Good afternoon. I'm Commander Ibad Khan, and I'm representing the Clinician Outreach and Communication Activity, COCA, with the Emergency Risk Communication Branch at the Centers for Disease Control and Prevention. I would like to welcome you to today's COCA Call: Updated Guidance for Clinicians on COVID-19 vaccines. All participants joining us today are in listen-only mode. Continuing education is not offered for this COCA Call.

After this presentation, there will be a Q&A session. You may submit questions at any time during today's presentations. To ask a question using Zoom, click the Q&A button at the bottom of your screen, then type your question in the Q&A box. The video recording of this COCA Call will be posted on COCA's web page and available to view on demand a few hours after this call ends. If you're a patient, please refer your questions to your healthcare provider.

For those who have media questions, please contact CDC Media Relations at 404-639-3286 or send an email to media@cdc. gov. I would now like to welcome our presenters for today's COCA Call. We are pleased to have with us Dr. Isaac See, a medical officer with the Vaccine Safety team as part of CDC's COVID-19 response, and Lieutenant Commander Sarah Oliver, lead of the COVID-19 Vaccines Workgroup of ACIP and a medical officer from the Vaccine Task Force as part of CDC's COVID-19 response.

It is now my privilege to turn it over to Dr. See. Dr. See, please proceed.

Thank you. I will be presenting updates on the thrombosis with thrombocytopenia syndrome or TTS. These updates were presented at yesterday's Advisory Committee on Immunization Practices meeting and provided some context for updates on guidance that you'll see explained on this call after my presentation. So, I'll start with some background and then I'll describe some of the characteristics of the disease and epidemiology, as well as the frequency of occurrence and complications. We can go to the next slide.

The thrombosis with thrombocytopenia syndrome, or TTS, is a new syndrome that's been recognized to occur after receiving adenoviral vector COVID-19 vaccines. As a reminder, in the United States, currently, the only authorized adenoviral vectored COVID-19 vaccine is the Janssen or Johnson & Johnson COVID-19 vaccine. As the name suggests, this syndrome is characterized clinically by thrombosis and thrombocytopenia. And this slide shows some screenshots of some of the early reports about TTS both in Europe after use of the AstraZeneca COVID-19 vaccine, which is not in use in the United States, and in the United States following use of the Janssen COVID-19 vaccine.

Next slide. Several of the slides later in the presentation will refer to cerebral venous sinus thrombosis or CVST. This is a somewhat rare type of thrombosis involving large veins inside the head such as those shown on this diagram. CVST can be a very serious condition, and the most severe TTS cases often involve CVST.

Next slide. CVST is often underdiagnosed due to its nonspecific presentation.

When patients die from CVST early in the disease course, the immediate mechanism of death is often brain herniation resulting from either a large hemorrhage in the brain, multiple

hemorrhages or diffuse brain edema. Reported prognostic factors for poor short-term outcome in CVST include anatomical characteristics of disease such as the presence of brain herniation and hemorrhage, or features of the clinical presentation such as seizures, depressed consciousness, and altered mental status. Next slide. This slide caps the initial US events concerning TTS that proceeded yesterday's ACIP meeting. On February 27th of this year 2021, the FDA granted emergency use authorization for the Janssen COVID-19 vaccine and the first post-authorization doses were given March 2nd.

On April 13th, the CDC and FDA announced a pause in the use of the Janssen COVID-19 vaccine after identification of six cases of CVST with thrombocytopenia following vaccination. On April 23rd, the ACIP reviewed data on TTS following Janssen COVID-19 vaccination and reaffirmed its recommendation, and the pause in vaccination was subsequently lifted. Around that time, CDC's website of interim clinical considerations for use of COVID-19 vaccines was updated to state that women less than 50 years should be aware of the rare risk of TTS and the availability of other COVID-19 vaccines without that risk. The FDA at that time also updated its emergency use authorization factsheet for vaccination providers and patients to contain information about TTS. Before yesterday, the most recent update to ACIP on TTS had been given on July 22nd, 2021, when an updated benefit/risk discussion occurred in light of the occurrence of Guillain-Barre syndrome after vaccination.

Next slide. So, the data that you'll see later in this presentation are public health surveillance data. And they come from a collaboration between the Vaccine Adverse Event Reporting System, or VAERS. Next slide. And CDC's Clinical Immunization Safety Assessment or CISA project, which is a collaboration between CDC and several medical research centers with vaccine safety experts.

Next slide. The initial case finding to look for TTS cases occurred through searches of the VAERS database. Confirmation required medical record review related to the case. And then the case presentations were presented to the CISA experts, including from fields of hematology and neurology. This was to confirm that the clinical syndrome was consistent with TTS, as well as to rule out other potential causes of thrombosis and thrombocytopenia.

Next slide. This slide shows our working case definition for TTS presented here. The criteria differs slightly between what we call tier one and tier two cases. Both required a platelet count of less than 150,000. But the tier one cases were those for us where there was thrombosis in an unusual location, such as a CVST.

