NetConference - CDC (US)

Moderator: Dale Babcock
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Coordinator: Welcome and thank you for standing by. At this time, all participants are in a listen-only mode until the question and answer session of today's call. At that time, if you would like to ask a question, you may do so by pressing star 1.

Today's conference is also being recorded. If you have any objections, you may disconnect at this time. I, now, would like to turn the meeting over to Dr. Raymond Strikas. You may begin.

Raymond Strikas: Well, thank you very much. Welcome to Current Issues in Immunization, a CDC NetConference. I'm Raymond Strikas, a medical officer in the Immunization Services Division of the National Center for Immunization and Respiratory Diseases or NCIRD at the CDC. And, I'll be the moderator for today's session.

To participate in today's program, you need a telephone connection and a separate Internet connection.

The learning objectives for this session are to describe an emerging immunization issue, to list the recent immunization recommendation made the Advisory Committee on Immunization Practices, be able to locate resources relevant to current immunization practice, and obtain, assess and apply patient information to determine the need for immunization.

Today is May, 20, 2015. We have two topics for today's NetConference. First, Susan Hariri, a senior research scientist from the National Center for HIV/AIDS, Viral Hepatitis, STD and Tuberculosis Prevention at CDC, will give an update on human papillomavirus vaccines and the current vaccine recommendations in the United States.

Then, Beth Hibbs, a nurse epidemiologist from CDC's Immunization Safety Office, will give an update on how that office tracks vaccine administration errors, what some of the common errors are, and how you can prevent them from recurring.

A question and answer session will follow. Please make a note of the following information. If you have technical trouble, please dial star 0 on your telephone, and if you'd like to ask a question when we get to the question and answer session, please press star 1 on the phone.

CE credit is available only through the CDC ATSDR Training and Continuing Education Online system at http://www.2a.cdc.gov/TCEOnline/. The CE credit for this session expires on June 22, 2015.

CDC, our planners, and our presenters wish to disclose they have no financial interest or other relationships with the manufacturers of commercial products, suppliers of commercial services or commercial supporters. Planners have reviewed the content of this program to ensure there is no bias.

Presentations will not include any discussions of the unlabeled use of a product or a product under investigational use, and CDC does not accept any commercial support. I will now turn the microphone over to Dr. Hariri. You may begin.

Susan Hariri: Thank you Dr. Strikas. I'm Susan Hariri, and today, I'll be giving an update on the HPV vaccination recommendations in the United States. I will briefly give an overview of HPV vaccines that are available in the U.S., each previously associated cancers due to the HPV types, and I'll review data from the 9-valent HPV vaccination trials, and review the updated recommendations of the ACIP.

Available prophylactic HPV vaccines are virus-like particle vaccines. These vaccines are made from the L1 major capsid protein of the virus, which is expressed through a recombinant technology, and these L1 proteins self-assemble VLP that are not infectious.

Until recently, there were two HPV vaccines available. The bivalent vaccine, which is also called Cervarix directed against HPV types 16 and 18, and the quadrivalent vaccine called GARDASIL, which is directed against 16 and 18 as well as HPV types 6 and 11.

HPV 16 and 18 are oncogenic types that cause cancer whereas HPV 6 and 11 cause genital warts. As I mentioned, both of these vaccines are similar in that they are VLP vaccines. In addition to differences between the - to the two vaccines due to the different types, the vaccines differ in their adjuvants.

The recently licensed 9-valent vaccine, which is also called GARDASIL 9, is directed against the same four types that are in the quadrivalent vaccine, 6, 11,

16 and 18, and five additional cancer causing types that are shown in red. The quadrivalent and the 9-valent vaccine are produced by the same manufacturer and they have the same adjuvants.

As I just mentioned, all HPV vaccines target oncogenic or high risk types, HPV 16 and 18, and these two types are responsible for the vast majority of cervical cancers and other HPV associated cancers.

So, this graph shows the percentage of cervical cancers that are attributed to high risk types world-wide, and you can see that HPV 16 and 18 accounted for 60% and 10%, respectively, of cervical cancers that were HPV positive.

And, the other high risk types each account for just a small percentage of cervical cancers. In addition to cervical cancer, HPV causes cancers at other anatomic sites. This slide shows data for the United States with the estimated number of cancer cases at anatomic sites where cancers have been attributed to HPV. Males are on the left and females are on the right.

The purple portion of the bar shows the cancer cases at these sites that are attributable to HPV. And as you can, most but not all of the cancers at these sites are attributable to HPV, and this varies somewhat by the type of cancer.

The most common HPV associated cancer for females is cervical cancer and the most common HPV associated cancer in males is cancer of the oropharynx.

These data were from a study conducted to examine HPV types in cervical and other HPV associated cancers in the U.S. In the first column are the cancers that are associated with HPV. The second column are the percent of the cancers at these sites in which HPV was detected.

And, the third column shows the percent that are attributable to HPV 16 and 18. Finally, the last column is the percent attributable to the five additional types in the 9-valent vaccine.

