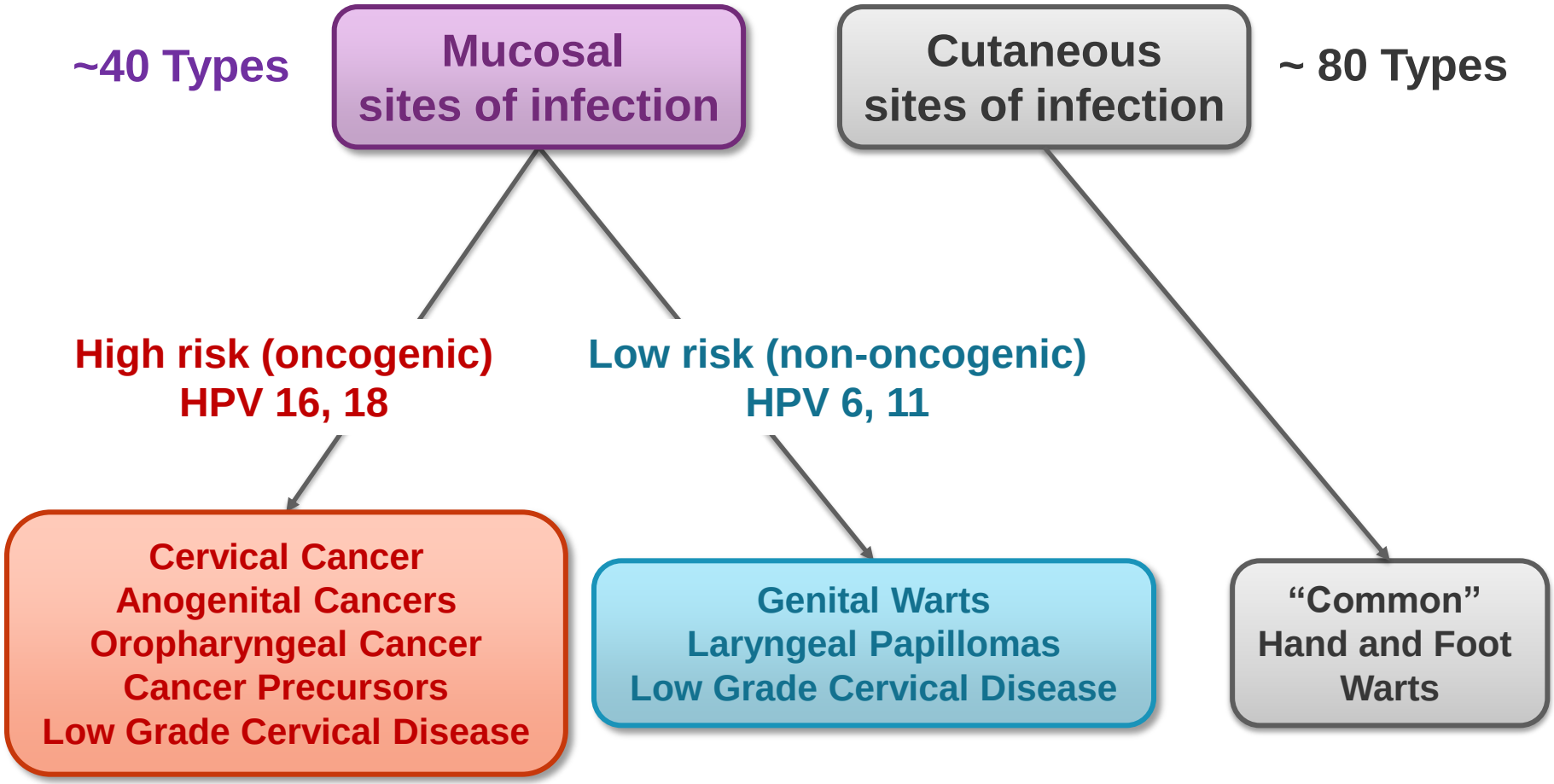
HPV Vaccines

Michael T. Brady, MD
Professor of Pediatrics
The Ohio State University
Associate Medical Director
Nationwide Children's Hospital

HPV Types Differ in their Disease Associations



HPV YOU ARE THE KEY TO CANCER PREVENTION

Disease Associations with Most Frequent Types of HPV

Diseases	HPV Type
Cutaneous warts	1, 2, 3, 4, 10 others
Cervical cancer	16, 18, 45, 31, 33, 35
Condyloma acuminata (anogenital warts)	6, 11
Recurrent respiratory papillomatosis	6, 11

Burd. *Clin Microbiol Rev* 2003;16:1-17

Risk Factors for HPV Infection

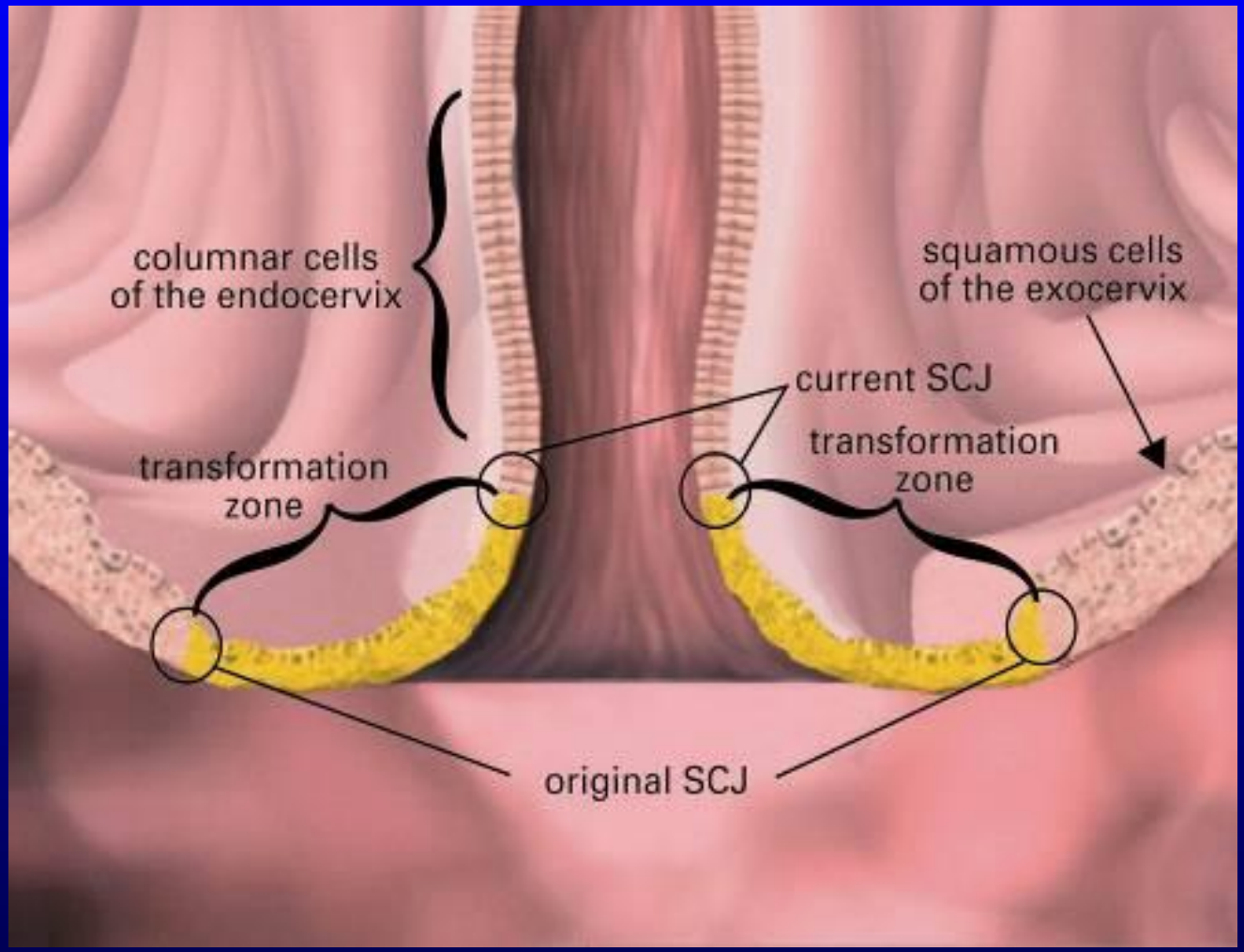
Women	Men
• Young age (peak age group 20-24 years of age)[1]	• Young age (peak group 25-29 years of age)[1]
• Lifetime number of sex partners[2]	• Lifetime number of sex partners[6]
• Early age of first sexual intercourse[3]	• Being uncircumcised[6]
• Male partner sexual behavior[3]	
• Smoking[4]	
• Oral contraceptive use[4]	
• Uncircumcised male partners[5]	

[1]Insinga RP, Dasbach EF, Myers ER. *Clin Infect Dis.* 2003;36:1397–1403.
[2]Burk RD, Ho GYF, Beardsley L, Lempa M, Peters M, Bierman R. *J Infect Dis*. 1996;174:679–689.
[3]Murthy NS, Mathew A. *Eur J Cancer Prev*. 2000;9:5–14.
[4]Winer RL, Lee S-K, Hughes JP, Adam DE, Kiviat NB, Koutsky LA. *Am J Epidemiol*. 2003;157:218–226.
[5]Schiffman M, Castle PE. *Arch Pathol Lab Med*. 2003;127:930–934.
[6]Svare EI, Kjaer SK, Worm AM, Osterlind A, Meijer CJLM, van den Brule AJ. *Sex Transm Infect*. 2002;78:215–218.

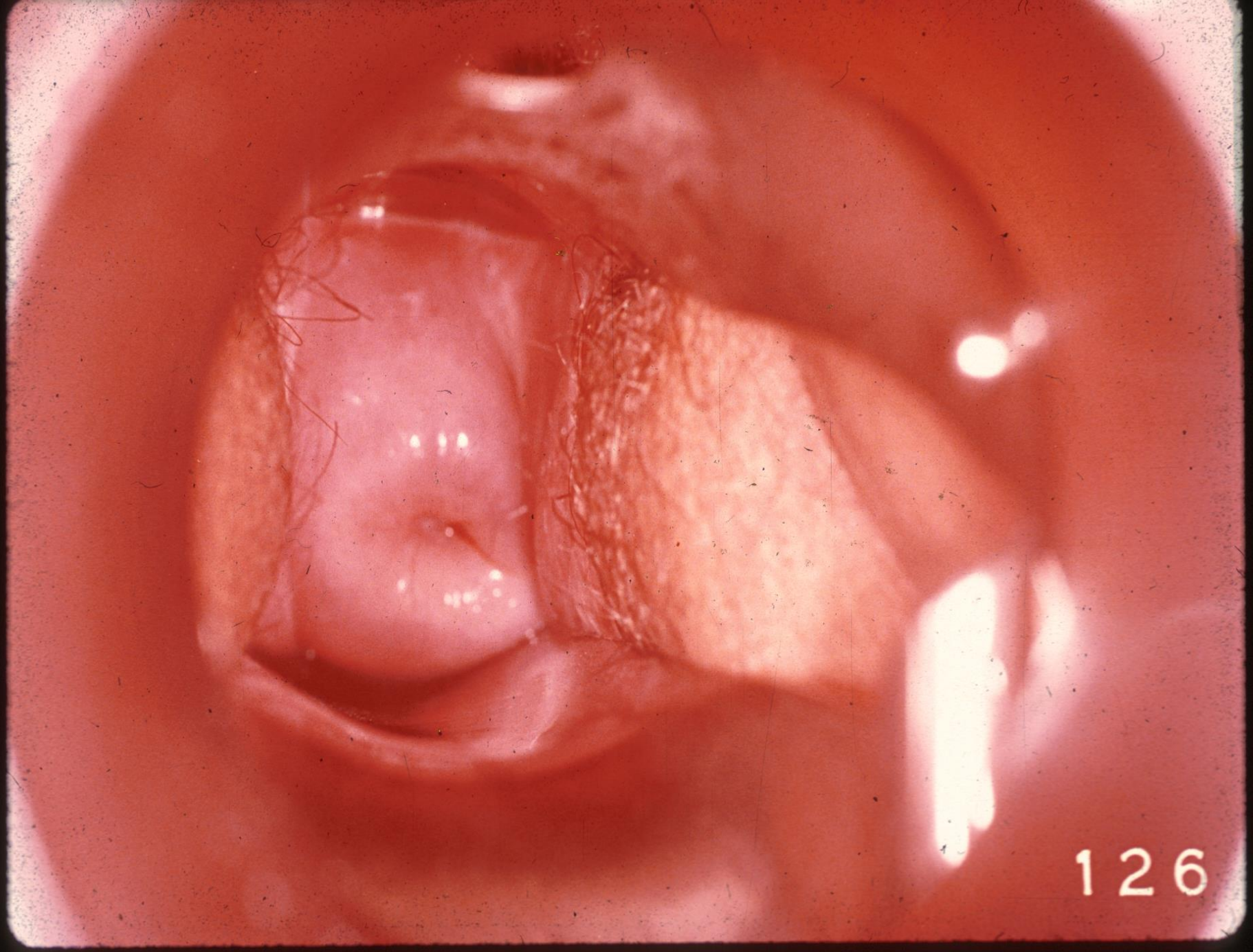
Human Papillomavirus: Risk factors

- Major risk factor: sexual activity
- Behavioral risk factors
  - Early age of first intercourse
  - Number of lifetime partners
  - Number of partner's partners
  - Older age of male partner
- Biologic risk factor
  - Immunosuppression
  - Cervical ectopy, anal transformation zone
  - Uncircumcised male

