Date: November 14, 2024

CDC COCA Call Transcript: 2024-2025 Recommendations for Influenza Prevention and Treatment in Children: An Update for Pediatric Providers

Good afternoon. I'm Captain Ibad Khan, and I'm representing the Clinician Outreach and Communication Activity, COCA, with the Office of Emergency Risk Communication at the Centers for Disease Control and Prevention. I would like to welcome you to today's COCA Call 2024 to 2025 Recommendations for Influenza Prevention and Treatment in Children: An Update for Pediatric Providers. 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, presenters, and moderators must disclose all financial relationships in any amount with ineligible companies over the previous 24 months, as well as any use of unlabeled product or products under investigational use. CDC, our planners and presenters/moderators 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 with the exception of Dr. Kristina Bryant, who would like to disclose that she is an investigator on multicenter vaccine trials with Enanta, receives an honoraria for a column in pediatric news and receives royalties from Oxford University Press. All of the relevant financial relationships listed for this individual have been mitigated. Content will also not include any discussion of the unlabeled use of a product or a product under investigational use, with the exception of Dr. Kristina Bryant's discussion by the American Academy of Pediatrics' recommendation that the use of HD influenza vaccine could be considered in children aged three to 17 years who have undergone hematopoietic cell transplantation. CDC did not accept financial or in-kind support from ineligible companies for this Continuing Education.

At the conclusion of today's sessions, participants will be able to accomplish the following: highlight key recommendations in the AAP influenza policy statement, "Recommendations for Prevention and Control of Influenza in Children 2024 to 2025" and in the CDC Advisory Committee on Immunization Practices' document, "Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices United States 2024 to 2025 Influenza Season. " Review strategies pediatric healthcare providers may implement to increase influenza vaccination rates and highlight current health disparities in vaccination coverage. Describe considerations and best practices for co-administering influenza vaccines and other childhood immunizations. List recommendations for influenza testing in outpatient and hospitalized pediatric patients with suspected influenza and describe test limitations and review antiviral medications for influenza and CDC recommendations for antiviral treatment of children with suspected or lab-confirmed influenza.

After the presentations, there will be a Q&A session. You may submit questions at any time during today's presentation. To ask a question, click the Q&A button at the bottom of your

screen, then type your question in the Q&A box. Please note, we often receive many more questions than we can answer during our webinars. If you're a patient, please refer your questions to your healthcare provider. If you're a member of the media, please contact CDC Media Relations at 404-639-3286 or send an email to media@cdc.gov.

I would now like to welcome our two presenters for today's COCA Call. We are pleased to have with us.

Dr Tim Uyeki, the chief medical officer of the Influenza Division in the National Center for Immunization and Respiratory Diseases at the Centers for Disease Control and Prevention and Dr. Kristina Bryant, who is a member of the Committee on Infectious Diseases at the American Academy of Pediatrics. AAP, a professor of Pediatrics at the University of Louisville School of Medicine, hospital epidemiologist at Norton Children's Hospital, and the medical director of the System Pediatric Epidemiology and Infectious Diseases Norton Children's Medical Group in Louisville, Kentucky. It is my pleasure now to turn it over to Dr. Uyeki.

Dr. Uyeki, please proceed.

Thanks so much. I'm very pleased to present in collaboration with the American Academy of Pediatrics and Dr. Bryant. Next slide, please. So, I'm going to try to cover influenza activity and disease burden.

I'll speak a little bit about influenza vaccine coverage and vaccine effectiveness and end by talking about influenza testing and antiviral treatment recommendations. Next slide. So, I'll start with influenza activity and influenza disease burden. Next slide. So, on the left, this is a slide that shows influenza positive tests reported to CDC by US clinical laboratories for the past season, and the point of that is that last season was a predominantly influenza A H1N1 pdm09 virus season.

We did have about a third of the influenza A viruses. A little bit more were H3N2 and we did have about 23% influenza B viruses. On the right, what you can see is, actually it's a different scale. So, this is to the far right, the latest influenza surveillance data of your [inaudible] data, and the point is, it's almost like the tail end on the left figure far right, influenza activity is very low in the US nationally at this time, but it is slightly increasing, still very low levels. But in recent weeks it has slightly increased, and we expect influenza activity only to increase in the coming weeks to months this fall, winter season.

Next slide. So, the spectrum of influenza virus infection varies, and disease severity and clinical manifestations vary by age, host factors, immunity and by influenza virus type and influenza A virus subtype. We know that asymptomatic infection can occur. Most people who are symptomatic experience uncomplicated illness after a short incubation period, about one to two days, and most people who are symptomatic experience upper respiratory tract illness with or without fever. Fever may not be present in all patients, particularly in elderly and immunosuppressed individuals, and the classic signs and symptoms are the abrupt onset of fever, cough, chills, myalgia, fatigue, headaches, sore throat, and runny nose.

But not everyone who is symptomatic with influenza manifests the classic signs and symptoms. In young children, gastrointestinal symptoms can occur more commonly and particularly are more common with influenza B, and just to say in young infants, they may manifest fever only and irritability and may not have respiratory symptoms, and so they may be considered to have rule out sepsis, but one should try to elicit a history of any close contacts in the household who might actually had acute respiratory illness symptoms, and one might sample the upper respiratory tract and test for influenza. And then there are, unfortunately, a minority of people who do experience complicated illness. Next slide. So, influenza complications, I would divide them into moderate as well as severe to critical illness.

