

Good afternoon. I'm Commander Ibad Khan, and I'm representing the Clinical 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 2021-2022 Influenza Vaccination Recommendations and Guidance on Coadministration with COVID-19 vaccines.

All participants joining us today are in listen only mode. Free continuing education is offered for this webinar. Instructions on how to earn in continuing education will be provided at the end of the call. In compliance with continuing education requirements, CDC, our planners, our presenters, and their spouses/partners wish to disclose to have no financial interests or other relationships with the manufacturers of commercial products, suppliers of commercial services, or commercial supporters. Planners have reviewed content to ensure there is no bias. This presentation will not include any discussion of the unlabeled use of a product or a product under investigation of use, except part of the presentation will address the use of COVID-19 vaccines outside of approved age group. CDC did not accept commercial support for this continuing education activity.

At the conclusion of today's session, the participants will be able to accomplish the following. Outline updates on the advisory committee on immunizations practices, recommendations for 2021-2022 influenza vaccination season, discuss general influenza vaccination guidance during the COVID-19 pandemic, and describe clinical considerations and best practices for coadministration of influenza vaccines and COVID-19 vaccines. After the presentation, there will be a Q&A session. You may submit questions at any time during today's presentations. To ask a question using Zoom, click the Q&A button at the bottom of your screen, then type your question in the Q&A box. Please note, we receive many more questions that we can answer during our webinars. If you are a patient, please refer your questions to your healthcare provider. And 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 presenters for today's COCA Call. We are pleased to have with us Captain Lisa Grohskopf. Captain Grohskopf is the CDC lead for the influenza work group of the advisory group on immunization practices. The primary focus of her work is on influenza vaccine policy. We would also like to welcome our other presenter for today's webinar, Dr. Andrew Kroger. Dr. Kroger is a medical officer for the National Center for Immunization and Respiratory Diseases, Communication and Education Branch at CDC. Most notably, Dr. Kroger authored the newest edition of CCD's General Best Practice Guidelines for Immunization and is currently also involved with the current issues in immunization webinar series.

It is my pleasure now to turn it over to Captain Grohskopf. Captain Grohskopf, please proceed.

Thanks very much. And thanks, everyone, for being here today. It's good to be able to talk with you. Next slide.

So, as mentioned, I'm going to present an overview of the updates of the ACIP influenza vaccine recommendations for the upcoming 2021-2022 season. But before we get started, just a quick reminder about the general vaccine types we have and the abbreviations we use, as you're going

to see those in the slides. We have three main types of influenza vaccines, generally speaking, inactivated influenza vaccines, or IIVs, recombinant influenza vaccine, or RIV, and live attenuated influenza vaccine, or LAIV. And when you see these letters, you will often see a number right behind it, and this indicates the valency of the vaccine. That is, how many viruses are represented in that particular influenza vaccine. Three is for trivalent, which have H1N1, H3N2, and 1 influenza B virus from 1 B virus lineage. And for the quadrivalent vaccines, which is pretty much all we're going to have for this season. Those vaccines contain an influenza A(H1N1) an A(H3N2). And 2B viruses, one from each lineage. And just lastly, we only have one LAIV and one RIV, but we have a number of different kinds of inactivated vaccines, or RIVs, and sometimes we'll see specific abbreviations and we'll need to refer specifically to those. CCIIV for the cell culture based inactivated vaccine, AIV for the adjuvated inactivated influenza vaccine. And HDIIV for the high dose inactivated influenza vaccine. Next slide.

So, getting onto the flu statement from ACIP for this season, the core recommendation, which has been in place since 2010-2011 season, is unchanged. And that is that annual influenza vaccination is recommended for all persons aged six months and older who did not have contraindications. Next slide.

The 2021-22 statement was published on August 27th, and contains updates on the following topics, each of which we'll touch upon in this presentation. These include the influenza vaccines expected to be available for this season, the U. S. influenza vaccine viral complications for the coming season, a change in the FDA approved age indication for Flucelvax quadrivalent, some updates to the timing of vaccination language, some information on coadministration of influenza and COVID-19 vaccines, and some updates to the contraindications and precautions to influenza vaccination specifically concerning persons who had had a previous severe allergic reaction to an influenza vaccine. Next slide.

So, this slide's a bit busy and colorful. But just to it's really just here to put into perspective just what an expansion we had in the number of different types of vaccines for flu that we've had since 2000. At the far left, that's the 2000-2001 season. And then at the far right, we have our most recent season. That's coming up. And these bars represent the number of unique vaccine products that have been available since basically 2000. Each color represents a different type. If we look at that sort of medium blue color that's all the way on the left, those are the trivalent inactivated influenza vaccines, which we had had for a good number of years before that. We had the introduction of the live vaccine in 2003 in green, high dose vaccine for the 2010-11 season in red. For a few seasons, in orange, we had an intradermal vaccine, which is currently not on the market anymore. And then we had the introduction to the cell based vaccine in purple, the recombinant vaccine in light blue, and then finally in pink for the 2016-17 season, the adjuvated influenza vaccine. Over time since about 2013-14, we've had a gradual transition of all of these vaccine types from trivalent versions to quadrivalent versions, which was kind of the crosshatch of coloring that you see as you move to the right on the slide. And the take home point here is really that, you know, we've had a decline in the number of all types of vaccine or individual brands of vaccine available, but we still have a total of nine different vaccines that are available for the season. And some of them have unique features, which we'll get to in the next slide. Next slide.

