Human Papillomavirus (HPV) Disease and the Status of HPV Vaccination in Wisconsin

Jeffrey P. Davis, MD

Chief Medical Officer and State Epidemiologist Bureau of Communicable Diseases and Emergency Response (BCDER) Division of Public Health Wisconsin Department of Health Services



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Objectives

- Describe the occurrence of HPV infections and their associated burden of disease among Wisconsin residents and other populations.
- Describe the efficacy, safety and importance of HPV vaccination to prevent HPV-associated cancers and other diseases.
- Describe the ACIP recommendations for HPV vaccination among males and females and how well we are doing with HPV vaccination in Wisconsin.
- Describe what is needed to improve HPV vaccination rates and reduce the burden of HPV related disease among Wisconsin residents.

Human papillomavirus (HPV) HPV infections HPV transmission Rapid acquisition of HPV infection after sexual debut

Human papillomavirus (HPV)

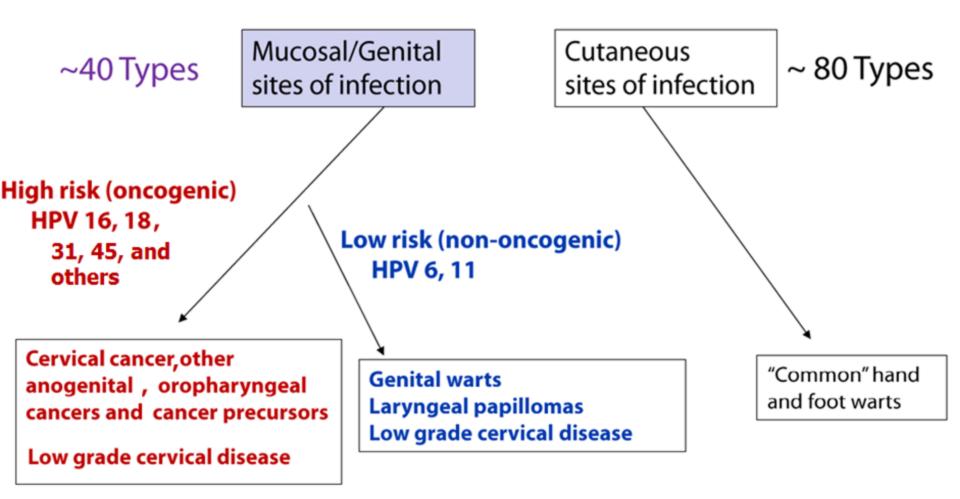
- HPV infections are the most common sexually transmitted infections in the United States.
- Relationship of cervical cancer and sexual behavior suspected for >100 years.
 - 1960s: established by epidemiologic studies.
 - 1980s: cervical cancer cells demonstrated to contain HPV DNA.
 - 1990s: results of numerous published studies consistently demonstrating association between HPV and cervical cancer.
- HPVs are small, double stranded DNA viruses.
 - Over 120 types identified: high risk (oncogenic) and low risk (nononcogenic).
 - Differentiated by the genetic sequence of the outer capsid protein L1.
 - Most HPV types infect mucosal epithelium or skin: infection begins at the basal epithelium.

CDC Pink Book. Epidemiology and Prevention of Vaccine-Preventable Diseases. Atkinson W, et al., eds. 12th ed., second printing. Washington DC: Public Health Foundation, 2012.

Laboratory diagnosis of HPV

- HPV has not been isolated in culture.
- HPV infection is diagnosed by detection of HPV DNA from clinical samples.
 - Variable sensitivity and type specificity.
 - Detection affected by specimen collection or anatomic site.
- Epidemiologic and research studies use nucleic acid amplification that generate type-specific results: wide array of HPV types can be detected.
- Current FDA-approved HPV DNA (nucleic acid hybridization) test detects 13 high-risk types:
 - HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68.
 - Results: positive or negative, not type-specific.
- Serologic tests (EIAs) are not standardized.

HPV types and disease association



Mona Saraiya, MD, MPH. Public Health Importance of HPV Infection and Disease. PowerPoint Presentation. CDC Pink Book. Epidemiology and Prevention of Vaccine-Preventable Diseases. Atkinson W, et al., eds. 12th ed., second printing. Washington DC: Public Health Foundation, 2012.

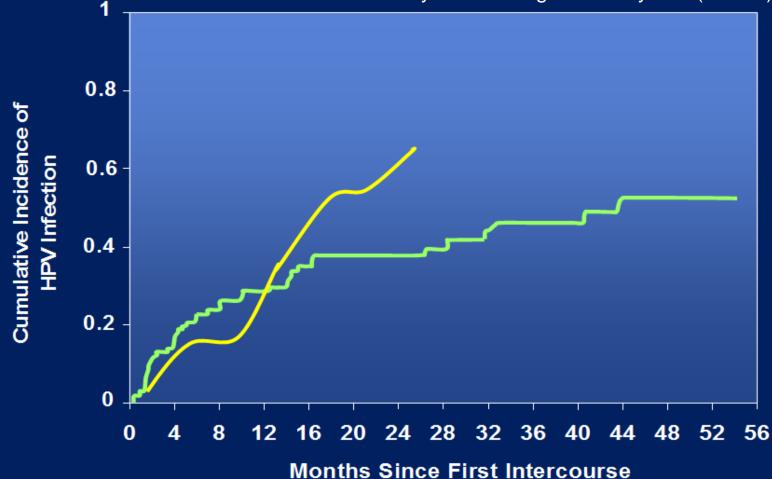
HPV transmission

- HPV: readily transmissible, infections are common
 - 1 in 4 people in the United States (nearly 80 million) currently infected with <u>></u>1 HPV types
 - 14 million new infections annually in the United States
 - Almost all sexually active men and women will be infected with HPV at some point in their lives, even those with only one sexual partner
- HPV: modes of transmission
 - Direct contact (usually sexual) with an infected person
 - Can occur during any type of intimate sexual contact (including nonpenetrative sexual activity)
 - Small longitudinal study of adolescent females without prior vaginal intercourse: prevalence of vaginal HPV infection was 46% (10/22)
 - Non-sexual transmission of genital HPV uncommon: woman to newborn infant during birth
- HPV infection
 - Acquired shortly after becoming sexually active
 - Most common among persons in their early 20's

Accelerating HPV Vaccine Uptake: Urgency for Action to Prevent Cancer. A Report to the President of the United States from the President's Cancer Panel. Bethesda, MD: National Cancer Institute; 2014. CDC Pink Book 2012. Shew ML, et al. *J Infect Dis* 2013;207:1012-1015. Hariri S, et al. *J Infect Dis* 2011;204:566-572.

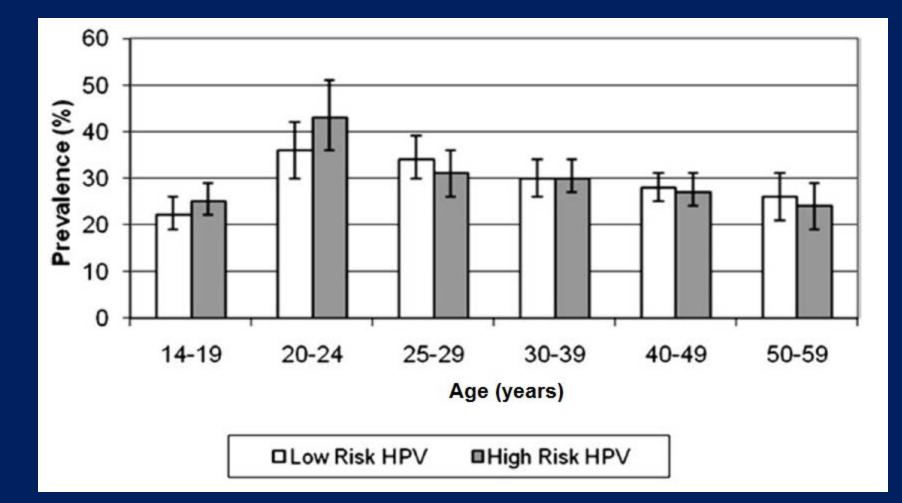
Rapid acquisition of HPV following sexual debut

Partridge et al. Male university students aged 18-23 years (N=240)
 Winer et al. Female university students aged 18-20 years (N=603)



Winer RL, et al. American Journal of Epidemiology 2003;157:218-226. Partridge M, et al. The Journal of Infectious Diseases 2007;196 (8): 1128-1136. CDC. You Are the Key to HPV Cancer Prevention. PowerPoint Presentation. September 9, 2013.

Prevalence of HPV infection among women aged 14-59 years, United States, NHANES*, 2003-2006



*National Health and Nutrition Examination Survey (NHANES)

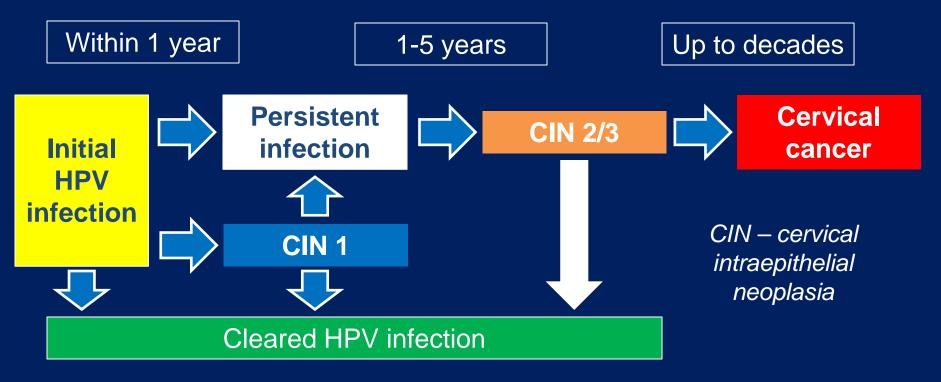
Hariri S, et al. *The Journal of Infectious Diseases* 2011;204:566-572. Mona Saraiya, MD, MPH. Public Health Importance of HPV Infection and Disease. PowerPoint Presentation.

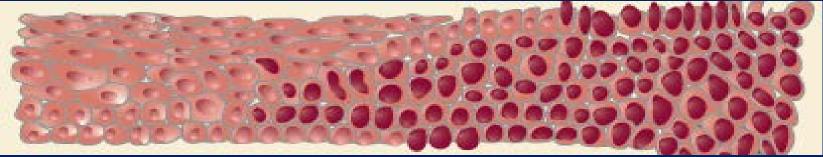
Natural history of HPV infections

HPV infections

- Most HPV infections are asymptomatic and cleared within two years with no resultant disease.
- If not cleared, clinical manifestations can include: anogenital warts, recurrent respiratory papillomatosis (RRP), cervical cancer precursors (cervical intraepithelial neoplasia = CIN), and cancer (cervical, anal, vaginal, vulvar, penile and oropharyngeal).