And for those cases, a positive PA-4 ELISA test which is a test often used in the diagnosis of heparin-induced thrombocytopenia is not required for our surveillance. There are two cases of those where thrombosis is only in a more typical location such as pulmonary embolism or deep vein thrombosis. And for these we do require a positive PA-4 ELISA test result for inclusion in this. Reports where the only signs of thrombosis are ischemic stroke or myocardial infarction are excluded. We also excluded reports with concurrent COVID-19 infection, because COVID-19 is known to be a cause of both thrombosis and thrombocytopenia.

I will note that these are the definitions we used for, you know, inclusion criteria for the presentation you're going to see. These are not necessarily the same as the criteria that might be used for the diagnosis of a patient. Next slide. So, I'll first present a description of the US TTS cases receiving the Janssen COVID-19 vaccine, patients who received a vaccine through August 31st, 2021. Then I'll summarize information about all deaths among TTS cases following Janssen that have been confirmed by December 9th, 2021.

And then find out actual calculations of TTS death reporting rates. The data for those calculations will match the time period for case reporting rates that I show in the first section, in other words, through August 31st, 2021. So, in the presentation, I will go back and forth a couple times between data that correspond to different time periods. So sometimes the numbers will change for that reason, but I'll try to make that clear as I go.

Next slide. So, I'll now present some data to you about the epidemiology and kind of an overall description of TTS cases following Janssen COVID-19 vaccination. And again, in this section, all the information will be on TTS cases in people vaccinated with the Janssen vaccine through August 31st, 2021. Next slide. This slide shows some overall basic information about the cases. The median age of patients with TTS was 44 and a half years.

Most were females, and almost half were women under 50 years of age. Most patients were reported to be white, non-Hispanic. 29 of our TTS cases involved a CVST. None of our patients with TTS were pregnant or within 12 weeks postpartum, and none occurred in a patient with a diagnosis of thrombophilia. Seven of the cases were in patients known to have a past SARS-CoV-2 infection.

Next slide. The median time from Janssen vaccination to TTS symptom onset was nine days. And then once symptom onset occurred, the median time from symptom onset to hospital admission was five days. 39 of the patients were vaccinated before the pause in Janssen vaccination occurred on April 13th. And all of these cases occurred after dose one of the Janssen vaccine. In other words, not after a booster dose.

Next slide. This slide shows the number of cases by month of vaccination, and the blue bars depict those vaccinated before the pause in the Janssen vaccine, and gray for those vaccinated after. You can see that most of these cases were vaccinated before the pause.

Next slide. This bar chart shows the distribution of time in days from vaccine to symptom onset for the patients. And most notable here is the clustering where symptoms almost all began within six to 15 days after vaccination.

Next slide. We do not know precisely what the specific risk factors for TTS are. But this slide shows a description of general risk factors for venous thrombosis in patients with TTS following Janssen.

The most common risk factor is obesity, occurring in 46%. 39% of patients did not have any of these venous thrombosis risk factors.

Next slide. Outcomes of TTS cases are shown on this slide. All of the patients were hospitalized, and 36 of them, or two-thirds, were in the ICU at some point.

For those patients who survived their hospitalization, the median length of their hospital stay was nine days with a range of one to 132 days. And the interquartile range for their hospital stay length was six to 17 days. Eight patients died during their hospitalization. Nine were discharged to a post-acute care facility, and 37 were discharged home.

Next slide. This slide shows reporting rates for TTS following Janssen COVID-19 vaccination in terms of cases per million doses. Rates for females are on the left, for males on the right. And each row represents the reporting rate for a different age group. Next slide. This slide highlights that the highest rates for TTS in terms of cases per million Janssen COVID-19 vaccine doses were in women between 30 to 39 years of age, and women between 40 to 49 years age. This has been seen previously.

Next slide. Now, although at the time of the ACIP presentation yesterday, the language on the CDC website had talked about increased risk of TTS in women less than 50 years, however, in our current data the reporting rate for women 18 to 29 years of age is actually similar to the reporting rates for women 50 to 64 years of age, and for men 40 to 49 years of age -- all around four to five per million doses.

Next slide. Now on this slide and the next, I will compare actually the reporting rates that were presented back in the July ACIP meeting in 2021 to the reporting rates that I just described on the previous slides.

So, this slide shows the comparison for female. The rates given at ACIP in July were on the left in gray, and our current rates in yellow on the right. And our current rates are now slightly higher for all age groups and overall 20% higher.

Next slide. This slide shows that comparison for males.

The rates for men 30 to 49 years of age are now about twice what was presented in July. And for men 50 to 64 years of age, there's about a 50% increase. Overall rates for men are about 50% higher than what was previously presented.

Next slide. So now I'm transitioning to focusing specifically on deaths in patients who had TTS following Janssen COVID-19 vaccination. And this slide shows information about all the deaths we have confirmed through December 9th. So, on a previous slide in the last section, I described that we had eight deaths in persons vaccinated with the Janssen vaccine by August 31st, 2021. We've also confirmed one TTS death in a patient who was vaccinated after August 31st. And so, the total number of deaths we have confirmed is now nine.