Moderate illnesses, some examples for children are otitis media. This is a recognized complication of influenza in young children, sinus infections can occur, and in all ages, exacerbation of underlying chronic disease definitely occurs. In some of these individuals, they may require hospitalization for severe exacerbation of chronic underlying conditions, but the most common respiratory complications leading to hospitalization are pneumonia, and this can be viral pneumonia, but also secondary bacterial infection complicating influenza. In addition, I would just note that although we focus a lot on parainfluenza virus as well as RSV, other viral etiologies of croup, influenza virus infection can precipitate croup. Influenza virus infection can precipitate bronchiolitis in young children and then Status asthmaticus can occur, even in children without a prior history of asthma or reactive airway disease, and then other really severe complications are bacterial tracheitis and acute respiratory distress syndrome.

There are rare cardiac complications such as myocarditis and pericarditis that have been reported in children, myocardial infarction is more of an issue in adults with underlying coronary artery disease, and there is a wide range of neurologic complications in children. Rare encephalopathy and encephalitis can occur in adults, cerebrovascular accident. Guillain-Barre syndrome is very uncommon, but it can occur with influenza, ADEM, and Reye syndrome can occur. Reye syndrome is more common with influenza B than influenza A, and typically in the past, it's been associated with influenza and salicylate exposure, and fortunately, we rarely see that anymore, and then bacterial co-infections, community-acquired, the most common pathogens both in children and in adults are Staphylococcus aureus, both methicillin-sensitive and methicillin-resistant, pneumococcus and Group A streptococcus, but it depends on the host and what they may be colonized with in terms of what they -- there could be an underlying exacerbation, such as a child who has different bacterial colonization with cystic fibrosis. There are musculoskeletal complications.

I would remind pediatric providers that school-aged children can present with abrupt onset of myositis. It's typically bilateral gastrocnemius, severe muscle pain in the calves, and they can actually progress to rhabdomyolysis. Multi-organ failure can occur with influenza with both respiratory and acute kidney dysfunction, septic shock, and then don't forget healthcare-associated infections, particularly in a child who is in the ICU and is ventilated. Ventilator-associated pneumonia can occur, but on the wards, it is possible for other healthcare-associated infections to occur. Next slide.

So, disease burden, we use a variety of methods to estimate, because it's -- we do not have influenza testing on every person that dies of suspected influenza or is hospitalized, but there's a

wide range, and the range of illnesses we estimate from anywhere from 9. 4 million to 41 million per year over the last quite a few seasons, but a wide range of hospitalizations, from 100,000 to 710,000 per season, and then deaths from about 5,000 to 52,000 deaths per year. And you can see in the figure that there some seasons are much more severe than others, so quite a variability in the severity of a seasonal influenza epidemic in the US. Next slide. This is a slide of influenza associated hospitalizations.

This is lab-confirmed hospitalizations in all age -- by age group through our population-based surveillance system. This is last season, and what you see is cumulative influenza associated hospitalization rates by far are dominated by people 65 years and older and then moderately high rates in those 50 to 64 but also see moderately high rates in young children less than five years and then younger adults and school-aged children hospitalization rates are low. Next slide, please. And this is showing just children less than 18 years cumulative pediatric age groups, laboratory-confirmed influenza associated hospitalization rates from last season, and what you can see is the younger you are, the higher the hospitalization rate for pediatric influenza associated illness with children less than six months old, the highest hospitalization rates, and then with age, increasing age, there is a decreasing hospitalization rate. So, adolescents have the lowest hospitalization rates for influenza.

Next slide, please. So, this is also data from last season showing underlying medical conditions in children who are hospitalized with lab-confirmed influenza, and what you see is, is that in the older age groups, which is the dark green there, you can see a higher prevalence of obesity and neurologic disease. Next slide, please. But I want to make the point that there are children who are hospitalized, who were previously healthy without known underlying medical conditions, that are hospitalized with lab-confirmed influenza, and these are data from last season. And you can see the younger you are, the higher percentage of children who do not have any underlying medical conditions, and it's about three quarters in young infants and still more than half of young children aged six months to less than two years, and you can see that with increasing age, it's fewer percentage of children who are hospitalized without any underlying medical conditions.

In the older-aged children, it is those typically who have underlying medical comorbidities. Next slide, please. So, this is recently published data from the end of October in the MMWR Surveillance Summaries. I just want to highlight these are pediatric age groups. The actual publication shows all adult age groups as well, but I've just highlighted here two pediatric age groups, and if you go to the far right column, this is the most recent season data from 2022 to 2023, I just want to highlight that in terms of pneumonia, you see about 30% of kids who are hospitalized had influenza-related pneumonia, and then about 19% or so of children were hospitalized in the PICU, you can see that a small, smaller percentage of about 4 to 5% were hospitalized and put on invasive mechanical ventilation, and then a very small number at the bottom, a very low percentage actually died in hospital.

Next slide. Now, here are some data from last season. This is hospital rate data, lab-confirmed influenza hospitalizations showing disparities in racial and ethnic groups with the highest rates of hospitalization in -- you can see for those Hispanic, Black, non-Hispanic and American Indian Alaska Natives Non-Hispanic. So, we have special considerations to try to reduce, you know, we

need to especially try to reduce these racial and ethnic disparities in severe influenza in children. Next slide, please.

This shows reported pediatric influenza associated deaths in the US reported to CDC by week of death and by season. This is the prior three seasons, and you can see during the 2022 2023 seasons, we had 187 pediatric influenza associated deaths, and last season, we had 204. These are -- most of these are vaccine preventable, and the ones that are six months and older, and the bulk of these children who have died, this has been a pattern for many, many years, have not been vaccinated for the current season. And then, so far this season, we have had one pediatric influenza associated death this season reported to CDC. This is very, very, very sad, and we need to do a better job at preventing these collectively.

