

24 July 2020

BRIEF19

A daily review of covid-19 research and policy.

RESEARCH BRIEFING

Another major trial finds hydroxychloroquine offers no covid-19-related benefit.

A new randomized controlled clinical trial comparing hydroxychloroquine (HCQ) to control has been [published](#) in *The New England Journal of Medicine*. No benefit was found. In the study from Brazil, covid-19 patients with mild or moderate disease (either not requiring oxygen, or less than 4 liters per minute) were randomized to one of three groups: 1. HCQ alone; 2. HCQ with azithromycin (an antibiotic) and; 3. No addition to the standard covid-19 treatments (“usual care”). The “primary” outcome was clinical status 15 days after entering the trial. To assess this, the investigators used a 7-point scale based on early guidance provided by the World Health Organization when this SARS-CoV-2. The scale is reproduced here:

1: Not hospitalized with no limitations on activities. 2: Not hospitalized but with limitations on activities. 3: Hospitalized, not receiving supplemental oxygen. 4: Hospitalized, receiving supplemental oxygen. 5: Hospitalized, receiving noninvasive ventilation or high-flow oxygen (pressurized air via facemask). 6: Hospitalized, receiving mechanical ventilation. 7: Death.

No significant changes in score were found. There were also no differences in “secondary” outcomes, including an analysis at 7 days, monitoring for blood clots, number of days alive and free from the need for breathing support (meaning no need for any extra oxygen, including by nose, face mask, high flow oxygen, or mechanical ventilation) up to day 15.

HCQ was seen to increase the time it takes the hearts of patients who took it to prepare for its next beat. When that time, known as the QT or QTc interval, becomes too elongated, it can cause life-threatening cardiac rhythms.

This trial comes in the context of two recent important clinical trials assessing HCQ. One American study assessed whether persons with substantial exposure to patients with covid-19 could be prevented from becoming infected by taking HCQ as prophylaxis. It did not work. Another, out of the United Kingdom found [no benefit](#) in hospitalized patients.

In the United States, HCQ prescriptions [skyrocketed](#) this Spring after President Trump and Elon Musk touted its benefit, without any quality evidence supporting the claims.

The nation of Brazil is led by President Jair Bolsonaro, a supporter of President Trump and a vocal proponent of HCQ. Mr. Bolsonaro recently became infected with SARS-CoV-2.

–Jeremy S. Faust, MD MS

Antibody levels fall after SARS-CoV-2 infection. What does that mean?

One of the important questions in covid-19 is whether we become immune after an infection. If so, for how long? A [correspondence](#) in the *New England Journal of Medicine* reports on the concentration of antibodies against SARS-CoV-2 over time in 34 subjects who recovered from mild covid-19. All participants had their antibody levels measured twice; once around a month after symptom onset and the second nearly 3 months after. Rather than just testing for the presence or absence of antibodies, the researchers quantified the amount of anti-SARS-CoV-2 antibody (Immunoglobulin G, or IgG) in each participant. After statistical modeling, they concluded that the concentration of antibodies quickly declined by approximately 50 percent in just over a month (36 days). At the individual level, there was variability. In fact, it

appears 7 patients had at least some *increase* over time. A small number of participants had minimal decreases, and others had rapid declines.

Before we panic about lack of immunity, it is crucial to consider that the human immune response is much more complicated than the concentration of antibodies against a virus. First, it is not uncommon for antibodies to peak, decline, and then stabilize at lower levels. As a novel virus, we don't know what quantity of antibody provides protection. Additionally, while antibodies are produced by B cells, another line of cells, T cells, can identify and kill viruses and infected cells. This form of immunity was not evaluated in this study, but hopefully future research can determine if and how immunity to SARS-CoV-2 is generated by humans.

–Lauren Westafer, DO MPH

POLICY BRIEFING

The AMA comes out against permanent relaxing of “scope of practice rules.”

Since President Trump declared a national emergency on March 13th, 2020, many temporary changes affecting how medical care is delivered have gone into effect. These changes are designed to allow healthcare workers to keep up with the demands and difficulties introduced by the pandemic. Some changes are here to stay, while others may not be permanent. For example, both patients and providers have quickly become accustomed to telehealth. While the federal government (namely, the Centers for Medicare and Medicaid Services, or CMS) has enacted temporary rule changes to support telehealth largely citing reasons stemming from the benefit of reducing in-person patient visits (i.e. decreasing exposure, decreased use of PPE, etc), a major reason why many in and outside of the medical profession appear to support permanent extensions to the telehealth rules comes down to convenience, as long as telehealth is used safely. Other changes, such as temporary legal rules that protect physicians from malpractice lawsuits during the pandemic are likely to sunset at the conclusion of the covid-19 emergency.

One temporary rule change that has healthcare advocacy groups up in arms concerns “scope of practice” changes. Normally, nurse practitioners (NPs) and physician assistants (PAs) require some degree of physician supervision. During the national emergency, those rules have been relaxed, allowing NPs and PAs to work alone and without supervision in some circumstances. While for years, some NP and PA organizations have advocated for extending the independence of these healthcare providers, physician organizations have pushed back on the grounds that doctors generally go through 10,000 hours of post-graduate training which is 5 times more than most PAs, and 10-20 times more than most NPs. The American Medical Association issued an [open letter](#) yesterday, signed by dozens of other professional organizations, calling for the federal government not to make the relaxed rules permanent after the covid-19 emergency ends. The main concern is safety to patients.

–Jeremy S. Faust, MD MS

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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.