

22 April 2020

## **BRIEF19**

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

### **RESEARCH BRIEFING**

**The hydroxychloroquine drama continues.** In a [preprint](#) study posted to medRxiv, NIH-funded researchers from the Veterans Affairs (VA) and University of Virginia looked at outcomes of 368 hospitalized patients in the VA system with confirmed SARS-CoV-2 infection. Patients received hydroxychloroquine (HC) or hydroxychloroquine and azithromycin (AZ), or standard of care (neither of these medications). The study assessed whether death or the need for mechanical ventilation was more frequent in any of the three groups. Patients who received HC were a bit sicker at the start of the study than those who did not receive the drug. Patient given only HC died 27.8 percent of the time. Those who received HC plus AZ died 22.1 percent of the time. Patients who received neither only died 11.4 percent of the time. Thus, the patients who received HC, or HC plus AZ died more often than those who only received “standard” treatment that did not include these medications. This is a large difference. In addition, there was no evidence that the medications reduced the risk for the need of mechanical ventilation. Is this another major blow to the use of HC for patients with severe covid-19? Possibly. However, this is an observational study that looked at patient information in medical databases, rather than a randomized trial that collected data in real time and divided patients into groups that were slated to either receive the drugs of interest or placebos. This means the patients in this study received the drugs that treating physicians deemed appropriate at the time. To overcome some of these limitations, the researchers performed statistical analyses that adjust for the increased severity of illness found in the patients who received HC. This is called “propensity score matching.” Propensity matching, while helpful, doesn’t completely negate the limitations of observational studies like these. Analysis: So far, there has been no high-quality evidence to support the use of HC. Other studies that have shown signs of benefit from HC have similar limitations to those found in this study. However, this study is an important reminder that it is unsafe and unwise to assume that giving an unproven drug to sick patients will either do nothing or help. That mindset is dangerous. Giving an unproven drug to patients will either help, not help, *or* harm patients.

**What happens to children diagnosed with covid-19?** A hot off the press systematic review published today in *JAMA Pediatrics* assessed the known literature (at the time of submission) of pediatric cases of SARS-CoV-2 infection. The authors found 18 studies with 1,065 patients (444 patients younger than 10 years, 553 were aged 10 - 19) with confirmed SARS-CoV-2 infection. Notably, all of the included studies came from China except for one case report from Singapore. Most children in the study had mild symptoms, including fever, dry cough, and fatigue. Many were entirely symptom-free. Interestingly, imaging (x-rays, ct scans, etc) found mildly symptomatic and asymptomatic children to be similar. No deaths were reported in children aged 0-9, and one death was reported in a person 10-19 years old. However, since these data were submitted, we know that a small number of children have died here in the United States. This study confirms prior observations that children tend not to have severe covid-19. However, these results reflect “publication bias.” The true case fatality rate, while likely extraordinarily low in children, remains unknown.

*—Joshua Niforatos, MD Research Section Editor.*

## **POLICY BRIEFING**

**A Bright spot at BARDA flames out.** The leader of the Biomedical Advanced Research and Development Authority (BARDA) and notable vaccine development researcher Rick Bright has [stepped down](#) from his position in the middle of the largest pandemic in the last century. BARDA is the government agency tasked with making sure that the United States has the medical supplies necessary to respond to emerging, natural, and deliberate threats. This includes development of vaccines and medical treatments. It also oversees the Strategic National Stockpile and encompasses all aspects of preparedness from research & development to assessing and improving manufacturing capacity. Bright, the second director in the history of BARDA, will be moving into a role at NIH geared toward diagnostics. BARDA is poised to play an outsized role in the coming months as the country responds to and eventually recovers from the SARS-CoV-2 outbreak. Its budget was tripled by the CARES Act package passed by US Congress last month. Prior to this package, BARDA had not been fully appropriated since its creation following the September 11th attacks. *STAT*. –Jordan Warchol, MD, MPH

**New stimulus package by the numbers.** On Tuesday, the US Senate [voted to approve](#) an additional \$484 billion stimulus package to reinvigorate the Paycheck Protection Program (PPP) and provide additional funding for national testing programs. The initial \$350 billion set aside for PPP in the second stimulus package was quickly claimed. This new bill allocates a further \$310 billion to replenish the program. Of these funds, \$60 billion has been reserved for under-banked and rural areas, \$60 billion is directed to the Economic Injury Disaster Loan (EIDL) program, with up to \$10 billion of the EIDL allocation available as grants. The package reserves an additional \$75 billion to reimburse healthcare entities for expenses and losses associated with covid-19, and directs \$25 billion to bolster national testing, with explicit instructions on distribution between federal and local entities. *US Senate*. –Joshua Lesko, MD

**Partisanship dominates pandemic management in Wisconsin.** Two weeks ago, Wisconsin drew national attention when it proceeded with in-person polling in the middle of the pandemic, and associated shelter in place orders. Democratic lawmakers requested mail-in ballots and voting extensions. Legal action was taken and the case eventually reached the federal Supreme Court. Ultimately, the primaries went on as scheduled. Since then, seven people have [fallen ill](#) and traced their infection to the election. In a new move, the Republican lawmakers in Wisconsin have filed suit against the state's Democratic Governor in response to shelter in place orders. They [allege](#) that shutting down the economy and requiring individuals to stay at home amounts to administrative overreach. However, state governments are given significant police powers in times of crisis. There is a reason we have not seen these orders challenged earlier; the suit is unlikely to be successful. *New York Times*. –Kimi Chernoby, MD JD, Policy Section Editor

*Jeremy Samuel Faust MD MS, Editor-in-Chief.*

*Kane Elfman PhD, Publishing and Design.*

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Twitter: [@brief\\_19](#)

[submissions@brief19.com](mailto: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.