The Cervical Transformation Zone



Castle PE. *J Low Genit Tract Dis.* 2004;8:224–230.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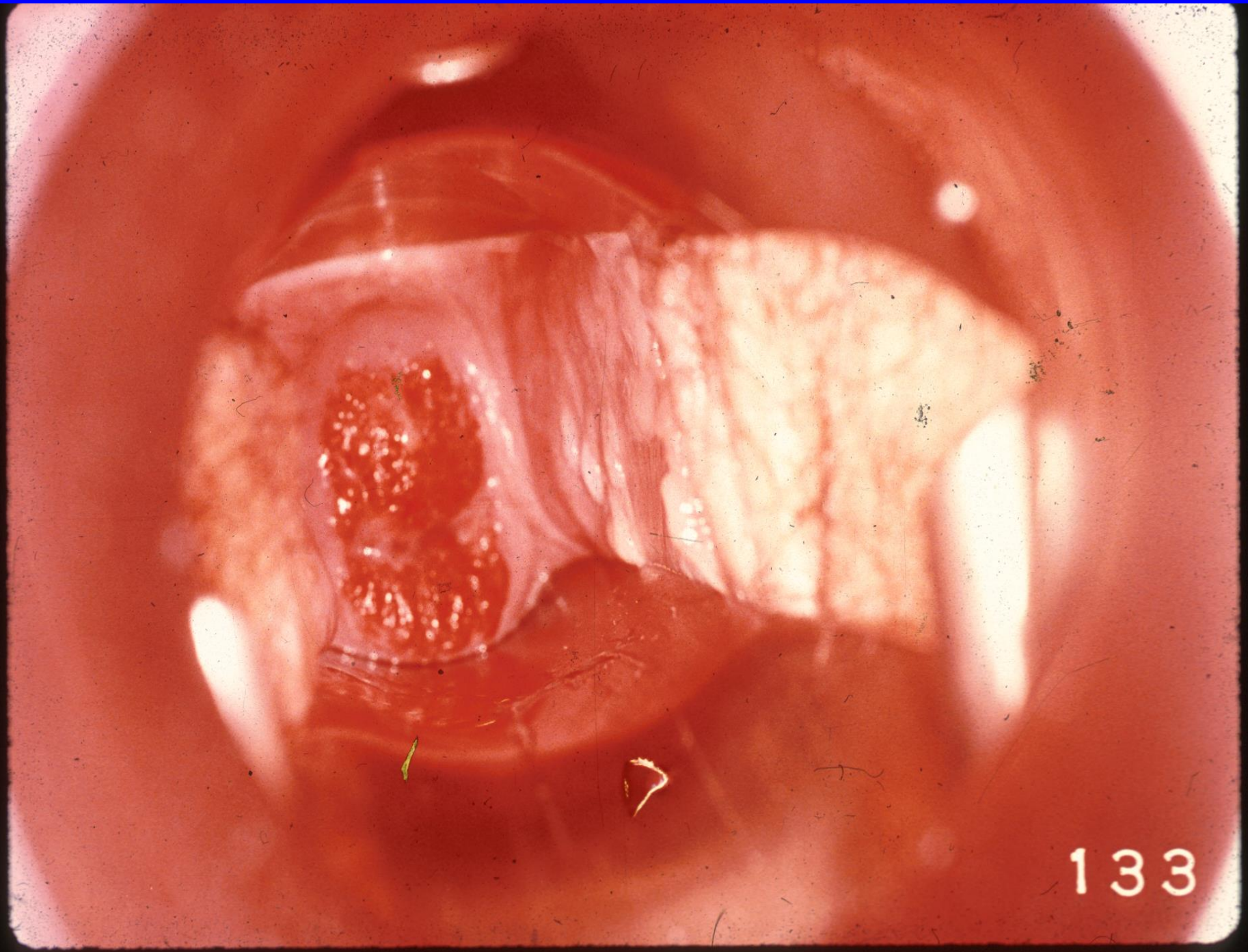
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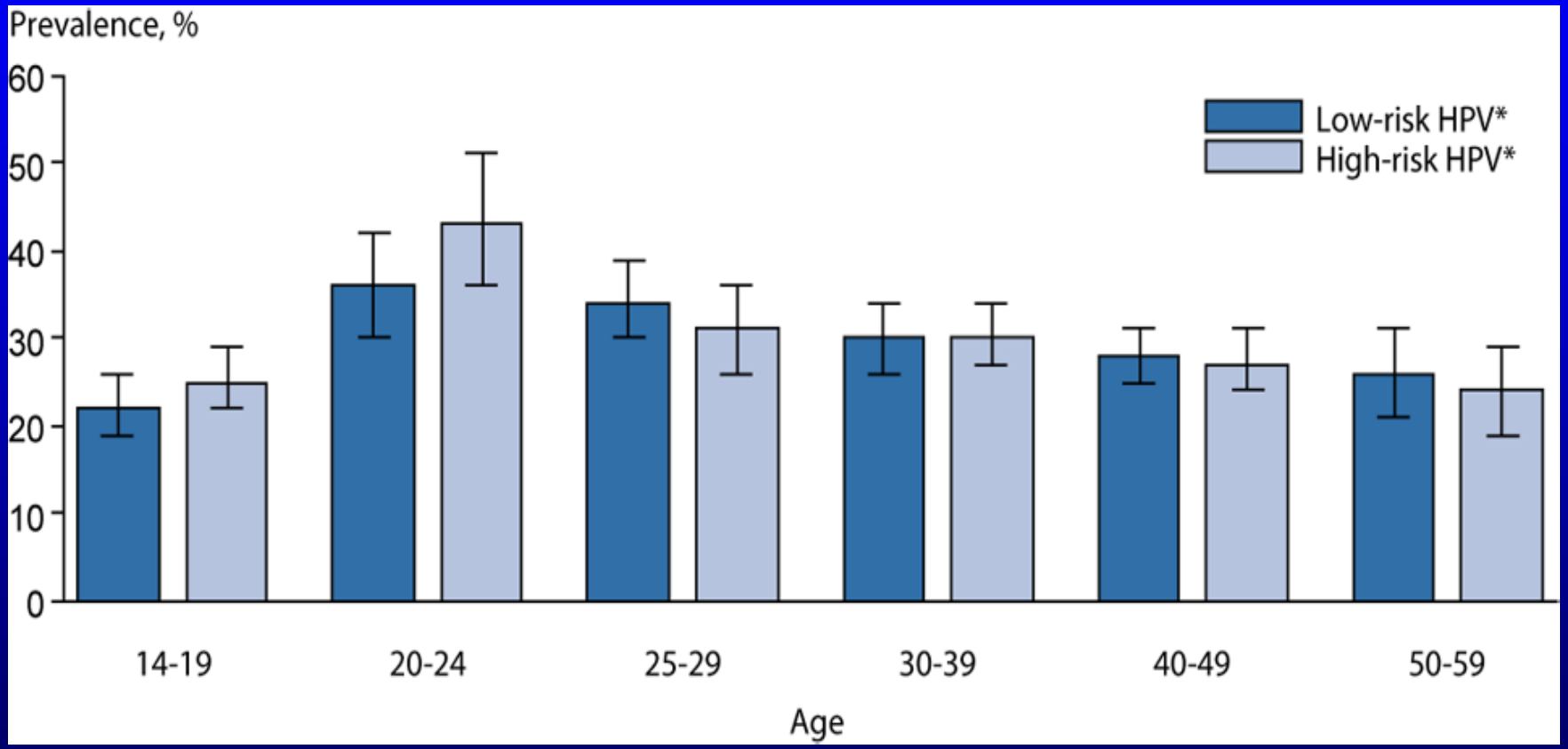
Human papillomavirus burden in adolescents and young adults in United States

- **Most common sexually transmitted pathogen**
  - **4.6 million new infections in 15-24 year olds each year**
  - **Infection commonly occurs shortly after sexual debut**
  - **62% of adolescents sexually active by 12th grade**
  - **Prevalence of HPV in adolescents/young adults is 25-40%**

Human Papillomavirus
Epidemiology

Approximately one-half of sexually active adolescents and young adults will acquire HPV within 5 years of initiating intercourse

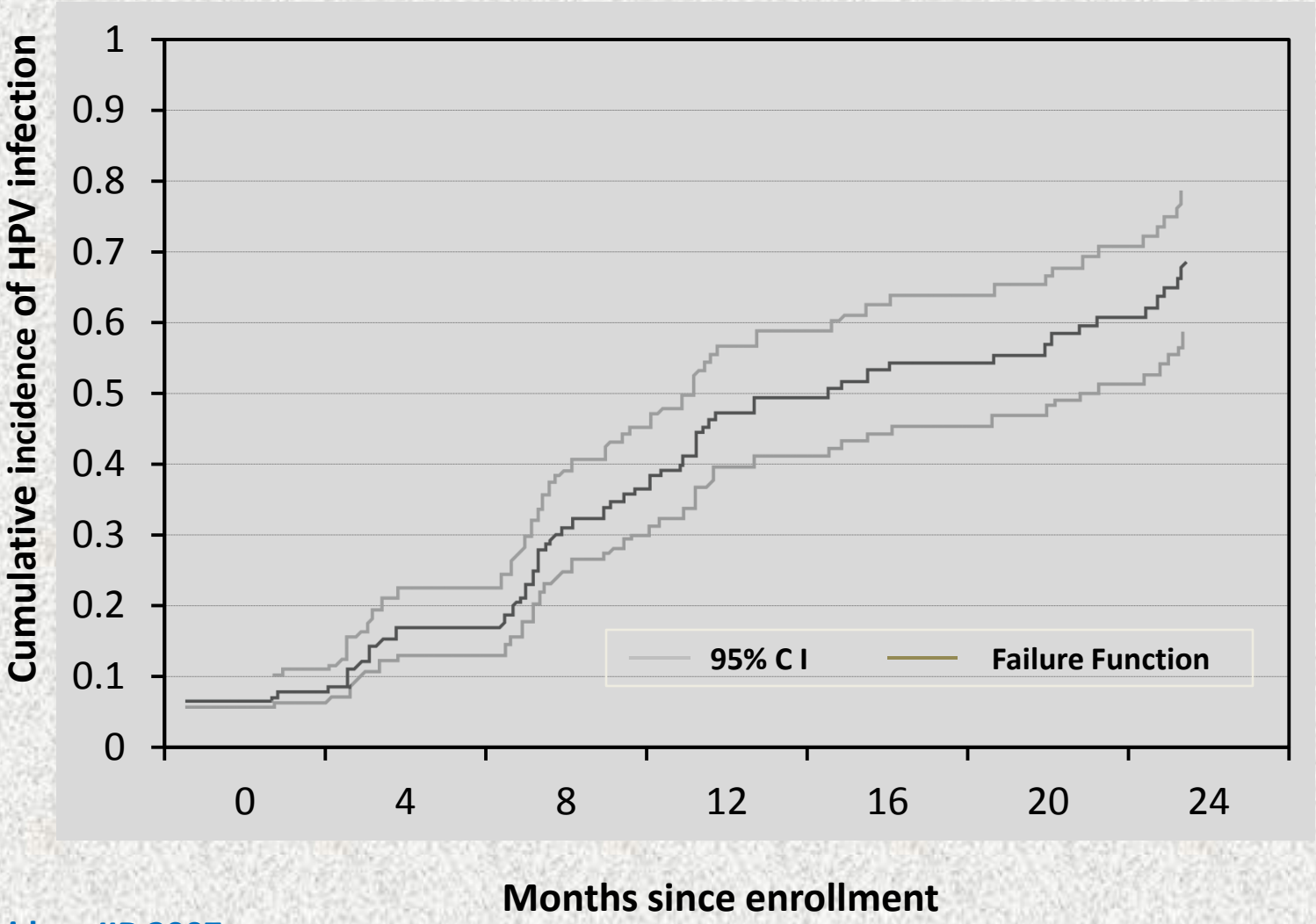
HPV Prevalence:
Females Aged 14-59



National Health and Nutrition Examination Survey, 2003 – 2006

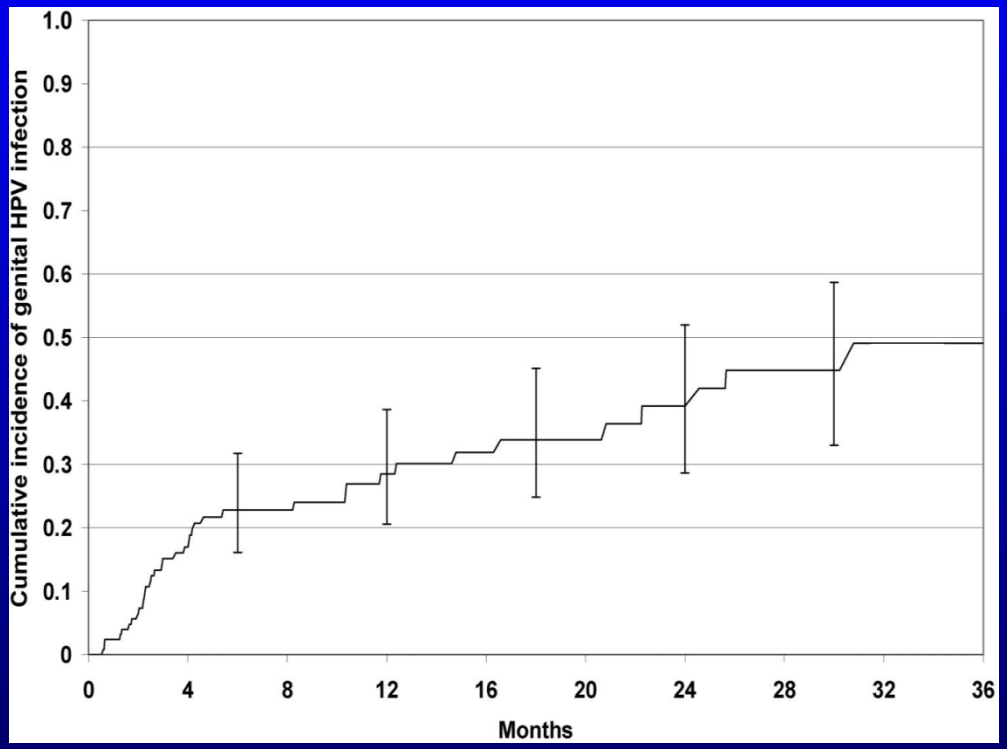
Source: Hariri J Infect Dis. 2011;204(4):566-73

Cumulative incidence of genital HPV infection among sexually active male University of Washington students, 18–23 years of age



Partridge, *JID* 2007

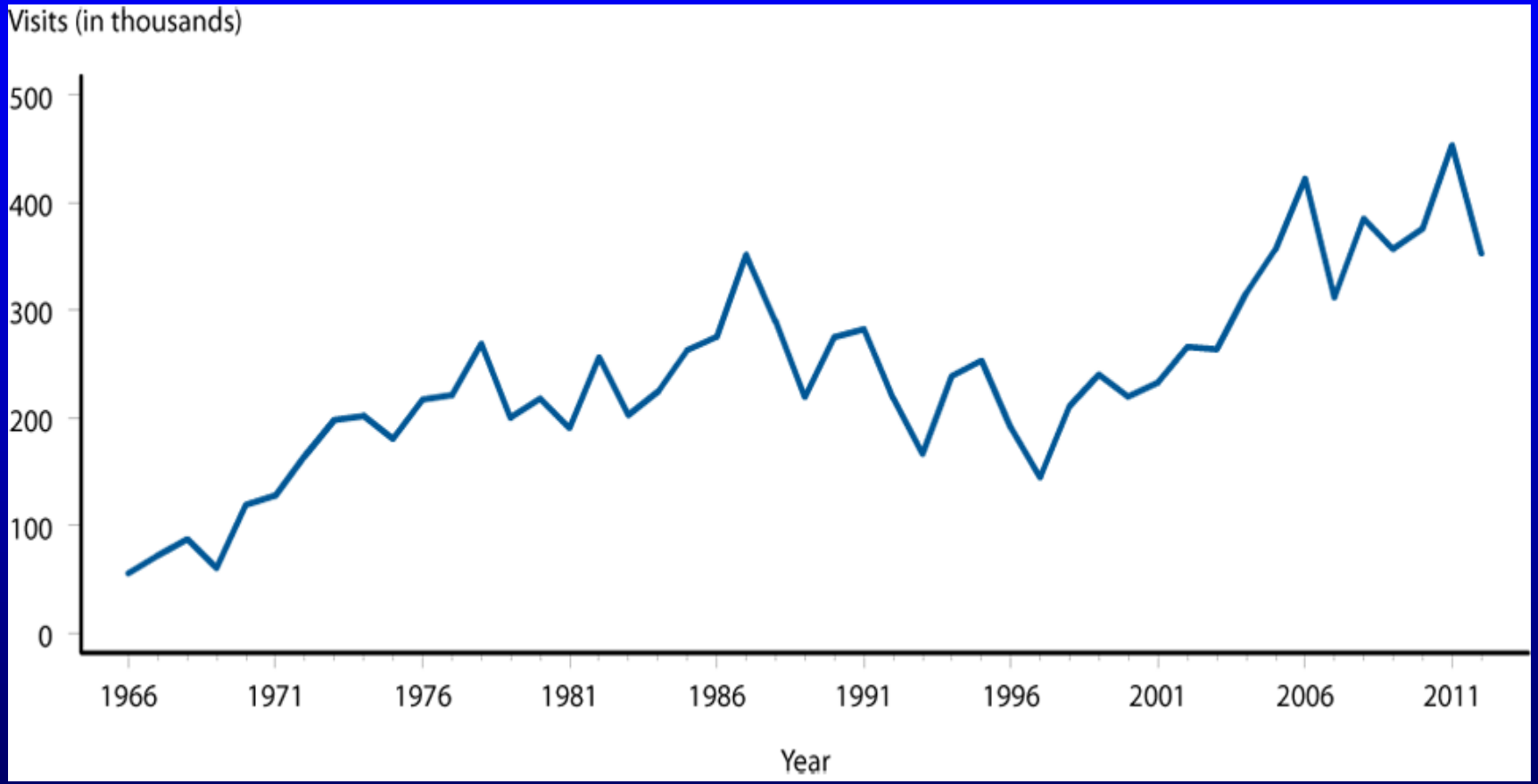
Risk of Acquiring HPV First Ever Male Sexual Partner