Next slide. So, among -- so I mentioned deaths, pediatric deaths that have been reported, and I mentioned in hospital deaths are low, and this is also data that was recently accepted and published online to the -- in the Journal, Clinical Infectious Diseases. This is data from the US CDC data. I'm just highlighting there are two pediatric age groups less than five and five to 17 years, and you can see in the far right column that in hospital deaths, this is through our FluSurv-NET surveillance platform very low percentage of children died, but they're -- and a very low percentage died after within 30 days after discharge from surviving hospitalization, but I just want to make the point that some children do die after they survive hospitalization, and, of course, in older adults, this is a much bigger problem, much greater burden. Next slide, please.

So overall, there are specific groups that are, we feel, at increased risk for influenza complications and severe illness, and I hope that I've convinced you that children less than two years old, and clearly, it's adults greater than 65 years old, are at increased risk for influenza complications. Also, it includes persons with chronic medical conditions, including pulmonary or cardiovascular, renal, hepatic, neurologic, neurodevelopmental, hematologic, metabolic or endocrine disorders, persons who are immunocompromised, persons with extreme obesity, children and adolescents who are receiving aspirin or salicylate containing medications, who might be at risk for Reye syndrome after influenza virus infection, residents of nursing homes and other long-term care facilities, and this includes children who are in pediatric long-term care facilities, pregnant persons and people up to two weeks postpartum, and I've shown you some racial and ethnic disparities, so people from certain racial and ethnic minority groups, including non-Hispanic Black, Hispanic or Latino, and American Indian or Alaska Native persons. Next slide, please. So, let me move on to a short presentation about influenza vaccine coverage and influenza vaccine effectiveness. Next slide, please.

So, this is some data from the past season. This is cumulative influenza vaccination coverage. This is weekly rates, and you can see that, basically in the lavender or light purple there at the top, that influenza vaccine coverage is higher in children less than five years old, and it's lowest in adolescents. And so, we really need to do a better job with that, and we still, in all of these pediatric age groups, we still need to get coverage up higher than it has been. Next slide, please.

So, this is data from -- since the 2019 2020 season, but also includes the current season, and the current season is in the far right columns for under each category, there light purple or lavender, and what you see is overall, to date, this season, about 30% of kids have received influenza

vaccination, and this is data through November the 2nd. So, there is a data lag, and coverage is probably a little bit higher than this, but basically, you can see, in comparison to the previous seasons, were either a little bit lower or on par with what's with coverage the last few seasons. It's still under what we would like to see, and we need to do a better job at advocating for influenza vaccination in children this season. Next slide. So, this is also data as through November the 2nd.

This is weekly influenza vaccination status and intent for vaccination, and to the far right column what you see in the dark blue and then the next slightly lighter blue, the two bottom colors are children who have received a vaccination or definitely will get a vaccine, in contrast to those who probably or definitely or probably will not get a vaccine. And so, you can see that we're still under 60% if you combine the bottom two categories, and so we all need to do a better job at trying to increase that and particularly talking to parents of children. Next slide. So, let me talk briefly about influenza vaccine effectiveness. So, influenza vaccine effectiveness varies by virus antigen and match to circulating virus strains, and we have quite a range in estimated vaccine effectiveness from season to season, and you see in the figure on the right there a range of anywhere from 19 to 60%.

This is in all ages. I'll just say that there is some interim -- there's an interim estimate from earlier this year from the Southern Hemisphere. Influenza vaccine effectiveness in young children was 39%, and so, you know, it's hard to say how that translates to this coming season in the US, but I just put that there for your information, and we know from other studies that have been done over a number of years that influenza vaccination effectiveness can be as high as 65% against reducing the risk of pediatric intensive care unit admission for children, and there was one study from my colleagues at CDC that reported vaccine effectiveness of 65% against influenza-related death in children. So, it's not just benefit of influenza vaccination to reduce mild disease, but actually influenza vaccination can prevent severe influenza and severe complications. Next slide, please.

So, let me move to influenza testing. Next slide. So first, let me start with talking a little bit about influenza viral shedding, and the point in the upper right is that influenza viruses can be detected in the upper respiratory tract the day before illness onset, but that virus levels typically peak in the upper respiratory tract within 24 hours after onset. The highest infectious period is within three days after onset and just to say a few notes that are exceptions, that there are young children can be infectious for longer periods. Immunocompromised children can be infectious for longer periods, and critically ill patients might have longer influenza viral replication, particularly in the lower respiratory tract.

Next slide, please. So, the optimal respiratory specimens to detect influenza viruses in the upper respiratory tract in pediatric patients who do not have severe disease, have clinically mild disease, the highest yield is in a nasopharyngeal swab, ideally collected within three to four days of illness onset. You can detect viral antigen for about three to four days after illness onset, but you can detect viral RNA a bit longer, because nucleic acid detection assays are more sensitive. Now, it depends on the assay, and so you should really check the manufacturer's package insert to see what specimens are approved for that specific test. Some tests, nasal swabs, nasal pharyngeal aspirates, nasal aspirates, or combined nasal and throat swabs may be acceptable.

There is slower clearance of influenza viruses and severe disease in, as I mentioned, immunocompromised children, as well as those who are on immunosuppressive therapy, including with corticosteroids, may have slower clearance of influenza viruses and prolonged infectious viral replication. Children who are hospitalized with severe lower respiratory tract disease may have prolonged viral replication in the lower respiratory tract, and when you sample the upper respiratory tract, they might have actually cleared virus from the upper airways, and so if you suspect influenza and you sample the upper respiratory tract and testing for influenza viruses is negative, you should definitely sample the lower respiratory tract. In an intubated child, you should collect an endotracheal aspirate specimen to test for influenza viruses if you suspect influenza and the diagnosis has not been made by testing upper respiratory tract specimens, and we have better data in adults to know that you can miss the diagnosis by only sampling the upper airways. Next slide, please. So, there are quite a few different influenza tests available in different clinical settings, and they differ by the time to produce results the information provided, approved respiratory specimens, and accuracy, and the two categories that I would really focus on are antigen detection or nucleic acid detection and just to say there are multiple, single-plex as well as multiplex assays that have been either cleared by FDA or authorized, including by emergency use authorization, and this includes both multiplex assays, and there are some assays that have been cleared or authorized for use in the home setting over the counter, so just to say that includes some multiplex assays.

