Importantly cannot determine causality of a diverse event. Next. Next slide.

As of October 10, 2021, there were 4,990 reports VAERS following dose two Janssen or dose three of mRNA COVID-19 vaccine. The median age was 64 years, and 63% of reports were from women. Next slide.

Race or ethnicity was unknown or incomplete for 49% of reports and 39% were from persons who identified as white/non-Hispanic. Next slide.

Overall, 94% of the 4,990 VAERS reports following dose two of Janssen or dose three of mRNA COVID-19 vaccination were nonserious. This varies slightly by vaccine manufacturer but is similar to what we've observed for COVID-19 vaccines overall and other vaccines in general. Next slide.

Among serious reports, the most common adverse event reported to VAERS was extra dose administered. Among nonserious reports, the most common adverse event was interchange of vaccine products. This may mean that the addition dose was given in error or given outside of recommendations at the time. Per federal law, serious reports include reports of hospitalization, prolongation of existing hospitalization, life threatening conditions, permanent disability, congenital deformity or birth defect, or death.

Also, please note that these adverse events are not mutually exclusive, and a report may include more than one adverse event. Next.

Among the millions of persons who have reported a third dose of mRNA or a second dose of Janssen COVID-19 vaccine, there were 30 reports of death to VAERS. There were no reports of death following dose two of Janssen. The median age was 79 years.

Median time elapsed from third dose to death was two days. A CDC physician received the available documentation, including death certificate, to determine a preliminary impression of cause of death. We were unable to determine cause of death due to insufficient data. Next. VAERS is also monitoring reports of adverse events following co-administration of COVID-19 vaccine and other vaccines.

Most reports to VAERS does not specify the vaccine type administered with the COVID-19 vaccine. Influenza and Zoster vaccine were among the most common vaccine types specified. The most commonly reported adverse events included extra dose or expired products, systemic symptoms, or adverse events unique to Zoster. VAERS will continue to monitor adverse events following co-administration. Next slide.

Now, I will review data from v-safe. v-safe is a voluntary, smartphone-based safety surveillance system. v-safe allows existing participants to report receiving an additional dose of COVID-19 vaccine and new participants to enter information about all doses of COVID-19 vaccine received and complete health surveys on the most recent dose. v-safe health surveys are sent during the week following each dose of vaccine and include questions about local injection site and systemic reactions and health impacts, including inability to perform normal, daily activities,

inability to work or attend school, and receipt of medical care. Additional health surveys are sent weekly through six-week factor vaccination and at three, six, and 12 months after vaccination. Next slide.

The key strengths of v-safe are that it's easy to use, includes active outreach to participants, and collects longitudinal data. The key limitations include that enrollment in v-safe is voluntary and requires a smartphone, and importantly cannot determine causality of adverse events. Next slide.

As of October 10, 2021, over 274,000 v-safe participants had reported an additional dose of COVID-19 vaccine. Sixty-two percent of participants were female. Thirty-nine percent were age 65 to 74 years. Ninety percent of participants identified as non-Hispanic, and 84% as white. Next slide.

This table shows the patterns of vaccination for v-safe participants who reported an additional dose. The column shows primary series received and rows show additional dose. Bolded in blue are those who received the same manufacturer for primary series and additional dose. Over 98% of participants reported a third dose from the same manufacturer as their primary mRNA vaccine series. Most participants report three doses of Pfizer BioNTech vaccine. Next slide.

This figure shows the top ten solicited reactions reported at least once during days zero through seven after dose three of Moderna or Pfizer BioNTech vaccine. Moderna shown in blue and Pfizer BioNTech in orange. Pain, fatigue, myalgia, and headache were among the most frequently reported solicited reactions for both vaccines. Next slide.

This figure shows reactions in health impact events reported at least once during day zero to seven after Pfizer BioNTech vaccination by dose. The odds of reporting and event following dose two and three were compared using a multivariable, generalized estimating equations model that accounted for the correlation between participants and adjusted for demographic variables. P values less than 0. 05 were considered to be statistically significant and are indicated here by an asterisk. Injection site reactions, systemic reactions, and health impacts including inability to perform daily activities and inability to work were all less frequent following dose three than dose two. Next slide.

This figure shows reactions in health impact events reported at least once during day zero to seven after Moderna vaccination by dose. Injection site reactions were more frequently reported following dose three of Moderna vaccine than dose two. While systemic reactions and health impacts, including inability to work, were less frequent following dose three than dose two. While these differences were statistically significant, the magnitude was small. Next slide.

v-safe is also monitoring reactions reported following co-administration of COVID-19 vaccine and other vaccines. Over 65,000 v-safe participants reported receiving another vaccine at the same time as their COVID-19 vaccine. Most were aged 18 to 75 years. Nearly 90% of co-administered vaccines was given with dose three of COVID-19 vaccine. v-safe will continue to monitor reactions reported following co-administration. Next slide.

