

HPV: A Brief Review and Results from 2 Recent Studies

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HPV: History

- ▶ 1940's, 1st seen on EM on wart particles
- ▶ 1954, epidemiologic evidence of infectious disease on genital warts on returning soldiers from Asia. Within 6 months of return, high % of wives developed genital warts.

(Oooops!)



Harald zur Hausen

- ▶ **1977 Isolated HPV6 centrifugation of genital warts**
- ▶ **1983 isolated HPV 16 Southern Blot Hybridization**
- ▶ **1984 HPV 18**
- ▶ **2008 Nobel Prize Physiology**

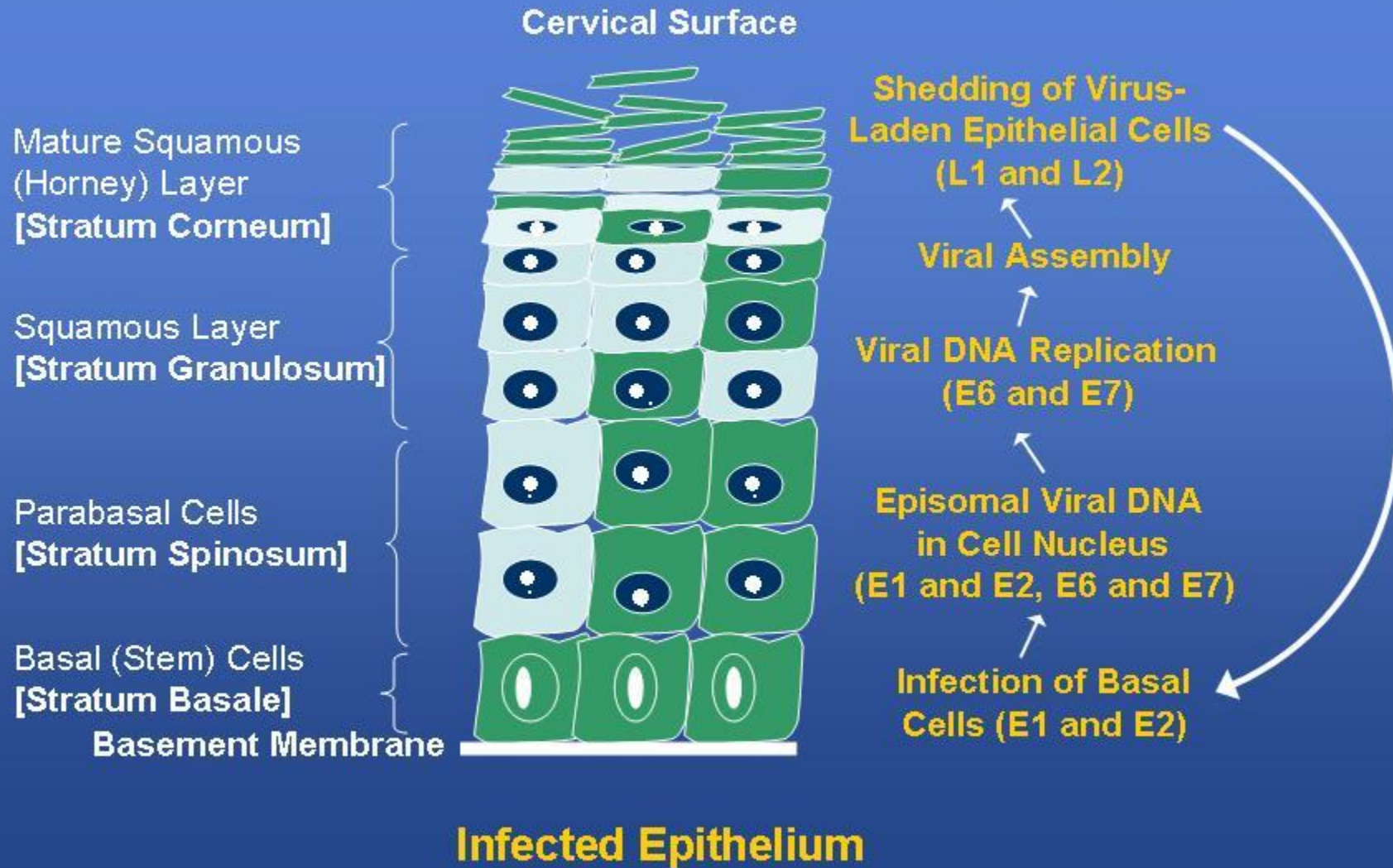
HPV: Virology (cont.):