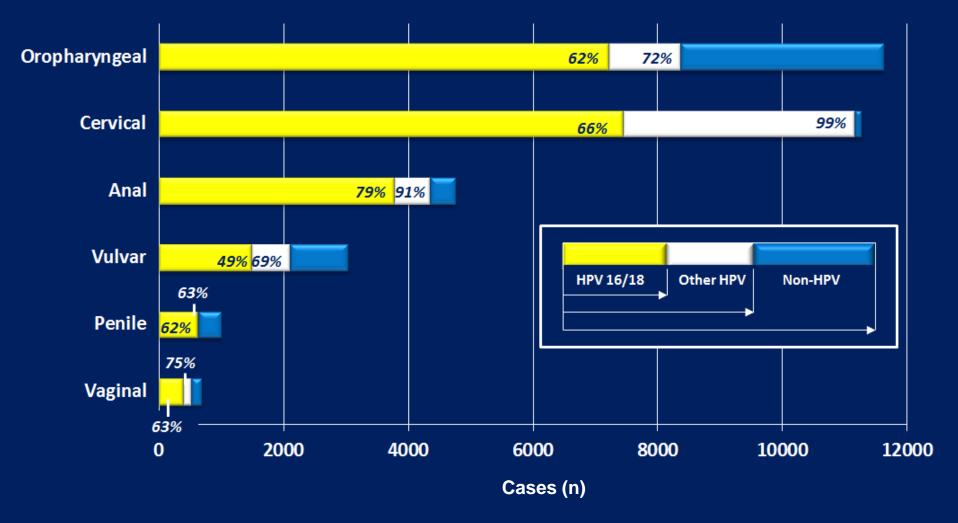
Natural history of HPV infections: cervix





CDC Pink Book. 12th ed. Washington DC: Public Health Foundation, 2012. Accelerating HPV Vaccine Uptake: Urgency for Action to Prevent Cancer. A Report to the President of the United 12 States from the President's Cancer Panel. Bethesda, MD: National Cancer Institute; 2014.

Distribution of cancers attributable to HPV, by anatomic site, United States, 2005-2008



CDC. You Are the Key to HPV Cancer Prevention. PowerPoint Presentation. September 9, 2013. Jemal A, et al. *Journal of the National Cancer Institute* 2013;105:175-201.

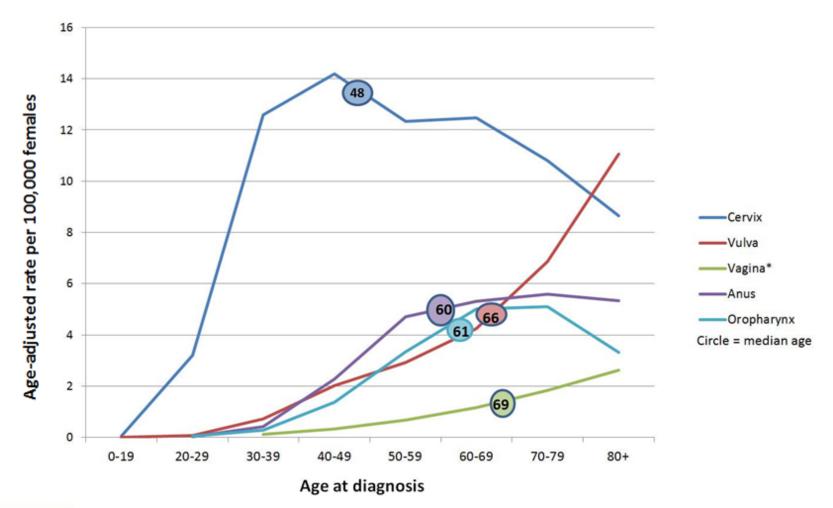
The burden of HPV infection and related diseases: United States

Number and percentages of new HPV-associated cancers by anatomic site and by gender, United States, 2005-2009

Total Men Women (n=12,002)(n=32,415)(n=20,413)Penis, 3% Vagina, Penis, 8% Vagina, 4% n=1,003 **2%** n=694 n=1.003 n=694 Vulva, 9% n=3,039 Vulva, 15% n=3.039 Anus, 14% **Cervix**, 35% n=1,687 n=11,279 Anus, 15% n=4,771 Anus, 15% **Cervix**, 55% n=3.084 n=11,279 **Oropharynx**, 78% n=9.312 **Oropharynx**, 36% Oropharynx, 11% n=11.629 n=2,317

Mona Saraiya, MD, MPH. Public Health Importance of HPV Infection and Disease. PowerPoint Presentation. 1 Jemal A, et al. *Journal of the National Cancer Institute* 2013;105:175-201.

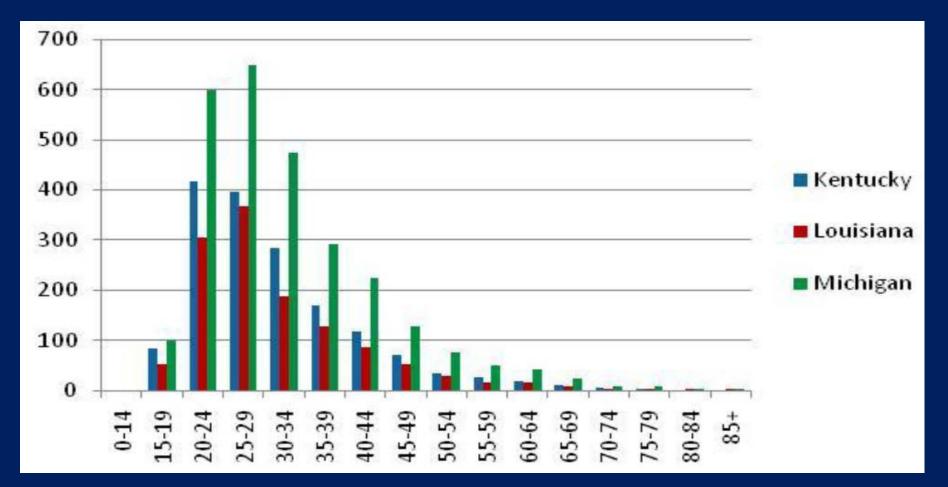
Rates of HPV-Associated Cancer and Median Age at Diagnosis Among Females in the United States, 2004–2008





Age-adjusted to the 2000 U.S. standard population.

*The vaginal cancer statistic for women between the ages of 20 and 39 is not shown because there were fewer than 16 cases. Data from population-based cancer registries participating in the CDC-supported National Program of Cancer Registries and/or the National Cancer Institute-supported Surveillance, Epidemiology and End Results Program, meeting criteria for high data quality, and covering 100% of the population. Published in: Watson et al. Human papillomavirus-associated cancers—United States, 2004–2008. *MMWR* 2012;61:258–261. Numbers of cases of CIN3 and adenocarcinoma *in situ* (AIS) by age group, Kentucky, Louisiana and Michigan cancer registries, 2009



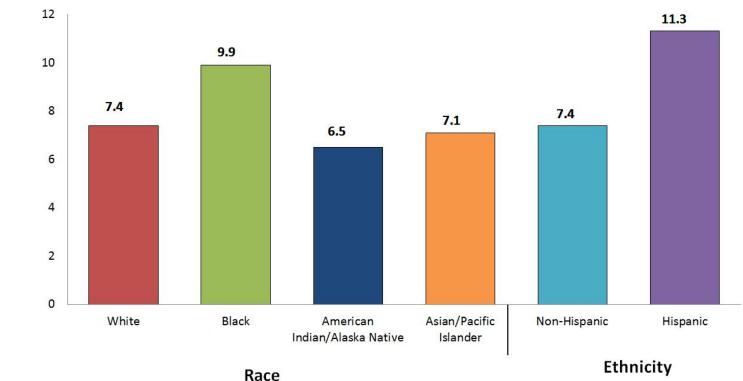
Flagg E. Population Based Surveillance for High-grade Pre-invasive Cervical Cancer in Three Central Cancer 17 Registries, United States 2009. PowerPoint Presentation. June 23, 2011.

CIN3 and AIS incidence (per 100,000), by age group, Kentucky, Louisiana and Michigan cancer registries, 2009

	Kentucky	Louisiana	Michigan
Age at			
Diagnosis			
0-14	0.00	0.00	0.00
15-19	59.75	33.21	27.91
20-24	287.43	178.70	175.69
25-29	265.25	215.90	211.74
30-34	207.29	130.58	165.19
35-39	117.48	91.89	89.74
40-44	78.98	59.00	64.61
45-49	43.29	30.33	33.24
50-54	21.74	17.60	19.26
55-59	18.06	10.33	14.38
60-64	14.69	12.55	14.62
65-69	11.68	9.81	11.20
70-74	8.09	5.51	4.21
75-79	4.90	3.30	4.96
80-84	0.00	2.03	1.67
85+	0.00	4.11	2.36

Flagg E. Population Based Surveillance for High-grade Pre-invasive Cervical Cancer in Three Central Cancer 1 Registries, United States 2009. PowerPoint Presentation. June 23, 2011.

HPV-Associated Cervical Cancer Rates by Race and Ethnicity, United States, 2004–2008



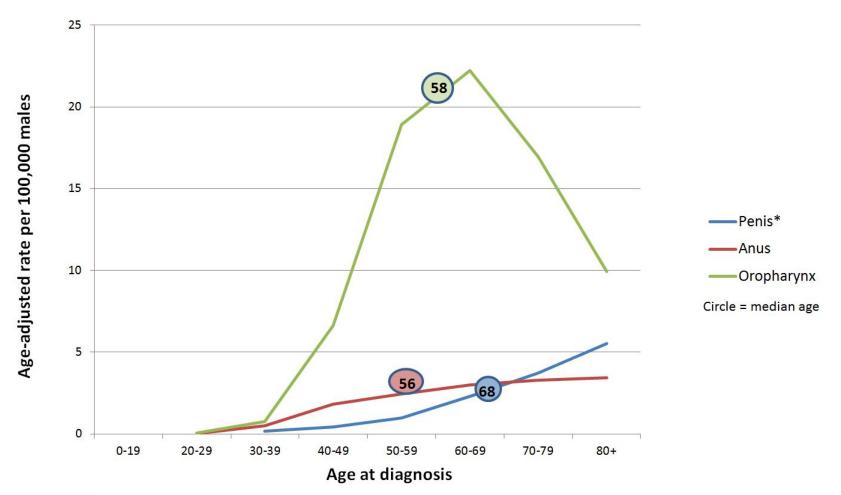


*Age-adjusted to the 2000 U.S. standard population.