All these deaths occurred after dose one of Janssen. The median age of patients who died was 45 years. That's similar to the overall median age of TTS patients on the previous section that we saw, 44 and a half years. Seven of the deaths were in females, all were reported to be in non-Hispanic white persons. And when we looked at all underlying medical conditions for these

patients, not just limiting to thrombosis risk factors, the most common underlying condition was obesity, present in seven of the nine deaths. Note though that two of the deaths occurred in patients without any known medical condition.

Next slide. This slide summarizes some of the clinical features of the nine deaths. All had features consistent with severe CVST, including either large or multiple cerebral hemorrhages, in some cases both. Evidence of intracranial edema and/or mass effect, and depressed consciousness, including many with seizures.

Seven of these deaths had confirmed CVST. The other two patients did not have specific brain imaging before death that would be needed to diagnose CVST, but the location of brain hemorrhages was suggestive of CVST. In other words, the clinical presentation for all deaths was consistent with what's seen from CVST in general. None received IV heparin for treatment. Four received craniectomy or craniotomy to try to treat brain hemorrhage.

The median time from symptom onset to admission was three days compared to five days for TTS overall. So, these patients are presenting for care sooner than the typical TTS patient. Moreover, the median time from admission to death is one day, with a maximum of two days. We've been struck when reviewing these cases that the patient's status often rapidly deteriorates, resulting in death.

Next slide. This slide shows a recap of the total TTS case and death counts previously presented to ACIP and the reasons for these presentations. First, on April 23rd, to discuss resolution of the Janssen pause, a general follow up on TTS in May, and then an updated benefit/risk discussion in July, including Guillain-Barre Syndrome data.

Next slide. And this slide revises the TTS case and death counts to show what we now have in our data for those corresponding time periods. So, in April, we were aware of and presented data on three deaths.

But we now know of five deaths in persons who were vaccinated with the Janssen vaccine during that time. In May, the number of deaths was three and is now six. In July it was four and now six. And finally, for the calculation of death reporting rates that I presented yesterday at ACIP and I'm about to show again now, we're aware of eight deaths in persons vaccinated by August 31st.

Next slide. So now I'm going to show you TTS death reporting rates. And again, I'll be switching now back to data on persons vaccinated by August 31st. And so, we're back to eight deaths, as I mentioned in the first section.

Next slide. The highest TTS death reporting rate was for women 30 to 39 and 40 to 49 years of age, of approximately two deaths per million Janssen vaccine doses.

I will mention that the ninth death, which is not used in these calculations because of vaccination after August 31st, was a woman under 30 years of age.

Next slide. Underneath the table, we've added now here data to show that the proportion of TTS cases resulting in death was 13% for those vaccinated before the pause, and 20% for those vaccinated after the pause.

Next slide. In addition to the nine deaths that we've confirmed to date, we also have identified two additional possible TTS deaths following Janssen vaccination.

Both were vaccinated before the pause, and these two possible TTS deaths share many clinical and epidemiologic features in common with the nine confirmed TTS deaths, including symptom onset between seven and four days after vaccination, large cerebral hemorrhage with mass effect, thrombocytopenia, and rapid progression from admission to death. The principal difference is that these two cases did not have definitive imaging to identify CVST, nor did they have imaging performed that might have identified other thromboses if those were present. We reviewed these two death presentations with CISA investigators, and they were difficult to confirm as TTS cases because without a documented thrombosis, they didn't technically meet the TTS case definition that we've been using. However, the CISA investigators were concerned that clinically it appeared that TTS with CVST could be the underlying cause of the patient's hemorrhage.

Next slide. The main limitations of this work are possible underdiagnosis of CVST, as well as the fact that VAERS is a passive surveillance system. Both of these limitations mean that the case and death reporting rates that I've shown could be underestimates of the true incidence rates for TTS following Janssen COVID-19 vaccine.

Next slide. So, to summarize, the US TTS case reporting rate following Janssen COVID-19 vaccination is higher than what had been presented to ACIP in July. And the case reporting rate for men 40 to 49 years, and for women 50 to 64 years, is similar to the rate for women 18 to 29 years.

As far as the US TTS deaths following COVID-19 vaccination go, they have typical features of severe CVST. And the clinical course from symptoms to admission, and then from admission to death is rapid. In addition, these deaths are more common than what we had known before, when the data were previously presented in July and earlier. With the TTS death reporting rate following vaccination of approximately two TTS deaths per million Janssen doses in women 30 to 49 years. Finally, the proportion of TTS cases with death did not decrease after the Janssen pause.

Next slide. I'd like to thank people from the VAERS program including both CDC and FDA teams, the CISA project, including the CISA site investigators, CDC's COVID-19 Response Vaccine Taskforce, the Vaccine Safety team within the Taskforce, CDC's Immunization Safety Office, and then those who brought these events to our attention by reporting them to VAERS. And that's the end of my presentation.