So, this slide breaks down the vaccines that are anticipated to be available this season by their FDA approved age indications, and also whether they're egg-based or non-egg-based. So, we have our egg-based vaccines are in green. Our non-egg-based vaccines are shown in blue. And we still have our three general basic categories; our IIVs, the inactivateds, our RIVs, RIV is one, the recombinant vaccine. And LAIV, the live attenuated vaccine. All told, we have nine vaccines for this season. So, one of the new things for this season is that they're all quadrivalent, there won't be any trivalent influenza vaccine anymore as of this season. For the standard dose, unadjuvanted, sort of classical inactivated vaccines that we've had for a while, those four are licensed down to six months of age. The cell culture based vaccine is for two years and older. Fluvad quadrivalent and Fluzone high dose quadrivalent are only licensed for 65 and older. Flublok quadrivalent, the recombinant vaccine for 18 and older. And FluMist for 18, I'm sorry, for 2 through 49 years. Next slide. Whoops, next slide. There we go.

Okay. So, you can break the various influenza vaccines that we have down by a number of different characteristics, and it's something that is very, very difficult to make a Venn diagram of, even though I've tried many times. But just to describe some general features and break them down into root of administration factors, most ordered vaccines, of course, are intramuscular, they're injectable intramuscular vaccines. The one exception is FluMist quadrivalent, which is intranasal. Just to go over some general features of the vaccines, for the inactivated influenza vaccines, or the IIV4s, these contain inactivated virus. Virus is grown up in large quantities in either eggs for most of them or in cell culture for the cell culture based vaccine. And then it is split. And in some cases, it's further purified, and that's what's referred to as a subunit vaccine. But all these vaccines have in common, that they start with virus that's basically inactivated and split. Most of these are egg based with the exception of the CCIIV4 for the Flucevex quadrivalent for which the viruses are grown up in canine kidney cells instead of eggs. Most contain 15 micrograms of hemagglutinin. That's HA, the sort of active ingredient that encourages the immune response that neutralizes flu. per virus. One contains 60 per virus. That's Fluzone high dose quadrivalent, or HDIIV4. And most are unadjuvanted. But there's one Fluvad quadrivalent that contains the adjuvant MF59. For the recombinant influenza vaccines, there's only one of them, that's Flublok quadrivalent. This vaccine uses no viruses and no eggs in production. It contains 45 micrograms of hemagglutinin per virus. And that hemagglutinin, instead of being derived from an actual virus, is made through recombinant methods; essentially they take the genetic sequence of the hemagglutinin protein and introduce it into an insect cell line using a viral vector, and that's how they appear in hemagglutinin. So, that one involves no viruses or eggs in its production. The live attenuated vaccine is an egg based vaccine. It contains live attenuated viruses, which need to be able to replicate in the nasopharynx, where they've been deposited in order to promote inadequate immune response. These are attenuated viruses, so they don't cause clinical illness. They're cold adapted, so they grow best at 25 degrees Celsius, so less than the core body temperature. And they're temperature sensitive, which basically means that their growth is restricted at 37 to 39 degrees Celsius, so closer to core body temperature. All of this encourages growth in the nose and not elsewhere essentially. This is licensed for ages 2 through 49 years. Next slide.

So, now that we've talked about the vaccines available, the next update concerns the vaccine viral composition for 2021-22. And all of our vaccines are quadrivalent for this year, so all of them are going to have representation of four viruses, and H1N1(PDM09) and H3N2, and one B

virus from each lineage; the Victoria lineage, and then the Yamagata lineage. For this season, the B viruses, composition wise, are the same as they were last season. The strains for the H1N1 PDM09 and the H3N2 have both been updated. One thing I just want to point out here is that when you, if you look, for example, at the FDA pages or any articles about strain selection for the flu vaccines, you'll notice that there will be a long taxonomic name like A Victoria 2570 2019 H1N1 PDM09, and then you'll see "-like virus". And the reason for this is that for any of these selected recommended viruses that go into the vaccine, there generally are a few different strains that are suitable and acceptable to you. So, it's not necessarily one virus that can be used. And this is why you will sometimes see, and we get questions about this, in the package insert, you'll see that the particular vaccine might have used a virus with a slightly different type of taxonomic name, but it's still like the recommended virus. It doesn't mean that they've chosen a different virus. That's just something to point out. Also, you'll notice sometimes in some seasons, last season this happened, also this season, sometimes there's a slightly different strain name recommended for the egg based vaccines versus the cell cultured vaccines, or the recombinant vaccines. So, for example, for this season, there's a slightly different name for the PDM09 viruses. Those are slightly different strains of the virus, but they are antigenically similar viruses. FDA has allowed for the last several years that the non egg based vaccines can use viruses that have been derived initially from cell rather than egg. So, sometimes you'll see a difference, but it doesn't mean that the viruses are actually different. Next slide.

The next update is a change in age indication for Flucelvax quadrivalent. This is the cell culture based inactivated vaccine, and it was previously licensed for ages four years and up. And then in March, 2021, it was approved for ages two years and up. This change was supported by data from a randomized control trial conducted among over 4,000 children age 2 through under 18 years, over 3 influenza seasons, where they compared the efficacy versus a non influenza control vaccine. The overall vaccine efficacy was 54.6% against RT-PCR or culture confirmed influenza associated with CDC-defined influenza like illness. And this new age indication has been reflected in both the text of the guidance and in table one in the statement. Next slide.

