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Time needed to complete: 60 minutes

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Increasing the Uptake of Flu Vaccines Across the Age and Risk Spectrum

Announcer Open:

Welcome to CME on ReachMD. This activity titled: Increasing the Uptake of Flu Vaccines Across the Age and Risk Spectrum is provided by Partners for Advancing Clinical Education, PACE, and is supported by an educational grant from Sequirus USA Incorporated. Prior to the beginning of the activity, please be sure to read the faculty and commercial support disclosure statements, as well as the learning objectives.

Ms. Knudtson:

Alright, welcome back, everyone. I am pleased to introduce our next speaker, Dr. Martin Mahoney. He is a Professor in the Department of Epidemiology and Environmental Health at the University of Buffalo in Buffalo, New York. Today Dr. Mahoney will be speaking about flu vaccines. So we're going to go ahead and get started.

Here are his disclosures.

And here are our learning objectives. We're going to implement the ACIP recommendation for influenza vaccine, updated for the 2022-2023 flu season, we're going to individualize immunization schedules and choices according to specific age and risk groups. And then lastly, we're going to use strategies and resources to address barriers to vaccines.

Alright, let's just go and get started. Dr. Mahoney?

Dr. Mahoney:

Thank you, Mary. Alright, so to start out, we'll just review a little bit of the epidemiology of seasonal influenza vaccine. And really, if we look back over the last several influenza seasons 2010-2011 through 2019-2020, we can see that the impact of each of those influenza seasons has been variable, but significant nonetheless; anywhere from you know, 9 million to 45 million illness episodes, 14 to 21 million outpatient medical visits, 140,000 to 810,000 hospitalizations, and anywhere from 12,000 to 61,000 deaths.

But like any other infectious disease, right, it's extremes of age who are going to be most impacted. Most typically, children less than 2 years of age, and adults over age 65, as well as anyone with medical comorbidities, which place them at increased risk for medical complications.

Speaking of complications, it's important to understand that just because somebody is infected with influenza, doesn't mean they're immune to other conditions. In fact, we see a lot of coinfections, so coinfections with other bacterial or viral pathogens, examples of that would be a bacterial sinusitis, a secondary bacterial otitis media, again, possibly pneumonia, either viral or bacterial in origin. And then the other thing that often occurs is that we see an exacerbation of an underlying medical condition, whether we're talking about diabetes, COPD, asthma, etcetera.

There have been a number of reports over the last several years documenting an increased risk of myocardial infarction within a week of influenza, and that risk is markedly increased. You can see there that figure of 6- to 10-fold increased risk within a week of influenza. And that risk extends as well to an increased risk of stroke, 3- to 8-fold risk or several weeks following a single influenza episode.

The other way to kind of think about that risk is to view it from a preventive potential. And there, there was a meta-analysis done a few years ago, which documented that the preventive potential of vaccinating a patient against seasonal influenza vaccine was comparable

to getting a patient to stop smoking or to be adherent to an entire year of statin therapy or blood pressure control. And I think when you put that into perspective like that, you know, to me, it's like why wouldn't you protect patients at high risk of a medical complication with something, with a therapy as simple as a seasonal influenza vaccine.

This next graphic, kind of busy, but what it's representing is the number of influenza-like illness episodes. So this is a barometer for the activity of influenza in a particular season. And you can see here, a number of seasons, in fact, the last 9 or 10 influenza seasons, and that red line is 21-22 influenza season. You can see that influenza season typically peaks sometime between December and February. That's the shaded area. Most of the time though, that peak is going to occur in January or February, or even later, and that works out to about 2/3 of the time, 65% of the time.

The other interesting thing to note from this particular graphic is the fact that, you know, that 21-22 season, that last influenza season was very different in terms of - the line was low, right? The threshold for background influenza-like illness is that dotted line, about 2.6% of visits for influenza-like illnesses. And you can see aside from a peak in late December, early January, that line kind of fell below the threshold. And that really reflected was a number of policies, right, masking, social distancing, and similar kinds of structural changes, if you will, reflecting, you know, what we did to manage the COVID pandemic.

