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All across the United States, the coronavirus is killing more men than women, data show

U.S. state data, along with figures from New York City, show a picture that matches one of the most mysterious global trends

By **Chris Mooney**, **Sarah Kaplan** and **Brady Dennis**

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As New York City erupts in coronavirus infections and deaths, Kaedrea Jackson has noticed something peculiar during her shifts inside the emergency department at Mount Sinai Morningside hospital.

“It seems there are more men coming in with really severe illness,” said Jackson, an emergency physician. “In general, I’ve seen more male patients. And when they do come in, they are at a sicker state.”

She and her colleagues on the front line of the pandemic have had little time to ponder why covid-19 seems deadlier for men than women — a phenomenon she could not recall happening with other diseases, such as the flu. “I don’t think there’s anything that’s very clear that shows me the etiology of why it’s been more males,” she said.

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Coronavirus data reported by more than a dozen states and the nation’s largest city support Jackson’s experience. In most states, slightly more women are getting infected than men. But of more than 3,600 deaths in 13 states and New York City that report fatalities by gender, the majority of victims are men.

The disproportionate toll of the virus appears to have deep biological roots. An emerging body of research has revealed that women's bodies are better at fighting off infection, thanks to the hormones in their systems and the genes on their two X chromosomes.

Scientists say these differences may partly explain why men have been hit hardest by the covid-19 pandemic. And they may provide a vital clue in the search for a cure.

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The Washington Post identified 37 states that provide a breakdown of how many men, and how many women, have tested positive for covid-19. In 30 of those states, including the large outbreaks in Massachusetts, Michigan and Washington, women had a higher number of reported cases, though not always by a large margin. In several large states, including California and Florida, and in the vast outbreak in New York City, the data swing the other way toward male cases, leaving an ambiguous picture overall.

Fewer states provide an analysis of the differing numbers of deaths among men and women. But at least 13 with substantial death numbers reported that data. (The Post did not analyze some states, like Alaska, where the death numbers remain small.) In every one of those states, men died more frequently, and that was the case even if they made up fewer total cases of the disease to begin with.

That's also true in the city with the country's biggest outbreak. As of Friday, men made up 59 percent of overall hospitalizations in New York City and 62 percent of more than 1,800 fatalities.

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"I've seen more males that need immediate respiratory support — to be intubated or supplemental oxygen," Jackson said. "That's been the major difference. They come in sicker."

Men in New York are dying at a disproportionately high rate, even when accounting for the fact that male cases are more numerous to begin with. Men make up 55 percent of cases there, but 62 percent of deaths.

A difference in the genes

Often, the virus doesn't start out feeling deadly, said Katrina Hawkins, an intensive care doctor at George Washington University Hospital in the District. Many patients experience mild symptoms for about a week, then recover.

But in a small fraction of cases, the disease takes a sudden, dramatic turn. A dry cough and shortness of breath will give way to acute respiratory issues and dangerously low blood-oxygen levels. The body's immune system unleashes a storm of protective cells and other molecules that can overwhelm vital organs, sometimes causing more damage than the virus itself.

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This progression suggests that the worst form of the disease is triggered in part by the patient's own immune system, Hawkins said. "There's probably something written in their DNA that we just don't know or understand yet," she said.

To Robyn Klein, director of the Center for Neuroimmunology and Neuroinfectious Diseases at Washington University in St. Louis, the combination of lopsided statistics and divergent immune responses is an indicator that sex differences may be at play.

For almost all infectious diseases, women are able to mount a stronger immune response than men, she said. Women with acute HIV infections have **40 percent less viral genetic material** in their blood than men. They are **less susceptible** to the viruses that cause hepatitis B and C. Men infected with coxsackie viruses — which in severe cases can cause inflammation of heart tissue — are twice as likely to die of the disease.

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That holds true even in other animals. Female birds show higher antibody responses to infection than males, especially during mating season. The immune cells that eat up microbes and cellular debris are less active in male lizards than in their female counterparts.

“With regard to viral infection, it’s been very well established that females have much stronger immune responses than males,” Klein said. “Not just as a result of exposures or behavior. But there are actual differences in the ways that immune cells respond.”

Some 60 genes involved in immune function are located on the X chromosome, said Sabra Klein, a microbiologist at Johns Hopkins University (who is no relation to Robyn Klein).

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Genetic females have two of these molecules — one from their mother, one from their father — whereas people who are genetically male have only one. When there are two copies of this genetic molecule, the gene on one copy is typically turned off. But as many as a quarter of X-linked genes can escape this inactivation, giving people with two copies of the chromosome a “double dosage” of the genetic instructions needed to fight disease.

One such gene codes for a protein called “toll-like receptor 7,” which gets its name from a German word for “great.” These receptors recognize strands of viral RNA and will alert the body to the presence of an invader.

“What we’ve seen in my lab is you get greater expression of this gene in immune cells in females,” Sabra Klein said, “which means you’re going to get all kinds of downstream effects.”

