Good afternoon! I'm Captain 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'd like to welcome you to today's COCA call. We must maintain measles elimination in the United States; measles clinical presentation, diagnosis, and prevention.

All participants joining us today are in listen-only mode. Free continuing education is offered for this webinar, and instructions on how to earn continuing education will be provided at the end of the COCA call. In compliance with continuing education requirements, all planners and presenters must disclose all financial relationships, in any amount, within eligible companies over the previous 24 months, as well as any use of unlabeled products or products under Investigational Use. CDC, our planners, and presenters, wish to disclose they have no financial relationships with ineligible companies, whose primary business is producing, marketing, selling, reselling, or distributing healthcare products used by or on patients. All of the relevant financial relationships listed for these individuals have been mitigated. Content will not include any discussion of the unlabeled use of a product, or a product under Investigational Use. CDC did not accept financial or in kind support from ineligible companies for this continuing education activity.

At the conclusion of the session, participants will be able to accomplish the following: identify the clinical presentation of measles, and other causes of febrile rash illness, which may mimic measles; diagnose measles infection with appropriate laboratory diagnostics; identify measles vaccine adverse reactions, and implement measles prevention and public health control strategies.

After the presentations, 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. Please note that we receive many more questions than we can answer during our webinars. If you're a patient, please refer your questions to your health care provider. If you're a member of the media, please contact CDC Media Relations at 404-639-3286, or send an e-mail to media@cdc.gov.

I would now like to welcome our presenters for today's COCA call. We are pleased to have with us, Miss Adria Mathis. Miss Mathis is an epidemiologist in the Division of Viral Diseases at the National Center for Immunization and Respiratory Diseases at CDC. Dr. Dan Filardo. Dr. Filardo received training in Internal Medicine with a subspecialty focus in Infectious Diseases, and is board-certified in both disciplines. He works as a medical officer in the Viral Vaccine-Preventable Diseases Branch in the Division of Viral Diseases in the National Center for Immunization and Respiratory Diseases at CDC. And our final presenter will be Dr. Stephen Crooke. Dr. Crooke is lead research microbiologist in the Viral Vaccine-Preventable Diseases Branch, where he oversees diagnostic and clinical serologic testing for measles and mumps in the Division of Viral Diseases in the National Center for Immunization and Respiratory Diseases at CDC.

Now, it's my pleasure to turn it over to Miss Mathis. Miss Mathis, please proceed.

Thank you. I'll begin our session with a discussion of measles surveillance data in the United States. Next slide, please.

Increases in US measles activity reflects global activity and importations into susceptible US populations. This figure shows the annual measles case counts in blue columns, and incidents per one million population in the yellow line. And the dashed red line indicates an incidence of one case per million population. From 2001 to 2022, a total of 4,056 measles cases were reported in the United States, with a median of 79 cases per year, ranging from a low of 13 cases in 2020, to a high of 1,274 cases in 2019. In 2023, a total of 19 cases were reported as of August 3rd. Annual measles incidence has remained below one case per million population in all but three years: 2014, 2018, and 2019. Large outbreaks were reported in each of these years, including two prolonged outbreaks in New York City and New York State that began in the fall of 2018, continued into 2019, and threaten the US elimination status. Elimination of measles is defined as the absence of sustained transmission within the country for any 12-month period. Next slide, please.

From 2001 to 2023, measles cases have been reported by 48 states and Washington D. C. 67% of all cases, and 72% of outbreak-related cases were reported by five states, New York, California, Ohio, Washington State, and Minnesota. Next slide.

Next, we will review the measles cases reported from January 2021 through July of 2023. There have been sporadic importations of measles during this time period, but most cases have been associated with two distinct outbreaks. Next slide.

During September to October 2021, an outbreak occurred, which was limited to military facilities participating in Operation Allies Welcome, which was the resettlement of over 80,000 Afghan evacuees in the United States. Forty-seven measles cases were reported as part of this outbreak, and due to a robust response that involved many public health and federal partners, there was no spread into US communities. These cases represented almost all of the measles cases reported in the US during 2021. Next slide.

During October to December of 2022, there was an outbreak in Central Ohio, and 85 cases were reported among Ohio residents during this time. Most cases occurred among children who are eligible to receive MMR vaccination by age, that is 12 months or older, and 94% of cases occurred among persons who were unvaccinated against measles. Next slide.

During 2023, there have been 19 cases reported to-date. 16, or 84%, were associated with international importations. And no outbreaks have been reported. We have seen an increase in the frequency of importations, as international travel by US residents to turn -- returns to pre-COVID levels. Next slide.

One key point that we'd like to highlight is that measles cases are imported primarily by unvaccinated US residents traveling abroad. This figure shows the number of directly imported cases annually. Cases among US residents are shown in blue, and cases among foreign visitors are shown in gray. Overall, 63% of importations occurred among US residents during this time period, including all of the importations during 2022 and 2023 to-date, as you can see on the

right. 86% of these US residents were unvaccinated, or had an unknown vaccination status. Next slide.

Among the international importations, 62% of patients reported travel to countries in the European and Western Pacific regions. This highlights that travel to many regions of the world, including to Europe, which is one of the most common vacation destinations for US residents, can pose risk for measles for those who are unvaccinated or under vaccinated. The top five source countries for imports since 2001 were India, the Philippines, China, Pakistan, and the United Kingdom. Next slide.