So, you can see that the majority of the cancers at all sites are attributable to HPV 16 and 18, and this ranges from 48% to 80%. The percent attributable to the five additional types in the 9-valent vaccine is much lower and it ranges from about 4% in oropharyngeal cancers in males to 18% of vaginal cancers.

This slide shows the estimated numbers of cancers at these anatomic sites that are attributed to HPV 16 and 18 and to the five additional types in the U.S., and these are data from 2006 to 2010. And, as I noted in the previous slide, the majority of all HPV related cancers are attributable to 16 and 18 types.

The blue bars here show the cancers attributable to the five additional types. The largest number of cases due to the five additional types are cervical cancers.

So, to summarize what I just reviewed, in the United States, approximately, 64% of invasive HPV associated cancers are attributable to HPV 16 and 18. HPV 16 and 18 account for 66% of cervical cancers, and for the other cancers, the percent ranges from 48% in penile cancers to 80% for anal cancers.

Ten percent of HPV associated cancers are attributable to the five additional types that are in the 9-valent vaccine. 15% of cervical cancers are attributed to these types. And, for the other cancers, the range is 4% to 18%.

So, due to the differences in HPV type attributable cancers at different sites, there are also differences by sex. The five additional types account for 14% of

HPV associated cancers in females and only 4% of HPV associated cancers in males.

For cervical cancer lesions - cervical pre-cancer lesions, sorry, or cervical intraepithelial neoplasia Grade II or worse, approximately 50% of those are caused by HPV 16 or 18, and another 25% by the five types in the 9-valent vaccine.

Now, I'm going to switch to talk about the 9-valent HPV vaccine clinical trials. The 9-valent vaccine was licensed by FDA in December of 2014. The trials conducted for licensure included a pivotal efficacy trial, immunogenicity and immunobridging studies, and concomitant use studies.

The 9-valent vaccine efficacy trial included about 14,000 women, ages 16 to 26 years, and they were randomized to receive either the 9-valent vaccine or the quadrivalent vaccine. There was no unvaccinated group for comparison in this study.

The objectives were to demonstrate efficacy for HPV 31, 33, 45, 52 and 58 related endpoints, and to demonstrate non-inferior immunogenicity for HPV type 6, 11, 16 and 18. Since both vaccines target the four types in the quadrivalent vaccine, it wasn't possible to evaluate efficacy against those types.

The 9-valent HPV vaccine efficacy trials showed very high efficacy against outcomes related to the five types in the pro-protocol population. So, efficacy against the combined endpoint of high-grade cervical, vulvar, and vaginal lesions due to the five additional types was about 97%.

And, other endpoints were also evaluated, and shown here is the efficacy against six month persistent infection, which was 96%. There were very few high-grade outcomes due to HPV 6, 11, 16 and 18. There was one in the 9-valent vaccine group and three in the quadrivalent group, since those vaccines protect against these types.

And so, because of this, efficacy was inferred from the immunogenicity trials. Antibody titers were evaluated for these types, and non-inferior immunogenicity was demonstrated for all four HPV 6, 11, 16 and 18. There was over 99% zero conversion of all types and the geometric mean titers were similar in the two groups.

This slide shows the results from the 9-valent vaccine adult adolescent immunobridging study. This is one of the studies that allowed licensure in the younger age group, and this study compared geometric mean titers in 9 to 15 year olds, shown here in green, and for females with those in 16 to 26 year olds, the age group that was in the efficacy trial, are shown in purple.

As you can see, not only was non-inferiority criterion met for all nine HPV vaccine types, but the GMTs were higher in the younger age group. This is a similar finding to what's been seen in the quadrivalent and the bivalent vaccine studies, previously, that the antibody response to vaccination is higher in the younger adolescents.

This slide summaries some of the data that I presented as well as data from other trials. So, the 9-valent HPV vaccine has about 97% protection against HPV types 31, 33, 45, 52 and 58 related outcomes. And, it has similar protection to the quadrivalent vaccines against HPV 6, 11, 16 and 18 related disease.

The 9-valent vaccine also showed non-inferior immunogenicity for HPV 6, 11, 16 and 18 compared with the quadrivalent vaccine in 16 to 26 and 9 to 15 year olds, and for all nine HPV vaccine types in adolescent females and males compared to adult females and adult males compared to adult females.

Concomitant use had no impact on immunogenicity or safety when 9-valent HPV was administered with meningococcal vaccine or Menactra or Tdap vaccine or Adacel.

As always, safety is evaluated and reviewed in the pre-licensure trials. Trials included over 15,000 9-valent HPV vaccinate, and 9-valent vaccine was generally well-tolerated and the safety profile was similar to the quadrivalent vaccine.

There were more injection site reactions with 9-valent vaccine, specifically swelling and erythema. And, erythema and swelling increased with the number of doses administered as was seen in the quadrivalent vaccine trials.

In the concomitant use studies, there was no difference in the safety profile when co-administered with the other vaccines. So, now, I will discuss the updated ACIP recommendations.

This slide shows the ACIP's previously published recommendations for the bivalent and the quadrivalent vaccine, and since 2011, recommendations have been for routine vaccination of boys and girls at age 11 or 12 years.