Data from population-based cancer registries participating in the CDC-supported National Program of Cancer Registries and/or the National Cancer Institute-supported Surveillance, Epidemiology and End Results Program, meeting criteria for high data quality, and covering 100% of the population. Published in: Watson et al. Human papillomavirus-associated cancers—United States, 2004–2008. *MMWR* 2012;61:258–261.

Age-adjusted rate per 100,000 females

Rates of HPV-Associated Cancer and Median Age at Diagnosis Among Males in the United States, 2004–2008

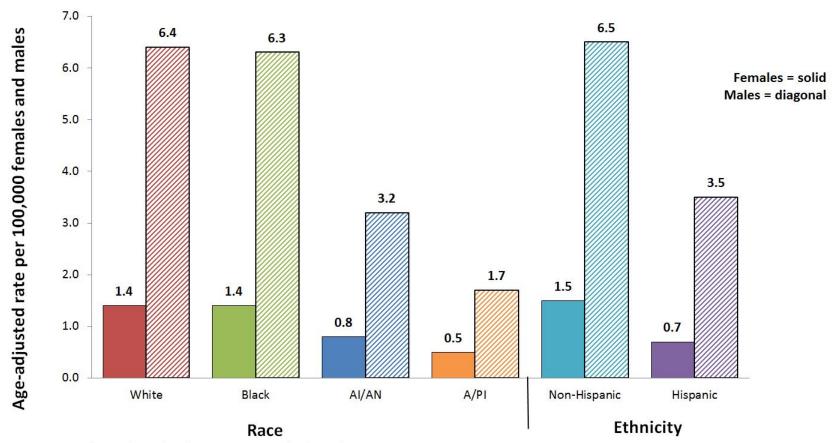




Age-adjusted to the 2000 U.S. standard population.

*The penile cancer statistic for men between the ages of 20 and 39 is not shown because there were fewer than 16 cases. Data from population-based cancer registries participating in the CDC-supported National Program of Cancer Registries and/or the National Cancer Institute-supported Surveillance, Epidemiology and End Results Program, meeting criteria for high data quality, and covering 100% of the population. Published in: Watson et al. Human papillomavirus-associated cancers—United States, 2004–2008. *MMWR* 2012;61:258–261.

HPV-Associated Oropharyngeal Cancer Rates by Race and Ethnicity, United States, 2004–2008



*Age-adjusted to the 2000 U.S. standard population.



Data from population-based cancer registries participating in the CDC-supported National Program of Cancer Registries and/or the National Cancer Institute-supported Surveillance, Epidemiology and End Results Program, meeting criteria for high data quality, and covering 100% of the population. Some cancers of the oropharynx (back of the throat, including the base of the tongue and tonsils) have been linked with HPV. Cancers in this area of the body are usually caused by tobacco and alcohol, but recent studies show that about 63% of oropharyngeal cancers are caused by HPV. These numbers are based on cancers in specific areas of the oropharynx and do not include cancers in all areas of the head and neck or oral cavity. Published in: Watson et al. Human papillomavirus-associated cancers—United States, 2004–2008. *MMWR* 2012;61:258–261.

Oropharyngeal cancers diagnosed during 1995-2005, United States

Residual Tissue Repository Program

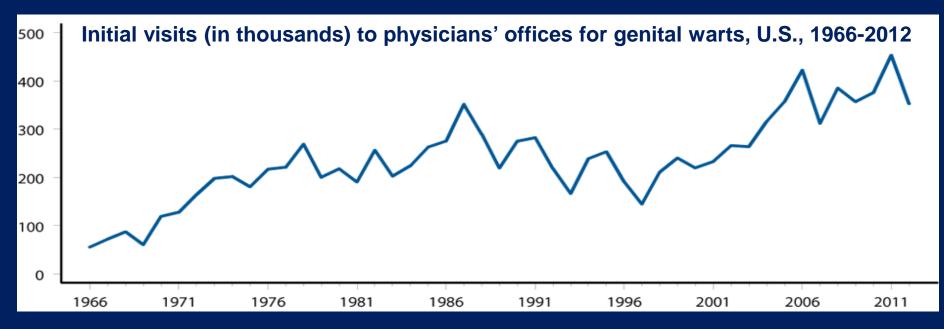
- Testing to establish a pre-vaccine baseline for monitoring impact of HPV vaccination
- Tumor tissue from 557 patients with invasive oropharyngeal squamous cell carcinoma
 - 72% HPV positive
 - 62% HPV 16 and 18
 - Males 66%, females 53%
 - Non-Hispanic blacks 31%, other racial-ethnic groups 68-80%
- **Conclusions**: HPV4 vaccine could prevent most oropharyngeal cancers in the United States, but efficacy may vary by demographic variables.

Complications related to current methods of cervical cancer management and prevention contributes to the burden of disease

- Infertility resulting from treatment of cervical cancer by hysterectomy
- Cervical conization and loop electrosurgical excision procedures (LEEP) are associated with risks and impacts during subsequent pregnancies
 - Perinatal mortality
 - Severe (32-34 weeks) and extreme (<28-30 weeks) preterm delivery
 - Severe (<1500-2000g) and extreme (<1500g) low birth weight
 - Long term impacts on mothers and infants
 - Costs of neonatal intensive care

Burden of disease caused by low-risk or non-oncogenic HPV types – anogenital warts

- 300,000-450,000 genital warts-related initial visits annually since 2006 in the United States
- Peak incidence among persons aged 20-29 years
 Over 90% associated with HPV type 6 and 11



CDC. 2012 Sexually Transmitted Disease Surveillance: <u>http://www.cdc.gov/Std/stats12/figures/46.htm</u> CDC Pink Book. Washington DC: Public Health Foundation, 2012. Mona Saraiya, MD, MPH. Public Health Importance of HPV Infection and Disease. PowerPoint Presentation.

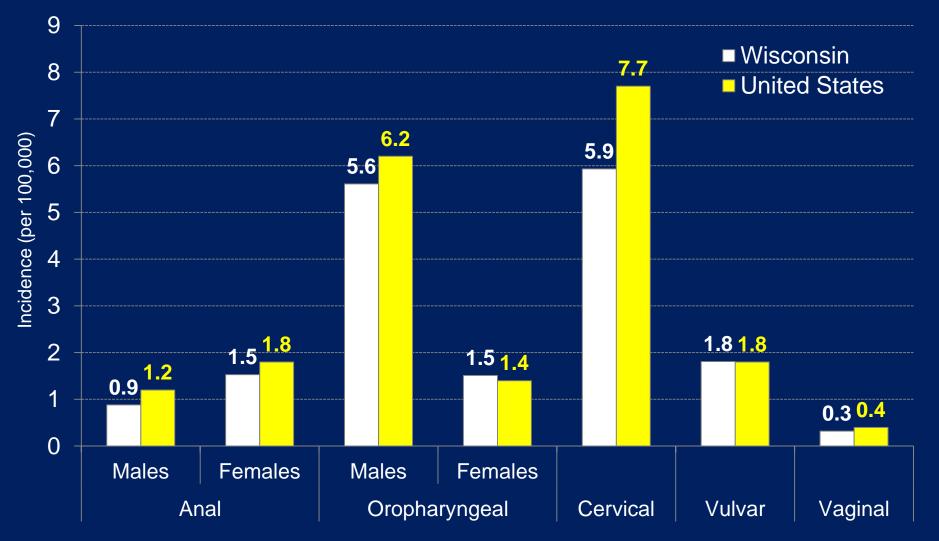
Burden of disease caused by low-risk or non-oncogenic HPV types – RRP

- Recurrent respiratory papillomatosis (RRP) or laryngeal papillomatosis
 - Caused by HPV types 6 and 11
 - Occur in children (juvenile-onset) and adults
 - Most common benign neoplasm of the larynx in children
 - Estimated 820 new cases of J-O RRP annually in US
- Can result in airway obstruction requiring multiple surgeries
 - 1%-3% of children with RRP die as a result of papilloma spread to lung parenchyma
 - Challenge to anesthesia administration

Accelerating HPV Vaccine Uptake: Urgency for Action to Prevent Cancer. A Report to the President of the United States from the President's Cancer Panel. Bethesda, MD: National Cancer Institute; 2014. Armstrong L, et al. *Clinical Infectious Diseases* 2000;31(1): 107-109.

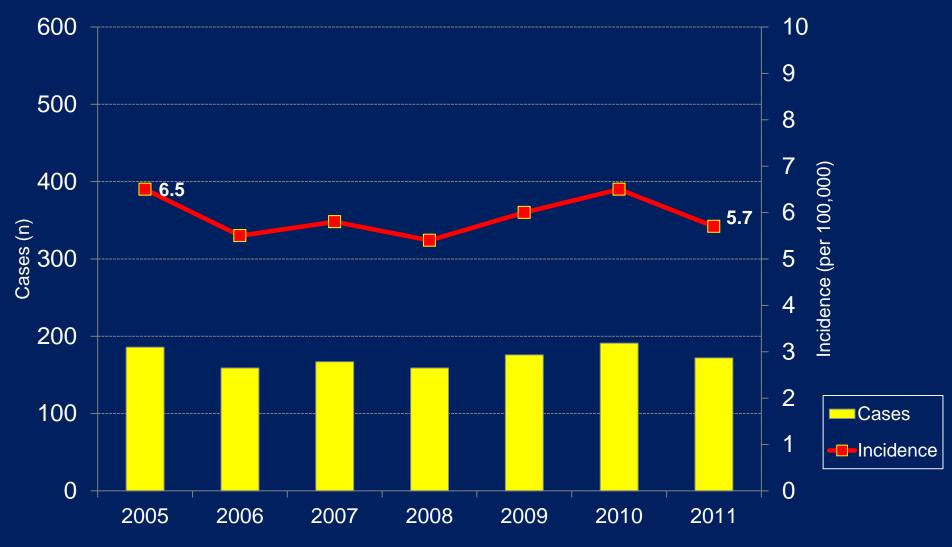
The burden of HPV infection and related diseases: Wisconsin

Incidence of HPV-associated cancers, by anatomic site, Wisconsin and United States, 2004-2008



