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BRIEF19

A daily review of covid-19 research and policy

RESEARCH BRIEFING

Coronavirus mRNA vaccines reduce the risk of asymptomatic infection.

While early clinical trial data largely focused on whether the coronavirus vaccines are effective at preventing severe covid-19 and hospitalizations, researchers and the public alike remained curious as to whether the vaccines would also prevent *asymptomatic* SARS-CoV-2 infections. This is important because people have had concerns that being vaccinated might protect themselves, but that they could in effect be unwittingly hurting others by passing on a virus that, once in a new host, causes significant disease. A new study published in *Clinical Infectious Diseases* suggests that both the Pfizer-BioNTech and Moderna mRNA vaccines were in fact able to stop infections, not just symptomatic disease.

This research, conducted by the Mayo Clinic health system across its hospitals in Minnesota, Arizona, and Wisconsin, recruited patients requiring covid-19 testing 48 to 72 hours ahead of planned procedures and surgeries. The patients were divided into two cohorts: those who had received at least one dose of either vaccine and those who hadn't had a shot yet at the time of the testing. Of the nearly 40,000 patients who were tested, 3.2 percent of the unvaccinated group tested positive, while only 1.4 percent of the protected group was found to have contracted SARS-CoV-2. This was a statistically notable difference and suggests a relative risk reduction of 44 percent after getting vaccinated for asymptomatic disease.

Although this was not a randomized clinical trial, it provides important information regarding the vaccines' abilities to reduce infection. That said, it is possible that patients preparing to undergo elective surgery are more likely to engage in safer behaviors and may have overall lower rates of asymptomatic covid-19 compared to the general population. Furthermore, the researchers did not follow-up to determine if the patients ever became symptomatic after their pre-procedural laboratory testing, so it is possible that that the final rate of symptomatic infection differs from reported results. But most importantly, the data strongly suggests that even asymptomatic covid-19 is lessened following vaccination. *—Joshua Niforatos, MD, MTS*

High dose blood thinners show no benefit for patients with severe covid-19.

For much of the past year, doctors and scientists have studied whether covid-19 is associated with potentially life-threatening blood clots. As a result, there has been a strong focus on whether and how to give blood thinning medications to covid-19 patients. The research to date has been mixed, as previously discussed on *Brief19*. Last week, a manuscript from the REMAP-CAP trial was published on the preprint server *medRxiv*, suggesting that patients with severe covid-19 did *not* benefit from "therapeutic" doses (i.e. not lower doses given for preventing clots) of blood thinning anticoagulation medications.

REMAP-CAP is an open-label randomized clinical trial (RCT). In this particular study, patients with severe covid-19 were randomized to receive either *therapeutic* anticoagulation or pharmacological *thromboprophylaxis* (doses meant for preventing clots), according to hospital policy. Briefly, the difference between therapeutic and prophylactic use of drugs like heparin (blood thinners) is chiefly of dosing, with the former being a higher dose than the latter. But higher dosing does not come without risks; therapeutic dosing of blood thinners, the risk of potentially devastating bleeding, a feared side effect, also increases.

Over 1,000 patients with confirmed covid-19 were included in this study, and the researchers were primarily trying to assess whether patients were less likely to die or need organ

support after 21 days. Therapeutic anticoagulation did *not* significantly improve the number of days that patients did not need organ support. The overall in-hospital mortality was 36 percent and 35 percent in the therapeutic group and prophylaxis group, respectively, which was not a statistically significant difference.

Patients receiving therapeutic anticoagulation had fewer major thrombotic (clotting) events compared to the prophylaxis group, which was significant; however, when combining the outcome of major thrombotic events *and* death, there were no significant differences between groups. Major bleeding occurred in 3 percent of patients in the high dose group and over 2 percent of patients in the low dose group. Notably, patients already deemed to be at high risk of bleeding were excluded from this study, so the potential risk for significant bleeding could be even higher among some patients requiring covid-19-related hospitalization.

The results of this study are meaningful, as it was the largest RCT to assess the safety and efficacy of therapeutic anticoagulation for covid-19 patients with serious disease. From this, we now know that routine therapeutic dosing should be avoided, as it did not provide an overall mortality benefit. Patients already requiring blood thinners for other reasons, however, should still continue to do so. This study is yet another instance from the covid-19 pandemic, that it is better to perform expeditious RCTs rather than subject hundreds of thousands of patients to theoretical treatments that may actually turn out to be harmful. *—Joshua Niforatos, MD, MTS*

POLICY BRIEFING

No good deed goes unpunished in federal spending.

This past week President Biden signed the latest pandemic stimulus package into law, the American Rescue Plan. Tipping the scales at $1.9 trillion, it is one of the most expensive pieces of Congressional legislation ever passed. While it does provide significant support for healthcare entities, it seems to fall short with respect to financial support for Medicare.

A balanced budget has long been the goal for Congressional spending. To achieve this, multiple mechanisms have been developed to limit the growth of the deficit. In 1985, the Balanced Budget and Emergency Deficit Control Act introduced "sequestration," in which spending on specified federal programs is reduced by a percentage for a given year to cut costs. Furthermore, a pay-as-you-go process (PAYGO), most recently implemented as the Statutory Pay As You Go Act (S-PAYGO) of 2010, scores new bills to determine the financial impact and makes reductions to existing entitlement programs to offset new expenditures. One of the biggest programs affected by both sequestration and PAYGO is Medicare.

Under the Budget Control Act of 2011, a new round of sequestration was initiated through 2021, but the CARES Act extended the program through 2030, and placed a moratorium on the 2 percent Medicare sequester through December 31, 2020. The Omnibus package passed at the end of the year further extended this deadline until March 31, but the American Rescue Plan did not address the sequestration.

What this means is that absent a new bill, providers and hospitals will immediately be subject to 2 percent reduction in all Medicare reimbursement, and according to the Congressional Budget Office (CBO), the additional budgetary strain could increase next year's sequester to 4 percent. While this may not seem like a consequential change, it amounts to $36 billion in lost funds for our healthcare system. *Various* *—Brief19 Policy Team*

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