

HPV Prevention: Where Are We and Where Do We Need to Go

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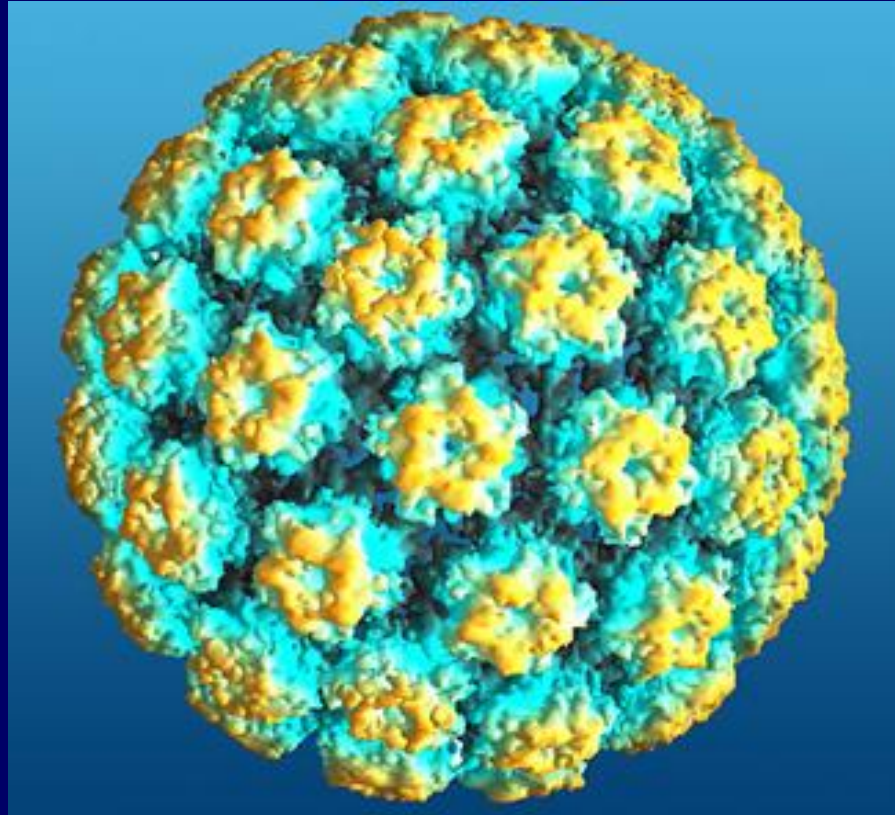
University of Illinois at Chicago



Disclosures

- I have no financial relationships to disclose
- I do not intend to discuss off-label uses for FDA-approved products

What you need to know about HPV



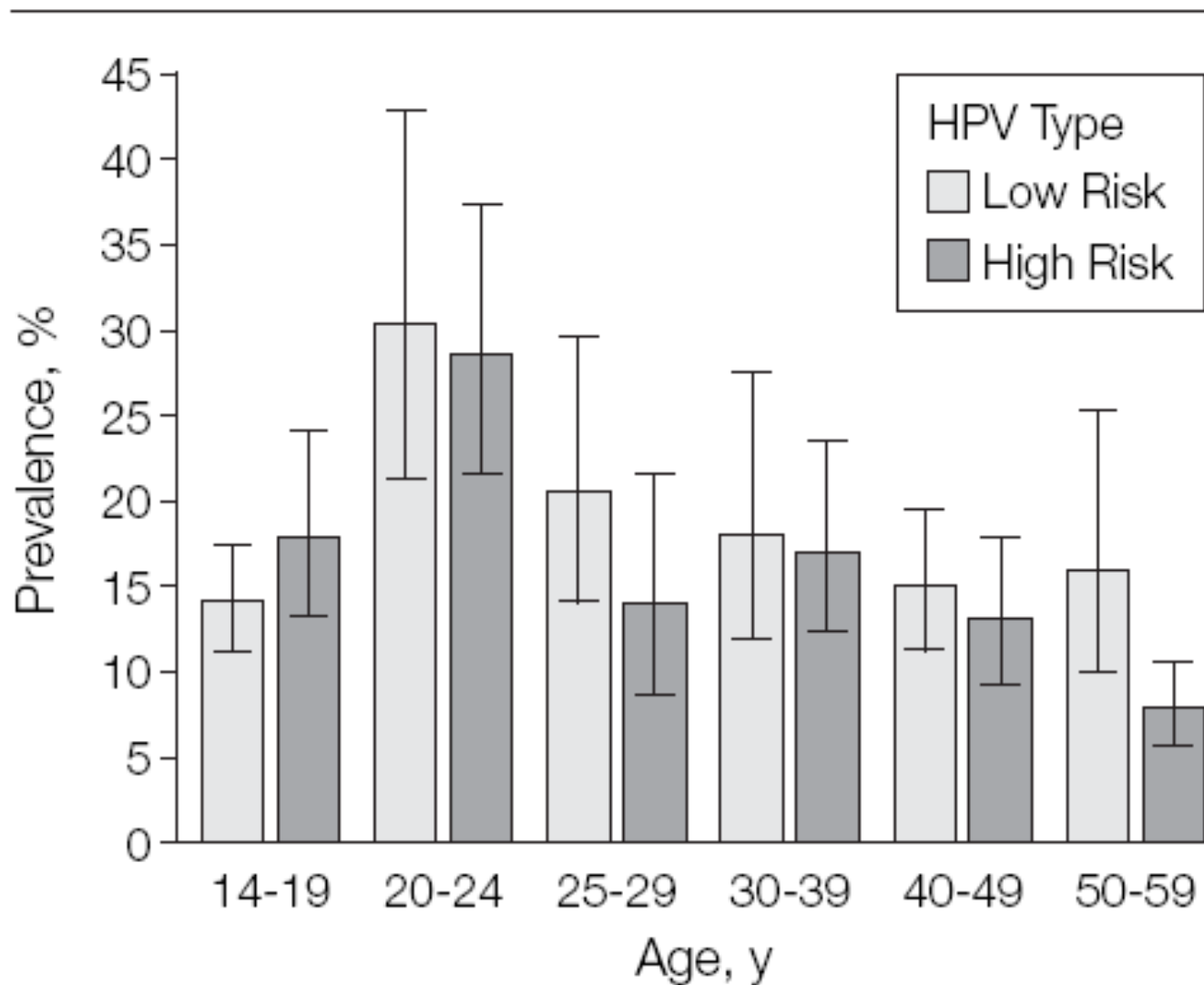
HPV in the U.S.

HPV is the most common sexually transmitted infection in the U.S.

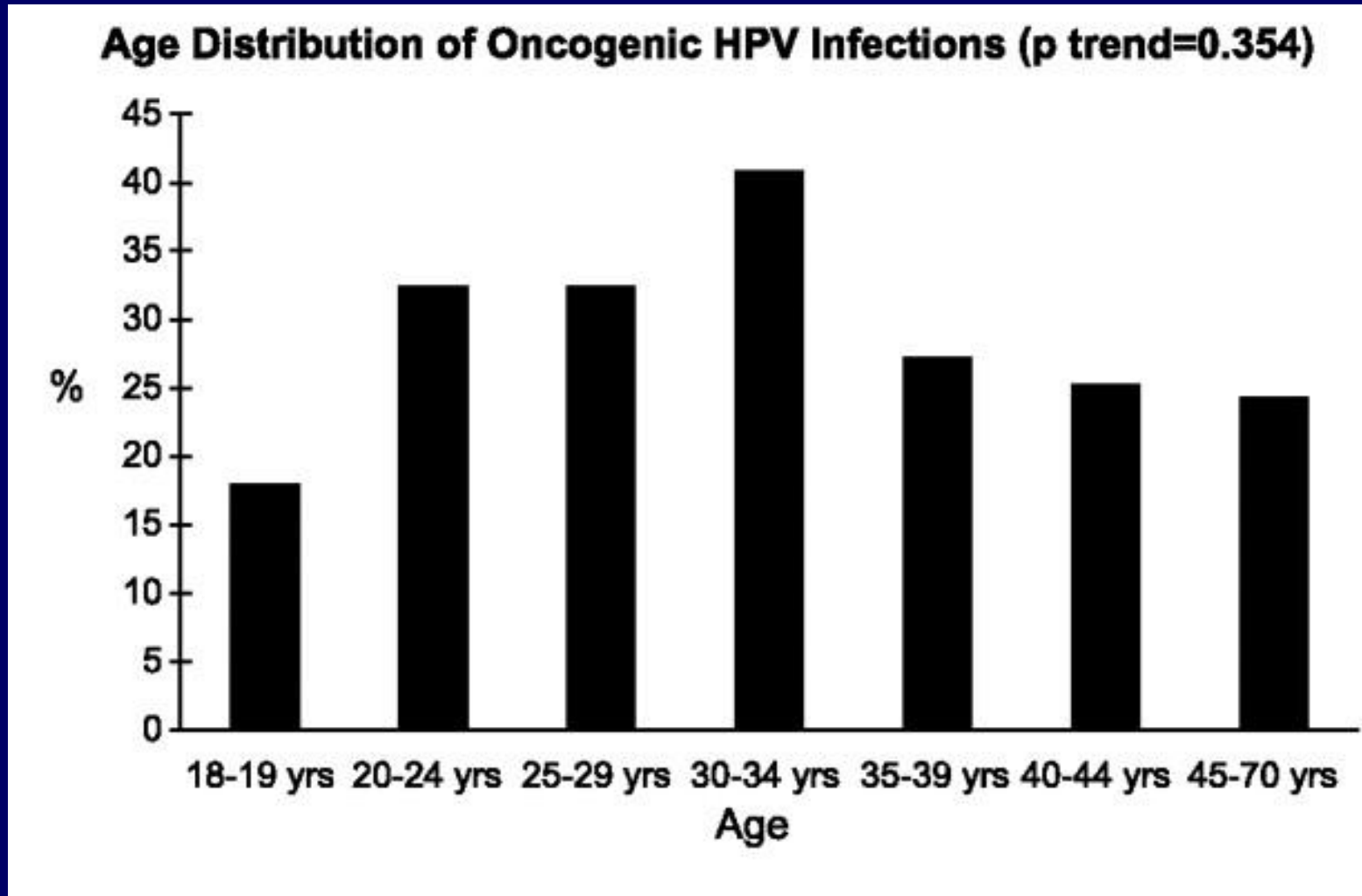
- Over 6.2 million new infections every year
- Nearly three-fourths new infections in 15-24yo