Alright, this cartoon here represents a influenza virion. And the important antigens on the outside would include hemagglutinin, and they look like the blue lollipops, and neuraminidase, abbreviated there as NA, is the white lollipops. There are actually 3 families of influenza viruses that infect humans, A, B, and C. We're all familiar, I think, with influenza A and influenza B. These are typical components of the, depending on what's circulating, the seasonal influenza vaccine, there is a family of influenza B viruses. We don't hear anything about them because we don't really track them. Because influenza C is thought really to result in subclinical cases of infection. So there's no disease burden, there's no significant illness or hospital burden, so we tend to skip over influenza C.

And then when we're talking about influenza A subtypes, remember that's based on the combination of the hemagglutinin and neuraminidase glycoproteins. There's about 18 different identified hemagglutinin glycoproteins, 11 neuraminidase glycoproteins, and they combine, right, you get an H designation and an N designation, and that kind of – that's classifying the circulating strains and those change, as we know, from year to year.

Ms. Knudtson:

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Alright, we're going to go ahead and do a case study. We have Sam, he's a 68-year-old Asian male. Sam visits your primary care practice in November for an annual checkup. He's 5 foot 7, 260 pounds, which gives him a BMI of 40. He does have type 2 diabetes. He had a knee replacement 1 month ago. He's unvaccinated against influenza. He says that he's taken the vaccine in the past, but he worries about side effects. He mentions that his wife has never believed in vaccines, even though she has asthma. And despite your counseling that both he and his wife are at high risk for influenza complication, Sam declines the vaccine. He also declines the COVID-19 vaccination. So Dr. Mahoney, back to you.

Dr. Mahoney:

Alright. So a typical patient by the way. You know, I see patients like Sam all the time, as I'm sure you do. But I think it's important to recognize patients like Sam carry with them a number of important risk factors for complications of an influenza illness episode.

On the left, we see demographic factors, patients over age 65, younger children, right, especially under 2 and especially under 6 months who are not eligible for influenza vaccination, pregnant women, including 2 weeks postpartum. You know, social inequities, health disparities, again, are reflected in influenza illness burden. So you see all of these different patient populations demonstrating increased risk. Well, we'll see that on a slide upcoming as well, as well as residents of nursing homes and other long-term care facilities.

Over on the right are a whole host of chronic medical conditions which increase risk of influenza complications. And just like we saw with COVID-19, morbid obesity is an important risk factor. And the callouts here, the boxed ones are the ones that really would apply to Sam or his wife, the age and those medical comorbidities including morbid obesity.

So the action item is remember to recommend influenza vaccine to all patients over 6 months of age.

Ms. Knudtson:

Back to you, Dr. Mahoney.

Dr. Mahoney:

Alright. So this next slide looks at rates of influenza vaccination, so completion of seasonal influenza vaccine by selected high risk of medical comorbidities, and this is adults 18 to 64 years of age. While the data are several years old, I can assure you that they have not changed for a more recent time period. Really, you know, we just reviewed some of the medical comorbidities that increase the risk of influenza complications. And, you know, despite those risk factors, patients, regardless of whether they have asthma, COPD, heart

disease, cancer, diabetes, they all hover at 50% or less. And if you look at a whole variety of medical comorbidities, right, these are the biggest ones, but if you include a broader mix of medical comorbidities, overall vaccination rates 37%. So, again, you know, even in these high-risk groups, not much better than the background influenza coverage rates.

We mentioned a couple of slides ago, social and social disparities, health inequities, and then that carries across to influenza vaccine completion rates. Two recent influenza seasons 2019-2020 on the left, 2020-2021 influenza season on the right, the blue bars are completion rates for black non-Hispanic, orange, Hispanic populations, the gray American Indian and Alaska Native populations, Asians are in green, and non-Hispanic whites are in yellow. And you can see that the highest rates of influenza completion tend to be in Asian and non-Hispanic white populations, with the lowest rates generally in Hispanic and non-Hispanic black populations. So unfortunately, longstanding disparities, which, you know, did not improve as a result of the COVID pandemic.

