Week in Review: 28 December – 1 January 2020

BRIEF19

A daily review of covid-19 research and policy.

RESEARCH BRIEFING

Moderna vaccine phase III trial results released in *New England Journal of Medicine.*

The phase III randomized double-blinded multi-center trial of the Moderna vaccine against SARS-CoV-2 has now been published. The trial enrolled 30,420 volunteers, randomly assigned to receive either two doses of the vaccine 28 days apart or a placebo injection. None of the study subjects who received the vaccine developed severe covid-19 (needing hospitalization). Among volunteers who received the mRNA vaccine, only 11 out of 15,210 developed covid-19, versus 185 out of 15,210 in the placebo group. This means that the vaccine was 94.1 percent effective in preventing covid-19 illness (though we do not know whether infections were prevented). Severe illness was only detected among test subjects in the placebo group, another promising sign. Subjects older than 65 years and those who had evidence of previous coronavirus infection also fared similarly.

Of note, an assessment of outcome 14 days after the first dose indicates early effectiveness. However, we do not yet know whether one dose would provide long-lasting immunity, which means that for now, the two-dose strategy must be continued. Data given to the FDA earlier this month suggested that one dose provided 92 percent efficacy compared to placebo, but only out to 28 days. Much longer follow-up is needed on this aspect in particular.

Side effects have been a closely watched area. Soreness or pain at the injection site was equally frequent in those who received the vaccine and those who received the placebo. Those who received the vaccine were more likely to report fever and generally feeling ill. No severe adverse events were reported in either group.

The Moderna vaccine (mRNA-1273) is a lipid nanoparticle that contains mRNA that encodes the virus's spike protein. The Moderna and Pfizer vaccines were developed using a novel strategy, using mRNA instead of a weakened, killed, or gutted virus, which are the usual mechanisms of action for vaccines in use for a variety of other diseases. Both the Moderna and Pfizer vaccines include the genetic code for just one part of SARS-CoV-2, the spike protein. Once injected, the human cells create that single viral protein (but not the 28 other proteins that would be needed for a complete and infectious viral particle) which is then recognized as "unusual" by our own immune systems. That our bodies "know" to turn around and make antibodies to a protein that it just manufactured itself is one of the remarkable achievements of our own immune systems. The rationale is that including part of the virus might limit side effects such as rash, fever without reducing effectiveness. Also, using mRNA instead of DNA eliminates the chance of the viral genetic material being incorporated a person's own DNA.

These results demonstrate that the Moderna vaccine is safe to administer and effective at preventing covid-19 serious enough to require hospitalization. It cannot assess for adverse events that occur more rarely than in 1 in 15,000 patients nor does the study speak to whether the vaccine reduces other complications such as an increased risk of blood clots in the lungs or persistent neurologic or psychiatric changes. The study did not analyze if there was a difference in vaccine efficacy for different strains of SARS-CoV-2, though experts believe that there is little cause to worry that it would not be effective against new strains such as the B.1.1.7 mutant which has now been detected in the US. *31 December 2020*.

—Michael Chary, MD PhD

B.1.1.7, A new variant of covid-19, isn't kidding around. What we know about a fast-spreading mutant and its effect on children.

Viruses mutate by changing their genetic code. SARS-CoV-2, the virus that causes covid-19, is no exception. The CDC estimates that any particular SARS-CoV-2 strain will acquire a new mutation around every two weeks. Not all of these mutations to viral genes will be evident to scientists, however. That is, unless the mutations change the structure of the virus itself, altering its efficiency, infectivity, and the severity of disease it causes, no one is likely to notice or even care when they occur. But when a mutation does cause a noticeable change in how the virus operates, we become acutely interested in understanding it.

On December 20th, a "new" strain of the SARS-CoV-2 started making global headlines. Public Health England (an agency in the United Kingdom which carries out many of the functions that the US Centers for Disease Control and Prevention does in the US) emphasized that this new version of the virus does not seem to cause more severe disease nor higher mortality rates. The concern is that this variant spreads faster than the "usual" strain of SARS-CoV-2. It also appears that children are more susceptible to this iteration, which has ramped up concerns but in the UK and around the world.

The rate of transmission for this new mutant—known as B.1.1.7—is 71 percent higher than seen among typical other viral variants of SARS-CoV-2. This is likely due to the strain's enhanced ability to find and enter human cells.

Children have never been immune to the novel coronavirus, but when kids come into contact with it, the virus less frequently enters the lungs and causes less significant disease, owing to differences between the respiratory tracts (as covered in *Brief19*) and lungs of children and adult. Changes in B.1.1.7 viral variant apparently make it easier for the virus to circumvent the advantages children have had in staving off clinical impactful covid-19 disease. The concern is that this new virus could cause symptoms and complications more frequently, though that has not yet been determined.

While the B.1.1.7 variant has been most closely tracked in the United Kingdom so far, is probably already in the United States. It started spreading back in September, though researchers did not begin to understand its enhanced features until more recently.

Before you panic, it is important to remember sly mutations like this are a typical part of the viral playbook. Also, the vaccines being rolled out were developed to account for the likelihood that small shifts in viral proteins would occur. Therefore, the current versions of the vaccines are likely to retain their ability to neutralize the virus and prevent most disease. However, this strain may yet change how most people view children as viral vectors and force policymakers to reassess safety in schools. One thing is certain: no mutation can evade the effect of the simple public health measures that experts have been emphasizing. Make it your New Year's Resolution to maintain safe physical distancing, wash your hands, and wear a mask. These precautions can still outsmart this prevalent pathogen, no matter how many mutations it accrues. *28 December 2020*.

—Joanna Parga-Belinkie, MD

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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.