Hello. My name is Lois Ramondetta and today I am going to talk to you about an introduction to HPV-related diseases. I'm a professor of Gynecologic Oncology & Reproductive Medicine at The University of Texas MD Anderson Cancer Center.

Upon completion of this lecture participants will be able to discuss the prevalence of HPV infections across the U.S. and the early effect of HPV vaccination on this prevalence. We will also be able to gain knowledge about HPV-associated cancers and understand data demonstrating that the HPV vaccine is safe and effective.

Almost all will be infected with at least one type of HPV at some point in their life. Most people will never know that they have been infected. An estimated 79 million Americans are currently infected and there are 14 million new infections per year. The infection rate is most common and the prevalence rate is most common in people in their teens to 20s.

There are hundreds of different types of HPV viruses. About 40 different types cause mucosal infections and about 80 different types cause cutaneous infections, the common wart. However, of the mucosal infections, some of those viruses are high-risk types and some of them are low risk types. The high risk types, the most commonly known are HPV 16 and 18 and those are the ones that we believe are responsible for cervix cancer, anogenital cancers, oropharyngeal cancers, cancer precursors of the cervix, low-grade cervical disease. Also HPV 6 and 11 are very likely to cause laryngeal papillomas, genital warts, and low-grade cervical cancer disease.

HPV infection can occur with an --- any intimate contact. Intercourse is not necessary for infection. Nearly 50% of high school students have already engaged in sexual intercourse. It's scary but one-third of ninth graders and two-thirds of twelfth graders have already engaged in intercourse and 24% of high school students have already had intercourse with four or more partners. Condoms do not totally prevent HPV infection.

In 2003 through 2005 through a number of different studies in STD, family planning, and primary care clinics they --- the prevalence rate of high-risk HPV types including 16, 18, and a number of different types listed here showed the overall prevalence rate was 23% and the prevalence age by group was highest in those women age 14 -19 and women age 20-29 and the rates --- the prevalence rate decreased at that --- from that point.

This is a very busy slide and I'm going to point out just a few important numbers. This shows the reduction in HPV prevalence in young women following HPV vaccine introduction in the U.S. through the National Health and Nutrition Examination Surveys. What you see on the left is the age of the person evaluated and the HPV type. Were these HPV types any types? Were the virus --- [sorry] --- the vaccine-specific types or were they specifically the high-risk viruses? And what you see in the next columns is ---,[let me use the --- the mouse to show you] --- in 2003 through 2006 these were the prevalence rates before the vaccines were re --- released and FDA approved and these 2007 through 2010 show the rates after the vaccine was imp --- was FDA approved. In the 14 to 19 year age group you can see that the high-risk subtype
prevalence rate was --- [I’m sorry] --- was the --- of any HPV prevalence rate was 7.2% but dropped to 3.6% in those --- in those years of 2007 through 2010. In the 20 to 24 year-old age group those women are the ones that we expect the highest prevalence rate. We saw a rate of 15% of the high-risk types and then 16% in the 2007 through 2010. And what you can s --- can gain from this is that those women who are vaccinated, those in the 14 to 19 age year --- age group, you saw a significant decrease in the vaccine prevalence rate.

And then you really see again in the age 25 through 29 and the age 30 through 39 there was really no difference pre- and post-vaccine for the prevalence rates for those age groups. And this slide shows the same for age 40 to 49 and 50 to 59.

This is another way of kind of showing the same information. This shows the prevalence of individual HPV types among females age 14 to 19 looking at these two different seconds --- sections of years, 2003 through 2006 and 2007 through 2010. And you see if you look at all --- vaccine type 16, 6, 18 and 11 those are types covered in the four-valent virus [speaker intended to say vaccine], you see a significant decrease, here's pre-vaccine and post-vaccine, in the prevalence of these types that are covered in the vaccines. But then you look at the other high-risk non-vaccine types and you really see very little difference although you still see some and I’ll explain why later on in this presentation. Other non-vaccine types, really no difference from pre to post vaccine FDA approval.

So what we’re doing in --- in these series is that we'll have a series of lectures going over HPV, its epidemiology, its effect on different cancer types, ways to prevent it through the vaccination and screening, but also how to cover patients for --- who are uninsured for treatment with --- with newly diagnosed cervix cancer. There are a series of talks. You can access them all on this website. They'll include an introduction which is this talk, the biology of HPV, cervical cancer screening and treatment, anal cancer, oropharyngeal cancer epidemiology and clinical implications, penile cancer, HPV vaccination, and the Medicaid as I explained before.