So for our first Knowledge Check question: "Measles cases in the US are most commonly the result of virus importation by unvaccinated foreign visitors. " A: true, or B: false? Next slide.

The answer is false. As we discussed, the most common cause of measles cases in the US is importation of the virus after travel abroad by unvaccinated US residents. Next slide.

And now I'll turn it over to Dr. Dan Filardo, who will discuss a clinical overview of measles.

Thanks, Adria. Next slide, please.

So measles is an acute febrile rash illness caused by measles virus. It is transmitted by direct contact with infectious droplets. It can also be spread by the airborne route. Measles is highly contagious, 90% of susceptible household contacts will develop illness if exposed to a measles case. And the estimated reproductive number, or R-naught, is 12 to 16 in an unvaccinated population, meaning that a measles case would be expected to result in 12 to 16 secondary cases. Next slide, please.

Because measles can spread so quickly among a susceptible or unvaccinated population, measles cases require a coordinated and robust public health response. Measles is, therefore, nationally notifiable, and cases should be reported immediately to the Health Department serving the jurisdiction in which the case is diagnosed. Health Departments can also assist with testing when measles is suspected, and we will discuss laboratory diagnosis of measles in later slides. Next slide, please.

So measles presents with a high fever, which can be up to 105 degrees Fahrenheit, and a rash, which we'll talk about shortly, and one of what are called the three C's, which includes: cough, coryza, or runny nose, or conjunctivitis, or some combination of these three C's. The fever is present when the rash starts, and the fever often peaks around the time the rash starts or after rash onset. According to the Council of State and Territorial Epidemiologists, or CSTE, case definition, fever, rash, and one of the three C's must be present to be considered a clinical measles case. Next slide, please.

So more about the measles rash. The measles rash is generally described as starting on the face, at the hairline, or behind the ears, and then subsequently spreading downwards to the neck, trunk, and extremities. The rash is maculopapular, being made up of small raised or flat red bumps, and as the rash progresses, the spots may join together or coalesce. The rash is not

usually itchy, and Koplik spots may be present as small white plaques on the buccal mucosa. These can appear before or at the same time as the rash, but they are hard to see, and not always present. The rash can present atypically in people with immunocompromising conditions, and in people who have been previously vaccinated against measles, but overall the presentation I've described here is fairly-consistent among people who develop measles, who have not been vaccinated against measles. Next slide, please.

These are a couple of additional photos of measles rashes. On the left is a photo of a child from Samoa during a measles outbreak in 2019, that occurred in Samoa. Most images of measles available on the Internet, and on CDC's website are among adults and children with light skin tones. But I wanted to highlight here an example of how measles may present in children with darker skin tone. On the left, we can see that the rash is patchy, and less red in color than it might appear on a lighter skin tone background seen on the right. Next slide, please.

Timeline is a very important piece of the history of illness to obtain once suspecting measles, and so let's review the typical timeline one would expect. After exposure to the measles virus on the left, there's an incubation period of on average 10 to 14 days, during which time the exposed person is asymptomatic. Next slide.

Around two to four days before onset of the rash, the prodromal symptoms begin. This includes fever, and at least one of the three C's, that is cough, coryza, or conjunctivitis. And following these prodromal symptoms, the rash begins. And the date of rash onset is considered days zero when discussing measles cases. On average, the time from exposure to developing the rash is 14 days, and the longest time period from exposure to developing the rash is considered to be 21 days. Next slide.

People who develop measles are considered contagious for four days before and four days after rash onset, and this informs isolation and exclusion policies for those who develop measles. As you can see, a challenging piece of measles control is that people are infectious before the rash, and can be infectious when they only have nonspecific symptoms that look like other respiratory illnesses. Next slide, please.

The most common measles complications are diarrhea, otitis media, or middle ear infection, and pneumonia. These occur in less than 10% of cases, but can cause substantial morbidity, especially measles pneumonia, which can cause severe disease in infants and immunocompromised people. Next slide.

More severe complications include hospitalization, which occurs in one in four cases; encephalitis, which occurs in one per a 1,000 cases, and deaths which occurs in one to three per 1,000 cases of measles. All of these complications of measles are more common in two age groups: those under the age of five, and those over the age of 20. And complications are more common among those who are unvaccinated against measles. Finally, subacute sclerosing panencephalitis, or SSPE, is a devastating neurologic complication that occurs a median of seven years after measles infection, and is more common for those who develop measles at less than two years of age. It's a syndrome of progressive neurologic decline, which is generally fatal within one to three years of onset. Estimates of how common SSPE is vary, but data from 2005

suggests that it occurs in about seven to 11 per 100,000 cases of measles. And measles vaccination also protects against this complication. Next slide.