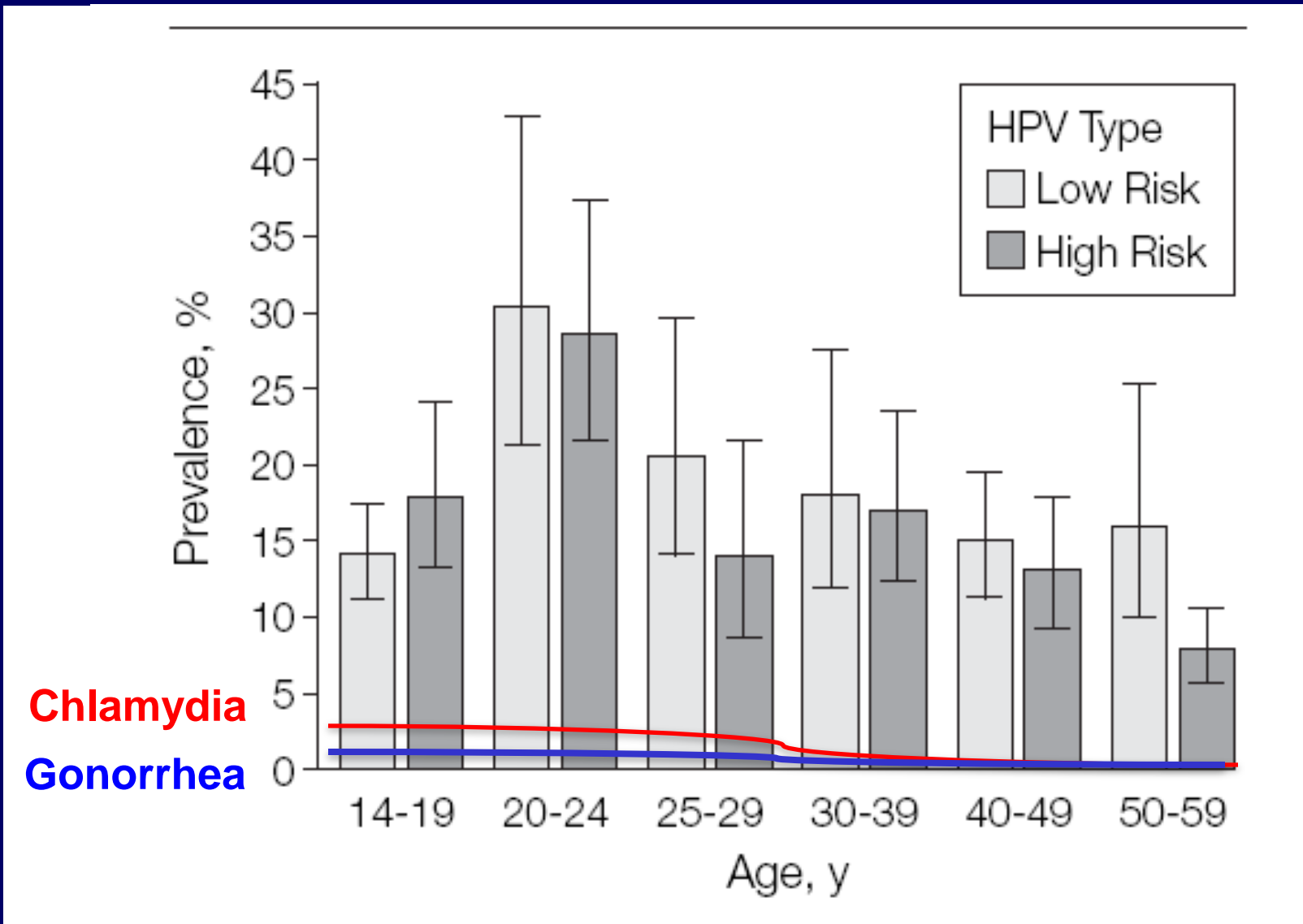
Prevalence of HPV Among FEMALES 14 to 59 years



Prevalence of HPV Among MALES 18 to 70 years



Prevalence of HPV Among Females 14 to 59 years



HPV in the U.S.

By 50 years old, 80% of women
will have acquired a genital
HPV infection...

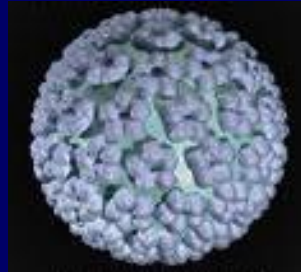
HPV is ubiquitous



HPV in the U.S.

By 50 years old, 80% of women
will have acquired a genital
HPV infection...

Most will not develop cancer

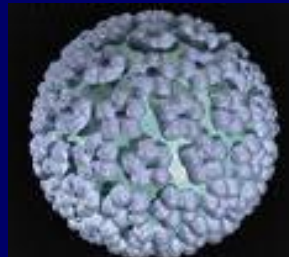


Transmission of HPV

Skin to skin contact!

HPV can spread through anogenital region

- Condoms only partially effective prevention
- Some adolescents found to test positive for vaginal HPV prior to first vaginal sexual intercourse



