**PB14**

**Welcome to today's session of *Epidemiology and Prevention of Vaccine-Preventable Diseases* webinar series for 2019. I'm Commander Tina Objio, a nurse educator in the Immunization Services Division of CDC's National Center for Immunization and Respiratory Diseases. I'll be the moderator for today's session. Here are our learning objectives. At the conclusion of this session, the participant will be able to describe the different forms of immunity; describe the different types of vaccines; for each vaccine-preventable disease, identify those for whom routine immunization is recommended; for each vaccine-preventable disease, describe characteristics of the vaccine used to prevent the disease; describe an emerging immunization issue; locate resources relevant to current immunization practice; and implement disease detection and prevention health care services, such as smoking cessation, weight reduction, diabetes screening, blood pressure screening, and immunization services, to prevent health problems and maintain health. Today's webinar will cover pneumococcal. Our presenter is Dr. Raymond Strikas, a medical officer in the Immunization Services Division of the National Center for Immunization and Respiratory Diseases.**

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**If you have a question during this presentation, please type your question into the Q and A pod on your screen. I will collect these questions during the presentation and we will address them during the question and answer period that follows the presentation. I will now turn today's session over to Dr. Strikas for his presentation.**

Thank you very much, Commander Objio. I'll discuss pneumococcal disease and the vaccines to prevent this disease during today's session. This material is from the Pink Book, chapter 17, and also includes updates from CDC web pages and more recent ACIP recommendations. So let's talk about pneumococcal disease.

Pneumococcal disease is caused by *Streptococcus pneumoniae* bacteria, which are lancet-shaped, gram-positive, facultative, anaerobic organisms. They are typically observed in pairs. They may also occur singularly or in short chains. There are 92 known serotypes. Some pneumococci are encapsulated. Their surface is composed of complex polysaccharides. The polysaccharide capsule is an important virulence factor, which means that encapsulated organisms can be deadly for humans and experimental animals, whereas organisms without capsular polysaccharides are not. Capsular polysaccharides are the primary basis for the pathogenicity of the organism. They are antigenic and also form the basis for classifying pneumococci by serotypes. Type-specific antibody of the capsular polysaccharide is protective. These antibodies and complement interact to opsonize pneumococci—that is, absorb them and destroy them, which facilitates phagocytosis and clearance of the organism of the same serotype. Antibodies to some pneumococcal capsular polysaccharides may cross-react with related serotypes, as well as with other bacteria, providing protection against these organisms. Most *Streptococcus pneumoniae* serotypes have been shown to cause serious disease, but only a few serotypes produce the majority of pneumococcal infections. The 10 most common serotypes are estimated to account for about 62% of invasive disease worldwide. The ranking and serotype prevalence differ by patient age group and geographic area. In the United States, prior to widespread use of the 7-valent pneumococcal conjugate vaccine introduced in the year 2000, the seven most common serotypes isolated from blood or cerebrospinal fluid or CSF of children younger than 6 years of age accounted for 80% of such infections. These seven serotypes account for only about 50% of isolates from older children and adults.

Pneumococcal disease is the second most common cause of vaccine-preventable disease in the US, causing thousands of cases of invasive disease, such as bacteremia or meningitis, every year. Pneumococcal pneumonia is the most common clinical presentation of pneumococcal disease among adults, although pneumonia alone is not considered to be invasive disease. The incubation period of pneumococcal pneumonia is short—about 1–3 days. Symptoms generally include an abrupt onset of fever and chills or rigors. Typically, there is a single rigor and repeated shaking chills are uncommon. Other common symptoms include pleuritic chest pain, cough productive of mucopurulent rusty sputum, dyspnea or shortness of breath, tachypnea or rapid breathing, hypoxia or poor oxygenation, tachycardia or rapid heart rate, malaise, and weakness. Nausea, vomiting, and headaches occur less frequently. CDC estimates as many as 400,000 hospitalizations occur from nonbacteremic pneumococcal pneumonia annually in the United States. The case fatality rate is 5% to 7%. Other clinical syndromes include the two most common forms of invasive disease, bacteremia and meningitis. Bacteremia is bloodstream infection and meningitis is infection of the meninges or the lining covering the brain. The clinical symptoms, cerebrospinal or CSF fluid profile and neurologic complications of pneumococcal meningitis, are similar to other forms of purulent bacterial meningitis. Symptoms may include headache, lethargy, vomiting, irritability, fever, nuchal or neck rigidity, cranial nerve signs, seizures, and coma.

This graph of invasive pneumococcal disease shows the rate of invasive disease per 100,000 population by age group and demonstrates that the highest rates of invasive disease occur in those younger than 2 years of age and those 65 years of age or older. These data are generated by CDC's Active Bacterial Core Surveillance System, or ABCS, and highlight age as an important risk factor for invasive disease.

