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BRIEF19

A daily review of covid-19 research and policy

RESEARCH BRIEFING

Russian Sputnik V vaccine data released.

Late 2020 and early 2021 has been marked by good news on the SARS-CoV-2 vaccine front, and bad news on almost every other aspect of the covid-19 pandemic. This week in [The Lancet](#), Russian researchers released results of the Gam-COVID-Vac, affectionately known as “Sputnik V.” Early media reports in Russia, where the trial occurred, were positive and the results, which provided data from the Phase 3 trials seem to confirm that hype and hope.

The Sputnik V vaccine is based on a reconfigured adenovirus, which unless altered, is a cause of the “common cold.” This is the same method employed by the [AstraZeneca/Oxford](#) and [Johnson & Johnson](#) vaccines, which have previously released positive data. Nearly 22,000 study participants came from 25 hospitals and clinics around Moscow and were slated to receive two doses 21 days apart. The average of participants was 45 years, and 98.5 percent were White. As with the other vaccine trials, participants were initially screened for covid-19 by PCR and antibody testing. The primary outcome tested was whether participants had covid-19 symptoms and a positive SARS-CoV-2 PCR test 21 days after receiving the first dose.

Vaccine efficacy was determined to be 91.6 percent and only 0.1 percent of those who received the vaccine tested positive for the coronavirus on the 21st day. Effectiveness against severe covid-19 was 100 percent. A scant number of serious adverse events were recorded, and in fact, the placebo group had more than the vaccine group—0.4 vs 0.3 percent, respectively. Four deaths occurred, none of which were attributable to the vaccine.

The demographics of persons included in the study population was rather homogenous, which is not unexpected given the country of origin. It is particularly interesting that despite the trial design to assess a two-dose regimen, the data still showed great efficacy against covid-19 after just the first dose. This would be an important consideration in resource poor countries where a single dose would be more cost effective and be easier to administer. Based on these interim results, it appears the world has another vaccine to use in the fight against covid-19.

—*Christopher Sampson, MD, FACEP*

Mix-and-match dosing regimens could ward off coronavirus variants.

Russian researchers released Phase 3 [data](#) from the Sputnik V vaccine trial (as per above), indicating an efficacy of 91.6 percent. Although this vaccine will not be available in the United States, these data underscore the importance of having more vaccines globally and the value of what scientists call “heterologous dosing regimens.” A [heterologous prime-boost](#) is a “mix and match” vaccine dosing schedule, in which the immune response is primed with a first shot of one type of vaccine and then boosted with a different vaccine. In this case, researchers used two different vaccines based on adenoviruses.

Both the AstraZeneca/Oxford and Sputnik V vaccines use adenoviruses (which are a family of DNA viruses that cause common colds) as “vectors.” Once injected, these vectors deliver the genetic code for the SARS-CoV-2 spike protein into our cells which then make that protein, eventually triggering an immune response. There are many different adenoviruses, and they can be engineered to safely deliver genes to a recipient via injection. However, it is important to understand that adenoviruses are *themselves* viruses. So, the immune system will also mount a response to the virus itself, not just the eventual spike protein it codes. Something called vector immunity can develop, meaning that the body creates a defense not just against the

SARS-CoV-2 spike protein that has been engineered into the virus, but the rest of the virus itself. In effect, the virus is a trojan horse delivering the code for the SARS-CoV-2 spike protein, and the body's immune system does not let the trojan horse in a second time. This means that subsequent boosters that use the very same adenovirus vector to carry the SARS-CoV-2 spike might be blocked, thereby preventing the second round of spike protein production that is meant to trigger the body to make antibodies. This could also explain why the full two-dose regimen of the AstraZeneca/Oxford vaccine (also an Adenovirus-vector vaccine) performed less well than regimens in which a half-dose was given the first time.

The Sputnik V vaccine uses two different adenovirus-vector vaccines: Ad26 and Ad5. Any antibodies that develop against the prime Ad26 vector will not subsequently block a booster that is riding on an Ad5 adenovirus. This is notable because the Johnson & Johnson vaccine—which could soon receive an Emergency Use Authorization from the US Food and Drug Administration in the coming weeks—is an Ad26-based vaccine. Its efficacy might be improved with a boost. While a two-dose regimen is still in trials, we very well might anticipate potential issues with vector immunity.

As vaccine manufacturers have announced plans to develop boosters for the variants, we should begin to look at “mix-and-match” boosting strategies that use a combination of vaccine platforms. For example, it may be possible to mix the active components of the Pfizer or Moderna vaccines with a boost that uses another vaccine platform. Such an approach may also improve the side effect profile. This would also help with some logistical issues, as individuals may be able to get a boost from any number of options, allowing them to receive any appropriate vaccine that is available to them. Currently, these data for heterologous “mix-and-match” dosing across platforms and manufacturers are not available, but they have important implications for adapting to new emerging coronavirus variants, and for flexible and equitable vaccine access.

—Angela Rasmussen, PhD

POLICY BRIEFING

Covid-19 will not delay the start of 2021 Major League Baseball season.

While some baseball stadiums are currently being used as covid-19 vaccination sites, they'll soon be used for something else: the start of major league baseball season in the US.

Major League Baseball (MLB) announced on Monday that the 2021 season will not only start on time but will allow a limited number of fans in the stands, risky though that may be. In order to attend a baseball game, fans won't need a covid-19 test, proof of vaccination, or a temperature check. All attendees will need to do is sit at least six feet apart from other attendees and wear masks unless eating or drinking. MLB has additionally added a “buffer zone” around the dugouts, meaning that fans will not be allowed to sit in the first three rows unless a team puts up a Plexiglass-type barrier.

Government officials from eight “Cactus League” (the name of the MLB spring training that takes place in Arizona) cities sent a letter to MLB asking that spring training currently scheduled to begin in mid-February be delayed due to the high rate of coronavirus infections in Arizona's Maricopa County. “[In] view of the current state of the pandemic in Maricopa County – with one of the nation's highest infection rates – we believe it is wise to delay the start of spring training to allow for the covid-19 situation to improve here,” officials said.

MLB initially discussed shortening the regular season and delaying the start by a month in order to give the country more time to vaccinate the population, believing that a delay was baseball's best hope for a successful season with more fans in attendance later in the year. However, the player's union rejected this plan in favor of playing the full 162 game season and reverting to pre-pandemic baseball rules, meaning that temporary changes that included

expanded playoffs, seven-inning double headers, starting extra innings with a runner on 2nd base, and no designated hitters in the National League will be eliminated. (This all came as news to *Brief19*'s editor-in-chief).

As of now, fans can begin attending games in-person as early as the opening of spring training, beginning February 27. This news comes as the United States continues to experience over 100,000 new coronavirus cases per day, with over 90,000 people currently hospitalized.

—*Miranda Yaver, PhD*

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