There are point of care assays that do not require a clinical lab, and there are others that are classified as moderately complex and highly complex that do have higher clinical laboratory requirements. Next slide, please. So, there are differences in the time to produce results. The antigen tests typically provide results in 10 to 15 minutes. The molecular assays, including rapid assays, molecular assays can produce results within 15 to 30 minutes, and then there are some others, including multiplex and molecular assays that take a bit longer, up to 45 minutes and then standard molecular assays that may take an hour or more.

And then there are assays that are performed in clinical laboratories, complex, highly complex clinical laboratories like public health laboratories that may take quite a few hours to produce results just to note that there are differences in the sensitivity. So typically, antigen detection tests have low to moderate sensitivity, whereas molecular assays have high to very high sensitivity or I would say moderately high to high sensitivity. All of these assays have very high specificity, so false positive results are uncommon, but false negative results can occur with antigen detection tests, and it's very important to really think about a lot of different factors and to really interpret the test properly -- test result properly, particularly negative test results during influenza season. Next slide, please. So, recommended tests in outpatients are rapid influenza molecular assays.

These are recommended over influenza rapid influenza antigen tests. For hospitalized patients, RT-PCR or other influenza molecular assays are recommended, and antigen detection tests are not recommended. Don't order viral culture for the initial or primary diagnosis of influenza. It's important for public health investigations. It may be actually very useful for immunocompromised patients and for outbreak settings.

Don't order serology for influenza. There are some companies that do offer influenza serology, but a single serum specimen and serology on that specimen is uninterpretable. You really need paired acute and convalescent sera, and serology needs to be done at specialized labs. Next slide, please. So, just to show that over time there has been a change in the kinds of influenza tests that have been performed.

These are data from recently published from the Influenza Hospitalization Surveillance Network, and what you see is that there's been a decrease over time of single-plex standard molecular assays and rapid influenza antigen tests and an increase over time of the use of rapid influenza molecular assays as well as multiplex molecular assays and which is a good thing, although there is a cost, a higher cost, of these molecular assays. Next slide. So, let me move on to influenza antiviral treatment. Next slide. So, there are four FDA-approved antivirals that are recommended for treatment of influenza in the US this season.

There's no evidence of resistance among circulating seasonal influenza A and B viruses. All of the recommended antivirals have demonstrated efficacy in randomized controlled trials for early treatment of outpatients with uncomplicated influenza, and early means less than two days after illness onset, and the two categories of drugs that are recommended are the neuraminidase inhibitors, Oseltamivir, Zanamivir, and Peramivir. These drugs block the release of influenza viruses from infected cells, and then the other category is the cap-dependent endonuclease inhibitor Baloxavir marboxil. Baloxavir inhibits influenza virus viral replication and can reduce viral load in the respiratory tract pretty substantially within 24 hours, and that is an advantage over the neuraminidase inhibitors. So, just to show you -- to highlight in the table below, to show there are differences in both the age of approval, the route of administration, as well as the dosing.

So, Oseltamivir is given twice daily for five days. It's recommended for all ages. Zanamivir is an inhaled powder. You need to use a disc inhaler device. It's administered twice daily for five days in children seven years and older.

Peramivir is a single intravenous infusion for children aged six months and older. Baloxavir is a single oral dose for children who are otherwise healthy age five years and older or for children aged 12 and older who are at high-risk of complications, have underlying medical conditions. Next slide, please. So, our antiviral treatment recommendations are focused on prompt treatment of persons with severe disease and those at an increased risk of influenza complications. We do recommend initiation of antiviral treatment as soon as possible, and it does have the greatest clinical benefit when you start it as soon as possible for patients with confirmed or suspected influenza who are hospitalized, and that includes without waiting for testing results, and that is oral or, for patients who are intubated, it can be administered enterically through an oral gastric or nasogastric tube.

For outpatients with complicated or progressive illness of any duration who do not require hospital admission, we recommend oral Oseltamivir. For patients, outpatients at high-risk for influenza complications, early initiation of either oral Oseltamivir or oral Baloxavir, and then for non-high-risk, otherwise healthy people with uncomplicated influenza, if they present within 48 hours of illness onset, antiviral treatment can be considered, they will benefit from a reduction in

the duration of their illness, but it's up to clinical judgment, and the drugs to consider would be oral Oseltamivir or oral Baloxavir. Next slide, please. So, let me just go over a few slides on also -- and this one is on Oseltamivir treatment efficacy from randomized control trials and effectiveness from observational studies, and so the bottom line is, for randomized control trials, Oseltamivir has significant clinical benefit when started within 48 hours after symptom onset versus placebo in children with influenza, uncomplicated influenza. And so, when you look at a meta-analysis, a pooled meta-analysis of five RCTs in children, this was powered for mild disease outcomes.

This is not looking at severe progression to severe disease. So, early treatment Oseltamivir reduced duration of illness by 18 hours overall, and when you exclude children that had asthma, the benefit is 30 hours. It also reduced the risk of otitis media by about one third, which is significant. When you look at observational studies in children who are hospitalized with lab-confirmed influenza, I'll just highlight some study findings. Starting Oseltamivir treatment within two days after symptom onset was significantly associated with shorter hospital length of stay.