Adding to the challenge of recognizing and diagnosing measles, there are other viral causes of a maculopapular febrile rash that are common in children, and often can be confused with measles. Most children will acquire these viruses sometime between the ages of one and six. First, Parvovirus B-19 causes what is known as "Fifth Disease", which can present with fever, and what is called the quote/unquote "slapped cheek" rash shown in the top photo, where a rash begins on the cheeks, and can then spread down to the trunk and extremities. So this rash can definitely mimic measles, but generally is not as confluent as a measles rash. And this infection, with Parvovirus B-19, is more common in school aged children than in infants. Human Herpesvirus 6, or HHV-6, can cause a viral illness known as "Roseola", or "Sixth Disease" HHV-6 also presents with a high fever and rash, although in this case, the rash generally follows a day after the fever breaks, and the rash results more quickly than it does for measles. Also, in contrast to measles, this rash generally starts on the trunk, and then spreads outward to the extremities, sometimes as far as the neck in the face, but not always. And, finally, enteroviruses can cause a fever and rash with a similar rash pattern to measles. The rash can be maculopapular, like measles, but it can also be urticarial or itchy, which is less likely measles appearance. The most common presentation is hand, foot and mouth disease, classically caused by Coxsackie virus, which is in the enterovirus family. A typical hand, foot and mouth rash is shown here in the bottom photos. And a key distinguishing feature is that the measles rash does not appear on the palms and soles of the hand, but this is a characteristic location for hand, foot and mouth disease. And, lastly, not a viral cause, but a maculopapular rash can be seen with antibiotic reactions to both Penicillin's and sulfur-containing antibiotics. And recent use of such antibiotics is an important question to ask in the history, when a provider is suspecting measles. Next slide.

So just a brief review of what we covered about the clinical presentation of measles. Measles is a highly infectious acute febrile rash illness. measles cases should be reported to health departments immediately. The clinical definition of measles includes fever, and a rash, and at least one of the three C's: cough, conjunctivitis, or coryza. Measles can cause severe complications, including pneumonia and encephalitis, and measles does have multiple mimickers, including parvovirus and HHV-6. Next slide, please.

So let's do our second Knowledge Check question. "What is the typical presentation of a measles rash?" Answer A. the rash starts on the trunk, then spreads up to the hairline and extremities; Answer B: starts on the extremities, and spreads everywhere on the body, including the palms and soles, or C. starts with the hairline or face then moves down to the trunk and extremities. And next slide.

So the answer is C. As we discussed, the typical measles rash starts at the hairline or on the face and then moves down to the trunk and extremities. Next slide.

So now I'm going to turn the presentation over to my colleague Stephen Crooke from the measles laboratory group to review the laboratory diagnosis of measles.

Thank you, Dan. Next slide, please.

So let's review our bottom line upfront when it comes to laboratory diagnosis of measles. First, clinical, epidemiologic, and laboratory data should all be considered when diagnosing measles infection. No one test alone can rule in or rule out measles. Second, using serology alone, in this case IgM, to test patients with a low pretest probability of having measles will result primarily and false positive results. And, third, both serum, and nasopharyngeal, or oropharyngeal swab should be collected for all suspect cases of measles. Next slide, please.

Let's discuss measles serology. The detection of measles antibodies is useful to help confirm the diagnosis of measles, but there are some limitations that we will highlight. Serology, which is testing for measles IgG and IgM, can increase the window in which measles can be diagnosed if diagnostic or reporting delays are encountered. IgM detection starts one to three days after rash onset and can be detected for up to six to eight weeks after infection. So early testing for IgM, that is before day three, following rash onset, can sometimes be negative just because measles IgM production has not become detectable Additionally, IgM may disappear rapidly, be delayed, or not appear at all in vaccinated people who develop measles, which is another diagnostic challenge. IgM testing, alone, that is without additional testing by PCR, can be problematic in settings with low measles incidence, which includes places like the United States that have maintained measles elimination. First, cross-reactivity with other causes a febrile rash illness has been documented, especially with HHV-6 and parvovirus, which can mimic measles as we've discussed. And second, false positive results are relatively common when the likelihood of measles is low. For example, when there isn't local active transmission, and patients have not traveled, and when patients have been fully-vaccinated and have no known exposure. Next slide.

Measles can also be detected by PCR, or polymerase chain reaction. The test for measles by PCR is called rRT-PCR, which stands for real-time reverse transcription-polymerase chain reaction. Real-time PCR testing can be performed on nasopharyngeal and throat swabs, as well as urine. Testing is primarily performed on nasopharyngeal or throat swabs. Specimens are ideally collected within three days of rash onset for optimal sensitivity, but can be positive up to 10 days after rash onset. It is best to collect specimens for real-time PCR as soon as possible after rash onset to optimize detection. Proper specimen collection, storage, and processing is critical to maintain the stability of viral nucleic acids. Most real-time PCR assays include a control for specimen integrity, also referred to as "a reference gene". Real-time PCR has much higher sensitivity and specificity than serology. False positive results can occur, but are much less common. False negative results can also occur primarily due to the timing of specimen collection, or transportation, or storage issues. Both CDC and State Public Health labs can perform real time PCR for measles. Next slide.

Additionally, some large commercial laboratories, such as Quest and LabCorp, are offering measles real-time PCR testing, and others are in the process of onboarding testing. Overall, commercial laboratories can expand access to testing, and can provide testing that goes through the typical workflows and EMR structure of a health system. However, there are some issues that arise with commercial testing. One is that there is loss of integration with public health departments, which as we've discussed, is critical to ensuring a robust public health response to measles. And second is that specimens that commercial laboratories are not always maintained appropriately, or for long enough to allow for genotyping or additional testing if needed. Next slide.