And, vaccinations also recommended through age 26 for females and through age 21 for males, who were not previously vaccinated. Vaccination is recommended for immunocompromised persons including HIV infected persons and for men who have sex with men through age 26.

They're administered as a three dose schedule, zero, one to two and six months, and the bivalent and the quadrivalent vaccine, either one is recommended for females and the quadrivalent vaccine for males.

So, before I review the updated recommendations, I want to mention the licensed age groups for the three available vaccines in the U.S. The bivalent vaccine is licensed for females ages 9 to 25 years, and the quadrivalent vaccine is licensed for females and males aged 9 to 26 years.

The 9-valent vaccine is licensed for females 9 to 26 years and for males 9 to 15 years. At the time of the first application to FDA, 9-valent vaccine trials in males 16 to 26 years hadn't been completed yet.

Immunogenicity data in the 16 to 26 year olds are now available and were reviewed by the ACIP last year, and these data have now been submitted to FDA.

When ACIP deliberated on the 9-valent HPV vaccine, they recommended use of the 9-valent vaccine in the currently recommended age groups, including for males. The recommendation for males older than age 15 would be an off-labeled recommendation.

So, these are the updated ACIP recommendations. The first three bullets are essentially the same, it's - HPV vaccination is still routinely recommended at age 11 or 12 years. Vaccination is recommended through age 26 in females and through age 21 in males, who were not previously vaccinated.

It's recommended for men who have sex with men and immunocompromised, including HIV infected persons, through age 26. And then, the last two bullets

are new. Vaccination of females is recommended with bivalent, quadrivalent as long as the formulation is available, or 9-valent vaccine.

And, vaccination of males is recommended with the quadrivalent as long as it's available or the 9-valent vaccine. The vaccinations used can be started as early as nine years of age.

The updated recommendations include some wording on the differences between the vaccines, including the following, the bivalent, quadrivalent, and 9-valent vaccines all protect against HPV 16 and 18, types that cause about 66% of cervical cancers and the majority of other HPV attributable cancers in the United States.

9-valent HPV vaccine targets five additional cancer causing types, which account for about 15% of cervical cancers. Quadrivalent vaccine and 9-valent vaccine also protect against HPV 6 and 11, the types that cause genital warts.

For administration, there are minor wording changes, but the recommendation is similar to what it was before, and that is, if vaccination providers do not know or do not have available the HPV vaccine product previously administered or are in settings, transitioning to 9-valent HPV vaccine.

For protection against HPV 16 and 18, any HPV vaccine product may be used to continue or complete the series for females. And, the quadrivalent or 9-valent may be used to continue or complete the series for males.

One question that's been raised is about 9-valent HPV vaccine for persons who completed an HPV vaccination series. And, I want to note that the manufacturer did not seek an indication for 9-valent vaccination for persons who previously completed an HPV vaccination series.

However, a study of the 9-valent vaccine in prior quadrivalent vaccinates was conducted mainly to evaluate safety. And, due to time limitations, this was not discussed at the last ACIP meeting and will be presented to ACIP at a subsequent meeting.

Okay. Sorry. Okay. I think I was on the last slide, but anyway, okay, so there are no changes in the recommendation regarding vaccination during pregnancy. HPV vaccine is not recommended for pregnant women. If a woman is found to be pregnant after initiating the series, the remainder of the doses should be delayed until after completion of pregnancy.

No intervention is needed and no pregnancy testing is needed before vaccination. A new pregnancy registry has been established for the 9-valent vaccine.

The vaccine of pregnancy registries have been closed for quadrivalent and the bivalent vaccine with concurrence from the FDA. Exposure during pregnancy of those vaccines can be reported to the respective manufacturers and to the Vaccine Adverse Event Reporting System or VAERS.

I think I just went over the slide on the issue about people who completed the vaccination series being vaccinated with the 9-valent vaccine. So, I am going to skip that and, to summarize, the 9-valent HPV vaccine was licensed by the FDA in December of 2014.

It has been available from the manufacturer since February of 2015 and it was recommended by ACIP in February of 2015. It is one of three HPV vaccines that can be used for routine vaccination of females and one of two for routine vaccination of males.

The 9-valent vaccine targets five additional high risk types. Overall, 14% of HPV associated cancers in females are due to these types and 4% in males are attributable to these types, and 15% of cervical cancers are attributable to the five types.

The 9-valent vaccine has received a Vaccines for Children contract, and so, really, now, what's really needed is efforts to increase vaccination coverage. And so, this graph shows the National Estimated Vaccination Coverage levels among adolescents aged 13 to 17 from the National Immunization Survey Team.

The red line is coverage with at least one dose of HPV vaccine in females and it increased initially, but then leveled off in recent years and has reached about 57% in 2013. The three dose coverage, you can see here, is in orange and it was 38% in 2013.

In blue, are the one and three dose male coverage estimates. The increase in coverage for males started after the vaccine was licensed in males in 2009, and then, increased further after the routine recommendation by ACIP in 2011.

In 2013, at least one dose and three dose coverage were 35% and 14%, respectively, in males. So, as you can see, further efforts are needed and they are ongoing to increase HPV vaccine coverage in the United States.