There are a number of cancers and genital warts attributed to HPV infections. This is a pyramid diagram showing the relative burden that the United States has related to HPV-related infections and you can see the largest burden are those who are infected with HPV and get genital warts. The second most common is cervix and that may change and oropharyngeal is next, followed by anal, vulvar. This section is called juvenile onset recurrent respiratory papillomatosis. And this is a picture of vocal cords with recurrent warts and this occurs in young children. We believe they get exposed through the birth canal. Then there's vaginal and penile cancer.

Cervical cancer is the most common HPV associated cancer at this point in time but expect this to change over the next two years. Right now it accounts for 500,000 cases worldwide and 11,000 cases in the United States. There are 4,000 deaths in the United States yearly related to HPV-related cervix cancer. Most of these cancers occur in women age 20 to 44, oftentimes women with young children.
This is a map of the United States showing HPV-associated cervical cancer rates and you can see that Texas where we are located is --- has one of the highest rates of cervical cancer and where --- this may be a combination of reasons. It may because of the large border with Mexico and a lot of immigrants as well as the fact that there are, at least prior to the Affordable Care Act, may uninsured.

Oropharyngeal cancer is the principal site of head and neck cancers related to HPV. It is HPV-related in not all but 60-80% of cases and the majority of these cancers are HPV 16-related and this is important because the vaccine covers HPV 16 and 18. In the U.S. there are 10,000 to 12,000 new cases yearly. You can see that this number already overlaps with the incidence for cervix cancer in the United States. And we expect over the next year or two for cervix cancer to --- [I'm sorry] --- oropharyngeal cancer to overtake the number of new cervix cancers and soon as we believe we'll be dealing with an epidemic of these new HPV-related head and neck cancers. The prevalence of the screening, here's the important part. We have a pap smear for cervix cancer but we have no pap smear-equivalent for oropharyngeal cancer. There is no way to detect an oropharyngeal cancer early which is why vaccination is so important.

There is more information about HPV-related oropharyngeal cancer in the other lectures but I'll touch on it briefly during this lecture. And in this slide you can see that the trends in cancer incidence and number for oropharyngeal versus cervix and you can see that cervix has declined because of the --- the use of pap --- the pap smear and now HPV DNA tests and the more screening we do the --- better we are at detecting this cancer in a pre-invasive state and eliminating it. But you can see in the oropharyngeal cancers we are starting to see this rise. Here it is again rising, the number of new cases total and the oropharyngeal cancer is rising overall in men significantly and cervix cancer is going down. Oropharyngeal cancer is also going up in women but not as high.

Penile cancer rates are also concerning and as I said 60% of these are related to HPV and these occur mostly in Hispanic men as well as African American men and Asian American.

It is estimated more than 1,000 new cases of HPV-associated penile cancers are diagnosed in the U.S. each year and it is more common as I said among Hispanic men. Anal cancer is occurring in more than 7,000 new cases yearly. We are starting to see an upward trend with anal cancer related to HPV as well and we are concerned that without vaccination that this will significantly increase over the next decade.

This is a breakdown of the number of HPV-associated cancers by sex and as I said before cervix cancer is about 11,000 new cases in women. The other cancers are also prevalent but not as prevalent as cervix and for men HPV-related oropharyngeal cancer is the most common HPV cancer followed by anal and penile cancer.
So not only is this a huge tragedy for a patient and for the physicians who are seeing these patients knowing that this could have been prevented with vac --- with vaccination or with screening test for cervix cancer, it is a huge economic burden primarily in the pre-invasive stages. The cervical cancer screening evaluations which involve pap smears followed by biopsies followed by colposcopies and sometimes pre-invasive procedure can cost up to 6.6 billion dollars. And if you look at the total cost for the U.S. per year we believe it’s 8 billion dollars spent on HPV-related diseases.

There are actually three vaccines now FDA approved but one of them is in its very early stages of introduction in the United States. There is the quadrivalent HPV4 vaccine which covers HPV 6, 11, 16, and 18 and the bivalent or HPV2 vaccine covering HPV 16 and 18. So remember that HPV 16 and 18 are the most high-risk types causing most of the cancers that I mentioned before. 16 --- 6 and 11 are the types that are most commonly causing a low-risk disease as well as warts. Both of them require a three dose series and I’m going to refer you to our vaccine talk which is also on this website.

The quadrivalent vaccine recommendat --- is the recommendation for males age 11 to 12 for the prevention of anal cancer and genital warts and we believe oropharyngeal cancer too based on the fact that since the vaccine we have seen a reduction in the prevalence of HPV virus detected in the oral cavity. HPV 13 --- [I’m sorry] --- In --- age 13 to 21 are supposed to get HPV quadrivalent vaccine if they haven’t started or completed the series. Men in the 22 to 26 age group may also get the vaccine and teens age --- through age 26 who identify as gay or bisexual or haven’t started or completed the series should also get the quadrivalent vaccine.

