

HPV Vaccination Program and Impact Monitoring

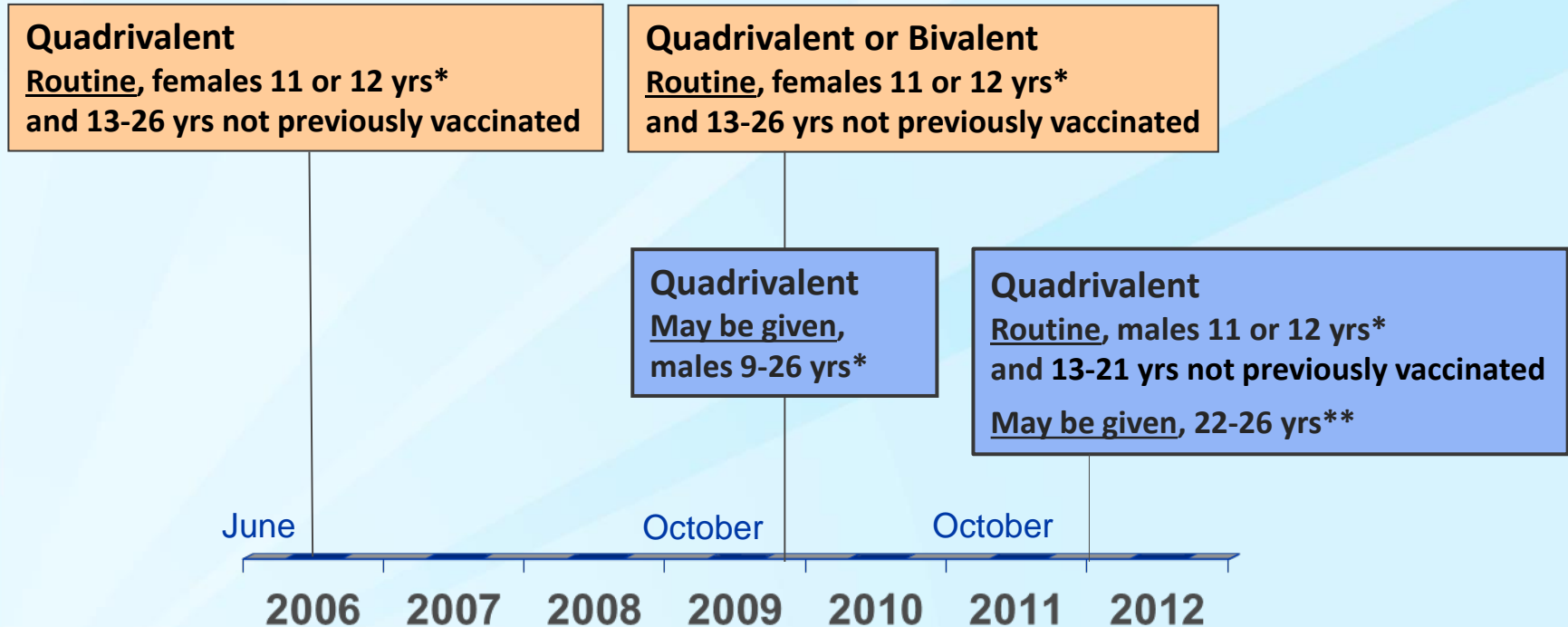
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Advisory Committee on Immunization Practices
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Overview

- ❑ HPV vaccination program
- ❑ Update on vaccine safety
- ❑ HPV vaccine impact monitoring

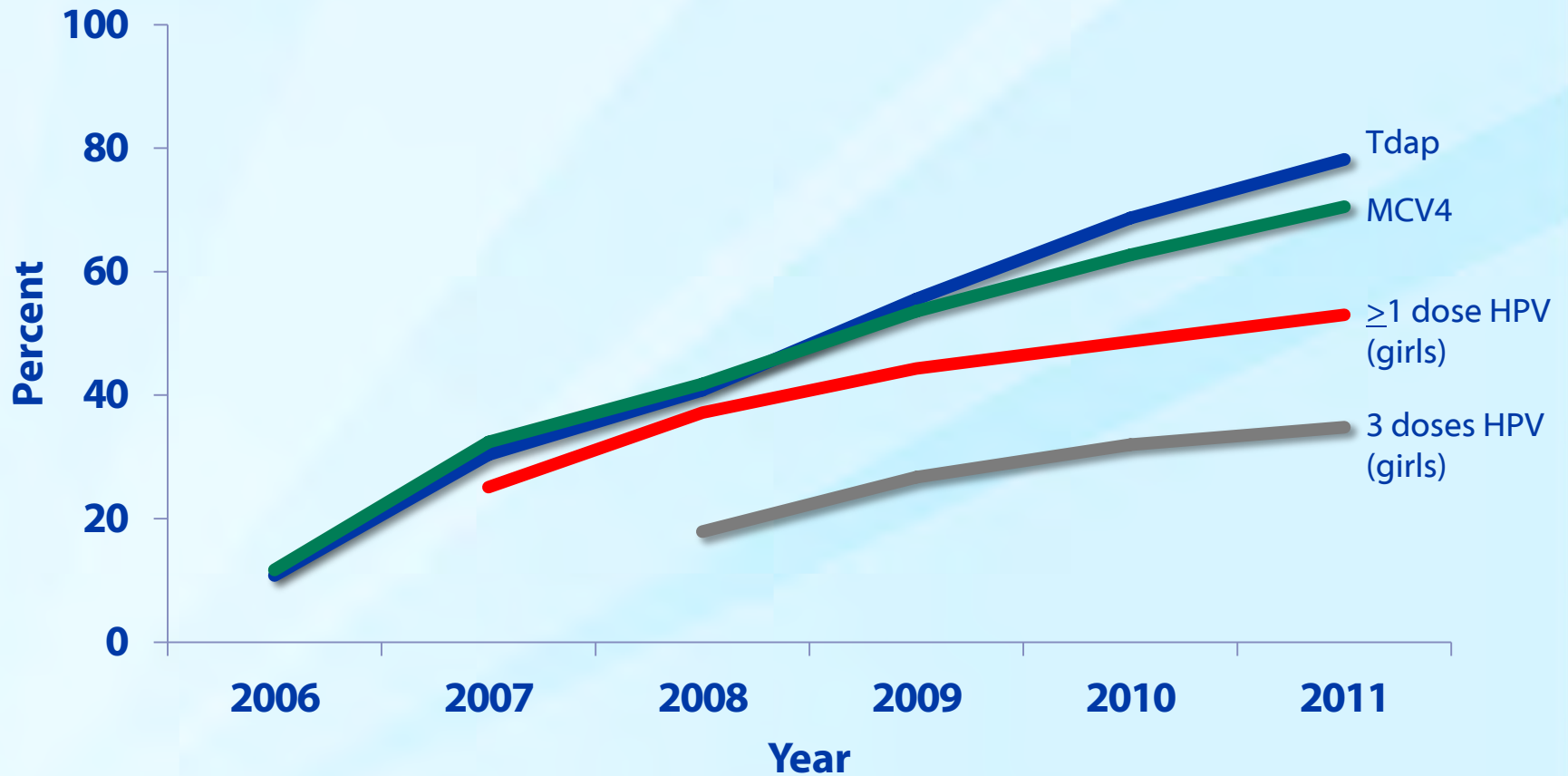
Recommendations for HPV vaccination in the United States