And, lastly, I just want to mention that there are a variety of resources that can be helpful for providers and for patients, and some of them are listed on this slide. And that's all I have, thank you.

Raymond Strikas: Thank you very much Dr. Hariri. Let me now turn the program over to Beth Hibbs.

Beth Hibbs: Thank you Dr. Strikas and good afternoon everyone. It is a pleasure and honor to have this opportunity to speak with you today about vaccination errors reported to the Vaccine Adverse Event Reporting System also known as VAERS.

This slide provides an overview of what I'll be covering in the presentation today. On the right, you will see a cartoon of a patient overhearing staff in a hospital. While vaccination errors are more likely to occur outside a hospital study, the feelings expressed about making an error are very similar.

Let's begin by discussing some background. In the year 2000, the Institute of Medicine published a report that focused attention on medical errors. In 2007, they followed with another report, specifically highlighting medication errors which stimulated a national discussion.

Previous studies describing vaccination errors to VAERS were reported in two articles covering VAERS data from 1990 to 2002. In those studies, less than 100 vaccination errors were identified.

This slide lists national organizations that accept reports of vaccination errors. The first one on the list, VAERS, will be covered in this presentation today. Other reporting systems include the Food and Drug Administration's MedWatch Surveillance System, which accepts reports about any medication or medical devices regulated by FDA.

The third and fourth organizations on this slide are non-governmental organizations and include the Institute for Safe Medication Practices, which

has collected and reported on different types of medication errors for several years.

Recently, in the past couple of years, they have partnered with the California Department of Health to develop a vaccination error reporting program. The last organization, MEDMARX, is national in scope, but is limited to hospitals that are part of their medication error program.

The picture on this slide depicts an engineering error that is obvious to anyone who looks at it. Vaccination errors are not as obvious and the reporting systems on this slide play an important role in helping us to see and understand them.

These are some definitions of terms I will using throughout this presentation. A vaccination error is any preventable event that may cause or lead to inappropriate use of patient harm. Such events may be related to professional practice, immunization products, storage, dispensing, and administration.

Vaccine adverse health events are health effects that occur after immunization, but may or may not casually be related to vaccination. So, what is the Vaccine Adverse Event Reporting System or VAERS? It was authorized by the National Childhood Vaccine Injury Act of 1986.

It is jointly administered by CDC and FDA, and is a national post-marketing passive reporting system for adverse events. It began receiving reports in 1990, and VAERS receives around 36,000 reports per year. The data from VAERS is available to the public at the link listed on this slide.

This slide lists some of the strengths and limitations of VAERS data. Strengths include that the data collected is national and VAERS accepts reports from anyone. Some of the other strengths we've already discussed.

There are also a number of limitations, including underreporting of adverse events, reporting biases, inconsistent data quality and completeness, and generally, VAERS cannot assess if a vaccine or a vaccination error caused an adverse health event.

And, VAERS's coding practices can affect the types and numbers of errors reported. Our research objective was to describe reports of vaccination errors to VAERS during 2000 through 2013, including the types and frequencies of errors and adverse health events reported.

This slide outlines the methods of our studies. We looked at all VAERS reports from 2000 to 2013. We identified vaccination error reports using codes that describe vaccination errors. Because we had almost 50 codes, we grouped these vaccination error codes into 11 error groups and characterized them.

I will show you the codes and the groups on the next slide. We looked at the top three error groups and performed a 5% random sample to help characterize the specific types of errors. We identified and clinically reviewed all contraindications of vaccination error reports.

The next analysis looked at errors and adverse health events. Errors where no health event occurred or the error was not serious, were summarized and based on the electronic data, and errors with a serious health event were all clinically reviewed and summarized.

The last analysis looked specifically at reports of errors that occurred to multiple individuals in the same location. We identified these reports using key word search techniques.

We reviewed the reports to confirm the existence of a cluster and documented the number of patients involved and described the cluster incidence by vaccines administered and the error groups.

This slide shows you the grouping that was 49 error codes into the 11 main error groups that were determined by the researchers. A sample of reports were reviewed to ensure (unintelligible) term consistency with a specified group.

There is one group I would like to point out in this slide and that is the general error grouping. These general error codes were used by VAERS to describe vaccination errors most commonly before 2007.

In 2007, VAERS adapted MedRA coding terminology, which provided a much broader choice for vaccination error coding terminology than the previous system did prior to 2007.

The use of general vaccination error terms are rarely used today in VAERS coding of vaccination error reports. Now, let's discuss the results of the study. This slide shows that there were 311,000 reports to VAERS during 2000 through 2013. Of these, around 20,000 or 7% of all reports to VAERS reported a vaccination error.

No adverse health events were reported in the majority of reports. Of the 25% that did report an adverse health event, most were considered to be non-serious reports. I will discuss more about these reports later.

This chart shows you the vaccination error reports by the number and percentage of all VAERS reports by year. If you look at the bottom of the chart, you will see the year the report was received by VAERS. The numbers on the vertical axis on the left of the chart depict the number of reports in thousands.

The numbers at the top of each bar, date the percent of reports that reported a vaccination error. As you can see, in the year 2000, VAERS received few vaccination error reports, less than 1%.