The next update concerns some modifications to the language regarding timing of influenza vaccination. And this is always a difficult topic because flu is unpredictable in terms of its timing, so it makes it difficult for us to tell people every year this is the exact time you should get vaccinated. First, a little more background on the timing of flu seasons. Timing of the onset and the peak of influenza activity varies from season to season. And within a season, the timing of activity can also vary geographically. You can see localized pockets of activity in some portions of the country before others in any given season. In the United States, generally, localized areas of increased activity can occur as early as about October. Over the 36 seasons between 1982-83 and 2017-18, peak activity varied. And the histogram graph on the right there is one that you can also find on the CDC website at the link at the bottom of the slide. But just to summarize it, the peak occurred in December in 19% of seasons, January in 17% of seasons, February in 42% of seasons. So, that was a pretty popular one. And in March in 19% of seasons. So, the take home point here is that, you know, February was a very common month for peaks among the 36 seasons that are represented here. But you also see a good number of peak seasons that occurred in December, and that as late as March, and we even had a couple of seasons where the peak was before December, one in October and one in November. So, all this to say that the peak of the

season, the time when the activity of flu is most intense is variable. And we really predict it in advance. Next slide.

So, some factors relevant to guidance for timing a vaccination. One concerns waning of immunity. Declines in influenza vaccine effectiveness over the course of the single season have been observed in many observational studies, so this poses some concern for getting vaccinated too early. It can be difficult to say what too early is exactly. July and August are probably too early in most season for some populations before we get to, which we'll get to a little bit more on the next slide.

But that's one factor that definitely plays into the special timing of vaccination. Waning of immunity appears to be more pronounced among older adults than younger adults or children. Overall, there appears so far to be less evidence of waning for children. It might also be more of an issue for H3N2 viruses say than H1N1 viruses, although there's a lot of variability in studies that are out there. Other considerations regarding the formulating recommendations for timing of vaccination include the unpredictability of timing of the onset and peak of the season, as we discussed on the last slide, wanting to avoid missed opportunities to vaccinate, if somebody's vaccination is deferred, are we going to be able to see them again to vaccinate them? And also programmatic constraints. Vaccination programs are huge and complex and have to be planned in advance and involve a lot of effort from a lot of people. And to have to try to vaccinate a given population in a more constrained time period can cause problems too. So, next slide.

So, the guidance for timing of vaccination has a lot of similarities with previous seasons, but with some updates. It includes discussion of the various factors that go into considering considerations that are relevant for timing of vaccination that we discussed on the last slide as it has in previous seasons. Also, as previously, it states that for all vaccination should be offered ideally by the end of October. Also, similar to last season, children who need two doses, these are those kids in the six months to eight years old age range to have either never been vaccinated, who haven't received a lifetime total of least two doses previously, or whose vaccination history is not known, those kids need two doses, and they should receive their first dose as soon as possible after the vaccine is available, mainly because they can't have the second dose until at least four weeks later, and won't allow enough time to get the second dose in. New for this season, it says that children needing one dose can also be vaccinated as soon as vaccine is available. And also that vaccinations soon after vaccine becomes available can be considered for pregnant persons in the third trimester. The reason being that this allows some opportunity for protection of the infant once born kids can't be vaccinated under age of six months because we don't have any licensed vaccines, and there is evidence that vaccination of pregnant people can offer protection during the first two months of life for the infant after birth. In general, for non pregnant adults, July and August should be avoided. It's probably too early in most seasons, especially for older adults, those 65 and older in particular, unless there is concern that later vaccination might not be possible for some reason. Similar to last year, vaccinations should continue to be offered throughout the season, as long as influenza viruses are circulating and unexpired vaccine is still available. Next slide.

So, there's also a brief update in the section on coadministration of influenza vaccines with other vaccines concerning COVID-19 vaccine. The ACIP influenza statement for this year cites the

current interim clinical considerations for the use of COVID-19 vaccines currently approved or authorized in the United States. This guidance states that COVID 19 vaccines may be administered without regard to timing with other vaccines, so they can be given with other vaccines, including influenza vaccine. Vaccines administered at the same visit, this guidance further says should be given at different sites separated by an inch or more if possible. And that guidance also notes that if COVID-19 vaccines are given with vaccines that might be more likely to cause a local reaction, they should be administered in separate limbs if possible. For the purposes of flu, most flu vaccines are pretty well tolerated. High dose and adjuvanted vaccines in some studies they've seen slightly higher frequency of some adverse events than non high dose or non adjuvanted influenza vaccines, if you compare high dose versus non high dose, adjuvanted versus non adjuvanted. So, for our purposes, those are the two vaccines that probably would be most likely to apply in this case. The guidance further notes that providers should check current CDC COVID-19 vaccination guidance for updated information concerning coadministration. Next slide.

The last general category of updates that we have concerns contraindications and precautions to influenza vaccination, and specifically these concern people who have had a severe allergic reaction; e. g. anaphylaxis, to a previous dose of an influenza vaccine. So, it's a fairly narrow group. And we'll get more into the details on that in the next few slides.

Just background on contraindications precautions, first, contraindications are conditions in recipient that increase the risk for a serious adverse reaction, and in which the vaccine generally should not be administered. Precautions, on the other hand, are conditions which might increase the risk for a severe adverse reaction, or which might cause a diagnostic confusion. For example, if they have an adverse reaction to the vaccine, is it a vaccine or is it some intercurrent illness that they have or something else? Or which might compromise the ability of that vaccine to produce immunity. In general, vaccinations should be deferred when a precaution is present, but a vaccine might be indicated to be given even if a precaution is present, if it's judged that the benefit of protection from the vaccine outweighs the risk for an adverse reaction. Contraindications and precautions for vaccines are listed in the vaccine package inserts. For the flu vaccines, the ACIP recommendations generally follow those listed in the package inserts, though there are some exceptions. And really the main one is egg allergy, which, for which severe allergic reaction to egg is a labeled contraindication for all of the egg based vaccines, but which for ACIP's purposes, ACIP has made for the last several seasons the recommendation that people with egg allergy of any severity can get influenza vaccine. And I have one slide with a bit more detail on that, just to remind folks of what the reqs are there later. Next slide.

