6 January 2021

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 supply of vaccines, 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 to 32 percent of covid-19 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.

—Joshua Niforatos, MD MTS

POLICY BRIEFING

Feds emphasize sticking to the existing vaccine timeline and dosing strategy.

With the US Food and Drug Administration (FDA) having granted Emergency Use Authorizations to both the Pfizer/BioNTech and Moderna vaccines, the race to herd immunity is on. As production and supplies lag behind demand, several news outlets have reported deviations

from the inoculation timeline used in the respective vaccine trials. In the United Kingdom, for example, the time between doses has been stretched to twelve weeks, as opposed to the studied three to four week gap. Another recommendation suggested individuals could get two doses of different vaccines, but that was quickly quashed.

Similarly in the United States, Operation Warp Speed chief Adviser Moncef Slaoui said that there was evidence of two half doses of the Moderna vaccine conveying the same immunity in healthy populations and that discussions were underway about the feasibility of such a change. To address these issues, on Monday the FDA released a statement roundly rejecting any deviations from the standards used in the clinical trials, emphasizing consistency between the manufacturer used and the 21-day period between the Pfizer doses and 28 days between the Moderna jabs. The statement further emphasized that any alternatively proposed plan was premature and that sufficient evidence is not available to support such changes. *Various.*

—Brief19 Policy Team

Are researchers and the FDA at odds on a vaccine rollout? Not necessarily.

Editor's Note: Today's Policy Briefing and the Research Briefing might seem contradictory. That's not entirely the case. Let's emphasize some key points.

While the FDA has discouraged straying from recommended vaccine delivery doses and timing (and importantly emphasized not mixing doses from two different vaccines), the discussion of how to most effectively inoculate the population is still an important one. The research briefing discusses a recent paper exploring a vaccine rollout that the FDA has now specifically recommended against—changing the way we might deliver the shots.

It's important to recognize that the authors of the modeling study *did not* recommend giving only a single dose, decreasing the dosage amount, or even extending the period between doses. They are merely surmising that harm reduction could be best achieved by giving out as many first doses as possible, rather than storing half the available vaccines. This of course relies on the assumption that incoming vaccine supply will be able to meet the second dose demand. By testing various scenarios, the researchers calculated that even if supply were to dwindle, a greater degree of infections could be prevented.

Most importantly, this paper was a "thought experiment" aiming to suggest how the country might most effectively handle the pandemic, not an overt recommendation to change rollout strategies. One hopes the FDA and other medical governing bodies will assess this study and make a recommendation based on their knowledge of the country's overall vaccine supply. It is clear that the US is behind schedule in bringing the vaccine to the population, and that trend needs to change.

—Fred Milgrim, MD Editor-at-Large

Shawnee Tribe prevails in DC circuit challenge to CARES act allocation.

Yesterday, the Native American Shawnee Tribe prevailed in the DC Circuit Court of Appeals in a case challenging allocation of funding under the Coronavirus Aid, Relief, and Economic Security Act (CARES). Congress enacted CARES on March 27, 2020 in response to the covid-19 pandemic. While the district court had previously found the case unreviewable, the Circuit Court reversed the lower court's holding.

Title V of the CARES Act appropriated $150 billion for "making payments to States, tribal governments, and units of local government [for] necessary expenditures incurred due to the public health emergency," with payments to be made within 30 days of enactment. Eight billion dollars of the $150 billion were reserved for payments to Tribal governments, as determined by Treasury Secretary, Steven Mnuchin, in consultation with the Secretary of the

Interior and Indian Tribes. Funding allocation was determined by the Indian Housing Block Grant (IHBG) program, which does not reflect actual tribal enrollment. Thus, the decision to use these data were found to have an adverse impact on the Shawnee Tribe such that they received only the minimum payment for tribes with a population of fewer than 37 ($100,000) though they counted 3,021 enrolled members and expenditures of $6.65 million in 2019. The Tribe claims that they made multiple attempts to correct the mistake, including seeking help through members of Congress, but were unable to do so. Shawnee Chief Ben Barnes noted that the $100,000 allocated under the CARES Act based on the faulty population data would not even cover the first order of protective equipment and the salary for a public health officer. "They treated us as if we didn't exist," Barnes said.

The Tribe contended that Secretary Mnuchin acted arbitrarily and capriciously, thereby unlawfully violating the Administrative Procedure Act by using IHBG population data rather than other available data and by refusing to adjust what the Tribe identified as errors in the IHBG data. Emphasizing the Secretary's discretion, the district court denied the Tribe's motion for a preliminary injunction, asserting that Mnuchin's decision to use IHBG data was not renewable under the Administrative Procedure Act, though they acknowledged that the Shawnee Tribe would suffer harm.

In response to the lower district court holding, the Shawnee Tribe urged the DC Circuit Court of Appeals to find that Secretary Mnuchin's funding allocation methodology based on IHBG data in fact ran afoul of the Administrative Procedure Act. The DC Circuit panel held instead that the district court should consider the challenge on the merits.

—Miranda Yaver, PhD

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