Starting neuraminidase inhibitor treatment, it's virtually all Oseltamivir within two days after symptom onset was significantly associated with shorter ICU length of stay, and then children treated with Oseltamivir within two days after hospital admission had shorter length of stay, lower odds of seven-day hospital readmission, fewer late ICU transfers and lower odds of the composites outcome of death or ECMO use, so some clinical benefit both in early treatment and outpatients, as well as treatment as soon as possible in hospitalized children with influenza. Next slide, please. So, moving to Baloxavir looking at efficacy studies in outpatients for early treatment of influenza, Baloxavir treatment has similar clinical benefit to Oseltamivir and significant clinical benefit versus placebo when started within 48 hours after symptom onset. So, in non-high-risk children aged one to less than 12 years in outpatients, a single dose of Baloxavir had a similar median time to alleviation of influenza signs and symptoms versus five days twice daily of Oseltamivir, and then in adolescents and adults, 12 years and older, a single dose of Baloxavir had a similar median time to alleviation of symptoms, as for five days of Oseltamivir treatment. Baloxavir significantly reduced influenza viral RNA levels in the respiratory tract at 24 hours and reduced infectious, so that's viral, infectious virus from viral culture detection versus Oseltamivir duration significantly, and then single-dose Baloxavir also reduced the median time to improvement of influenza B symptoms by 24 hours versus Oseltamivir.

So, for influenza B, Baloxavir has higher efficacy and clinical benefit than Oseltamivir. Next slide, please. So, special populations, Oseltamivir is recommended for treatment of pregnant persons. So, if you had a pregnant adolescent and up to two weeks postpartum, Baloxavir is not recommended for treatment of pregnant people or breastfeeding mothers. There's no efficacy or safety data for Baloxavir in pregnant or lactating people, whereas we have substantial evidence of Oseltamivir safety for pregnancy and birth outcomes globally from many countries.

For immunocompromised persons, because they can have prolonged influenza viral replication with emergence of antiviral resistant viruses during and after treatment, you definitely need to monitor these patients for antiviral resistance and implement infection prevention and control recommendations. We do recommend neuraminidase inhibitor treatment, so, sorry, Oseltamivir.

Baloxavir monotherapy is not recommended. Certainly, you could consider a combination antiviral treatment. Next slide, please.

So, I want to end with showing some real-world data. This is from last season, recent publication, in fact, so recent it's published today in the MMWR. This is showing data in children who are at high-risk of complications, who are recommended for early antiviral treatment of influenza. So, these are outpatients, and I've highlighted in the top three children aged less than five years, children with a high-risk medical condition, and children aged less than five years and a high-risk medical condition. And you can see a very low percentage of children, 28 to 39% who actually received antiviral treatment last season.

Next slide. And so, this one, this a slide looking at the same point published very recently in the MMWR Surveillance Summaries and then also some data from the publication today by Fritps and and colleagues in the MMWR. This is showing in children who are hospitalized with lab-confirmed influenza in the Influenza Hospitalization Surveillance Network, you can see that children less than five years, and children five to 17 years, there has been a decrease in antiviral treatment of children who are hospitalized with influenza over several years, including during the COVID-19 pandemic, and last season, less than 60% of hospitalized influenza patients received antiviral treatment, and this is pediatric patients. And then in two hospital networks, 29 to 33% of children hospitalized with influenza received antiviral treatment one day or more after hospital admission, and just to highlight again, we recommend prompt antiviral treatment for children at high-risk of influenza complications who are outpatients as soon as possible, and then for hospitalized patients, we recommend initiation of antiviral treatment with Oseltamivir as soon as possible, even after hospital admission, including before influenza testing results are available. So, if you suspect influenza in a child who's being hospitalized during influenza season, start Oseltamivir before even you have the results of influenza testing.

Next slide. And so, moving to a self-knowledge check, a four-year-old child with cystic fibrosis presents with a two-day history of fever, cough, myalgia, sore throat, and tests positive for influenza A by rapid molecular assay. What is the recommended antiviral treatment for this patient? A, intravenous Peramivir, B, inhaled Zanamivir, C, Baloxavir, D, Oseltamivir, E, A, B, C, or D are all recommended, or F, only C or D. Next slide. So, the answer is D, Oseltamivir, one oral dose twice daily for five days, and the rationale is also Oseltamivir is recommended for children of any age and for high-risk children.

Baloxavir is recommended for otherwise healthy children aged five years and older. This child is aged four years and so is actually not even if the child had been previously healthy, the child is not recommended for Baloxavir, is not approved in a child less than five years. So, children with high-risk medical conditions aged 12 years and older are recommended for Baloxavir. Inhaled Zanamivir is recommended for otherwise healthy children aged seven years and older. Peramivir can be given to otherwise healthy children aged six months and older but requires intravenous administration in a healthcare facility.

So, if this child does not require hospitalization, Oseltamivir would be the best choice. Next slide, please. With that, I'm going to turn it over to Dr. Bryant. Thank you.

Thank you. Good afternoon, everyone. Dr. Uyeki has shared information about the most recent influenza season, emphasizing that influenza causes a substantial burden of disease in children. Fortunately, we have safe and effective influenza vaccines, but last season and, in fact, the last few seasons, these vaccines have been underutilized.

Next slide, please. My job today is to share the American Academy of Pediatrics' recommendations for influenza immunization during the '24 '25 season. In particular, I want to offer some reminders about influenza vaccine administration and review some practical strategies to increase immunization rates, because, as you've heard, we urgently need to do that. We'll also practice using a presumptive recommendation for influenza vaccine. Next slide, please.

In the October issue of Pediatrics, the AAP published a new policy statement and technical report for the 2024 2025 influenza season. The policy statement that is depicted here is a succinct summary of the recommendations, while the technical report provides the why behind the recommendations. Next slide, please. In case you haven't had a chance to look at these yet, there is some important new information for the upcoming season. All flu vaccines available in the US this season are trivalent.

