What you need to know about COVID-19 vaccines with Sandra Fryhofer, MD

Featured topic and speakers

This comprehensive update from internal medicine specialist Sandra Fryhofer, MD, AMA trustee and the AMA liaison to the Centers for Disease Control and Prevention’s Advisory Committee on Immunization Practices, includes:

- A brief historical review.
- COVID vaccines currently available and who should get them.
- Expected vaccine side effects & more serious adverse.
- Virus variants of concern.
- Additional doses for immunocompromise and where we stand on boosters.
- Equity: Vaccine access and addressing vaccine hesitancy.
- Strategies for productive conversations about vaccination.

Find out the four keys for doctors to know on Pfizer COVID-19 vaccine booster and watch a recent episode of the “AMA COVID-19 Update,” with Dr. Fryhofer about the Pfizer COVID-19 vaccine booster shots. Learn more at the AMA COVID-19 resource center.

Speaker

- Sandra Fryhofer, MD, chair-elect, AMA Board of Trustees; AMA's liaison to the Advisory Committee on Immunization Practices

Transcript

Unger: Hello, I'm Todd Unger, AMA's chief experience officer in Chicago. The American Medical Association has been dedicated to providing physicians with timely up-to-date information throughout the pandemic. In the following program, brought to you in partnership with the Medical Society of the District of Columbia, vaccine expert Dr. Sandra Fryhofer explains what physicians wish patients knew about COVID vaccines. This broadcast provides comprehensive timely information on COVID vaccines for physicians. For more great content from the AMA, be sure to visit ama-assn.org/podcasts


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Dr. Fryhofer: Hello, I'm Dr. Sandra Fryhofer. I'm a general internist in private practice in Atlanta, an adjunct associate professor of medicine at Emory. I'm chair-elect of AMA Board of Trustees and serve as AMA's liaison to ACIP, the CDC's Advisory Committee on Immunization Practices. I'm also a member of ACIP's COVID vaccine workgroup. It's my great pleasure to present this update on what you need to know about COVID-19 vaccines.

Here's the plan. First, we'll set the stage with some historical highlights and equity issues. We'll then review COVID vaccines currently authorized or approved, as well as who should get them. We'll talk about side effects to expect and risk of more serious adverse events to look for. Next, Delta. Other variants of concern and who needs additional vaccine doses. We'll then circle back to vaccine hesitancy and how address it. Let's get started.

We're in a race against time and the variants to get everyone vaccinated. But having a vaccine won't end this pandemic if people aren't willing to take it. Vaccine hesitancy is not new. Early in the pandemic, themes from focus group discussions with frontline workers and traditionally underrepresented groups included concerns about the process, distrust of government, distrust of the health care system, concerns that politics and economics will be prioritized over science, fear based on past experiences and fear that the vaccine will not work for me or my community.

Minority populations have been devastated during the COVID pandemic. In a recent New England Journal of Medicine perspective, Sandra Quinn and colleagues address reasons for vaccine hesitancy in BIPOC communities. BIPOC stands for Black, Indigenous and people of color. Vaccination hesitancy does not mean vaccine refusal. The authors highlight broad systemic challenges, including an equitable distribution of vaccine doses and failure to place vaccination clinics in easy to access places. Online registration is also a disadvantage if you don't have access to technology. Barriers including work obligations, limited childcare options can make it harder to chase down vaccination appointments. Systemic racism and provider bias also play a role.

We must ensure institutions are trustworthy, transparent and engaged with communities. The authors also included a 'train the trainer' section with many commonly asked questions. They dispel this rumor. mRNA COVID vaccines will not give you COVID. They don't affect fertility for males or for females. They don't contain fetal tissue. They don't contain microchips or any other devices. That said, let's move on and answer the other questions. The first alert occurred New Year's Eve, December 31, 2019 with a mysterious cluster of pneumonia cases in Wuhan, China. Less than three months later, we had a global pandemic.

Enter, Operation Warp Speed. In less than a year, we had three safe and highly effective COVID vaccines. This is truly a remarkable achievement. To review, SARS-CoV-2 is the name of the virus. COVID-19 is the disease caused by it. The virus has protein spikes on its surface, a corona, a crown.
These spike proteins are the main target for vaccine development. Both Pfizer/BioNTech's mRNA BNT162b2 COVID vaccine and Moderna's mRNA-1273 COVID vaccine are nucleic acid vaccines. Both contain messenger RNA, which instructs the body's own cells to make the protein antigen, the COVID-19 spike protein, which then triggers the immune response. mRNA vaccines are somewhat new. For licensing this was uncharted territory. There had never, ever been a vaccine licensed by FDA, which used a nucleic acid platform.