We can examine health disparities, again through the lens of age-adjusted flu-related hospitalization rates. So over on the left, you see the highest rates of hospitalization rates related to influenza illness episodes occurring among non-Hispanic blacks, the lowest rates in non-Hispanic white and Asian/Pacific Islander population. And, you know, I think this reflects the number of factors, but primarily, this is driven by, what, completion of seasonal influenza vaccines as well as, you know, other social and medical comorbidities.

Ms. Knudtson:

Alright, let's go back to our case. Sam returns to the office after attending a New Year's Eve party and he's feeling sick 2 days later. His symptoms include fever 101.8, chills, body aches, and intense headache, extreme fatigue, and a cough. He missed work yesterday, he's unable to perform any household chores. His wife was with him at the party, but she has no symptoms. Influenza is highly prevalent in the community, but the rate of COVID-19 is low where he is.

Alright, back to you, Dr. Mahoney.

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Dr. Mahoney:

Alright. And the rationale for that is, you know, you presume that that patient has influenza, so, you know, you're going to give them an antiviral medication and also strongly encourage completion of seasonal influenza vaccine. Because again, there are 4 different strains in the seasonal influenza vaccine, and that would protect against a second illness episode from 1 of the 3 other strains, that, you know, that's why that recommendation is to treat and vaccinate.

So speaking of influenza antiviral medications, I think everyone is familiar with oseltamivir and zanamivir. Those products have been around for several years. More recently, there has been an expansion to some other antiviral medications to treat influenza episodes, including peramivir administered IV, and baloxavir which is an oral medication.

And again, just as a reminder, it has been many, many years since the CDC has recommended the use of amantadine or rimantadine as a influenza antiviral medication. The reason behind that non-recommendation are very high rates of resistance, so it is not going to help your patient to prescribe amantadine or rimantadine. Please use one of the 4 influenza antiviral medications you see at the top of the screen.

So this slide describes the current composition of the seasonal influenza vaccine for 2022-2023. Each year, the World Health Organization gets together in February to make some recommendations about what is circulating, based on what is circulating in the southern hemisphere for public health authorities in the northern hemisphere, to make some decisions about what that composition will be. The change from 21-22 was to change the H1N1 component, as well as one of the influenza B components. Remember when we saw that cartoon of the influenza virion, the A types are based on an H and an N designation, most flu seasons there's an H1N1 component and an H3N2 component. There is some slight variation. If you read across here, the H1N1 component is slightly different in the egg-based and live attenuated formulations, compared to the cell culture and recombinant versions. The other change for this current influenza season was to change one of the B components.

And the other important point to share with you is since 2021-2022, everything, all the seasonal influenza vaccines have been quadrivalent, meaning contained 4 antigens, 2 against influenza A and 2 against influenza B. And the reason for that was by adding another B, right, before that there 2 A and 1 B, there's only 2 lineages for the B. And although you would think it would be easy to predict the circulating strain if you look back over time, they were wrong about 50% of the time. So to eliminate that error and to reduce disease burden, provide broaden coverage, everything went quadrivalent in 21-22. And there's that basically the Yamagata lineage and the Victoria lineage and that covers all the B strains.

Alright. A busy slide here, but cover some important information, including what products are indicated for what age groups. If we just started out in the top row and look at inactivated influenza vaccines, again, everything is quadrivalent. When we speak about standard dose unadjuvanted or cell culture base, you can see a number of products listed there by brand. Those 2 classes of seasonal influenza vaccines have the broadest indication ranging from 6 months of age to 65 plus. If we continue down, looking at the next row, adjuvanted

inactivated influenza vaccines are indicated for patients ages 65 plus. High-dose products, the same age indication, 65 plus. Recombinant influenza vaccines are indicated for use in patients 18 of age - 18 years of age and above. And the live attenuated influenza vaccine, again all of these products are quadrivalent, is indicated for use in patients ages 2 through age 49. And then the blue block and the cell culture - I'm sorry the recombinant and cell culture-based products are identified as not having any egg components, no egg proteins, albumin. That's important as an option for patients who may be a egg allergic.