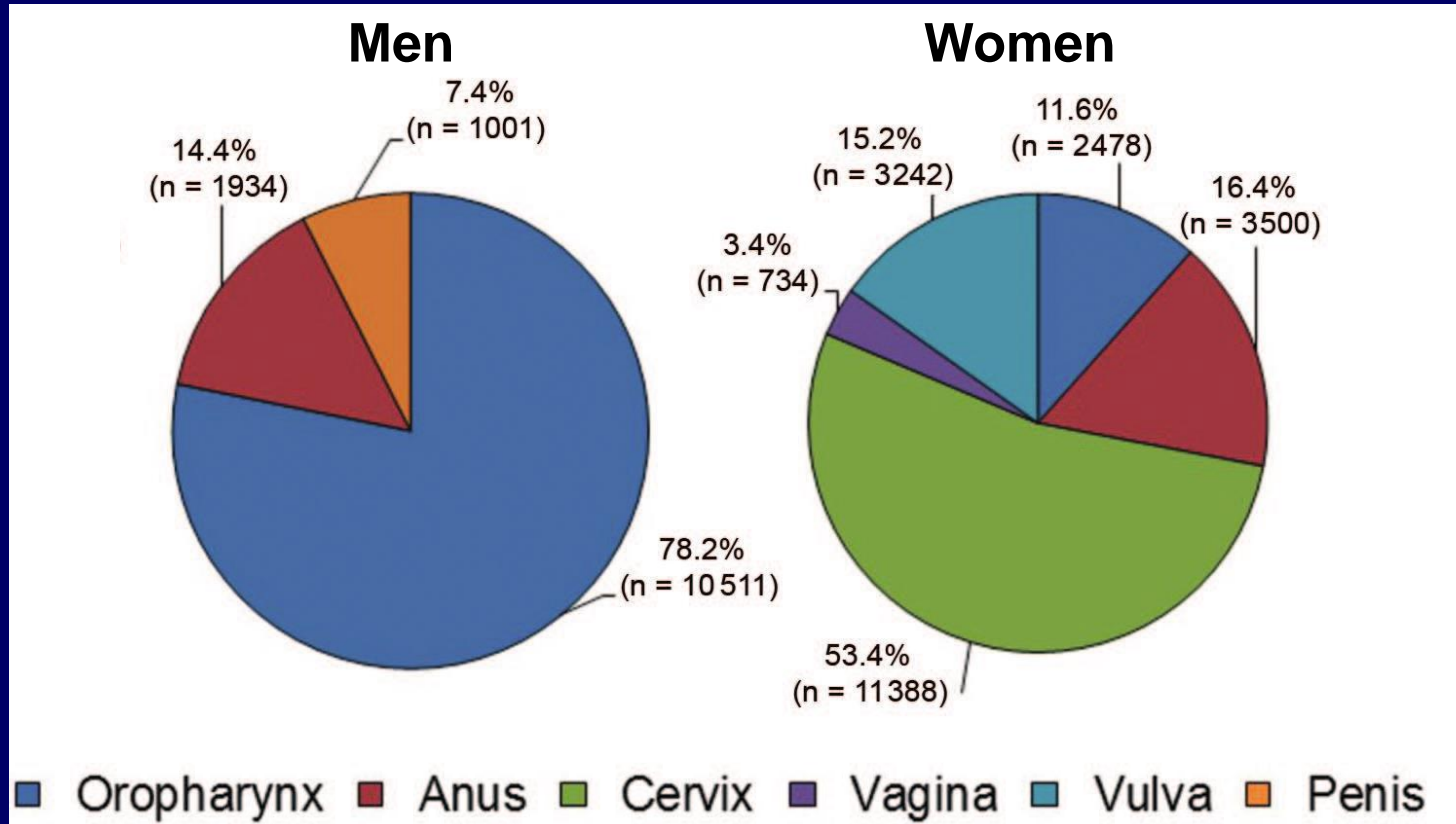
HPV-Related Disease in Adults

- Genital Warts
- Anogenital dysplasias and carcinomas
- Head and neck cancers

HPV-Related Cancer in 2014

Cancer Type	New Cases	Deaths
Oral, Pharyngeal	42,440	8390
Cervical	12,360	4020
Vaginal and Vulvar	8020	1910
Anal	7210	950
Penile	1649	320

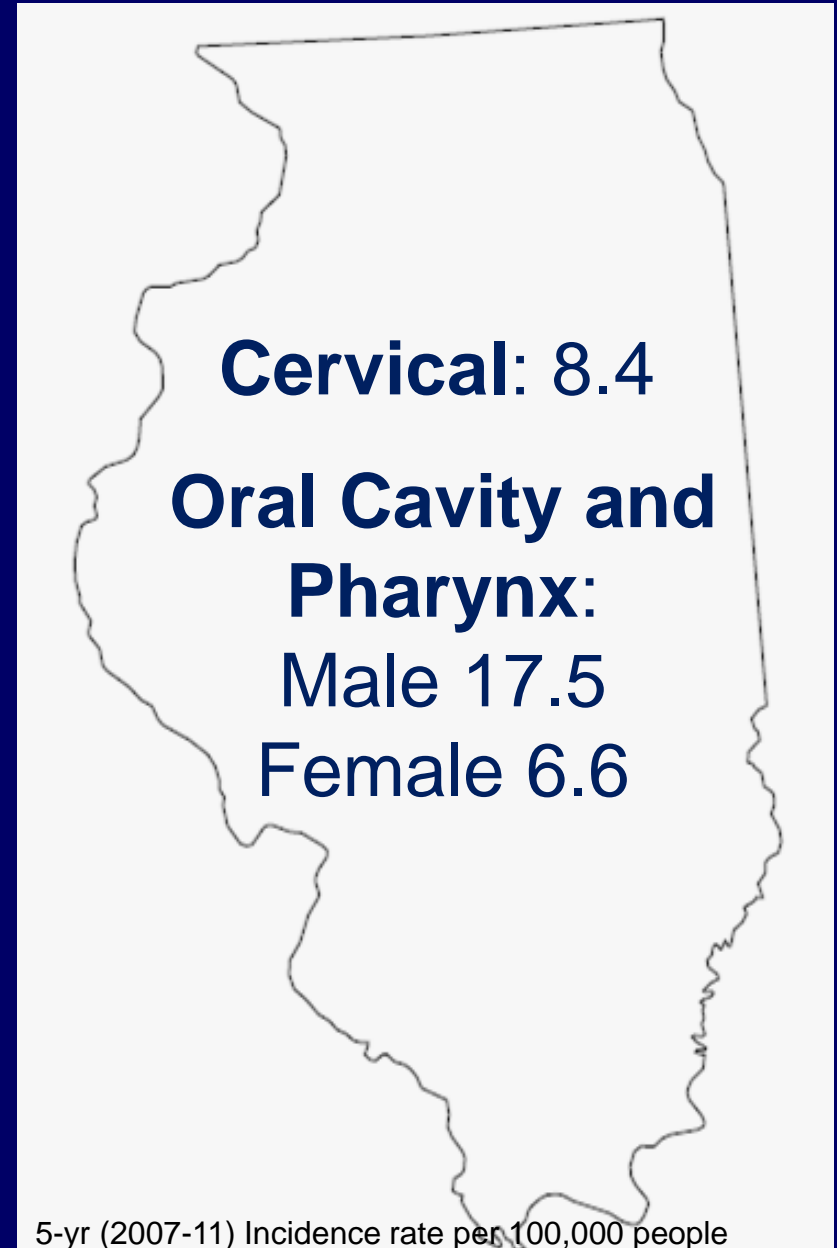
HPV-Related Cancer



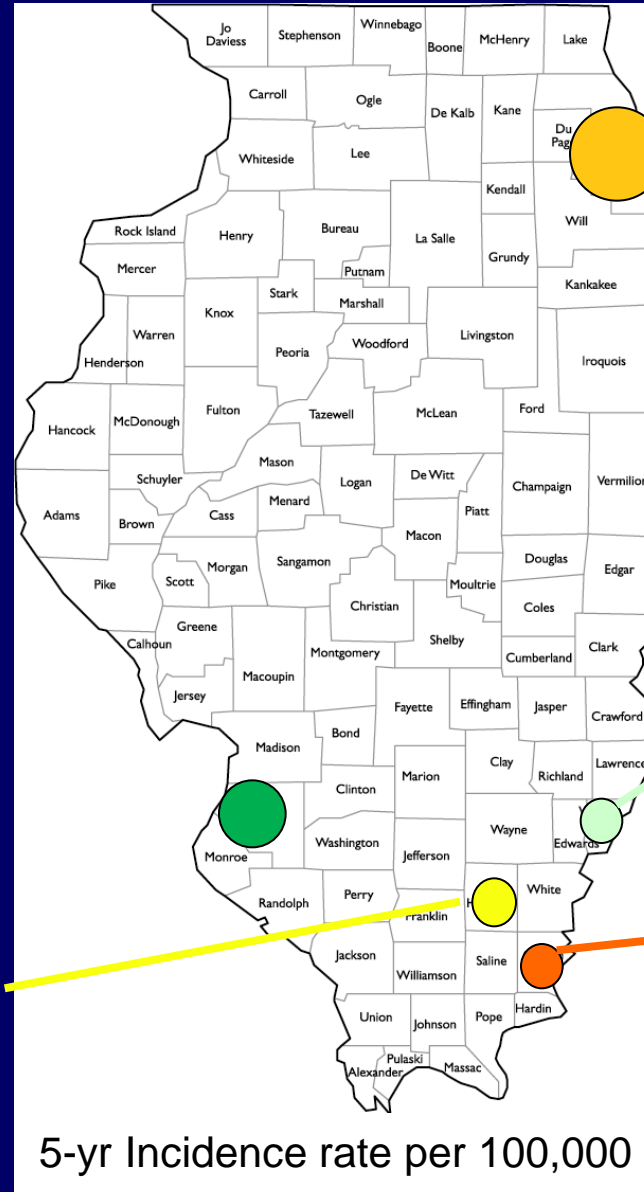
HPV-Related Cancers in Illinois

470 new cases
of cervical cancer
in 2014

6th highest incidence
for cervical cancer
in the United States



Incidence of HPV-Related Cancers in Illinois



Cook County

Cervical 10.2
Oral Cavity and Pharynx
Male 17.9
Female 6.6

Wabash County

Oral Cavity and Pharynx
Male 41.7

Gallatin County

Oral Cavity and Pharynx
Male 37.5

St. Clair

Cervical 8.4
Oral Cavity and
Pharynx
Male 17.5
Female 6.7

Hamilton County

Cervical: 30.5

5-yr Incidence rate per 100,000

HPV-Related Cancers in 2014

	Estimated New Cases			Estimated Deaths		
	Both Sexes	Male	Female	Both Sexes	Male	Female
All Sites	1,665,540	855,220	810,320	585,720	310,010	275,710
Oral cavity & pharynx	42,440	30,220	12,220	8,390	5,730	2,660
Tongue	13,590	9,720	3,870	2,150	1,450	700
Mouth	11,920	7,150	4,770	2,070	1,130	940
Pharynx	14,410	11,550	2,860	2,540	1,900	640
Other oral cavity	2,520	1,800	720	1,630	1,250	380
Anus, anal canal, & anorectum	7,210	2,660	4,550	950	370	580

Incidence of HPV-related oral pharyngeal and anal carcinomas are **increasing**

- Particularly among males
- 60+% of oropharyngeal carcinomas positive for HPV 16

HPV Oropharyngeal Cancers in U.S.