Additional testing is available with our Serology Lab at CDC. This includes performing paired IgG testing, that is acute and convalescent specimens, which can provide additional evidence of measles infection if data are inconclusive. And we also perform avidity testing, which is a specialized test of IgG antibody that can provide information about breakthrough measles cases among previously-vaccinated people. Most cases do not require these additional tests, but they are available if necessary. Next slide.

Additional molecular testing is also available. Genotyping assists with outright detection and tracking, and should be performed on all real-time PCR positive specimens. This is important to help document sustained elimination of measles in the United States. There is also a test called MeVA, which stands for "measles vaccine assay". This is a specialized real-time PCR assay which can determine if the detected measles virus is vaccine-derived or from community transmission, and a true measles infection. Among people recently exposed to measles but also recently vaccinated. This test can differentiate a vaccine reaction from a measles case. We will discuss vaccine reactions more in depth in a later slide. Both of these tests are performed at CDC, and that for vaccine-preventable disease reference centers in California, Minnesota, New York, and Wisconsin. Next slide, please.

Overall, to summarize what we've covered so far regarding laboratory diagnosis, measles serology is a useful piece of diagnostic testing, but is limited by cross-reactivity with other causes of febrile rash, and high dependence on disease prevalence, that is the pretest probability. Diagnostic evaluation of measles should include both molecular testing, real-time, which is real-time PCR, and serology, which is testing for both IgM and IgG. A consideration of the clinical and epidemiologic context, including travel history, and vaccination status to interpret lab results should also be included. Finally, additional testing is available at CDC and the VPD reference centers in coordination with state or local Public Health laboratories. Next slide.

So let's do our third Knowledge Check. "What testing is recommended for measles diagnosis?" Is it A. measles IgM only, B. a swab for nasopharynx or oropharynx for real-time PCR only, C. both serology and swap for real-time PCR, or D. none of the above -- measles is a clinical diagnosis. Next slide.

The correct answer is C. As we discussed, serology and real-time PCR are complementary tests, and should ideally both be performed when evaluating a suspect case of measles. Next slide.

Now, I'll turn it back over to Dr. Filardo to review some information about measles vaccination.

Thanks, Stephen. Next slide, please.

So measles vaccine was first licensed in the US in 1963, in combination, MMR vaccine was licensed in 1971. MMR is an attenuated or weakened live virus vaccine. And the vaccine cannot cause measles, mumps, or rubella, and cannot be transmitted from person to person. However, transient side effects can occur which can mimic these diseases. And we'll return to this point later in just a few slides. MMR vaccination is highly-effective. It's estimated that a single dose provided at the typical schedule, which we will review, is about 93% protective against measles.

And two doses provide about 97% protection. MMR also has an excellent safety record. And we'll discuss vaccine side effects in a few slides. Next slide, please.

So MMR is licensed for people aged six months and older. And according to the routine pediatric vaccination schedule, a first dose of MMR is given at age 12 to 15 months, and a second dose is given at the beginning of school age years at four to six years of age. A dose between six to 11 months of age can be given, if needed, to provide protection during international travel, or during an outbreak response. If what is called this quote-unquote "zero dose" is given between six to 12 months of age, either for international travel, or outbreak response, two more doses should be given on any routine schedule. And just to note, all doses of MMR should be separated or need to be separated by 28 days or more. Next slide, please.

So MMR vaccine recommendations for adults take prior immune status into consideration, as adults may have been vaccinated, or infected with measles previously. Aside from written documentation of age-appropriate vaccination, which itself can serve as evidence of immunity, adults are considered to have presumptive evidence of immunity if they were born before 1957, if they have laboratory evidence of immunity, and that is a positive IgG. Just a note here that a testing for IgM is not testing for evidence of immunity. So testing for evidence of immunity is performed by testing for measles IgG. And, finally, presumptive evidence of immunity can also include prior laboratory-confirmed measles. So a clinical diagnosis of measles alone is not sufficient here, partly because of the measles mimickers we've discussed previously, that could provide false reassurance about measles immunity, and adults without evidence of immunity generally should get one dose of MMR. Two doses may be required or recommended for some high-risk adults, including healthcare personnel, international travelers, and post-secondary school students, which includes all schooling after high school. Next slide.

CDC recommends that all US residents older than age six months, who will travel internationally, receive MMR vaccine prior to departure. They are otherwise without evidence of immunity. So for infants six to 11 months of age, this means one dose of MMR vaccine, and as we discussed, this should be followed by two more doses on a routine pediatric schedule, assuming that all doses are separated by 28 days or more. For children 12 months of age or older, this means two doses of MMR vaccine, separated by at least 28 days. And for teenagers or adults without evidence of immunity, this also needs two doses of MMR vaccine, separated by at least 28 days. A CDC HAN alert was recently published regarding protection for international travelers, and is linked here on the slide. Next slide, please.

