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BRIEF19

A daily review of covid-19 research and policy.

RESEARCH BRIEFING

Some patients have more severe covid-19 than others. A study suggests genetics play a role.

Why do some illnesses hit some patients harder than others? It may be that people are suffering from different illnesses with overlapping manifestations or that some have pre-existing conditions that leave them more vulnerable. But what about people largely comparable in age, gender, risk factors, and social determinants of health? Why should differences exist? Perhaps genetics play a role, as they are known to with respect to how well certain medications are tolerated by various individuals (for more on this, see our *Brief19 extra* below). The authors of a new [small study](#) appearing in *JAMA* set out to determine whether there was a genetic basis for why four healthy Dutch males between the ages of 21 and 32 became profoundly ill from coronavirus such that each had to be on a mechanical ventilator for 10 days and one died. The authors sequenced the entire genome of the four individuals and their immediate family and found that all four had mutations that prevented interferons from being activated. Interferons are proteins the body uses to interfere with viral infections. Without active interferons, a virus can wreak havoc relatively unchecked. Meanwhile, studies investigating the effectiveness of giving patients interferons as a treatment for covid-19 have yielded mixed results. None have demonstrated substantial efficacy, suggesting that there is more to the body's response against coronavirus than achieving a certain level of interferon activity.

This study demonstrates a genetic variant present in four Dutch men who became critically ill from coronavirus. However, it does not demonstrate that these men would have lived if they did not have this variant. The next steps are to see how widespread this variant is—the authors acknowledge this is a very rare mutation—and to investigate whether medications that bypass this blown fuse in the immune system might shorten the duration or reduce the severity of covid-19. It will also be important to look for other genetic variants that are associated with decreased duration or severity.

Even if this study's findings do not apply to the general population, a deeper biological understanding of the interaction between SARS-CoV-2 and its human hosts may inspire further research that may eventually lead to novel treatments.

—*Michael Chary, MD PhD*

Brief19 extra: Genetics are known to play a role in how medicines can affect various people in different ways. Guided by similar questions as the Dutch study discussed above, over the last few decades researchers have uncovered genetic variations among seemingly similar people. For example, some people metabolize codeine which is in “Tylenol #3” into morphine far faster than others. Children with such metabolisms become excessively sleepy when they receive standard doses of Tylenol #3. Their ability to rapidly convert codeine into morphine means that for them, Tylenol #3 is akin to a hit of morphine, and can sometimes deliver what amounts to an unintentional opioid overdose.

—*Michael Chary, MD PhD*

POLICY BRIEFING

Health care workers in the community.

In an attempt to keep with CDC guidance, many U.S. businesses are prohibiting entry to individuals who have had close contact with people suspected or confirmed to have a covid-19 infection. If applied literally, health care workers (HCWs) might never be allowed anywhere—but this would be a misinterpretation of the CDC’s more nuanced suggestions. The current [guidelines](#) for community transmission of covid-19 state that anyone who has had close contact with a patient suspected or confirmed to have covid-19, should quarantine for 14 days, regardless of mask or PPE use by either party. Close contact is defined as being within six feet for at least fifteen minutes. Such an application would sideline almost all HCWs from society. The caveat is that the CDC reasons that the general public is not trained in proper PPE use. Its specific [guidance](#) for HCWs only recommends quarantine if there was contact without adequate PPE. Therefore, work exposure should not generally be subject to the quarantine rules. Ultimately however, health care workers are not a protected class under the law. If businesses did decide to expressly prohibit HCWs from entry, they would be free to do so, but may have to face the court of public opinion. *Centers for Disease Control and Prevention.*

—*Kimberly Chernoby, MD JD*

Health justice demands global supply of remdesivir.

If not for patients in Liberia, Guinea and the Democratic Republic of Congo, no large-scale clinical trials of remdesivir would exist right now. A [commentary](#) traces the history of remdesivir and its origins as a novel treatment for the Ebola virus. Because of these willing patients, Gilead (the company that manufactures the drug) was able to conduct necessary safety trials, ultimately proving the drug was safe for humans, although it was not found to be effective against Ebola. With human safety trials therefore already having been completed years ago, Gilead was able to quickly secure orphan drug approval from the Food and Drug Administration in March and subsequently proceed to effectiveness trials. In a cruel twist however, the very same patients who risked their health as participants in early clinical trials for Ebola have no current access to the drug during the covid-19 pandemic, as the U.S. has purchased the entire global supply and has shown no indication of any willingness to share it. The issue of global access to costly drugs is not new to Gilead, as the company has faced [criticism](#) of its distribution of HIV and Hepatitis C drugs in the past, even finding ways to reap benefit by donating some of its products. The commentary authors suggest that Gilead place the patent for remdesivir in a United Nations patent pool that would facilitate low-cost generic manufacturing of the drug. Regardless of the lingering [questions](#) as to remdesivir’s effectiveness, it seems unconscionable to deploy the drug domestically knowing that those who paved the way lack access themselves.

—*Kimberly Chernoby, MD JD*

*Kimi Chernoby, MD, JD, Policy Section Editor. Joshua Niforatos, MD Research Section Editor
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Twitter: [@brief_19](#)

submissions@brief19.com

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.