- 18-22 year old university students
- Enrolled if never SA or within three months of first male partner
- One year cumulative incidence of first HPV infection: 28.5%
- Male partner with more partners increased risk

Winer RL JID 2008; 197: 279

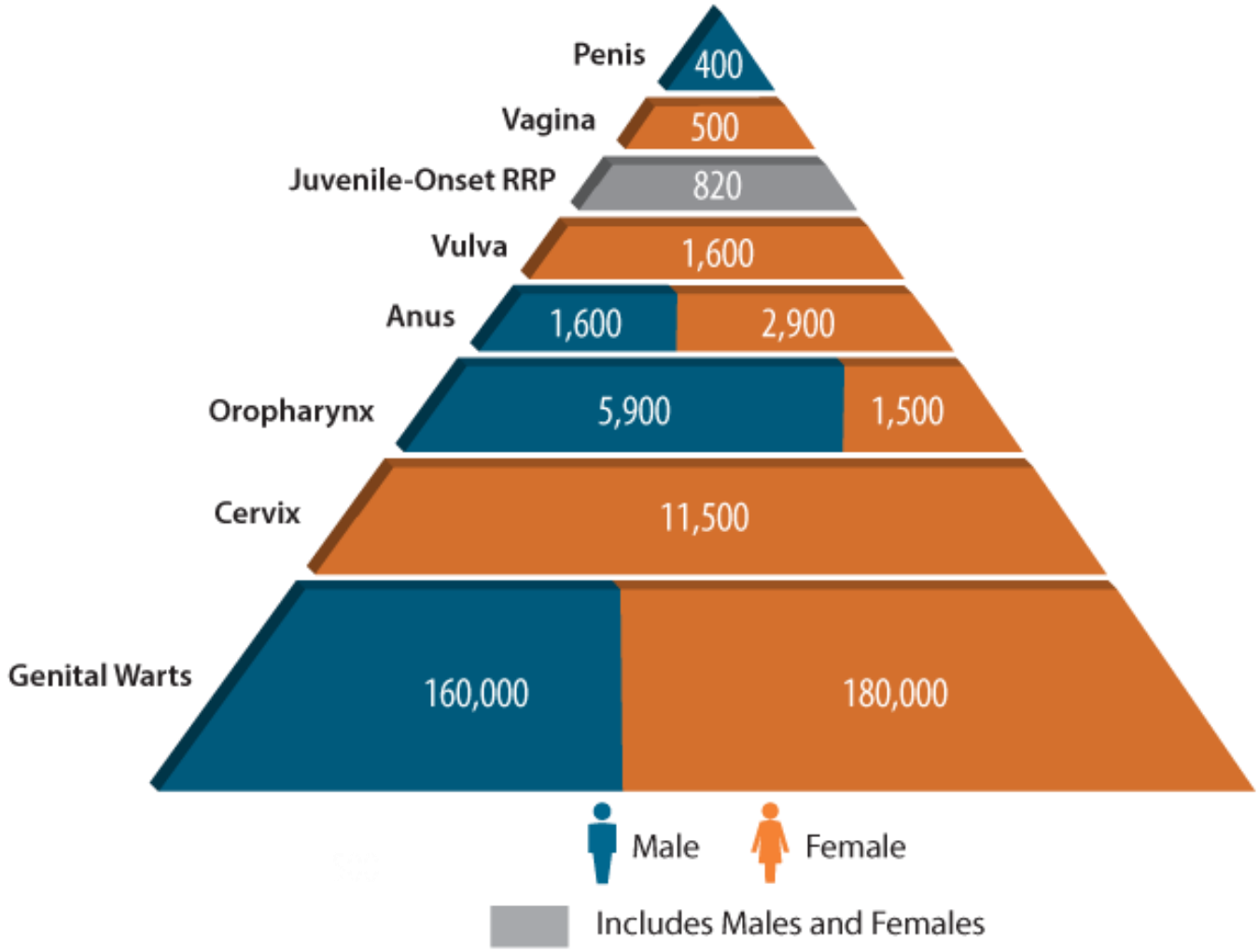
Human Papillomavirus and Diagnosis of Genital Warts



Initial Visits to Physicians' Offices, United States, 1966 – 2012

Source: CDC

Numbers of Cancers and Genital Warts Attributed to HPV Infections, U.S.



CDC. Human papillomavirus (HPV)-associated cancers. Atlanta, GA: US Department of Health and Human Services, CDC; 2013. Available at http://www.cdc.gov/cancer/hpv/statistics/cases.htm

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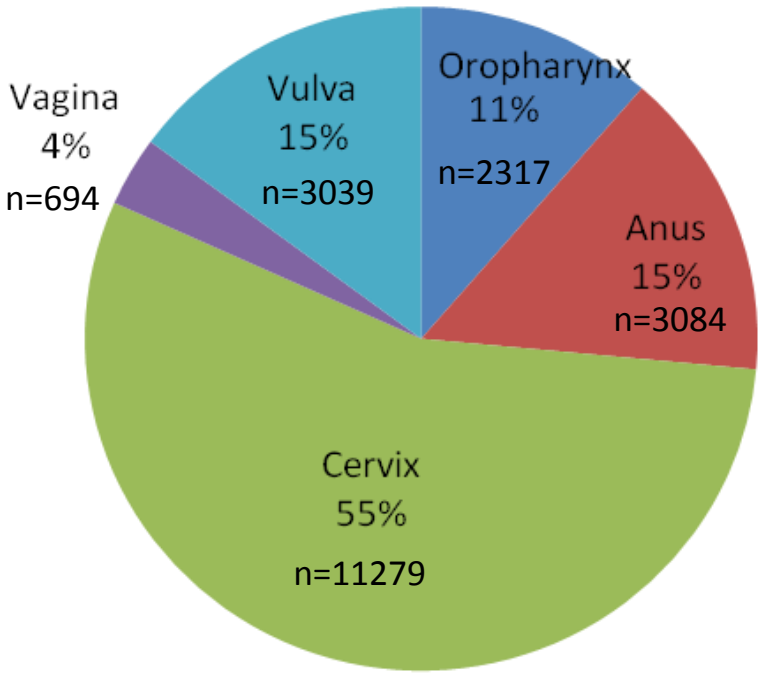
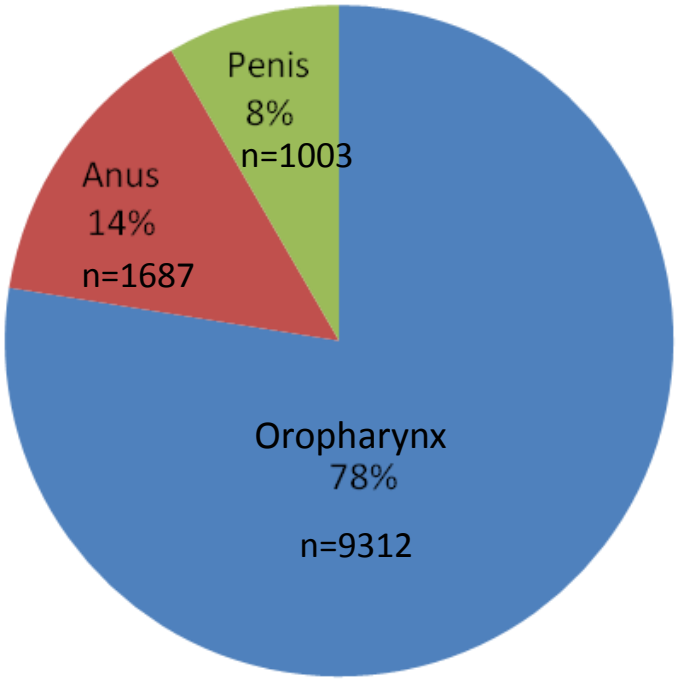
Average Number of New HPV-Associated Cancers by Sex, in the United States, 2005-2009

Women (N=20,413)



Men (N=12,002)



Jemal A et al. J Natl Cancer Inst 2013;105:175-201

YOU ARE THE KEY TO CANCER PREVENTION

Human Papillomavirus and Oropharyngeal Cancer

- HPV prevalence in oropharyngeal tumors
  - Increased from 16.3% in 1980s to 71.7% in 2000s
- Increase in oropharyngeal squamous cell carcinoma (OPSCC) 1984-2004
  - Among <age 60, men, and whites
  - Related to HPV positive cancers
- HPV positive OPSCC
  - Postulated related to sexual behavior (oral sex)
  - Have better survival than HPV negative (tobacco, alcohol)

Chaturvedi et al. J Clin Oncology, 2011; 32: 4294; Jemal et. Al J Nat Ca Institute 2013; 105: 175

Human Papillomavirus and Anal Cancer

- 2 fold increase 1975-2009 men and women
  - Burden >>Women
- Anal receptive intercourse risk factor not prerequisite
  - Most women no history of anal intercourse
- Women risk factors
  - Young age at 1st intercourse
  - Multiple partners
  - STDs
- Male risk factors
  - HIV positive MSM

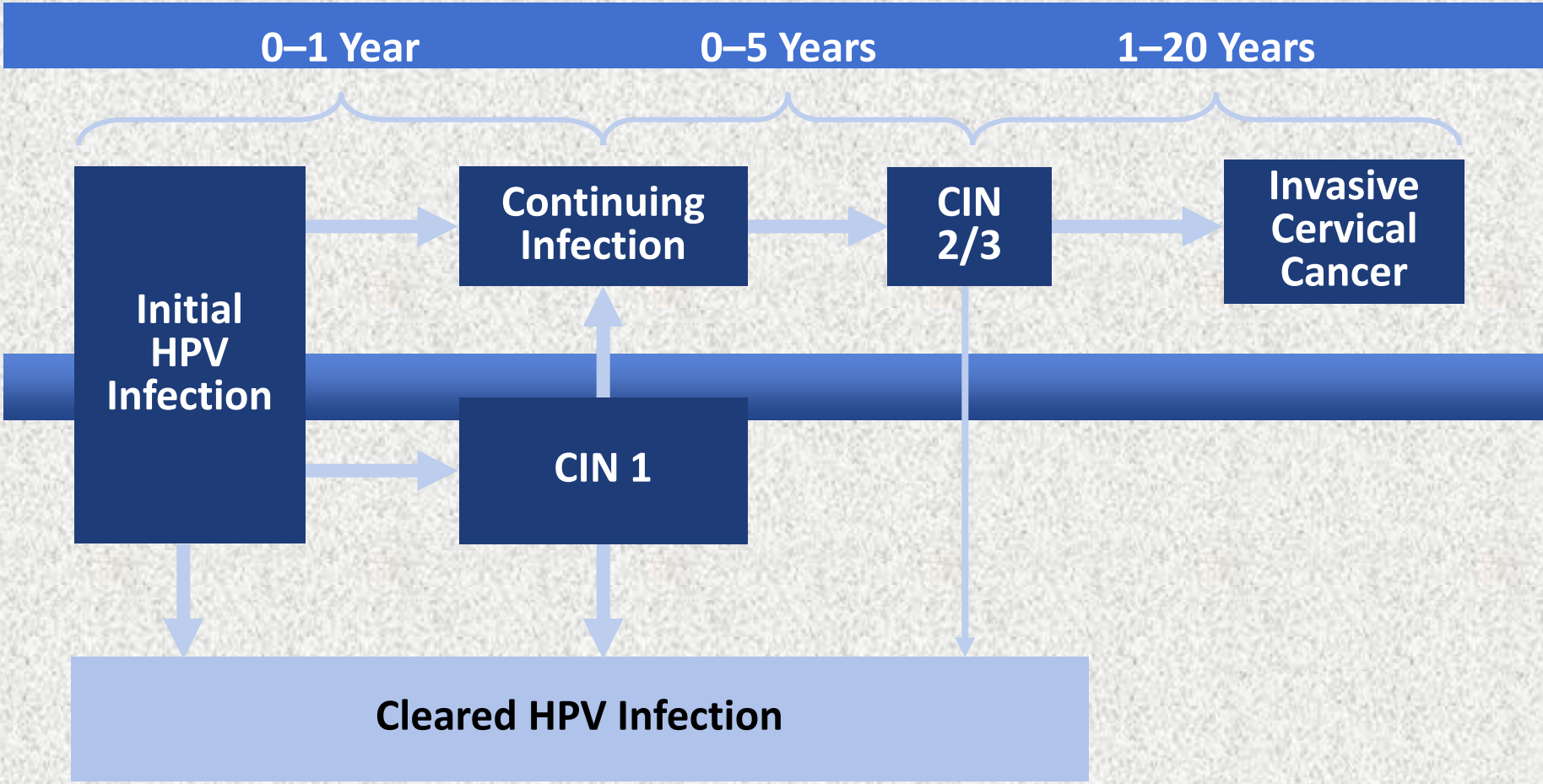
Jemal et. Al J Nat Ca Institute 2013; 105: 175

Human Papillomavirus:
Natural History

- Incubation period weeks-months
- Median duration of HPV
  - 6-8 months (F)
  - 5.9 months (M)
- Most individuals clear specific HPV type within 6-12 months
  - May be less likely to persist in males[1]
- First Pap smear age 21 unless immunocompromised
- Viral persistence: progression

1. Guiliano AR. Gynecol Oncology 2010; 117: S15

Natural History of HPV Infection and Potential Progression to Cervical Cancer[1]



1. Pinto AP, Crum CP. Clin Obstet Gynecol. 2000;43:352–362.

HPV Persistence

- Persistent infection: Detection of same HPV type two or more times over several months to 1 year[1]
- Widely accepted that persistence of high-risk types of HPV is crucial for development of cervical precancer and cancer[1]
- Other associated factors
  - Age (≥30 years)*, [2]
  - Infection with multiple HPV types[3]
  - Immune suppression[4]
- Currently, there are no antivirals available to treat the underlying HPV infection.[5]

*May be partially confounded by duration of infection

1. Schiffman M, Kjaer SK. J Natl Cancer Inst Monogr. 2003;31:14–19.
2. Hildesheim A, Schiffman MH, Gravitt PE, et al. J Infect Dis. 1994;169:235–240.
3. Ho GYF, Burk RD, Klein S, et al. J Natl Cancer Inst. 1995;87:1365–1371.
4. Kobayashi A, Greenblatt RM, Anastos K, et al. Cancer Res. 2004;64:6766–6774.
5. Stanley M. J Natl Cancer Inst Monogr. 2003;31:117–124.

