

Hello. I'm Commander Ibad Khan, and I'm representing the Clinical Outreach 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: 2019 to 2020 Influenza Season Update and Recommendations for Clinicians. Please stay tuned until the end of this COCA call for more information about two upcoming COCA calls on HHS guidance on opioid dosage reduction or discontinuation, as well as another one on the novel Coronavirus outbreak. Both calls will take place later this week. You may participate in today's presentation via webinar, or you may download the slides if you're unable to access the webinar. The PowerPoint slides and the webinar link can be found on our COCA webpage at emergency.cdc.gov/COCA. Again, that web address is emergency.cdc.gov/COCA.

Once you reach the webinar page, the PowerPoint slides can be found under the call materials tab. Free continuing education is offered for this webinar. Instructions on how to earn 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 they 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.

The presentation will not include any discussion of the unlabeled use of a product or a product under investigational use, except Dr. Angela Campbell would like to disclose that she will discuss the off-label use of antiviral medications for treatment of influenza. CDC did not accept commercial support for this continuing education activity. After the presentation, there will be a Q and A session. You may submit questions at any time during the presentation through the Zoom webinar system by clicking the Q and A button at the bottom of your screen, and then typing your question.

Please do not ask a question using the Chat button. Questions regarding the webinar should be entered using only the Q and A button. Those who may have media questions, please contact CDC Media Relations at 404-639-3286, or send an email to media@cdc.gov. If you are a patient, please refer your questions to your healthcare provider.

At the conclusion of today's webinar, participants will be able to accomplish the following. Describe the current status of influenza activity in the United States. Describe the circulating influenza viruses detected this season, and explain the implications for clinicians. And describe antiviral testing and treatment recommendations for patients with suspected and confirmed influenza. Now I would like to introduce our presenters for today's webinar.

Our first presenter is Miss Alicia Budd. Miss Budd is an epidemiologist in CDC's Influenza Division. Miss Budd has been at CDC for more than 13 years, and has worked on national influenza surveillance for most of that time. She also has experience in infection control, having spent 6 years at the Johns Hopkins hospital, in the Hospital Epidemiology and Infection Control department. Our second presenter is Dr.

Angela Campbell. Dr. Campbell is a medical officer in CDC's Influenza Division. Her projects focus on studies of influenza and antiviral treatment, and antiviral effectiveness, vaccine effectiveness, pandemic preparedness, and development of CDC clinical guidance related to treatment and prevention of seasonal and novel influenza viruses. She is an adjunct associate professor of pediatrics at Emory University School of Medicine, and has a professional staff appointment at Children's Healthcare of Atlanta.

I will now turn it over to Miss Alicia Budd. Miss Budd, you may proceed.

Thank you. So today I'll be giving an update on the current influenza season, based on activity that we've received-- or data we've received, rather, about activity occurring through January 18 of this year. Next. So before I launch-- oops. Next slide.

Before I launch into an actual update on activity, I just wanted to briefly explain how we get all this information in that I will be talking about. So flu surveillance on the national level is really a collaborative effort between those of us at CDC, and also our public health partners at the state and local level and territories, and also numerous other data providers, many of whom are at the clinical level. And our role at CDC is really to coordinate the system that all those various partners make possible. So we get data from five categories of flu activity from eight different sources. Three of those have to do with the virus tracking itself.

Two have to do with flu-related mortality, and then we have one each that focus on outpatient visits, hospitalizations and the geographic spread of flu activity in general. And every week we analyze that information, and we make it available to the public in the form of FluView which is a static report, and FluView Interactive, which is a system online that really lets you dive deeper into the data on different geographic levels, different time frames, and things like that. And those are both available on the internet, and in the resource slide at the end, you'll have those web pages. Next. So the goals with the flu surveillance really haven't changed, even though the system has been in place over many, many years.

Some of the systems have changed. Some of the data we get in have changed, but really all along, we're focused on identifying and characterizing the viruses that are circulating, with a special eye towards making sure that any viruses with pandemic potential would be recognized early. We also are doing flu surveillance to provide situational awareness about the onset of the season, where we are in the season in terms of activity increasing or decreasing, and where in the country activity is occurring. We're also of course looking at the severity of the flu season, and whether it looks like things are what we would expect, or maybe a bit higher or lower. And then, we're looking of course to describe the clinical infections, and those at most risk, and all of this really with the eye towards how we can guide decisions about interventions.

Next. So now I'm going to move into where we are with this season. So this slide shows what we're seeing in terms of influenza virus circulation, based on the data that have been reported to us from clinical labs and public health labs across the country. So clinical labs test specimens primarily for diagnostic purposes, and we use the data from these labs to calculate the percent of specimens that they're testing that are positive for influenza. And with this data, we can track the timing of the season, and the intensity of flu activity.

So this season, activity was low in October, and began to increase in November, but then really took off in December. We had a slight decrease in activity the first two weeks of January, and we're starting to see an increase again now in the third week of January. And there's a number of reasons that this might be occurring. That decrease could be related to a slight decrease in transmission that occurred because kids were out of school for a couple of weeks around the holidays. It could be that that highest peak there is somewhat impacted by changes in healthcare-seeking behavior over the holidays, and it was sort of an auto-data correction bit that we saw there with the decline.