- ▶ Replication is unique with some genes replicating early and others later in basal keratinocyte as it migrates away from basement membrane.
- ▶ As keratinocyte moves to upper layers, hpv replication slowly increases. The low viral load helps prevent immune detection.
- ▶ As the keratinocyte reaches the surface, hpv replicates its genome a lot.
- ▶ The dead keratinocyte releases the viral protein genomes that have been packaged into capsids (20 sided structure)
- ▶ **Role of Langerhans cells (antigen presenting cells)- (Martin Cast, USC)**

HPV Virology (cont.)

- ▶ **(Early) E6 & E7 oncogenes, causing abnormal or cancerous cells**
- ▶ **(Late) L 1 & 2 are capsid proteins & only expressed when viral replication complete and ready to infect next cell.**
- ▶ **Vaccine against L-1 antigen**

Life Cycle of HPV After Infection of the Epidermis¹



1. Frazer IH. *Nature Rev.* 2004;4:46–54.

Humoral Immune Response Against HPV Infection

- 2 classes of HPV antigens¹
 - Early proteins
 - Late proteins
- Late proteins (capsid) induce most consistent and strongest neutralizing antibody response^{1,2}
- Humoral response to early viral proteins typically modest or absent in most patients²
- Antibodies against HPV shown to be type specific³

1. Howley PM. In: Fields BN, Knipe DM, Howley PM, eds. *Fields Virology*. 4th ed. Philadelphia, Pa: Lippincott-Raven; 2002:2197–2229. **2.** Bonnez W. In: Richman DD, Whitley RJ, Hayden FJ, eds. *Clinical Virology*. 2nd ed. Washington, DC: American Society for Microbiology Press; 2002:557–596. **3.** Wang SS, Hildesheim A. *J Natl Cancer Inst Monogr*. 2003;31:35–40.

For a better start in life
start COLA earlier!



How soon is too soon?