- Increase in oropharyngeal cancers in past decades despite decrease in tobacco use
 - Tobacco and alcohol remain risk factors
 - Many HPV+ cancers among never smokers
- If trend continues oropharyngeal HPV-related cancers will exceed incidence of cervical cancer in coming years
 - **More MEN with HPV-related cancer than women**

HPV Oropharyngeal Cancers in U.S.

- Transmission is oral sex
 - Though not completely understood
- Why increase in younger individuals?
 - Different sexual norms
 - Oral sex at an earlier age
 - Decrease in other tobacco-related cancers
- Greater prevalence in men?
 - HPV burden in cervix greater than penis
- Oral HPV detected in 3-5% of adolescents, and 5-10% adults

HPV and SEX

Vaccination against HPV
does NOT affect
sexual behavior

HPV Prevention: Vaccination



HPV4 – Gardasil (Merck)

HPV2 – Cervarix (GSK)

HPV Vaccine: HPV4

- FDA licensed first HPV Quadrivalent Vaccine (HPV4) (Gardasil, Merck) June 8, 2006
- Initially indicated for prevention of disease caused by HPV types 6, 11, 16 & 18
 - Genital warts
 - Cervical Cancer
 - Cervical adenocarcinoma in situ
 - Cervical intraepithelial neoplasia grades 1, 2 and 3
 - Vulvar intraepithelial neoplasia grade 2 and 3
 - Vaginal intraepithelial neoplasia grade 2 and 3

HPV Vaccine: HPV4

Since then two additional indications have been licensed for the HPV4 vaccine

- Prevention of genital warts caused by HPV types 6 and 11 in MALES
- Prevention of anal cancer and associated precancerous lesions due to HPV types 16, 18 in both males and females

HPV4 Vaccine

Per Protocol Summary of Month 18 Anti-HPV Response

Parameter	Boys			Girls		
	n	Response	95% CI	n	Response	95% CI
Anti-HPV 6 % Seroconversion GMT (mMU/mL)	449	97.8 227	(95.9, 98.9) (204, 251)	481	97.9 213	(96.2, 99.0) (195, 232)
Anti-HPV 11 % Seroconversion GMT (mMU/mL)	450	99.3 292	(98.1, 99.9) (263, 323)	481	99.2 300	(97.9, 99.9) (273, 330)
Anti-HPV 16 % Seroconversion GMT (mMU/mL)	448	99.3 1,402	(98.1, 99.9) (1252, 1570)	478	99.8 1,250	(98.8, 100) (1134, 1378)
Anti-HPV 18 % Seroconversion GMT (mMU/mL)	451	92.5 233	(89.6, 94.7) (201, 270)	483	91.5 181	(88.7, 93.8) (159, 205)

Source: Reisinger KS, et al. *Pediatr Infect Dis J.* 2007;26(3):201-209.

Efficacy of HPV4 Vaccine

Analysis of Efficacy of GARDASIL in the PPE* Population** of 16- Through 26-Year-Old Girls and Women for Vaccine HPV Types

Population	GARDASIL		AAHS Control		% Efficacy (95% CI)
	N	Number of cases	N	Number of cases	
HPV 16- or 18-related CIN 2/3 or AIS					
Study 1***	755	0	750	12	100.0 (65.1, 100.0)
Study 2	231	0	230	1	100.0 (-3744.9, 100.0)
Study 3	2201	0	2222	36	100.0 (89.2, 100.0)
Study 4	5306	2	5262	63	96.9 (88.2, 99.6)
Combined Protocols†	8493	2	8464	112	98.2 (93.5, 99.8)
HPV 16-related CIN 2/3 or AIS					
Combined Protocols†	7402	2	7205	93	97.9 (92.3, 99.8)
HPV 18-related CIN 2/3 or AIS					
Combined Protocols†	7382	0	7316	29	100.0 (86.6, 100.0)
HPV 16- or 18-related VIN 2/3					
Study 2	231	0	230	0	Not calculated
Study 3	2219	0	2239	6	100.0 (14.4, 100.0)
Study 4	5322	0	5275	4	100.0 (-50.3, 100.0)
Combined Protocols†	7772	0	7744	10	100.0 (55.5, 100.0)
HPV 16- or 18-related VaIN 2/3					
Study 2	231	0	230	0	Not calculated
Study 3	2219	0	2239	5	100.0 (-10.1, 100.0)
Study 4	5322	0	5275	4	100.0 (-50.3, 100.0)
Combined Protocols†	7772	0	7744	9	100.0 (49.5, 100.0)
HPV 6-, 11-, 16-, or 18-related CIN (CIN 1, CIN 2/3) or AIS					
Study 2	235	0	233	3	100.0 (-138.4, 100.0)
Study 3	2241	0	2258	77	100.0 (95.1, 100.0)
Study 4	5388	9	5374	145	93.8 (88.0, 97.2)
Combined Protocols†	7864	9	7865	225	96.0 (92.3, 98.2)
HPV 6-, 11-, 16-, or 18-related Genital Warts					
Study 2	235	0	233	3	100.0 (-139.5, 100.0)
Study 3	2261	0	2279	58	100.0 (93.5, 100.0)
Study 4	5404	2	5390	132	98.5 (94.5, 99.8)
Combined Protocols†	7900	2	7902	193	99.0 (96.2, 99.9)
HPV 6- and 11-related Genital Warts					
Combined Protocols†	6932	2	6856	189	99.0 (96.2, 99.9)

HPV Vaccine: HPV2

- FDA licensed HPV Bivalent Vaccine (Cervarix, GSK) Oct 26, 2009
 - Females 9-25yo
- Indicated for prevention of disease caused by HPV types 16 and 18 (cancer prevention)
 - Cervical Cancer
 - Cervical adenocarcinoma in situ
 - Cervical intraepithelial neoplasia grades 1, 2 and 3

Unanimous ACIP Recommendation, 2007

“ACIP recommends routine vaccination of females aged 11-12 years with 3 doses of quadrivalent HPV vaccine. The vaccination series can be started as young as age 9 years.”

“Vaccination is also recommended for females aged 13-16 years who have not been previously vaccinated or who have not completed the full series.”

ACIP Recommendation, 2011

“Advisory Committee on Immunization Practices recommended routine use of quadrivalent human papillomavirus (HPV4) vaccine in males aged 11 or 12 years.”

“ACIP also recommended vaccination with HPV4 for males aged 13-21 years who have not been vaccinated previously or who have not completed the 3-dose series; males aged 22 through 26 years may be vaccinated”