These data are subject to a number of limitations. First, both VAERS and v-safe are volunteer systems and are likely not representative of the vaccinated U. S. population.

Second, additional dose recommendations include immunocompromised persons who completed a primary series of mRNA COVID-19 vaccine. However, v-safe does not include specific information about immune status. Additional dose recipients likely included immunocompromised and non-immunocompromised persons. And immunocompromised persons might have a different reactogenicity than immunocompetent persons.

Third, approximately half of mRNA third doses are among persons aged 65 years and older who might have different reactogenicity than persons in different age groups.

Fourth, at this time, data are limited to determine patterns of adverse events after receipt of second dose from Janssen or from the manufacturer different from the primary series. This also limited our ability to identify the rare adverse events. Finally, complete medical review of deaths following vaccinations reported to VAERS is dependent on availability of medical records, death certificates, and autopsy reports which may be delayed or not available. Next slide.

To summarize, we did not observe any unexpected patterns of adverse events. However, the data are limited at this point to identify rare adverse events. Nearly all reports of VAERS were nonserious. Most commonly reported were vaccination errors and systemic symptoms. Most v-safe participants reported a primary mRNA vaccine series followed by dose three from the same manufacturer. For Pfizer BioNTech, local and systemic reactions were reported less frequently following dose three than dose two.

For Moderna, local reactions were reported slightly more frequently, and systemic reactions slightly less frequently following dose three than dose two. Next slide.

VAERS and v-safe will continue to monitor safety of additional doses of COVID-19 vaccinations. Additionally, Vaccine Safety Datalink will incorporate additional doses into its ongoing safety monitoring. And CISA will be available to consult on clinically complex adverse events. We will update ACIP as additional data become available. Next slide.

The Vaccine Safety Team is incredibly grateful to all of the v-safe participants and to those who complete VAERS reports. We'd like to encourage everyone to report adverse events that occur following vaccination to VAERS, even if you're unsure vaccination caused the event. Also, please enroll yourself in v-safe.

If you're a healthcare provider, encourage your patients to enroll. If you're a parent, enroll your children and complete surveys on their behalf. The data collected through these systems are extremely valuable. Please get involved and encourage others to do so as well. Next slide.

Finally, thank you to the many people who contributed to these analyses. This concludes my presentation.

Good afternoon, everybody. This is Kathleen Dooling, and I will be reviewing the recommendations for COVID-19 vaccine booster doses and highlighting the evidence that ACIP examined to inform these recommendations. Next slide, please.

I'd like to start the presentation with the bottom line. The two recommendations made by ACIP last Thursday. The first was that the following recipients of mRNA COVID-19 vaccine primary series should receive a single dose at least six months or more after completion of the primary series. And those are people 65 years and older as well as people 18 years of age and older who reside in long-term care settings as well as people 50 to 64 years old with underlying, certain underlying medical conditions. In addition, the following recipients of mRNA COVID-19 vaccine primary series may receive a single booster dose six months or more after completion of the primary series based on their individual risks and benefits. So, those are people 18 to 49 years old with certain underlying medical conditions and people 18 to 64 years old at increased risk of SARS-CoV-2 exposure and transmission because of their occupational or institutional setting. Next slide.

The second recommendation was that CDC recommends that people who are 18 years of age and older who received a Janssen COVID-19 vaccine should receive a booster at a minimum of two months following the initial receipt of their Janssen vaccine. Another important aspect of the recommendations are that highlight that any of the authorized COVID-19 vaccine booster doses, so that's Pfizer BioNTech, Moderna, or Janssen, can be used following any of the primary series vaccinations. The term used for a booster which is different from your primary series is heterologous boosting, also known as mix and match. And now, I'll go on to share some of the evidence the ACIP used to inform these recommendations. Next slide.

As of October 20, more than 189 million people age 12 years of age and older have been fully vaccinated in the U. S. Approximately 66% of people have been fully vaccinated with the Pfizer primary series. Approximately 37% with Moderna primary series, and approximately 8% with a dose of Janssen COVID-19 vaccine. Next slide.

This slide shows the trends in the number of daily COVID-19 cases in the U. S. Now totaling approximately 45 million since the beginning of the pandemic. Currently, during which Delta variant has predominated, peaked in early September and has been on the decline since then. Next slide.