This figure shows changes in the incidence of invasive pneumococcal disease, or IPD, among children less than 5 years old from 1998 to 2016 in the United States. Rates of IPD expressed as cases per 100,000 population are shown on the Y axis and calendar year surveillance on the X axis. Blue bars represent overall IPD incidence, while the gray bars represent IPD incidence caused by serotypes included in the 13-valent pneumococcal conjugate vaccine, commonly abbreviated PCV13. Pneumococcal 7-valent conjugate vaccine, or PCV7, contains serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F was introduced for use among children less than 5 years old in the year 2000. PCV13, which contained the additional serotypes 1, 3, 6A, 7F, and 19A, was introduced for use among children less than 5 years old in the year 2010. The overall IPD incidence declined from 95 cases per 100,000 in 1998 to 9 cases per 100,000 in 2016, and this reduction is mostly due to drops in IPD caused by PCV13 serotypes declining from 88 cases per 100,000 in 1998 to 2 cases per 100,000 in 2016.

This figure shows changes in the incidence of invasive pneumococcal disease among adults 19–64 years of age for the same period as before, 1998 to 2016, also in the United States. Rates again are expressed as cases per 100,000 population on the Y axis and calendar year on the X axis. Blue bars represent overall IPD incidence. Orange bars represent IPD incidence caused by serotypes included in the 23-valent pneumococcal polysaccharide vaccine, commonly abbreviated PPSV23, while the gray bars represent IPD incidence caused by serotypes included in the 13-valent pneumococcal conjugate vaccine, PCV13. The overall IPD incidence declined from 16 cases per 100,000 in 1998 by half to 8 cases in 2016. IPD caused by PCV13 serotypes declined from 11 cases per 100,000 in 1998 to 2 cases per 100,000 in 2016. IPD caused by PPSV23 serotypes also declined from 14 cases per 100,000 in 1998 to 6 cases per 100,000. Most of these reductions were due to declines in IPD caused by the serotypes commonly found in PCV13.

This last figure shows changes in incidence of invasive pneumococcal disease for adults 65 years and older for the same time period, 1998 through 2016. The same denotations are of 100,000 population on the Y axis and calendar year surveillance on the X axis. Blue bars again represent overall IPD incidence, orange bars IPD incidence caused by serotypes in the 23-valent vaccine. All the gray bars represent IPD incidence from serotypes in the 13-valent PCV13 vaccine. The overall IPD incidence declined from 59 cases per 100,000 by more than half to 24 cases per 100,000. IPD caused by PCV13 serotypes declined from 44 cases per 100,000 to 6 cases per 100,000 in 2016 and IPD caused by PPSV23 serotypes also declined from 51 cases per 100,000 to 15 per 100,000 in 2016 but, yet again, these reductions were, as in younger adults, due to declines in IPD caused by serotypes in common with PCV13.

There are also medical risk factors besides age risk factors for invasive pneumococcal disease. These include functional or anatomic asplenia, and functional asplenia includes sickle cell disease because children with sickle cell disease slowly destroy their own spleen, making patients vulnerable to encapsulated organisms like pneumococcus. Other sickle hemoglobinopathies, including hemoglobin SC disease or S-beta thalassemia, are also indications for vaccination because they can also affect the spleen. Altered immunocompetence is a risk factor for invasive pneumococcal disease and also other underlying medical conditions like chronic renal disease, nephrotic syndrome, and conditions that predispose to cerebrospinal fluid or CSF leak. Other underlying medical conditions are risk factors for invasive disease, but the risk is lower. These include chronic heart disease, chronic lung disease, diabetes, alcoholism, chronic liver disease, and solid organ transplant. Also, patients with cochlear implants have an increased risk of pneumococcal meningitis and, both for these patients and those with CSF leak, this is because of continuous spread of pneumococcal bacteria through the source of the implant or the CSF leak.

The reservoir for pneumococcal disease is human—human carriers. Pneumococci are common inhabitants of the respiratory tract and may be isolate from the nasopharynx at between 5% and as many as 90% of healthy adults, depending on their age and situation. Rates of asymptomatic carriage vary by age, environment, and presence of upper respiratory infections. Only 5% to 10% of adults without children are carriers. On military installations, as many as 50–60% of service personnel may be carriers. The duration of carriage varies and is generally longer in children than adults. The relationship of carriage to the development of natural immunity is poorly understood. Transmission of *Streptococcus pneumoniae* occurs as the result of direct person-to-person contact via respiratory droplets and by autoinoculation in persons carrying the bacteria in their upper respiratory tract. Pneumococcal infections are more common during the winter and in early spring, when respiratory diseases are generally more prevalent. The period of communicability for pneumococcal disease is unknown. Presumably, transmission can occur as long as the organism appears in respiratory secretions.