Influenza B Yamagata has not circulated since 2020 and has been removed from vaccine formulations. Co-administration of influenza vaccine with other age-appropriate immunizations, including nirsevimab is emphasized. The recommendations for influenza treatment and prophylaxis hasn't changed, but the way the AAP presents the recommendations has been simplified. We've updated recommendations for influenza immunization of immunocompromised host, and we focus on evidence-based strategies to increase influenza immunization rates, including vaccine access. Next slide, please.

Of course, there are many things that haven't changed. You've already heard that influenza continues to cause morbidity and mortality in children. Annual influenza vaccination is recommended for all people six months and older, and any vaccine appropriate for age and health status can be used, and as Dr. Uyeki already highlighted, antiviral treatment is recommended for certain children with influenza. Next slide, please.

The number of influenza vaccine doses recommended for children remains unchanged this season, and it depends on the child's age at first dose administration and their influenza vaccination history. So, children six months through eight years of age who are receiving flu vaccine for the first time or who only received one dose prior to July 1st of this season or whose vaccination status is unknown need two doses of influenza vaccine administered four weeks apart, all other children receive one dose this season. If you have an eight-year-old who meets criteria for two doses, but they turn nine between the first and second dose, that child still needs to receive the second dose. Another thing to remember is that when two doses of influenza vaccine are required, they don't need to be the same brand or type. So practically, if you have a healthy three-year-old who has never received flu vaccine and needs two doses, theoretically, one dose could be an inactivated influenza vaccine, and one dose could be LAIV.

Next slide, please. The AAP's influenza policy statement emphasizes some practical tips for vaccine administration, and a few of those are listed on this slide. The maximum number of doses that can be drawn from a multidose vial is specified in the package insert, and this should not be exceeded. This varies by product, so be sure to look at the package insert. Residual product in the vial must be discarded, regardless of the remaining volume in the vial, and a 0.

5 ml unit dose of any inactivated vaccine should not be split into two separate 0. 25 ml doses. Next slide, please. Now, let's talk about co-administration. Inactivated influenza vaccine may be administered simultaneously with or at any time before or after other inactivated or live vaccines.

You can give flu vaccine on the same day that you give other routine vaccines that you give nirsevimab or when you give COVID-19 vaccine. LAIV may be administered simultaneously with other live or inactivated vaccines. LAIV is live attenuated influenza vaccine or the intranasal flu vaccine. If this vaccine is not administered simultaneously, at least four weeks should pass between the administration of LAIV and other non-oral live vaccines. Next slide, please.

So, thinking about co-administration brings us to this very practical question, are there maximum volumes of injectable vaccine, antibiotic, or other products that can be administered into each muscle group for different ages? For example, at the six-month well-child visit, you might have an infant who qualifies for nirsevimab, COVID-19 vaccine, influenza vaccine, PCV, and a DTaP-IPV-HepB-Hib vaccine. Can you really give all of those at the same visit? Next slide. The answer is that AAP continues to recommend all indicated age-appropriate vaccines be given during an office visit with very few exceptions. Neither the AAP nor the CDC have endorsed maximum volumes that can be injected into a particular muscle, although the CDC has suggested some typical ranges, and you see those on this slide. The infographic here was produced by the Alliance for Immunization in Michigan and suggests how to give all needed immunizations at the six-month visit, along with some practical considerations.

So, for example, when giving several injections at a single visit, separate intramuscular vaccines by at least one inch, if possible, to reduce the likelihood of local reactions overlapping. Now, this said, some practices and some healthcare organizations have nursing guidance that suggest limits on the volumes that can be injected into a given muscle. Some organizations have limits that suggest that the maximum volume that can be injected into the vastus lateralis is 1 ml. So, clinicians are encouraged to explore the existing guidance in their own organizations, and if volume limits are defined, share this information so that guidance can be updated and all indicated immunizations can be given on the same day. Next slide, please.

All right, let's shift gears and talk about how to protect immunocompromised children against flu. The AAP policy statement provides the recommendations you see on this slide. Children who are immunocompromised should receive an activated influenza vaccine, that's the flu shot, and the vaccine should be given at a time when the best immune response can be anticipated. So, for example, in children with malignant neoplasms, in general, flu vaccine is administered at least two weeks before the administration of cytotoxic chemotherapy. For hematopoietic stem cell transplants, inactivated influenza vaccine is generally administered four to six months after transplantation.

Next slide, please. This year, AAP has made a new recommendation related to hematopoietic cell transplant recipients. We know these children are at high-risk for severe influenza, and they may not develop a robust response to standard influenza vaccine. Although high dose inactivated influenza vaccine is not approved for use in children, the AAP suggests that clinicians could consider administering two doses of high-dose trivalent inactivated influenza vaccine 28 to 42 days apart in hematopoietic cell transplant recipients who are three to 17 years of age. This recommendation is based on a phase II multi-center, double blind, randomized, controlled trial that compared immunogenicity and safety between high-dose trivalent influenza vaccine and standard dose quadrivalent vaccine.

This trial was in children and adolescents three to 17 years of age who'd had a transplant three to 35 months earlier. As you see on this slide, two doses of high-dose trivalent vaccine resulted in higher antibody responses to influenza A antigens than standard dose quadrivalent vaccine. The overall safety profile was similar. So, this is a consideration, but let me emphasize, this is an off-label recommendation. Next slide, please.

Let's shift gears for a minute and talk about timing. For best protection, influenza vaccine is administered before flu vaccine starts circulating in a community. We know that it generally takes 10 to 14 days to develop an antibody response to the vaccine. That's why the AAP continues to recommend that influenza vaccine be offered to children when it becomes available, especially for children who require two doses, and it's a good idea to give all recommended doses by the end of October. All right, so now we're already in November.