Similarly, the daily trends in the number of hospitalized COVID-19 cases has been declining in the U. S. over the past several weeks. Next slide.

So, this figure is an update from COVID-NET which is a hospital-based surveillance system that allows for chart review of COVID cases.

The data shown here is for age adjusted weekly hospitalization rates, stratified by age group from January through August. Hospitalization rates among fully vaccinated people are shown in the green, and hospitalization rates in unvaccinated people are shown in the blue line. In July and August, as hospitalization rates increased dramatically among the unvaccinated, rates increased

only slightly among the fully vaccinated. Among the various age groups, hospitalization was nine to 15 times higher among unvaccinated compared to vaccinated. Next slide.

And of course, hospitalization is not the only debilitating consequence of COVID-19. Long COVID conditions are a wide range of new, returning, or ongoing health problems people can experience four or more weeks after being infected with the SARS-CoV-2 virus. Prevalence of post COVID-19 conditions, both among vaccinated and unvaccinated, has been reported to be from between 5% and 80% of COVID cases. The prevalence of long COVID among fully vaccinated persons who develop COVID ranges from reports stating 5% in a study among UK adults to about 19% in a study of Israeli healthcare workers. And among COVID-19 cases in that same UK study, the odds of long COVID were reduced by half among fully vaccinated people compared to unvaccinated. Next slide.

So, switching gears, now. I would like to review a summary of vaccine effectiveness of the primary vaccine series. Waning of mRNA vaccines has been more pronounced against infection shown in this graph in blue than against hospitalization shown here in red. Compared to the pre-Delta period, vaccine effectiveness has generally been lower in the Delta period. Next slide.

And as demonstrated in this figure of published vaccine effectiveness studies, mostly involving mRNA vaccines, waning against infection has been most pronounced in July during the Delta period. Nanduri et al. depicted in the light blue in this figure, reported that VE among nursing home residents that was lower than that found in younger adults, and it did wane over time. Next slide.

So, vaccine effectiveness against hospitalization, on the other hand, has remained fairly constant over calendar time. In this range of studies, all above 80%. Next slide.

And VE against hospitalizations was also constant when analyzed against time since vaccination. As seen here in the red, Janssen vaccine effectiveness was lower than that assessed, the vaccine effectiveness assessed for mRNA vaccines. Next slide.

So, to summarize the protection afforded by COVID vaccine primary series, more than 189 million people in the U. S. are fully vaccinated. That's approximately 57% of the total population.

Hospitalization rates are nine to 15 times higher in unvaccinated as compared to vaccinated adults. And the Moderna primary vaccine series has been used to vaccinate about 37% of those fully vaccinated, and protection with this vaccine declines against infection over time and during the Delta period. On the other hand, there have been minimal to no declines in vaccine effectiveness against hospitalization in younger adults and mild declines observed in some studies, in some study platforms, among older adults. Approximately 8% of fully vaccinated people received the Janssen COVID vaccine. This vaccine shows lower VE compared to mRNA vaccines, however most platforms show persistent vaccine effectiveness over time against infection and hospitalization even among older adults who receive this vaccine. Next slide.

And now, we'll review the evidence for benefits and harms of the Modern and Janssen COVID boosters. Next slide.

So, I know this slide is busy, but bear with me as I walk through it. So, the Moderna's data for immunogenicity of a 50-microgram booster, so that's important to know that that's a half dose as compared to the primary series.

So, for this boost, sorry, this booster, following their primary series, the evidence comes from a study of 149 subjects, and a larger group with immunogenicity data following the primary series was available as a comparison. So, at 28 days following the booster dose, the neutralizing antibody titers were about 1. 8 times those in the comparison group who just received the primary series. Thus, meeting the prespecified endpoint for noninferiority of this comparison. So, it's important to note that no clinical outcomes were assessed.

So, no actual outcomes against symptomatic disease were assessed. And that participants were not randomized to the intervention or comparison group, and therefore, the evidence tied to assess prevention of symptomatic COVID was type four. Or, in other words, very low quality. Sorry, very low certainty. There was no data available to assess the prevention of hospitalization, death, or transmission of SARS-CoV-2.

With respect to possible harms, no serious adverse events were attributed to Moderna booster doses in the 171 subjects assessed at the 50-microgram dose. The proportion with any serious adverse event was balanced between intervention or booster dose and comparison [inaudible]. In terms of reactogenicity at the grade three level, or in other words, early reaction to the vaccine that might interfere daily life in the seven days after receiving the vaccine, 10. 8% of the booster group experienced such a reaction compared to 19. 7% of the primary series comparison group. The certainty for both outcomes were judged as evidence type four or low certainty. Next slide.