Or it could be, and I'll talk about this a little bit more later, it could be that we're switching over from seeing sort of an increase in B activity, and now we're seeing more of an increase in A activity. But

things haven't quite evened out yet. So regardless, we are definitely seeing high levels of activity, and you can see with this increase in the most recent week, we're just about back up to where we were at the highest point this season. So we don't know yet at this point where things are going to go from here, but it's definitely something to continue to monitor. From the public health labs, that bottom panel there, you can see the information about the-- what types of flu viruses are circulating.

So this season, we've seen, for the season as a whole, predominantly B/Victoria lineage virus season. So that's the most common virus reported for the season as a whole. But in the most recent weeks, we've seen nearly equal numbers of B/Victoria viruses and Influenza A/H1N1 viruses. Very little B/Yamagata virus circulation, and not much H3 virus circulation, either. Next slide.

So this slide is a little busy, but I wanted to put into perspective how unusual it is that we are seeing so much Influenza B activity. So each individual pie chart here represents the distribution of influenza viruses by Influenza A subtype and B lineage where we have it, going back to the 1976-77 season. And then, on the bottom right there, in the red box, is this season's data to date. The red represents H3 viruses. The blue is the pre-pandemic H1 viruses.

The yellow or orange color is H1pdm09 virus, our current H1 virus since the last pandemic. And then the greens are the Influenza B viruses. Next slide. So now, that blue circle there is the 1992-'93 season. And that is the last time that we have had a B-predominant season here in the U.

S. And it was a B/Yamagata virus. And it accounted for almost 75% of the viruses that season. Next. More recently, there circled, are the 2000-2001 and 2002-2003 seasons.

These seasons were not B-predominant, but they were the last time that we saw such a significant amount of Influenza B activity. And in both seasons, it was actually H1 that was predominant. It was the pre-pandemic H1, but it was H1, just like we're seeing as our other sort of co-circulating virus this season. The 2000-2001 B's were of the Yamagata lineage, and the 2002-2003 B's were the Victoria lineage. Next slide.

So I think in general people tend to be a little bit less aware of some of this Influenza B history than we are of the Influenza A sub-type. So I just wanted to spend a quick minute talking about that. So it was the early to mid-1980s when the two separate B lineages, the Yamagata and Victoria, were identified. In 1988, rather, it was the B/Yamagata/16/88 strain was identified in Japan. Looking back earlier, it looks like maybe as far as the early '80s, it was also in some other countries in Asia.

And it's similar to a 1983 virus from Russia. So the specific date of when it emerged isn't known, but sometime in the early to mid-'80s. Despite that, it's still in the U. S. for the '88-'89 season.

Our B viruses were antigenically like the B/Victoria lineage viruses. It wasn't until the 1990-'91 season that we first saw B/Yamagata lineage viruses in the U. S. And the Yamagata viruses dominated the B circulation in the U. S.

throughout the 1990s. Victoria viruses were pretty much limited to China and Asia. Then in 2001-2002, we saw B/Victoria viruses circulate in the U. S. again.

It was the first time that we had had them since the '88-'89 season. And since then, we've seen co-circulation of the two lineages in the U. S. But both have been at relatively low levels, when you look at the relative proportions of the viruses every season. And typically when we think of B activity in the U.

S. , we think about sort of the later wave of flu activity that happens toward the end of flu season. Next slide. So you know, while in recent seasons, like I just mentioned, we typically see relatively low levels of flu, looking a little more closely at that 2000, and 2001, and 2002-2003 season, just a couple interesting things to point out. That first season where we had a predominant, or-- not predominant.

But a large amount of B viruses circulation, it was also H1 as I mentioned. But the A viruses came first, and the B's later, which is sort of the timing we're more familiar with. In the '02-'03 season, it was H1 again, and B/Yamagata viruses this time. And A's and B's seemed to increase at about the same time. B's dropped off first.

This season what's even more unusual than seeing so much B activity is that our B activity increased before our A activity. So that's definitely not something that we typically see with influenza B viruses. Next. So another interesting piece of Influenza B viruses epi is who tends to be more affected by these two different lineages of viruses? This slide shows pie charts for the Victoria viruses on top, Yamagata viruses on the bottom. Looking back at the last several seasons, back to '15-'16, and you can see that Victoria viruses impact kids more than the elderly with those 65 and older only accounting for 10% or less of the Victoria viruses in these recent seasons.

For the Yamagata viruses, the opposite is true. We see the elderly accounting for between a quarter and 1/3 of the Yamagata viruses in each season. That's a larger proportion than we see in the youngest kids, and it's certainly more than we typically see for the Victoria viruses. Next slide. So this is also looking at age distribution, but back to looking at just this season.

And with this sort of co-circulation of a large amount of B/Vic viruses and the H1 viruses, we're actually seeing a different predominant virus in the different age groups. So in our kids, B/Victoria viruses are predominant, and in our both adult age groups, it's the H1 virus that are predominant. Next. And another thing that I touched on earlier, just wanted to show a little bit closer, is while B/Victoria viruses are predominant so far this season, for the season as a whole, we are definitely seeing an increase in flu A activity recently. You can see that in the clinical lab data on the left, where we're looking at percent positivity.

That dark line is the overall percent positivity. But the dashed green line is percent B, and you can see it had a sharp decline there for a couple weeks. Now it's sort of leveled off. But percent A positivity and the yellow dashed line is continuing to increase quite steadily. You can also see that in the public health lab data, which is in the slide on the right.