In December of 2014 the HPV9 or nonavalent vaccine was approved and if you remember I mentioned that 16 and 18, 6, and 11 were the most common to cause disease but here are another type --- five different types who --- which also cause HPV-related head and neck --- [I’m sorry] --- oropharyngeal cancer as well as cervix cancer. This was FDA approved and actually yesterday the American College of Immunization Practice held their meeting. It was on February 26th and approved the HPV9 vaccine for use.

The vaccine is incredibly safe. Many, many different methods have been used to look at safety. The most common adverse events reported were considered mild for adverse events. There was no unusual pattern of cluster --- clustering that suggested that there was disease or serious side effects related to the vaccine. The reviews --- The safety reviews are similar to the meningococcal and the Tdap vaccines and further over 57 million doses have been given in the U.S. since 2006.

There are multiple methods for determining whether or not a vaccine is safe. There are no new safety concerns through the Vaccine Adverse Event Reporting System. Among the 7.9% of reports that co --- were coded as serious the most frequently sitied were headache, nausea, vomiting, fatigue, dizziness, syncope, and generalized weakness. There were multiple studies that looked for causal relationships between HPV vaccination and multiple different disease types including neurologic abnormalities or
immunologic diseases and there have been no evidence of connection between the HPV vaccine and any of these abnormalities. Syncope is frequently reported amongst adolescents. We believe this is partially related to giving the vaccine to young adolescent girls who are are sometimes more scared about getting a vaccine than a toddler might be. We do recommend an adherence to a 15 minute observation period after the vaccine is given to avoid fainting and then accidents that can happen after somebody faints.

So one of the concerns with the vaccine is that children would become more sexually active and this is really number one kind of a --- a silly comment. First of all, when you give a vaccine the easiest thing to do is to --- to talk to the patient about how they're getting a vaccine to prevent cancer later on in life. That said, there have been many studies. The most recent one was published in 2015 that showed there is no association between children who are vaccinated and children who weren’t vaccinated in terms of their markers of sexual activity which include pregnancy, counseling, and contraceptives or requests or testing for diagnoses of STDs.

Australia is doing much better than the United States in vaccinating their children. Up to 80% of school-age girls in Australia are vaccinated. Part of this is that Australia has taken on the vaccine project as a sign of --- of country pride. They believe that they are partially responsible for bringing the vaccine to --- to con --- to visualization and to bring it out and so they have vaccinated their kids in school-based programs. The proportion of genital warts has declined by 93% since introducing the vaccine in Australia. Genital warts declined by 82% among males of the same age indicating herd immunity which means that if you have say two schools that get the flu vaccine, you have one school that half the kids get vaccinated and one school where none of the kids are vaccinated just the school with the half vaccinated have a significantly lower rate than --- than the kids who didn’t because they are not carriers. Fortunately, even though we’re doing just a terrible job vaccinating in the United States we’ve already seen a decrease in the prevalence of vaccine --- HPV vaccine types.

Here’s an example of how we’re doing compared to other countries. The U.S. is only vaccinating 32% of its girls with all three shots required for full protection compared to 67% in Australia --- I’m sorry --- in Austria, 75% in Austria --- I’m sorry --- Australia, 79% in Switzerland, and up to 84-92% in the United Kingdom.

We have a long way to go and a lot of missed opportunities. We’re vaccinating close to 80% --- almost 90% of our kids with Tdap and this is the age group where these kids are supposed to get the HPV vaccine. So for every one of these children getting vaccinated with the Tdap or the meningococcal vaccine we could be vaccinating them with their first HPV test --- vac --- virus [speaker intended to say vaccine].

We are also not doing very well in vaccinating here in Texas and this is an example right here of where we’re vaccinating 25-35 --- 32% of our girls compared to other states which are vaccinating from 40-55% of their girls.
Well why is this? We mentioned in Australia they had a --- a high level of country pride and school-based vaccination rates. We thought many coun --- may states have considered HPV vaccine legislation and many have been proposed across the United States but only Virginia and Washington, D.C. have been successful in getting mandatory school-based vaccination legislation across. Unfortunately, because they have parent --- parental opt out options there --- they really haven’t increased vaccination rates through this legislation alone.

There were many that were proposed and only a few have been successful, as I said, Washington, D.C. and Virginia.

I want to talk just a few minutes about what these patients with cervical cancer look like. I work at Lyndon Baines Johnson Hospital which is part of the Harris Health System in the county and it is primarily a --- set up to take care of underinsured or uninsured individuals who live in Texas. It is a part of The U --- University of Texas MD Anderson Cancer Center outreach program.