This graph shows the incidence of invasive pneumococcal disease or IPD in adults ages 18–64 years who are healthy in the bar on the far lefthand side compared to those with selected underlying conditions progressing from left to right. Cases of IPD per 100,000 persons are shown on the vertical axis. The conditions are listed as you see on the horizontal axis. The two columns on the far right of the graph demonstrate that individuals with hematological cancer and HIV/AIDS have a more than twentyfold increased rate of IPD compared to persons without these conditions. Adults with other conditions on the graph in the center part have a three to sevenfold increased risk for IPD compared to persons without these conditions.

Let us now discuss pneumococcal vaccines in some more detail. These vaccines are composed of pneumococcal polysaccharide. The first vaccines licensed were pure polysaccharide vaccines and the first contained polysaccharide for 14 different types of pneumococcus and was licensed in 1977. In 1983, a 23-valent polysaccharide vaccine was licensed and replaced the 14-valent form. In 2000, the first pneumococcal conjugate vaccine, PCV7, was licensed, consisting of polysaccharides from seven types of pneumococcus conjugated to a protein. In 2010, as mentioned, an expanded 13-valent conjugate vaccine replaced the seven-serotype conjugate vaccine and is the conjugate vaccine we use now.

PPSV23 is a vaccine, as I said, with purified capsular polysaccharide antigen from 23 types of pneumococcus. It is licensed for adults 50 years of age and older, as well as for high-risk children 2 years and older. CDC recommends, as we will discuss, its use in younger high-risk adults as well. It has not been demonstrated that PPSV23 can provide protection against nonbacteremic pneumococcal pneumonia. For this reason, we recommend providers should avoid referring to PPSV23 as the “pneumonia vaccine.”

Regarding PCV13, as I noted, it contains 13 serotypes of *Streptococcus pneumoniae*. These are conjugated to a nontoxic diphtheria CRM197 carrier protein. Because this is a conjugate vaccine, it generates a long-lasting immune response that is useful in both children and adults. PCV13 was approved by FDA based on demonstration of immunologic noninferiority to PCV7 rather than clinical efficacy, and PCV13 is presently recommended for all children beginning at 6 months through 59 months of age and for older children at high risk, as well as for high-risk adults.

PCV7 was introduced into the routine schedule in 2000 and has been tremendously successful, as noted earlier, and I want to demonstrate again, in reducing the rate of invasive pneumococcal disease. These data between 1998 and 2009 show how PCV7 reduced rates of invasive disease, along with disease caused by serotype 6A, by 99%, seen in the lower line of the graph, and also reduced rates of invasive disease caused by all serotypes by 76%, seen on the upper line of the graph. In 2008, however, 61% of invasive pneumococcal disease cases among children younger than 5 were attributable to the serotypes in PCV13, but those types contained in PCV7 only accounted for 2% of the cases, the remainder being accounted by the additional six serotypes and serotype 19A, and this information supported the need with additional serotype protection, which was included in PCV13 when it was licensed in 2010.

In 2013, 20% to 25% of invasive pneumococcal disease cases among adults 65 years old and older were attributable to PCV13 serotypes. These serotypes accounted for about 10% of community-acquired pneumonia cases in adults as well, and this includes pneumonias with no bacteremia. You may wonder how it is possible to identify specific serotypes of *Streptococcus pneumoniae* in patients that have only pneumonia diagnosed with x-ray or clinically with no organism obtained from the blood. This is because the manufacturer of PCV13, the Pfizer company, determined type-specific nonbacteremic pneumonia cases using a urinary antigen test based on immunochromatographic membrane technique.

Having discussed burden of disease, I want to move on now to immunogenicity and effectiveness, beginning with PPSV23 vaccine. While 80% of healthy adults who receive PPSV23 vaccine develop antibodies against the serotypes contained in the vaccine, most estimates of effectiveness range between 60% and 70% against invasive disease among immunocompetent older persons and adults with underlying illnesses. Effectiveness among immunocompromised persons or very old persons has not been demonstrated. The confidence interval has become very wide in most studies looking at adults 40 years old and older, and some effectiveness estimates for invasive disease are as low as 10% in some populations and, as mentioned, the vaccine is not thought to be clearly preventive for noninvasive pneumococcal pneumonia.