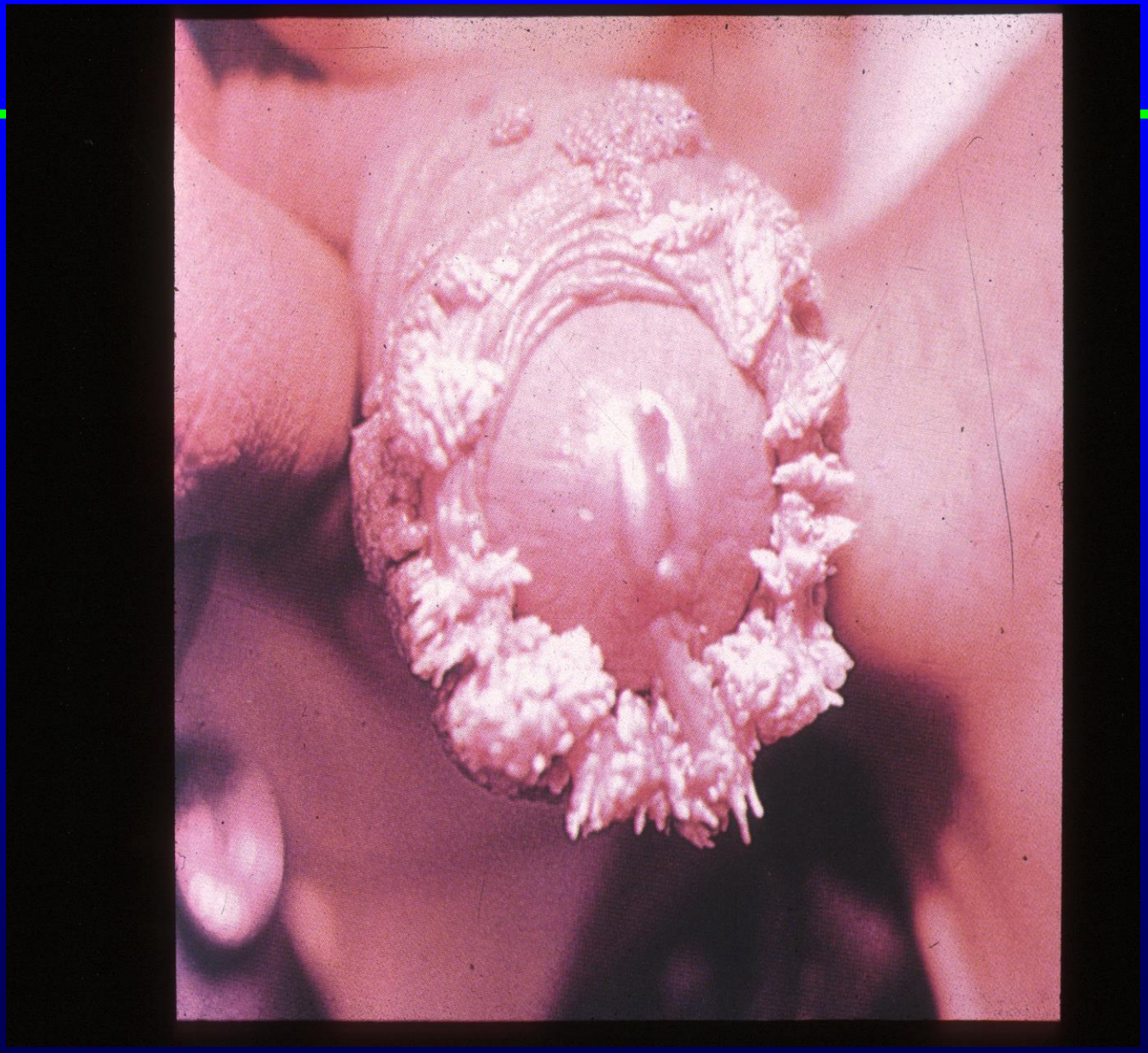
HPV Clearance

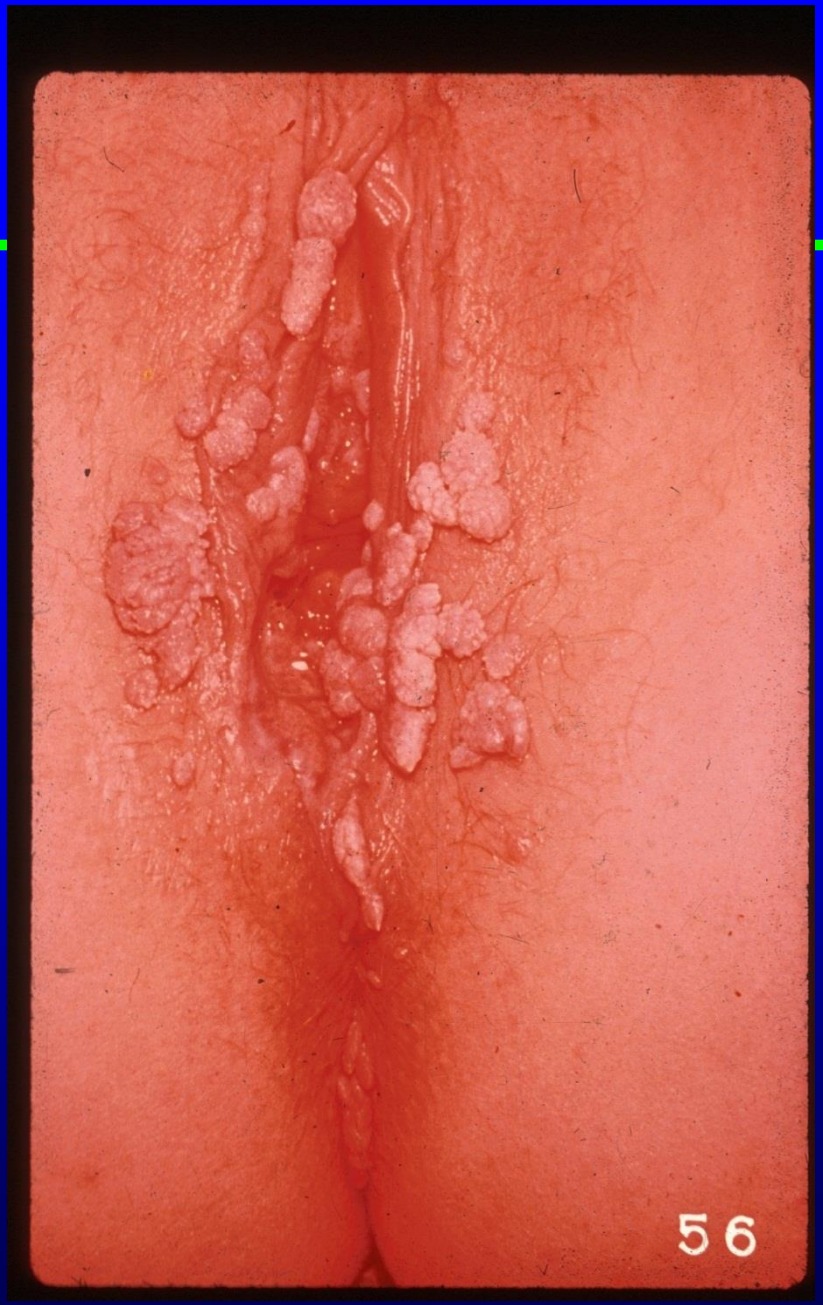
- In women 15-25 years of age, ~80% of HPV infections are transient.[1]
  - Gradual development of cell-mediated immune response presumed mechanism[2]
- In a study of 608 college women, 70% of new HPV infections cleared within 1 year and 91% within 2 years.[3]
  - Median duration of infection = 8 months[3]
  - Certain HPV types are more likely to persist (e.g., HPV 16 and HPV 18).

1. Meijer CJLM, Helmerhorst TJM, Rozendaal L, van der Linden JC, Voorhorst FJ, Walboomers JMM. Histopathology. 1998;33:83–86.
2. Schiffman M, Kjaer SK. J Natl Cancer Inst Monogr. 2003;31:14–19. 3.
3. Ho GYF, Bierman R, Beardsley L, Chang CJ, Burk RD. N Engl J Med. 1998;338:423–428.

Human Papillomavirus
Clinical Presentation: Genital Infection

- **Subclinical infection**
  - Most infections
  - Not all infections detected through cytology
  - HPV present 10-30 times more often than cytologic abnormalities
- **Genital Warts:**
  - Condyloma acuminata
- **Multicentric disease**
  - Multiple locations: concurrently and consecutively

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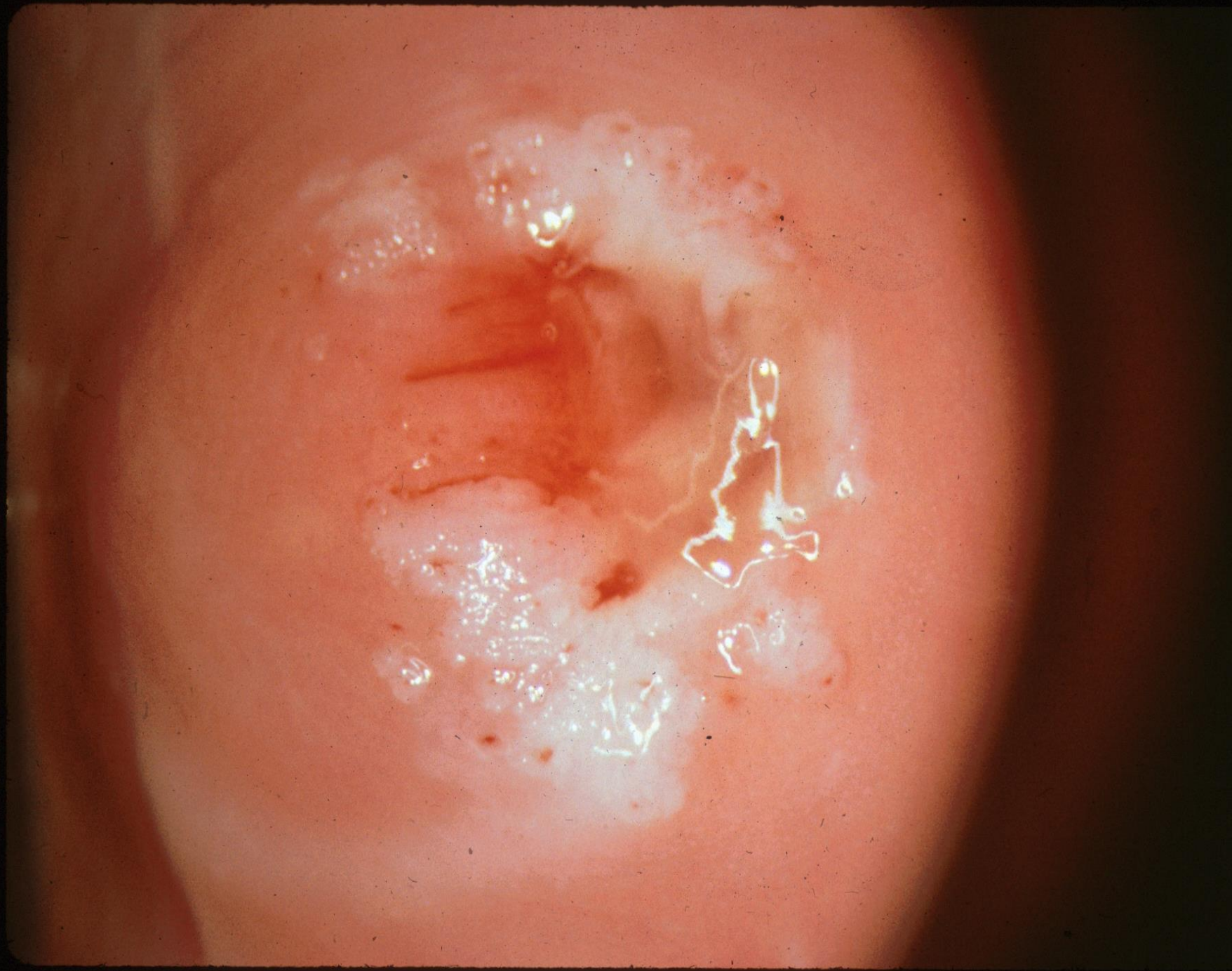


Human Papillomavirus: Diagnosis

- Visual inspection (genital warts)
- DNA
  - Not used to diagnose or manage visible warts
  - No role in diagnosis or treatment of genital disease in adolescents
- Cytological abnormality on Pap smear

Human Papillomavirus: Treatment

- Infection may not be completely eradicated with treatment
- Treat genital warts and precancer/ cancers
- Recurrence of genital warts is common; so is spontaneous resolution (30%)
- Treatment
  - Time consuming
  - Stressful
  - Uncomfortable

Human Papillomavirus: Treatment

- Podophyllin/ Podofilox
- Aldara- Imiquimod
- Sinecatechins 15% Ointment
- Trichloroacetic acid/ Bichloroacetic acid
- Liquid nitrogen, cryoprobe
- Electrodessication, cautery
- Laser, surgery, LEEP

Yellow highlighted: Patient applied

Human Papillomavirus: Prevention

- Only way to prevent sexual transmission is to refrain from sexual contact
- "Virginity" not 100% protective (skin-to-skin contact)
- Can acquire HPV by
  - Nonpenetrative genital-genital contact
  - Likely: oral-genital and possible: manual-genital contact

Human Papillomavirus:
Prevention

- Condoms not 100% protective
- Condom use reduces risk for reinfection or new infection which in turn:
  - May reduce genital warts and cervical neoplasia
  - More likely to clear HPV infection
  - More likely to resolve abnormal cervical cytology