Recommend is the same language for all other childhood vaccines

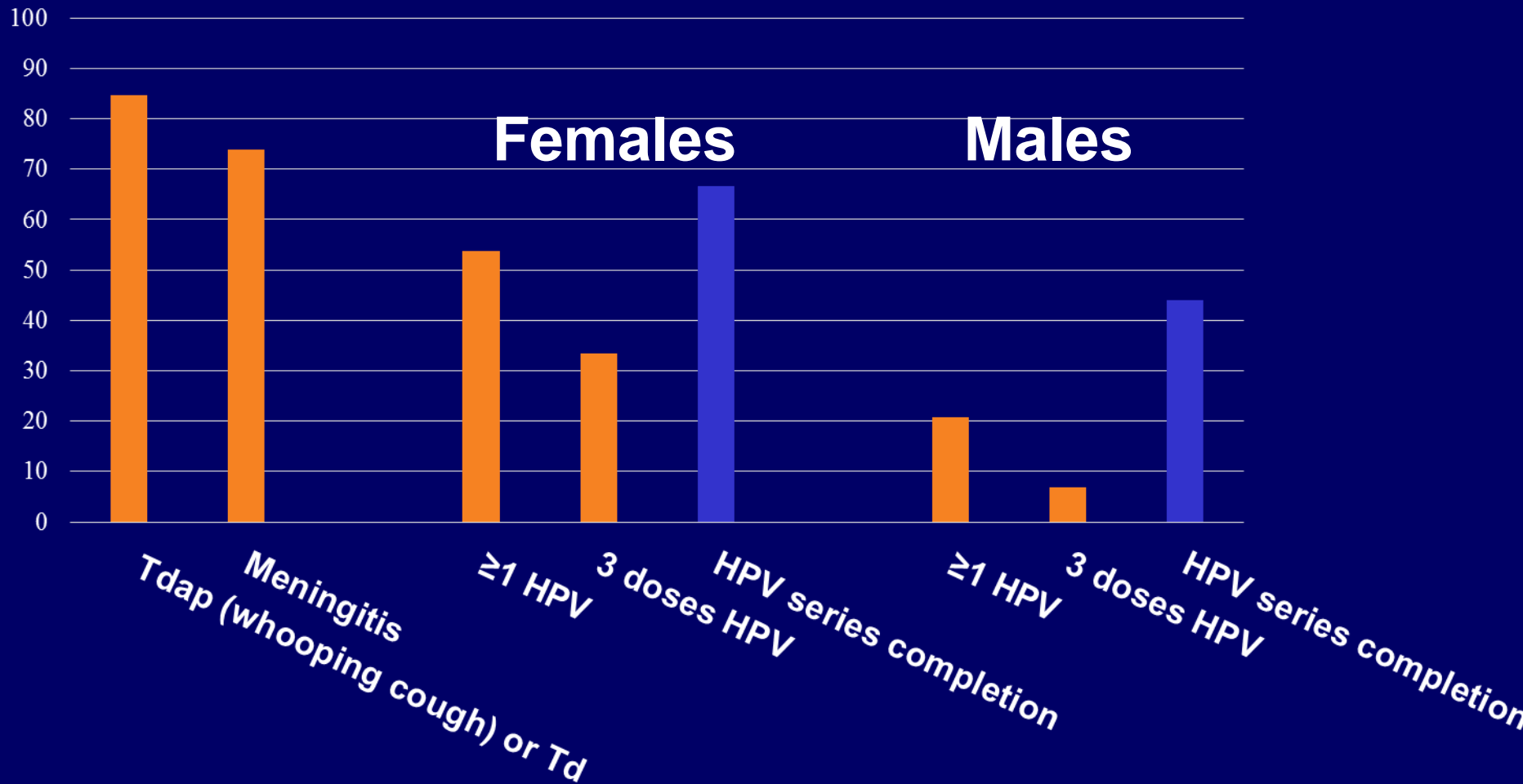
Seven Years of Vaccinating Against HPV

Where are we now?

Vaccination Coverage in the U.S.