Don't stop vaccinating. Continue offering vaccine to unvaccinated children and families throughout the season. As you've already heard, we have many children across the US who are not yet protected against flu, and we still have time to protect them. Next slide. Efforts should be made to promote influenza vaccination of all children, especially those at high-risk for complications, and you've already heard about children who are at higher risk.

Next slide, please. All right, now it is possible to increase influenza immunization rates by using some of the practical evidence-based strategies listed on this slide. Having an influenza vaccine champion in your office or practice can certainly be beneficial. Today, though, I want to emphasize the importance of the messaging. Effective messaging starts when a patient checks in at the front desk or maybe even earlier when the patient makes an appointment.

It's consistent across all team members, and it involves a strong presumptive recommendation that bundles the recommendation for flu vaccine with recommendations for other routine vaccines. Next slide, please. Now, let's spend just a minute talking about what a presumptive recommendation looks like. I hope some of you have seen this clinical report from the AAP that addresses strategies for improving vaccine communication and uptake. Next slide, please.

Let's practice the presumptive recommendation as suggested in the clinical report. It might go something like this. Sarah gets two shots today. It's time for her second HPV vaccine and her influenza vaccine. Next slide, please.

With the presumptive recommendation, it's not just the words we say, but how we say it, tone and body language matter. Before you deliver a presumptive recommendation, do square your shoulders and make eye contact. Don't make the presumptive recommendation sound like a question. So, for example, you wouldn't want to say, "Sarah is due for two vaccines today, including a flu vaccine. Is that okay?" The presumptive recommendation works best if you can focus on the patient and the parent and not the electronic health record, and so that's why it works well if you know what the patient needs before you enter the room.

Next slide, please. This may be counter-intuitive, but the presumptive format can be effective, even if a parent has voiced hesitancy at a previous visit or if another staff member lets you know that the parent is hesitant about flu vaccine. For the best chance of success, don't undermine the presumptive format by quickly reverting to the participatory format. Give the parent time to think and respond, and practically, this might involve being comfortable with some silence. Next slide, please.

After the presumptive recommendation, there are several possible outcomes. The parent may accept your recommendation for vaccine or they may respond with some simple questions. For example, they might say, "I'm not sure about the flu vaccine. Are there a lot of side effects associated with that?" Another possibility is that the parent will voice significant concerns. For example, they might say, "I'm fine with the HPV vaccine, because I know that prevents cancer, but I don't see the need for the flu vaccine.

" Next slide, the clinical report offers a general framework for addressing questions about vaccines, and this can be applied to influenza vaccine. So, for example, to the parent who wants to know about side effects, you might say, "Good question. The most common side effects of flu vaccine are a sore arm and only last a day or two. " To the parent who doesn't see the need for flu vaccine, you might say, "May I share my thoughts today on why I think the flu vaccine is so important, and why I recommend it for my patients and why my own children receive flu vaccine?" If the parent doesn't accept the vaccine after you've offered the questions, the recommendation is to move on to motivational interviewing, and the clinical report offers some suggestions for how to do this. Next slide, please.

The next few slides cover programmatic interventions that can be implemented at the practice or the health system level to increase influenza immunization rates, and the strategies on this slide are largely about improving access to vaccine and reliable information about vaccine. While it's tempting to chalk up some of our disappointing immunization rates to hesitancy, the information that Dr. Uyeki presented about disparities suggest that access continues to be a problem, and so one way to address access to vaccine is vaccinating at all visit types and in all healthcare settings. This includes emergency department visits and upon hospital discharge for eligible patients. Other strategies might include expanded office hours or vaccine-only clinics, and one way to address access to reliable information is to provide evidence-based information to patients and families and use scripting for staff to address common questions.

The next slide, if we can move to that, is just a reminder that AAP, if we can move to the next slide, please, this is just a reminder that AAP has a number of resources for patients and healthcare providers. Next slide, please. On this slide are operational strategies that could be

implemented by practices or health systems, including standing orders and clinical decision support in the electronic health record. Next slide, please. Community level interventions are also needed.

If we are to eliminate health disparities, we need to engage directly with affected communities to develop tailored strategies that resonate with those communities. We need to promote trust, encourage dialog, and increase access to preventative services. We also need to think about how we work with community partners to increase immunization rates. I just want to emphasize that the AAP continues to champion immunization within the medical home, particularly for the youngest children. However, in order to make sure that every eligible child receives flu vaccine, we have to work with stakeholders to support vaccine initiatives within the community, and this could include school-based programs or immunization at pharmacies.

Next slide, please. During the '25 '26 influenza season, the partnership with pharmacies could look a bit different. In September, the FDA approved self or caregiver administration of intranasal influenza vaccine for eligible patients, and, again, this will be for next season. The manufacturer of intranasal influenza vaccine has indicated that an online pharmacy will be utilized. Individuals will complete a questionnaire for themselves or their children.

Individuals' eligibility will be reviewed by a pharmacist, and then, if eligible, vaccine will be shipped to the person's home. Individuals 18 and older could self-administer the vaccine, and for children two to 17 years of age, the vaccine could be administered by a caregiver. The AAP understands that pediatricians and other clinicians who care for children have a lot of questions about how this is going to work. They anticipate questions from their patients. They want to know how they're going to learn how -- whether their patients are receiving flu vaccine through a pharmacy, and so the AAP anticipates developing additional guidance about this option and potentially FAQs before the next season.