Now, to summarize the evidence for grade of the Janssen booster. So, the evidence for use of the Janssen booster dose was primarily generated from a clinical trail where subjects were randomized to receive either two doses of Janssen vaccine 56 days apart or a placebo. Wherever possible, we tried to compare the effects of the booster dose administered to approximately 7,400 participants to a primary dose administered to a little over 19,000 participants in the initial clinical trial.

The Janssen COVID-19 booster dose is, appears to be more effective at preventing symptomatic, lab-confirmed COVID than the primary dose alone. However, because the participants were not randomized to the intervention and comparison groups and results were compared across two separate studies that differed in both time and geography, the evidence was type four or low certainty in the estimate. The Janssen booster dose may be more effective than the primary dose at preventing hospitalizations and deaths due to COVID, but because of concerns with study design and indirect comparison, and imprecision resulting in small numbers of outcomes, both of these outcomes were assessed to be type four evidence. There was no data to assess the prevention of transmission. For serious adverse events, over 8,000 participants received the booster dose were compared to placebo recipients.

The proportion with any serious adverse events were balanced between the booster and placebo arms. However, three serious adverse events were attributed to Janssen COVID booster dose by the study investigators. Those were facial paresis, pulmonary embolism, and cerebrovascular accident. With respect to reactogenicity, the proportion with a grade three reaction, remember those are ones that interfere with daily life, following a booster was similar to or less than the primary dose because of lost follow up, short duration of follow up, and indirect comparison and imprecision, meaning the evidence was type four or low certainty for both arm outcomes assessed. Next slide.

So, large scale and rigorous post authorization safety surveillance has identified safety issues that may be too rare to be seen in standard clinical trials. Myocarditis and pericarditis have been observed following Moderna COVID vaccine primary series. This has been noted and included in the emergency use authorization fact sheet available to clinicians and patients receiving the vaccine. The risk is noted particularly within seven days following the second dose and is highest among males under 40. Although most cases resolve, the long term sequelae are not fully understood.

The highest reporting rate is in 18-24-year-old males in the zero to seven days post dose two, and that's been reported as 39 cases for every million doses administered. Thrombosis with thrombocytopenia syndrome, also known as TTS, has been identified following Janssen primary vaccination. TTS involves blood clots with low levels of platelets and has been reported highest in females age 18 to 49. The highest reporting rate observed thus far is in 30 to 39-year-old females in the zero to 21 days post the vaccine dose and reported as ten cases per one million doses administered. And the third safety signal noted thus far is Guillan Barre syndrome or GBS has been identified following Janssen.

The unadjusted reporting rate in the one to 42 days following vaccination has been noted as 20 cases per one million doses administered. And sorry 16 cases per one million doses administered. And please note that all these reporting rates cited here will include some level of background incidence, and not all cases may be attributed to vaccination. Next slide.

So, heterologous boosting, which I mentioned earlier, also known as mix and match, could provide important immune benefits as well as enhanced feasibility and implementation of the booster dose program.

The National Institute of Health sponsored study showed that use of Moderna, Janssen, and Pfizer BioNTech COVID vaccine as booster led to a strong serologic response in groups primed by all three of those vaccines. And for a given primary COVID-19 vaccine, heterologous boosts elicited similar or even higher serologic response as compared to their respective homologous booster responses. mRNA vaccines resulted in higher antibody titers in the first 28 days after boosting. And although the study arms were each of them were small, containing about 49 to 53 participants, no safety concerns were identified in the over 400 study participants involved. Next slide.

Now, let's look at the feasibility implementation with regard to booster doses. Next slide.

From August 13th to September 23rd, approximately three million additional doses had been administered under the recommendation for use in immunocompromised people. So, following the Pfizer booster dose recommendation on September 23rd, the total number of booster or additional doses has increased to approximately 10. 9 million.

The majority of those booster doses has been administered in people 65 and older. Next slide.

So, this is a figure of the number of people who completed their primary vaccination regime over time. The Pfizer vaccine recipients in grey, Moderna in orange, and Janssen in blue. Next.

And for all three of these vaccines, most people who completed the primary vaccine regime did so more than six months ago. Next slide.

And here's a detailed breakdown of the number of people either six months post their mRNA primary series or two months post their initial Janssen dose. For Janssen, that's about 12. 9 million people, and for Moderna, almost 18 million people over the age of 65 as well as 21 million people, younger people, a portion of whom may be recommended as a result of the ACIP booster dose recommendations last week. Next.