Quadrivalent (HPV 6,11,16,18) vaccine; Bivalent (HPV 16,18) vaccine

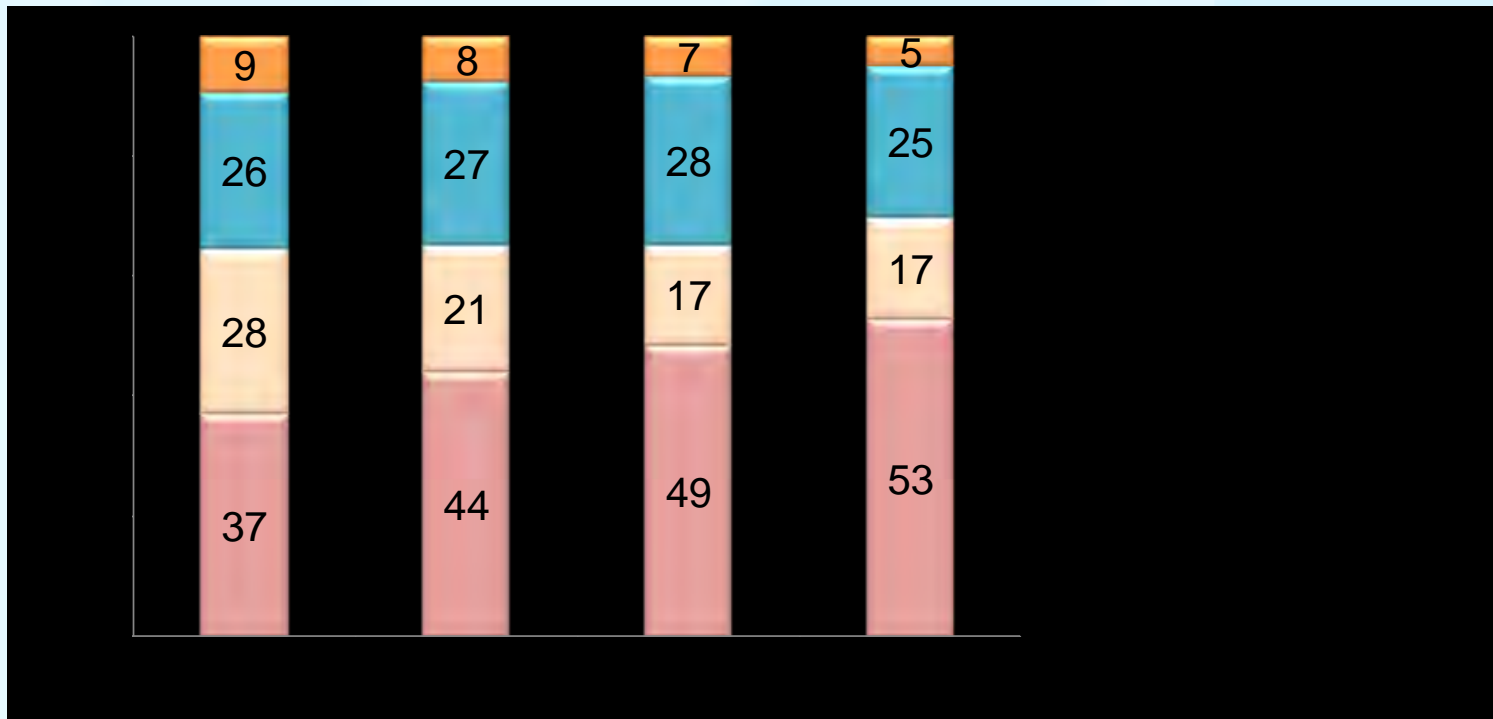
* Can be given starting at 9 years of age; ** For MSM and immunocompromised males, quadrivalent HPV vaccine through 26 years of age

National estimated vaccination coverage levels among adolescents 13-17 years, NIS-Teen, 2006-2011



National Immunization Survey (NIS)-Teen. MMWR 2012;61

HPV vaccine intentions (in the next 12 months) among parents of girls 13-17 years, NIS-Teen



NIS-Teen available at <http://www.cdc.gov/vaccines/stats-surv/nis/default.htm#nisteen>

Top 5 reasons for not vaccinating daughter, among parents with no intention to vaccinate in the next 12 months, NIS-Teen 2011

Reason	%
Not needed or necessary	23.2%
Not sexually active	19.5%
Safety concern/side effects	19.3%
Lack of knowledge	15.2%
No recommendation by provider	9.6%

Response categories are not mutually exclusive

Human papillomavirus vaccination among females (at least 1 dose) – NHIS, 2010 and 2011

Age Group (yrs)	2010 (%)	2011 (%)	Difference*
19-26	20.7	29.5	+8.8
19-21	28.2	43.1	+14.9
22-26	16.5	21.5	+5.0