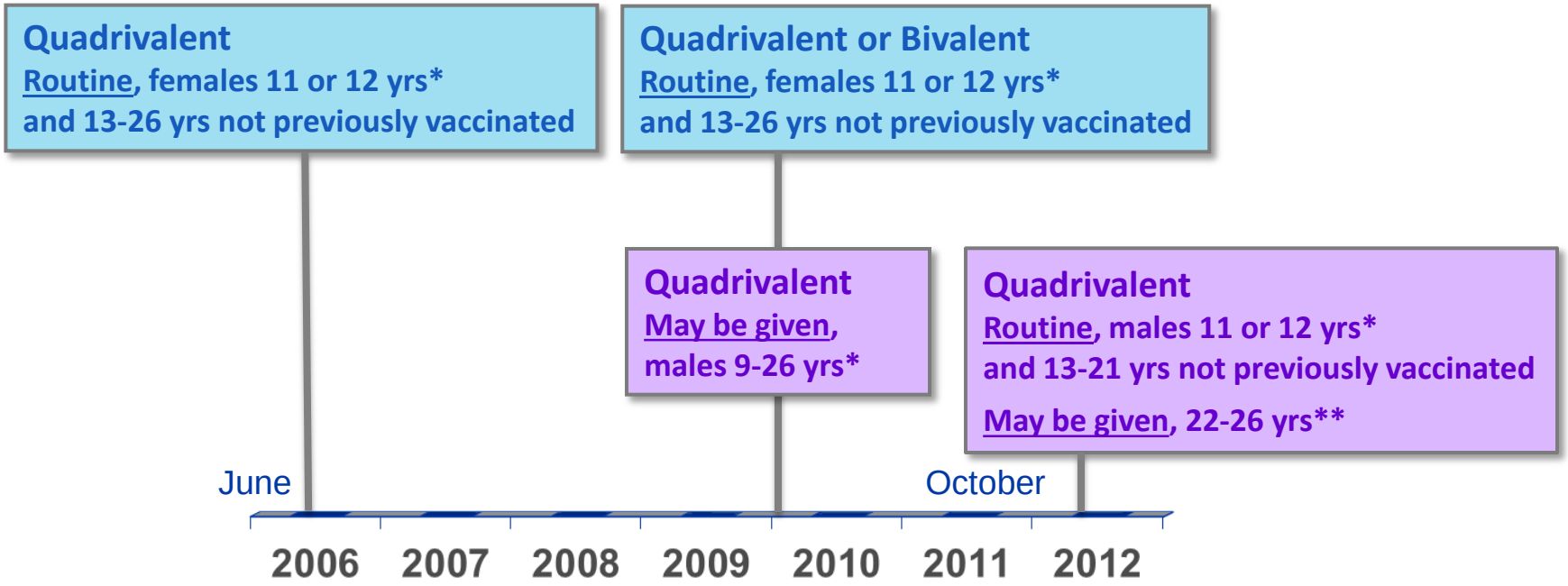
Human Papillomavirus: Prevention

- Long term monogamy (depends on sexual history of partner)
- Limit sexual contact to partner with longer periods of monogamy
  - Allows for spontaneous resolution of HPV
- Overall limit number of sexual partners

Human papillomavirus (HPV) vaccines licensed in the United States

Vaccines	Viral types	Date FDA Licensed
Quadrivalent (HPV4) (Gardasil)	6, 11, 16, 18	Females: June 2006 Males: October 2009
Bivalent (HPV2) (Cervarix)	16, 18	Females: October 2009

Evolution of 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 age 26

HPV YOU ARE THE KEY TO CANCER PREVENTION

Quadrivalent HPV vaccine indications

- **Prevention of the following diseases caused by HPV types 6, 11, 16, and 18:**
  - **Cervical cancer**
  - **Vulvar cancer**
  - **Vaginal cancer**
  - **Anal cancer***
  - **Genital warts***
  - **Cervical adenocarcinoma in situ (AIS)**
  - **Cervical intraepithelial neoplasia (CIN) grades 1-3**
  - **Vulvar intraepithelial neoplasia (VIN) grades 2 and 3**
  - **Vaginal intraepithelial neoplasia (VaIN) grades 2 and 3**

- **No data on efficacy against oropharyngeal cancer, penile cancer, RRP; no studies in progress**

***males and females**

http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM094042

Quadrivalent HPV vaccine efficacy vaccine type-related endpoints females, 16-26 years

Endpoint*	Vaccine N	Vaccine cases	Placebo N	Placebo cases	Efficacy %	Efficacy (95% CI)
CIN 2/3 or AIS	7864	2	7865	110	98%	(93,100)
VIN/VaIN 2/3	7900	0	7902	23	100%	(83,100)
Genital warts	7665	2	7669	190	99%	(96,100)

Per protocol population: received all three doses, cases, counted one month after dose 3, mean follow-up 42 months post dose 1
*HPV6,11,16,18 related

CIN 2/3: cervical intraepithelial neoplasia grade 2 or 3, AIS: adenocarcinoma in situ
VIN: vulvar intraepithelial neoplasia: VaIN: vaginal intraepithelial neoplasia

Kjaer et al. *Cancer Prev Res* 2009; future I/II Study Group. *Br Med J* 2010

Quadrivalent HPV vaccine efficacy
HPV vaccine type-related endpoints
males, 16-26 years

Endpoint*	Vaccine N	Vaccine cases	Placebo N	Placebo cases	Efficacy %	Efficacy (95% CI)
Genital warts⁺	1394	3	1404	28	**89%**	(65, 98)
AIN 2/3**	194	3	208	13	**75%**	(9, 96)

Per protocol population: received all three doses, naïve to vaccine type at baseline; cases counted one month post dose 3

***HPV 6,11,16,18 related; ⁺median follow-up 2.9 yrs post dose 1; ** median follow-up 3.2 yrs post dose 1**
AIN 2/3: anal intraepithelial neoplasia grade 2 or 3

Source: Food and Drug Administration. Highlights of prescribing information. Gardasil (human papillomavirus quadrivalent [types 6, 11, 16 and 18]). Available at http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM111263.pdf

AAP/ACIP Recommendations for HPV Vaccine

- HPV vaccine is recommended routinely for boys (HPV4)and girls (HPV2 and HPV4) at 11 or 12 years of age

- HPV Vaccine may be given as early as 9 years of age
  - Catch-up vaccination (routine)
    - Females: 13 through 26 years of age
    - Males: 13 through 21 years of age
    - MSM: 13 through 26 years of age
  - Catch-up vaccination (permissive)
    - Males 22 through 26 years of age

AAP/ACIP Recommendations for HPV vaccine

- 3- dose series (0,1-2; 6 months)
- 1st dose: Day 0
- 2nd dose: 1-2 months after dose 1 (minimum of 4 weeks after dose 1)
- 3rd dose: 6 mos after dose 1 and 16 weeks after dose 2 (minimum of 12 weeks after dose 2)
- Immunogenicity is good with longer durations between doses (no need to restart if doses are given with longer times between doses)

AAP/ACIP recommendations for HPV vaccine: Special situations

- **Vaccine can be given to women:**
  - **With equivocal or abnormal Pap smears; positive Hybrid Capture II or genital warts**
  - **Breast feeding**
  - **Immunocompromised**
- **Pregnancy – Not recommended at present time**
  - **Delay initiation of series until pregnancy completed**
  - **If patient becomes pregnant during vaccination series, delay next dose until pregnancy completed**
    - **Report to registry (800-986-8999)**
  - **No evidence of adverse fetal outcomes**

www.cdc.govnip/resc/provisional_recs/hpv.pdf

ACIP Recommendations for Special Populations

HPV4 is not a live vaccine and can be administered to persons who are immunocompromised as a result of infection (including HIV), disease, or medications. The immune response and vaccine efficacy might be less than that in immunocompetent persons

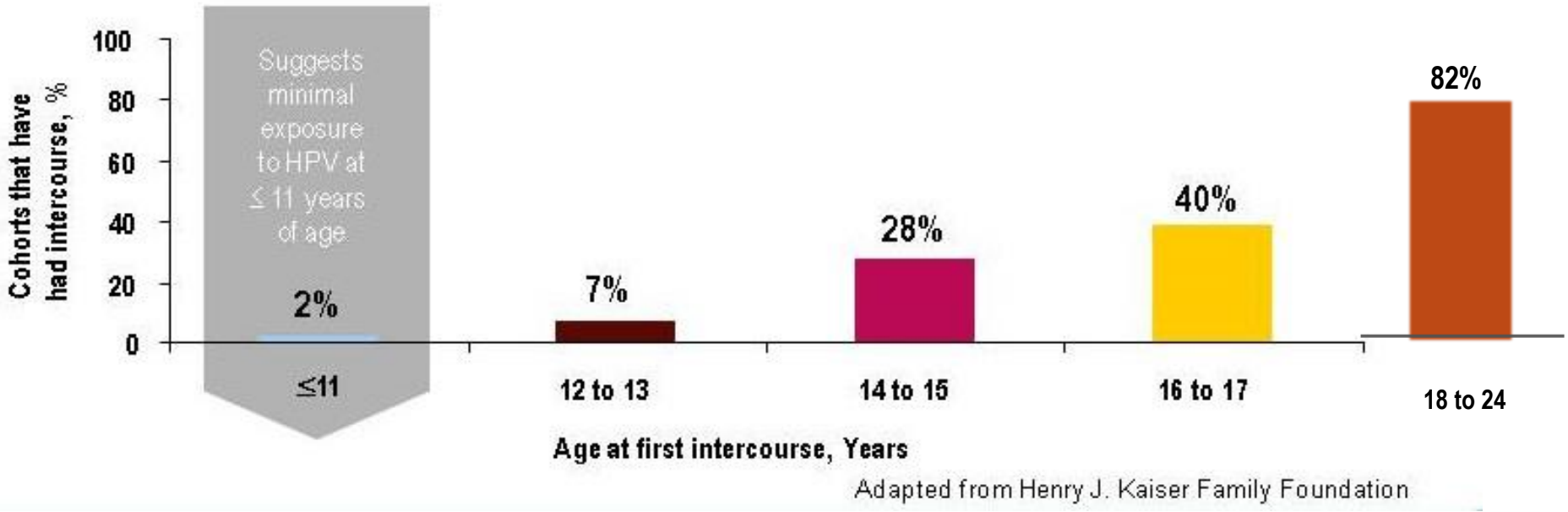
For immunocompromised males, ACIP recommends routine vaccination with HPV4 as for all males, and vaccination through age 26 years for those who have not been vaccinated previously or who have not completed the 3-dose series.

***MMWR* 2011;60:1705-8**

Why is just one vaccine recommended for males and two for females

- **Quadrivalent HPV vaccine was studied in males and is licensed for males aged 9-26 years**
  - **Bivalent vaccine has not been licensed in men**
- **Both vaccines prevent types of HPV most likely to cause cancers in men**
  - **Only quadrivalent HPV vaccine has been demonstrated to reduce genital warts and anal precancers in men**

Rationale for vaccinating early: Protection prior to exposure to HPV



Markowitz MMWR 2007;
Holl Henry J Kaiser Found 2003;
Mosher Adv Data 2006

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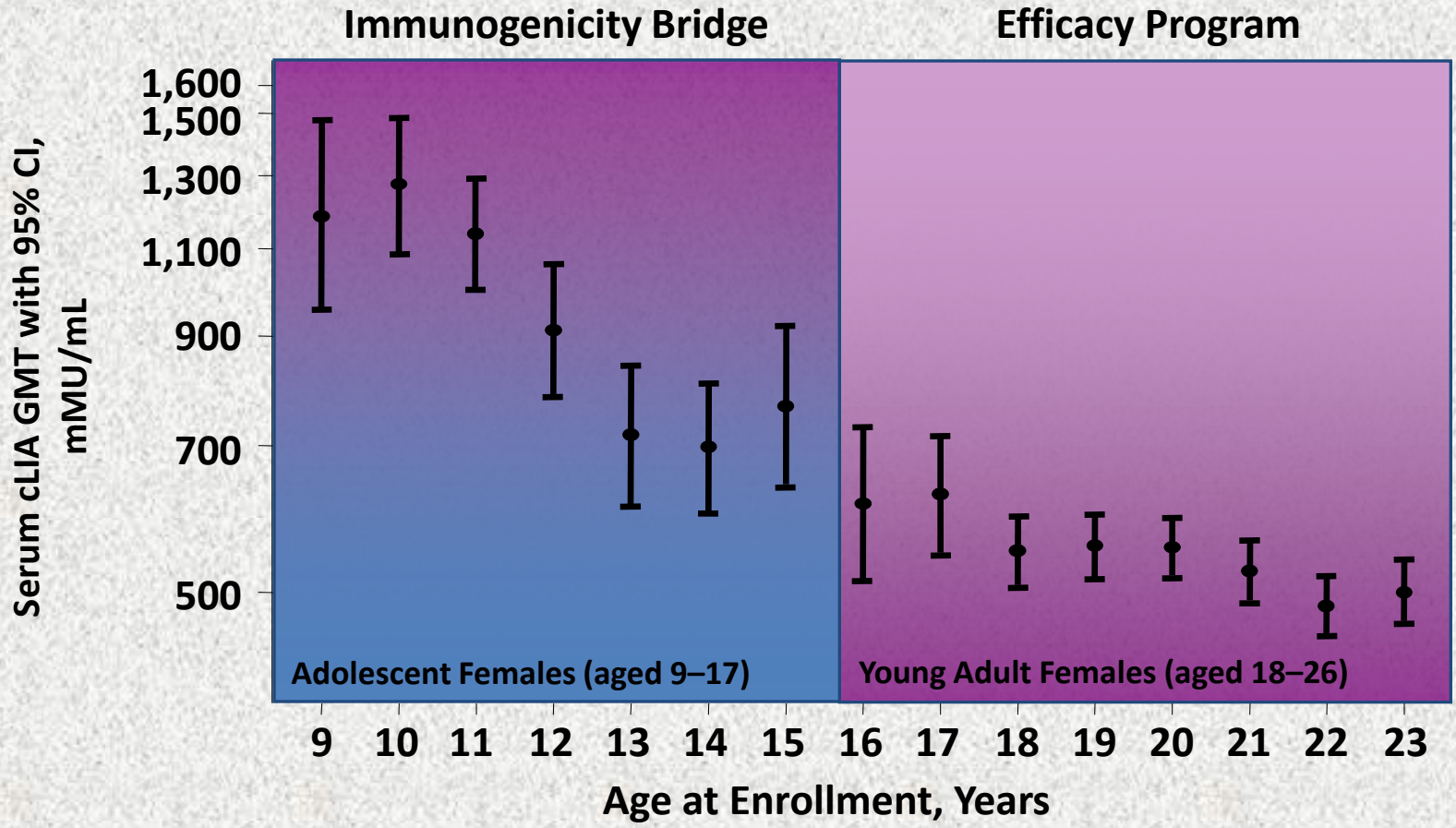
Neutralizing Antibodies by Age at Enrollment