So mRNA vaccines were new but not unknown. Researchers had been studying them for decades. Early stage clinical vaccine trials for flu, zika and rabies used mRNA vaccines in the past. In early January 2020, Chinese researchers posted the genetic sequence of this new coronavirus on the internet. mRNA vaccine companies got started right away and thanks to research on SARS back in 2002, and then MERS a decade later, scientists knew to focus on the spike protein. They knew how to purify the mRNA and how to stabilize it and protect it from degrading too quickly. The secret, a protective lipid nanoparticle coating. mRNA vaccines have been under great scrutiny. Because they were a new type of vaccine, many worried about safety. CDC guidance has been reassuring. mRNA vaccines do not contain live virus. They can't cause an infection. They can't give someone COVID.

mRNA vaccines do not affect or interact with our own DNA in any way. The messenger RNA never enters the nucleus of the cell. It doesn't hang around. The body breaks it down within hours. Trials for both mRNA vaccines enrolled diverse populations, including race, ethnicity and age, both young and old. They included patients with underlying medical conditions, most commonly obesity, diabetes and lung disease. Studies also included patients with stable HIV, Hep B and Hep C. Patients with immunocompromising conditions were excluded. Both companies disclosed details on diversity of their participants on their websites. They published their protocols online. Pfizer/BioNTech phase three, double-blinded placebo controlled trial enrolled about 44,000. Moderna's phase three trial enrolled more than 30,000 participants.

Tuesday, December 8, 2020, was V-Day in Great Britain. As COVID cases in the U.S. topped 15 million, the U.K. started vaccinating. On December 11, 2020 near the stroke of midnight, mRNA vaccines had their Cinderella moment. Pfizer/BioNTech's mRNA vaccine got the green light for those aged 16 and older and became America's first COVID vaccine and the first mRNA vaccine ever to win FDA's emergency use authorization. Two doses of Pfizer vaccine given 21 days apart were 95% effective at preventing COVID. One week later on December 18, FDA authorized emergency use of a second COVID vaccine, Moderna's mRNA vaccine for those 18 and older. Two doses of Moderna vaccine given 28 days apart were 94.1% effective at preventing COVID.

America's V-Day was December 14, 2020. That's the day we started putting vaccine into arms. First there was Pfizer. Then Moderna. Both are mRNA vaccines. Each requires two doses. Both were more than 90% effective. On February 27, 2021, Janssen's single-dose 'one dose and you're done' viral vector vaccine became number three. Janssen is the pharmaceutical arm of Johnson & Johnson.
Janssen's Ad26.COV2.S vaccine was authorized for emergency use in those 18 and older. It uses a completely different technology platform. With viral vector vaccines, you take a weakened version of a virus, which is the viral vector, then genetically engineer it to make coronavirus spike proteins in the body, which then trigger an immune response. Janssen's vaccine uses a modified cold virus, an adenovirus called Ad26 as its viral vector. Several genes have been removed from it, making it replication incompetent, so it cannot multiply in the body. The genes in the vaccine cannot incorporate into human DNA. The virus is basically dead.

The vaccine cannot give someone COVID. Janssen's COVID vaccine was 66.3% effective overall at preventing symptomatic COVID just 14 days after a single dose. It maintained at least 63% effectiveness across age, sex, race and ethnic categories. And also for those with underlying medical conditions. Janssen's phase three study included more than 40,000 participants spanning three continents and eight countries. It was effective across world regions like Brazil and South Africa, where variants of concern had already emerged. Efficacy did vary geographically. Highest in the U.S., 74.4% effective and lowest in South Africa at 52% where Beta, the B135i variant, dominated. There was a large body of research supporting Janssen's vaccine platform. More than 193,000 people, including patients of different age groups and conditions, elderly, children, as well as pregnant and lactating persons. They all had been vaccinated with Ad26-based vaccines during studies of vaccine candidates for Zika, HPV, RSV and HIV. In July 2020, an Ad26-based Ebola virus vaccine was approved in Europe.

Now, for differences in vaccine transportation and storage. Pfizer/BioNTech’s vaccine has complicated cold chain storage challenges. It has to be stored frozen, ultra-cold, in super freezers at -70°C, making vaccine distribution and administration cold, complex and somewhat cumbersome. Most physician offices don’t have access to these super freezers. Moderna's also stored frozen but at regular freezer temperatures around negative 20°C. Its cold chain requirements are much more user-friendly. Moderna’s vaccine can remain stable at 2°C to 8°C. The temperature of a standard refrigerator for up to 30 days and at room temperature for up to 12 hours. Both mRNA vaccines must be thawed before going into arms.