There are some contraindications to MMR, which are related to it being a live virus vaccine. So the main contraindications I'd like to highlight are first severe immunocompromising conditions, including hematologic malignancy, receipt of chemotherapy, or long-term immunosuppressive therapy. And this includes HIV. The CD4 percentage is less than 15%, or absolute CD for count as less than 200. Another country indication is family history suggestive of a congenital immunocompromising condition, unless the patient is assessed to be immunocompetent by a clinician or by laboratory testing. Another contraindication is a history of severe allergic reaction to MMR, or to an MMR vaccine component, such as gelatin. But note, egg allergy is not a contraindication to MMR vaccination, due to a good safety record of MMR vaccination in this population. However, people with any severe life-threatening allergies, such as anaphylaxis,

should talk with their health care provider to ensure it is safe to get MMR vaccination. And finally MMR should not be given to pregnant people. Next slide, please.

So MMR vaccine is generally very well-tolerated. Common side effects include fever, which occurs in less than 15% of recipients, a brief rash, which occurs in up to 5% of recipients, and lymphadenopathy, which is more common in adult recipients than in children. Rare serious adverse events do occur, but they are infrequent. Anaphylaxis occurs in two to 14 events per million MMR doses. Febrile seizures occur in one event per three to 4,000 doses, and a low platelet count can occur in one per 40,000 MMR doses. This low platelet count is often transient, and carries generally no long-term complications. But there is a higher risk of this occurring if the patient has a known diagnosis of ITP. Next slide, please.

So one thing to highlight here, that we've discussed, is that MMR itself can cause a self-limited rash, which is not contagious to others, and which is generally shorter in duration than the rash caused by wild-type measles infection. As we discussed, this can occur in up to 5% of MMR recipients. The photo on the right, which was a rash that was confirmed by testing to be related to overt vaccine reaction, shows that in some cases, this rash can be indistinguishable from the rash of a measles infection. Differentiating measles from an MMR reaction in the setting of an outbreak can be challenging, especially if MMR was given as post-exposure prophylaxis, which we'll touch on later. We want to highlight here that serology, that is testing for measles IgG, or IgM, cannot differentiate measles infection from MMR vaccination in this setting. However, molecular testing with MeVA can differentiate measles from an MMR reaction. And this is specialized testing that can be done only at CDC or at the vaccine preventable disease reference centers we discussed earlier. Overall, we think that this specialized testing shouldn't be required in most instances. Providers should carefully assess for measles risk factors, such as exposure, and travel history, if they're assessing a child or a patient, of any age, who develops a rash shortly after MMR vaccination. If there are no risk factors identified for measles exposure, then a rash after MMR vaccination would be presumed to be related to the vaccine itself. If there is concern for exposure, and there is recent vaccination, then specialized molecular testing can be performed in coordination with state or local public health authorities. Next slide, please.

Another note on this about commercial laboratories, so some commercial labs nationally have begun offering measles real-time PCR as part of a viral exanthem, or of an upper respiratory infection panel. Positive results from measles from these panel tests have so far only represented vaccine reactions based on investigations by state and local health departments. And clinicians should be aware that measles real-time PCR can detect vaccine derived measles virus 14 or more days after MMR vaccination, and even as many as 45 or more days after vaccination in some rare reports. This is another reason why obtaining vaccination history, especially about recent vaccinations, can be very important when assessing patients to present with a rash. Next slide, please.

So to review what we've discussed about MMR; MMR is a safe and very effective vaccine. MMR can be received by most people, but it's contraindicated for pregnant people and people who are severely-immunocompromised. International travelers should be assessed for prior vaccination or evidence of immunity, and international travelers should be provided MMR, if appropriate, for protection during the travel. And, finally, MMR can cause a self-limited febrile

rash, but molecular testing can distinguish between measles and a vaccine reaction, if it's necessary. Next slide, please.

So I wanted to talk a little bit more about the big picture of measles prevention with MMR vaccination. Next slide.

So, overall, despite high national and state level MMR coverage, regional differences in coverage can hinder measles control. This has been observed in prior measles outbreaks, which have occurred in geographic areas where vaccine coverage is lower than what is required to sustain elimination and prevent outbreaks. The map on the right highlights an example of regional heterogeneity and vaccination coverage, which has been documented by the New York City Department of Health and Hygiene after a polio case was detected in New York in 2022. These data show polio vaccination coverage, and not measles, but highlight the phenomenon of substantial heterogeneity in vaccine coverage by zip code, with darker shades of blue correlating to higher estimated coverage. Overall, New York City polio vaccine coverage was estimated to be 86. 2% at the time of this map in June 2022. But this number masks the substantial regional differences. Some zip codes have polio coverage estimates estimated and 99% or higher, while others have coverage estimates that are as low as 55 to 60%. CDC is working to estimate fine-area coverage for measles vaccination to identify regions where measles may spread more easily. And based on preliminary data, despite high national and state level MMR coverage, a substantial portion of census tracts in the US have coverage levels well below 95%, which is the level of measles vaccine coverage that is considered required to prevent community spread of measles. Next slide, please.

Overall, our data systems which track national coverage with MMR vaccination have not shown a decline in receipt of the first dose of MMR, also called "MMR1" here, with 91. 6% of children nationally born during 2018 to 2019, receiving MMR by 24 months of age. However, surveillance, which estimates two-dose coverage for children entering school, that is in the five to six-year age range, did show a decline from 95. 2% for the 2019 to 2020 school year, to 93. 9% for the 2020 to 2021 school year. This is lower than the 95% or higher vaccine coverage considered required to suppress the spread of measles within a community. And, again, if we take what we saw in the prior slide about regional heterogeneity, this declining percentage of two-dose MMR coverage likely reflects a number of communities with much lower vaccine coverage, and where many children are at risk of developing measles and its complications. Next slide.