A bit about general background about allergic reactions to flu vaccines. They are fortunately rather rare. So, if all vaccines, including flu vaccines, include multiple components, if you were to look at the package insert, you would see a lot of things that are listed there that can potentially trigger a severe allergic reaction, such as anaphylaxis. Fortunately, these reactions are rare. The figures vary a little bit with regard to rates, but in one vaccine safety data link study, the estimated rates of post-vaccination anaphylaxis among cases that involve the administration of a single vaccine at that visit, so without the confusion of multiple vaccines being given, the estimated rates were 1.31 cases per million doses for all vaccines, and 1.35 cases per million for inactivated influenza vaccine trivalent. So, again, rare. This affects a relatively small segment of

the population. However, for those who have experienced these reactions, it's a serious issue, it's frightening. And also it's complicated by the fact that if the reaction occurred in somebody who has no known history of reaction to any component of that vaccine, you don't know, and it can be very difficult to figure it out without allergy consultation, for example, what component in the vaccine was responsible for the reaction. Next slide.

Now, looking at influenza vaccine package insert language concerning previous allergic reactions to influenza vaccines, all vaccines, as mentioned earlier, have, in their package insert, listings for contraindications and precautions. And our older vaccines, specifically the egg based inactivated vaccines and the live attenuated vaccines, for many years have contained relatively consistent language about contraindications related to allergy to a previous dose of influenza vaccine. They generally read with some minor variation that these vaccines are contraindicated and those are the history of severe allergic reaction e. g. anaphylaxis to any component of that vaccine, or to a previous dose of any influenza vaccine. So, for example, if one has had a severe allergic reaction, such as anaphylaxis to Fluzone quadrivalent, that would also pose a contraindication not only of Fluzone quadrivalent, but the Fluarix quadrivalent, FluLaval quadrivalent, all of the other vaccines. And for many years, the ACIP recommendations reflected this and stated that if somebody has a severe allergic reaction to a previous dose of influenza vaccine, that's a contraindication to future doses of vaccine. In recent years, we've had the introduction of newer vaccines, and specifically here we're going to talk about the cell culture based vaccine and the recombinant vaccine for which the package insert language reads slightly differently. Contraindications here include those with a history of severe allergic reaction e.g. anaphylaxis to any component of the vaccine, so that's similar to the other vaccines. But they don't list a contradiction for those that have had a severe allergic reaction to any influenza vaccine. So, the one similarity, I just want to point this out before we move on, that for somebody with a known history of allergic reaction, severe allergic reaction to any component of a particular vaccine, that vaccine is contraindicated. That has not changed. What we're talking about in the next slides are those who have had a severe allergic reaction to a previous dose of flu vaccine, and we don't necessarily know what component caused it. Next slide.

So, in light of the package insert language and the fact that there's been more experience these newer vaccines, the cell based vaccine, and the recombinant vaccine have been out for a number of years now, but also be mindful of the fact that when somebody has a severe allergic reaction to a flu vaccine, we're not sure generally which component they reacted to. The components of the different flu vaccines vary from vaccine to vaccine. There is some agents that are present in multiple vaccines. But all of the components, all of the ingredient lists are different from vaccine to vaccine. This can make things very difficult for figuring out whether or not to give a future dose. Or if so, what vaccine you choose. With all those things in mind, the contraindications and precautions language specifically related to previous severe reaction to a flu vaccine dose have been modified. For any egg based IIV4s or LAIV4, our older vaccines, severe allergic reaction to a previous dose of any influenza vaccine is a contraindication. So, any. Not just the one that you're administering, but any flu vaccine. For cell culture based inactivated vaccines, severe allergic reaction to any cell culture based vaccine is a contraindication. So, CCIV3, the older version, or the current CCIV4, severe allergic reaction to any other egg based IIV, recombinant vaccine, or LAIV as a precaution for recombinant influenza vaccine, RIV4, severe allergic reaction to any RIV is a contraindication, whether it's RIV3, RIV4, any valence, central reaction

to any other influenza vaccine, and egg based IIV, CCIIV, or LAIV as a precaution. Where precaution is present at the potential benefit of vaccination is thought to outweigh the potential risk of a severe reaction, and has decided to proceed with vaccination. Vaccination should occur in a medical setting supervised by a provider who can recognize and manage a severe allergic reaction, and providers can also consider consulting with an allergist to hopefully help identify the vaccine component likely to be responsible for the previous reaction. Next slide.

So, stated another way, in the following situations where a precaution exists, and if the potential benefits of vaccine, potential benefits of vaccination are believed to outweigh the risks, for those with a previous severe allergic reaction to an egg based IIV, LAIV, or LAIV, CCIIV45 or RI4 can be considered. For those with a previous severe allergic reaction to a cell based influenza vaccine, CCIV3, CCIV4, for example, RIV4 can be considered. For those with a previous severe reaction to an RIV, RIV3 or RIV4, for example, CCII4, the cell based vaccine, can be considered. In each case when vaccinating in the setting of a precaution, it should occur in a medical setting, supervised by a provider who can manage a severe allergic reaction. And, again, an allergist consultation can be considered. Importantly, just to reinforce lastly, each vaccine is still also contraindicated, contraindicated in the setting of a previous severe allergic reaction to any component of that vaccine. Next slide.