This is looking at the relative proportions of each of the A subtypes and B lineages. The gray line is the B/Victoria viruses. It's been relatively high. A few bumps here and there, but pretty stable for a good part of the season, and then a slight decline in recent weeks, while the relative proportion of viruses from the public health labs that are H1, which are shown in the blue line, has continued to increase throughout the season. So we'll continue to watch and see how that plays out in the coming weeks as well.

Next. So the public health labs also, in addition to reporting their results, they send a subset of their specimens on to CDC or to a CDC reference lab for genetic and antigenic characterization, as well as antiviral susceptibility testing. And this is used to help monitor how the flu viruses are evolving. The pie chart there on the left is the same public health lab data that we've been looking at. I just put it in there for perspective, and a reminder that, you know, what we're seeing a lot of this season, we have a system in place we call right-sizing, where we try to get in as much as possible, similar amounts of all the subtypes and lineages for the characterization.

So just the fact that we are seeing a lot of a virus being tested for characterization doesn't mean that necessarily is the virus which is predominant, which is why I wanted to have that public health lab pie chart there as well. So for the H1's and the B/Yamagata viruses, the story's pretty straightforward for both of those viruses. Everything that we have genetically characterized belongs to a single genetic clade for each of those viruses respectively. And it's the same clade as the vaccine reference virus. All of those that have been tested antigenically are also considered similar to the cell-grown reference virus.

For the H3 viruses, which again, we're seeing very little of this season, the vast majority of those that have been genetically characterized belong to a different genetic subclade than our vaccine reference virus. But even so, we are seeing about 42% of the H3's that have been antigenically characterized are similar to the cell-grown vaccine reference virus. For the B/Victoria viruses, more than 90% belong to what we call the B1a.3 genetic clade, and the vaccine reference virus is actually the V1A.1 genetic clade.

But similar to the H3 viruses, despite that difference in genetic clade between the vaccine reference virus, and what we're seeing predominance of in circulation, about 60% of the viruses that have been antigenically characterized are similar to the cell-grown vaccine reference virus. And a last piece of good news on this additional testing front is that almost all of the viruses tested, and it's been more than 1,000, have been found to be susceptible to all four of the licensed antiviral medication. Next. Switching gears now to look at flu-related illness. This is data from our outpatient physicians, our provider network.

This season is shown in red. We've been at or above the national baseline for 11 consecutive weeks now, taking us back to early November. And all 10 of the surveillance regions have been above their region-specific baselines for several months as well. We see a similar dip here at the same time period that we did for the clinical lab data. Likely for all or any of those reasons that we talked about with the clinical lab data.

Then of course, we'll have to wait and see how this continues to play out, whether we're going to increase again, or start to decrease in the coming weeks. But either way, we are, again, seeing a lot of flu virus circulation at this point. Next. We also look at the same outpatient ILI data on a state level, and calculate the intensity of ILI activity for each state. The intensity level ranges from minimal to high.

And during Week 3, which was our most recent week, we had 37 jurisdictions experiencing high ILI activity, 7 at moderate, and the remaining 9 were either low or minimal. Next. So we track lab-confirmed flu hospitalizations in addition to outpatient illness. And we do this through a multistage population-based surveillance system. Just wanted to point out these data are presented somewhat differently than the rest of our flu surveillance data.

It's weekly data, but the data point for each week is where we are cumulative through the season up into, and including that week. So these data continue to increase with each week of the season. This season is again, shown in red, and you can see where we are with a overall rate of 24.1 flu-related hospitalizations per 100,000. Puts us right sort of in the middle of where we have been at this point in the season in past recent years.

Also not surprisingly, the highest hospitalization rate is in those 65 and older, at about 58 per 100,000. Next slide. So we have two systems for tracking flu-related mortality. The graph on the left shows data from the National Center for Health Statistics where we look at death certificates that have been coded

with a cause of death of either pneumonia or influenza. We compare that percentage to epidemic-- a baseline epidemic threshold.

And so far this season, with the exception of Week 1, so that first week of the year, we have been below the epidemic threshold. That one week we just touched it, barely. So as you can see, compared to some of the past seasons, we are still at quite low levels of flu-related mortality at this point. On the right is our second mortality surveillance system, which looks at laboratory-confirmed deaths in children. So far this season, 54 pediatric deaths have been reported to CDC.

Sixty-nine percent of those were associated with Influenza B virus infection, and 31% with Influenza A virus infection. Only a small proportion of the B's have been lineage tested, but all those that were are Victoria viruses. And for the A's, a small number have been subtyped, and all were H1 viruses. Next slide. Actually, I'm sorry.

Could you back one minute? Just one quick thing to point out, because I know there's always a lot of interest in this, is vaccination history for our pediatric deaths. This is information that we don't have on all the deaths for this season as of yet. We do know that typically only about 20% of the pediatric deaths have been vaccinated, looking back over a history of this system. Again, I mentioned we don't have all of that data for these deaths yet. That information tends to lag a bit more.

But what we do have so far this season seems to indicate that that vaccination percentage is even lower this year than we often see. So next slide. The last piece here is our geographic spread of flu activity. So this is where each jurisdiction reports, not the intensity of their activity, but how widespread it is across their jurisdiction. And during the week ending January 18, as you can see, almost all of the country was reporting widespread activity.