Pfizer’s vaccine has to be reconstituted. Modern does not. Neither does Janssen's. Janssen's viral vector vaccine has several advantages that make it convenient. Storage is much, much easier. Unlike for Pfizer, no fancy super freezers are needed. Janssen vaccine can be transported and stored for up to three months at regular refrigerator temperatures, 2°C to 8°C. Janssen doses don’t need dilution, which means one less step before putting vaccine into arms. Temperature and storage requirements, as well as vaccine expiration dates for all three vaccines keep changing as more study confirms vaccine stability. So be sure to check for the most up-to-date recommendations.

We now have three safe and highly effective COVID vaccines. There was diversity in trial participants for all three vaccines. There was transparency in the process. There's also been close post-
authorization safety surveillance. CDC monitors vaccine safety in several different ways. All look at safety data a little bit differently. VAERS, CDC's Vaccine Adverse Event Reporting System is a passive reporting system, meaning it relies on individuals to send in reports of their experiences. Anyone can submit a report to VAERS, including physicians, parents, patients and friends. VSD, CDC's Vaccine Safety Data link is a collaborative project between CDC and nine integrated health care organizations scattered throughout the country. CISA is CDC's Clinical Immunization Safety Assessment project and consists of seven participating medical research centers with vaccine safety experts. V-safe was created with the COVID vaccine rollout. It's a new smartphone-based tool that uses text messaging and web surveys to give personalized health check-ins after you receive a COVID vaccine.

Fast forward to May 2021, a belated Mother's Day present from FDA extended Pfizer vaccine EUA, emergency use authorization, to children 12 to 15. And on August 23, 2021, Pfizer/BioNTech's COVID vaccine received full FDA approval for those 16 and older. EUA, emergency use authorization, still applies to kids 12 through 15. Emergency use authorization is also in place for an additional mRNA vaccine dose for immunocompromised patients who received a two-dose mRNA vaccine series. Now we'll talk more about this later. EUA, emergency use authorization, is based on the best available evidence. FDA was transparent and made its requirements very clear. Full FDA licensing requires submission of a BLA, a biologics license application. FDA then reviews all this data with a fine tooth comb. Decision is based on substantial evidence.

Full FDA approval is a rigorous process. Next side effects. And most of us already know what that means. Getting a dose of COVID vaccine is no walk in the park, especially for the second mRNA vaccine dose but for full protection, you need that second dose. For Janssen, one dose and you're done also means only one set of side effects. Reactogenic side effects are similar for all three COVID vaccines. Expect mild to moderate, local and systemic reactions: pain, swelling, redness at the injection site, as well as localized axillary lymphadenopathy on the same side as the vaccinated arm. Expect fever, fatigue, headache, chills, muscle aches and joint aches. You may have to skip work the day after vaccination. Reactions are more intense after the second dose. Symptoms are also worse in younger as compared to older patients. But you can think of these symptoms as a sign the vaccine is working. The good news is symptoms seem to resolve within one to three days.

Another new convenience, COVID vaccines can now be co-administered with other vaccines but please consider vaccine reactogenicity of the other vaccine, especially for shingles vaccine and tetanus boosters. Let's compare vaccine ingredients. None of the available COVID vaccines contain egg, gelatin or metals. The stoppers of vaccine vials are latex free. Polyethylene glycol, aka PEG, is an ingredient in both mRNA COVID-19 vaccines. PEG is also the primary ingredient laxatives, including MiraLAX as well as colonoscopy preps including then GoLYTELY, Colyte and MoviPrep. Janssen's vaccine contains no adjuvants, no antibiotics and no preservatives but it does contain polysorbate 80. PEG and polysorbate are structurally related and cross-reactive hypersensitivity
between these compounds may occur. This nice color coded table on the CDC website shows contra-
indications in red and precautions in yellow. mRNA vaccines are contraindicated if you’re allergic to
any of the ingredients. History of an allergic reaction to any vaccine or injectable therapy is a
precaution for vaccination.

Injectable is the keyword here. This does not include allergic reactions to foods, pet dander, venom,
oral medications, latex, egg or gelatin, which are in the green column. For patients with precautions,
CDC suggests clearance by an allergist. People with precautions or any history of anaphylaxis have
to sit and be observed for 30 minutes after vaccination. Everyone has to sit and be observed for at
least 15 minutes. So plan your time accordingly. CDC also says have epinephrin and antihistamines
on hand. People who carry an epinephrine auto-injector should bring it with them. Next anaphylaxis,
several safety updates have looked at anaphylaxis risk. VAERS safety data as of January 2021,
initially reported 11.1 cases of anaphylaxis per million doses administered for Pfizer and 2.5 cases
per million doses for Moderna. A later VAERS update lowered Pfizer's anaphylaxis reporting rate to
4.7 per million doses. This is more consistent with ACIP's August VSD safety update. Five cases of
anaphylaxis per million doses for Pfizer and 4.9 cases for Moderna. Most cases were in females. To
put this in perspective, risk of anaphylaxis after flu vaccination is about one to two per million doses
administered.