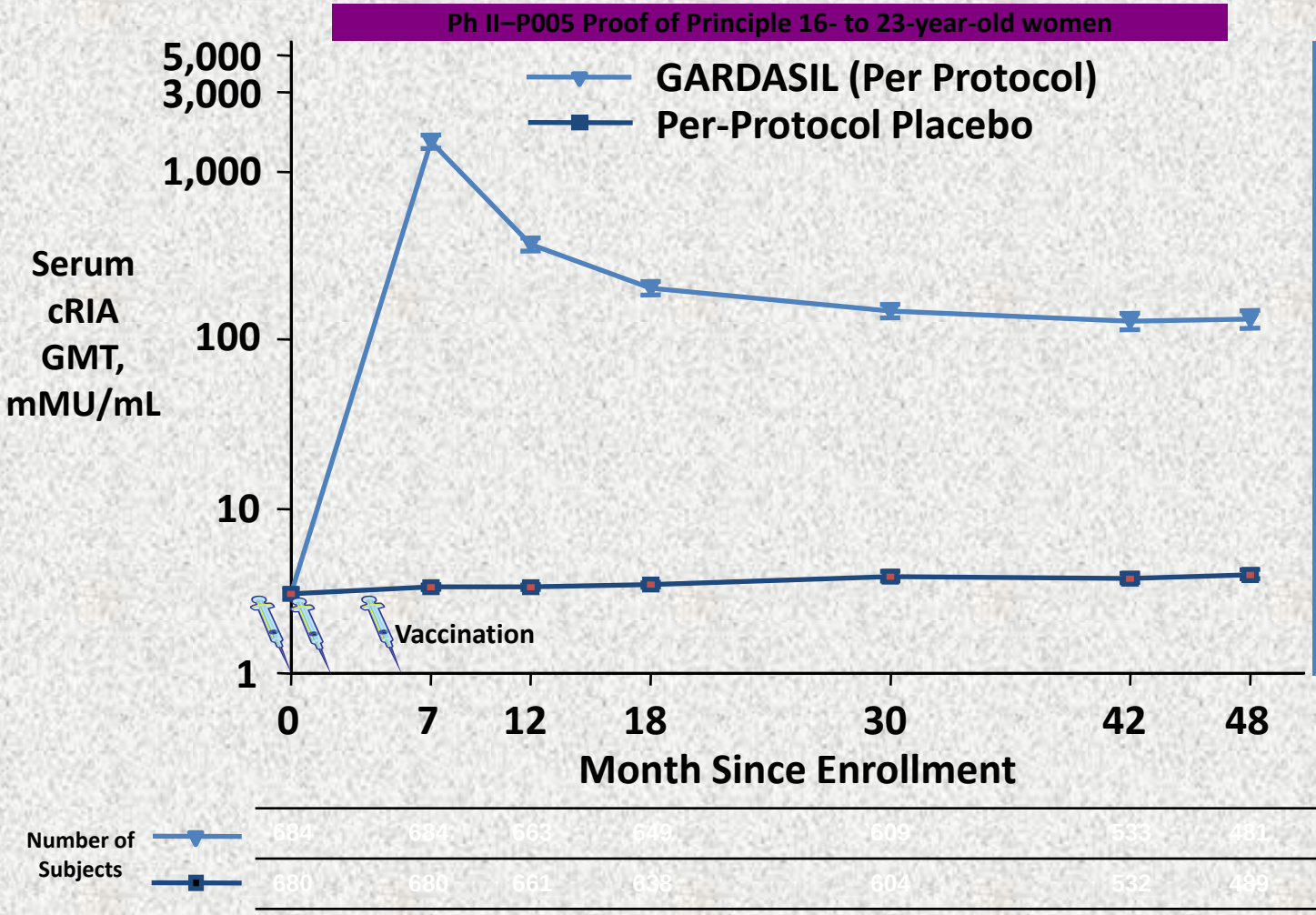
Per-protocol immunogenicity population (aged 9–26)*
Neutralizing anti-HPV 6 GMTs at Month 7

Ph III–P016, 018 Safety/Immunogenicity 9- to 15-year-old adolescents



*Inclusive of 5 study protocols; all GMTs measured using cLIA.
Data on file, MSD.

GARDASIL Maintained Type-Specific, Neutralizing Antibody Responses



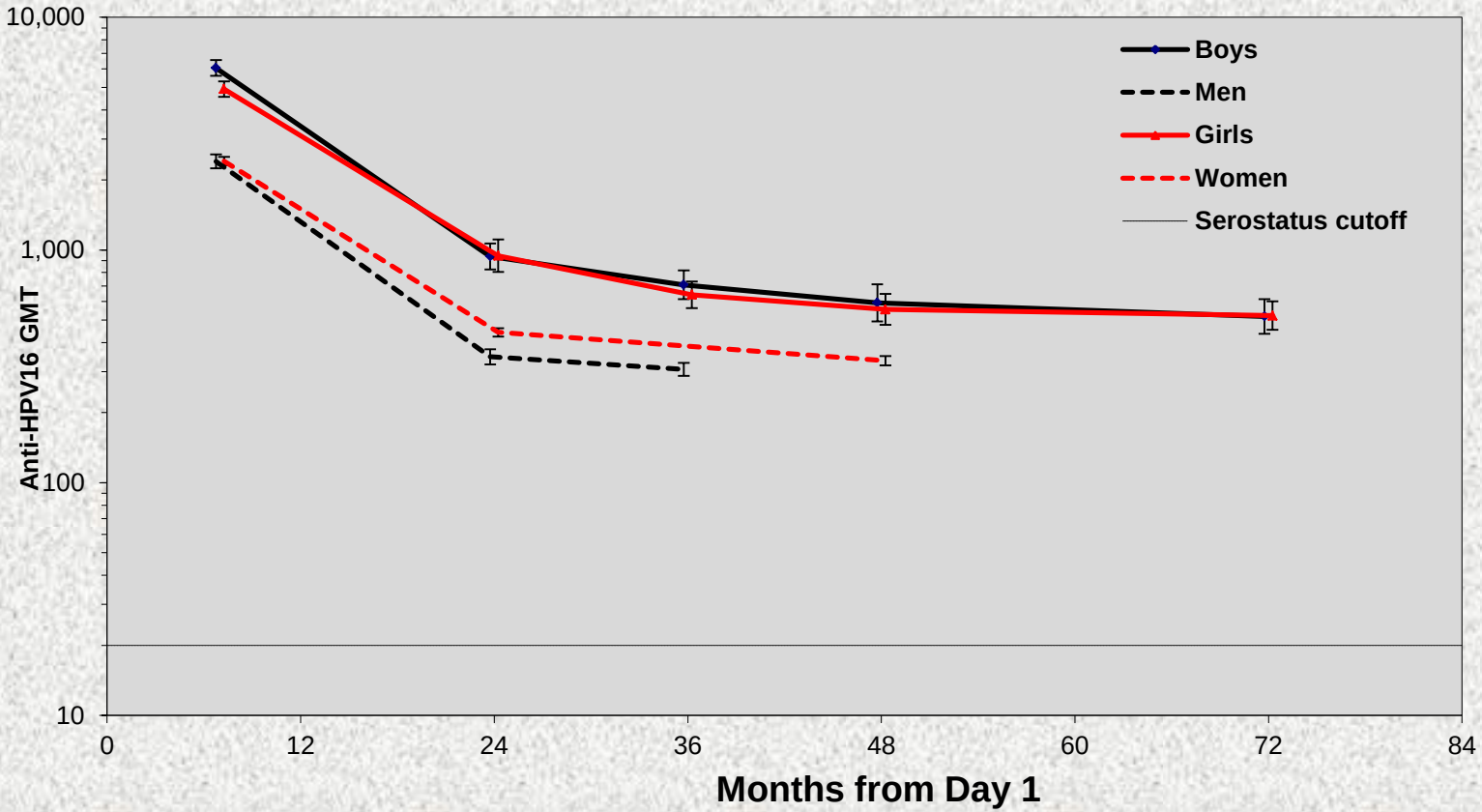
The duration of protection of GARDASIL is unknown beyond 48 months.

*Evaluated only the HPV 16 L1 VLP vaccine component of GARDASIL.

GMT = Geometric mean titer; cRIA = Competitive radioimmunoassay.

Data available on request from Merck & Co., Inc., Professional Services-DAP, WP1-27, PO Box 4, West Point, PA 19486-0004. Please specify information package 20651100(1).

Quadrivalent HPV Vaccine: Anti-HPV16 GMTs, by month post vaccination*



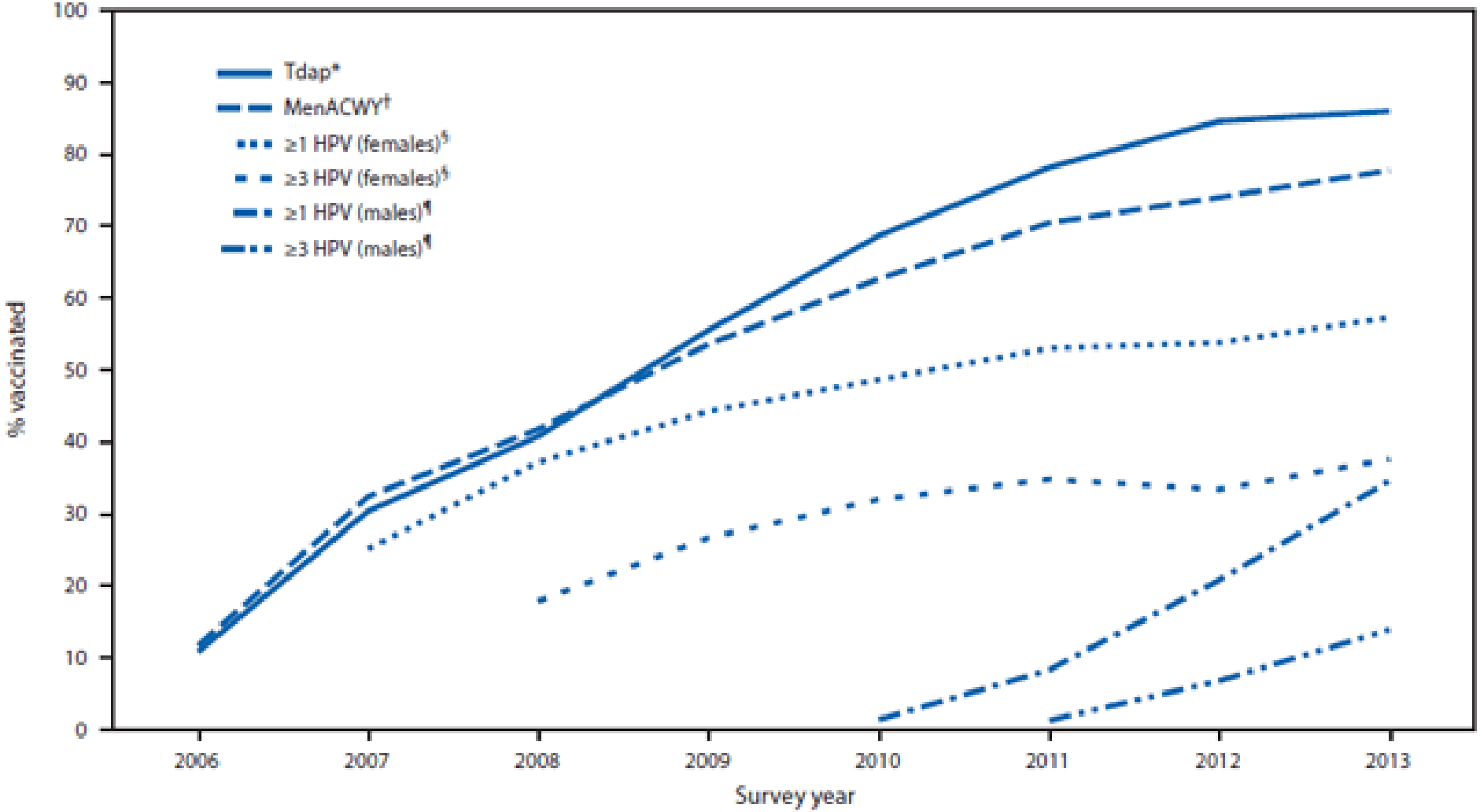
GMT – geometric mean titer by cLIA

* Per protocol population

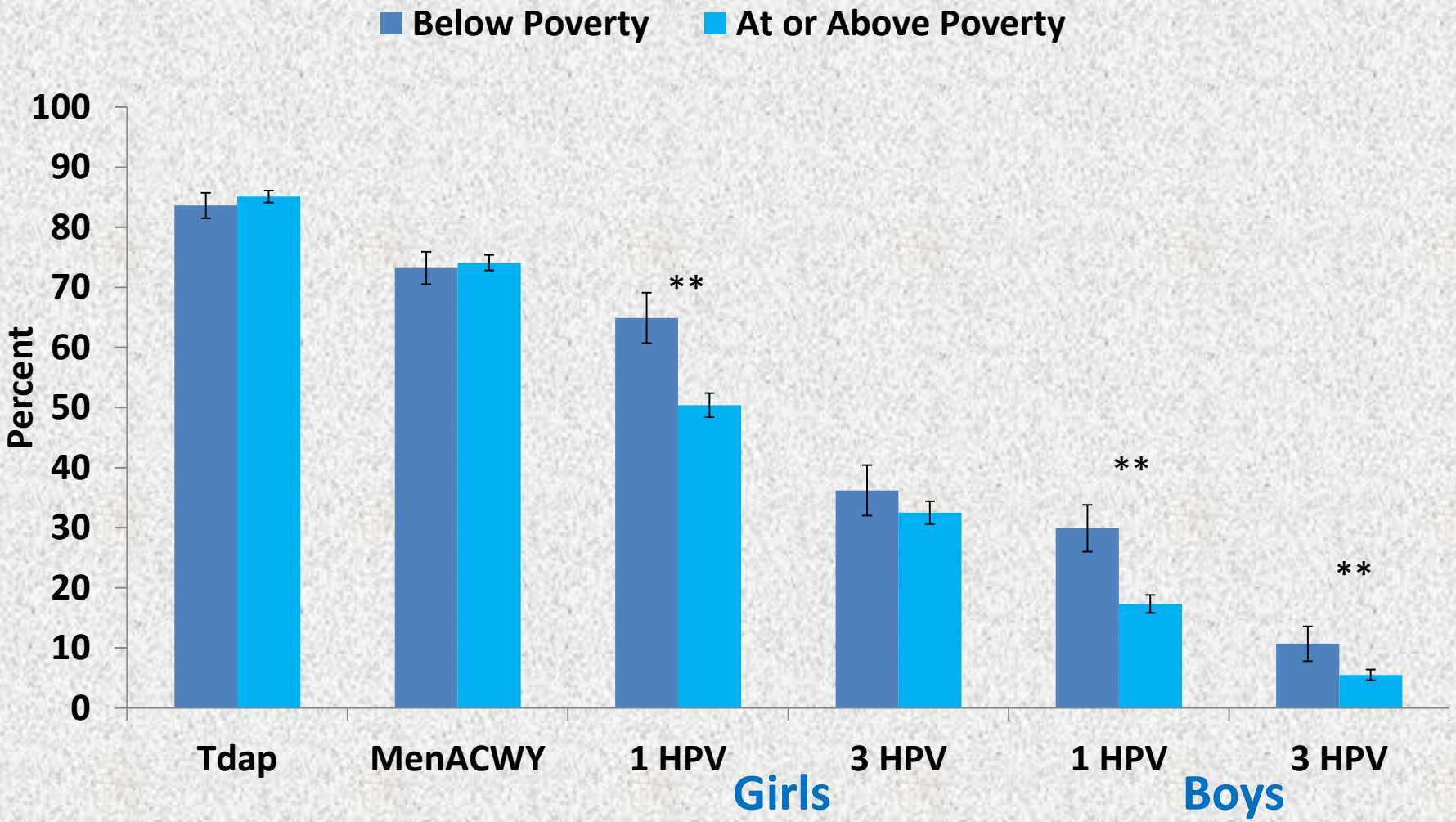
Courtesy, Al Saah

HPV Vaccine: Significant Benefits & Poor Immunization Rates

Adolescent Immunization Rates: 2006 to 2013



Vaccination Estimates Among Adolescents by Poverty Status, NIS-Teen, Unites States, 2012



**statistically different (p<0.05)

HPV Vaccine Effectiveness

- **Clinical trials that were performed to achieve FDA approval showed the following reductions:**
  - **HPV 16/18-related CIN 2/3 or AIS were reduced by 100%**
  - **Genital warts (females) were reduced by 97%**
  - **Genital warts (males) – were reduced by 89% after 3 doses; and 67% after one dose**