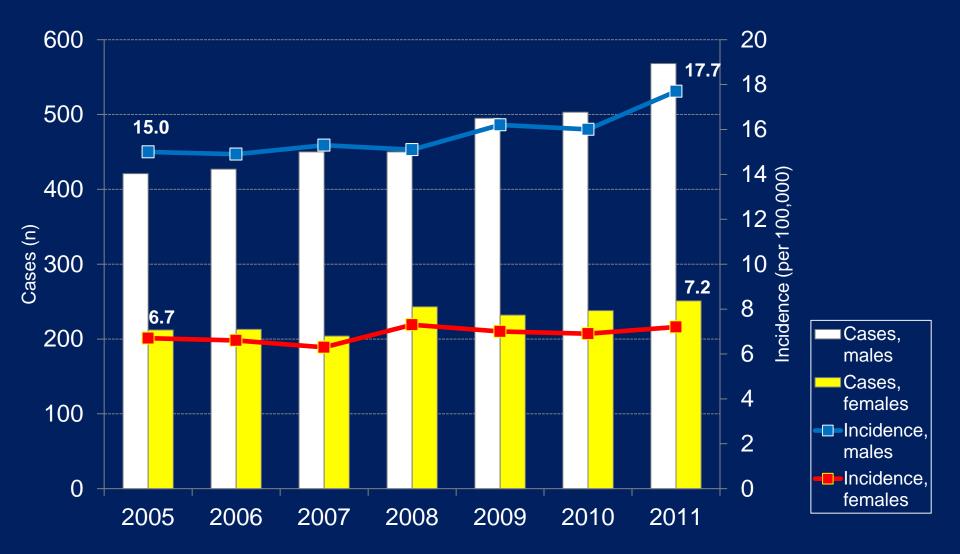
CDC. Human papillomavirus-associated cancers – United States, 2004-2008. *MMWR* 2012 Apr 20;61(15):258-61. 27 HPV-associated cancer rates by state: <u>http://www.cdc.gov/cancer/hpv/statistics/state/index.htm</u>

Number of cervical cancer cases and age-adjusted incidence, Wisconsin, 2005-2011



Incidence rate is age-adjusted to the 2000 U.S. standard population Data source: Wisconsin Interactive Statistics on Health (WISH) <u>https://www.dhs.wisconsin.gov/WISH/cancer/</u>

Number of oropharyngeal cancer cases and ageadjusted incidence by gender, Wisconsin, 2005-2011



Incidence rate is age-adjusted to the 2000 U.S. standard population. Data source: Wisconsin Interactive Statistics on Health (WISH) <u>https://www.dhs.wisconsin.gov/WISH/cancer/</u>

The burden of HPV infection and related diseases: Costs, United States

Economic impact (direct medical costs) of HPVassociated disease, United States, 2010

Event	Cost (\$ billions)		
Cervical cancer screening*	6.6		
Cervical cancer	0.4		
Other anogenital cancers	0.2		
Oropharyngeal cancer	0.3		
Anogenital warts	0.3		
RRP**	0.2		
TOTAL	8.0		

*Cervical cancer screening costs: ~80% routine screening and ~20% follow-up **RRP costs: ~70% juvenile-onset, ~30% adult-onset

Characteristics of episodes of genital warts involving physician management: private health plans, United States, 2000

Characteristic	Male patients $(n = 237)$	Female patients $(n = 299)$	$\begin{array}{l} AII\\ (n = 536) \end{array}$
Duration of episode, mean days (95% CI)	102.6 (77.8–127.4)	84.8 (67.5-102.1)	92.7 (85.3–100.2)
Mean no. of physician visits (95% CI)	3.1 (2.8–3.5)	3.1 (2.8–3.4)	3.1 (2.9–3.3)
Cost, mean US\$ (95% CI)	477 (365–590)	404 (316–492)	436 (365–508)
Therapy, % of patients			
Patient applied ^a	37	41	39
Physician applied	62	58	60
Patient and physician applied	21	21	21

^a Includes imiquimod and podofilox and reflects use of patient-applied therapy alone or in combination with physicianapplied therapy.

 Over 40% recurrence, resulting in repeat clinical visits, treatments, and psychological stigma

Summary of burden of HPV infection and related diseases: United States

- Over 60% of oropharyngeal, cervical, anal, penile, and vaginal cancers in the United States are attributable to HPV 16 and 18.
- Over 32,000 new HPV-associated cancers are diagnosed annually among men and women in the U.S.
 - 35% cervical and 36% oropharyngeal cancers
 - Variability by racial and ethnic groups
- Cervical cancer precursor data (state cancer registries) demonstrate peak incidence of CIN among women aged 20-34 years (detected among women aged as young as 15-19 years).
 - Adverse obstetric morbidity associated with current methods of cervical cancer management and prevention
- HPV 6 and 11 are associated with significant burden related to anogenital warts and RRP.

HPV vaccines and vaccine immunogenicity

HPV vaccines licensed in the United States

- Quadrivalent HPV (HPV4) vaccine (Gardasil®)
 - Contains HPV types 16 and 18 (high risk) and types 6 and 11 (low risk)
 - Approved for females and males aged 9 through 26 years
- Bivalent HPV (HPV2) vaccine (Cervarix®)

- Contains HPV types 16 and 18 (high risk)

Approved for females aged 10 through 25 years

CDC Pink Book. Epidemiology and Prevention of Vaccine-Preventable Diseases. Atkinson W, et al., eds. 12th ed., 35 second printing. Washington DC: Public Health Foundation, 2012.

HPV vaccines licensed in the United States

- HPV4 and HPV2 are inactivated subunit vaccines:
 - Antigens: L1 major capsid protein of each of the HPV vaccine types
 - Antigens produced using recombinant DNA technology
 - L1 proteins self- assemble to form non-infectious and non-oncogenic virus-like particles (VLP)

HPV vaccine immunogenicity

- Both HPV4 and HPV2 are highly immunogenic
 - Produce higher levels of neutralizing antibody than natural infection
 - More than 99% of recipients develop an antibody response to the HPV types contained in the respective vaccines one month post 3-dose series completion

HPV vaccine efficacy

- HPV4 vaccine efficacy (VE):
 - Two large double blind, placebo control trials among women aged 16-26 years
 - VE 97% against HPV 16 and 18-related cervical intraepithelial neoplasia (CIN) grades 2 and 3 (CIN 2/3) or adenocarcinoma insitu (AIS)
 - VE 95% against any CIN caused by HPV 6, 11, 16, 18
 - VE 99% against HPV 6, 11, 16, and 18-related genital warts
 - VE 90% against HPV 6 and 11-related genital warts
- HPV2 vaccine efficacy:
 - Two large randomized, double blind, controlled clinical trials among females aged 15-25 years
 - VE 93% against HPV 16 and 18-related CIN 2/3 or AIS

CDC Pink Book. Epidemiology and Prevention of Vaccine-Preventable Diseases. Atkinson W, et al., eds. 12th ed., 38 second printing. Washington DC: Public Health Foundation, 2012.

HPV vaccine immunogenicity (continued)

- Better antibody response is observed among preteens compared to older teens
 - Results of immunogenicity studies during VE trials
 - 18 months post HPV4 series completion, anti-HPV antibodies in females aged 9-15 years were two- to three-fold higher than those observed in females aged 16-26 years

HPV vaccine immunogenicity (continued)

- Duration of immunity
 - For both vaccines, subset of participants followed for >60 months with no evidence of waning immunity
 - Anti-HPV antibody titers decline over time after the third dose but plateau by 24 months
 - Vaccinated women given a challenge dose (revaccinated)
 5 years after enrollment demonstrated increase in antibody titer consistent with immune memory
 - This available evidence suggests protection for at least 8-10 years
 - Multiple cohort studies in progress to monitor duration of immunity

HPV vaccines: ACIP recommendations and vaccine safety

ACIP recommendations for routine HPV vaccination

- Three-dose series: females and males aged 11-12 years
 - Series schedule: 0, 1-2, and 6 months
 - Permissive recommendation: males and females aged 9-10 years
- Catch-up vaccination: females aged 13-26 years and males aged 13-21 years who have not completed the vaccine series

– Permissive recommendation: males aged 22-26 years

 Routinely recommended for men who have sex with men (MSM) and immunocompromised persons aged 22 through 26 years

HPV vaccine contraindications and precautions

Contraindication (vaccine should not be given)

• Severe allergic reaction (e.g., anaphylaxis) to a vaccine component or following a prior dose of the HPV vaccine

Precautions (assess benefits and risks)

- Moderate or severe acute illness with or without fever
- Pregnancy

HPV vaccines: safety monitoring

- For all vaccines, the CDC and FDA use the data sources below and continue to carefully monitor their safety:
 - Vaccine Adverse Events Reporting System (VAERS) postlicensure safety monitoring.
 - Vaccine Safety Datalink (VSD) post-licensure observational comparative studies.
- Other safety monitoring systems include:
 - Post-licensure commitments from vaccine manufacturers.
 - Registries for vaccines administered during pregnancy.
 - Long-term follow-up in Nordic countries.
 - Official reviews.
 - WHO's Global Advisory Committee on Vaccine Safety.
 - The Institute of Medicine's report on adverse effects and vaccines, 2011.

CDC. You Are the Key to HPV Cancer Prevention. PowerPoint Presentation. September 9, 2013.

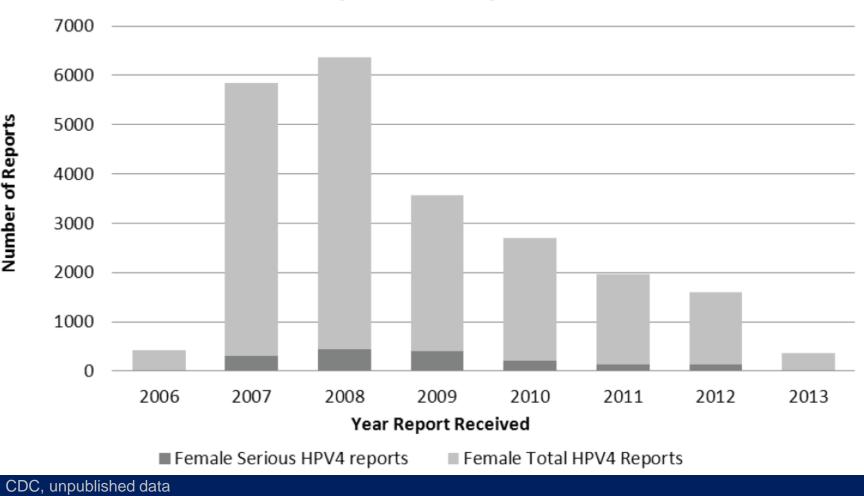
HPV vaccines: safety

- More than 57 million doses of HPV vaccine distributed in the U.S. since 2006 and more than 175 million doses worldwide.
 - Most common adverse events reported are local reactions at the site of injection (20-90%) and fever (10-13%).
 - No new safety concerns identified during post-licensure vaccine safety surveillance among vaccine recipients.
 - Among 7.9% of reports coded as "serious," most frequently cited include: headache, nausea, vomiting, fatigue, dizziness, syncope, and generalized weakness.
- Syncope continues to be a frequently reported adverse event among adolescents in general.