Next warnings, TTS, Thrombosis with Thrombocytopenia Syndrome and GBS, Guillain-Barre with
Janssen's viral vector vaccine. Myocarditis with mRNA vaccines. All COVID vaccines have side
effects but these warnings are different. First TTS. Janssen's viral vector vaccine has been linked to
rare types of blood clots in unusual places in combination with thrombocytopenia, really low platelets.
The syndrome has been named TTS, thrombosis with thrombocytopenia syndrome. FDA amended
Janssen's EUA. It warns of increased risk of thrombosis combined with thrombocytopenia occurring
one to two weeks after Janssen vaccination. Women under 50 need to be made aware of this rare
risk and that there are other COVID vaccines available that don’t pose this risk. TTS has not been
seen with mRNA vaccines. These are not the usual types of blood clots. Using heparin to treat them
could be harmful. Patients who’ve had the Janssen vaccine should seek immediate medical attention
if they develop shortness of breath, chest pain, leg swelling, persistent abdominal pain, neurological
symptoms, including severe or persistent headache or blurred vision or petechiae beyond the side of
where they got the vaccination.

For diagnosis and treatment, the EUA references ASH, the American Society of Hematology and
actually links to the ASH website. Consulting a hematologist is advised. Most TTS cases have
occurred in women under 50. However, cases have also been reported in men. As of May 24,
there’ve been a total of 32 confirmed TTS cases out of more than 10.2 million doses of Janssen
vaccine administered. There is risk but the risk is rare. Next GBS, in July 2021, CDC surveillance
revealed another safety signal concern. GBS, Guillain-Barre Syndrome after Janssen vaccination.
There had been around 100 preliminary reports of GBS out of 12.8 million Janssen COVID vaccine
doses administered. Most cases occurred in males, 15 and older, about two weeks after Janssen vaccination. GBS is a rare disorder, which the body's immune system damages nerve cells causing muscle weakness and in severe cases paralysis. Most people recover.

FDA has now amended Janssen's EUA and warns of an increased GBS risk during the 42-day window after Janssen vaccination. Another safety alert, myocarditis, heart inflammation and pericarditis, inflammation of the tissue surrounding the heart, after mRNA vaccines. Reports of myocarditis after mRNA vaccines had increased since April 2021, mostly in young males, 16 and older, several days after vaccination. More often after the second vaccine dose. Symptoms include chest pain, shortness of breath and palpitations. FDA amended EUA for both mRNA COVID vaccines. In its review of Pfizer's BLA, biologics license application, FDA took a rigorous look at risk of myocarditis and pericarditis after Pfizer vaccine. There is an increased risk, particularly within seven days after the second dose. Prescribing information includes a specific warning about this risk. The risk is higher in males under 40 and highest in young males aged 12 to 17. Some of these patients required hospitalization, some required ICU admission. Follow-up so far seems to show resolution of symptoms.

Overall, there've been more than 2,500 reports to VAERS of myocarditis or pericarditis out of more than 350 million mRNA doses administered. CDC and ACIP will continue to monitor cases and their clinical course. CDC is also beginning in enhanced surveillance for myocarditis outcomes after mRNA vaccination. ACIP reviewed all the data and determined the benefits of vaccination clearly outweigh the risk. If you have a patient, friend or family member with myocarditis or TTS or anything else unusual after COVID vaccination, please send a report to VAERS, CDC's Vaccine Adverse Event Reporting System, so they can check it out. Without this reporting, CDC can't know the scope of a potential issue, investigate it and provide communication. And if you do report a case and CDC asks for medical records, send them ASAP. It's not a HIPAA violation. Anyone can submit a report to VAERS. It's not just limited to health care providers.

Given the greater risk of other serious complications related to COVID-19 such as hospitalization, MISC, aka multi-system inflammatory syndrome in children and even death, CDC continues to recommend COVID vaccination for those 12 and older. MISC, multi-system inflammatory syndrome, is a severe hyperinflammatory syndrome that can occur two to six weeks after COVID infection. It can affect both children and adolescents. MISC can infect the heart, lungs, kidneys, brain, skin, eyes and gastrointestinal organs. Children with MISC can have fever, fatigue, abdominal pain, vomiting, diarrhea, neck pain, rash and bloodshot eyes. For MISC patients under age 21, as many as 60 to 70% require ICU admission. One to 2% of them die. As of June 2, 2021, there've been more than 4,000 cases of MISC. The estimated incidents is one in 3,200 COVID infections. More than a third of cases occur in young people aged 12 to 20. The majority of cases are in Hispanic, Latino or Black non-Hispanic children.
Another concern for kids is post COVID conditions. Kids can be long haulers too. Recent studies have shown evidence of new or persistent COVID symptoms in younger age groups. Symptoms include fatigue, insomnia, rhinorrhea, runny nose, muscle pain, headache, lack of concentration, exercise intolerance, shortness of breath and chest pain. As more older adults are vaccinated, young people make up a greater percentage of total cases. At least 33% of COVID cases reported in May were in young people, aged 12 to 29. COVID deaths continue to occur in adolescents and children. As of July 9, there were more than four million cases of COVID in children and at least 335 deaths. As of September 9, the total number of COVID cases in children was even higher, 5.3 million. As CDC director, Dr. Rochelle Walensky emphasized in a recent Senate hearing, 400 children have died from COVID. This is a huge number. Children are not supposed to die.