Next. So I just wanted to mention one other quick thing before I turn this over for the clinical portion, and that is our estimates of influenza-associated burden in the U. S. The surveillance systems that I've just gone through, are how we track trends of flu activity. It's how we get sort of real-time indications of what's happening.

But we take that information and run some mathematical models to find out what we think those trends might equate to if you try to estimate flu-related illnesses. So doing that so far for this season, again, same time period up through the week ending January 18th, we're estimating that so far in the U. S. this season, there have been at least 15 million illnesses, at least 140,000 hospitalizations, and at least 8200 influenza-associated deaths. So these are cumulative numbers.

We put them out this week, and they will continue of course to increase throughout this season. On the left-hand side, you can see the burden estimate ranges from 2010-'11 through '17-'18. You can see for the most part we are either at or below the lower end of that spectrum, but again, we are, you know, only probably about halfway through this season so, these numbers will continue to increase. And last slide for me is just a quick summary. So we are seeing indicators, our surveillance indicators that track flu activity itself, they're quite high.

And we expect them to remain high, or at least above baseline levels for many weeks to come. But despite this high level of flu activity, our markers of severe illness, the hospitalization and deaths really aren't high at this point in the season. By saying not high, it is for course, you know, it is flu we're talking about, so we are seeing a lot, but not compared to what we have seen in other seasons. And this

is likely due to the fact that we're seeing so much B/Victoria and H1N1 circulation. And these viruses on a whole are more likely to affect children and younger adults than they are the elderly.

And we know that the majority of hospitalizations and deaths occur among the elderly. And so with fewer illnesses in that group, we expect to see what we're seeing, which is on a population level, less impact on hospitalizations and deaths. So that concludes my activity update portion, and I will turn it over to Dr. Campbell for her clinical piece.

Great. Thank you. Good afternoon everybody. My name is Angie Campbell. And first I'm going to briefly review the clinical manifestations of influenza, especially in light of this current season, with the predominance of B viruses and H1N1pdm09 viruses.

So next. Influenza, as you know, can cause a spectrum of illness. And this can range from asymptomatic infection to a more typical upper respiratory tract illness, typically consisting of abrupt onset of fever and cough, with other symptoms that may include chills, muscle aches, fatigue, headache, sore throat, runny nose. I should note that the runny nose and nasal congestion symptoms do tend to occur with other more common cold viruses as well, but they may occur in young children with flu. And GI symptoms such as abdominal pain, vomiting, and diarrhea also tend to be more common in children.

Young infants may not actually have respiratory symptoms at all, and they may present with fever alone, often with irritability. And then on the other end of the age spectrum, elderly people and people who are immunosuppressed may have atypical symptoms, and may not have fever. And so all of these manifestations can occur with what we would generally call uncomplicated influenza illness. But as we all know too well, and as Miss Budd just showed us, that flu can also cause complications. Next.

So common complication is otitis media. And this can actually develop in up to 40% of children under the age of 3 with influenza. Influenza can also exacerbate chronic underlying conditions such as asthma. And then other common causes of hospitalization with flu include dehydration and pneumonia. And the pneumonia can be a primary viral pneumonia, or secondary bacterial.

Flu can also cause other respiratory syndromes, as well as a number of extra-pulmonary complications. There's a whole list there. It includes renal failure, myocarditis, pericarditis, myositis, or extreme rhabdomyolysis. Flu is known to cause encephalopathy and encephalitis, particularly in children. Guillain-Barre syndrome, acute disseminated encephalomyelitis or ADEM, as well as sepsis and multi-organ failure.

And in fact in a relatively recent review of death reports of children who died with flu, sepsis was actually found to be listed as a complication in up to 30% of those reports. Lastly, I do want to mention invasive bacterial co-infection, which can cause severe and fulminant disease when it's present with flu. The most common bacteria are typically pneumococcus, which is strep pneumo, staph aureus, and this is really either methicillin-susceptible or methicillin-resistant staph aureus, as well as strep pyogenes, or Group A strep. Next. So as you may be aware, on January 10th, CDC put out this health advisory.

And the point was really to notify clinicians that influenza activity remained and continues to remain high in the United States. At that time, and now, ongoing elevated activity was due to the Influenza B/Victoria viruses, with increasing circulation of Influenza A, H1N1pdm09 viruses, and then we still have very low levels of B/Yamagata, and A/H3N2 viruses. And you just saw that demonstrated really nicely with all of our surveillance data. Next. So since this season has been rather unusual with this early

predominance of Influenza B/Victoria viruses, I wanted to talk about what we know about B viruses, and specifically what we know regarding differences between Influenza A and B virus infections.

So there are a few papers that have addressed this question. This top bullet really is reflective of most. Among hospitalized adult influenza cases, and this was data from the '05-'06 through the '12-'13 flu seasons that was collected through the Flu Servnet Hospitalization Network that Alicia mentioned. In this paper, they found no difference in ICU admission, length of stay, or mortality between Influenza A and B infections. And that was after adjusting for high-risk conditions, antiviral treatment, and seasonality.

Next. This slide has the same-- you know, I think I didn't really want to say "next" yet. Could you just go back, please? I wanted to transition to children first before I showed you this figure. So among children, when we look at our surveillance data over time, it is actually interesting. The proportion of influenza-related pediatric deaths associated with Influenza B viruses has actually generally been higher than the proportion of Influenza B among circulating viruses.