So, in summary, next. The ACIP work group maintained that the top priority should be to continue vaccination of unvaccinated individuals. And that the goals of a booster program should be the prevention of severe disease, including hospitalization and death. However, the other considerations are important, such as maintaining the workforce and healthcare capacity, prevention of transmission, as well as considering individual benefit and risk.

And of course, we know that the balance of benefits and risks does vary by age. Sorry. Previous slide. So, adults 65 years of age and older have the clearest benefit risk when thinking about boosters, and for Moderna, the benefits are incrementally smaller with decreasing age. Given the high effectiveness maintained for the primary series.

Also, myocarditis risk is higher in young adults, especially males. For Janssen, the benefits may be smaller across age groups compared with mRNA vaccine. And it should be noted that the TTS risk is higher among young females. Next slide.

So, for people who've received Moderna COVID-19 vaccine as a primary series, the work group supports the use of a single booster dose at a minimum of six months following the primary series in certain populations, those that are consistent with the CDC recommended populations for Pfizer booster.

And for people who received the Janssen COVID-19 vaccine as a primary vaccination, the work group supported use of a single booster dose at a minimum of two months following the initial dose in all people 18 years of age and older. And a single dose of Janssen was noted by the work group resulted in a lower vaccine effectiveness in antibody levels compared to mRNA vaccine primary series. And the data demonstrated that a single does of Janssen or mRNA vaccine boosts immune response in these individuals. Next slide.

I'd like to thank the many people who made this presentation possible. Next slide.

And with that, I would like to hand the microphone over to Dr. Sujan Reddy.

Thanks, Dr. Dooling. You can go to the next slide.

We're reviewing the updates for our interim clinical considerations for the vaccine boosters. I wanted to start off with telling you the bottom line is, and these are the four points that I think I'd like you to take away here.

The first part is that the indication for and the timing of booster doses depend on a primary series that was administered. So, you'll hear me say the phrases like if the person received mRNA primary series, then you should do this. So, which people get the booster and when they get it will depend on what the primary series is. The second point I'd like to make is what Dr. Dooling had just mentioned that the booster product can be the same or different than a primary series.

So, any FDA approved or authorized COVID-19 vaccine can be used for the booster dose, regardless of the vaccine that was used for the primary series. So, in other words, you can use the same vaccine product for the booster dose, or you can do a mix and match with booster dose. The third point which I saw a lot of questions about was if you use the booster dose, the Moderna booster dose, the dose is half of the primary series. So, as a reminder, the primary and additional dose for Moderna is 0. 5 mL or 100 micrograms. Whereas the booster dose is only 50 micrograms and 0. 25 mL.

Lastly, I'll spend some time talking about special considerations for moderately and severely immunocompromised people, as I know there's some questions about that. Next slide.

So, let's start with people who completed their primary vaccine series with an mRNA product, either Pfizer BioNTech or Moderna. These categories have not changed since the Pfizer recommendations came out a couple weeks ago, and now they just apply for both mRNA products. The following groups who received mRNA primary series should receive a single mRNA COVID-19 vaccine booster at least six months after completion of their primary series. So, people that are over the age of 65, people over the age of 18 who reside in long term care settings, and people aged 50 to 60, sorry, 50 to 64 with certain underlying medical conditions that put them at risk for severe disease. The following groups who received mRNA primary series may receive a single COVID-19 booster shot at least six months after completion of their primary series. This is based off of the individual risks and benefits.

So, people at age 18 to 49 with certain medical conditions. Now, note these certain medical conditions do include pregnant people. I know that was a question I had. So, people that are pregnant may receive the COVID-19 booster as well as people that are 18 to 64 who are at increased risk of SARS-CoV-2 exposure and transmission because of their occupational or institutional setting. Now, if you're in one of these groups, the booster dose should be administered at least six months at the completion of the mRNA series, and as I noted before, any FDA approved authorized product, any of the three, can be used as a booster dose, regardless of the vaccine received in the primary series. So, even if you got an mRNA primary series, you

can get either that same mRNA product, a different mRNA product, or the Janssen booster. Next slide.

As a reminder, for the category of people who may, quote unquote, may receive a COVID-19 booster, we recommend risk benefit assessment considering these factors. Does a person have an increased risk for SARS-CoV-2 infection? This might come from increased risk to exposure from their occupational or institutional exposures. It also might be their risk related to other factors since their time from completion of their initial primary series.

If the individual were to be infected, they may want to consider what impact the virus could have on themselves as well as those around them. Individuals with underlying medical conditions are at increased risk for severe infection, but also importantly, people may want to consider their person circumstances. So, such as if they live or are caring for people who are at risk for severe disease. They may even want to consider nonsevere infections and the consequences they may have on their ability to do other obligations such as work because if they get infected. The person should also consider the benefits of the booster shot.