Thank you very much, Dr. See. Now, let's turn it over to Lieutenant Commander Oliver. Please proceed.

Thank you so much. So good afternoon, and today I'll walk through the benefit/risk discussion and results from yesterday's ACIPP meeting. We'll walk through updates to this benefit/risk assessment applying this evidence recommendation framework very similar to what was done back in April, when there was the initial pause.

Next slide. Our policy question remains the same: should vaccination with the Janssen COVID-19 vaccine as a single dose be recommended for persons 18 years of age and over under an EUA?

Next slide. So, we've hit an unfortunate milestone and now have over 50 million cases of COVID reported in the US. After steady declines in case counts through September and October, there have been an increase in cases reported through November and to date in December, with a recent seven-day average of around 117,000 cases.

Next slide. This slide shows the variant proportion circulating in the US.

Orange is the Delta variant and has clearly represented nearly all circulating COVID for the recent weeks. However, the Omicron variant is in the purple on the slide. And you can see that it currently is estimated to represent around 3% of circulating strains in the US.

Next slide. So, you've just heard in detail about TTS after the Janssen vaccine in the US from Dr. See, so I won't go into detail here. But just summarizing that again through August, there have been 54 cases of TTS identified for an overall reporting rate of 3. 8 per million, and rates are the highest amongst females in that 30 to 49 year age group, but that the risk is not exclusively clustered in this population. And through December there have been nine TTS deaths for an overall rate of. 57 per million doses.

And again, the TTS deaths are highest among females 30 to 49, but not exclusively in that population.

Next slide. And we know that this appears to be associated with other adenovirus vector vaccines. And so, we presented to ACIP what is known around TTS after the AstraZeneca vaccine in Europe. In April, the European Union or the EU was reporting around 10 cases per million vaccinated adults.

At that time, most cases were in women less than 60 and within two weeks of receiving the first dose. Through an update in September, the European Medicines Agency Safety Committee or the PRAC updated their product information by removing the previous statement reporting that TTS cases occurred mostly in women less than 60. In fact, they showed 40% of cases were in males, and nearly 40% occurred in those over 60 years of age. In updated data through December from the UK, they've reported over 400 cases of blood clots with low platelets for an overall reporting rate of 15 per million doses. Half of their cases were in women with a broad age range shown here.

They've reported a 17% case fatality. And most cases occurred after the first dose, but they've seen 47 cases and six deaths reported after a second dose.

Next slide. So, based on reports of TTS after the adenoviral vector vaccine, some countries have updated their COVID-19 vaccine policy. We evaluated vaccine policy from 16 countries highlighted here, primarily higher-income countries with broad access to mRNA adenoviral vector vaccines.

To note, this isn't meant to be globally representative of all adenovirus vector vaccine policy. All 16 countries with publicly available vaccine policy and broad vaccine access had recommendations for use of the AstraZeneca vaccine. 30% had halted use of the vaccine. 44% used the vaccine but had a preferential recommendation for other COVID vaccines. 12% recommend only in some ages, and 12% recommend use of the vaccine in all ages and populations.

Then of those 16 countries, 12 also had recommendations for the Janssen vaccine. And you can see very similar patterns. Around a quarter halted use, around a third have preferential recommendations for other COVID vaccines, some used in only older ages. And around a third have recommendations for use in all ages and populations.

Next slide. So then going into the benefit/risk analysis for the Janssen vaccine. Next slide. This slide shows the timeline of the Janssen benefit/risk analyses that have been presented to ACIP. Again, the first in April of this year when we presented the benefit/risk analysis to inform decision making during the pause. Next in July, when we presented the benefit/risk review for all COVID vaccines, including TTS and Guillain-Barre syndrome or GBS seen after the Janssen vaccine, and myocarditis after the mRNA vaccines.

Today then we'll present an updated benefit/risk analysis of the Janssen vaccine in the context of both the additional data that we have and sufficient vaccine supply.

Next slide. So, for this assessment of the benefit/risk balance, the benefits were calculated per 1 million fully vaccinated people, stratified by the age groups 18 to 49 years, 50 to 64 years, and 65 plus. We use age- and sex-specific hospitalization rates from COVID-NET, and age- and vaccine-specific VE estimates from the Ivy Network. Benefits were calculated over a 180-day period.

Harms were calculated per 1 million fully vaccinated people. TTS rates were from the presentation we just heard. We also included previous presentations on data from the Guillain-Barre syndrome or GBS and myocarditis rates from VAERS.

Next slide. So, these are the vaccine-specific estimates of effectiveness against COVID-19 hospitalization from the Ivy Network that were used as inputs for the model.

You can see for the Janssen age-specific estimates range from 69 to 76% and the mRNA age-specific estimates range from 88 to 92%.

