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BRIEF19

A daily review of covid-19 research and policy.

RESEARCH BRIEFING

Another remdesivir trial reported by press release. Gilead Science released preliminary results via press release of the SIMPLE trial, a randomized clinical trial of remdesivir versus standard of care for patients admitted to the hospital with moderate covid-19 illness. To be included in the study, patients had to have laboratory confirmed SARS-CoV-2 infection with evidence of pneumonia but *without* reduced levels of oxygen. Patients were given either five days of remdesivir (and other treatments considered "standard of care"), 10 days of remdesivir plus standard of care, or standard of care alone (essentially placebo). The primary outcome that the researchers tracked was improvement or worsening in clinical status by day 11, ranging from release form the hospital to death. Patients receiving remdesivir for 5 days were 65 percent more likely to have clinical improvement by day 11 compared to the placebo group. Interestingly, patients receiving remdesivir for 10 days did not have significant improvement compared to the placebo group, raising questions. Without more information including the characteristics of the patients who were in each group, and without access to the statistical analysis plan (which has not yet been made public), it is difficult to fully understand why patients receiving a drug for covid-19 did not improve when given this medication for 10 days instead of merely 5 days. What is encouraging, however, is that these data provide more evidence that remdesivir appears to be well-tolerated; there were non-statistically significant differences in the rates of adverse event (i.e. side effects) between patients who received remdesivir and those who did not. Overall, there are two major problems of which to be aware. Firrst, the data was unveiled via press release. Because we do not have the full methods and data, interpretation is severely limited. Second, it is unclear why the study changed its focal point to clinical status after 11 days as opposed to 14 days, which had been the original plan. However, 11 days is a conspicuous choice. In the recently published ACTT-1 trial, the median recovery time in patients receiving remdesivir was 11 days, 3 days faster than patients who received placebo. *–Joshua Niforatos, MD*

April study on the ineffectiveness of some masks retracted by major journal. In April, *Brief19* mentioned a study regarding the effectiveness of surgical and cotton masks that appeared in *The Annals of Internal Medicine.* In the study, patients with SARS-CoV-2 infection coughed towards petri dishes held 20cm (7.9 inches) in front of their faces while wearing one of the two types of masks or no mask at all. The goal was to determine whether non-PPE masks are effective in preventing the spread of viral particles on large droplets that are emitted during coughing. At that time, *Brief19* linked to the study in question, but did not report the conclusions of the authors because the data were collected from no more than four patients. We deemed the data insufficient to provide actionable information. Now that study has been retracted. While corrections are not uncommon, wholesale retractions in major journals are. (The findings have been so completely disavowed that the prior hyperlink leads not to the article accompanied by prominent notices of retraction, but instead to a "404 Not Found" message). The specific problem that led to the paper's retraction is that the authors of the study failed to fully recognize the implications of what is known as "limit of detection," or LOD. The idea is that if a measurement (such as the number of viral particles) falls below the LOD of a particular test, no *quantitative* information can be gleaned. For example, if a test has an LOD of 5,000 viral copies

per milliliter, and the test detects 3,000 copies of virus, there is no way to determine whether the true number of viral copies was zero, five-hundred, or 3,000; once a number is below the LOD for a particular test, the numbers themselves cease to have any reliable meaning. Therefore, the findings in the original paper, which included quantitative data that was under the LOD for the viral assay in use, were invalid. The authors offeed to provide corrected data; that offer was declined by the journal. This is the first retraction of a study previously covered by *Brief19.* We anticipate that other major retractions may soon be made by other journals. It appears that the rapid pace of peer review during the covid-19 pandemic has led to occasional breakdowns in the vetting process. *–Jeremy Samuel Faust, MD MS*

POLICY BRIEFING

White House floats plan to end surprise billing. Surprise medical billing occurs when a patient receives care at a healthcare facility that is in-network but the medical care is provided by a physician who is actually not in that network, leaving the patients responsible for paying for the care. Patients can find themselves with bills running into the thousands of dollars. Lawmakers in both parties have voiced support for ending this practice, but the question of how payment disputes should be resolved has proved more difficult and has been the subject of intense lobbying by hospitals and insurers. The White House said in April that any hospital accepting stimulus funds would have to agree not to send patients unexpected bills related to the coronavirus, but no mechanism was established for complaint resolution. More recently, the White House announced an initiative to permanently end the practice of surprise billing. Again, however, the proposal does not create any process to resolve disputes over billing, leading some experts to worry that battling parties will turn to litigation. *Politico.* *–Joshua Lesko, MD*

House seeks to give businesses more flexibility in using bailout loans.
On Thursday the House passed the Paycheck Protection Program Flexibility Act, aimed at giving small businesses greater leeway in using their bailout loans by relaxing forgiveness requirements and reducing financial burdens on participants. The bill would increase the time for business to use funds to twenty-four weeks from eight and reduce the percentage of funds that have to be directed to payroll to 60 percent from 75 percent. Businesses who receive forgiveness will also qualify for payroll tax exemption. The bill would extend the timeline for repayment to five years from two years and add protections for businesses required to open at fifty percent capacity. These provisions were also included in the House-passed HEROES Act, but given the unlikelihood of that bill passing the Senate, Representative Dean Phillips, Democrat of Minnesota, drafted this new language. The Senate is drafting similar language to address difficulties with the program but the two pieces of legislation will need to be reconciled before changes can take effect. *House of Representatives.* *–Joshua Lesko, MD*

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