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Arizona Vaccine News
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Human Papillomavirus (HPV) and HPV Vaccine Issue

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ECONOMIC IMPACT OF HPV INFECTIONS

Economic Impact of HPV-Associated Diseases in the U.S.

- The cost of preventing and treating HPV-associated diseases in the U.S. was estimated to be $8 billion. This includes estimates of about:
    - $6.6 billion (82.3%) for routine cervical cancer screening and follow-up.
    - $1 billion (12.0%) for cancer (including $0.4 billion for cervical cancer and $0.3 billion for oropharyngeal cancer).
    - $0.3 billion (3.6%) for genital warts.
    - $0.2 billion (2.1%) for Recurrent Respiratory Papillomatosis (RRP).

See the abstract in *Vaccine*, September 14, 2012.

HPV INFECTIONS IN THE U.S.

Prevalence of Cervical HPV Infections in the U.S., 2003-2004

- Pre-vaccine HPV infections in females in the U.S. were measured between 2003-2004 by the National Health and Nutrition Examination Survey.
    - The overall HPV prevalence was 26.8% among U.S. females ages 14 to 59 years old.
    - Prevalence of HPV infection was highest among females aged 20 to 24 years old (44.8%).
    - Females ages 14-24 years old had an HPV prevalence of 33.8%.
    - There was increasing HPV prevalence with each year of age from 14 to 24 years, followed by a gradual decline in prevalence through 59 years.

See *Journal of the American Medical Association* (JAMA), February 28, 2007.

Prevalence of Oral HPV Infection in the U.S., 2009-2010.

- Oral HPV infections were identified among men and women ages 14-69 years old using PCR analysis of oral rinse samples.
- The prevalence of any type of HPV was 6.9%. For high-risk (oncogenic) HPV types the prevalence was 3.7% and for low-risk HPV types it was 3.1%.
- The prevalence of the high-risk HPV type 16 in oral rinse samples was 1%.
- Men were more likely to have oral HPV infection (10.1%) than women (3.6%).
- Oral HPV infection was uncommon among sexually inexperienced individuals. In comparison, oral HPV was 8-fold higher among sexually experienced people, and increased with the number of sexual partners.

See JAMA, February 15, 2012.

Prevalence of HPV Anal Infections among Young Men who Have Sex with Men, 2009-2010

- Among young men in Seattle, Washington who had sex with men (mean age of 21 years), 70% were infected with at least one type of HPV, and 37% were infected with the oncogenic types HPV-16 and/or HPV-18.
- Nineteen percent had persistent infection with HPV-16/18.
- Prevalence of HPV-16/18 was 6% among those with a history of 1 sexual partner, and 31% among those with $\geq$ 2 sexual partners.
- Although HPV prevalence was high, many of the younger men who have sex with men had not yet acquired the oncogenic types HPV-16 or HPV-18. Therefore, they could still benefit from HPV vaccination.

See the abstract in *Journal of Infectious Diseases* (JID), February 1, 2014.

Genital Warts in the U.S, 2011

- Among individuals examined at sentinel surveillance sites, the 2011 median prevalence of genital warts in women was 1.7%, in men who have sex with men was 5.5%, and in men who have sex with women was 5.8%.
- Graph of initial visits to physician's offices for genital warts, 1966-2011.
- Table with numerical estimates of initial visits to physician's offices for genital warts from 1966-2011.

The above data is from the CDC 2011 Sexually Transmitted Diseases Surveillance website.

Recurrent Respiratory Papillomatosis (RRP) in the U.S.

- RRP is a rare but potentially fatal complication of HPV infection with a prevalence of about 4 per 100,000 children.
- The disease is caused by HPV-associated warts on the mucosal surface of the respiratory tract, usually on the larynx. These warts often cause blockage of the airway.
- HPV is thought to spread to infants at birth by contact with HPV-infected secretions in the birth canal.
- Children with RRP often need multiple surgical procedures to keep their airways open.
- The HPV types most commonly involved in RRP are HPV types 6 and 11 which are also the types associated with maternal genital warts.

See *Archives of Diseases in Childhood,* August 2006.

HPV-ASSOCIATED CANCERS

HPV-Associated Cancers in the U.S, 2004–2008

- Oncogenic HPV types have a causal role in nearly all cervical cancers and in many vulvar, vaginal, penile, anal, and oropharyngeal cancers.
- HPV types 16 and 18 are responsible for 70% of cervical cancers. HPV type 16 is the most common HPV type found in the other cancers often associated with HPV.
- Most HPV infections clear within 1–2 years, but those that persist can progress to precancer or cancer.
- During 2004-2008, every year an estimated 21,290 HPV-associated cancers occurred in females and an estimated 12,080 HPV-associated cancers occurred in males.
- Many HPV-associated cancers likely are preventable through the use of HPV vaccines.