The booster, as Dr. Dooling mentioned, the boosters may reduce their risk for infections, including the risk for severe infection. And lastly, a person should consider the potential risks, including the common risks such as the transient and local systemic symptoms that come after a vaccination, but also the rare risk of booster shots. Next dose. Sorry, next slide.

People who received an mRNA or Janssen primary dose, the indications for boosters are simpler. All people age over 18 who received a single dose of Janssen primary series should receive a single COVID-19 booster dose at least two months after completing their primary series. And again, they can receive any of the three vaccine products as long as it is over two months from their primary dose. I should, as there's some questions in the chat. The risk groups that I went over before only apply to the mRNA, the people that got an mRNA primary series.

So, anyone over the age of 18 who got a Janssen dose is at least two months from their primary, from their Janssen dose is eligible for a booster shot. Next slide.

I wanted to lay out where we stand in terms of the dosing, number of doses recommended, and the age recommendations from the primary series and the booster dose. So, for the Pfizer BioNTech recommendations, these recommendations are unchanged for the primary and booster doses. The dose of the Pfizer primary and booster doses are the same.

I would also note that even though adolescents age 12 to 17 should receive a primary series of Pfizer, they are not eligible for a booster dose at this time. For the Moderna vaccine, you can also see that the booster dose is half of the primary dose, the 0. 25 mL. Excuse me. As for the Janssen, as I mentioned, people over the age of 18 who receive Janssen would, should be getting a booster dose at least two months from their initial.

The dose of the booster, the Janssen booster dose is the same as the primary series. Now, when heterologous booster doses or mix and match booster doses are administered, the booster dose

eligibility criteria in the interval for receiving the booster dose are those that for the vaccine that was received for the primary vaccination. Next slide.

Now, let's talk a little bit more about heterologous booster doses, known as mix and match booster doses. Heterologous dosing may be considered only for the booster dose, so all primary doses and additional doses should utilize the same vaccine product.

And as I'll describe later, just as a reminder, additional doses refer to those that are indicated for moderately and severely immunocompromised people who had received two doses of an mRNA product. I also just mentioned that the interval between the booster dose and the primary series dose should follow the interval recommended by the primary series. So, people who receive Janssen primary dose can receive an mRNA booster dose at least two months after the Janssen dose. A common question may be which product should your patient use. As Dr.

Dooling described, there is evidence supporting the use of either homologous or heterologous booster dosing. People may consider this election of a booster dose just simply by based off of what's available. They may also want to talk to their providers about the risk profiles of different vaccine boosters, including rare events. Next slide.

So, the previous presenters talked about this, but just to remind, the potential risks associated with the COVID-19 vaccine boosters are based off of the rare events that were observed after primary vaccination. So, for the Janssen vaccine, thrombosis with thrombocytopenia syndrome or TTS is a severe adverse event. The highest risk has been observed in women age 18 to 49, so women in this age category should be counseled about this risk and made aware of the options to receive an mRNA booster dose. Other rare risks include Guillain Barre syndrome which is highest risk observed in men age 50 to 64. For the mRNA vaccines, the Pfizer and Modern vaccines, myocarditis and pericarditis has been observed after the vaccine, and the highest risk observed in men age 12 to 30. Next slide.

So, we've received many questions about moderately and severely immunocompromised people, so I wanted to review a recommendation for this population. Next slide.

So, just to review a few definitions. We use the term "additional dose" to refer to a subsequent vaccine dose in people who likely did not mount a protective immune response after their primary vaccination in order to optimize their vaccine induced protection. In other words, their initial response was likely insufficient.

A booster dose is a subsequent dose administered when the initial sufficient immune response to the primary series is likely to have waned over time. So, in other words, the initial response was fine, but over time, the response has decreased. We worry about people who are immunocompromised fall into that first category where their initial response to the vaccine is insufficient, so they need an additional dose. Next slide.

So, our recommendation for moderately and severely immunocompromised people age 12 or older for the Pfizer or over 18 for Moderna who received an mRNA COVID-19 vaccine primary series should receive an additional mRNA vaccine dose at least 28 days after their second dose.

I would note that even though we are allowing mix and match for booster doses, the primary series and additional doses should be the same as the initial dose. I would also mention that the recommendation does not apply to immunocompromised people who receive Janssen as a primary series, as you'll see in a couple of slides. Next slide, please.