And so the next slide. Next. Will actually show this in a figure from a recent paper. It has the same words I just said on the side, and let me just walk you through this. So the solid light gray lines are the percentage of Influenza A in the U.

S. Flu Virological Surveillance System, and the solid black are Influenza A among pediatric deaths. And I know the colors are not that distinct, but you can see in the very top line is the gray line that represents virologic surveillance. And it shows that the Influenza A viruses were predominant during all six of the seasons. It's the top line across the board.

But the percentage of A viruses among children who died was below that line. And then, if you look at the dotted lines-- that's switched. So the dotted lines represent Influenza B. And among virologic surveillance in the dotted light gray, and the pediatric deaths in the dotted black, you can see that the proportion of Influenza B virus is detected among those children who died was higher than the proportion of the Influenza B virus as detected in children for the overall surveillance for those six seasons. So it is interesting.

B viruses do tend to cause severe illnesses in children. OK. Back-- next. So back to this slide, and one last bullet. Next.

This was another paper that was recently published. This was actually in Canada. And they found that the mortality from Influenza B-associated hospitalizations was actually higher than Influenza A-associated hospitalizations among children. Next. The other thing that came out the same day as the health advisory was this recent MMWR that you may have seen.

And this described the early season pediatric Influenza B/Victoria virus infection specifically in Louisiana. Louisiana had very early activity this season. And nearly all of the viruses from these children belong to the recently emerged genetic subclade, the B1a. 3 subclade that Miss Budd mentioned. And so the objective of this investigation was to evaluate clinical features of this new subclade in children.

Especially because many young children have never been previously exposed to this new subclade. And really, the bottom line of the investigation is at the bottom. Next. It's that the early activity in Louisiana did result in illnesses that were generally typical to seasonal influenza. However, even though most of

the illnesses were uncomplicated flu, some illnesses were severe, and there was actually one death in this study.

Next. So because we've also now seen this increase in Influenza A/H1N1pdm09 viruses, I wanted to briefly highlight what we know about illness with these viruses. There was actually a systematic review done in 2018 to try to get at this question. And they found weak evidence that A/H1N1pdm09 viruses were more often associated with secondary bacterial pneumonia, ICU admission, and death in the post-2009 pandemic period. So this subsequent paper, which actually the first author was Miss Budd, who just presented, is really an interesting analysis.

Because this looked at U. S. Influenza Surveillance data by birth cohort, rather than traditional age groups. Usually we look at children, adults, and elderly. And this divided it into different birth cohorts, depending on the year of birth.

And it suggested that on a population level, the initial Influenza A virus subtype that you're exposed to may affect the clinical impact of influenza in subsequent years. And so specifically, since the pandemic, more severe disease and death occurred during H1N1 predominant seasons than H3. And this was particularly true in adults who had not originally been exposed to the currently circulating H1N1pdm09 viruses. So a really interesting paper to take a look at, that gets at this idea of your first influenza exposure which is often termed imprinting. Next slide.

So now I'm briefly going to discuss vaccination, and just a little comment on vaccine effectiveness. Next. So I think everyone on this call is likely already convinced that flu vaccination is the best way to protect against influenza, and you also all likely know that the ACIP and CDC recommend annual vaccination for everyone 6 months of age and older, who don't have any contraindications. This is recommended to be received by the end of October, but we always emphasize that as long as influenza viruses are circulating, vaccinations should continue throughout influenza season, even into January or later. I think that's really evident this season, with this switch that we're having from B viruses to H1N1 viruses.

But if you've-- obviously if you've had one viral infection with B early in the season, you're still at risk of having another infection. So even people who've had flu that have not been vaccinated should be encouraged to do so. Next. This slide lists the composition for vaccines available this season. Note that there were two changes from the 2018-'19 season.

Both the H1N1 and the H3N2 viruses were updated. And also note that the B/Victoria virus is included in both the trivalent and quadrivalent formulations. Next. And although we know vaccination's important, one thing we always struggle with is that communicating influenza vaccine effectiveness is challenging. The VE can vary by population, as well as by what viruses are circulating, and vaccine type in any given season.

And so I just want to remind you that CDC has developed a model to translate VE, or vaccine effectiveness, into the number of influenza-related outcomes that are prevented by vaccination. Next. So another way to say this is really, what is the burden averted by influenza vaccination? And this graphic shows the numbers for the 2018-'19 season. That it was estimated that 4.4 million illnesses, 58,000 hospitalizations, and 3,500 deaths were averted by vaccination.

So we expect our preliminary vaccine effectiveness estimates for this season to be available by the end of February. And then once we have those VE estimates, this averted burden graphic, and these estimates can then be estimated. Next. OK. I'm moving on to the diagnosis of influenza.

I have multiple topics I'm squeezing in here. Next. I do want to make sure you're all aware of the IDSA clinical practice guidelines that were published in December of 2018. Next. And I also wanted to draw your attention to the main CDC page on flu virus diagnostics, which has a lot of information that I won't touch on today.

Next. I do just want to remind you that flu testing should really be performed in a couple of instances. One is when results are likely to influence clinical management, in that they may decrease unnecessary laboratory testing for other etiologies. They may decrease unnecessary use of antibiotics. The result might facilitate implementation of infection prevention and control measures.