So the action item is be familiar with the age indications for the available influenza vaccine products.

Mary?

Ms. Knudtson:

So back to you, Dr. Mahoney.

Dr. Mahoney:

Alright. Thank you. Alright, some other important points to keep in mind if your patient is less than 9 years old. So between the ages of 6 months through 8 years, you need to ask the question whether that particular patient has received 2 or more doses of a seasonal influenza vaccine, either the trivalent for the 2019-2020 product or earlier, a season earlier, or the quadrivalent influenza prior to July 1st of 2022. It doesn't - the 2 doses don't have to have been received during the same or consecutive seasons, it just needs to be a total of 2 or more doses previously. If the answer is yes, you go ahead and administer a single dose of the 22-23 seasonal influenza vaccine and that patient is considered vaccinated. If the answer is no or you don't know, that patient needs 2 doses of the 22-23 influenza vaccine administered 4 or more weeks apart. The reason for that is simply if you think of years of potential exposure to the components of the influenza vaccine, so developing kind of a broad exposure, if you will, to the antigens in the vaccine. So that's just a question you need to ask if your patient population involves the younger children.

So the action item is remember that some children under 9 years of age will require 2 doses of influenza vaccines this season.

Alright. Very important new recommendation from the Advisory Committee on Immunization Practices as it relates to the current seasonal influenza vaccine. And that is what to do - what to recommend in patients 65 years of age and above. The ACIP came out in their updated MMWR recommendation for the 22-23 influenza season, stating that patients ages 65 and older over should preferentially receive one of the following: high-dose or adjuvanted influenza vaccine. So the high-dose inactivated influenza vaccine, high dose because it contains an increased level of antigen, right, standard dose vaccine is 15 micrograms of antigen per type or per strain, high dose contains 60 milligrams, as does the recombinant influenza vaccine is also a higher dose vaccine, instead of 15 micrograms, excuse me, per strain it is 45, so 3 times as much antigen. And then the adjuvanted inactivated influenza vaccine, the adjuvant is included as a strategy to kind of stimulate an immune response though so as we age, our immune systems weakened the 2 ways, 3 ways really, to overcome that weakening immune system are multiple doses, higher antigen, or use of an adjuvanted. And here we see the strategy higher dose along with adjuvanted products to overcome that the sleepy or weakened immune system as we age.

The CDC and ACIP take a pragmatic approach, however, and recognize that if none of these products are available when you're making a recommendation for a patient to receive seasonal influenza vaccine, and as an alternative any other age-appropriate influenza vaccine can be used.

So the action item, if available, give patients over age 65 years of age either a higher dose or adjuvanted seasonal influenza vaccine.

Ms. Knudtson:

So let's go back to Dr. Mahoney.

Dr. Mahoney:

Alright. So the next slide talks about influenza vaccine contraindications and precautions. And whether we're talking about the eggbased quadrivalent formulation, cell culture, or recombinant seasonal influenza vaccine, a real contraindication is a history of a severe allergic reaction to any of the - any component of the vaccine or any other influenza vaccine. And by severe allergic reaction here we're talking about anaphylaxis.

The other precautions really are, you know, a history of Guillain-Barre syndrome within 6 weeks of influenza vaccine, moderate or severe illness with or without a fever, that involves more of a conversation with the patients using good clinical judgment, balancing risks and benefits to the patient.

If we continue on to the other vaccine type, live attenuated influenza vaccine, here's the list of contraindications. It is a bit broader. It's going to, again, include a prior history of anaphylaxis to any component of this particular product or any other influenza vaccine. It's a

live vaccine, contraindicated for use in pregnancy, as well as in immunocompromised patients. Use good clinical judgment if you're going to administer this patient - or this product to a patient who lives in a household with someone who is severely immunocompromised. Concomitant use of aspirin or salicylates in children and adolescents is another contraindication, as is a history of asthma or wheezing in children 2 to 4 years of age. And cochlear implants, CSF, cerebral spinal fluid leaks, would be another contraindication.