Within these data, there were also some apparent disparities I wanted to highlight. When first dose of MMR coverage by 24 months was examined by insurance status in a recent CDC publication, we see the children receiving Medicaid coverage, other insurance, that is neither private nor Medicaid, and uninsured children have lower coverage than children who are privately-insured. And uninsured children particularly had coverage estimates as low as 80%, leaving many vulnerable to measles infection and complications. Next slide.

To more effectively address declines in routine immunizations resulting from the COVID-19 pandemic, CDC has developed the RISE Initiative, which stands for "Routine Immunizations on Schedule for Everyone", which aims to get all Americans back on schedule with a routine

immunizations to protect everyone from vaccine-preventable disease and disability. And additional information is available at the website linked here. Next slide, please.

So for the last part of the presentation, I'll focus on measles outbreak response, and then we can take questions. Next slide, please.

So here's an outline, overall, of measles outbreak response activities, which are most relevant to bedside providers. We'll walk through each of these pieces of the measles outbreak response in more detail. Next slide.

So a key step for providers is to identify cases and establish the diagnosis of measles. At the bedside, there are some important pieces of history that can help determine whether or not there should be concerned for measles. First, does the person meet the clinical case definition? Recall as we discussed that this is fever, and rash, and at least one of the three C's, that is cough, coryza, or runny nose, or conjunctivitis. A detailed clinical history could also provide clues potentially to other viral illnesses which can mimic measles, and as we discussed earlier. And second, what is the person's vaccination history? Have they received any doses of MMR or other measles containing vaccine? And, finally, has the patient traveled in the last 21 days internationally or domestically to a place where measles is circulating. All of these factors can change how likely it is that someone presenting with a rash, or other clinical symptoms, has measles. Next slide.

Another key piece of this we want to highlight is to involve Public Health early when measles is suspected. Public health departments can help advise on the need for testing, and on the appropriate routing for specimens. As we've discussed, testing should ideally include serology and real-time PCR. And real-time PCR is most commonly-performed in state public health labs. So reaching out to a local or state public health department can help with testing coordination. And because controlling measles transmission requires a detailed and coordinated response, early involvement of public health departments is critical to prevent measles outbreaks. Next slide.

So if an outbreak is declared, clinicians and their health department can work together to identify and prioritize susceptible contacts to measles cases. And those without presumptive evidence of immunity are at high-risk to develop measles. There are also specific groups that are at high-risk for serious disease if they were to develop measles, including infants aged less than one year, pregnant people, and people with immunocompromising conditions, or taking immunocompromised medications. Next slide, please.

Also, as we've discussed, vaccination is key to measles control, and community vaccination campaigns can be implemented to control an outbreak. First, providers can ensure patients are up-to-date with MMR vaccine requirements or recommendations. If preschool-aged children are particularly at risk due to the outbreak location, or outbreak transmission settings, a second dose early before the routine schedule, between age one and four years, could be considered as long as the dose is 28 days after a prior dose of MMR vaccine, or 28 days after any other live virus vaccine. And, finally, if infants less than 12 months of age are at risk due to the outbreak characteristics, a zero dose, quote/unquote "zero dose" between age six and 11 months could be considered, but this should be followed by two or more, two more doses on the routine pediatric schedule as we discussed. Next slide, please.

Next, there's post-exposure prophylaxis or PEP. Two options are available for PEP; MMR vaccination or immunoglobulin. PEP may provide protection from developing measles, or may modify the clinical course of disease and protect against severe complications. MMR should be given within 72 hours or three days of the initial measles exposure to be effective as PEP. Vaccination can be given after this window, but it would only be expected to protect from future exposures. Immunoglobulins should be given within six days of exposure to be effective, and can be given intramuscularly, that is IMIG, or intravenously, or IVIG. IVIG should be prioritized for adolescent or adult contacts who are at high-risk of severe disease, primarily pregnant people or people with immunocompromising conditions because IMIG, or intramuscular immunoglobulin, may underdose people weighing over 30 kilograms. Immunoglobulin is also the only post-exposure prophylaxis available to groups that cannot get MMR vaccination, including infants under six months of age, pregnant people, and people who are severely-immunocompromised. Next slide, please.

So case patients with measles should be isolated for four days after rash onset. People with immunocompromising conditions may require more prolonged isolation, given the possibility that they can shed measles for longer, and isolation should be tailored individually in coordination with the Health Department. Susceptible contacts without presumptive evidence of immunity should be offered post-exposure prophylaxis, or PEP, while otherwise excluded from congregate settings, such as schools, healthcare settings, or daycare. There's a lot of nuance to the exclusion of context, including the type of congregate setting, and the choice of PEP. So we won't go into a lot of detail here, but more information is available in "The Vaccine Preventable Disease Surveillance Manual" from the CDC, which is linked at the bottom of this slide. Next slide, please.

