COVID-19 vaccine boosters mix and match: What the evidence shows

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Patients have more options than ever before to protect against COVID-19. Boosters are now available for the three COVID-19 vaccines, made by Pfizer-BioNTech, Moderna and Johnson & Johnson. And the Centers for Disease Control and Prevention (CDC) has given the green light for safely mixing and matching the shots.

COVID-19 vaccines continue to protect against severe disease, hospitalization and death, but studies show waning immunity over time, noted Sandra A. Fryhofer, MD, the AMA’s liaison to the CDC Advisory Committee on Immunization Practices (ACIP) and a member of ACIP’s COVID-19 Vaccine Workgroup.

With the Delta variant on the scene and concerns over new variants emerging, “it’s important to keep antibody levels high,” said Dr. Fryhofer, chair-elect of the AMA Board of Trustees. Mixing and matching boosters will increase options for physicians and patients and enhance vaccination programs, she added.

Early study results demonstrate that boosters work effectively against some of the stronger variants. Dr. Fryhofer drilled down on these findings and the safety of mixing and matching boosters in an episode of the “AMA COVID-19 Update.”

Ongoing trial supports mix and match

A clinical trial that’s evaluating mixed COVID-19 vaccine regimens in 450 patients found that boosters from all three vaccines increased neutralizing antibody titers, irrespective of the kind of booster or primary vaccines series used.
The study, funded by the National Institute of Allergy and Infectious Diseases, isn't powered to compare which booster combinations work best, but the initial findings are interesting, said Dr. Fryhofer.

The two mRNA vaccines seemed to do a better job of boosting than the J&J shot, triggering stronger antibody responses. All boosters worked well in neutralizing Delta and Beta variants. No new safety concerns have emerged so far, and reactogenicity and adverse events have been similar across boosters.

“This is very reassuring,” said Dr. Fryhofer.

**All booster strategies work**

The CDC doesn't specify which kind of booster to give to patients, said Dr. Fryhofer. This is not an oversight—the bottom line is you can boost with any of the three COVID-19 vaccines. It doesn't have to match the primary series shot, she clarified. This is called heterologous boosting, whereas boosting with the same type of vaccine is called homologous boosting. “Either strategy is permitted,” she said.

The AMA recognizes the critical importance of scientific integrity, transparency and public trust in the fight to contain the global spread of COVID-19. Stay updated with the AMA on COVID-19 and vaccine development.

**Dosage varies among MRNA vaccines**

Eligibility, dosage amounts and time frames vary among the three COVID-19 vaccines.

The booster recommendation for Moderna is the same as Pfizer, the other mRNA vaccine. Boosters only apply to certain adults at least six months after a two-dose Moderna primary series. Patients must be 65 years old, have underlying health conditions, or work in a high-exposure job or living condition to qualify.

Where the two mRNA vaccines differ is on dosage. Pfizer requires the full 30-microgram dose. For Moderna, 50 micrograms, or half a dose, is enough to boost immunity.
J&J calls for shorter timeline

Anyone 18 or older who received the J&J primary series shot should get a booster two months after the original shot.

J&J has shown lower effectiveness compared with the mRNA vaccines, said Dr. Fryhofer. However, a company study from Janssen, its manufacturer, found that two doses given two months apart increased vaccine effectiveness from 70% to 94%. The Food and Drug Administration has yet to verify this data.

Vaccine booster administration relies on an honor system, said Dr. Fryhofer. If someone says they’re eligible, they’ll probably get a booster.

News reports indicate that people 40 or older might be next in line to receive a booster. However, “there’s nothing official yet from FDA,” she cautioned.

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