And depending on whether the patient has received an influenza antiviral medication, it's important to be aware of the washout period. So I will call your attention back to agents like baloxavir with a half-life of 79 hours, or peramivir which has a half-life of about 20 hours. So you need to be very careful to allow sufficient time to elapse if a patient has received one of those particular antiviral products and you're thinking about administering the live attenuated influenza vaccine.

What about the timing of flu vaccination? It seems to me that I know that summer is ending when I go by the local drugstores at the end of August and see the signs flu vaccine available now. And, you know, there's not the - I know some patients tend to rush out and get vaccination, their seasonal influenza vaccine in August or September, and there's a lot of vaccination that occurs in October. But as reflected in this slide, is, you know, if you look at the last influenza season, cumulative dose distribution, 23% got distributed in August, that percentage increased to 58% August and September, 86% August, September, and October, but by November, Thanksgiving, about 95% of the influenza vaccine that was administered last year was provided, meaning that during December, January, February, and March of last year, we didn't do a whole lot of vaccinating. And you know, there are continued opportunities with patients who come into the office in late November throughout December, January, and February. Remember, seasonal influenza most typically peaks in January, February, or March. So plenty of opportunities to continue to promote seasonal influenza vaccination beyond Thanksgiving.

We talked earlier about pregnant women, including in the third trimester, those individuals should receive influenza vaccine as soon as it is available. The reason for that is it reduces risk of complications to them. So maternal-related comorbidities as well as it helps to form a protective cocoon around the infant. So there would be some transmission of maternal antibodies into the infant. But if the mom is protected, the mom is going to be spending a lot of time with the infant, she would help to kind of create that protective cocoon until the infant can be vaccinated upon reaching 6 years of age – 6 months of age, excuse me.

So the takeaway there, continue to administer influenza vaccine throughout the influenza season.

Ms. Knudtson:

So Dr. Mahoney, back to you.

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Dr. Mahoney:

Alright. So the AARP recently surveyed a population of folks here in the U.S. age 45 and above, looking at attitudes and beliefs about out vaccines, including influenza vaccine. And you can see here a summary of some of the more common responses to the question, why do you rarely or never get a flu shot? And aside from the fact that people responded that they just didn't want one, the other leading responses included the fact that they were concerned about possible side effects and they don't believe in them or didn't think they're safe. And really, you know, influenza vaccines have been around for decades, so the efficacy and safety is has been demonstrated, you know, continuously and probably characterized in a way that is far in excess of any other vaccine product.

Ms. Knudtson:

Alight back to our case study. So given the high prevalence of influenza in the community and Sam's negative swab test for COVID-19, you prescribe an influenza, antiviral. Within 3 days, his symptoms subside and he's able to return to work. You recommend that he received a higher dose or adjuvanted vaccine to avoid further infection during the remainder of the flu season. And he refuses, saying he's worried about the side effects. So Dr. Mahoney, back to you.

Dr. Mahoney:

So really, Sam is demonstrating what we refer to as vaccine hesitancy. So, you know, I think again, COVID-19, you know, if you try to find some silver linings, it really opens up the conversation about vaccine hesitancy. It is complex and context specific. And, you know, every patient kind of comes at it from a slightly different perspective. The question is, you know, what do you do about it? You know, the Centers for Disease Control has developed a share model, SHARE, share the reasons when a flu vaccine is right for your patients. So kind of individualizing it, highlighting positive experiences with flu vaccines, addressing patient questions and concerns, reminding patients that flu vaccines do have demonstrated efficacy in terms of protecting them and loved ones from illness and complications, and explaining the potential costs of getting a flu.

You know, the CDC has this SHARE method. Some other academic health centers have developed other models, but the bottom line, the most important factor is your clear, concise recommendation for patients to get the flu vaccine. Patients trust you. You are their clinicians. And as a result, patients are more likely to get the vaccine if you, their clinician, recommends it to them.

We also often get a lot of questions about where can I go for a valid and unbiased evidence-based information about influenza? Two websites that I will recommend the CDC branches off to an area addressing seasonal influenza vaccines. The second resource I would recommend for you as clinicians is immunized.org. Standing orders, a bunch of questions and answers that are all vetted by vaccine experts.