Markowitz L. HPV Vaccination Program and Impact Monitoring: <u>http://www.cdc.gov/vaccines/acip/meetings/downloads/slides-jun-2013/04-HPV-Markowitz.pdf</u> CDC Pink Book. Epidemiology and Prevention of Vaccine-Preventable Diseases. Atkinson W, et al., eds. 12th ed., 45 second printing. Washington DC: Public Health Foundation, 2012.

Trends in total and serious female HPV4 vaccine reports to VAERS, 6/1/2006-3/31/2013

(N=21,194)



Markowitz L. HPV Vaccination Program and Impact Monitoring:

http://www.cdc.gov/vaccines/acip/meetings/downloads/slides-jun-2013/04-HPV-Markowitz.pdf

HPV vaccination: Measures of early program impacts

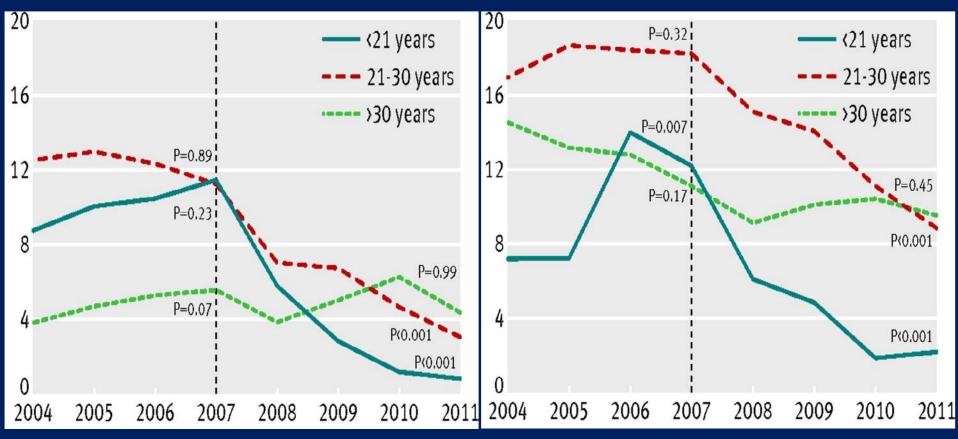
HPV vaccination: examination of trends of genital warts occurrence as a measure of early program impact Australia

- Nationally funded HPV4 vaccination for girls and young women began in 2007.
 - Females 12-13 vaccinated in schools:
 - Coverage in 2010: Dose 1 83%, Dose 2 80%, Dose 3 73%
 - Catch-up programs during 2007-2009 for females aged 13-18 years in school and females aged 18-26 years in the community.
 - Males not routinely vaccinated.
- HPV data among 85,770 patients seen for 1st time at 8 sexual health services clinics: 2004-2011.
- Declines in prevalence of genital warts diagnoses from 2007 to 2011
 - Females aged <21 years: 93% decline (11.5% to 0.85%, p<.001)
 - Females aged 21-30 years: 73% decline (11.3% to 3.1%, p<.001)
 - Males (heterosexual) aged <21 years: 82% decline (12.1% to 2.2%, p<.001)
 - Males (heterosexual) aged 21-30 years: 51% decline (18.2% to 8.9%, p<.001)
 - Females and males aged >30 years: no significant decline
- **Conclusions**: High efficacy of HPV4 within and outside trial setting among females. Significant declines of genital wart prevalence among males suggest herd immunity.

Proportion of Australian-born women and heterosexual men diagnosed with genital warts at first visit, by age group, 2004-2011

Females (%)

Heterosexual males (%)

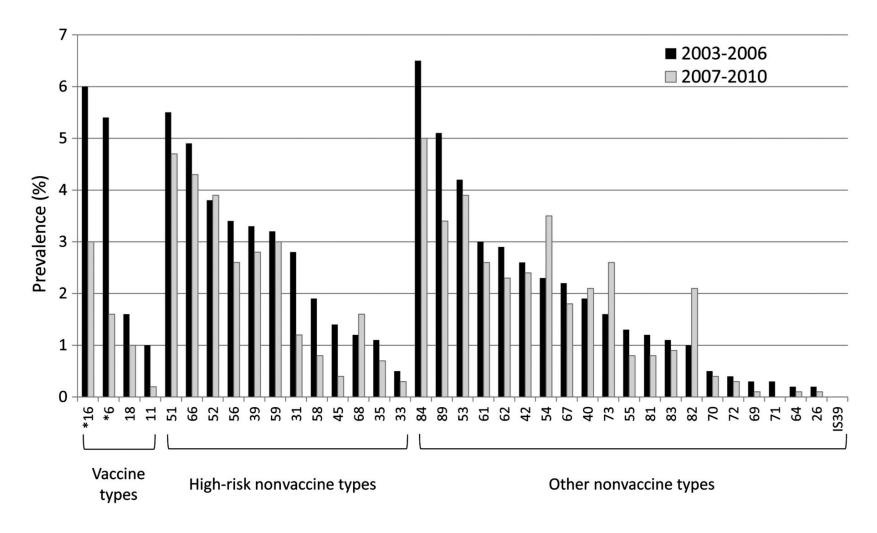


Ali H, et al. Genital warts in young Australians five years into national human papillomavirus vaccination programme: 49 national surveillance data. *British Medical Journal* 2013:346.

HPV vaccination: early measure of impact United States, NHANES, 2003-2010

- CDC study using data from the National Health and Nutrition Examination (NHANES) Surveys.
- Compared vaccine-type (6, 11, 16, 18) HPV prevalence among cervicovaginal swab samples (Linear Array HPV Assay) collected pre-HPV vaccine licensure (2003-2006) to HPV prevalence among samples collected during the first four years following HPV vaccine licensure (2007-2010). ACIP recommendations for routine and catchup vaccination during 2006. HPV vaccination data collected during 2007-2010.
 - 3-dose HPV vaccine coverage among females aged 13-17 was only 32% during 2010.
 - Among females aged 14-19 years, vaccine-type HPV prevalence decreased 56% from 11.5% (9.2-14.4) during 2003-2006 to 5.1% (3.8-6.6) during 2007-2010.
 - Estimated vaccine effectiveness (VE) of \geq 1 dose was 82% (53-93).
- **Conclusions**: Significant decrease of HPV vaccine strain prevalence among females aged 14-19 years despite low vaccine uptake. The estimated VE was high.

Prevalence of individual human papillomavirus (HPV) types among females aged 14–19 years, 2003–2006 and 2007–2010



Markowitz L E et al. J Infect Dis. 2013;infdis.jit192



HPV vaccination: early markers of impact Indiana, urban primary care clinic

- Compared at-risk sexually active females aged 14-17 years attending 3 urban primary care clinics (Indiana) during 2010 (n=75; 89.3% received >1 HPV4) to age-matched historic controls (2:1 match) who attended the same 3 clinics during 1999-2005 (pre-vaccine).
- Self-collected vaginal swabs from all participants in both groups, plus completion of sexual behaviors survey during interview.
- Significant decrease in detection of HPV4 types (6, 11, 16, 18) from 24.0% during 1999-2005 to 5.3% during 2010 (OR 5.6; CI 1.9, 16.5; p=0.002) despite incomplete vaccination and high risk sexual behaviors.
- Only behavioral difference (among many assessed) was 2010 group used condoms more often.
- Data suggest sexual behaviors were not altered because of the vaccine.

Cummings T, et al. Vaccine 2012;30:5496-5499.

HPV vaccination: early markers of impact Indiana and Ohio, 2 urban primary care clinics

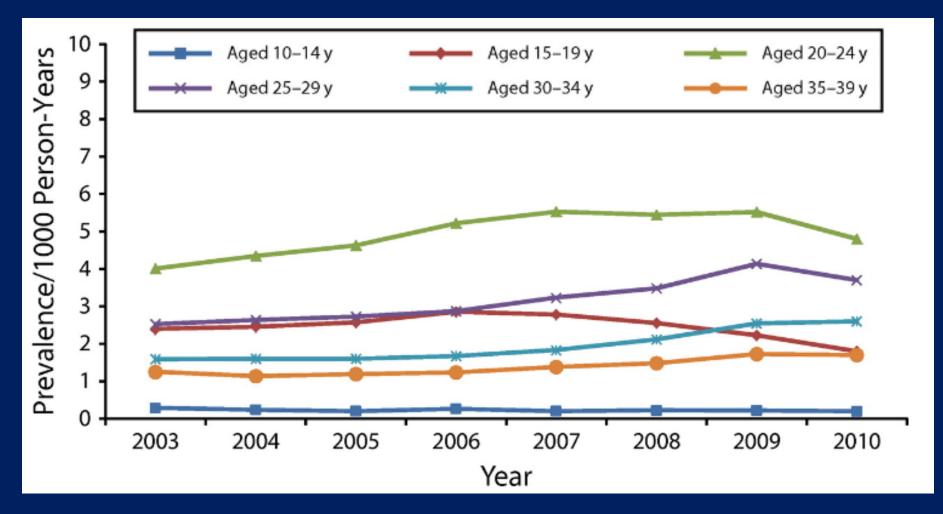
- Females aged 13-26 years: all had sexual contact, completed questionnaire, tested for cervicovaginal HPV DNA
 - Pre-vaccine period (2006-2007), N=368
 - Post vaccine period (2009-2010), N=409, 59% HPV vaccinated
 - Both groups comparable R/E and mean age (19 years)
- Vaccine-type HPV prevalence among pre-vaccine period vs. post-vaccine period participants:
 - Pre- vs. post-vaccine period -- All: 31.7% vs. 13.4%, p<0.0001
 - Pre- vs. post-vaccine -- vaccinated: 31.8% vs. 9.9%, p<0.0001
 - Pre- vs. post-vaccine -- unvaccinated: 30.2% vs. 15.4%, p<0.0001
- Four years after HPV vaccine licensure: decrease in vaccine-type
 HPV prevalence and evidence of herd protection in the community

HPV vaccines: early markers of impact Health claims data

- Ecologic analysis used health claims data to examine trends in anogenital warts during 2003-2010 among a large group of private health insurance enrollees.
 - Significant declines after 2007 among females aged 15-19 years (38% decrease from 2.9/1000 person-years during 2006 to 1.8/1000 person-years during 2010).
 - Smaller declines were observed among females aged 21-30 years, but none among those aged >30 years.
- Study evaluating genital wart trends in males and females attending public family planning clinics.
 - Significant decrease of 35% (.94% to .61%) among females aged <21 years and a 19% decrease among males <21 years.
 - No decreases reported among older males and females.