Pneumococcal conjugate vaccine, PCV13, is highly immunogenic in infants and young children, including those with high-risk medical conditions. The efficacy of PCV7 was 97% for prevention of invasive disease caused by vaccine serotypes and, furthermore, children who received PCV7 had 7% fewer episodes of acute otitis media or ear infections and underwent 20% fewer tympanostomy tube placements than did unvaccinated children. PCV13 was licensed in the US in 2010, based upon studies that compared the serologic response of children who received PCV13 to those who received PCV7, and those studies demonstrated that PCV13 induced levels of antibodies comparable to those induced by PCV7 and shown to be protective against invasive disease. In other studies of PCV13, children 7–71 months of age who had not received pneumococcal conjugate vaccine doses previously were administered 1, 2, or 3 doses of PCV13, according to the age-appropriate immunization schedules that existed for PCV7. This type of study is called “bridging” to reduced dose complete series of PCV7. These schedules resulted in antibody responses to each of the 13 serotypes that were generally comparable to those achieved after the 3-dose infant PCV13 series in the US immunogenicity trial.

Looking at adults, a randomized placebo-controlled trial, the CAPITA trial, was conducted in the Netherlands among approximately 85,000 adults 65 years old and older between 2008 and 2013 to evaluate the clinical benefit of PCV13 in the prevention of pneumococcal pneumonia. PCV13 demonstrated 75% efficacy against vaccine-type invasive pneumococcal disease and 45% efficacy against PCV13 serotype nonbacteremic pneumonia.

Now let us look at clinical considerations of using these vaccines. I'll discuss recommendations for the use of these two vaccines. The PCV13 recommendations, as well as those for PPSV23 for infants and children, were published in the *MMWR* on December 10, 2010, and I'll begin with PCV13 vaccine.

PCV13 is presently routinely recommended for children 2 months through 59 months of age. The vaccine should be administered as a 4-dose series at 2 months, 4 months, 6 months, and 12–15 months of age. Fewer doses are needed to complete the series if the series is started at 7 months of age or older. The number of doses depends on the child's current age and the age at which the first dose was given. Children who have received 1 or more doses of PCV7 can have those doses count, but they should complete the immunization series with PCV13.

Here is the routine catch-up schedule for unvaccinated older children—that is, older than 7 months. It's derived from table 8 in the 2010 pneumococcal recommendations for infants and toddlers, so these are children who begin the series with PCV13, but they begin the series late. If the age at first dose is between 7 and 11 months of age, a primary series of 2 doses should be administered, with 4 weeks in between those doses, followed by a booster dose after 12 months of age and at least 8 weeks after the second dose. If the PCV13 series is begun at 12–23 months of age, then 2 doses are recommended, separated by 8 weeks. If the series is begun between 24 and 59 months of age and the child is considered healthy, then only 1 dose of vaccine is necessary. However, if the child has an underlying medical condition—and I'll talk about those more shortly—and begins the series between 24 and 71 months of age, then 2 doses are recommended, with 8 weeks between the doses. These underlying medical conditions include chronic heart disease, chronic lung disease, diabetes, CSF leak, cochlear implant, sickle cell disease, other hemoglobinopathies, functional or anatomic asplenia, HIV infection, and other immunocompromising conditions, so this is the table that should be used, along with table 9 of the 2010 recommendations document, to determine whether high-risk children 24–71 months of age have a complete schedule or an incomplete schedule.

A note on the complexity of recommendations for PCV13. PCV13 is approved by the Food and Drug Administration or FDA for children 6 weeks through 17 years of age and for adults 50 years of age and older and, since August 2016, FDA has added approval for all adults 18 years of age or older. ACIP's recommendations and CDC's guidance recommended this for broader use earlier in all populations at high risk or by age, such as the children just discussed. Beyond the routine infant and toddler recommendation, which we'll discuss more later, ACIP recommended use for PCV13 for immunocompromised persons 6 years of age and older in 2012 and 2013. ACIP recommended use of PCV13 for all adults 65 years and older in 2014 and that recommendation was altered in 2019, and I'll discuss that altered recommendation shortly.

A single dose of PCV13 should be administered for children 6 through 18 years of age who did not receive PCV13 previously and are at increased risk for invasive pneumococcal disease because of the high-risk conditions mentioned earlier, again anatomic or functional asplenia, sickle cell disease and hemoglobinopathies, immunocompromising conditions such as HIV infection, cochlear implant, or CSF leak. These recommendations are in force regardless of prior vaccination with PCV7 or PPSV23.

Pneumococcal conjugate vaccine should be administered only via intramuscular injection using a 5/8- to 1-1/2-inch needle, 22-–25 gauge, depending on the age and size of the patient. The preferred site is the vastus lateralis muscle in either the thigh in infants or in the deltoid muscle in the upper arm in older children and adults. Please always follow aseptic technique when preparing and administering vaccines. A new needle and syringe should, of course, be used for each injection. A single-dose vial is for one patient only. An adhesive bandage may be applied to the site if bleeding occurs and, as discussed, pneumococcal conjugate vaccine can be administered in the same clinical visit as other indicated vaccines, except one meningococcal conjugate vaccine, Menactra, in asplenic persons.

