Week in Review: 12 – 16 October 2020

BRIEF19

A daily review of covid-19 research and policy.

RESEARCH BRIEFING

Excess Deaths in the United States among the worst when compared to similar nations.

One measurement of the toll of the covid-19 pandemic is the excess number of deaths from all causes. The term *excess deaths* refers to the difference between the expected number of deaths estimated from previous data and the observed number of deaths. Excess deaths counts not just the number of deaths attributed to a particular cause (such as SARS-CoV-2, the virus that causes covid-19), but to all causes. This allows epidemiologists to measure the impact of an outbreak even in the absence of adequate testing. However, when deaths from a particular cause of interest closely parallel the number of all cause deaths, as they have in the United States this year, it is highly likely that the excess deaths are simply a better window into the number of fatalities caused by the illness of interest, rather than other causes such as a decrease in medical care for other reasons.

In a previous brief, we discussed an article in the *JAMA Internal Medicine* that estimated that between March 1 to May 30, 2020 there were 122,000 excess deaths in the United States. In a Research Letter published today, the same authors extend their analysis through July 30. They found 225,530 excess deaths of which 150,541 (67 percent) were directly attributed to covid-19. Heart disease during March and April and complications from dementia during June and July drove the remaining deaths, largely concentrated in areas where the largest covid-19 outbreaks occurred. Most excess deaths were in the Northeast in the spring and in Texas, Florida, and Arizona during the last two months, rather than spread out evenly among the rest of the country where decreases in emergency care were seen, regardless of whether covid-19 surges occurred.

Another Research Letter in the published today reports that an United States all cause excess death rate of 65 more deaths per 100,000 people, approximately 100 times worse than South Korea. The United States has the worst death rate (27 per 100,000) since June 7 of the countries analyzed in the study. The authors note that a perfect comparison between the US and other countries is difficult because the US population is younger but has more chronic medical conditions (diabetes, high blood pressure, heart disease, kidney disease) than other countries. There will soon be enough data to isolate the effect of the most common pre-existing conditions.

Covid-19 has exposed inequities in our healthcare system that reinforce social determinants of health and put entire groups at higher risk of death. We previously remarked on the racial disparities in hospitalizations. The Financial Times columnist Anjana Anhuja labelled covid-19 a *syndemic* this week (paywall), referring to how the infectivity of the virus may synergize with pre-existing conditions to be especially lethal to certain groups. Pre-existing conditions reflect a combination of genetic predisposition, lifestyle, and, most crucially, social determinants of chronic health that affect health outcomes during acute crises.

These updated analyses suggest that the U.S. is performing more poorly than countries it considers comparably developed and that it continues to underperform. Pre-existing conditions and a lack of preparation may have led to excess death early in the pandemic. Meandering political actions and geographically varying responses to science-based policy may have also prevented effective action. However, neither paper covered here was able to include the increases in cases reported in many European countries that have occurred in the last few weeks. *12 October 2020*. —*Michael Chary, MD PhD*

Monoclonal antibody trial halted for safety concern. The ACTIV-3 monoclonal antibody trial for the treatment of covid-19 has been paused due to a potential safety concern. The ACTIV-3 trial is a randomized blinded clinical trial testing the safety and effectiveness of a monoclonal antibody (Ly-CoV555) produced by the pharmaceutical giant Eli Lilly in combination with remdesivir, an anti-viral with emergency use authorization for covid-19. This trial is designed to test this combination against a

combination of remdesivir and placebo alone. No details regarding the nature of the safety concern have been obtained. However, this is the same kind of compound that President Trump received at the beginning of this month (made by Regeneron). President Trump also received remdesivir at that time.Very few patients have received monoclonal antibodies designed to target SARS-CoV-2. Even fewer have received them in combination with remdesivir. Therefore, other than investor slide decks and press releases from the companies that make these compounds, little to nothing is known about how well they combat SARS-CoV-2 and how safe they are alone and in combination with other treatments. This news casts doubt as to the wisdom and safety of the approach used by President Trump's medical team. Trump, who became infected with SARS-CoV-2 sometime in late September, received a combination of medications, including a cocktail of monoclonal antibody for which there is scant clinical and safety data. Whether this current setback will turn out to be a small safety problem or a large one remains to be seen. Either way, this episode highlights the perils of proceeding with giving patients unvetted treatments on the basis of the fool-hardy premise that says, "what's the harm?" *14 October 2020*.

—Jeremy Samuel Faust MD MS

Covid-19 thought to increase abnormal blood clots. What do the CT scans say?

In addition to the direct effects of the SARS-CoV-2 virus and the typical manifestations of covid-19, several studies have found a higher than expected proportion of patients suffer abnormal blot clot formation, or what physicians call thrombotic events. Most of the research describing the potential increase in these conditions which are thought to be among the many complications of covid-19 has been performed in the inpatient hospital setting, where patients are generally on the sicker end of the spectrum, and in whom, the baseline occurrence may be more common.

Now, in the journal *Academic Emergency Medicine*, a group of researchers have reported data from a single-center retrospective study in which they assessed the number of computed tomographic pulmonary angiograms (CTPAs) ordered by emergency physicians looking either to diagnose or rule out pulmonary embolisms (blood clots in the lungs). They gathered data from April 1 through May 1, 2020 and compared the findings with data from the same time period in 2019.

In 2020, two times as many CTPAs were positive for blood clots in the lung compared 2019 (19 percent versus 8 percent). Over half of the patients with blood clots in the lungs (60 percent) in 2020 were positive for SARS-CoV-2, 88 percent of whom tested positive during the same emergency department visit, rather than during prior medical encounters, either in the emergency department, or any other clinical setting.

These data add to the emerging literature suggesting SARS-CoV-2 may increase the risk of blood clots to the lungs. However, there are several potential alternative explanations for these findings, including a change in the composition of emergency department patients during the peaks of covid-19 surges. Further, there may have been changes in clinician practice patterns and decisions regarding who was determined to require testing for these clots may have changed.

Regardless, this study provides an important reminder to avoid what physicians call "premature diagnostic closure"; while the symptoms of covid-19 and blood clots in the lungs may be similar (shortness of breath, low oxygen saturations, for example) and patients may have a positive test for SARS-CoV-2, these patients could still also have pulmonary embolisms simultaneously. *Abbreviated from Brief19 for 16 October 2020.*

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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.