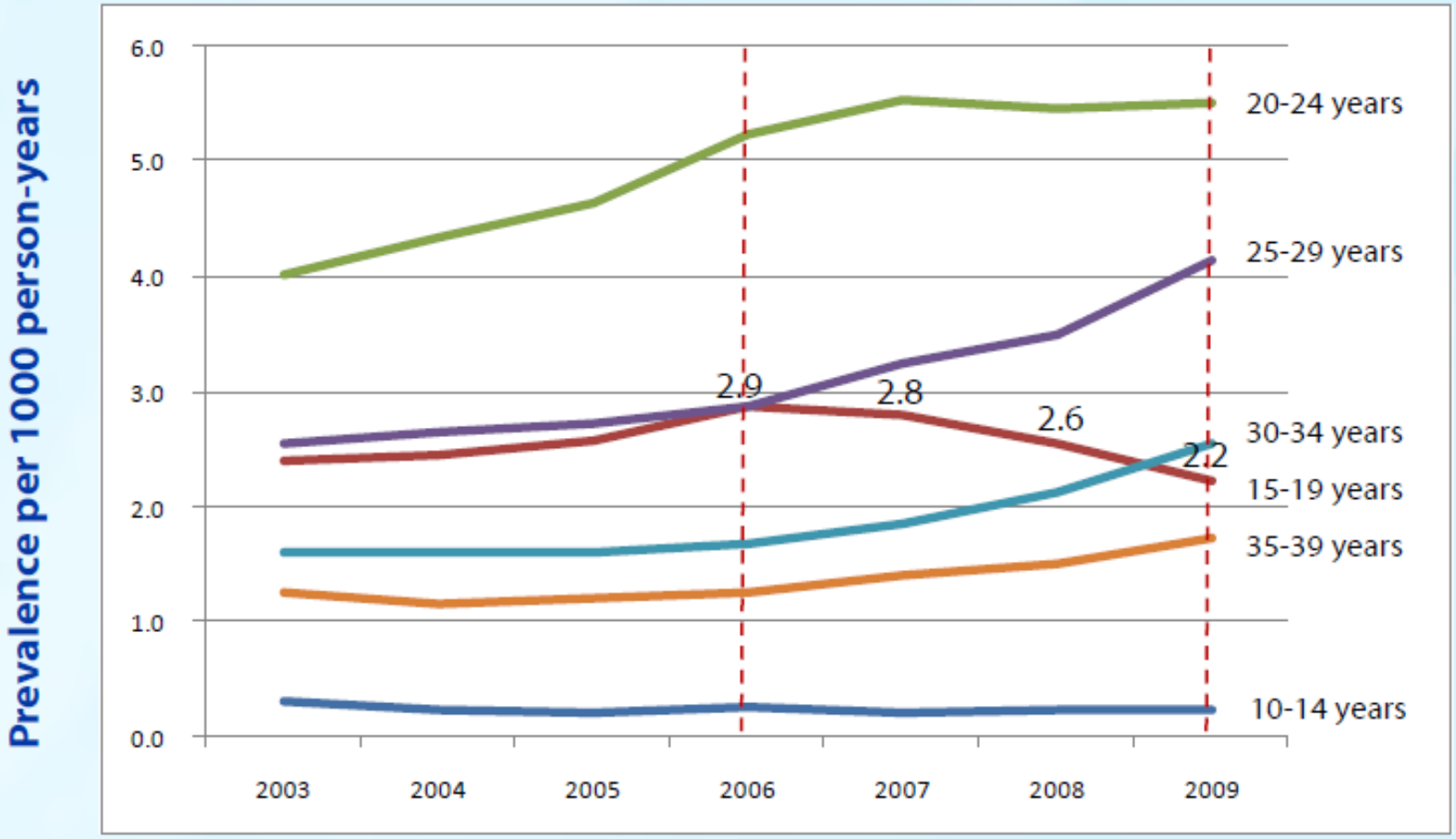
HPV Vaccine Effectiveness

- **Post-marketing surveillance in "real world" settings showed dramatic benefit already:**
  - **56% reduction in prevalence of HPV strains 6, 11, 16 & 18 in adolescent girls in United States (NHANES) despite low HPV immunization rates in the United States of 33% of girls receiving 3 doses**
  - **77% reduction in prevalence of HPV strains 6, 11, 16 & 18 in adolescent girls in Australia within 3 years vaccine introduction (3 dose immunization rates of 70%)**
  - **75% reduction in low grade cervical abnormalities in Australian girls <18 years of age within 3 years of vaccine introduction**

HPV Vaccine Effectiveness

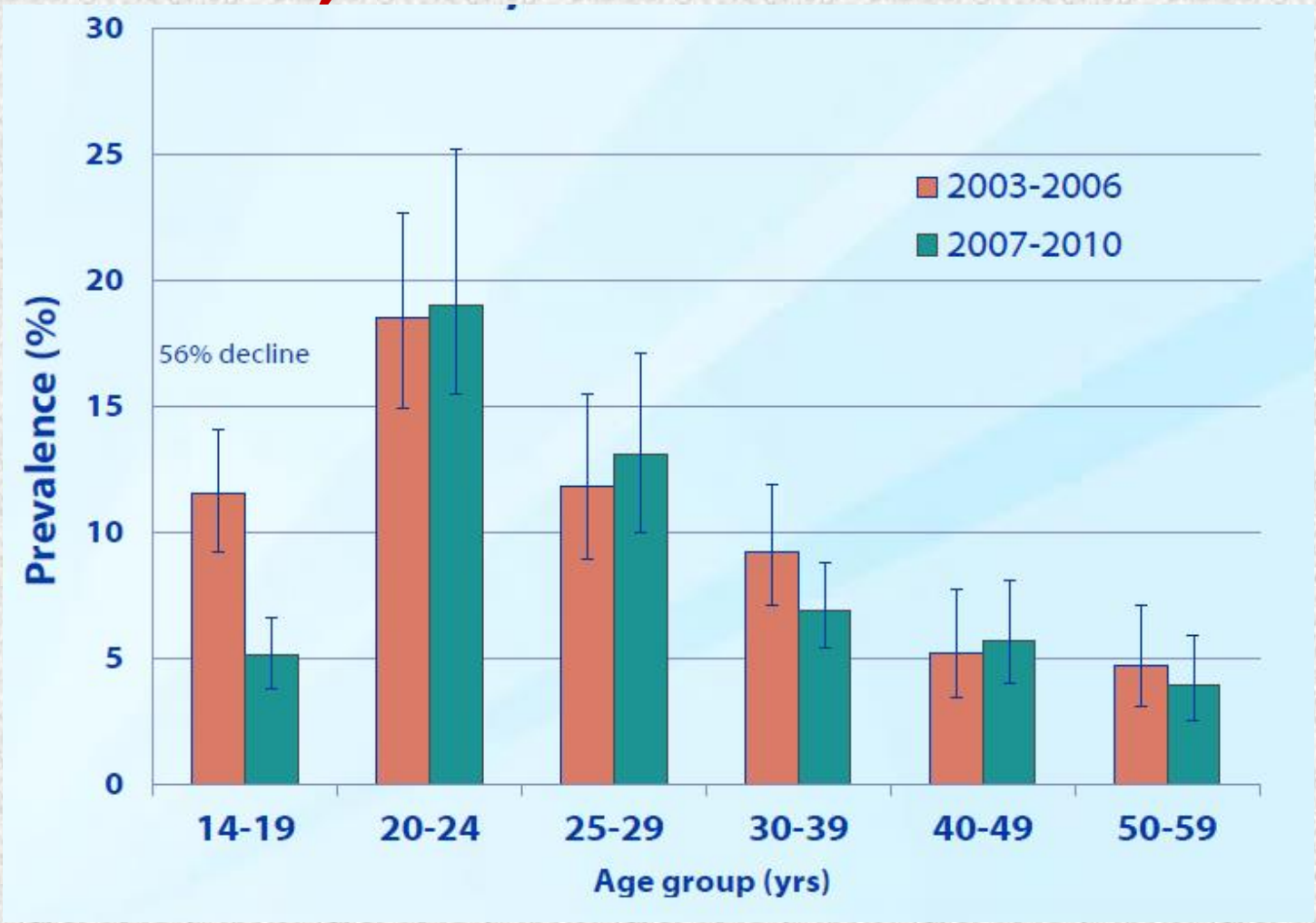
- **Post-marketing surveillance in "real world" settings showed dramatic benefit already:**
  - **45% reduction in genital warts in girls 16-17 years of age in Denmark**
  - **36% reduction in genital warts in girls 15-19 years of age in US despite low HPV immunization rates**
  - **88% reduction in genital warts in Australian females <21 years of age**
  - **Data on cervical cancer reduction will take a longer time to obtain due to the time between HPV infection and development of cancer. But data on prevention of pre-cancerous lesions make it clear that the HPV vaccine is having its desired effect.**

Prevalence of anogenital warts by age 2003-2009, US females



Flagg E. National STD Prevention Conference, May 2012

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



Markowitz, et al. *JID* 2013 (in press) *weighted prevalence

HPV Vaccine Safety

- **Safety**
  - **More than 57 million doses of HPV vaccine have been given in the United States through 2013.**
  - **More than 175 million doses have been given worldwide.**
  - **Post-marketing surveillance has not identified any new safety concerns in female or male HPV vaccine recipients.**
  - **Injection site discomfort is the most common adverse event.**
  - **Syncope is the most common safety concern. Adherence to a 15-minute observation period after vaccination should prevent significant adverse consequence due to syncope.**

HPV Vaccine Safety

- **Safety**
  - **Reports of adverse events to VAERS have declined dramatically since 2008 with no serious adverse events reported in 2013.**
  - **Post-marketing surveillance has not shown any increased risk following HPV vaccine and the following conditions: Guillain-Barre Syndrome, seizures, stroke, venous thromboembolism, appendicitis, anaphylaxis or other allergic reactions.**
  - **While not approved to be given during pregnancy, there have been no identified safety concerns in the HPV pregnancy registry. (Reports of girls who have been immunized with HPV vaccine while pregnant).**

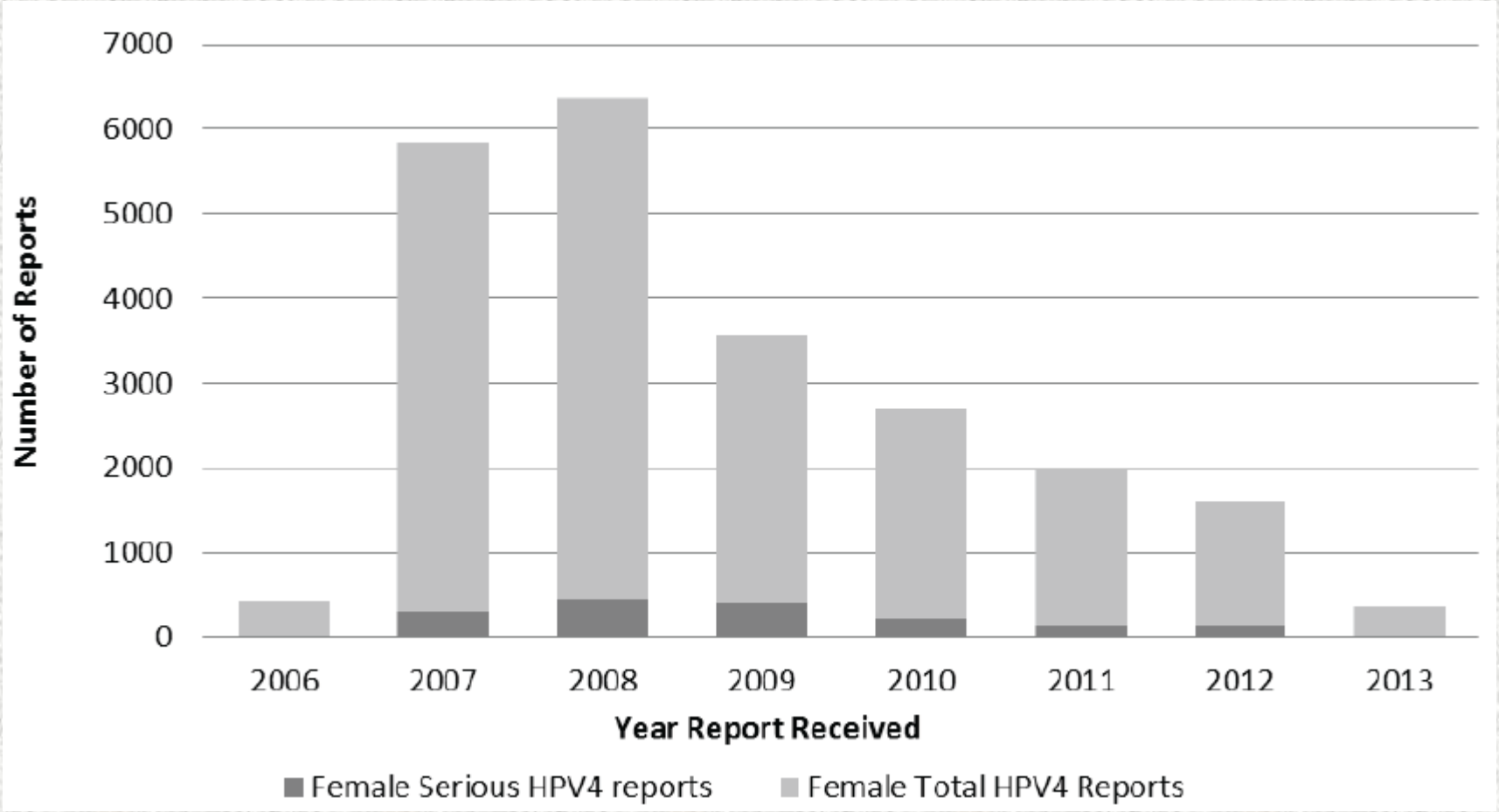
HPV vaccine safety monitoring - VAERS

- 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)



CDC, unpublished data

VAERS Serious Reports of Syncope Following HPV4*

- Total number of serious reports: 202
- Injuries resulting from syncopal event:
  - Fractures (nose, skull, maxillary)
  - Dental injuries
  - Contusions
  - Concussions
  - Intracranial hemorrhages (subdural hematoma, subarachnoid hemorrhage)
- No reports of death resulting from injury following a vasovagal syncopal event

*Unverified reports coded as syncope or syncope vasovagal

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MMWR Weekly

May 2, 2008 / 57(17);457-460

Syncope After Vaccination --- United States, January 2005--July 2007

Syncope (vasovagal reaction), or fainting, can be triggered by various stimuli, including medical procedures (*1*--*3*). Syncope has been documented to occur after vaccination, most commonly among adolescents, and can result in hospitalization for a medical evaluation or because of injury (*2*,*4*). During 2005 and 2006, the Advisory Committee on Immunization Practices (ACIP) recommended use of three newly licensed vaccines for adolescents*: the quadrivalent human papillomavirus recombinant vaccine (HPV) (Gardasil®, Merck & Co., Inc., Whitehouse Station, New Jersey) in a 3-dose series, the quadrivalent meningococcal conjugate vaccine (MCV4) (Menactra®, Sanofi Pasteur, Inc., Swiftwater, Pennsylvania) in a single dose, and the tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine (Tdap) (Adacel®, Sanofi Pasteur; Boostrix®, GlaxoSmithKline Biologicals, Research Triangle Park, North Carolina) in a single dose. To describe trends in occurrence of postvaccination syncope, CDC and the Food and Drug Administration (FDA) analyzed data from the Vaccine Adverse Event Reporting System (VAERS) for January 1, 2005--July 31, 2007, and compared the results with VAERS reports received during January 1, 2002--December 31, 2004. The findings indicated that, since 2005, reports to VAERS regarding postvaccination syncope have increased, primarily among females aged 11--18 years, and rarely, subsequent serious injuries have occurred. To prevent syncope-related injuries, vaccine providers should follow the ACIP recommendation to strongly consider observing patients for 15 minutes after vaccination (*4*).