Ms. Knudtson:

Alright, back to our case. Sam agrees to be immunized with an adjuvanted flu vaccine. He experiences an injection site pain for a few days, but he otherwise has no adverse reactions. He didn't have any flu-like symptoms for the rest of the flu season. When his wife presented for care, you successfully employed the SHARE method to persuade her to be immunized as well.

So Dr. Mahoney, will you review our action plan?

Dr. Mahoney:

I sure will. Recommend influenza vaccine to all patients 6 months of age and older. Be familiar with the age indications for the specific influenza vaccine products. Remember that some children under age 9 will require 2 doses of influenza vaccine this season, if available. Patients over age 65 should be offered a high dose for adjuvanted vaccine, and continue to do administer influenza vaccine throughout the influenza season.

Ms. Knudtson:

Alright, so let's go ahead and do some questions. The first one is from Mitzi. How long do you have to wait to get a flu shot after an injectable steroid?

Dr. Mahoney:

Interesting question. I think it would depend on the dose, right? We're really concerned about impact of a long-term steroid use with interfering with response to an influenza vaccine. So I would think that in acute injection, whether it was, you know, into a joint, or perhaps for some other reason, I would go ahead and administer the vaccine when you're making the recommendation. In my opinion, you would not have to wait because that would be an acute treatment episode, not chronic long-term use of steroids.

Ms. Knudtson:

Alright. The next one is from Fran. I know high-dose is only for those over 65. Why aren't they used for immunocompromised patients as well?

Dr. Mahoney:

I think that's a great question. You know, and, you know, the label is 65 plus based on the clinical trial data. Those were the populations studied. I don't know whether there are plans to study younger, so-called middle-aged adult populations. But, you know, taking that thought a little bit further, you would have the option to use the recombinant influenza vaccine in a younger adult, immunocompromised population, right. That's also a higher dose product, it's got 3 times the antigens in there and it's labeled for use in adults ages 18 and above. So, you do have options to, you know, utilize what your new knowledge or existing knowledge, as it were, about the antigen content in vaccines to again better try to meet the medical needs of your particular patients.

Ms. Knudtson:

Okay, the next question is from Ludi, the flu and COVID vaccine should be separated by 4 weeks, is that correct?

Dr. Mahoney:

No Ludi, that recommendation has changed. Remember with the availability of COVID vaccines, initially we were very cautious and recommended that, you know, that this 4-week interval be observed. But once we developed additional experience and understood, you know, yes, COVID-19 is reactogenic in terms of, you know, side effects, the current recommendation from the CDC is to go ahead and administer those vaccines to that patient which are recommended at that visit. So, if that patient is due for COVID-19 booster and a seasonal influenza vaccine, the recommendation would be to go ahead and give it at the same time. But I would add that, you know, administer them in different anatomic locations, left deltoid, right deltoid, you're going to record what goes where, so if there is an adverse reaction, a side effect that needs to be explored or even reported, you can attribute that side effect to one of those particular vaccines.

Ms. Knudtson:

Okay, the next question is from Olga. Can you please clarify why children have to have 2 doses of the flu vaccine?

Dr. Mahoney:

Yeah. So Olga, again, just to kind of review, think of it as, you know, acquiring or developing a robust immune response; the more times you see that antigen, the stronger and broader that antibody response is going to be. So that's really the rationale. If a child under 9, so

between age 6 months through 8 years of age, you want to query immunization information system, a vaccine registry, electronic health records, or whatever the source is to identify at least 2 prior doses of seasonal influenza vaccine. If you can identify 2 prior doses, that patient needs just the single dose for the current influenza season. If not, they need 2 doses. And those doses would be administered 4 or more weeks apart.

Ms. Knudtson:

Okay, this next one is from Gabrielle. How long do you have to wait to get a flu shot after you've been diagnosed with the flu?

Dr. Mahoney:

Yeah, so that's a very relevant question. I would say wait until the acute illness episode has passed. For most individuals, that's, what, 3 days, 5 days maybe a week, and then they would be eligible. And I hope the reason for that question, Gabrielle, was that you're thinking, hey, the flu vaccine is quadrivalent, and in several the past influenza season, a predominant strain has actually slipped late in the season. So again, the rationale would be all those someone had an influenza episode with the quadrivalent product, you have the ability to protect against 2 A strains and 2 B strains.