See *Morbidity and Mortality Weekly Report* (MMWR), April 20, 2012.

Report of Cancers in the U.S., Focusing on HPV-Associated Cancers

- HPV-associated cancers diagnosed in 2009 accounted for 3.3% of cancers in women and 2.0% of cancers in men.
- Cervical cancer represents 53.4% of the HPV-associated cancers among women.
- Oropharyngeal cancer accounts for 78.2% of HPV-associated cancers among men, and 11.6% of HPV-associated cancers among women.
- Color figures are available in this article for:
    - The number and percentages of new HPV-associated infections in the U.S. in 2009 (overall and by sex). See page 188.
    - A comparison of three-dose HPV vaccination coverage by state in 2010 among U.S. girls 13-17 years old. See page 194.

See *Journal of the National Cancer Institute*, February 6, 2013.

Increase in HPV-Associated Oropharyngeal Cancers in the U.S.

- The presence of HPV in oropharyngeal cancers (OPC) from 1984-1989 was compared with OPC from 2000-2004. Both these periods were before HPV vaccine was licensed.
- The incidence of HPV-positive OPC increased by 225% from 1988-2004 while HPV-negative OPC decreased by 50%.
- Median survival was longer for HPV-positive OPC than for HPV-negative OPC.

See the abstract in the *Journal of Clinical Oncology*, November 10, 2011.

HPV VACCINE SAFETY

HPV4 Safety Monitoring after Licensure in the U.S.

- There were about 56 million doses of HPV4 vaccine distributed in the US from 2006-2013, and 21,194 reports of adverse events following HPV vaccination were made to the Vaccine Adverse Event Reporting System (VAERS) during this time period.
- Most of the VAERS reports (92.1%) were classified as not serious.
    - The most common generalized symptoms were fainting, dizziness, nausea, headache, fever, and hives.
    - The most common injection-site symptoms were pain, redness, and swelling.
- Events classified as serious (7.9%) were most commonly headache, nausea, vomiting, fatigue, dizziness, fainting, and generalized weakness.
- A report to VAERS does not mean that there was a cause-and-effect relationship between the vaccine and the adverse event.

See MMWR, July 26, 2013.

Adverse Events Reported to VAERS after HPV4 in the U.S., 2006-2008

- In 2006-2008, there were 772 serious adverse events following HPV4 vaccine (6.2% of all reports) including 32 reports of death.
- Rates of reports of adverse events per 100,000 HPV4 doses were 8.2 for fainting; 7.5 for local site reactions; 6.8 for dizziness; 5.0 for nausea; 4.1 for headache; 3.1 for hypersensitivity reactions; 2.6 for hives; 0.2 for venous thromboembolic events, autoimmune disorders, and Guillain-Barré Syndrome; 0.1 for anaphylaxis and death; 0.04 for transverse myelitis and pancreatitis, and 0.009 for motor neuron disease.
- Of these serious adverse events, the only positive signals were for fainting and venous thromboembolic events.

For in-depth details, see JAMA, August 19, 2009.

Large Scandinavian Study Shows Excellent Safety Profile of HPV Vaccines

- A study of almost a million Swedish and Danish adolescents showed no causal relationship between HPV vaccination and autoimmune diseases, neurologic events, or venous thromboembolism.

For more details, see the *British Medical Journal* (BMJ), October 9, 2013.

HPV VACCINE COVERAGE LEVELS

HPV Vaccine Coverage in Arizona Compared with Overall U.S. Coverage, 2012

- According to the National Immunization Survey-Teen from the CDC, as of 2012, HPV vaccine receipt by adolescents ages 13-17 years old is as follows:

	Arizona	Overall U.S.
Females receiving ≥ 1 HPV vaccine	54.3%	53.8%
Females completion of 3 HPV doses	36.9%	33.4%
Males receiving ≥ 1 HPV vaccine	19.7%	20.8%
Males completion of 3 HPV doses	N/A	6.8%

See MMWR, August 30, 2013.