Next slide. This slide shows the reporting rates of TTS following Janssen. As you can see again, TTS is most common among women 18 to 49 years, with a reporting rate of 8. 7 TTS cases per million doses.

Next slide. So, to guide the benefit/risk discussion, we'll first present the benefits and risks of the Janssen vaccine compared with no vaccine by age and by sex. Then we'll consider the differential benefits and risks for the Janssen vaccine compared with the mRNA vaccines and we'll include the risks of GBS and myocarditis.

Next slide. So, on this slide, you can see COVID-19 associated hospitalizations prevented by the Janssen vaccine compared with the TTS cases expected, with results presented per million fully vaccinated people.

On the left side of the figure, COVID hospitalizations prevented in males are represented by the blue bars, and COVID hospitalizations prevented in females are the red bars. Then on the right side of the figure, expected TTS cases among males are in the light gray bars, and expected TTS cases among females are in the darker gray bars. As you can see, over the course of six months, we would expect many more COVID hospitalizations to be prevented than TTS cases expected for all age and sex groups.

Next slide. This slide focuses only on the benefits and risks among females and shows COVID hospitalizations prevented by Janssen compared with the expected cases of both TTS and GBS.

COVID-associated hospitalizations again are on the left in the dark red and on the right side of the figure, expected TTS cases are in the darker pink, and expected GBS cases are in the lighter pink bars. When including other potential risks, there are still more hospitalizations prevented than TTS and GBS cases expected.

Next slide. So now on this slide, we're still only focusing on females, but we've added the benefits and risks of the mRNA vaccines to the figure. On the left side, the figure shows COVID-associated hospitalizations per 1 million single doses of the Janssen vaccine in red, and per 1 million two-dose primary series of mRNA vaccines in gray.

On the right side of the figure, you see expected number of TTS cases and GBS associated with the Janssen vaccine in pink, compared with the number of myocarditis cases associated with the mRNA vaccines in gray. When comparing the Janssen vaccine with the mRNA vaccine in females, the mRNA vaccines prevent more COVID hospitalizations and have fewer cases of myocarditis expected than TTS or GBS for Janssen.

Next slide. So next we have the exact same analysis, but we're looking exclusively at the benefits and risks among males. The left side shows COVID-associated hospitalizations per 1 million single dose Janssen vaccines in blue, and per 1 million two-dose primary series of mRNA COVID vaccines in gray.

On the right side of the figure, we see the expected number of TTS and GBS with the Janssen vaccine in blue, and expected number of myocarditis cases associated with mRNA vaccines in dark gray. Again, when comparing the Janssen vaccine with the mRNA vaccine in males, the mRNA vaccines prevent more COVID hospitalizations than the Janssen vaccine in all age groups. In the 18- to 49-year-olds, we would expect to see more cases of myocarditis from the

mRNA vaccines than TTS or GBS cases from the Janssen vaccines. But in the older age groups, we see GBS become the largest vaccine-associated risk.

Next slide. It is important to note that there are differences in the severity of these vaccine-associated events. For myocarditis after the mRNA COVID vaccines at three-month follow up, over 90% are fully recovered by a cardiologist or a healthcare provider, and there have been no confirmed deaths. For TTS after the Janssen vaccines, there's about a 15% mortality rate and 17% required discharge to a post-acute care or rehab facility. For GBS after the Janssen vaccine, there's about 1% mortality rate and around 10% required mechanical ventilation.

Next slide. We do want to note some limitations to the benefit/risk analysis. It considers the direct benefits and risks over 180-day period, comparing the vaccine to no vaccine. It looks at the single-dose Janssen vaccine with the two-dose mRNA vaccine. We assume a static hospitalization rate and VE over six months, and it doesn't account for booster doses or for prior infection.

Next slide. So, in summary of the benefit/risk assessment, we looked at the direct benefits and risks for Janssen vaccines and TTS, which considered individual benefits of vaccination and individual risks. Using the current VE estimates, the benefit/risk balance of the Janssen vaccine is still favorable for all age and sex groups compared with no COVID vaccine. When compared to the benefit/risk balance for the mRNA COVID vaccines, the Janssen vaccine prevents fewer COVID hospitalizations, ICU admissions and deaths. There are more severe health impacts from TTS and GBS after a Janssen vaccine compared to impacts from myocarditis after the mRNA COVID vaccines. So, in settings where the mRNA and Janssen vaccines are both available, the benefit/risk balance for mRNA vaccines is likely more favorable across all age and sex groups.

Next slide. So next, we can quickly walk through the ETR domains of values, acceptability and feasibility, which really think through some of the practical how the Jenson vaccine was being used.

Next slide. Over 488 million COVID doses have been administered in the US, with 17. 2 million doses administered of the Janssen vaccine.

Next slide. And additionally, we've had around 56 million people in the US who've received a booster dose. And of those, around 800,000 have been of the Janssen vaccine.

Next slide. So, this figure looks at people who are fully vaccinated and have received a booster dose.