So another aspect of outbreak control lies with the healthcare setting. Clinicians can help prevent spread of measles in these, in healthcare settings if a suspect cases identified by doing a few things. First, encouraging patients or families to contact the healthcare facility before arrival, if they are known to be a suspect case, so that the facility can prepare. Second to provide the patient a face mask, if they're old enough to wear one, and to promptly isolate the patient in a room with the door closed. And third, to implement standard and airborne precautions as soon as possible in an airborne infection isolation room, or AIIR, if available. If there's no airborne isolation room available, such as might occur in a clinic, a single room with closed door, away from possible susceptible contacts, may be use pending transfer to an airborne isolation room. Another note here is that all healthcare personnel evaluated suspected or confirmed measles cases should observe airborne isolation, including a fit-tested N95, or equivalent. And this is regardless of the vaccination status or presumptive immunity to measles for the healthcare provider. The links to guidance for infection prevention in healthcare settings will be linked at the bottom of this slide, when slides are shared. Next slide, please.

So I just wanted to highlight here, at the conclusion of our talk, some resources for clinicians that CDC has prepared. This includes vaccine information for patients, families, and clinicians about MMR vaccination, and information about campaigns from the CDC regarding Vaccinate with Confidence prepared by our colleagues in the Immunization Services Division from CDC. Next slide, please.

So I'll turn it back to our moderator, and thank you so much for the opportunity to present today.

Presenters, thank you for providing this timely information to our audience. We will now go into our Q&A session. In addition to our presenters joining us for the Q&A session are from the National Center for Immunization and Respiratory Diseases, Captain David Sugerman, a medical officer and team lead for the Measles Rubella CMV team; Dr. James Lee, a medical officer in the Immunization Services Division; Dr. Andrew Beck, a microbiologist with the lab team, and Ms. Raydel Anderson, a microbiologist with the lab team, with the Center, again, with the National Center for Immunization and Respiratory Diseases at CDC. For our audience, please remember that to ask a question using Zoom, click the Q&A button at the bottom of your screen, then type your questions in. Please note, we often receive many more questions than we can answer during our webinar.

So our first question for our presenters is: "Can you talk a little bit about the adverse events that you referred to from the vaccine?" We have a few questions regarding that. One of our questions asks: "If you suspect that your patient has had an adverse reaction, is there a way that the clinician should report this adverse reaction?".

Yeah, this is Dan Filardo. I can take that question. You know, overall, in terms of reporting of adverse reactions, to vaccines in general, there is a mechanism by which anyone can report possible vaccine side effects, and that's a system called the VAERS, or V-A-E-R-S, which is co-managed by CDC and FDA. CDC's website on MMR vaccination does have additional information about VAERS, and how to report a potential side effect if encountered. Reporting is not mandatory, and so for, say, an expected side effects that occurs in five to 15% of patients, such as a self-limited rash, or self-limited fever, it's certainly not mandatory to report those adverse reactions. But the VAERS platform is a place where any provider can go to report adverse reactions, if they'd like to do so.

Thank you very much! We have some questions regarding signs and symptoms of measles infection. Our first question asks: "Can the koplik spots appear in areas other than the buccal mucosa?".

Hi, this is Dan Filardo. I can take that question. It's an interesting one. I think, you know, I've seen reports that kolpik spots are almost always discussed as pathognomonic for measles, meaning that they, you know, really generally only occur with measles infection, and not other infections. And in resources that discuss koplik spots, they're pretty much always mentioned to be on the buccal mucosa. I've seen one reference that mentioned that they could occur on the labial mucosa meaning, you know, on the mucosa, behind, or, you know, inferior to the lips, over the front teeth. But I think that that is probably a very unlikely occurrence. And just, overall, in terms of Koplik spots, I do want to highlight that they are considered to be pathognomonic for measles. And so providers can certainly evaluate for them when they're evaluating a case in which they're concerned for measles, but their absence certainly does not rule out measles, like any exam finding that they only have limited sensitivity or specificity for measles infection. So, really, the overall pieces of history and clinical examination that I highlighted should be taken into consideration.

Thank you!.

Thank you very much! We also have questions regarding specimen collection and testing. One question asks: "When swabbing, is there a preference between nasal versus oral?".

Hi, this is Dr. Kirk. I can take that one. No, to my knowledge, there's no preference upon which swab to take, which is why we typically recommend them as sort of with the slash in the text, just to show that it can be either. Over.

Thank you very much! Another question asks, and this is regarding complications of measles infection: In your knowledge, are there any patient criteria or demographics that generally make the complications more likely?".

I can take that question. This is Dan Filardo. I think age is, we highlighted on a slide earlier, you know, groups that are at highest risk of developing severe complications of measles. So that's really age, and we do see somewhat of a bimodal distribution there with age under five and age over 20. Those two groups having a higher rate of complications, overall. But specifically with severe complications, including hospitalization, or pneumonia, age under one is really probably the largest risk factor when it comes to demographics. Pregnant people are also at risk of developing more severe manifestations of measles, or more severe complications. And, finally, people who are severely-immunocompromised are at higher risk of complications. Over.

Thank you! Our next question is regarding some of the PEP discussions, I assume. The question asks: "Do you have recommendations for MMR vaccination for patients who have received IMIG or IVIG?" I suspect they want to know how long after IMIG, IVIG, etc. , can a person receive MMR vaccination?