*Increase in percentage points, $p < .05$

VACCINE SAFETY UPDATE

CDC Immunization Safety Office post-licensure vaccine safety monitoring infrastructure

System	Collaboration	Description
Vaccine Adverse Event Reporting System (VAERS)	CDC and FDA	US frontline spontaneous reporting system to detect potential vaccine safety problems
Vaccine Safety Datalink (VSD)	CDC and 9 Managed Healthcare Plans	Large linked database system used for active surveillance and research ~9.2 million members (~3% of US pop.) -Conducts monitoring & evaluation -Rates & risk estimates can be calculated
Clinical Immunization Safety Assessment (CISA) Project	CDC and 7 Academic Centers	Expert collaboration that conducts individual clinical vaccine safety assessments and clinical research

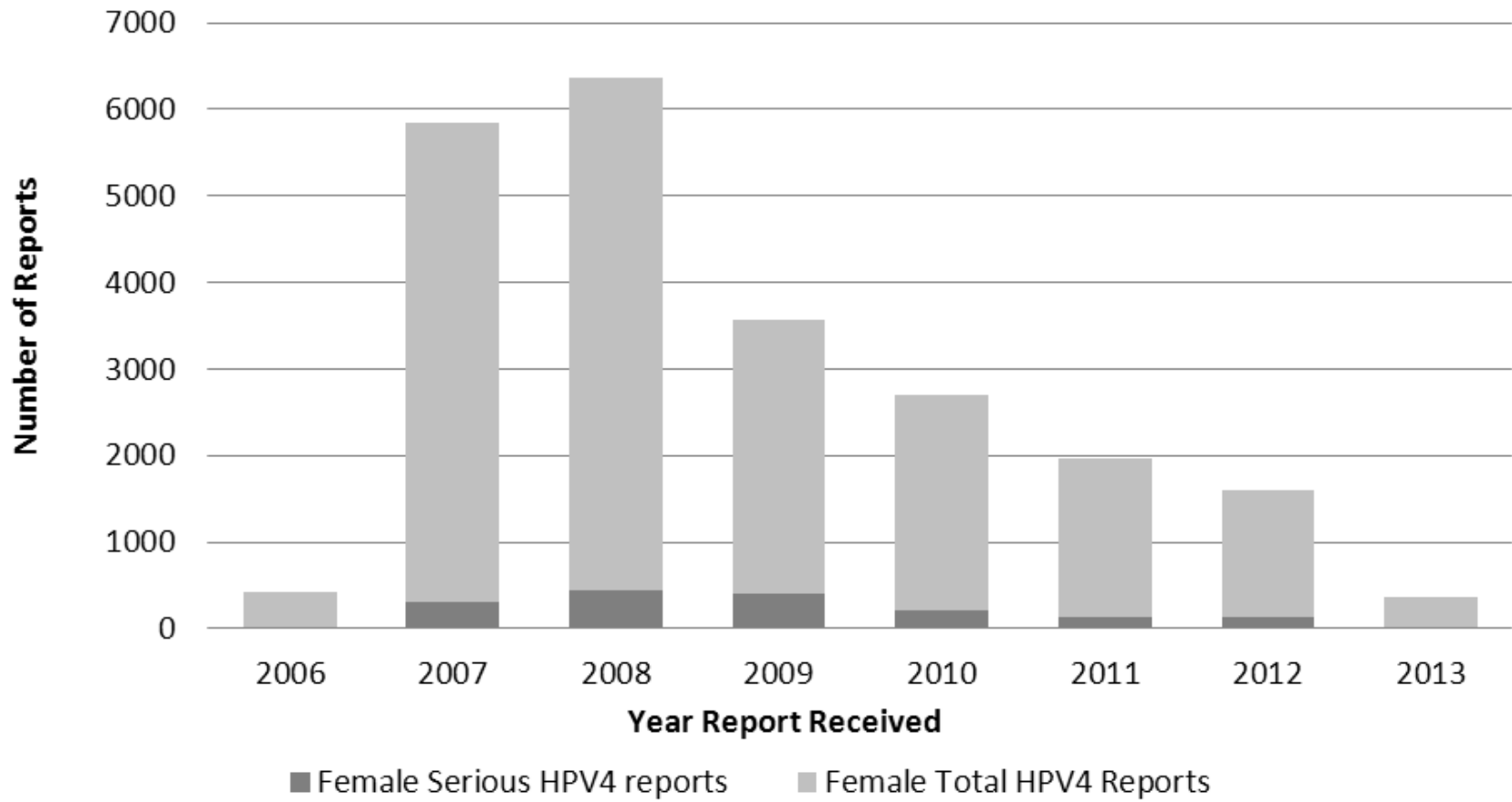
HPV vaccine safety monitoring - VAERS

- ❑ From 6/2006 through 3/2013 ~56 million HPV4 doses distributed in the United States

- ❑ No new safety concerns have been identified in post-licensure vaccine safety surveillance among male or female recipients of HPV4 vaccine
 - Among the 7.9% of reports coded as “serious”, most frequently cited are headache, nausea, vomiting, fatigue, dizziness, syncope, generalized weakness

- ❑ Syncope continues to be a frequently reported AEFI among adolescents
 - Adherence to a 15-minute observation period after vaccination is encouraged

Trends in Total and Serious Female HPV4 Vaccine Reports to VAERS by Year, 6/1/2006-3/31/2013 (N=21,194)



VSD active surveillance of HPV4 vaccine

- ❑ **HPV4 vaccine doses administered through March 2013**
 - > 1.8 million doses; ~270,000 doses given to males
 - Rapid cycle analysis of male data to begin late 2013
- ❑ **VSD Rapid Cycle Analysis publication (*Vaccine* 2011)***
 - Among 600,588 doses administered to females 9-26y/o, there was no significant increased risk for pre-specified AEFIs[†]
 - Guillain-Barré Syndrome (GBS), seizures, stroke, venous thromboembolism (VTE), appendicitis, anaphylaxis, and other allergic reactions
- ❑ **Longer-term surveillance of GBS and stroke among females 9-26 y/o following HPV4 vaccine evaluated after 1.5 million doses[‡]**
 - No increased risk of GBS or stroke observed

* Gee, et al. *Vaccine*. 2011; 29(46):8279-84.