We look at the vaccine manufacturer of the COVID primary series received, as well as the manufacturer of the booster dose received. You can see for the mRNA vaccines, most people received the same vaccine type for their primary series and their booster dose. For those who received J&J for their primary series, 41% received Moderna which is the green color for their booster. 31% received Pfizer in yellow, and 28% received a Janssen dose in blue.

Next slide. So, this figure shows the administration of the Janssen vaccines in the US since authorization by age and by sex, including both the primary series and booster doses. You can see that most doses were administered pre-pause. So, we have the pause in administration, and doses administered since the pause. Doses administered to males are in blue, and doses to females in red, and the darker shades are the younger ages, getting lighter with the older ages. We'll zoom in just a bit on doses administered since the pause in April.

Next slide. This looks at doses administered since the pause among males, and booster doses are now in orange to distinguish them. Specifically, among males, since early September, there've been around 65,000 doses administered per week, and since authorization around 50,000 booster doses per week.

Next slide. And this slide focuses on doses administered among females, again with booster doses now in green.

The scale is the same as the previous slide to allow for comparison. You can see around 45,000 primary doses are administered weekly since early September, which is lower than what we see among males. However, since the booster dose authorization for Janssen, similar numbers of booster doses have been administered each week among males and females -- around 50,000 doses.

Next slide. This slide shows administration of Janssen vaccines by race and ethnicity.

While not specifically shown here, you can see that the patterns are very similar for what we see among mRNA vaccines.

Next slide. But similar to what we did in April during the pause, jurisdictions were surveyed to get a better sense of their use of the Janssen vaccine. They report that overall, the Jensen vaccine is available to nearly all populations. And many specific populations are highlighted here, including those experiencing homelessness, homebound populations and incarcerated individuals.

Next slide. So, in summary, next slide. To revisit our timeline, back in April after the initial benefit/risk discussions. Just a reminder for the context, back in April, there was a limited supply of mRNA vaccines. It's estimated that if use of the Janssen vaccine was not resumed, it could take nearly three months for all vaccine attending adults to complete a COVID vaccine series based on supply at that time.

So, at that time and in that context, ACIP reaffirmed its interim recommendations for use of the Janssen vaccine in persons 18 and over under the EUA, which now included a warning that the rare clotting events might occur after vaccination primarily among women 18 to 49. An MMWR that was published shortly thereafter stated education around the risks of TTS as well as the availability of alternative COVID vaccines is required to guide vaccine decision making. Next slide. Then in July, GBS after the Janssen vaccine was identified, and the benefit/risk balance was reassessed. ACIP determined that overall, the benefits of the COVID vaccine in preventing

COVID morbidity and mortality outweighed the risks for these rare serious side effects but acknowledged that the balance of benefits and risks vary by age and by sex.

Next slide. In today's review, an additional case review and ongoing safety surveillance have identified TTS cases, both previous and newly occurring, including deaths. We presented the benefit/risk balance for the Janssen vaccine and acknowledge that we're no longer in the setting of limited mRNA vaccine supply in the US.

Next slide. So, the data was presented to the ACIP workgroup this past week and then also discussed at the ACIP meeting yesterday.

Yesterday the ACIP discussed each of these policy options and the pros and cons for each. I won't walk through all of that, but the slides are available on the ACIP website. They go through each of these options.

Next slide. So, the summary of what was discussed when the workgroup reviewed the data, discussed the policy options and the pros and cons, they had several conclusions.

First, in the setting where there are no alternative COVID vaccines, the benefits of the Janssen vaccine outweigh the risks. This is important for global situations where there may not be other COVID vaccines available. Then, due to both higher vaccine effectiveness for the mRNA vaccines and the severity of safety issues with the Janssen vaccines, in the setting of widely available mRNA vaccines in the US, the benefit/risk balance for the mRNA vaccines is more favorable than for the Janssen vaccines.

Next slide. They also felt that based on reviewing the totality of the data, the workgroup supported a preferential recommendation for the mRNA vaccines.

This is similar to many other countries with mRNA and ad vector vaccines both widely available. We'll continue to review available data on both effectiveness and safety, and so updates to the recommendation can be made as needed. Education around the risks with these ad-vector vaccines will be critical for those who may choose to receive a Janssen vaccine. And importantly, ensuring access to mRNA vaccines in all individuals is critical. We learned through the jurisdictional survey that there are some populations in settings where the Janssen vaccine is being used as the main vaccine offered.

If the Janssen vaccine is only offered to some of those harder-to-reach population, this could result in an inequitable distribution of risk for TTS and GBS, with some populations bearing a greater risk of the severe adverse events.

Next slide. So, the ACIP vote was unanimous at 15 to zero, that voted that mRNA COVID-19 vaccines are preferred over the Janssen COVID vaccines for the prevention of COVID-19 for those 18 years of age and over.

Next slide. So then, we will see the updates to the clinical considerations will hopefully be posted later today.