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Generally, female immune cells respond faster and more powerfully to viral attacks, producing higher amounts of interferons — proteins that stop viruses from replicating — as well as antibodies that neutralize the invaders.

Sex hormones also play a role in the body's response to infection. Testosterone, which is produced in abundance by male testes, has been shown to tamp down inflammation. Estrogen, meanwhile, can bind to immune cells and activate the production of disease-fighting molecules.

"It does seem like everything is designed so that females are going to have a more robust immune response," Robyn Klein said.

Yet this forceful immune response can be a double-edged sword. It accounts for why women have autoimmune diseases at a higher rate than men. It also may explain why women are more likely to die of the common flu. Studies of influenza viruses in mice have shown that females have a "hyper-responsive" immune reaction to the pathogen — their lungs fill up with chemicals that damage tissue as well as fight germs.

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The best immune system is one that is well-regulated, Sabra Klein said; disease-fighting cells must be kept in check, lest they become marauding armies. Women's bodies tend to give their immune systems a bit more freedom, while male systems are more frequently held back.

Those tendencies can be harmful or hurtful, depending on the disease in question. In the face covid-19, it is increasingly apparent that the male system fares worse.

Strong evidence from the states — and beyond

The 50 states, and the District of Columbia, have very different practices for reporting on the outbreaks within their borders. Some provide downloadable spreadsheets of all fatalities with ages and genders listed. Some give a daily update containing the same information. Others merely provide a percentage figure for the distribution of cases by gender, but not for fatalities. The Post searched each state's coronavirus website or page for gender-based information, but it's possible that journalists did not identify everything that is available.

In the United States, women make up a slightly larger percentage of the population to begin with, which may help explain why in many states, they're contracting somewhat more cases of the disease.

But men consistently die more often. That's true in Michigan, where men represent 61 percent of the state's 479 deaths so far. Of the 284 people killed by the coronavirus in Washington state, 57 percent are men.

In Florida, men made up more than 61 percent of the 163 fatal cases as of Friday. There, 53 percent of cases are in men.

This trend holds in at least 10 other states (and New York City) that report gender-identified mortality data. And it matches a pattern now recognized by epidemiologists around the globe. From China to South Korea to Italy to France, men are dying more frequently of covid-19 than women.

Efforts to explain the disparity initially focused on social differences, such as the higher rate of risky behaviors among men. In China, where the mortality rate for men was almost twice as high as that for women, nearly half of men over 15 smoke, compared with just 2 percent of women.

Recent polling by Reuters found that men are more likely to downplay the risk from the coronavirus, which may lead them to behave in ways that expose them to the virus. And at least one study of more than 3,000 people found that half of men don't wash their hands with soap after using the bathroom.

"Women generally are more likely to seek care than men are," added Tara Smith, an epidemiologist at Kent State University in Ohio. "So this could just be a bias in that aspect: As a gender, we're just more likely to go see a doctor when we're sick, so we're more likely to have a test done in the first place."

Men are also more likely to have underlying conditions that make them vulnerable. According to the World Health Organization, American men live on average five years shorter than their female counterparts and have a higher probability of dying of heart disease, cancer, diabetes and respiratory illnesses.

Behavioral factors are important, said Sabra Klein. But she noted that men and women are falling ill in roughly equal numbers in most countries the coronavirus has hit. It's only once the disease takes a turn for the worse, triggering severe respiratory problems, that sex differences emerge.

"That it seems to be occurring to a significantly greater degree in men than women, it does speak to biology," Sabra Klein said.

The disease is so new, and scientists still have so little data about it, that no one can pinpoint the source of these biological differences. But the differences are important to consider.

Robyn Klein pointed out that fast-working female immune systems may be more effective at clearing the virus from the body in the first week after infection, making women less likely to reach the later stage of precipitous decline.

"How the inflammatory response develops in the presence of this virus should be studied in the different sexes," she said. "Because the more you understand how a process may differ, the more you can develop treatments that are going to be effective."

Sabra Klein also speculated that the disease may repress testosterone in men, exacerbating their intense inflammatory response. Testosterone levels decline as men age, she noted, which could explain why older men are most vulnerable to the disease.

These are just theories, the scientists noted. Until governments give detailed, gender-identified reports on illnesses and deaths, and until researchers are able to probe potential sex differences in the lab, no one will know for sure whether the disparity in deaths is biological, or why.

At the moment, the majority of states do not appear to break down fatalities by sex, nor, it seems, does the Centers for Disease Control and Prevention.

And many researchers still don't analyze their results by sex or even perform experiments on both male and female models, Sabra Klein said. The fact that women have lower survival rates from heart attacks and more adverse drug reactions than men has been blamed on this disparity.

"We really are in our infancy" in the study of sex differences, she said. "Maybe the coronavirus is going to be that call to really take this very seriously."

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