PCV13 was licensed, as I mentioned, among adults 50 years of age or older on December 30, 2011. FDA approved this use under the accelerated approval pathway and it was based on serologic studies that compared the response of PCV13 recipients to the response of PPSV23 recipients. ACIP recommended 1 dose of PCV13 for adults 19 years and older at increased risk of invasive pneumococcal disease, such as those with asplenia, HIV infection, cancer, and cochlear implants in 2012. In 2014, ACIP recommended 1 dose of PCV13 for all adults 65 years and older who had not previously received a dose. That recommendation was revised this year, 2019, to allow a vaccination but only after shared clinical decision-making between the patient and the health care provider.

Now pneumococcal polysaccharide vaccine, but not the conjugate vaccine, is recommended for persons 2 years old and older with normal immune systems who have chronic illness like heart disease, pulmonary disease, including asthma, in adults, diabetes, liver disease, alcoholism, cigarette smokers 19 years of age or older, and patients with CSF leak or cochlear implants. The polysaccharide vaccine is also recommended for persons 2 years old and older who are immunocompromised, either due to disease or immunosuppressive drugs. Immunocompromising conditions include the ones I've mentioned before—functional or anatomic asplenia, chronic renal failure, nephrotic syndrome, Hodgkin disease, or other hematologic malignancies such as lymphoma and leukemia, multiple myeloma, organ transplant, and HIV infection, or any other condition or treatment that is considered immunocompromising. When both PCV13 and PPSV23 are indicated, ACIP and CDC recommend you administer PCV13 first for a better immune response. PCV13 and PPSV23 should not be administered at the same visit.

Pneumococcal polysaccharide vaccine or PPSV23 is routinely recommended for adults 65 years and older at least 1 year after receiving PCV13 if they received it and at least 5 years after the most recent PPSV23 dose. It is also recommended for adults 19–64 years at increased risk as I defined just on the last slide. When both PCV13 and PPSV23 are indicated, administer PCV13 first. Again, PCV13 and PPSV23 should not be administered at the same visit.

Routine revaccination of PPSV23 vaccine is not recommended for patients with the high-risk conditions grouped under immunocompetent conditions, nor with CSF leak and cochlear implants. However, revaccination is recommended for persons 2–64 years of age who are at highest risk of serious pneumococcal infections, and these include with a 5-year interval, as listed at the top of the slide between the 2 doses, and these patients, again, are those with functional anatomic asplenia, including sickle disease and other hemoglobinopathies, immunosuppression, including HIV infection, transplant, chronic renal failure, nephrotic syndrome, generalized malignancy, and hematologic malignancy. Once someone turns 65 years of age, a dose of PPSV23 is recommended, regardless of previous doses of PPSV23, but only 1 dose is recommended at 65 or older. Therefore, the maximum number of recommended doses of PPSV23 anyone should receive is 3 in a lifetime.

So what do you think? We've got a 6-year-old patient who’s got sickle cell disease. Her immunization history includes a complete PCV13 series and PPSV23 at 4 years of age. Should PPSV23 be administered today? And the answer is no, the next dose should be 5 years after the previous PPSV23 dose.

Now, pneumococcal polysaccharide vaccine or PPSV23 can be administered either by intramuscular (IM) or subcutaneous injection. You should choose a needle size based on the route and patient age and/or patient size. If you're using an intramuscular site, again, the vastus lateralis in children through about 3 years of age—the deltoid muscle may be used if the muscle mass is adequate—and for those 4 years of age or older, in general, the deltoid muscle is preferred, but you may use the vastus lateralis muscle if necessary. The subcutaneous site, if you choose that route of vaccination, is over the upper outer triceps of the arm.

So adults 19 years of age or older with one of these risk factors should receive a dose of PCV13. Note that both PCV13 and PPSV23 are recommended. A dose of PCV13 should be administered first, followed by the PPSV23 at least 8 weeks later. Adults with one of these immunocompromising conditions and functional or anatomic asplenia will then be recommended for a second dose of PPSV23 5 years or more later. PCV13 and PPSV23 adult vaccination recommendations are divided between the two age groups I've already mentioned. These are persons 19–64 years of age and those 65 years of age or older. Immunization recommendations for those 19–64 years of age are based on risks, including those at high risk. This means those with chronic medical conditions, but who are not immunocompromised or at more than moderate risk of pneumococcal infection. There are those at higher risk, and this specifically means those with cochlear implants and cerebrospinal fluid leaks, and at highest risk, which includes those persons mentioned earlier who are immunocompromised for one or more reasons. Those at high risk include persons with chronic pulmonary disease, including asthma, cardiac disease, excluding hypertension, liver disease, including cirrhosis, diabetes, alcoholism, smokers, and residents of a long-term care facility. These persons are recommended to receive just 1 dose of PPSV23 before 65 years of age. A higher-risk person—those with cochlear implants or cerebrospinal fluid leaks—should receive a dose of PCV13 first,followed by PPSV23 in 8 weeks. No revaccination is presently recommended for these persons until they reach 65 years of age. If these persons have already received PPSV23 as adults, they should receive PCV13 at least 1 year after the PPSV23 dose. Adults 19–64 years of age with immunosuppression, including HIV infection, generalized or hematologic malignancy, organ transplant, functional or anatomic asplenia, including sickle disease or other hemoglobinopathies, chronic renal failure, and nephrotic syndrome are deemed to be highest risk for invasive pneumococcal disease and should receive PCV13 once, followed by PPSV23 in 8 weeks, and these folks are recommended to be revaccinated with PPSV23 5 years after the first PPSV23 dose before age 65, and they would get a final dose once they reach 65 years of age or later.