But trying to give people an understanding of what that means and what type of language CDC will be saying. What we're saying now is that in most situations, mRNA COVID-19 vaccines are preferred over the Janssen COVID vaccine. This includes for both primary and booster vaccination, including those who received a Janssen vaccine for their single-dose primary series. Janssen vaccines may be offered to the following populations: persons with a contra indication to the mRNA vaccines, which can include severe allergic reaction or after a previous dose or to a component of the mRNA vaccines. Those who would otherwise remain unvaccinated for COVID due to limited access to mRNA vaccines, and persons who would prefer the Janssen vaccine despite safety concerns identified.

Next slide. Then persons who elect to receive a Janssen vaccine should be informed as a part of this pre-vaccination discussion with the vaccine provider about both the risk and symptoms of TTS that could occur after vaccination and the need to seek immediate care should symptoms develop, as well as the availability of the mRNA vaccines. Vaccine providers should start the two-dose mRNA vaccine series even if there's uncertainty around how the patient will receive their second dose. The two-dose mRNA vaccines can be used in any population or setting. And then one of the things that FDA did when they updated their EUA earlier this week is they came out with a contraindication to administer the Janssen vaccine to persons with a history of TTS after a previous dose of a Janssen or another adenovirus vector vaccine such as AstraZeneca's vaccine.

Next slide. It's a huge team of people that have helped kind of pull this together, so definitely want to thank them. And next slide is just thank you. So, I think I'll turn it back over to Dr. Khan and we're happy to walk through some questions.

Thank you so much, presenters. Thank you for providing our audience with this timely information. We will now go into our Q&A session. For our Q&A session, in addition to our presenters, we would also like to welcome Dr. Agam Rao, Dr. Anthony Fuhr, Mr. Chris Duggar. Dr. John Sue, and Dr. Tom Shimabukuro, from the Vaccine Task Force as part of CDC's COVID-19 response.

They'll be joining us for the Q&A session. For our audience, please remember to ask a question using Zoom, click the Q&A button at the bottom of your screen and then type your question.

Our first question asks, based on this information that you have provided, if a patient received a Janssen vaccine dose, are they still considered fully vaccinated?

This is Sarah. Absolutely. So a person is considered fully vaccinated against COVID two weeks or more after the receipt of the second dose in a two-dose series, or two weeks after receipt of the single dose of the Janssen vaccine. So yesterday's decision didn't change the recommendations around who's considered fully vaccinated. We will note that people are recommended who received Janssen as their primary dose, recommended to get a booster at two months. But the recommendations for fully vaccinated did not change.

Thank you very much.

Our next question asks, what is your recommendation if we have a patient who had a severe allergic reaction to first dose of an mRNA vaccine? Do they get a Janssen vaccine? Do they get two doses of Janssen vaccine? What would you recommend for such a patient that has had that severe allergic reaction to a first dose mRNA?

Agam, I know we've been talking about this. Do you want to summarize our recommendations for that one?

Yes, I can do that. So this is Agam. What I can say is that the Janssen vaccine is a consideration for people when there is a contraindication to an mRNA COVID vaccine. And if someone's had a very severe allergic reaction after a previous dose, you know, they would fall into that contraindication category. So being vaccinated is certainly better than not being vaccinated.

But it is a decision that needs to be made, you know, with the patient or the patient's guardian or parent and a healthcare provider to ensure that the risks and the benefits are understood. Is there anything that you wanted to add, Sarah?

No, I think that's perfect. We are aware that -- you know, we'll just kind of say that there are other vaccines that are not currently under EUA in the US yet. The protein subunit vaccines, either the Novavax or the Sanofi. And so those could potentially one day be an option if they submit data to FDA and authorization or approval is granted. So, we may be in a situation at one point where we have other vaccines. But I think everything Agam said applies for right now.

Thank you very much.

We have received a few questions along these lines. So I'll try and sum them up in one.

Essentially, the question boils down to as a provider, if we are uncertain whether the patient is going to come back in 21 or 28 days for their second dose of mRNA vaccine, should we still give the mRNA vaccine? Or if there's a chance that this may be the only dose they get, give the Janssen vaccine?

This is Sarah, I'm happy to take that one. And I think this is a great question and a really important question that we want to highlight.

So, I think you can absolutely start that mRNA vaccine series. We know that in many kind of instances in settings where people were worried about, you know, individuals returning for a second dose, they were more inclined to give the J&J vaccine. I think now that we have kind of a broader understanding and broader picture, we just want to say that, you know, give somebody that first dose of the mRNA vaccine, and then take the opportunity, you can do second-dose reminders or, you know, continued outreach.

But we wouldn't ever want somebody to only ever be offered a J&J vaccine strictly because there was concern that they may not come back for a second dose of an mRNA vaccine. So, as we do for all other vaccines, if they're in your clinic, or you're in a situation where you can start the series, do that. That's great. And then, you know, think through creative ways to get them back or

follow up with that second dose. But take the opportunity to start the first dose now, and we would not want anybody to not have an informed discussion about a J&J vaccine strictly because there was uncertainty around that second dose.