There is risk of myocarditis after mRNA vaccines but myocarditis can also occur with COVID infection and it occurs at higher rates after COVID infection, then after mRNA vaccination. Patients with COVID had 16 to 18 times higher risk for myocarditis as compared to those without COVID. Risk did vary by age and sex. Risk of myocarditis due to COVID infection was six to 34 times higher compared to those who received mRNA vaccine. New COVID hospitalizations are increasing among young people. CDC says, "Hospitalizations for children are rising as Delta surges." And this visual from the New York times is quite sobering. Two new studies published in MMWR on September 3, looked at COVID hospitalization among children and adolescents. Weekly COVID associated hospitalization rates among children and adolescents rose nearly fivefold from late June through mid-August. Hospitalization rates were 10 times higher among unvaccinated than among fully vaccinated adolescents.

From June to August emergency department visits and hospitalizations increased among kids and teens through age 17. Hospital admission among children and adolescents were four times higher in states with low vaccination rates as compared to states with high levels of vaccination.

The benefits of COVID vaccination for adolescents and young adults clearly outweighs the risk. CDC continues to recommend COVID vaccine for everyone 12 and older.

And with the Delta variant dominant, risk of getting infected with COVID is high.

Next, variants. Variants are wild cards. Vaccine researchers understand this and as long as people keep getting infected new variants will appear. Variants of concern may be more transmissible, cause more severe disease and may be more resistant to vaccines and antibody therapies.

Each variant now has two names. There at least four VOCs, variants of concern, that CDC is watching closely. Alpha B.1.1.7, also called the U.K. variant. Our vaccines work against this one. Next, Beta B.1.351, the South Africa variant. The South Africa variant is one of the most resistant to vaccines. So is the P.1 variant Gamma, first detected in Japan and Brazil. Both B.1.1.7 and B.1.351,
the South Africa variant, are 50% more transmissible. India’s B.1.617.2, aka the Delta variant, now dominates. It was first detected in India in March and it's gone global.

Delta now makes up more than 90% percent of new COVID cases. Delta is a super spreader, it's super transmissible, it's super contagious. It's twice as contagious as previous variants. It's the most contagious variant we've seen yet.

New COVID cases and hospitalizations around the rise. Since July 1, there have been a 700% increase in the seven-day average for COVID cases. We're also seeing more COVID-related deaths.

Even though this variant is hyper transmissible a full vaccination series seem to protect against it but you need both doses of a two-dose series, one mRNA vaccine dose may not be enough. The greatest risk of transmission is still among unvaccinated people but fully vaccinated people with Delta breakthrough infections can also spread virus to others. However, fully vaccinated people with Delta seem to be infectious for a shorter period of time than unvaccinated persons.

A study out of LA County as cases of the Delta variant surge and this study was published in MMWR, showed unvaccinated people had five times more infections and 29 times more hospitalizations from COVID as compared to those full vaccinated.

A study published on September 10 at MMWR shows vaccination offers strong protection against COVID. Data collected after Delta became the most common variant shows the unvaccinated had five times greater risk of infection and more than 10 times greater risk of hospitalization and death as compared to those fully vaccinated.

Delta is also the reasons masks are mostly back on for everyone. CDC says both unvaccinated and fully vaccinated people need to wear masks in public indoor settings and areas of substantial or high transmission, which now is just about everywhere.

Next, why additional doses are now recommended for immunocompromised persons.
Immunocompromised persons were not included in the phase three trials. We now know that COVID vaccines don't work as well in immunocompromised people. Immunocompromised patients are more likely to have breakthrough infections. Studies show 40 to 44% of hospitalized breakthrough cases are in immunocompromised people. Vaccine effectiveness ranges from 59 to 71% in immunocompromised patients, that's compared to 90 to 94% effectiveness in patients who are not immunocompromised. Immunocompromised people make up about 2.7% of U.S. adults, that's about 7 million people. They're more likely to transmit COVID to people they live with as well as other household contacts. Immunocompromised patients are also more susceptible to infection with COVID variants. They're also more likely to stay sick with COVID longer. Prolonged infection gives the virus more time to evolve and mutate, and to transform into new variants.