And it may increase appropriate use of influenza antiviral medications, which I'll discuss soon. And potentially decrease hospital length of stay. Another reason for testing is, if it will influence a public health response. Can be very useful for outbreak identification and interventions. And one of the most common situations where this is the case is in long-term care facility or nursing home outbreaks.

Next. So this is an algorithm from the IDSA guidance, and it's also on our webpage. It's a guide for considering influenza testing when flu is circulating in the community. And this should really be used regardless of flu vaccination history. It starts by asking, does the patient have signs or symptoms suggestive of flu, including atypical clinical presentation, or findings suggestive of complications associated with flu? And if the answer is no, then testing is probably not indicated.

But now, moving to the left of this diagram-- next. If the patient with suspected flu is being admitted to the hospital, testing is actually recommended both by IDSA and CDC, along with empiric antiviral treatment while results are pending. If not being admitted, but if results will influence clinical management, the same recommendation applies. If results aren't going to influence management, that is, if the result of the test isn't going to change whether empiric treatment can be initiated based on a clinical diagnosis, then there's probably no need for it. And that's often the case in some outpatient settings.

Also empiric treatment is recommended if the patient is at high risk or has progressive disease. I'll get to the treatment recs in just a little bit. Next. OK. So if testing is performed, what test should be used? The main point of this whole slide is that molecular assays are the most sensitive.

So for outpatients, rapid molecular assays exist now that have a very high sensitivity, and will improve detection over rapid influenza diagnostic tests that use antigen detection. And for hospitalized patients, molecular assays, which include both single PCR, or other multiplex molecular assays should be used to improve the detection of influenza. For immunocompromised patients, and often critical care patients in particular, multiplex molecular panels are recommended. Next. The last topic I'll cover today is our antiviral treatment recommendations.

Next. So influenza antiviral medications are an important adjunct to vaccination. The focus of CDC's treatment guidance is on prevention of severe outcomes. In other words, we treat those with severe disease and people who are at highest risk of severe disease. And really these antiviral recommendations are common to multiple organizations, including IDSA, PIDS, AAP, and ACOG.

Next. So in one slide, I did want to provide a very summarized overview of a lot of data regarding the efficacy and effectiveness of antivirals for influenza. And I do want to preface by saying that no antiviral is specifically approved for severe influenza. All the antivirals are approved for acute uncomplicated flu. But observational studies do support an effect on reduction of complications, and most experts support the use.

So what we do now, the first bullet. Clinical trials and observational data show that early antiviral treatment can shorten the duration of fever and flu symptoms. Next, meta-analyses of randomized controlled trials have demonstrated that early treatment reduces the risk of otitis media in children, and lower respiratory tract complications that require antibiotics and hospital admission in adult. And lastly observational studies and meta-analyses of observational data have reported that among high-risk outpatient children and adults, early antiviral treatment reduced the risk of hospital admission. Early treatment of hospitalized adult patients with oseltamivir reduced the likelihood of death, and shortened hospitalization.

And in hospitalized children, it's been shown that early antiviral treatment with oseltamivir shortened duration of hospitalization. So there's a whole body of evidence, some on randomized trials, and some observational, on which we base our recommendations. Next. So antiviral treatment is recommended as early as possible for any patient with suspected or confirmed influenza who is hospitalized; who has severe, complicated, or progressive illness; or who is at high risk for influenza complications. Next.

So the people who are at high risk for complications, for whom treatment is recommended, include children less than 2 years, and even though we know all children less than 5 years are considered at high risk for complications, the highest risk is for that youngest group. It also includes adults age 65 and over, pregnant and postpartum women, American Indians, Alaska Natives, children who are receiving long-term aspirin therapy. People with a number of underlying medical conditions, and residents of nursing homes and chronic care facilities. Next. So clinical benefit is absolutely greatest when antiviral treatment is initiated as close to illness onset as possible.

Treatment really shouldn't be delayed while testing results are pending. An antiviral treatment initiated after 48 hours can still be beneficial in some patients. There are been observational studies of hospitalized patients that suggest that treatment might be beneficial even when initiated 4 or 5 days after symptom onset. And similarly, there have been observational data in pregnant women that have shown treatment to provide benefit when started 3 to 4 days after onset. But by and large, the earlier the better, even within the first 12 hours is better than 24 and 48.

Next. So this is just to remind you of the initial recommendation, and then next. Antiviral treatment can also be considered for any previously healthy, symptomatic outpatient not at high risk, who has suspected or confirmed influenza. And that's on the basis of clinical judgment, if treatment can be initiated within 48 hours of illness onset. Next.

This is a little table of the four FDA-approved antivirals that are recommended for use this season in the United States. Three are neuraminidase inhibitors. There's oral oseltamivir, inhaled zanamivir, and intravenous peramivir. And the fourth is a cap-dependent endonuclease inhibitor. It's oral baloxavir.

And so this table really summarizes the differences. Oseltamivir can be given to anyone of any age. Zanamivir, for treatment of children age 7 and up. Peramivir, age 2 and up. And Baloxavir, 12 years and up.

And the treatment course for oseltamivir and zanamivir is one dose taken twice daily for 5 days. For peramivir and baloxavir, a course is just one dose. And then two of these drugs are approved and recommended for chemoprophylaxis. That's oseltamivir for ages 3 months and up, and zanamivir, 5 years and up. The most common adverse events are listed.