So, what do we mean by moderately and severely immunocompromised people? I know this is a challenge to assess, but one way of categorizing it is thinking of people who had a solid organ transplant or equivalent level of immunosuppression. Here, I provide a list of immunocompromised conditions that may warrant additional doses, such as people who have, that are receiving treatment for a solid tumor or hematological illness, people that are receiving CAR-T-cell therapy or stem cell transplant. People with severe primary immunodeficiencies or advanced HIV. And I know there's a long list of immunosuppressants that I've listed here, and consulting with their provider may help decide if an additional dose is indicated. Next slide, please.

So, I wanted to summarize how to approach vaccination in this immunosuppressed population. If the person received an mRNA primary series, they should get an mRNA additional dose at least 28 days after their second dose.

Note, if that dose is a Moderna dose, they should get a full dose of Moderna which is a 0. 5 mL. Then, six months later, after their additional dose, they can receive a COVID-19 vaccine booster, and that could be any of those three authorized products. And again, if Moderna is used for a booster dose, that should, they should receive the half dose as a booster dose. And I would also note, if Pfizer is used for any of these doses, it's the same doses as for the primary, additional, and the booster dose.

Now, if the person received a Janssen primary series, they should receive any of the COVID-19 vaccine boosters at least two months after the initial Janssen dose. And again, if Moderna is used in this situation, the Moderna booster dose should be used which is the half dose, 0. 25 mL. Next slide, please.

Now, I wanted to move on to a couple of additional considerations for the booster regime. Next slide.

Briefly, the definition of fully vaccinated has not changed with these booster recommendations. People who completed a primary series are considered fully vaccinated at least two weeks after their completion of their primary series which involves a two dose mRNA vaccine series or a single dose of Janssen. So, even if people are recommended to get an additional dose or recommended to get a booster dose, as long as they received that primary series, they're considered fully vaccinated. Next slide, please.

Given that we're ramping up influenza vaccination, we wanted to reiterate the points about co-administration with other vaccines. The COVID-19 vaccine booster is similar to the primary and additional doses may be given with other vaccines, regardless of timing. This includes all three of the authorized vaccines. This is also includes simultaneous administration of COVID-19 vaccines and other vaccines on the same day. Next slide.

I think I'm going to actually skip this slide. Just know that you know, the clinical considerations document that I'll link in the next slide have a lot of other recommendations, and we did update a few others that I mentioned here. I'd also mention that document is very long, and so we are updating a lot of our provider-facing documents that give nice, clear summaries that providers can utilize. So, look for those in the next couple of days as well. I think that's all from my slides, so thank you, and I think we can take Q and A according to the moderator.

Thank you very much, presenters. I appreciate your providing our audience with this timely information. We will now go into our Q and A session. We would also like to welcome Captain Tom Shimabukuro who is on the Vaccine Taskforce as part of CDC's COVID-19 response for joining us for the Q and A session along with the speakers. Please remember to ask a question using Zoom, click the Q and A button at the bottom of your screen and type your question.

So, our first question for the presenters is what recommendations do you have for boosters for people who are now back in the United States who may have gotten the Astra Zeneca vaccine or the Sinovac vaccine while abroad?

Thanks. I can take that question. So, for people that received an FDA authorized series, either the homologous series or a mixed series, we would recommend a booster according to what we just discussed. Now, people that received other vaccines that are emergency use listed by the WHO such as the Astra Zeneca vaccine, we actually, we do consider those people fully vaccinated, but at the moment, we don't have booster recommendations for that population. We continue to work with our international colleagues to try to figure that out. But at the moment, we have no recommendation for that.

Thank you very much. Our next question is regarding the long-term care setting aspect of consideration when discussing boosters. You've had multiple questions around this. Essentially, it boils down to should we consider other settings similar to long term care settings such as correctional facilities or college students dwelling together in dorms as being at an increased risk for SARS-CoV-2 infection and thereby being possible candidates for boosters?

Yeah. I can take this as well. And so, this falls into the category of, well, first, I would say if they received a Janssen dose and they're over the age of 18 and it's been at least two months, then they should receive a booster dose. Now, if they received an mRNA primary series and then six months later, then they may fall into that may receive a booster shot. And I would say there's a CDC website that says who's eligible for a COVID vaccine booster.

And it goes into this a little bit more detail. But basically, it's based off of where you work or reside, and it does include healthcare settings, correctional facilities, homeless shelters, where they might be at an increased risk of being exposed to COVID-19 and could be spreading in that workplace or where they reside. So, I'd probably refer people to that, and that does have a list of occupational settings and other institutional settings that might be helpful for people that are asked those types of questions.