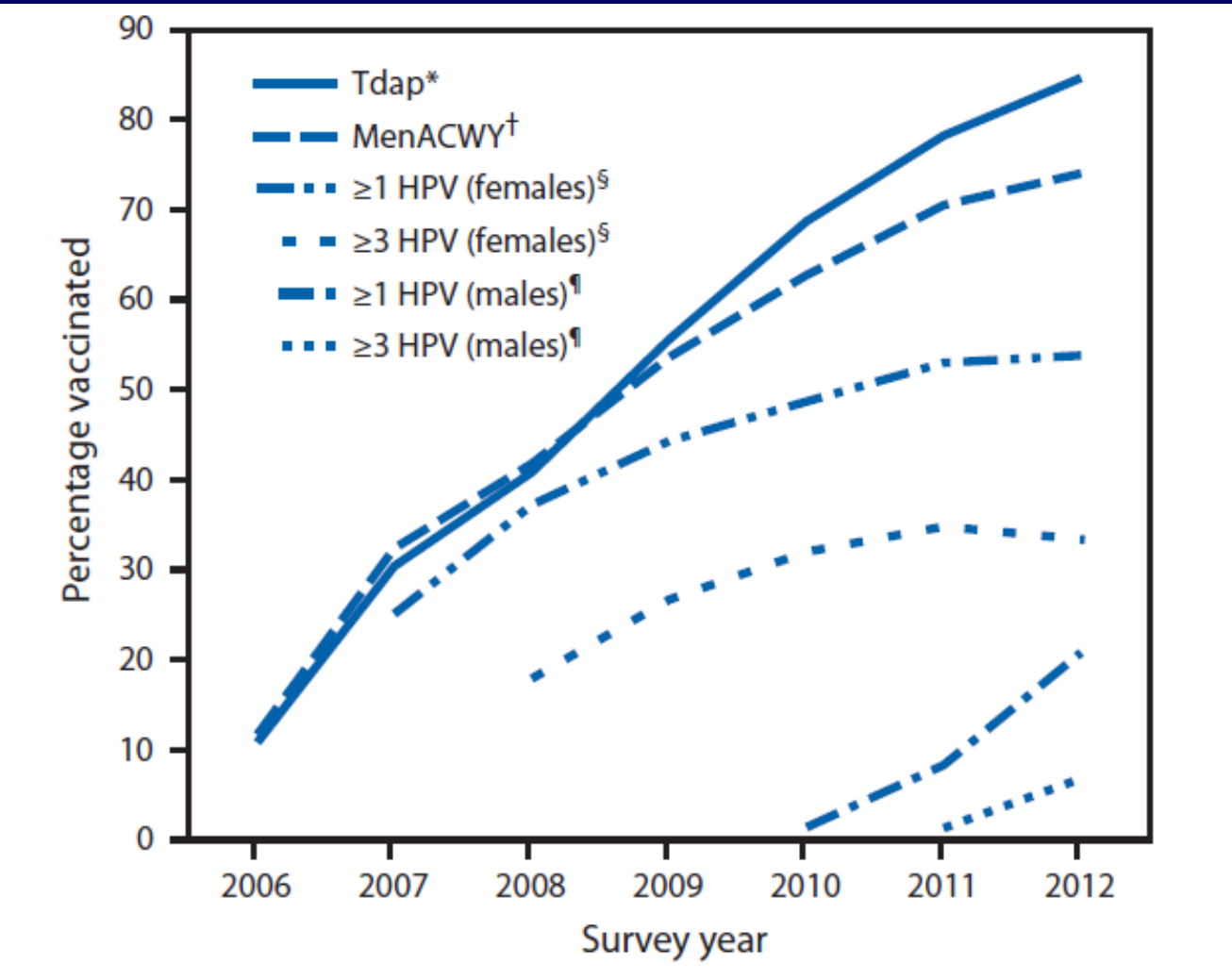


Current HPV Vaccination Rates

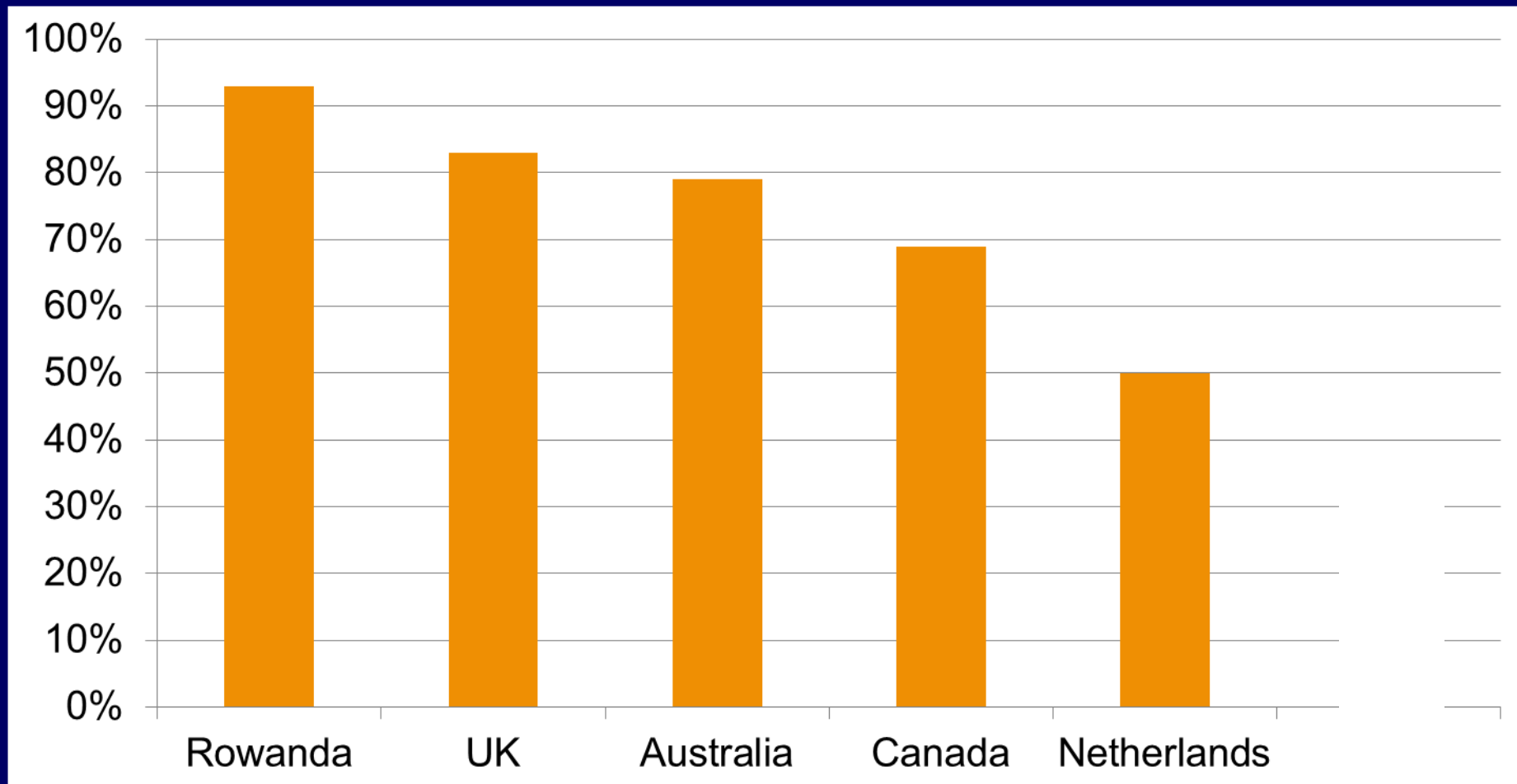


Estimated Vaccination Coverage Among 13-17yo

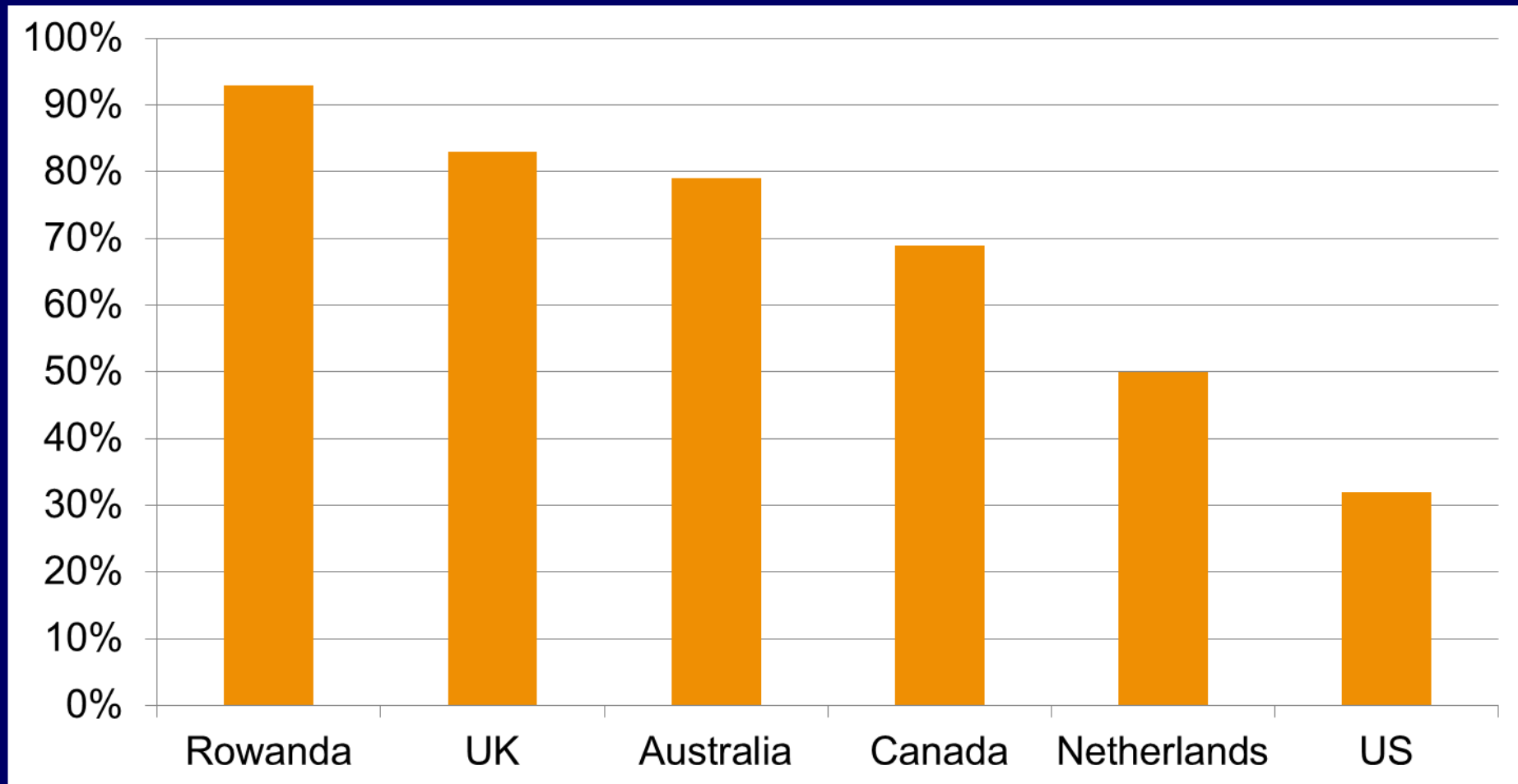
National Immunization Survey – 2006-2012



International HPV Vaccine 3 dose Coverage, by Country



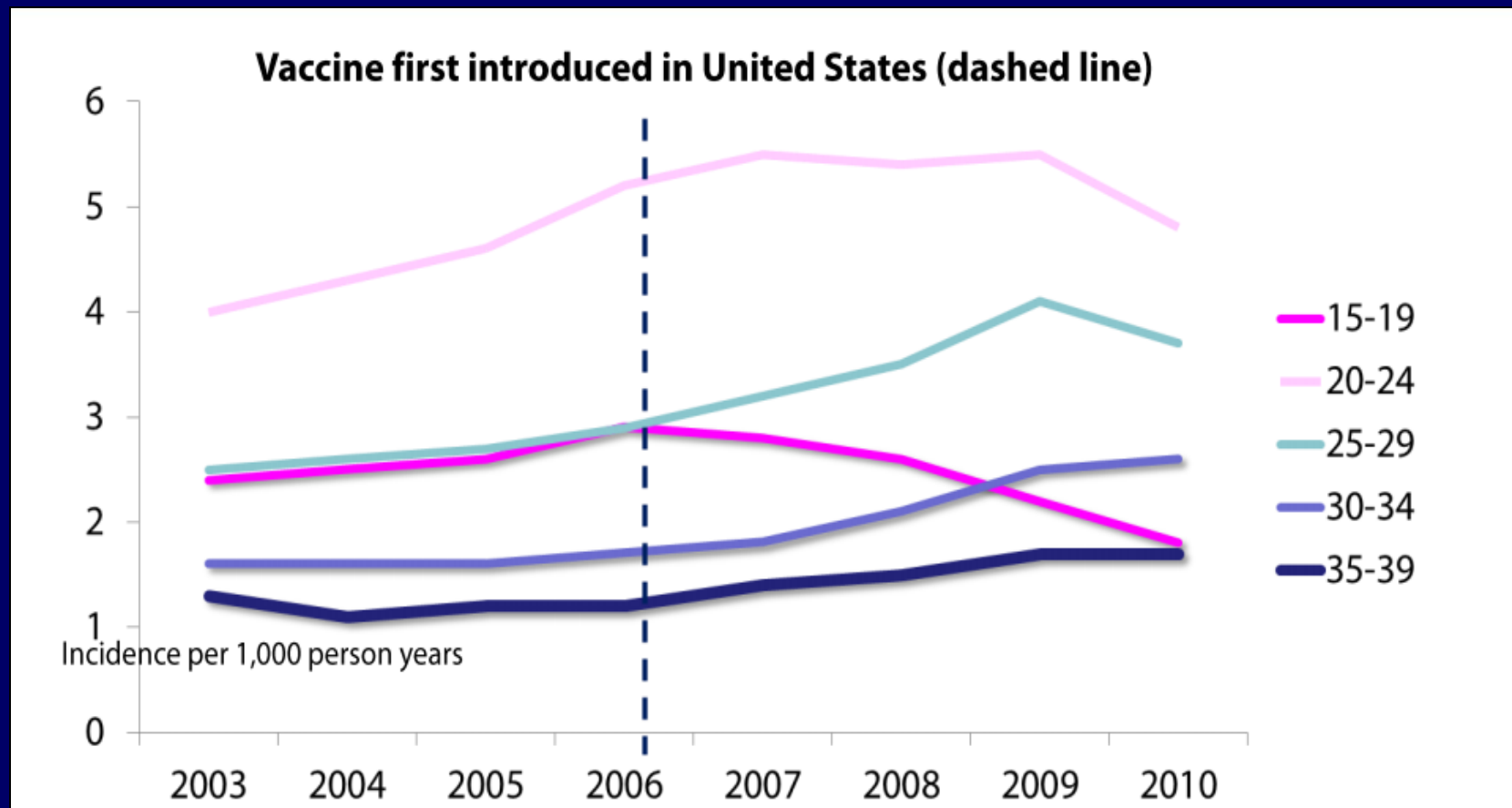
International HPV Vaccine 3 dose Coverage, by Country