On August 12, FDA authorized an additional COVID vaccine dose for certain immunocompromised people. This extra dose gives these vaccinated but still vulnerable patients a greater chance of making enough antibodies to protect them from COVID.

But even with this third dose protection's not guaranteed. Immunocompromised patients still need to follow prevention measures such as wearing a mask, practice social distancing and avoid crowds in poorly ventilated indoor spaces. And of course, all close contacts should be fully vaccinated.

The type of vaccine you initially received matters. For immunocompromised persons, ACIP recommends an additional dose of either Pfizer for those 12 and older or Moderna for those 18 and older, following a primary mRNA vaccine series. Get the additional dose at least one month after the primary series and try to get the same type of additional dose as the original series if you can.

The recommendation only applies to those who got Pfizer or Moderna, it does not apply to those who received a single dose of Janssen's viral vector vaccine. The effectiveness of two doses of the Janssen vaccine is being studied, new data about Janssen's durability just published in the New England Journal of Medicine demonstrates strong immune response eight months after vaccination. Pre-print release of this company study of an additional Janssen dose boosting immune response is also encouraging. Safety of a second Janssen dose must also be verified. How this will affect recommendations for immunocompromised adults who receive Janssen's vaccine is still not clear. That said, since Janssen vaccine was authorized much later the number of immunocompromised patients who may have received it is probably small. I look forward to ACIP review of these studies and their possible impact on future recommendations.

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CDC has posted detailed guidance on specifics of who qualifies as immunocompromised on the CDC website. For immunocompromised patients to get the additional dose, it's the honor system. No prescription is needed, a doctor's note is not required and you don't need to check for antibodies. For immunocompromised patients, you just give the additional mRNA dose. Antibody testing post vaccination is not recommended.

At the ACIP meeting the list of immunocompromised patients included active or recent treatment for solid tumor and hematologic malignancies. Patients who've received organ or stem cell transplants. Those with moderate or severe primary immunodeficiency or advanced or untreated HIV infection. Those with chronic medical conditions such as asplenia and chronic renal disease were mentioned at the ACIP meeting but are not on the CDC website. Their omission may be an oversight. In addition, those on active treatment with high dose corticosteroids, meaning 20 milligrams per day or higher, or other immunosuppressive treatments, including alkylating agents, anti-metabolites, tumor necrosis factor inhibitors and other biologic agents that are immunosuppressive should also receive an additional vaccine dose.

We are so fortunate here in the U.S. to even be discussing giving additional doses. So many people around the world have not received even a first COVID vaccine dose and what happens in the rest of the world does effect us. No one is safe unless everyone is safe. The next variant is only a plane ride away. We need to get everyone in the world vaccinated.

Here's where we are today. On Monday, August 23, Pfizer BioNTech mRNA vaccine, aka BNT162b2 became the first COVID vaccine ever to receive full FDA approval, a two-dose series is now fully approved for those 16 and older. Data submitted to FDA had a cutoff of March 13, so much of this data was pre-Delta. The Pfizer vaccine was overall 91% effective in preventing COVID vaccine. Pfizer's full FDA approval for those 16 and older, along with ACIP thumbs up review, which included some post Delta studies, should instill greater confidence in the vaccine’s safety and effectiveness. Pfizer's EUA, emergency use authorization, still applies to those 12 through 15, and for an additional dose for immunocompromised patients who received a two-dose mRNA vaccine series.

Both Moderna mRNA vaccine and Janssen’s viral vector vaccine are authorized under EUA for those 18 and older. Moderna's also submitted data for full FDA approval.

An additional vaccine dose for immunocompromised patients is not a booster, it's part of an augmented primary series when the regular primary series was not protective. A booster is given when protection begins to wane over time.

So what about boosters? Many kinds of booster studies are underway and we'll probably all need a booster eventually. The question is of what and of course when.

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Vaccine effectiveness has seemed to decrease of the last one to two months. Vaccine effectiveness pre-Delta was high, about 87%. Studies done as Delta became dominant show VE against infection is 39 to 84%.

FDA's Independent Advisory Committee plans to meet on September 17 to discuss booster data submitted by Pfizer. Booster protection studies out of Israel will also be reviewed. ACIP has tentatively planned a meeting for the following week, so more to come. The top priority, however, is still to vaccinate those not yet vaccinated.

Question, now that Pfizer vaccine is fully licensed for those 16 and older, and authorized for emergency use in children 12 to 15, can doctors just go off label and vaccinate younger children, those five to 11? FDA says no, you should not. We need to follow the science.

AAP, the American Academy of Pediatrics also says no, please don't. Don't give vaccine off-label to young kids, those under 12. The dose may be different for younger children but all age eligible adolescents should be vaccinated now. And as of August 19, there were 180,000 new COVID cases in children and adolescents.

