OPINION

What's Really Behind the Gender Gap in Covid-19 Deaths?

When in doubt, look to social factors first, not biology

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More men than women are dying of Covid-19. The numbers are striking. In Italy, men in their 50s died at four times the rate of women in their 50s. Globally, twice as many men than women may be dying of Covid-19.

When a sex difference is observed with some magnitude in deaths across diverse populations, it is commonly assumed that factors in women's and men's bodies drive the difference. This assumption has even led some clinicians to experiment with injecting estrogen into men suffering from Covid-19. However, early indicators and past experience with similar diseases suggest that social and other demographic factors, including age, race or ethnicity and class, and comorbidities, not sex, most likely explain a far greater portion of variation in Covid-19 outcomes between women and men. Appreciating the role of these factors is important, because understanding what's really driving these outcomes helps better target both the research and the public health efforts that can save lives.

As we report this week, emerging Covid-19 data already shows an important role for social context in generating sex disparities. In Connecticut and Massachusetts there is no sex difference in confirmed Covid-19 fatalities, while in New York and Florida, men account for about 60 percent of Covid-19 deaths. Globally, the male-to-female death ratio varies from a staggering 2:1 in the Netherlands to 1:1

in Iran and Canada. It's too early to say what accounts for these levels of variation; what they do seem to indicate is that sex difference alone isn't meaningful without incorporating other factors.

During the 1918 Spanish flu pandemic, with which the coronavirus pandemic has been widely compared, men also died in larger numbers in many places. But this wasn't because of sex alone. It was because of sex and gender-related differences in both occupations — a social variable — and pre-existing health conditions. During the Spanish flu, men in the military and unskilled manual laborers working outside the home died at far higher rates than the general population, probably because they had less freedom to engage in social distancing; it's noteworthy that nonmilitary and upper-class males perished at rates similar to women overall. For similar social reasons — they were less able to social distance than women — men in 1918 already carried a significantly higher burden of tuberculosis relative to women when the pandemic began. This, when combined with influenza-induced pneumonia, proved deadly.

Covid-19 is similar in important ways to the diseases caused by other recent coronaviruses, such as SARS and MERS. Like Covid-19, SARS and MERS exhibited male-female differences in fatalities. As with Covid-19, this difference was initially claimed as a "sex" difference. But careful analysis showed that gendered behaviors, pre-existing conditions, and gender-segregated occupational exposures explained these sex differences. All signs point to Covid-19 following a comparable pattern.

SARS emerged in early 2003 and quickly reached pandemic levels. Men overall indeed died at a higher rate than women. But a closer inspection of the data soon showed that sex differences varied considerably by age group. At older ages, there was no significant difference between the female and male fatality rates, but younger men died at markedly higher rates than younger women. For instance, in Hong Kong, only 5.9 percent of women ages 35 to 44 died, compared with 15.3 percent of men. Between the ages of 35 and 64, men who developed SARS were 10 percent more likely to die than women.

Taking a cue from these patterns, researchers ran analyses accounting for age, occupation and pre-existing conditions. The results showed that after accounting for these factors, women and men actually had similar fatality rates for SARS for all age groups. The lower fatality rate among women was driven by particularly high infection rates among health care workers, who were predominantly young, healthy and female. So women were both disproportionately likely to be infected and disproportionately likely to survive, compared with men in that age group. Among older women and men, and those with comorbidities such as heart disease, cancer, asthma and liver disease, there was little difference in SARS outcomes. The apparent sex difference was caused by gender-related occupational differences and diseases with complex, often socially rooted causes.

MERS offers an even more clear-cut example. The disease overwhelmingly affected, and continues to affect, older men. Primary transmission from camels remains a key source of infections, and camel handling and slaughtering are predominantly male occupations in Saudi Arabia. As with SARS, a comprehensive study published in 2017 found that fatalities did not differ by sex after accounting for age and pre-existing health status. The sex difference here, in other words, is produced by who is getting infected, not who dies once they're infected.

A key factor most likely related to male-female differences in Covid-19 fatalities is that men overall are in a poorer state of health than women. In a study examining sex differences in outcomes among Covid-19 patients in China, men were more likely than women to have any comorbidity or two or more of them. Of people with Covid-19 and chronic obstructive pulmonary disease, 83.3 percent were male. Of people with diabetes and cardiovascular disease, 58.9 percent and 62.1 percent, respectively, were male. To be sure, sex-linked biology may play a role in the development of some chronic diseases, but always in complex interaction with class, race or ethnicity, and gender-related variables. Several analyses have already demonstrated that in places where men have higher Covid-19 fatality rates than women, men also, on average, have far higher rates of behaviors such as smoking and comorbidities related to smoking, such as heart disease.

A paper out this month in The Lancet by researchers at the Harvard T.H. Chan School of Public Health underscores this point. In absolute numbers, men had higher death counts from Covid-19 during the first two weeks of April in Massachusetts. But when adjusted for men's higher baseline mortality rates by age, researchers found that women and men actually had an identical risk of dying from Covid-19.

A few months into the first wave of the Covid-19 epidemic, men in aggregate appear to have higher fatality rates. But ascribing this outcome to biological sex-related variables, as some have rushed to do, is unlikely to lead to effective interventions. In past epidemics, what at first appeared to be a sex difference turned out to be largely a result of the difference in life experiences between women and men. Occupations, behaviors and pre-existing conditions mattered more than whether one was a woman or a man.

As evidence from this pandemic continues to emerge, we should keep these past lessons in mind. It is possible that some aspect of sex-linked biology contributes to the differences in Covid-19 fatality rates. But framing female-male differences in those rates as driven primarily by innate sex differences distracts researchers, clinicians and policymakers from the far more likely culprits. If gendered behaviors and gender-segregated occupations are responsible for greater Covid-19 vulnerability, we owe it to people of all genders to address these urgent, controllable risk factors.

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