In 2013, 15% of reports to VAERS documented a vaccination error. This next slide shows you the number of reports by error group reported to VAERS, with the most frequently reported error group being inappropriate schedule errors at the top of table, and the least frequently reported group, product labeling and packaging at the bottom.

The top three error groups are highlighted in orange and we will be discussing these in the next few slides. The most common error reported was inappropriate schedule errors which included wrong age at vaccination and wrong timing between doses. The most common age for this error was in children ages zero to one year. This was not surprising because of a number of vaccines given to this age group.

The most common vaccines involved in wrong timing of vaccines included HPV vaccine, with a sample of reports describing delays between dose one and dose two, and giving the third dose too soon before the 12 week minimum interval.

Rotavirus vaccine was another common inappropriate schedule error with the most frequent issues described as giving the first dose late, greater than 15 weeks, and the last dose given late, after the 32 week cut-off. Both rotavirus and HPV vaccine involved complex timing schedules compared to other vaccines.

Vaccines with complex schedules may require more careful training and attention by vaccine providers. The second most common error were vaccine storage errors. The most common specific storage error was expired vaccine administered, found in more than half of the storage error reports, involving, most commonly, LAIV influenza vaccine.

The second most common storage error was incorrect storage describing vaccines being kept outside of proper storage temperatures. Patients receiving these vaccines were documented in almost all reports.

The most common reason for the error documented in a sample of the reports was that the vaccine storage unit was not holding the proper temperature and the provider did not recognize the temperature problem until after vaccination.

The Vaccine Storage and Handling Tool Kits may be a helpful reference pictured in this slide, and the link to this tool kit is found in the footnote at the bottom of the slide. The third most common error was wrong vaccine administered, found in 15% of vaccination error reports.

The chart shows you the most common vaccine mix-ups. This type of error occurs among vaccines with similar names, acronyms, and antigens. Some of these vaccine mix-ups have different age indications, and so, they would be more likely to occur in vaccination settings that carry vaccines for both adults and children.

This next slide looked at contraindications of vaccination errors where a patient receives a vaccine that is contraindicated for their specific condition. We were interested in identifying these and understanding them, since we believe these types of errors could potentially have an adverse impact on patients.

All reports were clinically reviewed. The most common contraindication error found in over half of the reports was a mother's exposure during pregnancy to a vaccine that was contraindicated. Most of the reports involved live attenuated influenza vaccines.

When we looked closely at these reports, we found that few described an adverse health event. Of the health events reported, seven described pregnancy-related adverse health events, including spontaneous abortion in six reports and vaginal bleeding in one report.

Other contraindication errors we found included live vaccines given to persons with immunodeficiency conditions, and vaccines given to persons with a history of an allergic reaction to a vaccine component. And, live attenuated influenza administered to persons with asthma.

Now, let's discuss what we found about reported adverse health events. The most common adverse health events reported were similar to the most common adverse health events that we've seen reported to VAERS overall, and included injection site redness, injection site pain and fever.

About 8% of reports also documented a health event and were considered to be serious reports. A physician reviewed all serious reports and medical records, when available, and classified them into body system categories.

The most common adverse health events described included conditions describing injection site reactions, pain in the extremity, and headache. The last analysis we did was to look more closely at error reports that involved multiple individuals affected by the same error in the same location.

We found 936 error clusters. Cluster size ranged from two to 501 patients. 110 clusters involved more than ten patients. In a large number of the cluster reports, a specific number of patients affected was unknown and stated as unknown number of patients affected, multiple or several patients.

The most common specific type of error identified in these reports were vaccine storage errors, which included incorrect product storage and expired vaccine administered. Half of the expired vaccine administered involved the live attenuated influenza vaccine.

This next table documents who is reporting vaccination errors to VAERS. In the first column, you will find the reporter type. In the next column, the number of errors reported by frequency and percent, and then, the last column lists the number and percent over all VAERS reports.

Interestingly, you can see the vaccine manufacturers are reporting more than half of the vaccination error reports to VAERS, compared with only 23% of reports to VAERS overall.

This next slide lists some potential strategies for reducing vaccination errors including education and training on vaccine timing, spacing, proper administration techniques, improved monitoring of vaccine storage temperatures, increased awareness and establishment of procedures to monitor the relatively short expiration date of live attenuated influenza vaccines.

Improvement in differentiating vaccines and other products with similar sounding names and acronyms, and, implementation and enforcement procedures to properly screen for vaccines contraindicated for individuals such as live vaccines and pregnant women.

In summary, vaccination error reports comprise 6% to 15% of all reports to VAERS in recent years. The number and percentage of vaccination error reports have increased during the period from 2000 to 2013.

Three-fourths of vaccination error reports have no reported adverse health events. However, errors can affect cost, convenience, effectiveness, and competence in vaccination programs.

I would like to thank my CDC co-investigators on this study, listed on this slide. Our study is currently in press and will be published in the journal Vaccine in the next few weeks. Next, I would like to discuss some other errors reported to VAERS that may be of interest.