COVID vaccination is recommended for all pregnant and lactating people. CDC recommends it. So does ACOG, the American College of Obstetrics and Gynecology, and the Society for Maternal Fetal Medicine, they recommend it too.

COVID hits pregnant of women hard, harder than the general population. There's a clear link between COVID and pregnancy complications like preeclampsia, blood clotting problems and still birth.

So far safety studies for people vaccinated during pregnancy have been reassuring. Many women have become pregnant after receiving COVID vaccine.

And if you're breastfeeding, you need to get vaccinated too. Another recent report says COVID antibodies are present in breast milk for at least six weeks after COVID vaccination. These antibodies could protect babies. And remember that none of the three FDA authorized COVID vaccines can cause infection. The vaccines cannot cause infection in mom or in baby.

COVID vaccines do not affect fertility in females or in males. They don't adversely affect sperm. ACOG says claims leaking COVID vaccines to infertility have been scientifically disproven.

COVID vaccination is recommended for those trying to get pregnant now and for those who might become pregnant in the future.

So who are the unvaccinated? This topic has been addressed in several recent articles in the New York Times. They typically fall into two categories, the vehemently opposed and the still on the fence.
Those vehemently opposed the vaccination are mostly white and live in rural areas. They also tend to be Evangelical Christian and politically conservative. Several studies suggest affiliation with the Republican party is one of the best predictors for this group. They're overrepresented in the South and Midwest, and these also happen to be areas of the country with dramatic surges and COVID cases fueled by the Delta variant.

The other groups that still deciding includes a broader range of people, Black men and women, Latinos and some Democrats. This wait and see group tends to be younger and tends to have concerns about vaccine safety, vaccine side effects and the newness of the vaccine. A Kaiser Family Foundation survey found 44% of this group would be more likely to get the vaccine once it's fully licensed by FDA. And remember, Pfizer's now has that approval for those 16 and older.

A professor at the Harvard School of Public Health analyzed the unvaccinated in a different way. His take is we can't rely on a one size fits all approach to convince people to become vaccinated. Vaccine enthusiasts have already been vaccinated. We need develop new methods and techniques to reach those who, for whatever reason, are still reluctant.

Some of what we call vaccination hesitancy could just be vaccination inconvenience. Unvaccinated Hispanic and Black adults are more likely than whites to worry about missing work and having to pay for the vaccine as major reasons for not being vaccinated. They must not realize the vaccine's free for everyone. In addition, unvaccinated Hispanic adults are more likely than unvaccinated white adults to say they're too busy. They have difficulty traveling to a vaccination site or they're not sure where to go to get the vaccine. Some of the unvaccinated are not opposed to vaccination, they may just need a nudge. Many creative incentives, free food, free beer, cash, scholarships, lotteries have been offered to make it happen. Barbershops, hair salons and pop stars have also been enlisted in the COVID vaccination push, those were the carrots.

Next came sticks, mandates. AMA joined forces with more than 50 other major medical organizations calling from mandatory COVID vaccination for all health care workers. We expected to see more companies making vaccination mandatory. Once vaccine was fully licensed by FDA and we have. On September 9, the White House raised an even bigger stick, the president announced COVID vaccine mandates that will affect a hundred million workers, that's about two-thirds of the U.S. workforce. Employers with a 100 or more workers must require the vaccine or conduct weekly COVID testing of unvaccinated employees. They also have to provide pay to time off for getting and recovering from the shot. This mandate does not apply to smaller private businesses, all federal employees and employees of government contractors must be vaccinated. The mandate includes workers at nursing homes and hospitals that receive Medicare and Medicaid funds. The President also called for large entertainment venues to require proof of vaccination or testing for entry. Vaccination mandates are already in effect for the military. Mandates may be here just in time, the COVID surge is putting strain on health care resources. Many states are facing ICU bed shortages, ICU beds are filling up, at least

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16 states are over 80% of ICU capacity.

I want to circle back to racial and ethnic disparities. There have been disparities regarding access to vaccines. Early in the pandemic, Black and Hispanic people received smaller shares of vaccinations compared to their shares of cases and as compared to their shares of the total populations in most states. Much of this is due to historic inequities and discrimination in our health care system. But there is some good news, recent vaccinations are reaching larger shares of Hispanic, Asian and Black populations.

