Week in Review: 14 – 18 December 2020

BRIEF19

A daily review of covid-19 research and policy.

RESEARCH BRIEFING

Covid-19 and pregnant women—to vaccinate or not to vaccinate?

As is the case with many medicines, the question of covid-19 vaccine safety for pregnant women is now coming to the forefront as vaccines are starting to receive emergency authorization from the Food and Drug Administration.

Should pregnant people vaccinate? It is a complicated question, but fortunately the new vaccine technology being utilized by Pfizer/BioNTech and Moderna may offer specific benefits for such women. Of course, the underlying context to this question is our knowledge that pregnant women have fared worse with covid-19. This fact must be taken into account.

The race for vaccine distribution is now on. The Pfizer/BioNTech vaccine has already received Emergency Use Authorization (EUA) and Moderna's candidate is likely not far behind. Unfortunately, neither trial (which included 30,000 participants in each) was designed or intended to be conducted with pregnant women. Such exclusions are standard practice for obviously reasons. However, in the Pfizer trial, 12 participants who received the vaccine *became* pregnant between the first and second doses. So far, no adverse events have been reported. Incidentally, two of the 11 women in the *placebo* arm who became pregnant had miscarriages. However, the follow-up time is still too short to determine outcomes of the pregnancies or the fetuses themselves. This will be watched closely in the coming months.

Nevertheless, what sets these two vaccines apart is that they use messenger RNA (mRNA), which is a "novel" vaccine approach. While science and medicine have never used this particular method of vaccine delivery before (i.e. there are no vaccines for other diseases that work on the same biological principles), this technology has distinct advantages; they actually mimic how our bodies' own biochemical machinery works. In essence, the mRNA in the vaccine acts as a recipe card of sorts, telling our cells to manufacture a small part of the virus (the spike protein), to which the body then develops its own immune response. By comparison, some of our traditional vaccines are called "live" vaccines, meaning that a weakened version of a virus is injected into a patient to create the immune response. Unfortunately, these vaccines are specifically contraindicated for pregnant patients due to the theoretical risk of infecting the fetus. With mRNA delivery this shouldn't be a problem. That means that the mRNA technology is also a potential breakthrough for a slew of other viruses that pregnant women may want to take in the future, if and when such options become available.

In fact, The Society of Maternal and Fetal Medicine (SMFM) issued a statement reporting that the risk of the mRNA vaccine appears low. Furthermore, the statement even mentions that the mechanism used in AstraZeneca's vaccine is similar to that of an Ebola vaccine (*not* mRNA, but rather a "viral vector," as described above), which also has thus far had an, "acceptable safety profile" during pregnancy.

It should also be noted that for lactating women, mRNA is likely too fragile to reach the breastmilk. If any of the resulting protein were to be ingested by a child, it would simply be digested like any other protein. As a result of this, the SMFM recommends individuals be offered the SARS-CoV-2 vaccine and the decision to receive the vaccine should be guided by an individual's risk of contracting covid-19 and other individual factors. *14 December 2020*. *—Lauren Westafer, DO, MPH, MS*

Tocilizumab not the blockbuster drug for patients with covid-19 pneumonia as hoped.

A new randomized clinical trial published in *The New England Journal of Medicine* looks at the efficacy of tocilizumab for patients hospitalized with covid-19 when given in combination with remdesivir, a now-approved though underwhelming covid-19 treatment. Tocilizumab is a "monoclonal antibody" that targets receptors in our immune system called interleukin 6 (IL-6). IL-6 plays an important part in the body's

inflammatory response and suppressing its action was hoped to combat counterproductive immune activity mounted by our own defenses.

In this study of 328 patients hospitalized with covid-19 and evidence of pneumonia, patients were randomized to receive standard of care treatments plus one or two doses of either tocilizumab or a placebo. The primary outcome of the study was a meaningful one: how long it was before mechanical ventilation (i.e. intubation) was necessary or death by day 28.

Patients were less likely to progress to mechanical ventilation *or* death by day 28 in the tocilizumab group (12 percent) compared to the placebo group (19.3 percent). In addition, only 8.6 percent of patients in the placebo group died compared to the 10.4 percent in the tocilizumab group; however, this difference was not statistically significant, meaning that it's impossible to rule out that chance alone accounted for that difference. A slightly higher number of patients in the placebo group received steroids (which have been proven to lower mortality in patients with serious covid-19 illnesses) compared to the tocilizumab group, though it is uncertain whether this contributed to fewer deaths in the placebo group. There are some patients in whom steroids help, and others it may hurt. We don't know enough about the breakdown of the patients in this study to glean that information. Length of stay in the hospital, another important outcome that patients tend to care about, was not statistically significantly different between groups. Tocilizumab appears safe as serious adverse events were not significantly different between the study groups.

In summary, tocilizumab appears to be safe and *might* prevent patients from progressing to requiring mechanical ventilation, though the total effect appears to be small. Overall, tocilizumab seems slightly less effective than remdesivir, which has been shown in one major study to reduce hospital length of stay. It is unlikely that this randomized clinical trial will significantly change current practice. *18 December 2020.* *—Joshua Niforatos, MD, MTS*

Female physicians less likely to be interviewed by cable news for covid-19 related content. While women represent a growing proportion of physicians and medical school faculty (41 percent currently), it seems that cable news networks have missed the memo. An article published this week in *JAMA Internal Medicine* found that female physicians were less likely to be interviewed on Fox News, CNN and MSNBC related to the covid-19 pandemic. The study assessed patterns during "primetime." The investigators obtained data from 220 guest speakers discussing covid-19. Only 30 percent of those speakers were women and they were allocated just a quarter of the total speaking time. Fox News was much less likely to have women speak on covid-19 compared to CNN and MSNBC. With respect to physicians, Fox News had *zero* experts speaking during primetime during the five-week inclusion period between May and June but did interview some women PhDs and a nurse. More specifically, of the 220 speakers, 47 were physicians, of which only 12 were women. The women were allocated only 15.5 percent of primetime programming time. In the non-physician PhD group, only 6 percent of speakers were women and were allocated only 15.1 percent of primetime programming time. The results of this study are informative and disappointing. During the peak of the pandemic, cable news networks were less likely to interview females regarding information related to covid-19. In addition, this study did not assess racial or ethnic differences, the results of which would likely be sobering as well. There really is no reason for this other than bias, or other related factors related to sexism in the workforce. Better female physician representation is needed and going forward. The television networks should address this. *16 December 2020.* *—Joshua Niforatos, MD MTS, Research Section Editor.*

Kane Elfman PhD, Publishing and design. *Anna Fang, Week in Review.*
Jeremy Samuel Faust MD MS, Editor-in-Chief.

http://www.brief19.com/ *Twitter: @brief_19* *submissions@brief19.com*

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.