We looked at oral rotavirus vaccine errors and found a couple of unexpected errors. The first unexpected error involved 39 reports of oral rotavirus vaccine being injected into infants. In the upper right, you can see pictures of the two rotavirus vaccines, which is given by mouth using the oral applicators pictured in the top-right.

The vaccine most commonly reported was Rotarix, in 33 reports. As you can see in the picture, the Rotarix applicator looks like a syringe you might attach a needle to, compared to the RotaTeq applicator. Interestingly, we tried and failed to attach several different types of needles to the end of the Rotarix applicator and were unsuccessful.

Adverse health events were described in half of the reports, and included irritability and injection site reactions. Reasons for the error specified in some reports that included vaccine providers stating that they misinterpreted instructions or they confused the Rotarix vial for an injectable vaccine. They had inadequate training or they did not read the package insert administration instructions.

The second unexpected error with rotavirus vaccine involved eye splashes. The eye splash occurred when the infant coughed, sneezed, or spit the rotavirus vaccine out its mouth and into eyes. Health care providers were most commonly affected in most reports, but there were reports of the eye splash occurring to the infant or parent.

Adverse health events were described in the majority of reports and included eye irritation, redness, itching, and blurred vision. Proper administration of rotavirus vaccine includes the use of the manufacturer's oral applicator devices to squirt the vaccine gently and slowly into the child's cheek.

The last error I would like to highlight is reports of administration of expired live attenuated influenza vaccine. We found 866 reports to VAERS concerning this error. LAIV generally has an 18 week shelf life. Inactivated influenza vaccine generally lasts until the end of flu season, June 30.

No health events were documented in 98% of the reports. In 95%, expired LAIV reports the vaccination occurred after the first week in November which is approximately 18 weeks from July 1.

Vaccination errors are an important area in vaccine safety research and surveillance. Continued study will be key to understanding risk factors and

developing prevention strategies. Focus of continued study in VAERS will be vaccination errors that occur frequently, the errors that may be associated with an adverse health outcome, and prevention of vaccination errors.

And, with that, I would like to thank you for your attention to this presentation.

Raymond Strikas: Thank you very much Ms. Hibbs. I would now like to invite our listeners to call in and ask questions. To do that, please dial star 1 as it's portrayed on the slide on your telephone.

Please be sure to restrict your questions to the contents of the presentations discussed today. Please tell us your first and last name and where you're from, and now I'll temporarily turn the mic over to our Operator.

Coordinator: Certainly. Once again, if you would like to ask a question, you may do so at this time by pressing star 1. Please wait for the prompt and record your first and last name as your name is required to introduce the question.

To withdraw your question, you may do so by pressing star 2. Again, at this time, if you would like to ask a question, please press star 1 now.

Raymond Strikas: While we wait for the first question, I'd like to provide some additional information. First a recast as well as the slide sets from these presentations will be available at www.cdc.gov/vaccines/ed/ciinc, and they'll be available during the week of June 1 of this year.

Also, for continuing education credit, please go to the Website I mentioned earlier, www.2a.cdc.gov/TCEOnline/. The course number for this program is

EC2064. The verification code in all caps is HPV-VAERS and the CE credit expires in about a month on June 22, 2015.

So, now let's see if there's a question in the queue.

Coordinator: And there are no questions in queue. Just as a reminder, if you would like to ask a question, you may do so at this time by pressing star 1.

Raymond Strikas: Okay. Well, let me ask a question we received earlier. This is for Dr. Hariri. Could you tell us, again, in case I missed it, how much additional protection against various types of cancers does the 9-valent HPV vaccine provide overall, and is that protection similar between males and females?

Susan Hariri: Sure. So, the - both the quadrivalent and the 9-valent vaccines protect against the two types, Type 16 and 18, that are associated with the majority of HPV associated cancers.

The 9-valent vaccine protects against five additional types that are not targeted by the quadrivalent vaccine, and these five types account for 14% of HPV associated cancers in females and 4% in males.

So, there is a difference by gender. The additional protection of the five types is 10% overall, but much higher, as I mentioned, in females 14% versus 4% in males.

Raymond Strikas: Okay, thank you. Operator, do we have anybody in queue for a question?

Coordinator: There are no questions in queue at this time.

Raymond Strikas: Okay. Let me ask Ms. Hibbs, could you tell us why you think reporting of vaccination errors has increased over time to VAERS?

Beth Hibbs: Well, Dr. Strikas that's a really good question and our study wasn't able to reallydetermine that, specifically, but we felt that contributing factors might include increased attention and focus on medication errors in general, including the Institute of Medicine's report, preventing medication errors.

There could also be changes in reporting practices by vaccine providers and vaccine manufacturers, who are more willing to report the amount of errors than they were in the past. The increased complexity of the immunization schedule or increased attention to storage and temperature lapses may also be contributors to why we were seeing more reports in VAERS.

Raymond Strikas: Okay. Thank you very much. Operator, has anyone queued for a question?

Coordinator: There are no questions in queue at this time.

Raymond Strikas: Okay, thank you. Dr. Hariri, I guess I'll ask, you mentioned that there's relative difference in vaccine coverage for HPV vaccines in the United States among both, well adolescent girls as well as adolescent boys.