Here's a snapshot of where we are now. This data is from our August 30 ACIP meeting, important strides have been made towards equitable vaccine administration over the course of the COVID vaccine rollout, American Indian and Alaskan Native people now have the highest coverage with more than 50% of the population receiving at least one dose. Coverage among Black people is lower at just under 31%. coverage for white is also lower than it should be but likely for reasons other than vaccine access. There have been marked racial and ethnic disparities in COVID related hospitalization and deaths. This figure shows trends in COVID-19 associated hospitalization, since the pandemic began through mid-August. Compared to whites, Hispanic adults experienced twice the rate of hospitalization, Black adults, almost two and a half times and American Indian and Alaska Natives have experienced three times as much hospitalization.

The previous slide included data on all adults but didn't consider age structure of different populations. This graphic focuses on excess death rates due to COVID and adults 25 to 64. The pandemic has hit everyone hard, all groups experienced excess deaths in 2020. However, compared to white and Asian adults under 65, Hispanic, Native Hawaiian, Pacific Islander, Black and American Indian, Alaska Native young adults had two to four times excess deaths. Many of these communities still experience low vaccine confidence. Many still have questions about vaccination. Everyone must have access to vaccine. Improvements have been made in equitable coverage but we still must make sure everyone has access to up-to-date information about the need for vaccination, as well as the safety and efficacy of COVID vaccines.

AMA's joined the COVID Collaborative and teamed up with the Ad Council on a new initiative called, It's Up to You. The goal is to answer vaccine questions, all in one place, so check it out. AMA also has some other great resources, there's a section dedicated to COVID on our website. JAMA continues to provide great content and guidance for those of us in the trenches to guide patient care. Check out AMA's COVID Daily Update Video blog series available on AMA's YouTube channel, on Apple Podcast and on Spotify. They can help keep you informed with the latest news COVID and COVID vaccines.

More and more patients are relying on social media for medical information. And there's a lot of dangerous misinformation on social media about vaccines and public health issues, this is concerning. New AMA policies strongly urges social media companies to do a better job of
moderating and monitoring medical and public health information content. We need stronger integration of verified health information. AMA has put together a 12 page COVID-19 guide with specifics on media messaging, including how to say and what not to say to get your message across. In July, the Federation of State Medical Boards warned that physicians who spread COVID-19 vaccine misinformation may be putting their medical license at risk. Three primary care boards have now issued a joint statement supporting this position. Unethical or unprofessional conduct could also put board certification at risk. Please understand we're all learning about COVID and COVID vaccines in real time, so information keeps changing. My favorite go-to side is CDC’s Interim Clinical Considerations for use of COVID-19 vaccines, this live document is being constantly updated.

So how will things change now that Pfizer's vaccine has full FDA approval? All doses distributed in the U.S. are still owned by the federal government, so physicians can't buy them from the company like we do other vaccines. They're still free or rather they've already been paid for with our tax dollars. Vaccine hesitant patients concerned about safety because the vaccine wasn't fully approved don't have that excuse anymore. Now that the vaccine's fully licensed, the company can advertise it but don't look for the name BNT162b2. Pfizer's vaccine now has two new names. The generic name is tozinameran, the brand name is Comirnaty. The generic name is crafted according to strict nomenclature, as per USAN, the United States Adopted Names Council. The drug company gets to decide on the first part, tozina, the last part, meran, applies to all mRNA vaccines. The Co in the brand name Comirnaty is for COVID, mirna, is for mRNA. The brand, Comirnaty, sort of sounds like a cross between community and immunity and that's no coincidence.

My preferred strategy for initiating healthy conversations about vaccination is the AIMS method, announce, inquire, mirror and secure trust. I call it AIMS for Success. It was created by John Parrish-Sprowl, director of global health communications at Indiana University. A is for announce, announce that your patient is due for a vaccine and you will vaccinate today. Assume that vaccination will occur, that it will happen, if it doesn't, I is for inquire. So you can inquire in order to understand their concern and get a feel for their level of vaccine hesitancy. Listen, don't interrupt, let them finish. M is for mirror, make the person feel heard, make sure they know you've listened and that you understand by repeating what they said, then you respond to their concerns in a way that, S, secures trust. They will either agree to become vaccinated at that time or, if not, one hopes that securing trust will help keep the door open and enable another opportunity for discussion. The way you respond is important, try not to trigger new concerns in the process. Don't repeat a myth to debunk it.
The most important thing is to keep the line of communication open. Each of us has the responsibility of building vaccine confidence and vaccination success. Those of us who can be vaccinated must be vaccinated to help protect the vaccinated but still vulnerable, as well as those not yet able to receive the vaccine. Remember, patients trust their physician. Physician recommendation is one of the most effective motivators for successful vaccination. We must get vaccine into arms, that's the only way we can end this pandemic. For the American Medical Association. I'm Dr. Sandra Fryhofer.

**Unger:** That concludes our program. Special thanks to Dr. Sandra Fryhofer and the Medical Society of the District of Columbia. We hope you found it informative. For more great content from the AMA, be sure to visit ama-assn.org/podcasts.

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