

Females more likely to suffer with long COVID, underscoring a critical need for sex-disaggregated research

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A new study published today in the journal *Current Medical Research* and *Opinion* reveals that females are "significantly" more likely to suffer



from long COVID than males and will experience substantially different symptoms.

Long COVID is a syndrome in which complications persist more than four weeks after the initial infection of COVID-19, sometimes for many months.

Researchers from the Johnson & Johnson Office of the Chief Medical Officer Health of Women Team, who carried out the analysis of data from around 1.3 million patients, observed that females with long COVID are presenting with a variety of symptoms including ear, nose, and throat issues; mood, neurological, skin, gastrointestinal and rheumatological disorders; as well as fatigue.

Male patients, however, were more likely to experience endocrine disorders such as diabetes and kidney disorders.

"Knowledge about fundamental sex differences underpinning the clinical manifestations, disease progression, and health outcomes of COVID-19 is crucial for the identification and rational design of effective therapies and public health interventions that are inclusive of and sensitive to the potential differential treatment needs of both sexes," the authors explain.

"Differences in immune system function between females and males could be an important driver of sex differences in long COVID syndrome. Females mount more rapid and robust innate and adaptive immune responses, which can protect them from initial infection and severity. However, this same difference can render females more vulnerable to prolonged autoimmune-related diseases."

As part of the review, researchers restricted their search of academic papers to those published between December 2019–August 2020 for



COVID-19 and to January 2020–June 2021 for long COVID syndrome. The total sample size spanning articles reviewed amounted to 1,393,355 unique individuals.

While the number of participants sounds large, only 35 of the 640,634 total articles in the literature provided sex disaggregated data in sufficient details about symptoms and sequalae of COVID-19 disease to understand how females and males experience the disease differently.

When looking at the early onset of COVID-19, findings show that female patients were far more likely to experience mood disorders such as depression, ear, nose, and throat symptoms, musculoskeletal pain, and respiratory symptoms. Male patients, on the other hand, were more likely to suffer from renal disorders—those that affect the kidneys.

The authors note that this synthesis of the available literature is among the few to break down the specific health conditions that occur as a result of COVID-related illness by sex. Plenty of studies have examined sex differences in hospitalization, ICU admission, ventilation support, and mortality. But the research on the specific conditions that are caused by the virus, and its long-term damage to the body, have been understudied when it comes to sex.

"Sex differences in outcomes have been reported during previous coronavirus outbreaks," authors add. "Therefore, differences in outcomes between females and males infected with SARS-CoV-2 could have been anticipated. Unfortunately, most studies did not evaluate or report granular data by sex, which limited sex-specific clinical insights that may be impacting treatment." Ideally, sex disaggregated data should be made available even if it was not the researcher's primary objective, so other interested researchers can use the data to explore important differences between the sexes.



The paper also notes complicating factors worthy of additional study. Notably, women may be at greater risk of exposure to the virus in certain professions, such as nursing and education. Further, "there may be disparities in access to care based on gender that could affect the natural history of the disease, leading to more complications and sequela."

The latter serves as a rallying cry: Availability of sex disaggregated data and intentional analysis is imperative if we are to ensure that disparate outcomes in disease course are addressed. No research is complete unless the data is made available to people who want to answer the question: Do sex and gender matter?

More information: Sex differences in sequelae from COVID-19 infection and in long COVID syndrome: a review, *Current Medical Research and Opinion* (2022). DOI: 10.1080/03007995.2022.2081454

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