So, I'm going to go through the last slides briefly, but these reflect some situations and guidance where the language hasn't changed, but for which questions often come up. One is vaccination in children aged six months through eight years. The algorithm for this has not changed. The only thing updated has been the seasons in the flowchart. But as previously, children in this age group who haven't received at least two doses of trivalent or quadrivalent influenza vaccine before July 1st, 2021, or for whom you don't know their vaccination history, need two doses of the 2021-22 influenza vaccine spaced at least four weeks apart. The two previous doses don't have to be from the same seasons or from consecutive seasons. They could be from different non-consecutive seasons. And for an 8 year old to determine need two doses, the second dose is still recommended even if they turn age nine years before dose one and dose two. Next slide.

Vaccination of pregnant persons, as previously, the vaccines recommended in this population, are they inactivated and the recombinant vaccine, and age appropriate inactivated vaccine, or the recombinant vaccine if appropriate for age, LAIV4 is not recommended in pregnancy. Vaccination can occur in any trimester. And, again, as noted earlier in the timing section, vaccination soon after vaccine is available can be considered for pregnant persons. Next slide.

With regard to egg allergy, the recommendations are similar to those of last year. History of severe allergic reaction to vaccine components, including egg, if applicable, is, again, is a labeled contraindication in package inserts. However, ACIP recommends that all persons with egg allergy receive influenza vaccine. The one additional recommendation is that those with a history of severe allergic reaction to egg, any symptom other than hives should be vaccinated in the medical setting, supervised by a provider who can recognize and manage a severe allergic reaction if the vaccine other than the cell culture based or the recombinant based vaccine is used. Next slide.

And for those 65 and older, as noted earlier, this is a population, which unfortunately has, bears a lot of the burden in terms of food deaths and hospitalization every year. They're at high risk for higher degree of complications from influenza if they get influenza. There are two vaccines that are approved specifically for this age group that are both available this season; the high dose inactivated vaccine, and the adjuvanted inactivated vaccine. Both are quadrivalent. The high dose has a higher concentration of hemagglutinin and antigen, or a dose four times higher than a standard dose. And the adjuvanted contains an adjuvant agent called MF59. Both of these are things that are intended to produce a stronger vaccine immune response, and both of these vaccines have been shown in some studies to be more effective in this population than non adjuvanted vaccines, or the standard dose vaccines. With that being said, ACIP and CDC still make no preferential recommendation for any one vaccine for any age group, including this age group. So, the important thing is to get vaccinated. Vaccinations shouldn't be unduly delayed to find a specific product of one that suitable is already available. Next slide.

And lastly, just a little bit on the benefits of flu vaccination. As we're aware, vaccines, in general, as far as flu vaccines go, they're not 100% effective. The vaccine effectiveness of flu vaccines varies from season to season. It's affected by the season, the predominant virus that is circulating, the degree of match between the circulating and the vaccine viruses, and also on host factors such as the age and the immunity of the recipient. In a season where most circulating viruses are similar to those represented in the vaccine, where there's a good match, or you can generally expect about 40 to 60% effectiveness overall, generally it's better for children and younger adults. Generally, it's better for H1N1 than H3N2 viruses. But one thing, the last thing I want to point out is that vaccination still provides important benefits even in a setting, a season of moderate to lower effectiveness. Last slide.

CDC publishes every year estimates of vaccine effectiveness for flu vaccines, and also for the past several seasons has published estimated benefits in terms of the burden averted through vaccination each season, burdens such as illnesses, hospitalizations, medical visits, and influenza associated deaths. The most recent example that we have is from 2019-20, where the estimated vaccine effectiveness for that season was 39% overall. However, the estimated burden averted was still substantial, including about 7.5 million illnesses, 105,000 hospitalizations, and 6,300 deaths. So, just to keep in mind that even in the setting of moderate vaccine effectiveness for flu, we're still, by vaccinating, preventing a substantial amount of burden to the United States and the people in it. And that's my slide, I think. And I'll close here and turn it over to Dr. Kroger.

Thank you, Dr. Grohskopf. I'm now going to discuss specific issues related to vaccine coadministration. My title slide shows some bias towards COVID-19 vaccination. I'm going to be talking about COVID-19 vaccination, influenza vaccines, as well as vaccines generally. As we begin the school year, and as influenza season gets into full swing, coupled with the increasing use of COVID-19 vaccines, and our need to catch up on vaccines that may have lapsed as a result of the COVID pandemic, we need to perhaps administer two or more vaccines at the same clinic visit takes on increased importance. Next slide, please.

So, every clinical visit might be an opportunity to vaccinate. Pictured here is CDC's handout on the adult standards for immunization. Coadministration is an issue that does apply across the lifespan, and, of course, children, as mentioned, are going to need to be caught up on vaccine

doses they might have missed. But I wanted to focus on adults. They don't see their provider as often as children, and so there's a need to emphasize that attention has to be given to assessing the immunization status at every encounter. Assessment of status is the first pillar of the CDC adult vaccination standards. You definitely don't want to miss an opportunity to vaccinate. The second pillar of our standards is that if a vaccine is indicated, the provider needs to make a strong recommendation to vaccinate. Vaccination coverage rates can rise by as much as 50% with a provider recommendation. The third pillar of our standards for adult immunization practices is that if you have a vaccine, you should administer the vaccine. Granted, some adult venues don't have every vaccine, so you may not be able to do this. But if you do have the vaccine that needs to be administered or coadministered, you should administer it. And then finally, document every dose of vaccine you administer. Make sure a patient has their own administration record, vaccination record. And make sure that, you know, the immunization information system or registry has a record so that you don't put a patient in the position of having to receive an unnecessary repeat dose of vaccine at some point in the future. And so more, you can look up more on the standards for adult immunization practices at the title URL at the top of the slide. Next slide, please.