[†]AEFIs - adverse events following immunization; [‡]Unpublished data from VSD

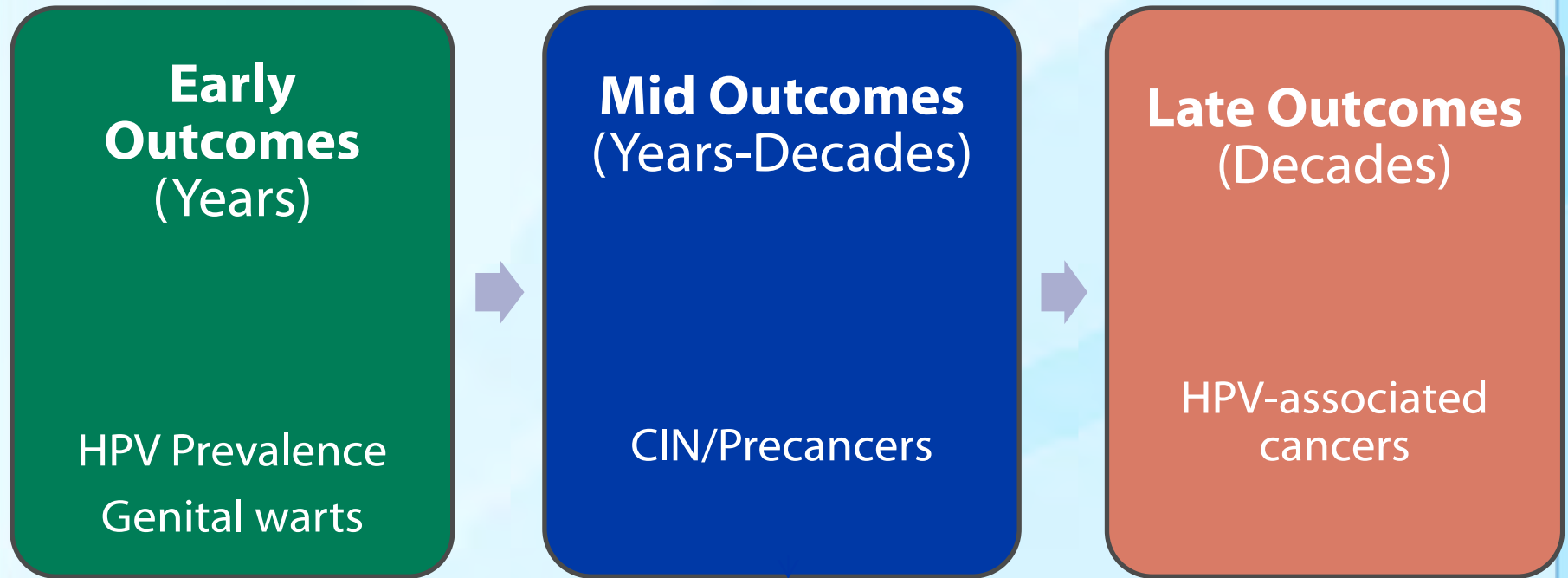
Inadvertent administration of HPV vaccine during pregnancy

- ❑ **No safety concerns raised by HPV4 in pregnancy registry**
- ❑ **CDC/FDA continue to monitor the safety of HPV vaccines, including reports in pregnant women through VAERS**
- ❑ **A retrospective analysis of pregnancy-associated HPV4 VAERS reports is in progress (2005-2012)**
 - **>85% of reports were submitted from the Merck Pregnancy Registry so anticipate a similar safety profile**
- ❑ **For VSD, descriptive data of adverse events following inadvertent exposure to HPV4 during pregnancy by 2015**

*death, life-threatening illness, hospitalization, prolongation of existing hospitalization, persistent or significant disability, congenital malformations

HPV VACCINE IMPACT MONITORING

Monitoring impact of HPV vaccine programs: HPV-associated outcomes



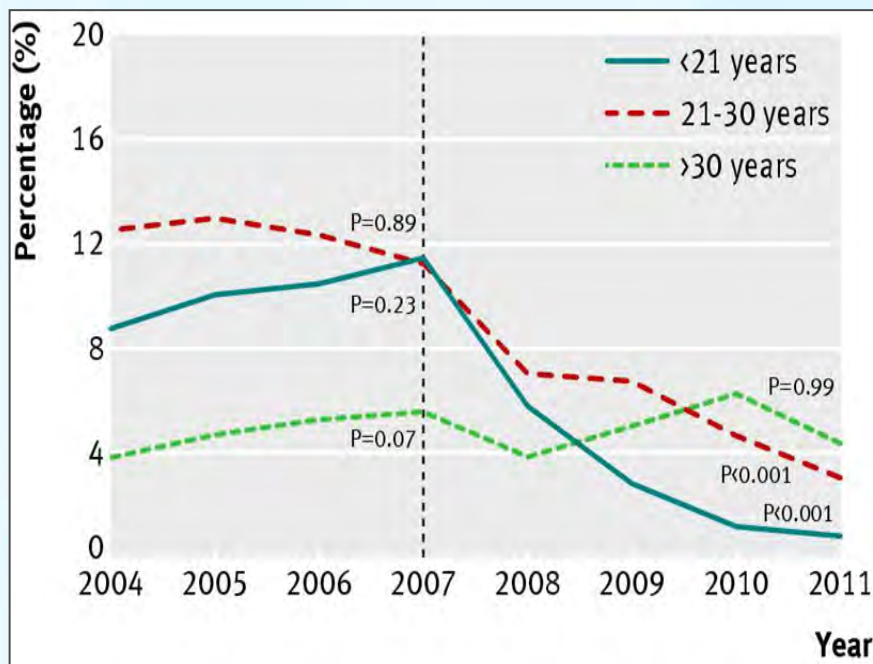
HPV immunization program in Australia

- Introduced in 2007 as school-based program
- Publicly funded: quadrivalent vaccine
- Target age group: 12-13 year-old girls
- Catchup program (2007-2009)
 - Age 14 - 17 years in schools
 - Age 18 - 26 years in community (primary care providers)
- Coverage
 - > 70% 3-dose coverage in target age group (school-based)
 - 52% 1-dose coverage among those 20-26 years