Next slide, please. Dr. Uyeki talked about testing for influenza. The AAP continues to recommend testing of children with signs and symptoms of influenza when testing will impact clinical management, and this could include the decision to start antiviral treatment, although I'll emphasize, as you heard before, a positive test is not required to start antiviral therapy when influenza is suspected. At-home tests for flu have proliferated, and clinicians should anticipate calls from parents saying, "Hey, my child has tested positive for flu on an at-home test.

What should I do now?" Next slide, please. The next two slides list AAP resources that you can use to communicate with patients and families about flu vaccine and implementing vaccine programs. Next slide, please. Now for a knowledge check, influenza vaccination should only occur in the medical home, true or false? Next slide, please. The answer is false.

Although vaccination in the medical home is optimal, administering influenza vaccine in diverse locations, such as subspecialty practices, urgent care clinics, emergency departments, schools and pharmacies may increase uptake among patients who do not have or who can't readily access their medical home, and this includes patients at high-risk for influenza-related complications. When flu vaccination takes place in a non-traditional setting, appropriate documentation should be provided to both the patient and the medical home. Settings that offer influenza vaccination

should submit details about that vaccination to the appropriate immunization registry, including all content needed to support communication to the patient's medical home. Now, I'll turn things back over to Captain Khan. Thanks so much.

Presenters, thank you so much for sharing this timely information with our audience. In the interest of time, we have time for a couple of questions. So, our first question asks, "Can you please speak to the ability for Oseltamivir or Baloxavir, any data that they have shown to keep kids out of the hospital, to reduce hospitalizations, or to reduce mortality?".

Yeah, hi. This is Tim Uyeki. I'll take that question. So, the studies that I presented, the randomized control trials have all been done in outpatients. They were powered for mild disease outcomes.

There are observational studies that have looked at this. There are studies in adults, a meta-analysis showing that -- it was published in 2015 showing that Oseltamivir treatment, early treatment, reduced the risk of all cause hospitalization in adults. There was a recent publication in the last year that was a meta-analysis looking at randomized, controlled trials and looking at the outcome of hospitalization. And the bottom line was, although they reported no statistical significant benefit of Oseltamivir treatment in outpatients to reduce the risk of hospitalization, it was tremendously underpowered. And actually, if you do read that article, it was published in JAMA Internal Medicine, you should read the letters to the editor that were published subsequent to that article, emphasizing this point in that actually to do a clinical trial to look at severe disease outcomes, you need probably more than 30,000 patients, and they only had a little more than 6,000 patients in their meta-analysis.

So, the bottom line is that there are some data from observational studies, but at least from randomized controlled trials, they did not address severe disease outcomes. And the same is true for Baloxavir, that although both Oseltamivir and Baloxavir have been shown to reduce some mild complications, and so I mentioned Oseltamivir reduces the risk of otitis media when treated early for children with influenza, but Baloxavir also in adolescents and adults has been shown to reduce the risk of some mild to moderate complications, but none of these -- no clinical trial, particularly in children, has looked at the outcome of mild, sorry, of severe influenza outcomes over.

Thank you, Dr. Uyeki, and our last question is sort of an amalgamation of a lot of counseling type questions we have received. So, for the audience that are curious, can you please share your recommended tips for providing counseling to parents, guardians, or caregivers when discussing the influenza vaccine for their children?

This is Kris Bryant. Yes, that's an important question. So, I begin with a presumptive recommendation. I -- so the child, let's say Sarah, Sarah is due for influenza vaccine today, we have safe and effective influenza vaccines. They're recommended for everyone six months and older.

You know, some parents, I think don't know or have forgotten that influenza is not just a cold. Dr Uyeki shared with us that influenza can be a severe disease. I think parents don't know that kids

can die of flu, and some of those kids are previously healthy kids, and so if the parents will allow me, I share that I have cared for patients with severe flu. Choosing flu vaccine is a way that parents can choose to protect their children against severe complications of flu, and I share that I give it -- I gave it to my own children. I make sure my grandson gets it, and so sometimes I think that that personal experience can be helpful, and, of course, I share that I always choose to get a flu vaccine.

Great, thank you very much. I want to thank everyone for joining us today with a special thank you for our presenters for sharing their time and expertise with us today. This year, CDC is moving from the Training and Continuing Education TCEO system that provides access to CDC educational activities for continuing education to CDC TRAIN. If you do not already have a TRAIN account, please create one at www. train.

org/cdctrain. All new activities that offer CE from CDC will only be listed in CDC TRAIN. CDC TRAIN is a gateway to the TRAIN Learning Network, the most comprehensive catalog of shared public health training opportunities. This transition will allow you to access non-credit and for-credit educational activities and track your learning, including CE in one place. Many CDC-accredited activities are already listed in TRAIN.

The move to one system improves efficiency and makes it easier for learners, CDC staff, and partners to offer and earn CE in one place. You can continue to use TCEO for existing activities that have CE set to expire in 2024, since these courses will not move to CDC TRAIN. You may also use TCEO for existing activities with CE set to expire in 2025 before the courses transition to CDC TRAIN sometime next year. If you begin one of these courses in TCEO, we will let you know when the course will move to CDC TRAIN. You can access and download CE transcripts and certificates in TCEO through the end of 2025.

Instructions will be available on both platforms, and a learner support team will be available to answer questions. All Continuing Education for COCA Calls is issued online through CDC TRAIN. Those who participated in today's live COCA Call and wish to receive Continuing Education, please complete the online evaluation and posttest by December 16, 2024 with the course code WC4520R-111424. The registration code is COCA111424. Those who will participate in the on-demand activity and wish to receive Continuing Education should complete the online evaluation between December 17, 2024 and December 17, 2026 and use course code, WD4520R-111424.

The fully closed caption video and transcript for today's COCA Call will be available on-demand about one week after the live session at emergency. cdc. gov/coca. 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 Calls 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. Thank you for joining us for today's COCA Call and have a great day.