HPV Infections Decreased, US, 2007-10

- In 14-19 year olds, vaccine-type HPV prevalence decreased from 11.5 percent (2003-6) to 5.1 percent (2007-10)
 - Other age groups did not show a statistically significant difference over time
 - Research showed that vaccine is very effective for prevention of infection (estimated >82% effective)

Genital Warts, Females by Age Group, US, 2003-2010



HPV Vaccines are Safe

- > 60 million doses distributed in US
- Most common adverse events were mild
 - Sore arm, myalgias
- Serious adverse events: **No** patterns to suggest any events caused by the vaccine
- Findings similar to the safety of all other adolescent vaccines

Population-based, Post-licensure Observational Safety Studies of HPV4 Vaccine in US Females Aged 9–26 Years

Organization	System or review	No. of doses evaluated	Description	Methods	Findings
CDC	Vaccine Safety Datalink ²	600,559	Safety assessment of 7 prespecified health outcomes among female HPV4 vaccine recipients at 7 managed care organizations ³	Cohort design with weekly sequential analyses of electronic medical data ⁴	No statistically significant increase in risk for the outcomes monitored
Manufacturer	Postmarketing commitment to FDA ⁵	346,972	General study assessment of HPV4 vaccine after routine administration at 2 large managed care organizations	Self-controlled risk interval design, supplemented with medical record review	HPV4 vaccine associated with syncope on the day of vaccination and skin infections ⁶ in the 2 weeks after vaccination
Manufacturer	Postmarketing commitment to FDA ⁷	346,972	Assessment of 16 prespecified autoimmune conditions after routine use of HPV4 vaccine at 2 large managed care organizations	Retrospective cohort using electronic medical data, supplemented with medical record review ⁸	No confirmed safety signals for the outcomes monitored

1. *MMWR*. July 26, 2013, Vol. 62, No. 29. 2. Gee J, et al. *Vaccine*. 2011;29:8279-8284. 3. Prespecified outcomes included Guillain-Barré syndrome, stroke, appendicitis, seizures, allergic reactions, anaphylaxis, syncope, and venous thromboembolism 4. Comparison groups included historic background rates for Guillain-Barré syndrome, stroke, appendicitis, venous thromboembolism, and anaphylaxis; concurrent preventive health visits for seizures; or adolescent vaccination visits for syncope and allergic reactions. 5. Klein NP, et al. *Arch Pediatr Adolesc Med*. 2012;166(12):1140-1148. 6. Medical record review suggested some cases might have been local injection site reactions.

7. Chao C, et al. *J Intern Med*. 2012;271(2):193-203. 8. Comparison group included background incidence rates.

US Post-licensure Safety Surveillance Study: Autoimmune Safety Results

Condition	Vaccinated	Nonvaccinated	Incidence Rate Ratio (95% CI)
	Incidence/100,000 Person-Years		
Graves disease	18.2	25.8	0.72 (0.50–1.01)
Hashimoto disease	104.8	81.1	1.29 (1.08–1.56)
Type 1 diabetes	10.3	18	0.57 (0.47–0.73)
Immune thrombocytopenia	6.8	5.9	1.16 (0.85–1.83)
Juvenile rheumatoid arthritis	3.4	7.7	0.48 (0.26–0.91)
Multiple sclerosis	3.4	2.5	1.37 (0.74–3.2)
Optic neuritis	5.7	3.9	1.45 (1.00–2.91)
Other demyelinating CNS diseases	1.1	1.6	0.71 (0.38–2.13)
Rheumatoid arthritis	4.6	7	0.71 (0.39–1.45)
Systemic lupus erythematosus	11.4	10.3	1.07 (0.69–1.6)
Uveitis	8	11.9	0.67 (0.49–1.02)

CNS=central nervous system

Chao C, et al. *J Intern Med.* 2012;271(2):193-203.

Australia

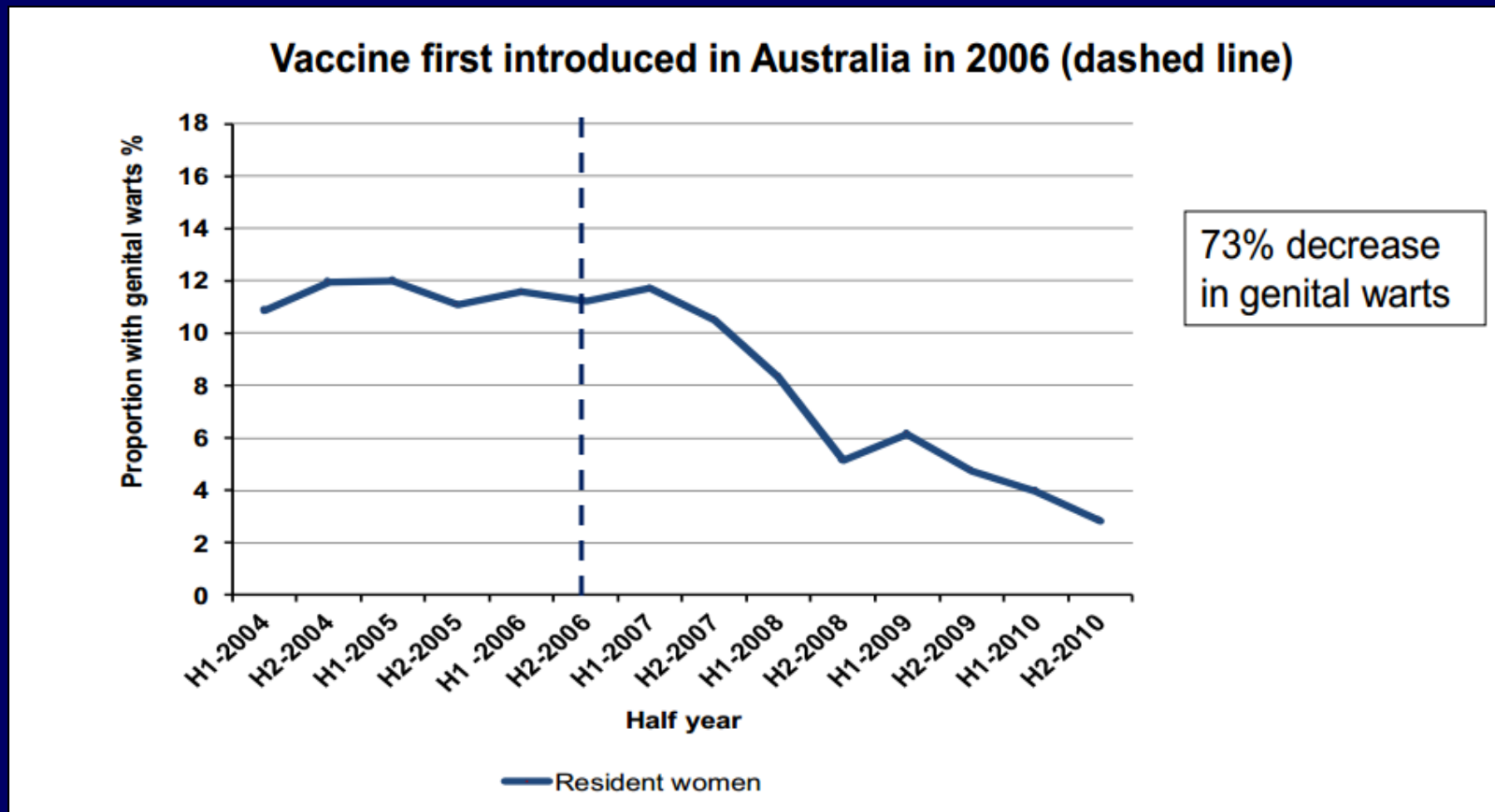


Australia

- >80% of school-age girls are fully vaccinated
- High-grade cervical lesions have declined in women <18 years
- Among vaccine-eligible females, 93% decline in cases of genital warts
 - 82% decline among unvaccinated males of the same age