Thank you very much. Our next question is regarding v-safe, and the question asks do patients need to sign up again with v-safe when receiving boosters?

Hi. This is Dr. Hause. Patients do not need to register again for v-safe. If they go ahead and go to the v-safe homepage and enter their information, they'll be sent a hyperlink through text that will link them to their profile.

Thank you very much. Our next question is regarding the difference in concentration or dose between the additional dose of Moderna versus the booster dose. And the questions essentially are inquiring about elaborating on the immune response difference between the additional dose versus the booster dose, considering that they are not the same.

This is Dr. Kathleen Dooling. I can take that one. So, we have a number of studies to help us sort out this question. You're absolutely right.

Primary series for Moderna is given at 100 microgram dose, and now we authorize booster dose is a 50-microgram dose. And it's the same formulation. It's just half the volume that should be given to the patient in the booster dose. So, in small studies, Moderna tested both the 50 microgram as well as 100 microgram as a booster dose, and it turns out that they provided fairly similar amount of serologic boosting to people who previously received the primary series. In terms of the mix and match studies done by NIH, a number of the listeners here noted that that was at 100 microgram level which is true.

So, that would be, you know, different from what has been authorized for a booster at the 50-microgram level, but I think those studies done early on by Moderna that showed that, you know, 50 or 100 micrograms provide an adequate boost is, it's a good footing for us to move forward with the authorized 50 microgram booster dose.

Thank you. Our next question asks for a person who received a full course of an mRNA vaccine, is there ever a reason for them to receive the J and J vaccine as their booster?

So, this is.

Hi. This is Dr. - Go ahead.

Yeah. Sure. I think they can. And to be clear, you know, let's say they'd received the two dose mRNA series, and it's been over six months. Yes, they may receive the Janssen dose, or they may receive any of the mRNA products at that time.

We don't necessary state a preference about which they should utilize, and I think they should consider those factors that we talked about before, what's available and potential rare side effects, along with some of the details that Dr. Dooling just mentioned about some of the mRNA vaccines. They can receive the Janssen dose equally.

Thank you. Our next question asks will those who received an additional mRNA dose based on perhaps their immune status, are they eligible for a booster six months after that additional dose as well, and how about annually?

This is Sujan Reddy again. So, if it's immunocompromised person who received two doses of an mRNA vaccine, they can get a third additional dose 28 days later of an mRNA vaccine, and then six months after that third additional dose, that third mRNA dose, six months later, they can receive any booster dose of the three vaccines. Now, after that period of time, I think obviously time will tell, and we will be ready to update our guidance as more data comes out. But at the moment, they can receive up to those four doses.

Thank you very much. And in the remaining time we have, we have time for really one last question, and this is a question that we've seen a lot in the Q and A box. And it might be good for you to elaborate or reiterate some of the things the three presenters talked about. And that's essentially are there any changes in timing and duration in how long to wait between first, second, booster, etc. when mixing and matching the various vaccines?

So, I can try to take a stab, answer that. So, just to be clear, if we're mixing and matching, we're only recommending mixing and matching for the booster dose. So, if it's a primary series or even that additional dose for immunocompromised people, they should stay with the same series, same vaccine product that they used as an initial dose. And then, the recommendation for the booster dose doesn't necessarily change if you used a homologous dose or a mix and match dose, if I understood the question correctly.

Thank you very much.

This is Dr. Dooling.

Yes, Dr. Dooling.

If I can add to that. I would say that the timing of the booster dose really depends on what you received as your primary dose. If you received a Janssen primary dose, then those people are eligible for their booster at a minimum of two months after that dose for anybody who's 18 and older. If you received an mRNA vaccine as your primary series, those folks are eligible for a booster dose at a minimum of six months after the second dose in that series. And with the recommendations for who should and who may receive a dose that we mentioned earlier.

Thank you very much. That is very helpful. I want to thank everyone for joining us today with a special thanks to our presenters. Today's COCA Call will be available on demand a few hours after the live call. You can find the video recording of today's COCA call at emergency.cdc. gov/coca. Join us for our next COCA call on Thursday, November 4 from 2:00 PM to 3:00 PM Eastern where the topic will be pediatric COVID-19 vaccines, CDC's recommendations for COVID-19 primary series in children five to 11 years old. However, please note that this COCA call is contingent on upcoming FDA and CDC meetings. As such, it is subject to change.

We will keep you posted. Continue to visit emergency. cdc. gov/coca to get more details about upcoming COCA Calls, as we intend to host more COCA calls to keep you informed of the latest guidance and updates on COVID-19. Please share these call announcements with your clinical colleagues.

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