Oseltamivir can cause GI symptoms. The most common are nausea and vomiting. This can be lessened if it can be taken with food. And it tends to be just about 5% over placebo in studies that have compared this. So it's a relatively small increase in nausea and vomiting.

Zanamivir can cause bronchospasm, and is not recommended for anyone with underlying airway disease. And peramivir has been shown in clinical trials to cause more diarrhea than placebo. Baloxavir has not actually had adverse events reported more commonly than placebo in the clinical trials. Next. So this just lists the neuraminidase inhibitors.

A reminder that it's actually FDA-approved for treatment of acute, uncomplicated influenza. And then I wanted to give you a little more information about baloxavir. It interferes with viral RNA transcription, and it blocks viral replication. It was first approved in December of 2018, again for treatment of acute, uncomplicated flu. And then in October of 2019, FDA added an indication for treatment of acute, uncomplicated flu specifically in people at high risk for influenza-related complications.

This was based on a trial in which early initiation of antiviral treatment in high-risk adolescents and adults showed that baloxavir was superior to placebo, and had a similar efficacy to oseltamivir, with the outcome being time to alleviation of symptoms. There currently are no available data for baloxavir treatment of flu in pregnant women, highly immunocompromised people, those with severe or progressive disease, or in hospitalized patients. Next. So my last slides, I'm going to review the principles of treatment in some specific groups. First in hospitalized patients, treatment with oral or enterically administered oseltamivir is recommended as soon as possible.

And just to emphasize, there really are insufficient data for use of inhaled zanamivir, IV peramivir, or oral baloxavir in patients with severe influenza disease requiring hospitalization. For patients who can't tolerate or absorb the oral or enteric-administered oseltamivir, the use of IV peramivir should be considered. And the optimal dosing and duration of treatment are actually kind of uncertain for severe flu. It's often given longer than the typical treatment course. Next.

So for treatment of pregnant women, or women who are up to 2 weeks postpartum, oral oseltamivir is the preferred and recommended agent, because it has the most studies available to suggest that it is safe and beneficial. And baloxavir, I just wanted to mention again, isn't recommended for treatment of pregnant women, or breastfeeding mothers, because right now, we don't have available efficacy or safety data in pregnant women, or anything about-- no data on the presence of it in human milk, or the effects on breastfed infants, or on milk production. Next. The last treatment slide just has a couple important additional considerations. I mentioned that invasive bacterial infections can occur.

And bacterial co-infection should really be investigated and empirically treated in patients with suspected or confirmed flu who initially present with severe disease, such as extensive pneumonia, respiratory failure, hypotension and fever, in addition to antiviral treatment. Bacterial infections should also be investigated, and empirically treated in patients who deteriorate after initial improvement. And it should be considered in patients who fail to improve after starting antiviral treatment. And lastly, I just wanted to mention corticosteroids. They really are not recommended as an adjunctive therapy for

suspected or confirmed flu-associated pneumonia, respiratory failure, or ARDS, unless they're indicated for some other reason.

Next. So this is the slide that has some additional resources. As Alicia mentioned, the FluView and FluView Interactive links are there, as well as a number of our pages for professionals, including antiviral recommendations, vaccination recommendations. And I would be remiss if I didn't mention this adorable baby who is a friend of our flu division, and wore her Fight Flu t-shirt to receive her 6-month influenza vaccine. So with that, that's the last slide I had today, and thank you all for attention, and we're happy to take questions.

Thank you so much, Miss Budd and Dr. Campbell for providing our audience with this important update on seasonal influenza. We appreciate your time and value your insights. We will now begin our Q and A session. Audience, please remember you may submit questions to the webinar system by clicking Q and A button at the bottom of your screen, and then typing your questions.

Again, please do not ask a question asking the Chat button. Our first question is regarding influenza activity. When can we expect to see flu activity decline? Dr. Campbell, or Miss Budd, if you're speaking, you might be muted. Please unmute your phone.

I think Alicia was trying to speak, but I couldn't hear it either. This is Dr. Campbell. I think it's really difficult for us to predict that. We know from last season, we had one of the longest seasons we had had in years.

And with this season being rather unusual, it's hard to say how long this current circulating H1N1-- I don't want to call it a peak, but it does seem that the H1N1 virus is on the rise. And so I think it's very hard to predict when we'll see it decline.

Thank you. We have a couple of questions regarding complications. And I'll try to compile them into sort of one question with two parts.

The first part is, you mentioned data related to cases and deaths. Do you also have data on increasing number of complications this flu season as well? And then Part 2 is, out of the complications that you listed, what are the most serious complications for young children?

This is Angie. I'm not sure if Alicia's microphone is working, so I'll take a stab at the data question as well. I was going to say that while we do get data eventually on complications of influenza, this comes from our surveillance systems, and so we tend to know numbers of people hospitalized with influenza fairly quickly. But then, we do get a lot of epidemiologic and clinical information on those people that takes a little longer. And so once we have that, we gain information on heart, lung, kidney, other organ complications, but we don't have that right now.

The same is true for the pediatric mortality. Once the data are all in, that can be reviewed, but at this point it's too early. And the second part was--.

I'm happy to repeat it.

Thanks.