Now there are new PCV13 recommendations, as many of you may be aware, for persons 65 years of age or older, adopted by the ACIP at its meeting in June of 2019, and the rationale is briefly as follows. PCV13-type disease has been reduced to historically low levels among adults 65 years old through pediatric PCV13 use, as I demonstrated on the last graph of the three graphs showing vaccine impact earlier in the presentation. The 2014 PCV13 recommendation for all adults 65 years of age seems to have had minimal impact, based on CDC's analyses on PCV13-type disease. However, we do know PCV13 is a safe and effective vaccine, so balancing this evidence, ACIP recommended that PCV13 can be administered to adults 65 and older based on shared clinical decision-making between the provider and the adult, and this is for adults who do not have immunocompromising conditions, a CSF leak, or cochlear implant. ACIP still recommends all adults 65 years or older should routinely receive 1 dose of PPSV23.

So let's go through some scenarios then for older adults. Again, as of June 2019, ACIP recommends receipt of PCV13 be decided by shared clinical decision-making for adults 65 years or older who do not have an immunocompromising condition and who have not previously received PCV13. All adults 65 or older should receive a dose of PPSV23. Persons 65 and older who have not received PCV13 may receive 1 dose following shared clinical decision-making, and then a PPSV23 dose can follow in 8 weeks if they've not received a dose of PPSV23 at 65 years or older and they have an increased risk for IPD as described earlier. If the patient has already received a dose of PPSV23 at 65 or older, 1 dose of PCV13 may be given 1 year after the PPSV23 dose. Giving the dose sooner than 1 year may impair the response to PSV13. If the patient has received PPSV23 before 65 years, PCV13 may be given at 65 or older, again after shared clinical decision-making between patient and provider, so long as at least 1 year has passed since the PPSV23 dose. A final dose of PPSV23 should follow in 8 weeks if they have an increased risk and if they don't have increased risk for invasive disease, a 1-year interval between PCV13 and PPSV23 is indicated.

Frequent vaccine administration errors of pneumococcal vaccines are what you might expect. The wrong vaccine, the wrong population—that is, PPSV23 vaccine to an infant— that is, a child less than 2 years of age, or a schedule error where more than 1 PPSV23 revaccination dose is administered to immunocompetent at-risk persons, where we recommend no more than 1 dose and, in most cases, only 1 dose at 65 or older.

Known adverse reactions do occur with these vaccines. Local reactions occur with 30–50% of doses of PPSV23, the rate of fever and myalgia of less than 1%, and severe adverse reactions are rare. For PCV13 local reactions, these are similar to those of PPSV23, but the rate of fever is higher, with febrile seizures, while rare, occurring in only 1–14 out of 100,000 doses and have a slightly higher rate when other vaccines are administered concomitantly with PCV13, particularly influenza vaccine. If both vaccines are administered simultaneously, the rate of febrile seizures can rise to between 4–45 out of 100,000 doses. Severe adverse local reactions occur in 8% of vaccinees and this grading of severe includes tenderness that affects limb movement.

The last topic I'll address are contraindications and precautions for pneumococcal vaccines and, thankfully, these are straightforward. The only contraindication to both of these vaccines is a severe allergic reaction to a vaccine component or following a prior dose of vaccine, and the only precaution is moderate to severe acute illness at the proposed time of vaccination. Please wait until the patient is over the illness and then you may vaccinate.

A reminder about storage and handling. Pneumococcal vaccine should be stored in the refrigerator at between 36 and 46 degrees Fahrenheit, which is between 2 degrees and 8 degrees Celsius. We frequently hear about vaccine administration errors related to the wrong formulation being administered, such as PPSV23 being administered when PCV13 was indicated and vice versa. Strategies which may help prevent these errors include storing the vaccine formulations separately in the original packaging because when both formulations are mixed together in the same bin or area, it is too easy for staff to grab and administer the wrong formulation.