Do you have some explanations or ideas on why those differences might be, and what types of strategies we could use to improve coverage?

Susan Hariri: Well, that's a great question. So, as I mentioned, the coverage in the U.S. is lower than what we would like to see right now and National Immunization Survey data indicates that only 57% of females and 35% of males received at least one dose of HPV vaccine in 2013.

Now, the - coverage in males is increasing probably, you know, at the same rate or maybe even a little bit faster than it did in females, but they just haven't had enough time to sort of catch up to the females because the vaccination in males started later after 2009, whereas females have been - the vaccines been available for females since 2006.

As far as strategies to increase coverage, the CDC is, and, you know, immunization experts are using a variety of methods to try to increase coverage in adolescents.

Most importantly, they're trying to increase education and training in providers to make sure that providers treat the vaccine, the HPV vaccine, just like any other adolescent vaccine and recommend it to their patients, and to make sure that there are no missed opportunities when an adolescent comes into the clinic and receives vaccination for another - against another disease or just comes in for a routine health visit.

Just make sure that they get the HPV vaccination, and then, there's a lot of effort around improving communication and education to the general public and also to parents.

One of the problems is, as was mentioned earlier, that the dosing schedule is really complicated, and so, one of the, well the sort of barriers has been trying to get three doses and completion of the three doses in adolescents.

So, hopefully, that will sort of improve over time if, you know, new vaccines become available, and if the dosing schedule or dosing number changes.

Raymond Strikas: Okay, thank you very much. I'll add that CDC has part of it's Website at cdc.gov/vaccines/teen dedicated to adolescent vaccination and HPV is

prominent there, and you highlighted one of the important roles we see for the provider is that there be a strong provider recommendation for this vaccine as an anti-cancer vaccine, and as part of the routine adolescent preventive health regime and we hope that works to improve coverage.

Operator, have we got any questions waiting for us?

Coordinator: We do have one question in queue. Angela Swanson, your line is now open.

Angela Swanson: Yes, hi, my name is Angela Swanson. I'm calling from Central California and I work for the King's County Health Department. I've got two questions. One has to do with the HPV. Has there been any direct studies in regard to with males receiving and having partner protection for their female or male partners?

Like that's - that them getting vaccinated then protects the partner because we know that males, maybe - they don't have as much to worry about as far as because they don't have a cervix or a uterus to worry about, but about them protecting their partner. That's my first question.

Susan Hariri: Yes, hi. So, thank you for the question. So, you're right. Vaccinating males does help increase protection, sort of through (herd) immunity in females, however, the most cost effective way to reduce the burden of disease is really to increase coverage in females.

So, that's something that we really want to underscore and make sure that providers understand that the coverage is low and it needs to be improved, and that they need to get vaccinated prior to exposure to the HPV types in the vaccines, so at 11 or 12 is the optimal age.

Males, of course, are being vaccinated for protection against other HPV associated cancers that they're susceptible to, and you're right, the burden of disease is mostly in females and, as I said, I mean, we really want to increase coverage in both males and females, but the objective really is not to vaccinate males in order to protect females. Although that does happen as a consequence.

Angela Swanson: Okay, my next question - I'm sorry.

Raymond Strikas: No, go ahead Ms. Swanson.

Angela Swanson: My next question has to do with could someone speak to how VAERS and the Vaccine Safety Datalink actually, if - how they might work hand-in-glove as far as to determine any side effects or adverse events because I know that they each have their strengths and weaknesses.

Raymond Strikas: Ms. Hibbs?

Beth Hibbs: Yes, thank you for your question. Is this in regards - are you thinking about HPV vaccines?

Angela Swanson: No, I'm talking about in general with error reporting...

Beth Hibbs: Oh, okay.

Angela Swanson: ...because, as I understand with VAERS as the adverse event reporting system that, you know, you can report anything, and it doesn't necessarily mean that whatever's reported necessarily came about due to the vaccine itself.

But, that the Vaccine Safety Datalink is maybe a little better at honing that down and how VAERS actually acts with the Vaccine Safety Datalink in order to determine things like that.

Beth Hibbs: You're exactly right and thank you. I was misunderstanding your question at first. Yes, we have been very interested to see how we might be able to use the VSD for looking at vaccination errors.

However, the ICD codes that the VSD uses , are based on medical diagnoses. Because of this VSD data does not have codes for vaccination errors because an error is not a medical condition.
And so, that's the problem we have with specifically looking for vaccination errors using the VSD data.

Raymond Strikas: Ms. Swanson, does that answer your question?

Angela Swanson: Yes, thank you.

Raymond Strikas: Thank you. Operator, do we have others waiting in line?

Coordinator: Yes, we have a few questions in queue. Kathy Harriman, your line is open ma'am.

Kathy Harriman: Thank you. This is Kathy Harriman from the California Department of Public Health. I just wanted to thank you for mentioning the ISMP VERP Vaccine Error Reporting Program because it's great, and so, the main thing that we're hoping to accomplish is to be able to quantify the types of errors that happen, as Beth so rightly pointed out.