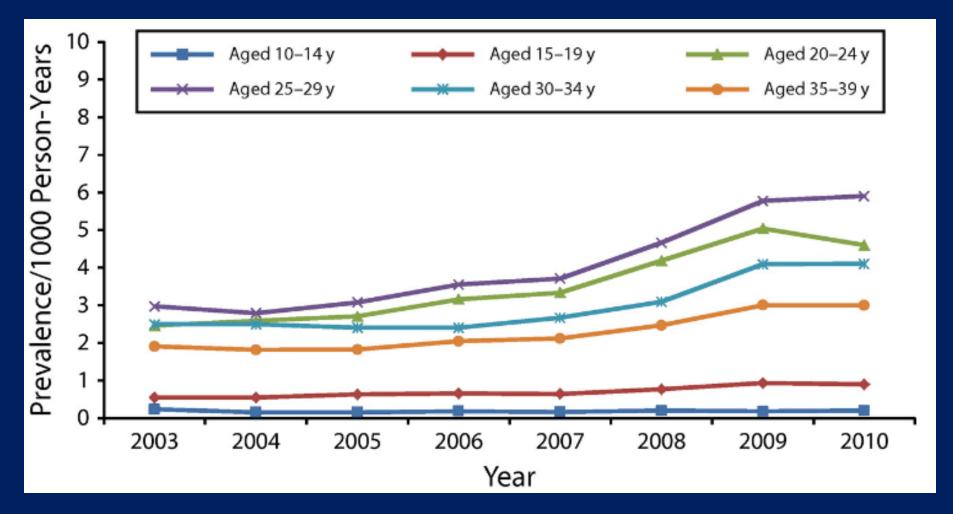
CDC. You Are the Key to HPV Cancer Prevention. PowerPoint Presentation. September 9, 2013. Markowitz L. HPV Vaccination Program and Impact Monitoring: <u>http://www.cdc.gov/vaccines/acip/meetings/downloads/slides-jun-2013/04-HPV-Markowitz.pdf</u>

Anogenital wart prevalence among females with private health insurance, by age, U.S., 2003-2010



Flagg E, et al. *American Journal of Public Health 2013;103(8):1428-1435.* (Data source: Truven Health Analytics MarketScan Commercial Claims and Encounters Database, United States, 2003–2010.) Markowitz L. HPV Vaccination Program and Impact Monitoring: <u>http://www.cdc.gov/vaccines/acip/meetings/downloads/slides-jun-2013/04-HPV-Markowitz.pdf</u>

Anogenital wart prevalence among males with private health insurance, by age, U.S., 2003-2010



Flagg E, et al. *American Journal of Public Health 2013;103(8):1428-1435.* (Data source: Truven Health Analytics MarketScan Commercial Claims and Encounters Database, United States, 2003–2010.) Markowitz L. HPV Vaccination Program and Impact Monitoring: <u>http://www.cdc.gov/vaccines/acip/meetings/downloads/slides-jun-2013/04-HPV-Markowitz.pdf</u>

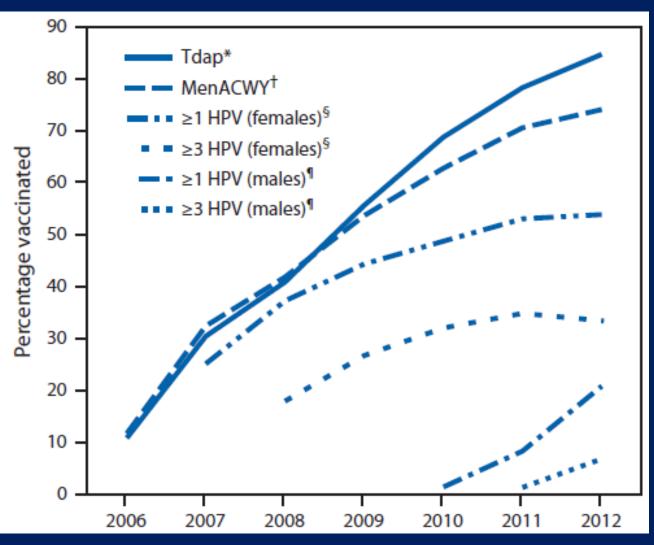
HPV vaccines: new 9-valent HPV vaccine

- Currently under FDA review
- Strains included in 9-valent HPV vaccine
 - Current strains in HPV4 (HR 16, 18 and LR 6, 11)
 - Additional HR strains: 31, 33, 45, 52, 58
- Includes HR strains that cause about 90% of invasive cervical cancers, 80% of high grade cervical dysplasia and 70% of oropharyngeal cancers

Steinau M, et al. *Emerging Infectious Diseases* 2014; 20: 822-828. Serrano B, et al. *Infectious Agents and Cancer* 2012;7:38 De Sanjose S, et al. *Lancet Oncology* 2010;11(11):1048-56.

HPV vaccination: Measures of HPV vaccine uptake, United States and Wisconsin

Estimated vaccination coverage with selected vaccines among adolescents aged 13-17 years, by survey year – National Immunization Survey (NIS)-Teen, United States, 2006-2012



* ≥1 dose Tdap vaccine on or after age 10 years.

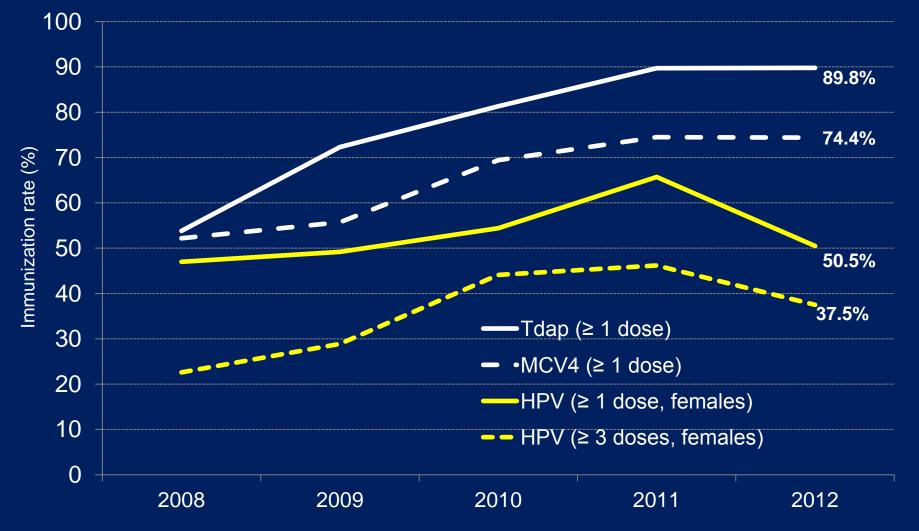
 $\dagger \geq 1$ dose MCV4 vaccine.

§ HPV vaccine, either bivalent or quadrivalent, among females. ACIP recommends either bivalent or quadrivalent vaccine for females.

¶ HPV vaccine, either bivalent or quadrivalent, among males. ACIP recommends the quadrivalent vaccine for males; however, some males might have received bivalent vaccine.

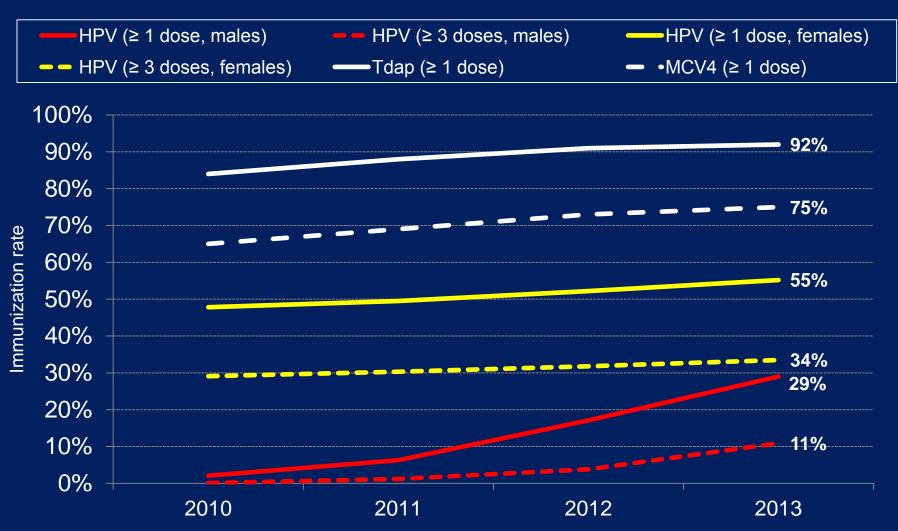
CDC. MMWR 2013: 62(34);685-693: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6234a1.htm

Estimated Tdap, MCV4, and HPV vaccine coverage among adolescents aged 13-17 years, NIS-Teen, Wisconsin, 2008-2012



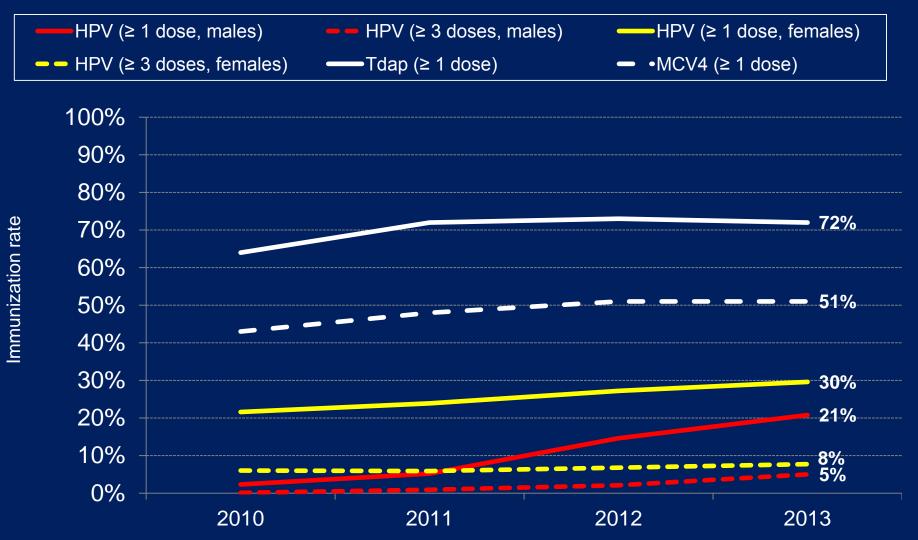
Because of inadequate sample sizes, the \geq 3 dose HPV coverage estimates during 2011-2012 and the \geq 1 dose rate during 2011 are not available for male adolescents in Wisconsin. During 2012, the \geq 1 dose HPV coverage rate 60 among males in Wisconsin was 19.3% ± 8.0%.