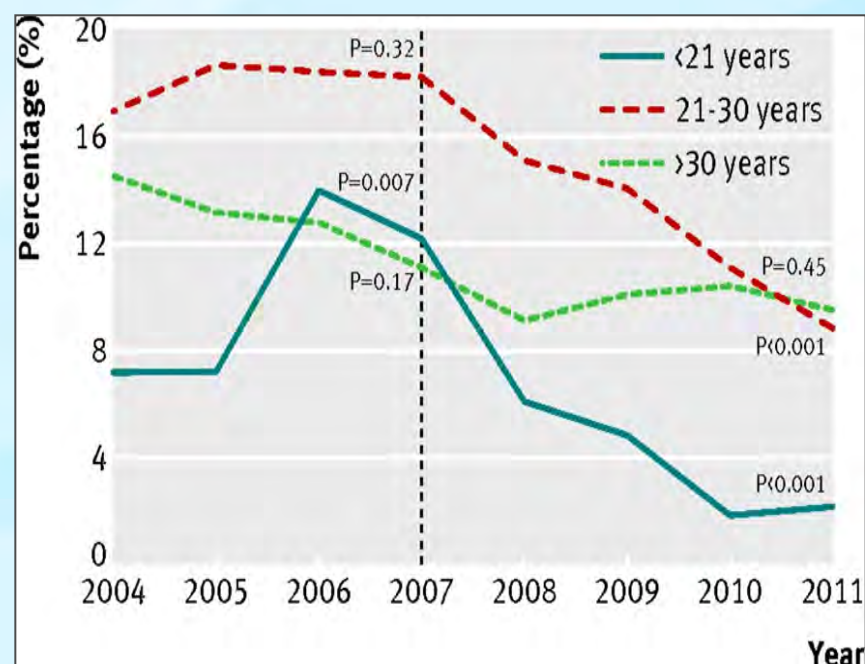
Impact of HPV vaccination in Australia

Proportion of Australian born females and males diagnosed as having genital warts at first visit, by age group, 2004-11

Females

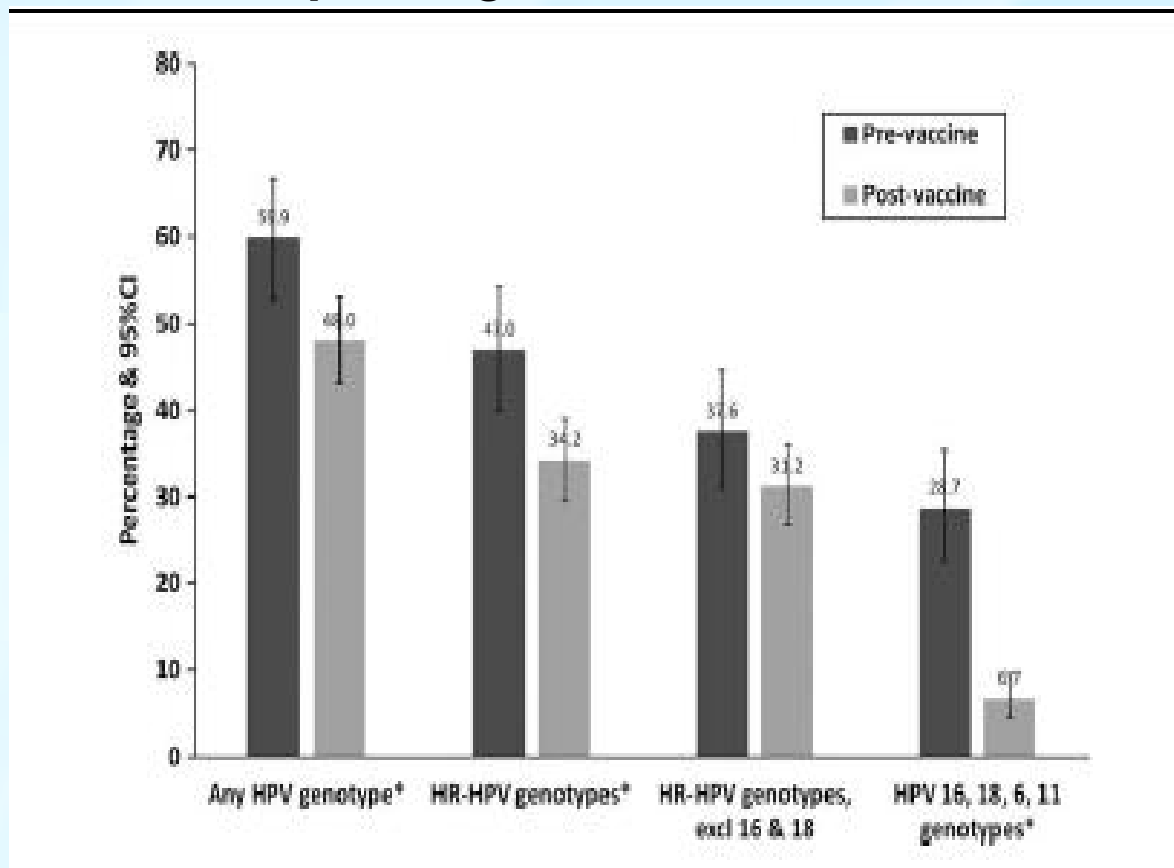


Males



Impact of HPV vaccination in Australia

HPV prevalence in women 18-24 years of age attending family planning clinics, Australia



