Week in Review: 4 – 8 January 2020

BRIEF19

A daily review of covid-19 research and policy.

RESEARCH BRIEFING

Modeling the most effective vaccine rollout strategy. Should second doses be reserved? Or should more people get vaccinated now and play catch-up on the booster later?

With the roll out of the Moderna and Pfizer vaccines has come criticism of the currently chosen strategy by which extra doses of the vaccines are being allocated. In an effort to ensure individuals receive the two-dose vaccine series three or four weeks apart, batches of second dose vaccines often remain in freezers unused even as the covid-19 pandemic worsens.

A new modeling paper in *Annals of Internal Medicine* attempts to characterize the pros and cons of different vaccine roll out strategies. Researchers simulated two conceptual models. The first model is our current (fixed) strategy, which reserves 50 percent of each vaccine shipment for second doses to be given a few weeks later. The second model is a so-called flexible strategy model, where different proportions of first batches are reserved for second doses each week. Researchers were interested in predicting the number of covid-19 cases prevented over an eight week period for each model assuming that just one dose of the vaccine is 52.4 percent effective, while the well-studied two-dose series is 94.8 percent effective in preventing symptomatic covid-19.

Based on the analysis, assuming a steady weekly vaccine supply, a flexible strategy that does not set aside 50 percent of each vaccine shipment for second doses could decrease covid-19 vaccine cases between 23 and 29 percent compared to a fixed strategy. This was driven by the fact that if more individuals receive the first dose of the vaccine upfront with variable reservation of second doses throughout each week, many more people will ultimately receive the full two-dose series compared to a fixed model. If there were a shortage of vaccine shipments such that each shipment was 50 percent decreased, the flexible strategy still prevented 27-32 percent of cases compared to the fixed model.

A major caveat is that modeling studies are always subject to large margins of error. The results of these types of studies are highly predicated on the assumptions and inputs made by the researchers—a kind of omniscient tinkering. One researcher might not agree on the assumptions and characteristics of the model made by another. Changing assumptions on how durable (i.e. how long immunity lasts) could easily alter the results in a substantial way.

That said, the most interesting result of this paper was the overall finding that two key determinants influenced prevention of covid-19 cases regardless of the model. Namely, more individuals vaccinated equates to more prevented cases, but that this finding relies on a *stable* vaccine supply. It's fair to say that the randomized clinical trial data of the Pfizer and Moderna vaccines suggests that the vaccines are effective, and those receiving the vaccine will be protected, particularly if they receive two doses. What we do not know is the stability of the supply chain. That implies that this debate will be more informed by conditions on the ground than by thought experiments. *6 January 2021*. *—Joshua Niforatos, MD MTS*

Abortions plummeted during Texas' policy to postpone most surgeries and medical procedures during March and April, 2020.

Early in the covid-19 pandemic, many states recommended halting procedures that were not deemed to be medical emergencies. The reason for this was simple: hospitals were overwhelmed with patients sick with covid-19, and surgical floors and post-anesthesia care units needed to be converted to covid-19 care areas. Additionally, decreasing surgeries meant more availability of PPE for providers taking care of hospitalized covid-19 patients.

Many procedures, surgical removal of cancerous tumors for example, do not fall under the definition of "emergent," and yet are often urgent in nature. Another procedure widely regarded as urgent—and depending on the gestational age might be considered emergent—is the surgical termination of early pregnancy, often simply referred to as an 'abortion'.

In a new paper published in *JAMA*, researchers assessed the changes in abortions following an executive order by Texas Governor Greg Abbott on March 22, 2020 that required postponing surgeries and

procedures not deemed medically necessary. Controversially, the order included abortion. To determine changes in the number of abortions that occurred during the pandemic in Texas, researchers analyzed monthly data from 18 of 24 abortion facilities which account for 93 percent of abortions performed in Texas. Data also included Texas residents obtaining abortions at 30 of 37 "open facilities" in nearby states, including Arkansas, Colorado, Kansas, Louisiana, Oklahoma, and New Mexico from February 2020 through May 2020. These data were compared to rates recorded during previous years.

When compared to the previous year, the researchers found a 38 percent reduction in abortions in Texas during the time that executive order issued by Texas Governor Greg Abbott was active. Additionally, there was a 17 percent increase in medication-induced abortions and a concomitant decrease in procedural abortions during this time period. When the executive order was lifted, there was an 83 percent increase in procedural abortions among pregnancies that were 12 weeks or higher when compared to May 2019. This means that some women waited weeks longer than they wished to in order to receive an abortion and that many more second trimester abortions occurred than usual. Finally, Texas residents receiving care at out-of-state facilities substantially increased (by *785 percent*) during the month of April, meaning that women who normally would not have to travel (and incur expenses) had no option but to do so in order to obtain their usual legal access to medical care. *4 January 2021*. *—Joshua Niforatos, MD, MTS*

Convalescent plasma: a rare win, if you squint hard enough.

Prior trials of convalescent plasma in patients hospitalized with severe covid-19 have fallen short of expectations. Many have argued that the benefit to this therapy is in preventing severe covid-19 and that patients in these trials received the plasma too late in their course for any difference to be seen. Now, in the *New England Journal of Medicine*, researchers report on a trial in which 160 patients over the age of 65 with mild covid-19 symptoms less than 72 hours in duration were randomized to receive either convalescent plasma (from donors who recovered from covid-19) or a saline placebo. The average age of the patients in the study was approximately 77 years age, and subjects reported around a day and a half of symptoms. Measured viral loads of SARS-CoV-2 were high on average and 81 percent had at least one medical comorbidity.

Overall, 16 percent of patients with received convalescent plasma had severe respiratory disease by day 15 compared with 31 percent of patients who received the placebo. This translates to nearly half the risk of disease progression. Unfortunately, the trial was stopped early due to a decreasing number of cases in the locales where the study was carried out (Argentina). Thus, the results could be turn out to be more or less impressive in larger trials. Additionally, the trial was too small to detect differences in specific outcomes such as death or the need for invasive or noninvasive mechanical ventilation; however, the numbers favored the convalescent plasma group in all of these end points.

One reason why this trial may have succeeded where others have not is that the investigators specifically used plasma with high concentrations (or "titers") of antibodies. Some previous trials did not control for that, meaning some donor plasma was stronger than others. In addition, other trials had younger adults with longer bouts of symptoms. The signs of benefit in this trial are therefore relatively narrow; older patients who are very early in their disease course.

This study provides some hope for convalescent plasma, yet it is important to recognize that the patients in this study were a very small cross-section of those with covid-19. The results may not be generalizable to younger people, those without comorbidities, patients with vital sign abnormalities, severe symptoms, or more than 2 days of symptoms. *7 January 2021*. *—Lauren Westafer, DO MPH*

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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.