HPV Vaccination Coverage in U.S. Teenage Girls, 2007-2012

- If the U.S. were to increase the 3-dose HPV vaccination coverage from 33.4% to 80%, an estimated additional 53,000 cases of cervical cancer could be prevented over the lifetimes of girls ≤ 12 years old.
- For every year that there is delay in increasing 3-dose HPV vaccine coverage, approximately another 4,400 women will go on to develop cervical cancer.
- Health-care providers need to strongly recommend of HPV vaccination to their adolescent and young adult patients.

See MMWR, July 26, 2013.

Geographical Differences in HPV Vaccine Uptake within the U.S., 2008-2011

- HPV vaccine uptake (receipt of one or more doses) and 3-dose completion in women 18-26 years old between 2008 to 2011 were analyzed by geographical areas in the U.S.
  - U.S. Overall: 28.0% uptake and 17.0% completion.
  - South: 14.0% uptake and 6.6% completion.
  - Midwest/West: 28.7% uptake and 19.3% completion.
  - Northeast: 37.2% uptake and 23.1% completion.

See the abstract from *Vaccine*, November 12, 2013.

EFFECTS OF HPV VACCINE ON HPV INFECTION AND ASSOCIATED DISEASES

Reduction in HPV among Young Women Following Use of HPV Vaccine in the U.S., 2003-2010.

- HPV4 vaccine was introduced into the routine U.S. immunization schedule in 2006 for girls and women starting at ages 11-12 years old and extending through 26 years old.
- By 2010, 3-dose HPV vaccine coverage was only 32% among 13-17 years-old females.
- Cervicovaginal HPV prevalence data from the prevaccine era (2003-2006) were compared with HPV prevalence data from the vaccine era (2007-2010) in females ages 14-59 years old.
- Among females aged 14-19 years, the HPV types contained in the quadrivalent HPV vaccine (types 6, 11, 16, or 18) decreased by 56%, from 11.5% in 2003-2006 to 5.1% in 2007-2010.
- This decrease in vaccine-type HPV prevalence occurred among females 14-19 years old despite only about a third of the females in this age group reporting having received at least one dose of HPV vaccine.
- Among the other older age groups, HPV prevalence did not differ significantly between the two time periods.

For more details, see JID, August 1, 2013.

Effectiveness of HPV4 Vaccine in Decreasing Cervical Cancer

- Australia started a publicly funded national vaccination program in 2007 with HPV4 vaccine in 12-13 year old girls along with a catch-up program through 26 years old.
- Over a four year period, HPV4 vaccine provided 46% protection against high-grade cervical abnormalities (adenocarcinoma *in situ*, cervical intraepithelial neoplasia 2, or worse) and 34% protection against other cervical abnormalities.
- Partial vaccination with two doses of HPV vaccine doses provided 21% protection against both high-grade and other cervical abnormalities.
- The vaccine seemed more effective in younger than older women.

See BMJ, published online March 4, 2014.

HPV4 Vaccine Prevents Cervical Cancer in Thirteen Countries

- HPV type 16 (HPV-16) and HPV type 18 (HPV-18) are the cause of about 70% of cervical cancers throughout the world.
- In a double-blinded, randomized study in HPV-negative women ages 15-26 years old, giving three doses of HPV4 vaccine had a 98% efficacy in preventing HPV-16/18-related high-grade cervical lesions.

See *New England Journal of Medicine*, May 10, 2007.

Reduced Prevalence of Oral HPV Types 16 and 18 after Bivalent HPV Vaccination (HPV2)

- Young women in Costa Rica who were 18-25 years old were given HPV2 vaccine (against HPV types 16 and 18). Four years later, they were tested for the presence of HPV16 or HPV18 in the oropharynx.
- HPV 16/18 vaccine was 93% effective in preventing against oral HPV16 or HPV18 infections.

For more details, see *PLOS ONE* on July 17, 2013.

HPV4 Vaccine Decreases Genital Warts by Danish National HPV Vaccine Program

- In Denmark, HPV4 vaccine was licensed for use in October 2006.
- Since January 2009, HPV4 vaccine has been offered at no cost to all girls 12 years of age as part of the national childhood vaccine program, with catch-up vaccination of girls up to 15 years of age, resulting in about 80-85% HPV vaccine coverage.
- The incidence of HPV and other sexually transmitted infections were studied between January 1995 and July 2011 to see the effect of HPV vaccination in teenage girls. The incidences of genital *Chlamydia*, syphilis, and gonorrhea for both sexes were stable or increased during the study period, as well as genital warts in males.
- The overall incidence of genital warts in women increased significantly until 2007, followed by an average yearly decline of 3.1% reflecting the increased number of HPV4 vaccinated women.
- Women aged 16 to 17 years had genital warts virtually eliminated, showing the benefit of high coverage levels of HPV4 vaccination.