Vaccine era = 2005-2007 Post vaccine era = 2010-2011

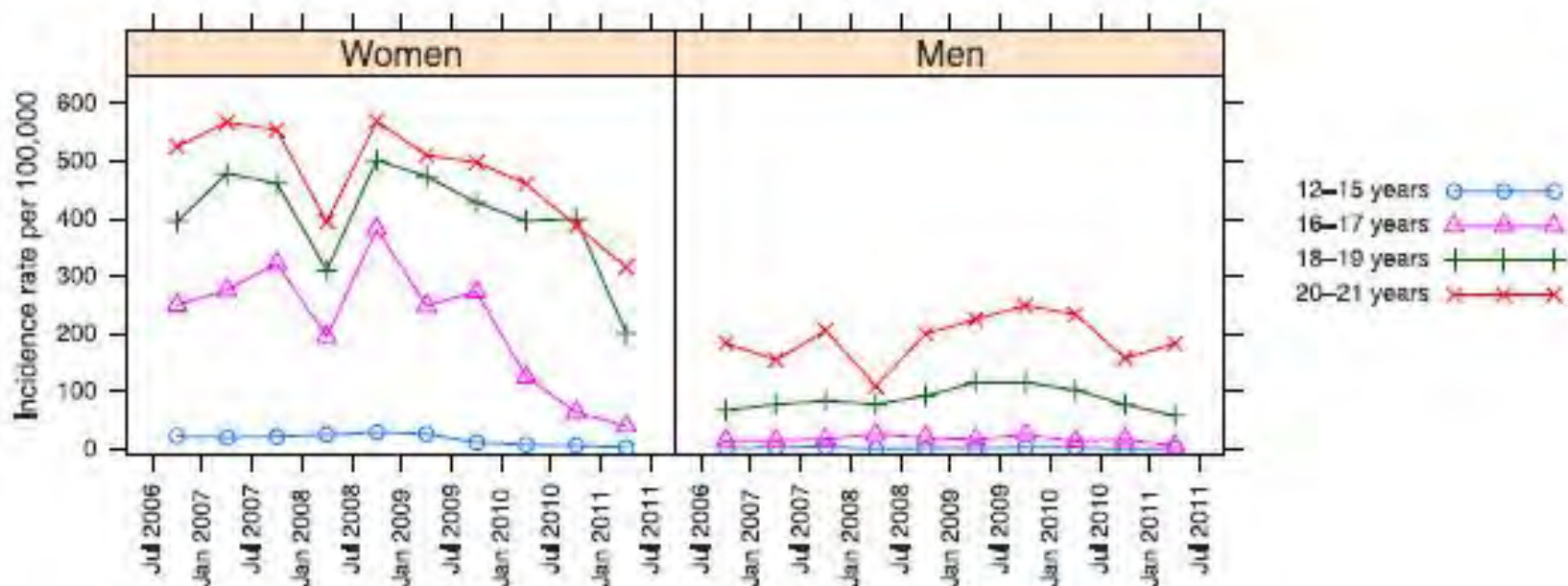
Tabrizi, et al. JID 2012

HPV immunization program in Denmark

- Introduced in 2009; vaccine delivered by general practitioners
- Publicly funded: quadrivalent vaccine
- Target age group: 12 year-old girls
- Catch-up program: 13 to 15 year-old girls (late 2008)
- >80% 3-dose coverage in target and catchup age groups

Denmark: nationwide incidence of genital warts per 100,000 person-years, by sex and age

- Significant decline in young women
- Average annual percentage change -45% among those 16-17 yrs



Monitoring impact of HPV vaccination on infection and disease, CDC efforts

- ❑ **Type-specific HPV prevalence**
 - National survey
 - Routine Pap specimens
- ❑ **Genital warts**
 - Network of STD clinics
 - Administrative data/Health information exchanges
- ❑ **Cervical precancers**
 - Sentinel sites* and cancer registry-based
 - Administrative data/Health Information exchanges
- ❑ **HPV-associated cancer**
 - Cancer registries*