And now this is unpublished data hopefully soon to be published showing a study population of the women that I see at this hospital. Most of the people that I see are of minority status. As is the case many of those are uninsured and so are seen at the Harris County system. Many of them are single or divorced and many of them have had less than a ninth grade education. Unfortunately they are also the primary caregivers for up to five children in 25% of these cases. When we lo --- talk about cervix cancer which we'll talk about in a different presentation, women who present with stage IB1 or below are treated with surgery. Women who present with stage IB2 or above have to get an eight week course of chemotherapy and radiation. It’s burdensome for the patient. It has many side effects. It requires daily visitations to radiation centers. And unfortunately due to a large tumor as well as the radiation have increased side effects. The majority of people that we see at this --- in this county system are in this IB2 and above group.

At diagnosis 75% of them have presented with bleeding, 66% had already presented to an emergency room, and 67% said they did not have a primary care physician. Many of them also received transfusions for bleeding.

If you looked at what were the differences between those women who presented with an early stage cancer versus a late stage cancer what really stood out is that --- that those with an early stage cancer had already had the Harris County insurance s --- card so that they could see a primary care physician. Those who had higher cancers and obviously bigger cancers presented to the ER more often and were less likely to have a primary care physician. In addition, what stood out is that those pe --- women who had ha --- larger cancers also took care of many of their family members and this made it difficult for them to take care of themselves.

So bottom line is we need better HPV --- better rates of HPV vaccination in 12 year olds, boys and girls. We need it for the girls to prevent cervix cancer, anal cancer, and
oropharyngeal cancer as well as vulvar and vaginal. For the boys we need them to also protect carrying in to the --- to women but to protect themselves against penile cancer, anal cancer, and oropharyngeal cancer. Currently 26 million girls --- Currently there are 26 million girls under the age of 13 in the U.S. If none of these kids are vaccinated then over the course of their lifetime we will expect 54,000 deaths from HPV-related cancers. Vaccinated 30% would prevent 45,000 of these cases. Vaccinating 80% would present --- prevent 98,000 cases.

MD Anderson is working hard to prevent cervical cancer as well as all HPV cancers. Over the last three years we’ve held a summit to try to bring together experts in the area to work together to try to raise the vaccination rates. We’ve also worked with the College of American Pathologists to do --- to work with their See-Test-Treat program where they --- we work hand-in-hand with The University of Texas Health Science Center and The Methodist Hospital and Baylor Hospital in order to do free pap screening. We, in collaboration with the Texas Medical Association, the Texas Pediatric Society, Texas Family Practice and Texas School Nurses’ Association, are working together to see what we can do to raise vaccination rates.

Right now we have a research initiative involving all the specialties that in --- that involve taking care of patients who have HPV-related cancer. We held our first retreat on August 9, 2014 and our next retreat will be planned for September 2015. During this time we spend a full Saturday where we work on issues related to policy, education, basket trials where we look at developing targeted trials for women and men who have HPV-related cancers as well as genomic and --- and other studies to see what connects these cancers. And further, we will be holding our ne --- our --- our fourth annual HPV summit this year in June to try to attract a larger group of school-based healthcare providers.

This is --- You can find this online at the Texas Cancer Information website. We will be hosting it at the The Univer --- at the United Way on June 18th.

What we really need is survivor support. This is an area where up until recently we’ve had no real lo --- no real survivor voice partially because of the stigma associated with HPV vaccination and the fact that many of these women who are getting cervix cancer didn’t have access to computers or didn’t even speak the same language. Fortunately and unfortunately now that men are getting an oropharyngeal cancer related to HPV and often in a different socioeconomic group we are able to start developing an HPV survivor support group where can bring this information to school educators, to legislators, and to the public to know how important it is for them to get vaccinated.

In summary, almost all people will be HPV positive at some point in their lives. Cervix cancer is the most common HPV cancer right now but may soon be second to HPV-associated oropharyngeal cancer. HPV also causes most penile and anal cancers as well as vaginal and vulvar cancer. The cost of continued prevalence of HPV disease is not just in the treatment of HPV-related cancers but primarily related to the screening and treatment of pre-invasive disease. Remember that there are actually three HPV
DNA ap --- [I'm sorry] --- D --- FDA approved vaccines with extensive safety data. The vaccination rates and vaccine series completion rates are extremely low and this is tragic in the United States. The cost of not vaccinating our children against cancer is unimaginable. I want to thank you for listening and tell you that you are able to contact us through the website if you have any questions and I encourage you to listen to the rest of our HPV vaccination and HPV canc --- HPV-related cancer se --- lecture series. Thank you.