

## **BRIEF19**

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

### **RESEARCH BRIEFING**

#### **School closures correlate with decreased covid-19 incidence.**

Amongst the many changes to daily life during the early covid-19 pandemic, school closures may have been the most noticeable and most hotly debated. A [study](#) in *JAMA* sought to elicit the effects of school closures on incidence of covid-19 cases and deaths. By examining the timing of school closures across all 50 U.S. states, the study's authors hoped to determine if there was a temporal component to such an effect. In a time series analysis performed from March 9, 2020 and May 7, 2020 they found a decline in incidence of cases and mortality by 62% and 58%, respectively. Furthermore, the data revealed that states where closures occurred early, when cumulative incidence was low, had the largest reductions—72% for the states in the lowest quartile for incidence versus 49% for the highest. Based on these percentages, the authors' model predicted an overall decrease of 1.4 million cases over a 26-day period and 40,000 fewer deaths over a 16-day period.

Of course, time series (before-and-after) studies are fraught with limitations as a number of behavioral (“non-pharmaceutical”) interventions were enacted in quick succession across many states. As states started to take the drastic measure of closing schools, they were also educating the public about improved hand hygiene, social distancing, and mask usage, not to mention restaurant, office and public space closures. While the authors made statistical adjustments for many of these factors, not all of them could be directly accounted for with data, making it difficult to accurately separate out school closures from many other simultaneous interventions. Another limitation included analysis at the state level, which can't account for differences amongst counties or individuals who traveled between states. Furthermore, as has been a centerpiece of all covid-19 related discussions, testing ability and reporting between states can vary greatly, possibly misrepresenting the number of actual cases in each state.

Ultimately, closing schools seemed an unavoidable step in the fight against the covid-19 pandemic and coincided with a significant decrease in disease burden and mortality, as this study shows. While adjusting for many other factors still resulted in a statistically significant difference, one would be hard pressed to take this data as decisive or definitive given the variety of measures each state enacted concurrently with school closures. [30 July 2020](#). —Fred Milgrim, MD

#### **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. 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. [28 July 2020](#). —Michael Chary, MD PhD

### **A decline in heart transplants due to covid-19, the waitlist actually dwindles.**

Another area of medicine affected by the pandemic: organ transplants. A [Brief Report](#) in *JAMA Cardiology* focused on the rate of heart transplants during the covid-19 shutdown this spring. Taking data from the United Network for Organ Sharing (UNOS), researchers looked at adult candidates for transplant. Inactivations and additions to the waitlist along with heart transplants performed over eight weeks were compared to an 8-week period during the pre-covid period.

UNOS is broken up into 8 regions: Northwest, North Midwest, Great Lakes, Northeast, Mid-Atlantic, Southwest, South Midwest and Southeast. During the study period, there was a 75% increase in waitlist inactivations (343 vs. 600). Patients were given the option of reporting to researchers whether the inactivation was related to covid-19 concerns or not. Of those who inactivated plans for a transplant, 67% were reported as being a result of covid-19 precautions and concerns. The highest region of inactivation was the Northeast (91%) followed by the Southwest (81%). A 38% decrease in additions to the transplant waitlist was also observed. The region with the largest decrease in additions was Northeast, where a 69% decrease was found (31 additions during the covid-19 period, down from 101 during the pre-covid “control” comparison period). One region, “South Midwest”, actually saw a waitlist addition increase of 8.5%, increasing slightly from 47 before to 51 during the covid-19 period. Not surprisingly, the number of heart transplant surgeries decreased by 26% nationwide during the covid study period (525 transplants took place during the pre-covid19 versus just 389 during the covid-19 period). No significant regional variation was seen with respect to this decrease in surgeries. The largest declines occurred at the end of March,

The researchers suggested several factors contributing to these declines. One primary concern is on the donor side. There is the possibility that individuals who otherwise would have been suitable organ donors might have had covid-19 at the time of their death. Even in the absence of infections, it is likely that the lack of ability to test potential donors was a supply-limiting factor. Additionally, decreased intensive care unit space was another likely factor. While these data may not be unexpected given our knowledge of how covid-19 has affected hospital capacity, what cannot yet be calculated **are** the costs to those waiting on the heart transplant lists hoping for a life-saving match. [27 July 2020](#).

—Christopher Sampson, MD, FACEP

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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.