Some of them are systematic errors, and if we can get data on those, then we should be able to present that to FDA, and hopefully that may lead to some changes say in packaging or, you know, the devices themselves, and really unless we get enough information to be able to show that errors are consistent and happening a lot, then that probably won't be possible.

So, I really applaud CDC for trying to do more to collect these errors, and that's all I wanted to say. Thank you.

Raymond Strikas: Thank you. Ms. Hibbs?

Beth Hibbs: Yes, Dr. Harriman, thank you so much. We also believe that the Vaccine Error Reporting Program will be very instrumental and helpful in helping us to learn more about vaccination errors. , This particular surveillance system uses a much more detailed than the form for collecting specific information about the error than the form we use for the Vaccine Adverse Event Reporting System.

So, we are looking forward to learning more about the reports that that system is collecting and analyzing.

Raymond Strikas: Thank you. Operator, the next question please.

Coordinator: Yes. Just as a reminder, if you would like to ask a question, please press star 1. Our next question comes from (Denise) with the (Columbus Immunization). (Denise), your line is open.

(Denise): Yes, I have a question regarding an error, like if you gave like Pentacel to a one year old, but then it's going to make the polio part of that Pentacel be the

fourth dose for the one year old, where they will mostly like need another when they turn four.

Is that considered an error for that fourth dose of polio, even though, you know, you're giving - it's (the mess) in the amount shots by giving a combo?

Beth Hibbs: Yes, thank you for that question. The reports that we receive at VAERS, rely on the health care provider to make a determination about whether they believe an error has occurred.

VAERS, is primarily concerned with monitoring adverse health events.

We have stated on our Website that health care professionals can decide whether or not to report a medical error at their own discretion, and, for example, a health care professional may elect to report vaccination errors that do not have an associated adverse health event, especially if they believe the vaccination error may pose a safety risk.

an example of that might be administering a live vaccine to an immunocompromised patient or if they believe that the error would be preventable with some kind of public health action or education. Something that we could act upon.

Raymond Strikas: Thank you. Operator, do we have another question?

Coordinator: Yes. (Hope Wood), your line is open.

(Hope Wood): Yes, please. I came on late, and I'm sorry, I couldn't log in. Was there mention on is there going to be a booster required if you got the quadrivalent and now the 9-valent is available?

Raymond Strikas: Dr. Hariri, can you address that?

Susan Hariri: Sure. So, are you specifically talking about 9-valent vaccination of someone who's received the full series of the quadrivalent or the bivalent vaccine?

(Hope Wood): Yes, please, thank you.

Susan Hariri: Yes, so this is something that is going to be discussed at a subsequent ACIP meeting. There was one study that was done by the manufacturer, it was mostly a safety study, and it looked at 9-valent vaccination among girls who were vaccinated previously with the quadrivalent vaccine.

And, the data are available and they will be presented to the ACIP for deliberation. At the last ACIP meeting, the meeting was abbreviated and we didn't have a chance to discuss that.

(Hope Wood): Thanks, and...

Raymond Strikas: Okay.

(Hope Wood): ...can you please give the Website to go to download the slides again? I didn't hear it all.

Raymond Strikas: Yes, I'm going to repeat that in a second for the entire audience. I just want to see if we can do one more question, if anyone else is waiting. Operator?

Coordinator: There are no questions in queue at this time.

Raymond Strikas: Okay. Well, then we'll go to closing. Thank you very much and we'll have to move onto closing information and the information folks need to follow the continuing education guidelines that we have.

So, as I've said earlier, please go to www.2a.cdc.gov/TCEOnline/ as it says on the slide now. The course number is EC2064. The verification code, in all caps, is HPV-VAERS. And, again, the CE credit will expire on June 22, 2015.

Once you become familiar with CDC's online system, you'll find it's pretty easy to use and a good way to keep track of your CE credit earned from CDC training programs.

If you have any difficulty or are new to this system, you can get assistance by phoning 1-800-41-TRAIN, that's T-R-A-I-N or 418-7246, and there is staff available from 8:00 a.m. to 4:00 p.m. Eastern Time to assist you.

Get help by way of e-mail, you can contact CE@cdc.gov. We received many helpful questions today to clarify the points made by our speakers. If you were unable to ask your question or think of one later to relate it to this NetConference, you can contact us by e-mail, and e-mail us at NIPinfo@cdc.gov and put NetConference in the body or the subject line of your e-mail.

Another way you can ask a question is to contact the CDC-INFO Program. It answers lots of questions about CDC activities, including immunization. You can dial 1-800-CDC-INFO from 8:00 a.m. to 8:00 p.m., Monday through Friday.

Another way to contact CDC-INFO and this is not up there, but go to CDC.gov and go to the bottom of the page and you'll see CDC-INFO at the

bottom and you can send them an e-mail through our Website. It's a general question and answer service that answers many questions for CDC.

Finally, I want to thank everyone for joining us today, with a special thanks to our subject matter experts, Dr. Susan Hariri and Ms. Beth Hibbs. Thank you very much and so long from Atlanta.

Coordinator: This now concludes today's conference. All lines, please disconnect at this time.

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