Estimated Tdap, MCV4, and HPV vaccine coverage among adolescents aged 13-17 years, Wisconsin Immunization Registry (WIR), 2010-2013



Estimated immunization rates are based on the number of persons recorded in the WIR as having received a valid 61 dose(s) of vaccine by antigen and the Wisconsin Interactive Statistics on Health (WISH) population estimates.

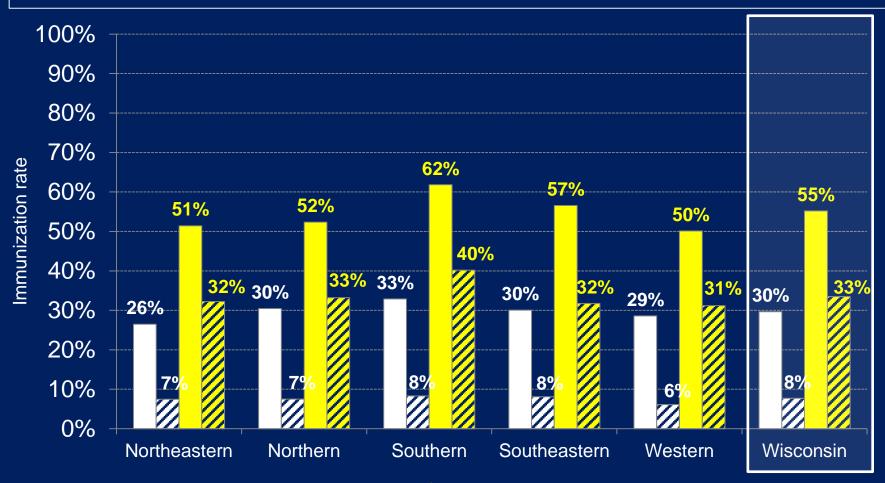
Estimated Tdap, MCV4, and HPV vaccine coverage among adolescents aged 11-12 years, Wisconsin Immunization Registry (WIR), 2010-2013



Estimated immunization rates are based on the number of persons recorded in the WIR as having received a valid 62 dose(s) of vaccine by antigen and the Wisconsin Interactive Statistics on Health (WISH) population estimates.

Estimated HPV vaccine coverage among adolescent females aged 11-17 years, by public health region, Wisconsin Immunization Registry (WIR), 2013

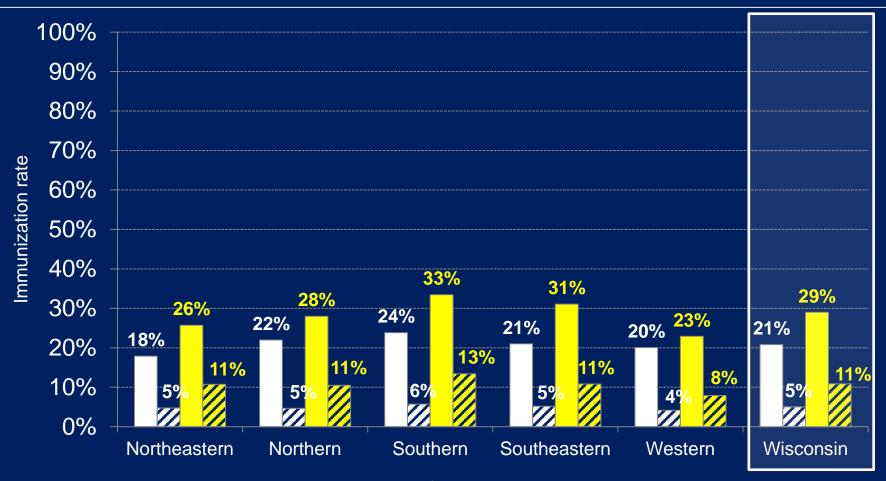




Estimated immunization rates are based on the number of persons recorded in the WIR as having received a valid 63 dose(s) of vaccine by antigen and the Wisconsin Interactive Statistics on Health (WISH) population estimates.

Estimated HPV vaccine coverage among adolescent males aged 11-17 years, by public health region, Wisconsin Immunization Registry (WIR), 2013

■ \geq 1 dose (11-12 years) $\boxtimes \geq$ 3 doses (11-12 years) $\square \geq$ 1 dose (13-17 years) $\boxtimes \geq$ 3 doses (13-17 years)

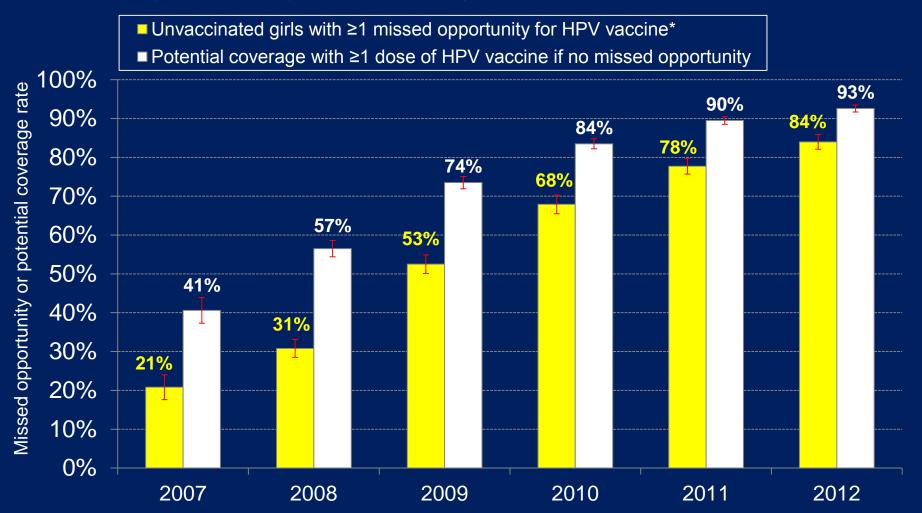


Estimated immunization rates are based on the number of persons recorded in the WIR as having received a valid 64 dose(s) of vaccine by antigen and the Wisconsin Interactive Statistics on Health (WISH) population estimates.

HPV vaccination:

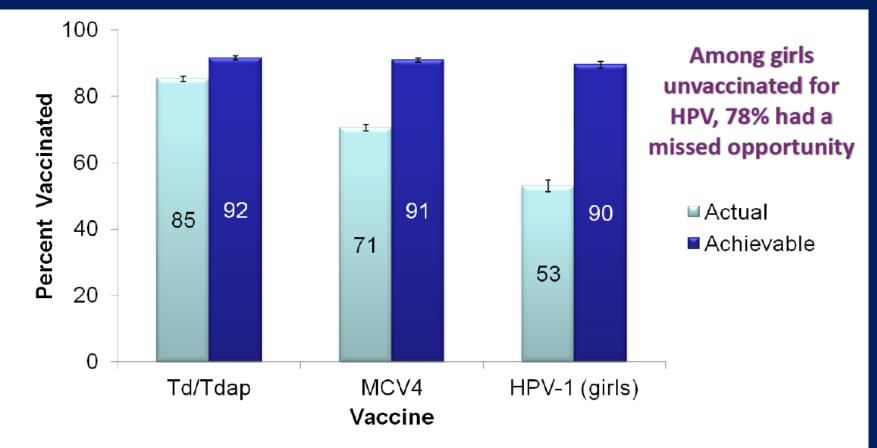
Missed opportunities to vaccinate and the impact of eliminating missed opportunities to vaccinate

Percentage of HPV-unvaccinated females aged 13-17 years with \geq 1 missed opportunity for HPV vaccination and the potential HPV vaccine coverage if all missed opportunities for HPV vaccination had been eliminated, NIS-Teen, United States, 2007-2012



*Missed opportunity: health-care encounter occurring on or after 11th birthday and on or after March 23, 2007 (ACIP HPV4 recommendation publication date), during which at least one vaccine was given, but not 66 HPV vaccine. CDC. *MMWR* 2013: 62(29);591-595.

Actual and achievable vaccination coverage if missed opportunities were eliminated: adolescents aged 13-17 years, United States, NIS-Teen, 2011



Missed opportunity: encounter when some but not all ACIP-recommended vaccines are given

HPV-1: receipt of at least one dose of HPV

2011 NIS-Teen available at http://www.cdc.gov/vaccines/stats-surv/nis/nis-2011-released.htm#nisteen



Eliminate missed opportunities to vaccinate

Centers for Disease Control and Prevention (CDC) estimates that increasing HPV vaccination rates from current levels to 80% would prevent:

- An additional 53,000 future cervical cancer cases in the United States among girls who now are aged <12 years during the course of their lifetimes.
- Thousands of other HPV-associated cancers in the United States would likely be prevented during the same timeframe.
- A growing proportion of these cancers—most notably, oropharyngeal cancers—will occur among males, who currently are vaccinated at very low rates.

Accelerating HPV Vaccine Uptake: Urgency for Action to Prevent Cancer. A Report to the President of the United 68 States from the President's Cancer Panel. Bethesda, MD: National Cancer Institute; 2014.

HPV infection prevention: Where to go from here

Prevent HPV-related cancers, cancer precursor lesions and genital warts

- Emphasize HPV vaccination as a standard and routine part of adolescent health care.
- Eliminate missed opportunities to vaccinate.
 - Take advantage of the adolescent immunization visit and every other potential visit.
- Do not delay vaccination.
 - Start the conversation regarding HPV vaccination during the first adolescent visit.
- Share a personal story and welcome questions from parents, especially about HPV vaccine safety.