See *Sexually Transmitted Diseases*, February 2013.

Genital Warts Decrease Due to Australian National HPV4 Vaccination Program

- Australia implemented a nationwide HPV4 vaccine program in 2007 by giving free HPV4 vaccine to school girls ages 12-13 years old, and free "catch up" vaccination to females through age 26 years old.
- The proportion of new patients diagnosed as having genital warts in the pre-vaccination period (2004 to mid-2007) were compared with patients with newly diagnosed genital warts in the vaccination period (mid-2007 to end of 2011).
- Over the first five years of Australia's national HPV vaccination program for females 12-26 years old:
    - The incidence of genital warts in teenage and adolescent girls fell by 92.6%.
    - Genital warts occurred 72.6% less often in women 21-30 years old.
    - No significant decline in genital warts occurred in women over 30 years of age.
    - Even though the national HPV vaccination program did not offer HPV vaccination to males, there was an 81.8% decrease in the diagnosis of genital warts in heterosexual males under 21 years old, and a 51.5% decrease in the diagnosis of genital warts among heterosexual young men between the ages of 21-30 years old, suggesting herd immunity.

For more details, see BMJ, April 18, 2013.

OVERCOMING BARRIERS TO HPV VACCINATION IN THE U.S.

Barriers to HPV Vaccination for Adolescent Girls in the U.S.

- Health care professionals cited financial concerns, and parental attitudes and concerns as barriers to HPV vaccination of adolescent girls.
- Parents had concerns about the HPV vaccine's effect on sexual behavior and the HPV vaccine cost. Other barriers were parents perceiving the risk of HPV infection to be low, social influences, and irregular preventive care visits.
- Some parents of boys reported not vaccinating their sons because they perceived a lack of direct benefit to their son.
- Parents often reported needing more information about the HPV vaccine.
- Parents consistently cited health care professional recommendations for HPV vaccination as one of the most important factors in their decision to vaccinate their children.

See the abstract at *JAMA Pediatrics*, January 2014.

No Increase in Markers of Sexual Activity Seen after HPV Vaccination

- To assess whether girls who received HPV vaccination were more likely to be sexually active, Kaiser Permanente researchers reviewed records on 11-12 year olds who received HPV vaccines and compared them with those who did not receive HPV vaccination.
- Over a three year period, markers of sexual activity were measured, such as seeking birth control advice, tests for sexually transmitted diseases, tests for pregnancy, or having become pregnant.
- There was no significant elevation in the rates of sexual activity markers among HPV-vaccinated girls in the first three years after vaccination compared with HPV-unvaccinated girls.

See *Pediatrics,* November 2012.

Provider Recommendation Is a Strong Predictor of HPV Vaccine Receipt

- HPV vaccination coverage was assessed for female adolescents ages 13 to 17 years old using data from the 2009 National Immunization Survey–Teen.
- More than half (56.9%) of the adolescents received a recommendation for the HPV vaccine from their healthcare provider.
- The adolescents with a healthcare provider recommendation were almost 5 times as likely to receive an HPV vaccine as those without a provider's recommendation.
- Racial/ethnic minorities were less likely to receive a recommendation for HPV vaccine. However, the positive association between healthcare provider recommendations and the patient's receipt of HPV vaccine was strong for all racial and ethnic groups.

See the abstract in *American Journal of Public Health,* January 2013.

HPV VACCINE RESOURCES

Centers for Disease Control and Prevention (CDC) HPV and HPV Vaccine Resources

- HPV Infections website
- HPV Vaccinations website
- Tips and Time-savers for talking with parents about HPV vaccination
- HPV-Associated Cancers. Webpages in English and Spanish
- CDC Cancer Prevention Campaign Promoting HPV Vaccine
    - "You Are the Key to HPV Cancer Prevention."
        - Video (Continuing education credit available until February 26, 2016)
        - Power Point Presentation to be used for community presentations

TAPI Campaign to Promote HPV Vaccines

- HPV vaccine oriented posters, banners, parent educational materials, teen-focused materials, and reminder recall posters are available to down load and order from the website of The Arizona Immunization Partnership (TAPI).

➢ Please feel free to distribute ADHS' *Arizona Vaccine News* to any of your partners who may be interested. Past issues of *Arizona Vaccine News* can be found at: http://www.azdhs.gov/phs/immun/vacNews.htm