Now that I've discussed vaccine recommendations for PCV13 and PPSV23, I'd like to briefly discuss how to use the vaccines together. These recommendations are based on CDC guidance—not the FDA license. If PCV13 is indicated or decided upon for an older adult based on shared clinical decision-making, note that PCV13 and PPSV23 should not be administered during the same clinic visit. Either vaccine may be administered simultaneously with influenza vaccine and most other routinely recommended vaccines but, again, do not give these two pneumococcal vaccines together and, ideally, administer PCV13 before PPSV23. In children, this means finishing the series of PCV13, then waiting 8 weeks and administering PPSV23, either 1 or 2 doses, depending on the risk condition.

So a last question before we wrap up the talk. We've got a 70-year-old patient who is immunosuppressed. Her immunization history includes PCV13 and PPSV23, which were administered on the same day when she was 65 years of age. Should she receive PPSV23 today? The answer is no, we do not recommend repeating either vaccine in adults, even though both were given together, and this is primarily to avoid severe local reactions.

Comment about resources on pneumococcal vaccines. This is a link for our resource page, which is going to be updated in the near future, so please bookmark it but, at present, it needs updating and I'll leave it to you for future reference. Thank you for your attention. Commander Objio.

**Thank you very much, Dr. Strikas, for an excellent presentation. On the screen, you can now see continuing education information, including the access code for today's webinar. The access code is Pneumo with a capital “P.”
The access code applies to the live program only. Things to remember about access codes. Please write the access code down now. The access code cannot be given out at any time other than during this presentation—not by email request or any other means. The access code is case-sensitive. There is no access code for the enduring archived program. Let me repeat the access code. It is Pneumo with a capital “P” and, as a reminder, the resources pod on your screen contains the CE instructions for download. Now let's take our remaining time to review some of the questions we've received during the program.**

**Here's the first question. Have the 2019 ACIP recommendations been published in the *MMWR* yet? If not, when will it happen?**

Thank you for the question. The *MMWR* has not yet been published, so ACIP has made its recommendations that I discussed about shared clinical decision-making. The *MMWR*—we anticipate it to be published in the near future but, I'm sorry, I cannot give you a date when it will appear.

**Okay, thank you. The next question: is there a risk if a patient receives 1 dose of a pneumococcal vaccine too close to another?**

Yeah, the risks are at least twofold. The risk is if you gave—say you had a patient who received PPSV23 as an adult at 65 or older and is now beyond that and you want to give PCV13—if you wait less than a year to give the PCV13, you may have a suboptimal immune response and they won't be as well-protected as you would like if you choose to offer PCV13 to that patient. The other possibility is some chance, though it's not well identified, of increased local reactions—one vaccine close to the other—because you are engendering immune response to similar antigens across the two vaccines but, otherwise, if you gave PPSV23 in a shorter window than 8 weeks after PCV13, we generally don't recommend repeating the dose. The only risk there, again, is possibly modified immune response or a local reaction, but we don't recommend repeating the dose in either case.

**Okay, thank you. Here's another question we received. All of this data about invasive pneumococcal disease—I believe this applies to the data slides we were going through—only applies to bacteremia and meningitis, correct?**

So invasive pneumococcal disease, as some of you may recall from training, does include other syndromes. The two most common are bacteremia and meningitis but, less commonly, you can see a pleural infection in the sterile space between the chest wall and the lung, so one could have a pleural abscess. That counts as sterile space or invasive infection, and even less common would be infection in a joint where there's been bacteremia in a joint infection that may manifest as a joint abscess but, generally, the most common, as you point out, are bacteremia and meningitis.

**Excellent. Let's go ahead and take another one. Can an adult receive PCV13 while taking antibiotics?**

An adult or a child, for that matter, could receive any vaccine while taking antibiotics. My concern is not the antibiotics. There is not documentation of interference, but is the person still having a moderate to severe acute illness from which they are recovering? If they're well past the illness, recovering from the illness and feel well and are up and around and doing things and just finishing a course of antibiotics, then vaccination with PCV13 or PPSV23 is perfectly appropriate. If they have any lingering remnants of illness, to avoid having an adverse event following vaccination conflate or confuse the course of the acute illness from which they are recovering, I might hold off until they've recovered from the illness, but antibiotics alone are not a reason to avoid vaccination.