The second part was what are the most serious complications that can occur in young children? You had mentioned complications in 2-year-old children, or younger.

Right. I think that we do see sepsis in children. We also see the encephalitis and encephalopathy manifestations associated with flu tend to be more common in children. Unfortunately, I think there have even been media reports to that effect this season. In particular, I'm thinking of this one child that was reported to have at least maybe temporary, but have enough damage to her brain that she's currently blind.

And that was on the news, so I'm not really saying anything private. But you know, children do tend to have some severe neurologic manifestations of flu. I would say there's not-- children can have any of the complications listed if the infection is severe enough, and really if the subsequent immune response and cytokine storm is severe enough, any of the manifestations I listed can actually occur in children or adults.

Thank you.

We also have multiple questions related to oseltamivir. I'd like to compile them as well into sort of a theme. One of the themes seems to be a concern about development of resistance.

The first inquirer asks if there is a concern that there could be resistance developed in the future if Tamiflu is used readily in not-at-risk persons.

And the second question related to resistance asks that is there concern with resistance developing now that Sanofi is pursuing over-the-counter status for oseltamivir?

Sure. So this is Angie Campbell. You know, I think it's important to think about resistance for oseltamivir differently than we think of it for antibiotics for bacterial infection. So when someone takes an antibiotic, all of us have bacterial flora in our bodies all the time, that live in our respiratory tract, in our GI tract, and when you take various antibiotics for whatever need, those bacteria that currently live within you can change to become resistant to that antibiotic. And so it's possible when you become sick again, you could be sick with that resistant bacteria in your urinary tract, and you have a urinary tract infection with a resistant organism.

But that's actually a different phenomenon than what happens with viral infections. Because influenza is really only present in your body when you're sick with it. And so, when someone is being treated for influenza, and receiving oseltamivir, it's true that resistance can develop. When we typically see that, is in a patient who's immunosuppressed and sheds virus for a long period of time. But there have been other reports where resistance can occur early in the course of treatment.

But the point is that you have to be currently infected with influenza for resistance to occur. So someone who takes it, whether or not they're at high risk for complications, or a previously healthy person, someone who takes oseltamivir for their influenza, it treats that infection, and then the flu eventually goes away. Likewise, if someone is given oseltamivir, and they don't currently have an influenza virus infection, there's no mechanism by which when they do acquire the flu, it would become resistant from having taken that oseltamivir. So I think it's a very different process. One thing we worry about sometimes is that if chemoprophylaxis is given, in which a dose is taken only once daily, instead of treatment dose, which is twice daily.

If chemoprophylaxis, for example, is given to someone who is already coughing and having symptoms of flu, that's sort of an undertreatment. And that is a situation where resistance is more likely to occur. Which is actually-- I didn't talk about chemoprophylaxis, but it's part of the reason that it's not something we generally recommend. But when treatment doses are given, it's not something that is the same as development of resistance with bacteria. I guess the other thing I should mention is, there are countries such as Japan where oseltamivir is used much more widely than here, and there have not been increased levels of resistance, sort of on a widespread scale.

Thank you for that. And I appreciate you also putting in some information about chemoprophylaxis, because we did have a couple of questions on that. We have time for one more question.

And my question to you is, now that we are as far along as we are, is there a need to recommend vaccinations to our patients, even if they may have already had influenza this season?

So this is Angie Campbell. I think so. I say that because, kind of dovetailing at the beginning of the Q and A session, we really don't know how long the influenza season is going to go on. But we expect it still maybe several more weeks, especially given the data that you saw where the virologic surveillance is actually increasing again. So every Friday you want to check FluView and watch and see what that's doing, because that's when it's released.

Around noon on Friday. But I think if someone has had influenza, it's very likely-- I guess if you're a betting person, odds are that they had Influenza B early in the season, and right now we're actually seeing more Influenza A/H1N1pdm09. So there could still be real benefit from vaccination.

Thank you for that explanation. And that concludes our Q and A session. If we were unable to ask your question, please submit it via email to coca@cdc.gov and we will provide you a response from our presenters. On behalf of COCA, I would once again like to thank our audience for joining us today.

And I'd especially like to thank our presenters. The recording of this call will be posted within the next few days to the COCA website, and available on demand in a few days at emergency.cdc.gov/COCA. Again that web address is emergency.cdc.gov/COCA. All continuing education for COCA calls are issued online through TCEO, the CDC Training and Continuing Education Online system. The web address is tceols.cdc.gov. Again, that's tceols.cdc.gov.

Those who participated in today's COCA call, and wish to receive continuing education should complete the online evaluation by March 2, 2020, with the course code WC2922. The access code is COCA012820. Those who will participate in the on-demand activity, and wish to receive continuing education should complete the online evaluation between March 2, 2020, and March 3, 2022, and use course code WD2922. The access code is COCA012820.

Please join us later this week for two upcoming COCA calls. The first COCA call will be held this Thursday, January 30th at 2 P. M. Eastern, and the topic will be HHS Guide for Clinicians on the Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesics. The second COCA call will be held this Friday, January 31st at 2 P. M. and the topic will be the Outbreak of 2019 Novel Coronavirus-- Interim Guidance for Clinicians.

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the COCA mailing list" link. To stay connected to the latest news from COCA, be sure to like and follow us on Facebook at facebook.com/cdcclinicianoutreachandcommunicationactivity.

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