Thank you for that.

Next question asks, based on these findings and the recommendations coming from the ACIP, from other agencies, are there differing guidance you have for completing reporting systems such as VAERS or V-safe? Are there any changes to those procedures or recommendations?

Dr. Shimabukuro, do you want that one?

Could you repeat that question again? I'm sorry.

Sure. Yeah. The question essentially asks, based on these recommendations coming out of ACIP, are there any changes to the guidance for reporting in VAERS or V-safe that clinicians should be aware of?

So, V-safe is a voluntary self-enrollment program that we encourage all healthcare providers to encourage their patients to enroll in and we encourage all patients to enroll in. And that's a smartphone-based text messaging and web survey type process. So those questions are basically sent out in a survey, so there's really no difference in the process. And then for the other vaccines, for vaccines that are under emergency use authorization the FDA reporting requirements to VAERS for emergency use authorization still apply. And CDC encourages reporting of all clinically significant or medically important adverse events, even if the doctor or the patient isn't sure if the vaccine caused the adverse events.

The reporting requirements for adverse events really haven't changed as a result of this.

Thank you very much.

The next question asks for a little bit of clarification.

So, people who have already received the Janssen vaccine, which booster should those people receive? And in which cases should those people receive a Janssen vaccine?

Yeah, this is Sarah. So, people who got this the Janssen for their primary vaccines are recommended to get a booster dose at two months or eight weeks after their primary dose. And after the vote yesterday now, an mRNA vaccine is preferred over a Janssen for that booster dose vaccine. Obviously, for individuals, as we kind of mentioned before, those who have a contraindication to an mRNA vaccine, you know, if there's somebody who after having kind of informed discussion with their provider still wants to choose a Janssen vaccine, they may still be offered a Janssen vaccine, but the booster recommendation is the same -- two months after the first dose of the Janssen vaccine. And then an mRNA vaccine is now preferred for that booster.

Agam, did I catch everything?

Yeah, you did. It's a preferential recommendation, which means that whenever possible an mRNA vaccine should be given. So, in this case, if someone already got the Janssen vaccine, then they've gotten that primary vaccine series and the booster really should ideally be with an mRNA vaccine. If, however, our guidance does say that persons would prefer the Janssen COVID-19 vaccine despite the safety concerns identified, then that is something that clinicians can provide to patients. But they really should ensure that as part of the pre-vaccination counseling that is done that they inform that patient about the risk and symptoms of TTS that could occur, particularly in the two weeks after vaccination and the need to seek immediate medical care should symptoms develop.

So those are just -- I mean, if someone wants to get the Janssen vaccine despite the counseling, they can receive it. But whenever possible, an mRNA vaccine should be given as the booster for this particular example.

Thank you very much.

Next question asks, are you aware if there were any changes to the Janssen vaccine during the pause period where the administration was paused, if there were any attempts to address the formulation at all? If you're aware of anything like that.

Yeah, this is Sarah. I'll say something and then I'm going to toss it to Chris Duggar. But I will say people have said, "Well, why did it seem like most J&J occurred -- you know, most cases of TTS occurred early?" That really has to do with that's when the most Janssen vaccine doses were given, was before the pause. If you kind of look back, the majority of doses were given pre-pause, and then there have been kind of a slower number of doses over time. So, it's a little bit more of a rate kind of numbers thing.

But, Chris, do you want to say anything about kind of formulation or anything like that with Janssen?

Oh, sure, thanks. So, no changes made to the NDC, packaging, formulation, storage and handling. The only changes that have occurred for this product is stability data allowed for extension of the shelf life. So now you can hold Janssen in your refrigerator for up to six months. That's a benefit because demand has been slow.

Over.

Thank you very much. We have time for one more question actually related to Janssen vaccine as well.

And the question asks that, if a facility has a stockpile or an amount of Janssen vaccine that has been, you know, properly stored, and like you mentioned, is in date, et cetera, should we look to get rid of it or donate it, or try and return this unused Janssen vaccine in preference of mRNA vaccines? Do you have any guidance on that?

Yes, and thanks for asking. So, at this time, if you do have a provider that no longer wants to use this vaccine, we ask them to keep it at the appropriate storage temperature, mark it "Do not use," and then contact your jurisdiction. There may be some demand and they could transfer that physical inventory to where it's needed or wanted. But for now, please just hold onto it and mark it "Do not use. " We do not have a return program.

So, as we approach expiration, we will send out information on proper disposal.

Thank you very much. I want to thank all our presenters today with a special thanks to our SMEs who also joined during the Q&A session. For our audience, please note that a lot of the references that we talked about including the ACIP slides and other guidance documents can be found under the additional resources section of this COCA Call's webpage, which you can access at emergency. cdc. gov/coca.

And 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 call at emergency. cdc. gov/coca. And that link will also have those additional resources.

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Again, I want to thank everyone for joining us for today's COCA Call. Have a great day.