So, are there concerns about giving two doses of vaccine on the same clinic day? This topic is covered generally in the ACIP's general best practice guidelines. And they state that two different vaccines may be simultaneously administered as a general rule. Simultaneous is a synonym for coadministration. Essentially, it means giving two doses of vaccine on the same clinic day or visit. You should never miss an opportunity to vaccinate. This might mean several vaccines at one visit. But the immune system definitely has the capacity to handle the multiple vaccines. There are a few exceptions to the allowance for simultaneous vaccination, but they're rare. They generally involve children that have conditions like functional anatomic asplenia, complement component deficiency, or HIV, and is limited to a few vaccines; PCV13 and Menactra is the, you know, the classic exception to this general rule about simultaneous vaccination. ACIP also defines non simultaneous. It's just the issue of a prior vaccine having been given recently, but more than one full day ago. There is a full day between two separate vaccines. This also generally is not a problem. There are some exceptions here, as well. There are non live vaccines; DTaP and Menactra. Again, that exception applies to certain risk groups, such as asplenia, HIV infection, and complement component deficiency. Another exception to this rule about non simultaneous vaccination occurs with essentially every, every single live injectable and live intranasal vaccine. And the reason for this is that the generation of immune responses to the first vaccine may inhibit the replication of the second live vaccine administered. And so we state that if, for these exceptions, if two live injectable or intranasal vaccines are not administered on the same clinic day, they should be separated by 28 days. And this is relevant for today's topic because, of course, live attenuated influenza vaccine is influenza. And so that is an issue of that particular vaccine and other live vaccines. Yellow fever vaccine is a live vaccine. That needs to be separated by 30 days from other live vaccines, including LAIV. But the general rule, of course, is that two different vaccines may be given simultaneously, or at any interval with another vaccine. I'll point out that in the vaccine specific influenza document, there's a lot of really good discussion of this question with other vaccines, looking at the data, but the answer comes out the same, that generally influenza vaccines may be administered and co administered with other vaccines. So, I can refer you to the influenza specific document to look at what has

been examined and demonstrated that there, indeed, can be coadministration. Why don't we go to the next slide?

So, with respect to COVID-19 vaccine, this is, of course, a pertinent topic. And as Dr. Grohskopf mentioned, there's not content published in an MMWR but it is available online at the clinical considerations webpage, which you can see on this slide, and you see the link below. Next slide.

The rules are straightforward with respect to timing. COVID-19 and other vaccines may be administered without regard to timing. So, simultaneously or non simultaneously, coadministration is a go. And this makes sense. First of all, COVID-19 is a non live vaccine. We don't expect effectiveness concerns. We have local reactogenicity in mind. It's not known if coadministration increases the risk of local reactions, particularly with other adjuvanted vaccines or live vaccines. When deciding on whether you're going to coadminister COVID 19 vaccine, consider whether the patient is behind on their vaccines, the risk of vaccine preventable diseases, whether during an outbreak or an occupational exposure, and the reactogenicity profile of the vaccines. And as mentioned from our general principles, the immunogenicity and adverse event profiles are generally the same, when two vaccines are administered simultaneously versus alone or even at an interval from each other. Next slide, please.

So, some administration pearls you need to keep in mind when you're administering more than one vaccine. Be sure to label each syringe so you know which vaccine is in which syringe, if it's back to the documentation issue and avoiding administration errors. Make sure that your coadministered vaccines are separated by at least one inch. Different sites need an inch apart so that if a local reaction occurs, you can identify which vaccine may have been responsible to document the precise location in the chart if you are able to see the patient when they report the adverse reaction. There are no particular requirements which vaccine you administer first. And this is in the context of COVID-19 vaccines and influenza vaccines. There are some rules for some of the other vaccines I mentioned as exceptions on the previous slide with pneumococcal vaccine. But for the purposes of influenza and COVID, there is no requirement to get one before the other. Some providers do, want to put separate vaccines into separate limbs. And we do have some guidance on this for COVID-19 vaccine specifically. So, you're still vaccinating at the same time, at the same visit. But instead of an my apart, you're vaccinating in different limbs. Next slide, please.

And this local reactogenicity we are concerned about when we talk about making sure they're in separate limbs, and the lists of vaccines that we would want to be separate from COVID-19 vaccine include adjuvanted vaccines. It's a long list. Hepatitis A, hepatitis B, DTaP, Tdap, TD, the adjuvanted influenza vaccine, FLUAD, AIV, HPV vaccine, Shingrix, abbreviated RZV, which is a recombinant zoster vaccine, MenB vaccine, and a number of combination products as well. Pentacel, Quadracel, Kinrix, Twinrix, and VAXELIS. Now, note authorization for COVID-19 vaccine is for persons 12 years old and older. So, the adjuvanted vaccines you really need to be concerned about is limited. We're talking Hep B, Tdap, TD, adjuvanted IIV, HPV, RZV, MenB, and Twinrix. So, a daunting list, but we talked about COVID-19 vaccine, it's really not that long a list. As Dr. Grohskopf mentioned, on the list of place in a separate limb is high dose influenza vaccine, so that's important. And our COVID-19 clinical considerations states tetanus-

toxoid containing vaccines, these are all adjuvanted, so in the list in the first bullet as well. Next slide, please.

And then just to bring us back to the topic of influenza vaccines, an important take home is for a separate limb when you're talking about FLUAD and high dose Fluzone that you should try to place, you should administer in a separate limb if feasible. Next slide, please.