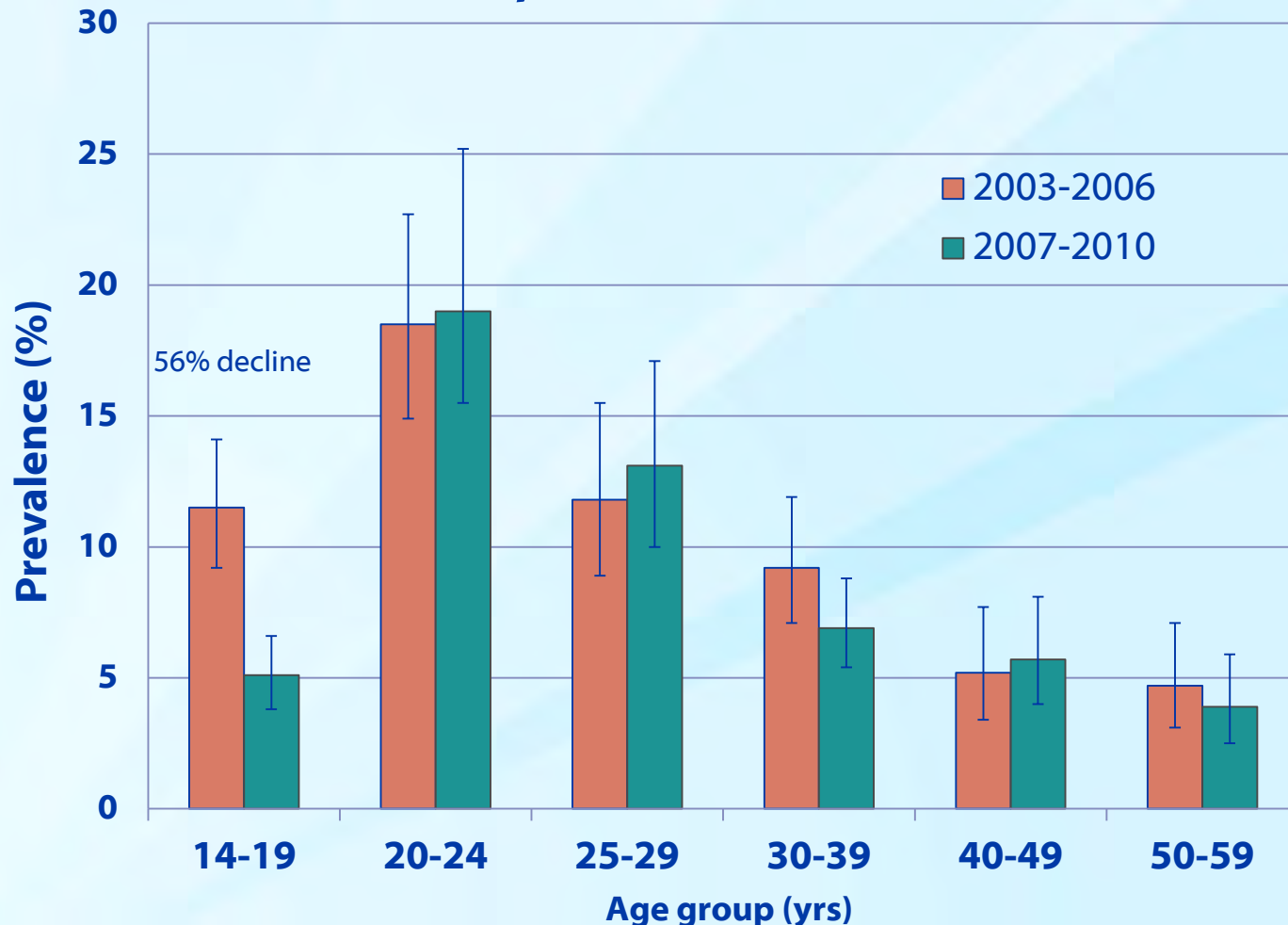
*with HPV type-specific determination

National Health and Nutrition Examination Surveys (NHANES)

- Representative survey of the U.S. population
- Home interviews & examination in mobile exam center
- HPV evaluation (ages 14-59 yrs)
 - HPV DNA testing in cervicovaginal swabs from females added in 2002
 - Demographic, sexual behavior data
 - HPV vaccine questions added in 2007
 - HPV DNA testing in genital swabs for males added in 2013



Prevalence of HPV 6, 11, 16, 18* in cervicovaginal swabs, by age group NHANES, 2003-2006 and 2007-2010



HPV vaccine impact monitoring

Early outcomes: genital warts

- ❑ **Administrative data/Health information exchanges**
- ❑ Network of STD clinics in 12 states
- ❑ Vaccine effectiveness study

Analysis of genital warts – MarketScan® Commercial Claims and Encounters Database, 2003-2010

□ Objectives

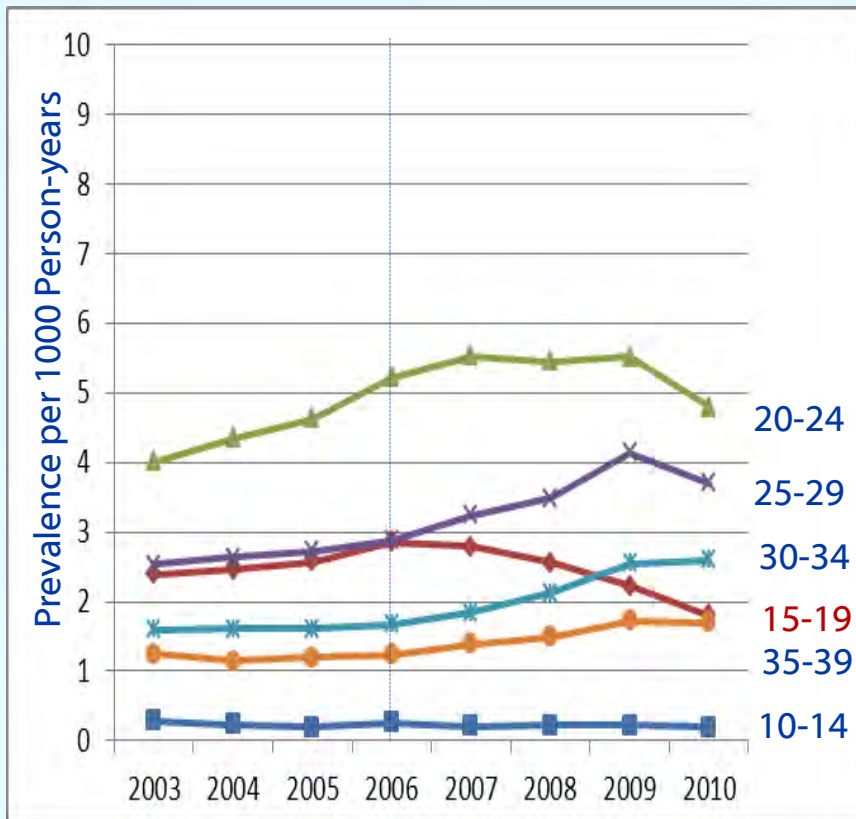
- Estimate annual prevalence of anogenital wart diagnoses from 2003 to 2010 in a large group of privately insured US patients

