COVID-19 impacts men more seriously than women, critical information that resulted from research examining how the virus progresses differently based on sex.

But including sex as a variable in scientific research has been historically rare, leading to dangerous gaps in understanding how diseases, drugs and vaccines impact men and women differently.

A new Northwestern Medicine study, published June 9 in the journal *eLife*, has found females are still an afterthought in most scientific research.

The study is a 10-year follow-up to a 2009 groundbreaking study that found females were left out of biomedical research because of how their hormones might skew fragile study designs, an idea that has repeatedly been proven false. That left only male subjects to represent both men and women in research findings.

Over the past decade, there have been numerous efforts to increase the representation of females as research subjects, including a 2016 policy by the National Institutes of Health (NIH) requiring scientists to "consider sex as a biological variable" in order to receive NIH grant funding.

Today, Northwestern investigators have discovered while scientists are increasingly including females in their research, they're still not breaking down their findings by sex.

"The implications of not analyzing research data by sex are endless," said Nicole Woitowich, associate director of the Women's Health Research Institute and research assistant professor at Northwestern University Feinberg School of Medicine. "Without this, we have no way of telling if or how new drugs and therapies may work differently in men and women. It hinders progress toward personalized medicine and it also makes it difficult for scientists to repeat studies and build upon prior knowledge."

The study authors analyzed more than 700 scientific articles across nine biological disciplines in order to determine if a sex bias still exists within biomedical research. They recorded if each study used male, female or both sexes and whether or not they reported and analyzed data by sex. They also recorded if scientists provided a reason for single-sex studies or for why they did not analyze data by sex.

The number of studies to include both male and female subjects increased from 28% in 2009 to 49% in 2019, the new study found, but there was no increase in the number of studies to analyze data by sex between 2009 and 2019.

In some cases, scientists did not provide an exact number of the males and females studied, the report found. And only 4% of published papers provided a reason why they did not use both sexes or why they failed to analyze data by sex. Of those, many claimed to use only males in order to limit the influence of female hormones.

Not analyzing data by sex might lead scientists to have to make assumptions based on the missing information, which requires additional time, resources and ultimately taxpayer-funded research dollars, Woitowich said.

"When we fail to consider the influences of sex in biomedical research, it's like we're trying to put together a puzzle without all the pieces," Woitowich said. "In order for us to improve our understanding of health and disease, it is essential that we include both sexes in research studies and analyze data accordingly."


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