And so a long list that I went through of adjuvanted products, and many providers have a tendency probably to place vaccines in separate limbs anyway. There are naturogenic vaccines that are not adjuvanted; IPV and PPSV23 come to mind. So, for practical purposes, you really need to make a decision in the context of whichever vaccines are indicated at a particular time. Keep in mind the influenza vaccines as most relevant for this discussion, separate limb from COVID-19 vaccine, if feasible, note also that while the deltoid is the preferred site for adults, you may use the anterolateral thigh for vaccination as well. There are challenges. The clinic setting may not permit use of the anterolateral thigh. It may not be convenient to access that site. But you should be aware that that site does exist as an option, particularly for persons who may be indicated for both COVID-19 and influenza vaccine. It's not the preferred, but it is acceptable to use. In some circumstances, where you are going to be limited to your deltoid, your deltoids, you know, you may have to make a decision that you are going to actually give the two vaccines in the same muscle. Make sure you separate the doses by around an inch. Next slide, please.

I'm just going to conclude with some important resources to assist clinicians in the administration of vaccines, and particularly COVID vaccines. The next slide.

So, for product specific information about the three COVID-19 vaccines, as well as various links that will take you to the clinical considerations, I will point you to this website, our main portal for COVID-19 vaccination, with the URL listed on the slide, with the link listed on the slide. Next slide, please.

A subpage to the page I showed you on the last slide lists important information about the training of healthcare professionals on how to administer COVID-19 vaccine. Additionally, your links to the specific administration guidance for each of this particular brand of COVID-19 vaccine are listed as links on the bottom of this slide. Next slide, please. And with that, I will turn it back over to our moderator. Thank you very much.

Thank you very much, presenters. Thank you for providing our audience with this timely information. We will now go into our Q&A session. Please remember to ask a question using Zoom. Click the Q&A button at the bottom of your screen, type your question. Please note, we have received many more questions that we can answer during the time we have remaining.

So, our first question asks, do you anticipate ACIP's recommendations to change as more emergency authorizations are issued by the FDA or the next several months for additional age groups when it comes to COVID-19 vaccine administration?

So, that's, this is Andrew. That's probably mine since it deals specifically with COVID-19 vaccine. I always expect change to accompany changes to authorizations or licensure, so I do expect that pattern to continue. As to whether, you know, specific coadministration recommendations change, it's hard for me to speak to that because I can't speak to something that hasn't necessarily happened yet. But I think there is a lot of attention to trying to adhere to general principles regarding coadministration. But, in general, with respect to usage of COVID-19 vaccines, I do expect change, I don't have specific timelines, but I always am expecting that type of change.

Thank you. Our next question asks, in light of the COVID 19 pandemic, do experts expect influenza activity, cases and hospitalization to be similar to last influenza season?

This is Lisa Grohskopf, I'll take that one. Always impossible to predict what the upcoming season is going to be like. We did have a very quiet little activity season last season, as I'm pretty sure everybody noticed. The closest we came to having a season like that was 11-12, which was also relatively low activity, but this was clearly lower this past season than even that was. It's probable that some of the same sorts of mitigation strategies that were employed to diminish the spread of COVID-19, things like the social distancing and masking and also things such as school closures also had a lot of influenza prevalence and activity of other respiratory viruses in the country last season, because a lot of the same mechanisms can also inhibit spread of those viruses. As things are going forward, children are back in school in a lot of places, and depending on the extent to which mitigation strategies continue to be employed in various areas, you know, it's conceivable that we're going to see increased activity of various respiratory viruses in the coming months, including flu. It's always impossible to predict how severe a season is going to be, just like it is, you know, when it's going to start and when it's going to peak and when it's going to end. But we always need to be prepared for the possibility that it's going to be significant. And there has been a bit of an uptick in other respiratory viruses over the past several months. So, always good to keep in mind that, you know, we could see more, and vaccination is always important.

Thank you. Our next question asks, can you please share any updates, if you have available, on many factors like Moderna making the news, saying that they're working on combo vaccines of influenza with COVID boosters?

Speaking for myself, I don't have any information about those particular things. And combination vaccines are always appealing from the point of view that it allows, you know, vaccination with more than one thing at the same time, but I don't have any specific information about that particular combination.

This is Andrew. I do not either.

Thank you very much. Next question. Can a pregnant adult receive an influenza vaccine in the first or second trimester as well?

Yes. The recommendation since 2004, coming from both the ACIP and the American College of Obstetricians and Gynecologists has been that vaccination can occur in any trimester.

Thank you very much. Can you also discuss vaccination administration either at or near surgeries, as well as any other imaging procedures that may be not advised for vaccine administration or coadministration?

So, this is Andrew. I can kind of approach this from the general perspective. Well, first, from the issue of coadministration, I'm not aware of any impact of specific clinical settings, whether they're upcoming surgeries or use of anesthesia or hospitalizations that truly impacts to coadminister or not to coadminister. I don't that intersection is new for me, so I don't think there's anything that bears on that issue. I will say that we generally consider, you know, severe or moderate acute illness a precaution to vaccination generally. So, that is going to often be a situation with hospitalization or upcoming use of anesthesia or surgeries. So, you know, the precaution will be applied in many circumstances. And, you know, we have often said that there's no evidence to recommend a specific number of days to kind of give a vaccine before. But we do want to emphasize that you don't want to miss an opportunity to vaccinate. And so if deferral occurs during a surgery or a hospitalization that one should try to make sure those vaccines are given, perhaps prior to this charge or at the first follow up visit, as soon as possible.