Accelerating HPV Vaccine Uptake: Urgency for Action to Prevent Cancer A Report to the President of the United States from the President's Cancer Panel

Accelerating HPV Vaccine Uptake: **Urgency for Action to Prevent Cancer**

	PART 3: ACCELERATING HPV VACCINE UPTAKE IN THE UNITED STATES
HPV Vaccines Preve	Goal 1: Reduce Missed Clinical Opportunities to Recommend and Administer HPV Vaccines
	Objective 1.1: CDC should develop, test, disseminate, and evaluate the impact of integrated, comprehensive communication strategies for physicians and other relevant health professionals
	Objective 1.2: Providers should strongly encourage HPV vaccination of age-eligible males and females whenever other vaccines are administered
A Report to th from The President's	Objective 1.3: Healthcare organizations and practices should use electronic office systems, including electronic health records (EHRs) and immunization information systems (IIS), to avoid missed opportunities for HPV vaccination
	Objective 1.4: Healthcare payers should reimburse providers adequately for HPV vaccines and for vaccine administration and services
	Objective 1.5: The current Healthcare Effectiveness Data and Information Set (HEDIS) quality measure for HPV vaccination of adolescent females should be expanded to include males
	Objective 1.6: Create a <i>Healthy People 2020</i> HPV vaccination goal for males
	Goal 2: Increase Parents', Caregivers', and Adolescents' Acceptance of HPV Vaccines
	Objective 2.1: CDC should develop, test, and collaborate with partner organizations to deploy integrated, comprehensive communication strategies directed at parents and other caregivers, and also at adolescents
	Goal 3: Maximize Access to HPV Vaccination Services
	Objective 3.1: Promote and facilitate HPV vaccination in venues outside the medical home
	Objective 3.2: States should enact laws and implement policies that allow pharmacists to administer vaccines to adolescents, including younger adolescents
	Objective 3.3: Overcome remaining barriers to paying for HPV vaccines, including payment for vaccines provided outside the medical home and by out-of-network or nonphysician providers
	PART 4: INCREASING GLOBAL HPV VACCINATION

PART 4: INCREASING GLOBAL HPV VACCINATION

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Current CDC activities to increase HPV vaccine coverage

- Communication and media campaign to public
- American Academy of Pediatrics (AAP) funded activity to focus on provider outreach
- Prevention and Public Health Fund (PPHF) awards to 11 State/local awardees to increase HPV vaccination
- State and local health department "Call to Action" with follow-up with health departments to discuss developing a plan
- Partnership building activities between immunization and cancer prevention programs and coalitions

What can you do to improve HPV vaccination coverage among adolescents in your area?

- Measure adolescent HPV immunization coverage rates in your county on a regular basis (e.g., quarterly).
 - Use the Wisconsin Immunization Registry (WIR) adolescent assessment and benchmark reports
 - Simple to run, measure HPV coverage rates in a few minutes
- Use the WIR reminder/recall functionality to generate list of persons due or overdue for HPV vaccination: for mailings or telephone reminders
- These are important evidence-based tools that can help improve HPV vaccination coverage.

What can you do to improve HPV vaccination coverage among adolescents in your area? (continued)

- Share county-level HPV immunization coverage levels with health care providers (HCPs) in your area.
- Encourage HCPs to assess HPV coverage rates within their own practices using the WIR adolescent reports.
- Promote the use of WIR reminder/recall functionality.
 Refer questions to the WIR Help Desk, 608-266-9691.
- Use and share free CDC tools and resources with HCPs
 - HPV Vaccine Resources for Healthcare Professionals "You Are the Key to Cancer Prevention" Campaign: <u>http://www.cdc.gov/vaccines/who/teens/for-hcp/hpv-resources.html</u>

Additional resources for health care professionals

- Tips and Time-savers for Talking with Parents about HPV Vaccine: <u>http://www.cdc.gov/vaccines/who/teens/for-hcp-tipsheet-hpv.html</u>
- Accelerating HPV Vaccine Uptake: Urgency for Action to Prevent Cancer. A Report to the President of the United States from the President's Cancer Panel. Bethesda, MD: National Cancer Institute; 2014. <u>http://deainfo.nci.nih.gov/advisory/pcp/annualReports/HPV/ind</u> <u>ex.htm</u>
- CDC Public Health Grand Rounds. Reducing the Burden of HPV-associated Cancer and Disease through Vaccination in the US, February 19, 2013: <u>http://www.cdc.gov/about/grand-</u> rounds/archives/2013/February2013.htm

Additional resources for patients and parents

http://www.cdc.gov/vaccines/who/teens/index.html

 CDC print materials (fact sheets, flyers, posters) for preteens and teens – available in English, Spanish, Vietnamese, Korean, and for American Indian/Alaska Native populations: <u>http://www.cdc.gov/vaccines/who/teens/products/print-</u>

materials.html

Multimedia Products



Web features

Health e-cards

Web button

- Posters, flyers, and fact sheets
- Podcasts and PSAs
- Videos

You may have heard that some kidd faint when they get vaccinated. Fainting is common with presense and teams for many medical procedures, no just the HPV tho. Be sure that your child east something before going to get the vaccine. It's a good ides to have your child is to full down while getting any vaccine, and for 15 minutes afterwards, to prevent fainting and any injurise that could happen from fainting.

The HPV vaccine can safely be given at the same time as the other recommended vaccines, including the Tdap, meningcocccal, and influenza vaccines. Learn more about all of the recommended preteen vaccines at www.cdc.gov/vacclnes/teens

Jacquelyn's story: "I was healthy—and

When I was in my late 20's and early 30's, in the years before my daughter was born, I had some abnormal Pap smears and had to have further testing. I was told I had the kind of HPV that can cause cancer and mild dvsblasia.

For three more years, I had normal tests. But when I got my first Pap test after my son was born, they told me I needed a biopy. The results came back as cancer, and my doctor sent me to an oncologist. Fortunately, the cancer was at an early stage. My ymph nodes were clear, and I din't need radiation. But I din ead to have a total hysterectomy.

My husband and I have been together for 15 years, and we were planning to have more children. We are so grateful for our two wonderful children, but we were hoping for more which is not going to happen now.



For more information about the vaccine 800-CDC-INFO http://www.cdc.g

Help paying for vaccines

As parents, you do everything you can to protect Ayour children's health for now and for the future. Today, there is a strong weapon to prevent several types of cancer in our kids: the HPV vaccine.

HPV and Cancer

HPV is short for Human Papillomavirus, a common virus. In the United States and view, there are about 17,000 women and 9,000 men affected by HPV-stated anners. Many of these cancers could be prevented with vaccination. In both women and men, HPV can cause and anner it can also how women and (copphanyaga) anner. It can also cause cancer of the gents', vulva and vagina in women; and cancer of the gents', vulva and vagina in women; and cancer of the gents'.

For woman, screening is available to descre most cass of cervical cancer with a Pay mean Unfortunately, there is no routine screening for other HPV-related cancers for women or men, and these cancers can cause pain, suffering, or even death. That is why a vaccime that prevents most of these types of cancers is so important.

More about HPV

HPV is a virus passed from one perion to another during skin-to-kin sexual contact, including vaginal, oral, and anal sex. HPV is most common in people in their late teens and early 20x. Almost all sexually active people will get HPV at some time in their live though most will never even know it.

Most of the time, the body naturally fights of HPV, before HPV cases any hashit problems. But in some case, the body does not fight of HPV and HPV can cause hashit problems, like cancer and genital wars. Genital warts are not a life-freeseming disease, but they can cause emotional trees, and their restances can be very uncomfortable About in 100 sexually active adults in the United States have genital warts at any given time.

Why does my child need this no

HPV vaccines offer the best protection to gifts an three vaccine does and have time to develop an they begin sexual activity with another person. Th preteen is ready to have sex. In fact, it's just the to get your child protected before you or your chill issue. The immune response to this vaccine is bu could mean better protection for your child. \diamondsuit DISEASES and the VACCINES THAT PREVENT THEM Updated March 2014

HPV vaccination is recommended for preteen girls and boys at age 11 or 12 years

HPV vaccine is also recommended for girls ages 13 through 26 years and for boys ages 13 through 21 years, who have not yet been vaccinated. So if your son or daughter han's started or finished the HPV

> Si hubiese una vacuna contra el cáncer, ¿se la pondría a sus hijos?

La vacuna contra el VPH previene el cáncer.

Consulte a su médico sobre cómo vacunar a sus

hijos e hijas de entre 11 y 12años contra el VPH. Your efforts to prevent HPV-associated cancers and other diseases are important and greatly appreciated.

Thank you

You're not opening the door to sex.

You're closing the door to cancer.

HPV vaccine is cancer prevention.

Talk to your child's doctor about vaccinating your 11-12 year old against HPV.

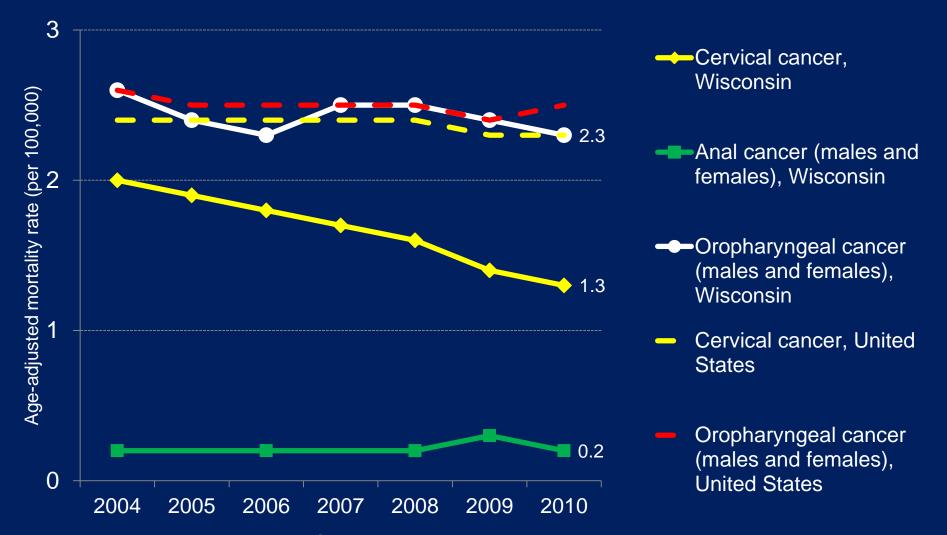
www.cdc.gov/vaccines/teens



U.S. Department of Health and Human Services Centers for Disease Control and Prevention



Age-adjusted mortality rate: cervical, oropharyngeal, and anal cancers, United States and Wisconsin, 2004-2010



Incidence rate is age-adjusted to the 2000 U.S. standard population.

Data sources: Wisconsin Interactive Statistics on Health (WISH): <u>https://www.dhs.wisconsin.gov/WISH/cancer/mortality.htm</u> 79 United States Cancer Statistics (USCS), National Program of Cancer Registries: <u>http://apps.nccd.cdc.gov/uscs/index.aspx</u>

Public funding for HPV vaccines, Wisconsin

- Vaccines for Children (VFC) Program
 - Medicaid eligible
 - American Indian or Alaska Native
 - Uninsured or underinsured
- Males aged 9 through 18 years: HPV4 only through VFC program
 - Males aged 19 through 26 years: HPV4 only through Medicaid
- Females aged 9 through 18 years: HPV4 or HPV2 through VFC program
 - Females aged 19 through 26 years: HPV4 or HPV2 through Medicaid

VFC-ACIP vaccine resolution for HPV vaccine: http://www.cdc.gov/vaccines/programs/vfc/providers/resolutions.html 80