Genital Warts among Females < 26 years, Australia, 2004-2010



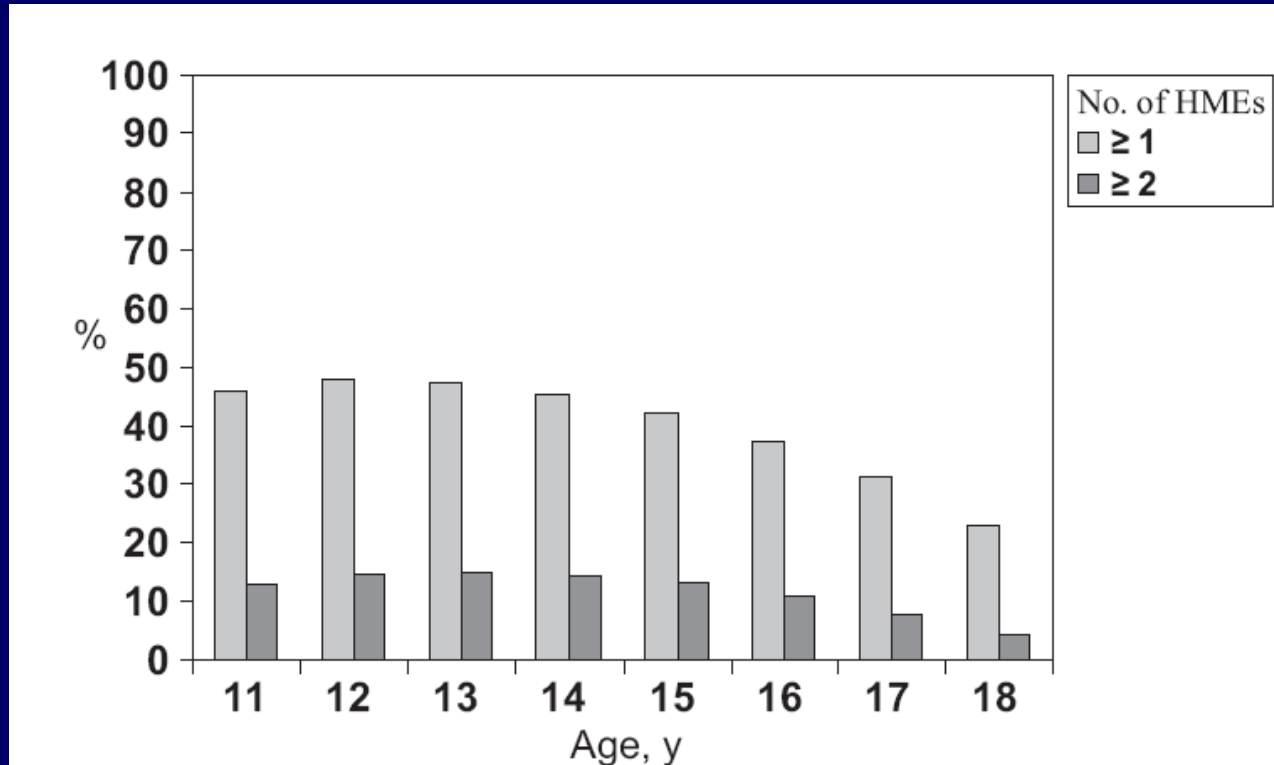
Challenges and Barriers to Vaccinating Adolescents

Challenges to Vaccinating Adolescents

- Knowledge
- School Requirements
- **Access**
- Concern about HPV

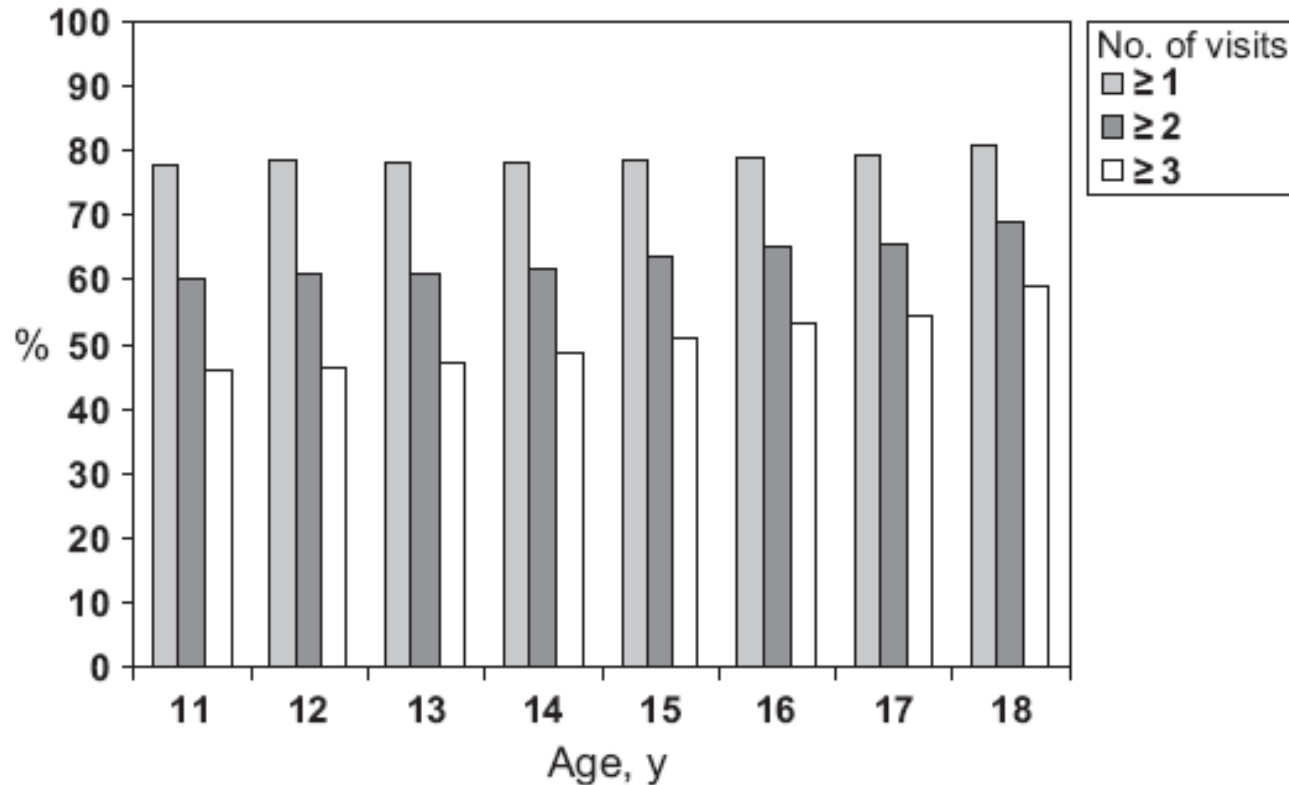


Proportion of Medicaid-Enrolled Adolescents Receiving Health Maintenance Exam



Less than 50% of 11-18-year-olds on Medicaid had a health maintenance visit in a 2-year period

Proportion of Medicaid-Enrolled Adolescents Receiving Problem Focused Care



Strategies to Vaccinate

Capture missed opportunities

- Non-primary care visits: acute care visits, urgent care, ED
- Standing immunization orders
- Extended immunization hours
 - Flu clinic model
- HPV: normalize vaccination

Challenges to Vaccinating Adolescents

How we present the vaccine

**Considerations
&
Solutions**

How We Present the Vaccine: Considerations

***“Sex during adolescence
is for other peoples kids”***

#1: Parents do not want to think about their kids being sexually active

#2: Immunization 101: Vaccines can only prevent disease you have not yet had

- Important to immunize **before** exposure
- Most parents do not know how immunizations work

How We Present the Vaccine: Considerations

For many parents this vaccine is simply 'new' and they have questions

- What does it do?
- Who is it for?
- Is it safe?

How We Present the Vaccine: Solutions

Potential Solutions

Approach to *Avoid*: A Focus on Sex

“HPV stands for human papillomavirus and causes genital warts and cervical cancer. It is a sexually-transmitted disease. Many kids become sexually active by age 14.

Do you want this vaccine for your
11 year-old?”



Approach to Consider: *Less is More*

“Today your son is due for three routine vaccines which include meningitis vaccine; Tdap which is tetanus, diphtheria, and whooping cough; and HPV which is human papillomavirus vaccine. Someone will be right in to administer those vaccines and I look forward to seeing you next year.”

Approach to Consider: *Less is More*

If questions arise about the HPV vaccine:

“Has anyone that you care about had cancer?”

“What was it like for them? For you?”

“We can reduce the chances of your son having a cancer experience. Do you want to reduce the chances of your son having cancer?”

Most Important Final Message

**Your Recommendation
Matters Most!**

