

## **BRIEF19**

*A daily review of covid-19 research and policy.*

### **RESEARCH BRIEFING**

#### **Adverse reactions to the first dose of a covid-19 vaccine does not preclude a second dose.**

As more and more of the coronavirus mRNA vaccines are administered, the rate of serious hypersensitivity reactions (i.e. inappropriate immune responses) has apparently declined by more than 50 percent. The latest estimates are that as few as 5 cases of hypersensitivity reactions per million doses have occurred as a result of the Pfizer/BioNTech vaccine and less than 3 cases per million such cases after the Moderna vaccine. Not a single death stemming from the vaccines has been reported.

Current US Centers for Disease Control and Prevention guidelines are to avoid a second dose if a recipient exhibits a hypersensitivity reaction following the first dose. There may be a better option, though.

A [letter](#) published in the *Annals of Internal Medicine* described two case reports of the successful administration of a second dose of the Moderna vaccine following an immediate hypersensitivity reaction upon receiving a first dose. Both cases come from this past winter during the initial rollout phases of the vaccine. In the first case, a 64-year-old woman with a shellfish allergy developed symptoms within 10 minutes of her first dose. She developed generalized itching, hives, and the self-reported sensation of an elevated heart rate. When examined by healthcare responders, she was found to have no significant swelling of her skin, mouth, or airway, no respiratory or gastrointestinal symptoms, and her blood pressure was normal. She was given 50mg of oral diphenhydramine (i.e. Benedryl) by the vaccine administration staff and had resolution of symptoms by 90 minutes. The second patient was a 39-year-old woman with a history of nasal allergies who developed chest and neck hives within 15 minutes of receiving her first dose. She received 25 mg of oral diphenhydramine at the vaccination site, but did go on to develop mild swelling (i.e. “angioedema”) within 30 minutes. The patient was transported to a local hospital where she received famotidine (“Pepcid,” an antihistamine) and steroids. Her symptoms did not worsen after two hours of observation and she was released to go home. Both patients were referred to an allergy clinic, staffed by the author of the letter, Rochester, NY. Skin testing was performed using polyethylene glycol (a substance used in the Moderna vaccine that was the target of some negative social media attention early in vaccine distribution) as well as some residual contents from previously used vials of the Moderna vaccine. All of the skin testing results were negative.

Both of the patients described in this report worked in healthcare and had increased covid-19 exposure risk. Therefore, following a detailed discussion with the allergy specialist, both patients opted to proceed with the second vaccine dose. The second dose was given without premedication (i.e. without the administration of prophylactic medications that *might* decrease hypersensitivity or allergic symptoms). However, a “graded dosing protocol” that often used for other vaccines that have caused similar adverse events was used. The protocol consisted of five small doses of diluted or partial vaccine given every 15 minutes. The first patient developed no symptoms. The second patient complained of itching after dose #2 and dose #5, both of which resolved without any medication or other medical intervention. Follow up antibody testing showed that the vaccinations were successful.

Although only two patients, these important case reports show that with close observation, it is possible to administer mRNA vaccines in patients who may have increased hypersensitivity or allergic risks. This is great news because many people with a history of drug allergies or side effects may be nervous about receiving these new vaccines. This report should help alleviate some fears, and thus encourage the march towards herd immunity, though larger studies are necessary. The nature of

a report such as this does not prove that such an approach is guaranteed to be safe, but rather that it certainly might be in some if not many instances. [9 April 2021](#).

—*Christopher Sampson, MD, FACEP*

### **Sex disparities in covid-19 mortality vary across racial groups in the United States.**

Inequities in covid-19 outcomes in the United States have been clearly documented for sex and race: men are dying at higher rates than women, and Black people are dying at higher rates than White people. Unexplored, however, is how sex and race interact in covid-19 outcomes.

Our new [paper](#), published in the *Journal of General Internal Medicine* based on work at the [GenderSci Lab](#) at Harvard University shows that Black women are dying from covid-19 at significantly higher rates than White men, and that disparities in mortality rates among women of all races are greater than those between White women and White men. These findings complicate the simple narrative that men are dying of covid-19 at greater rates than women.

Our study is the first to our knowledge to quantify the imbalance in covid-19 mortality looking at both race and sex simultaneously. We used US Census Bureau data and publicly available data from Michigan and Georgia (the only two states that currently report the relevant statistics by age, race, and sex) to calculate and compare covid-19 mortality rates. Key findings of the study include:

- Black women have covid-19 mortality rates that are nearly four times higher than White men, three times higher than Asian men, and higher than White and Asian women.
- Black men have far higher covid-19 mortality rates than any other sex and racial group, including over six times higher than the rate among White men.
- The disparity in mortality rates between Black women and White women is over three times greater than the disparity between White men and White women.
- The disparity between Black men and Black women is larger than the disparity between White men and White women.