**Okay, thank you. Should the 6-year-old in the first example that we covered receive PPSV23 at 5-year intervals? If so, the child would get more than 3 doses in a lifetime.**

Thank you for the question and for allowing me to clarify it. CDC does not recommend that PPSV23 be offered more than twice in anyone prior to the age of 65 years. There were parties that recommended PPSV23 every 5 years or every 10 years in years past. CDC has never recommended that frequency, so our present recommendation is—in this case, we'll go back to the 6-year-old sickle cell child who got a dose of PPSV23 at 4 years of age after completing PCV13. That child should get another dose of the polysaccharide vaccine 5 years after the dose given at 4 years of age, so at about 9 years of age, and no more doses at present are recommended to be given until she reaches 65 years. One wonders will she maintain pneumococcal immunity for that long a period of time and that's really unknown, but there is concern that if you give too many doses of PPSV23—significant local reactions have been documented when a number of doses have been given close together—so there's some more work to be done there to understand if that is the optimal number of doses. But to avoid adverse events, we've limited to 2 doses at least 5 years apart before age 65 and then 1 more dose at 65 or older.

**Okay, thank you. Here's another question. Is hepatitis C virus a risk factor or is it just cirrhosis for administering PPSV23 for individuals younger than 65 years old?**

Yeah, if the patient who has hepatitis C virus infection, hopefully under treatment, is stable, is not immunosuppressed, then that individual is not necessarily recommended to receive PPSV23 or PCV13 vaccine. It's a matter of judging the severity of the illness— whether they've got acute hepatitis going on or some other dysfunction—so it's a clinical judgment for you to make but, in general, one would not offer pneumococcal vaccine to that person if they're not immunocompromised and not seriously ill and we limit that for patients with liver cirrhosis.

**Excellent. Another question. If someone reports having received a dose of pneumococcal vaccine, but they don't have any documentation, can that count?**

Yes, it can count, but the present recommendation from ACIP is only counting pneumococcal polysaccharide vaccine—not the conjugate vaccine. We accept self-report for the polysaccharide and we want to avoid too many doses of the polysaccharide vaccine more often than every 5 years, so that's one of the reasons we accept self-report in the absence of a record to avoid too many doses. We realized in the last five years, we've used a lot of PCV13 in patients and they may be understandably confused or not have a record of which pneumococcal vaccine they received, so they may receive an extra dose of PCV13 or a missed dose of PPSV23. We think this is to discounting prior doses of pneumococcal vaccine or PCV13 and missing the dose for those for whom it's indicated. This is an issue that's being reviewed now because, again, we've got two pneumococcal vaccines and understanding how to use self-report in the best fashion is important.

**Thank you and here's a timely question since we're coming upon flu season. The package insert suggests that the antibody response is lower for some serotypes of *Streptococcal pneumoniae* and some subtypes of influenza when the two vaccines are administered simultaneously, so what should we do if both are recommended?**

We still recommend—CDC and ACIP—that you should administer for those for whom it's indicated pneumococcal vaccine—PCV13 in this case—and influenza vaccine and the antibody response to all serotypes of PCV13 was not lower in persons 65 or older and in some populations younger than 65, though there were some reduced antibody levels in three of the 13 serotypes. If the person needs both vaccines, we recommend they receive them because it's not clear that the lower immune response for those three serotypes compromises their ability to respond to illness. Antibody levels were also looked at for three influenza subtypes among patients 50 years old and older and only among persons 65 and older were there reduced antibody types and only to the type influenza AH3N2. There are some limitations to these studies and we'd rather err on the side of administering vaccines indicated for persons—in this case, both influenza vaccine and pneumococcal vaccine—and not miss an opportunity for protection rather than withholding a vaccine and perhaps limiting their ability to be protected against influenza and/or pneumococcal infection.

**Thank you and we're going to take just this one last question and then we'll close it out and repeat that CE information for you. Here's the last question. What if a child is catching up on PCV13 doses as a toddler, is high risk and recommended for 2 doses after 24 months of age and then receives PPSV23 in error for the second dose of PCV13? Do you give a dose of PCV13 in this circumstance?**

Yeah, so this is a substitution error or administration error—not really a spacing error. We would recommend you give PCV13 and the current recommendation is to space the dose out by 8 weeks from that inadvertent PPSV23 dose. However, if for some reason, the PCV13 dose was given before 8 weeks had passed, we would not recommend repeating the PCV13 dose.

**Thank you. Let me go ahead and review the continuing education information. Please go to the web page shown on the screen to obtain credit. Search for today's live CE event course number, which is WC2645-091819. To repeat, WC2645-091819. The numbers after the dash are today's date and differentiate this presentation from others in the series. CE credit for the live course will expire on October 21, 2019. The access code for today's live session is Pneumo and remember the code is case-sensitive. If you are watching the archived version of this webinar, search for the course number, which is WD2645-091819. It is slightly different from the live webinar course number. CE for the enduring archived program lasts until June 1, 2020, and no access code is needed.**

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**Thank you very much for joining us today. Have a wonderful day.**