□ Methods

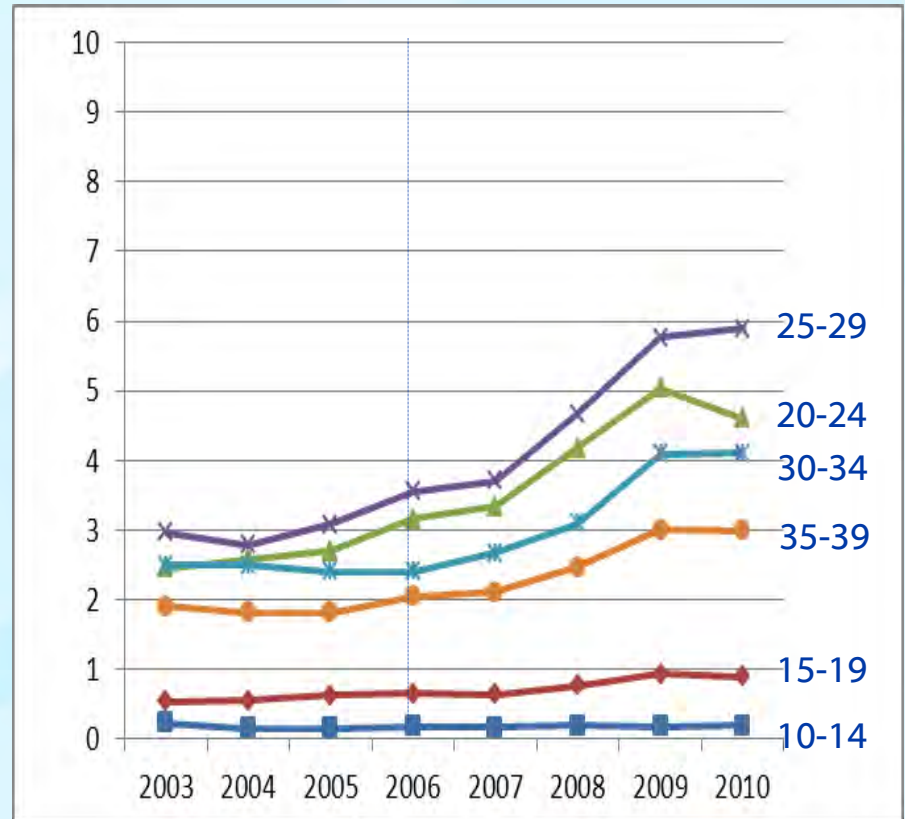
- Persons aged 10-39 years; continuously enrolled within a given year
- >64 million person-years of data
- Cases defined using ICD-9-CM codes
 - condyloma acuminata (genital warts) diagnosis or
 - non-specific viral warts diagnosis combined with anogenital neoplasm diagnosis or destruction/excision of anogenital lesion, excluding cervix or genital wart medication combined with anogenital neoplasm diagnosis or destruction/excision of anogenital lesion, excluding cervix

Anogenital wart prevalence per 1000 person-years, private insurance enrollees, by age, 2003-2010

Females



Males



HPV vaccine impact monitoring

Mid outcomes: cervical precancers

- ❑ **Population-based assessment in sentinel sites through EIP (with HPV typing)**
- ❑ County and state-wide assessments through cancer registries
 - Population-based cancer registries in 3 states and 1 county (Los Angeles) conduct surveillance for cervical pre-cancers.
- ❑ Administrative data and health information exchanges

Monitoring vaccine impact on high grade cervical lesions: HPV-IMPACT

Sites	Alameda Co, CA New Haven Co, CT Monroe Co, NY Portland metro, OR Davidson Co, TN
Outcomes collected	CIN2, CIN3, AIS
Reporting source	Histopathology labs
HPV typing	Linear Array DNA testing at CDC
Vaccination history	Actively investigated in all sites using variety of sources

EIP Network: HPV vaccine impact on HPV 16/18-related CIN2+

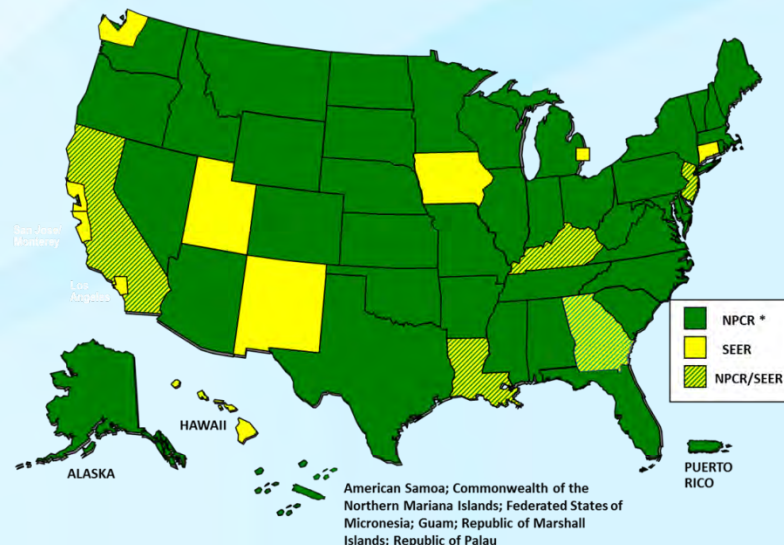
Diagnosis/Timing of vaccine initiation	N	HPV 16/18 N (%)	PR (95% CI)	aPR* (95% CI)
CIN 2+				
Not vaccinated	682	382 (56.0)	ref	ref
On/after trigger Pap	300	174 (58.0)	.98 (.88 – 1.10)	.95 (.85 – 1.07)
1-12 months before trigger Pap	95	53 (55.8)	1.00 (.82 – 1.21)	.93 (.77 – 1.13)
13-24 months before trigger Pap	96	50 (52.1)	.93 (.76 – 1.14)	.90 (.74 – 1.10)
> 24 months before trigger Pap	53	21 (39.6)	.71(.50 – .99)	.67 (.48 – .94)

PR - prevalence ratio
*adjusted for race and site

HPV vaccine impact monitoring

Late outcomes: Cancers

- ❑ **Cancer registries in all states: 100% population covered**
 - Regular updates on HPV-associated cancers, overall and by state*
 - Cervical, vaginal, vulvar, penile, anal, oropharyngeal
- ❑ **Typing of HPV-associated cancers (2007-2011)⁺**
 - Selected registries



Summary

- ❑ Vaccination coverage has increased since 2007 but very limited increase observed in recent years
- ❑ Post licensure monitoring data continue to show good vaccine safety profile
- ❑ Variety of early, mid and late HPV-associated outcomes being monitored
 - Data suggest impact on early and mid outcomes in the United States

Selected CDC plans

- ❑ HPV specific MMWR - end of July
 - 2007-2012 NIS-Teen data and vaccine safety
- ❑ 2012 NIS-Teen MMWR - end of August
- ❑ Utilizing IIS to conduct reminder/recall and vaccination coverage assessment of providers reporting to the IIS
- ❑ Tip-sheet for talking with patients about HPV vaccine
<http://www.cdc.gov/vaccines/who/teens/for-hcp-tipsheet-hpv.html>
- ❑ Developing speakers bureau to present at meetings
- ❑ Continued evaluation of barriers to vaccination and understanding what 'safety concerns' truly means
- ❑ Communication of safety data to providers and parents

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