Ms. Knudtson:

Okay, and this question is from Gay. Now, would your recommendation on how long should wait to administer the vaccine change is if they've actually been treated with medication for influenza?

Dr. Mahoney:

Yes, absolutely right, because antiviral medications are going to interfere. I'm sorry, repeat the question, Mary was at the live vaccine or a inactivated?

Ms. Knudtson:

She didn't clarify about which vaccine, but just if somebody has been treated for influenza, how long would you wait to administer a vaccine?

Dr. Mahoney:

So remember the case where the patient came in with influenza-like symptoms and the decision, the recommendation for optimal management is to administer a influenza antiviral and to give, in the case of the 65-year-old patient, either a higher dose or an adjuvanted influenza vaccine. So you're managing the current episode, but providing the patient with the ability to be protected throughout the influenza season.

The only caveat where antiviral, influenza antivirals would come into play is with use of the live attenuated influenza vaccine, where if you have had administered either peramivir or baloxavir, those half-lives are pretty substantial, especially in the case of baloxavir of 79 hours. So you would have to go out to, what, 4 or 5 half-lives in terms of delaying administration for the live attenuated influenza vaccine.

Ms. Knudtson:

Alright, and then we have a couple questions. Same sort of a question. We have one from Gabrielle and one from Barbara. When do you think we will have a combination flu/COVID-19 vaccine? Is that in our future?

Dr. Mahoney:

Yes, it is. That's a great question. Very soon. You know, I think people with the mRNA platform, I think the ability to combine various antigens into the same vaccine are not far off in the future. So great question.

Ms. Knudtson:

Alright. And then this one is from Kim. Does immunity wane by February or March if they've gotten their vaccine in the fall, especially in the elderly?

Dr. Mahoney:

Oh, I love that question. Yes, the CDC doesn't like to talk about it, but if you read their MMWR statement each influenza season, they will acknowledge that immunity decreases. A typical influenza vaccine for a typical patient, in quotes, is thought to protect for somewhere between 5 and 6 months. From a quantitative standpoint, how much does immunity decline? It declines somewhere between 7 and 10% a month, which means if you were one of those folks who when CVS or Walgreens put up their sign in August, went out and got vaccinated, well, September, October, November, December, January, you know, come January or February, you might be out of protection in terms of, you know, falling antibody levels. And that again, really speaks to, it is a, you know, it's a marathon, not a sprint in terms of getting patients vaccinated. Excuse me.

And probably when you think about waning immunity and the need for protection to last through the end of March and sometimes longer,

I think it makes a lot of sense to really delay seasonal influenza vaccine until late October or early November. There isn't a lot of influenza circulating currently. There will be after people start to socialize for Thanksgiving and other upcoming holidays. But you know, the downside of delaying is, will the patient come back in? So it's always kind of balancing risks and benefits and, you know, the likelihood of that patient coming back to get a vaccine at a later date, versus the ability to provide them with protection.

Ms. Knudtson:

Alright, this will be our last question. Is there any point in getting a flu shot in August and a second one in February?

Dr. Mahoney:

Yeah, so the current recommendation is for a single dose of vaccine. That's really based on a number of pragmatic considerations. It's hard enough to get enough people protected with a single seasonal influenza vaccine. And number 2, it takes a lot of effort to produce a batch of seasonal influenza vaccines. You know, the manufacturers are, I don't know what their current capacity is, I would say in the U.S., it's probably approaching 300 million doses. They have an obligation to produce influenza vaccine outside the U.S. So right, it's globally. And this is something that's occurring in the fall and winter for the northern hemisphere. And, you know, the alternative 6 months or 7 months in the southern hemisphere, I don't – I wonder whether there's capacity to produce that much vaccine. And then again, from a pragmatic standpoint, you know, are people going to be willing to get 2 doses of a vaccine? It's hard enough to get 1.

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