Yes, I can take that. This is Dan Filardo. After receipt of immunoglobulin, there is a period in which people should not receive MMR vaccination, because the circulating immunoglobulins would be expected to interfere to -- with the sort of robust response to that vaccination. And so for immunoglobulin, which is given intramuscularly, or IMIG, MMR should be administered no earlier than six months after IMIG. And for intravenous immunoglobulin, or IVIG, MMR should be administered no earlier than eight months after IVIG.

Thank you very much! That's very helpful. Our next question is regarding some of the data around outbreaks, recent outbreaks that was shared the beginning of the presentation. The question asks: "Can you please explain how this latest rise in cases that you referenced is similar or different from the rise encountered in 2014?".

Hi, this is Adria Mathis. I can take that question. In 2014, there was a very high global incidence of measles that resulted in a lot of importations into the US, followed by a large outbreak that began at the end of 2014 and went into 2015. So this year, we are just trying to raise awareness that we are starting to see an increase in international importation into the US, due to an increase in global measles incidence and increased travel. So we have not seen any outbreaks at this time, but we do want to make everyone aware that it is possible to have outbreaks, and that everyone

should be aware of measles on the differential if you see a patient that meets the clinical case definition for measles. Thank you!

Thank you! That's very helpful. Our next question is along similar lines, but focusing more on the vaccination side of it. And the question asks: Does MMR immunity wane, and should fully-vaccinated adults get boosters?".

Hi, this is Dan Filardo. I can touch on that, and answer that question. Overall, you know, the routine schedule that is provided to US residents, that I highlighted, we believe confers for really most people, lifelong immunity. Like any vaccination series, there can be some people, who have a waning antibody response. Overall, our recommendations for most adults in the United States is that receipt of age-appropriate MMR vaccination is presumptive evidence of immunity, and most adults do not require antibody testing to evaluate for, say, an IgG response that would suggest measles immunity. There are some higher-risk groups that may undergo screening, such as healthcare workers depending on the policy of the individual healthcare institution. But, overall, CDC does not recommend routine antibody testing for adults that have received age-appropriate vaccination.

Thank you very much! Our next question is regarding the timeline of developing symptoms during a measles infection. The question asks: "Can the order of the nonspecific and specific symptoms change in patients?".

This is Dan Filardo. I can answer that question. There are, there are some nuances to the timeline. Any infection can present outside the textbook. You know, it's one thing I learned in my infectious disease training. The presentation of measles, among those who are susceptible to measles, meaning they have not had measles before, and they are unvaccinated against measles, is pretty stereotypical. And so the onset of prodromal symptoms, preceding the rash, is really seen for the vast majority of people, to my understanding. For people, who it's quite rare for people to develop measles after a prior measles infection. Because measles infection, we think confers quite robust and lifelong immunity. There are rare cases of breakthrough cases among people who have previously received measles vaccination. And sometimes in those cases, the presentation can be atypical, and that maybe the prodromal symptoms occur at the same time as rash onset, or in a slightly different order. And as I said, the rash characteristics can be somewhat outside the typical in those cases. But, really, the majority of measles cases occur among those who are otherwise susceptible, meaning, no history of measles infection and unvaccinated. And for those individuals, the presentation typically goes along the timeline that I presented with prodrome, followed by rash. Over.

Thank you very much! And we just have time for one last question. This question is regarding testing. And the question asks: "What is the specimen type used for the MeVA assay, and what is the turnaround?".

Sure. This is Dr. Crooke. I can take that one. So the MeVA test is a specialized real-time PCR test. So it's the same specimen types that you would submit for a routine real-time PCR test. That's a nasopharyngeal, oropharyngeal swab, or urine. I can't speak to the turnaround times for the reference centers. I know that for the test at CDC, we do have up to seven days for

turnaround. We frequently beat that, but that is the turnaround time that's listed on our test directory. Over.

Thank you! That's very helpful. At this point, I want to thank everyone for joining us today with a special thanks to our presenters for sharing their expertise and answering these questions.

For our audience, please note that all continuing education for COCA calls is issued online through the CDC Training and Continuing Education Online system at tceols.cdc.gov. Those who participate in today's live COCA call, and wish to receive continuing education, please complete the online evaluation and posttest before September 18, 2023, with the course code WC4520-081723. The access code is COCA081723. Those who will participate in the on-demand activity in wish to receive continuing education should complete the online evaluation and posttest between September 19, 2023, and September 19, 2025, and use course code WD4520-081723. The access code is COCA081723. Continuing Education certificates can be printed immediately upon completing your online evaluation.

A cumulative transcript of all CDC's CE's obtained through the CDC Training and Continuing Education Online system are maintained for each user. Today's COCA call will be available to view on-demand a few hours after the live Coker call at emergency.CDC.gov/coca.

We invite you to join us Thursday, August 31st at 2:00 p.m. Eastern for our next COCA call. The topic will be "2023 to 2024 Recommendations for Influenza Prevention and Treatment in Children: An Update for Pediatric Providers".

You can visit emergency.cdc.gov/coca for more details about this COCA call and other upcoming COCA calls. We invite you to subscribe to receive announcements for future COCA recalls by visiting emergency.cdc.gov/coca/subscribe.asp. You will also receive other COCA products to help keep you informed about emerging and existing public health topics.

Again, thank you for joining us for today's COCA call, and have a great day!.