Thank you. And as a follow up, any consideration to vaccination when, for the second part of this question regarding imaging, whether it's something superficial like mammogram or something more involved than say contrast media, et cetera.

Right. So, we've, there has been some that's a good follow up. And it reminds me that there were some recommendations regarding COVID-19 vaccines and the impact of lymphadenopathy on potentially and this, again, gets to the, you know, the precaution issue that there may be diagnostic, what the general best practices refers to as diagnostic confusion if lymphadenopathy caused by a COVID-19 vaccine, you know, distorts or creates an artifact on a breast image. So, there are, you know, specific recommendations to try to, you know, defer, you know, vaccination in that circumstance, or, you know, defer the imaging with respect to COVID-19 vaccines.

Thank you. Next question asks, can you please also share the ideal range for influenza vaccination when it comes to time frame? I guess this question is referring to months, which months to vaccinate. Can you please also share ideal range of influenza vaccination for residents of the southern hemisphere?

That is an interesting question, since our guidance is formulated for the U. S. , so it focuses on the northern hemisphere. The southern hemisphere, influenza season, influenza varies there just as it does here in terms of the intensity of activity and the timing of onset of the season. Roughly September through April is the sort of common month range that we hear about for their influenza season in general. I am not, I'm not aware of the exact recommendations of timing of influenza vaccination, for example, countries in the northern, in the southern hemisphere, such as Australia, and such. But ideally you would, you know, if they were to model based on our, what we have in terms of our recommendations, October for the West surveillance tends to be a month where we begin to start to see localized pockets of activity, you know, even if it's not intense enough at that point to reach the threshold that we say the season has begun. And so ideally you would, you know, the general guidance is, you know, ideally you want to be vaccinated a few weeks before influenza starts to circulate in your community. So, that would be, you know, that's

really sort of the real crystalline guidance for when is the best time to be vaccinated, it takes about two weeks to develop immunity through vaccination. There's some variation in that, depending on your health and your immune system and such. But ideally that time is a couple of weeks before the virus is circulating in your community. And that's just something that we never know exactly when that's going to happen. I'm not sure what the official recommendations are for the various Southern hemisphere countries, unfortunately.

Thank you. And we have time for one last question. And our question is a bit similar to the previous one. And the question asks, for our healthcare facilities that are still seeing cases of influenza, how do we determine that it is the 2020, 2021 to 2022 season and no longer the 2020 to 2021 season?

That's, okay, so that actually has a couple of parts to it. So, from the point of view of the vaccines, the influenza vaccine from a given season is, all of it will have expired by June 30th of that year. So, from the point of view of selecting a vaccine, after June 30th, your, whatever was, for example, after June 30th, 2021, the 2020-21 season vaccine is all expired, it's all set to expire no later than that date. Some lots in some specific brands that have shorter shelf lives will expire before that, but that's sort of like the final date by which a given season's vaccine will expire. So, from the point of view of the vaccine, you know, if there were an outbreak setting where a setting in a community with a lot of activity, you're going to be vaccinating with what is available and licensed and approved for that season after June 30th. Generally, vaccine is not really in supply in July. Sometimes we start to see vaccine come around in late July, and definitely through August. But there's sort of this during the month of June sometimes vaccine is hard to come by. As far as what season you would ascribe a specific isolate to, that, some of that depends on surveillance information, which isn't my primary expertise. But that's something I can try to get more information about from our surveillance folks. In general, as far as our surveillance activity, the more detailed reports in FluView, the CDC Influenza Surveillance Report that comes out weekly, it runs year round, but we start to have more detailed information usually by the beginning of October in anticipation of activity beginning to increase by that point.

Thank you. And that concludes today's webinar. I want to thank everyone for joining us today with a special thank you to our presenters, Captain Grohskopf and Dr. Kroger, all continuing education for COCA calls are issued online through the CDC Training and Continuing Education Online System at <https://tceols.cdc.gov>.

Those who participate in today's COCA Call and wish to receive continuing education, please complete the online evaluation by October 11th, 2021, with the course code WC2922-090921. The access code is COCA090921.

Those who will participate in the on-demand activity and wish to receive continuing education should complete the online evaluation between October 12th, 2021 and October 12th, 2023, and use course code WD2922-090921. Again, that access code is COCA090921.

Continuing education certificates can be printed immediately upon completion of your online evaluation. A cumulative transcript of all CDC/ATSZR continuing education obtained through the CDC training and continuing education online system will be maintained for each user.

Today's COCA Call will be available to view on demand a few hours after the live call. You can find the video recording of today's call at emergency.cdc.gov/coca.

Join us for our next COCA Call on Thursday, September 30th, from 2:00 p. m. to 3:00 p. m. Eastern, where the topic will be Evaluating and Supporting Patients Presenting with Fatigue Following COVID-19. Free continuing education will be offered. Call announcements will be available soon for this COCA Call.

Continue to visit emergency.cdc.gov/coca to get more details about upcoming COCA Calls as we intend to host more COCA Calls to keep you informed of the latest guidance and updates on COVID-19. Please share these call announcements with your clinical colleagues. You may also sign up to receive weekly COVID-19 Science Updates by visiting the web link provided below. COCA Call announcements for upcoming COCA Calls and other COCA products are sent via e mail. In addition to visiting our webpage, please remember to subscribe to COCA to receive notifications about upcoming COCA Calls or other COCA products and services. Be sure to subscribe to receive notifications by going to emergency.cdc.gov/coca. Again, that's emergency.cdc.gov/coca.

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Again, thank you for joining us for today's COCA Call. Have a great day.