two age groups.

The researchers then used a statistical technique called LASSO to determine the most predictive long-term COVID symptoms and included them in their "PASC research index," with PASC referring to the technical name for long COVID: post-acute sequelae of SARS-CoV-2 infection.

Symptoms included in the index for children were trouble with memory or focusing, back or neck pain, stomach pain, headache, fear of specific things (phobias), refusing to go to school, itchy skin or rash, trouble sleeping, nausea or vomiting, and feeling lightheaded or dizzy.

In adolescents, the most predictive symptoms were change in or loss of smell and/or taste, body, muscle, or joint pain, daytime tiredness, tiredness after walking, back or neck pain, trouble with memory or focusing, headache, and feeling lightheaded or dizzy.

Interestingly, the research team found that the proportion of children reporting at least one symptom was not that different in those with and without a prior COVID infection. The research index (which measured a group of symptoms) was more capable of distinguishing between those with and without an infection history.

Finally, the researchers found four distinct symptom clusters in school-age children and three in adolescents, with the existence of the groups suggesting that there may be different types of long COVID that children experience.

Moving forward, the research team will seek to determine whether these pediatric clusters are associated with different disease mechanisms,

which would be critical in identifying treatment targets for future pediatric clinical trials.

More information: Characterizing Long COVID in Children and Adolescents, *Journal of the American Medical Association* (2024). DOI: 10.1001/jama.2024.12747

Provided by NYU Langone Health