VAERS, a passive surveillance system operated jointly by FDA and CDC, receives reports of vaccine adverse events (VAEs) and is designed to generate, not test, vaccine-safety hypotheses (*5*).† Detecting new or rare VAEs, monitoring trends in known adverse events, and identifying risk factors for particular types of VAEs are the primary objectives of VAERS (*5*). Reports included in this analysis were those received by VAERS during January 1, 2005--July 31, 2007, that had VAEs

HPV4 Safety Data

- **Favorable safety profile: no association between vaccination with GARDASIL and**
  - **Congenital anomalies, miscarriages**
  - **16 pre-specified autoimmune conditions**
  - **Venous thromboembolism**
  - **Death**
  - **Any other general safety events (except syncope & possibly local skin infection)**
- **Syncope associated with GARDASIL infection-related**
- **Local skin infection (cellulitis/abscess) possibly associated with GARDASIL could be injection site reaction**
- **All safety conclusions were made by independent, external Safety Review Committee of 5 experts.**

Velcer C. Garadsil Female Safety Study Team

HPV Vaccine Safety

- **Safety**
  - **There is no evidence to suggest that HPV vaccine is responsible for ovarian failure. Genetic, infectious, inflammatory, autoimmune and toxin-related conditions are most likely responsible for ovarian failure in adolescent girls who have received HPV vaccine. (The relationship of ovarian failure and HPV vaccine area a temporal but not causal relationship).**

HPV Vaccine Safety

- **Safety**
  - **As of June 2013, 85 deaths have been reported to VAERS in individuals who have received HPV vaccine. A majority of these deaths have been reviewed by CDC. Their findings were:**
    - **There is no diagnosis at death that would suggest that the HPV vaccine caused the death**
    - **There is no pattern of death occurring with respect to time after vaccination**
    - **There is no consistent vaccine dose number or combination of vaccines given and the death**

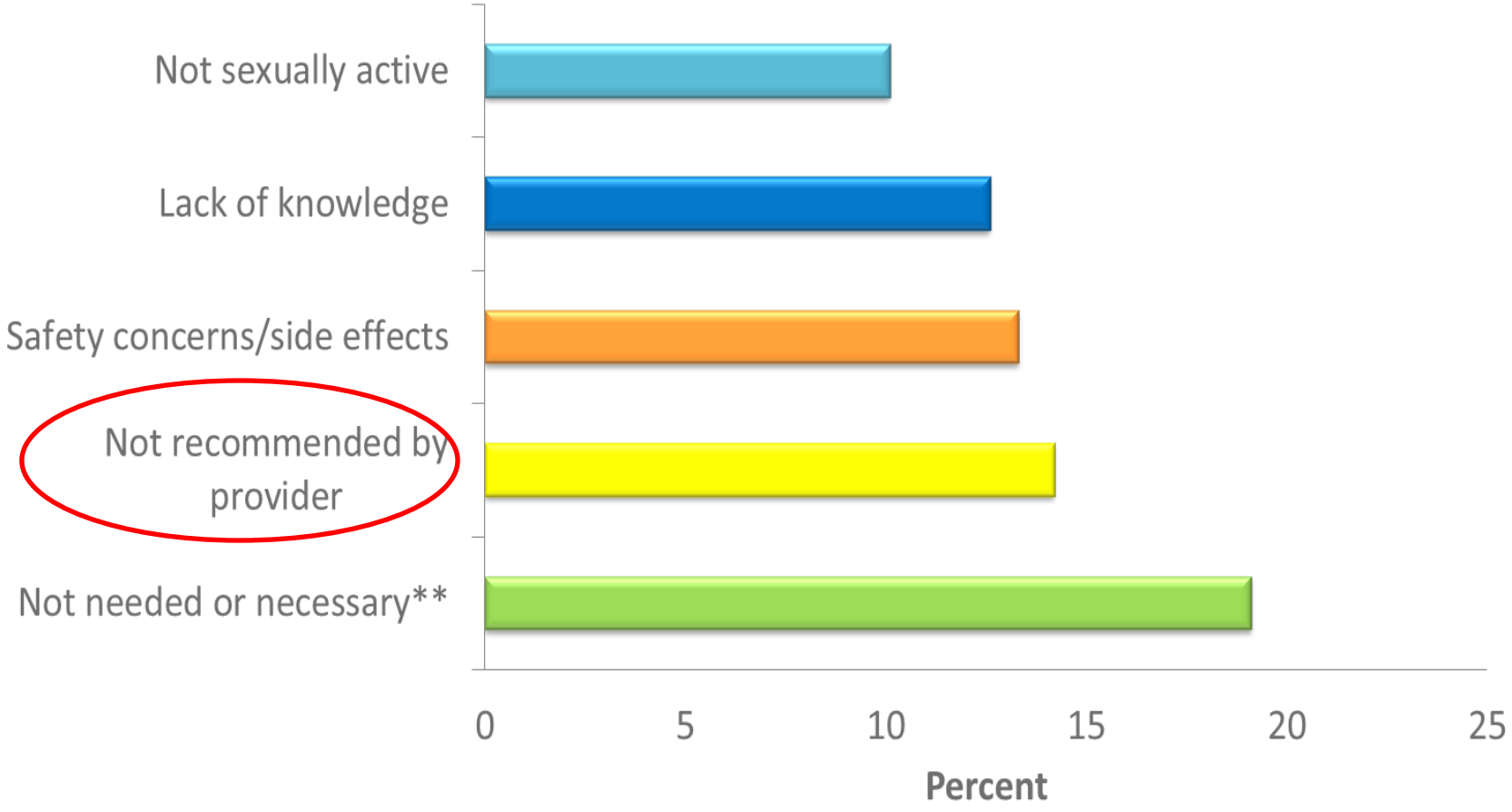
Vaccine Decisions Should Be Appropriately Informed

Recommendation From a Healthcare Provider for HPV Vaccination is Key

- HCP barriers to HPV vaccination include financial concerns and parental attitudes and concerns
- Parental barriers to HPV vaccination
  - Needing more information
  - Concerns about the vaccine's effect on sexual behavior
  - Low perceived risk of HPV infection
  - Perceived lack of direct benefit in boys
  - Social influences
  - Irregular preventive care
  - Vaccine cost
- Parents consistently reported a healthcare provider recommendation as one of the most important factors in their decision to vaccinate their children

Holman DM, et al. *JAMA Peds.* 2014;168:72-84.[15]

Top 5 reasons for not vaccinating daughter, among parents with no intention to vaccinate in the next 12 months, NIS-Teen 2012



* Not mutually exclusive.
** Did not know much about HPV or HPV vaccine

CDC. National and State Vaccination Coverage Among Adolescents Aged 13–17 Years — United States, 2012
MMWR 2013; 62(34);685-693.

YOU ARE THE KEY TO CANCER PREVENTION

Parents do weigh risks and benefits

- Parents who declined vaccine and those who accepted had similar concerns
- Both had concerns related to safety and sexuality but *accepters weighed cancer prevention more heavily*
- Most parents also believed their daughters would at some point be at risk for STIs
- Providers overestimated parents concerns

Perkins et al, Clin Peds 2013; Perkins et al J of Peds 2010; Perkins et al J Healthcare Poor Underserved 2013

HPV Vaccine Communications During the Healthcare Encounter

- HPV vaccine is often presented as 'optional' whereas other adolescent vaccines are recommended
- Some expressed mixed or negative opinions about the 'new vaccine' and concerns over safety/efficacy
- When parents expressed reluctance, providers were hesitant to engage in discussion
- Some providers shared parents' views that teen was not at risk for HPV and could delay vaccination until older

Goff S, et al. *Vaccine* 2011;10:7343-7349
Hughes C, et al. *BMC Pediatrics* 2011;11:74

But she's too young!!!

- Parents might believe their child won't be exposed to HPV because they aren't sexually active or may not be for a long time
  - In focus groups, some moms couldn't understand how their child could become infected even if they waited until marriage to have sex
  - Some moms stated that they didn't think HPV infection was very common because they had never heard that it was or didn't know anyone who had an HPV infection or HPV disease

Unpublished CDC data, 2013.

HPV YOU ARE THE KEY TO CANCER PREVENTION

Try saying:

We don't wait until exposure occurs to give any other routinely recommended vaccine.

HPV vaccine is also given when kids are 11 or 12 years old because it produces a better immune response at that age.

That's why it is so important to start the shots now and finish them in the next 6 months.

YOU ARE THE KEY TO CANCER PREVENTION

Is vaccine a green light for sexual activity?

- Parents may be concerned that vaccinating may be perceived by the child as permission to have sex
  - In focus groups, some parents expressed concern that in getting HPV vaccine for their child, they would be giving their child permission to have sex
  - This was one of the top four reasons respondents gave when asked why they would not vaccinate their daughter
  - A few parents expressed that while they wanted their child to “wait to have sex” they understood that might not be the case

Unpublished CDC data, 2013.

HPV YOU ARE THE KEY TO CANCER PREVENTION

Try saying:

Multiple research studies have shown that getting the HPV vaccine does not make kids more likely to be sexually active.

These studies have also shown that getting the HPV vaccine does not make kids more likely to start having sex a younger age.

YOU ARE THE KEY TO CANCER PREVENTION

Receipt of HPV vaccine does not increase sexual activity or decrease age of sexual debut

- Kaiser Permanente Center for Health Research
- 1,398 girls who were 11 or 12 in 2006, 30% of whom were vaccinated, followed through 2010
- No difference in markers of sexual activity, including
  - Pregnancies
  - Counseling on contraceptives
  - Testing for, or diagnoses of, sexually transmitted infections

Bednarczyk Pediatrics Oct 2012

HPV YOU ARE THE KEY TO CANCER PREVENTION

Would you give it to your child?

- Emphasizing your personal belief in the importance of HPV vaccine helps parents feel secure in their decision
  - Some respondents in focus groups stated that they would feel more comfortable knowing that the doctor had vaccinated their own child or was planning to (if the child was <11)
  - Respondents in an online survey stated that knowing that oncologists supported the recommendation made them more likely to get their child vaccinated

Unpublished CDC data, 2013.

HPV YOU ARE THE KEY TO CANCER PREVENTION

Try saying:

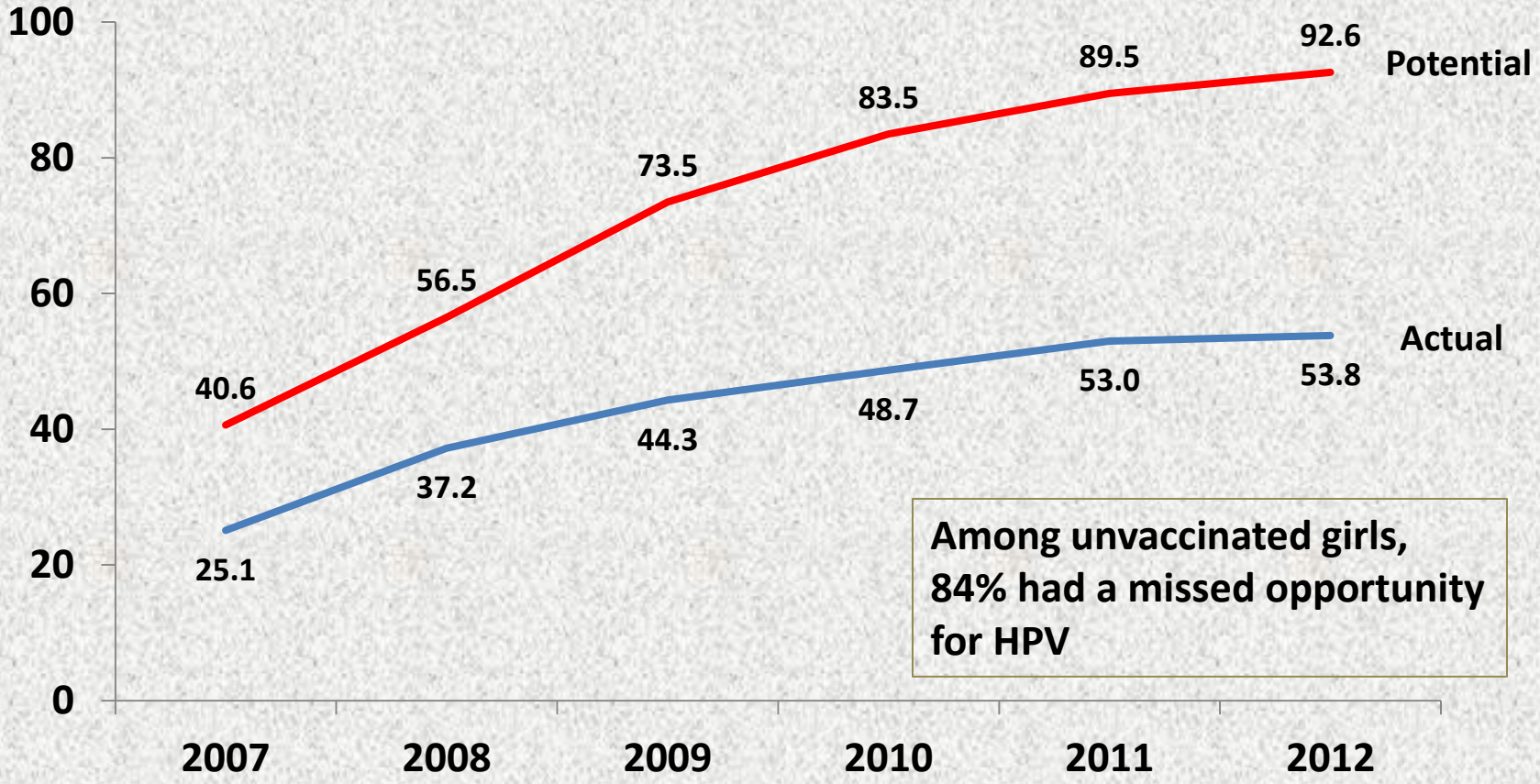
I strongly believe in the importance of this cancer-preventing vaccine.

I have given HPV vaccine to my son/daughter (or grandchild/niece/nephew/friend's children).

Experts, such as the American Academy of Pediatrics, cancer doctors, and the CDC, also agree that getting the HPV vaccine is very important for your child.

YOU ARE THE KEY TO CANCER PREVENTION

Actual and potentially achieve vaccination coverage of ≥ HPV among adolescent girls if missed opportunities* were eliminated, NIS-Teen



*Missed opportunity defined as having a healthcare encounter where at least one vaccine was administered but HPV was not.

MMWR. 2013; 62:591-5

Strategies to Improve Implementation of HPV Immunization in Adolescents

- HPV vaccine is a cancer vaccine not STI vaccine
- HPV immunization is routine and not “optional”
- Gender neutral
- Early age of administration (9-12 years) since this results in far superior immune response at this age → longer protection
- Early age of administration to ensure it predates greatest time of acquisition
- Give when given Tdap and/or MCV4 and don’t differentiate