While, overall, men have higher covid-19 mortality rates than women, our paper shows that this sex disparity does not hold across racial groups. These findings demonstrate the limitations of uni-dimensional reporting and analyses and highlight the ways that race and gender have intersected to shape covid-19 outcomes.

It is well understood that racism and [social inequities](#), rather than genetics, are responsible for racial disparities in covid-19 mortality. However, some researchers and other commentators continue to focus on differences in biology in an effort to explain the sex disparity in covid-19 mortality. Our paper's findings challenge a sole focus on biology as an explanation for sex differences in covid-19 mortality and argue that societal factors related to gender, combined with racism and socioeconomic stratification, are important explanatory factors. [8 April 2021](#).

—*Ann Caroline Danielsen and Tamara Rushovich*

### **Moderna mRNA vaccine shows durable antibody response six months later.**

Early in the pandemic, some people were concerned that the antibodies generated in response to natural coronavirus infection would fade rapidly, raising the specter of a never-ending crisis in which repeat infections were common. Mostly, these fears came out of reports stemming from antibody tests that we now know were not adequately vetted. While repeat infections have been reported widely, they remain rare occurrences. But what about antibodies our bodies make in response to vaccination?

Now, months removed from the initial dissemination of the two approved mRNA vaccines (from Pfizer/BioNTech and Moderna) and the groundbreaking clinical trials for each which have finally begun to turn the tide of the pandemic, new data suggests that the Moderna vaccine provides

persistent immunity at least six months after inoculation. A research letter, which was [published](#) in *The New England Journal of Medicine* yesterday showed significant evidence for the durability of neutralizing antibodies elicited by the vaccine.

Blood taken from a group of 33 individuals enrolled in Moderna's clinical trials were evaluated 180 days after receiving their second dose and tested for antibody activity against SARS-CoV-2. In all age groups, antibody levels were orders of magnitude above the detectable limit six months out, and the blood taken from the vaccine recipients was also able to neutralize live virus at that time as well. It does appear, however, that antibody activity was slightly lower for individuals over 56 years of age.

The takeaway here that we know the Moderna covid-19 mRNA vaccine maintains efficacy six months after the second dose. Research is ongoing about just how long that immunity will last, whether any of the newer variants muddy this picture, and whether or not we will eventually require a booster shot at some point down the road. [7 April 2021](#). —Joshua Niforatos, MD, MTS

### **Excess deaths from covid-19 in the United States.**

As we learned last summer, the United States experienced an approximately 20 percent increase in excess deaths during the first few months of the covid-19 pandemic. Now, a new paper published in [JAMA](#) provides data for the remainder of 2020. The findings are similarly bleak. The results indicate that 22.9 percent more deaths occurred than expected between March 2020 and January 2021. Typically, the annual increase in mortality is only 2.5 percent.

The data were collected from the National Center for Health Statistics (at the US Centers for Disease Control and Prevention) and the US Census Bureau. Mortality data from 2014 to 2019 was used to model anticipated mortality in the U.S. for 2020, and to compare the predicted trend to actual mortality data. Over the ten months included in the study period, there were 2.8 million deaths in the US, which was 522,368 more deaths than expected. Rates were significantly higher among the Black population. Furthermore, excess deaths from heart disease, dementia and diabetes also increased throughout the study period, though there was no attempt to control for whether some of these deaths were actually uncoded covid-19 deaths (which seems to be possible, given that many of these deaths occurred early in the pandemic, and coincided with covid-19 spikes). The authors also found that “the 10 states with the highest per capita rate of excess deaths were Mississippi, New Jersey, New York, Arizona, Alabama, Louisiana, South Dakota, New Mexico, North Dakota and Ohio.”

While the data are limited by their provisional nature (the CDC won't finalize the 2020 data until later this year), by death certificate accuracy, and by the inherent incomplete understandings around the circumstances of each death, the results are important nonetheless. First, the signal in the literature is incredibly clear that minoritized populations suffered disproportionately during the pandemic in the United States. Second, some of the states with high excess deaths rates during the pandemic were those that either did not embrace or actively discouraged pandemic control measures. In other words, political proclivities can have a significant impact on public health and mortality. Finally, more work needs to be done to look into the causes of excess deaths in the US during the pandemic, many of which may be preventable, whether caused by covid-19 directly or otherwise. [6 April 2021](#). —Joshua Niforatos, MD MTS

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*Brief19* is a daily executive summary of covid-19-related medical research, news, and public policy. It was founded and created by frontline emergency medicine physicians with expertise in medical research critique, health policy, and public policy.