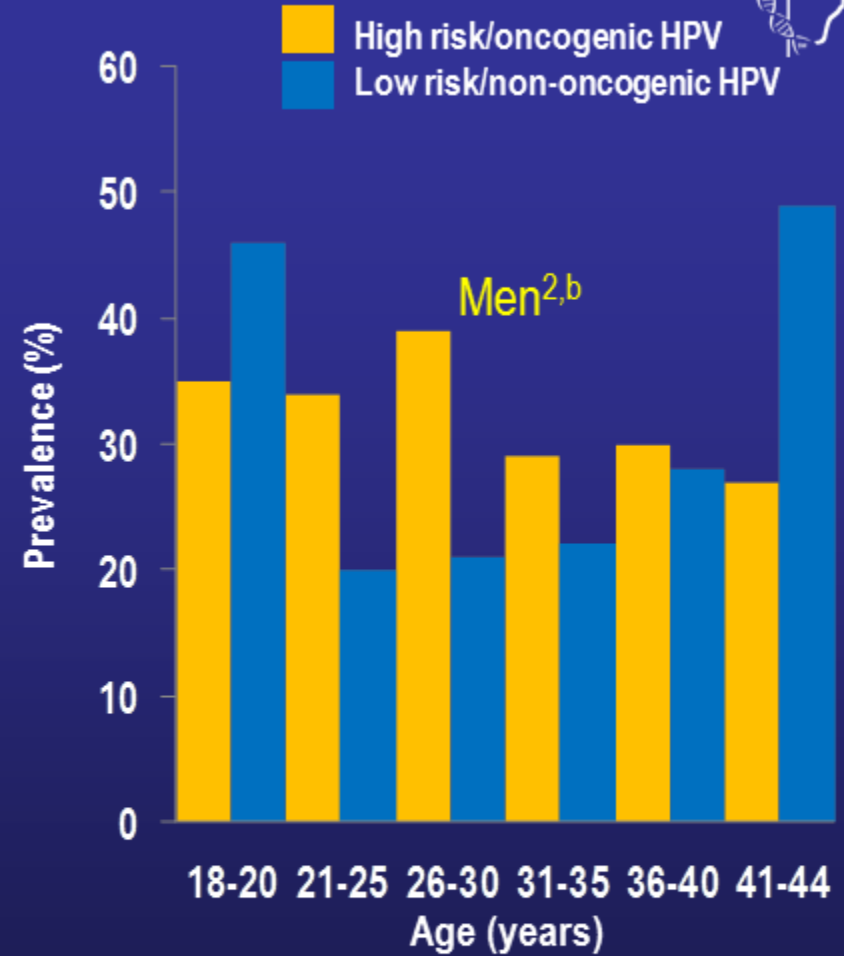
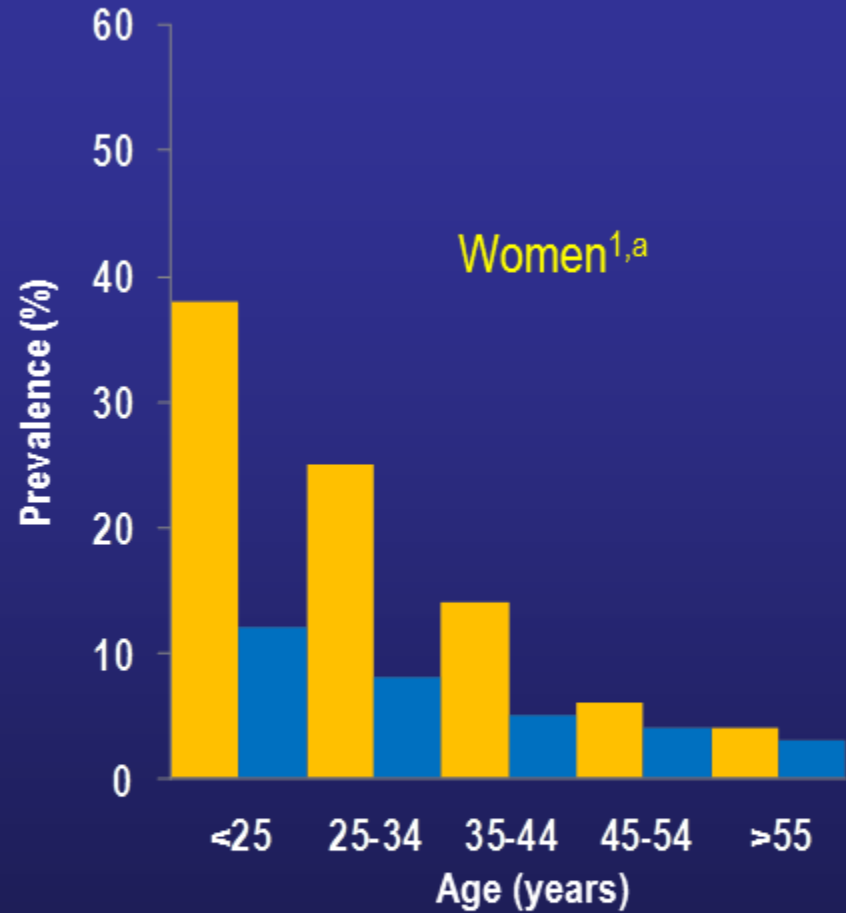
- Promotes Active Lifestyle!
- Boosts Personality!
- Gives body essential

Not soon enough. Laboratory tests over the last few years have proven that babies who start drinking soda during that early formative period have a much higher chance of gaining acceptance and "fitting in" during those awkward pre-teen and teen years. So, do yourself a favor. Do your child a favor.

From ACIP meeting February 2014

- ▶ % of cancers attributed to HPV keeps climbing- some because of better testing methods. By DNA detection method:
- ▶ 91% Cx Ca HPV (66% 16/18, 15% more in HPV 9 vaccine).
- ▶ 99% In situ Cervical Ca
- ▶ 69% vulvar, 75% vaginal Ca
- ▶ 70% oropharyngeal Ca
- ▶ 91% anal Ca (80% anal Ca HPV 16/18).
- ▶ 63% penile HPV

Prevalence of HPV Infection



HPV = human papillomavirus.

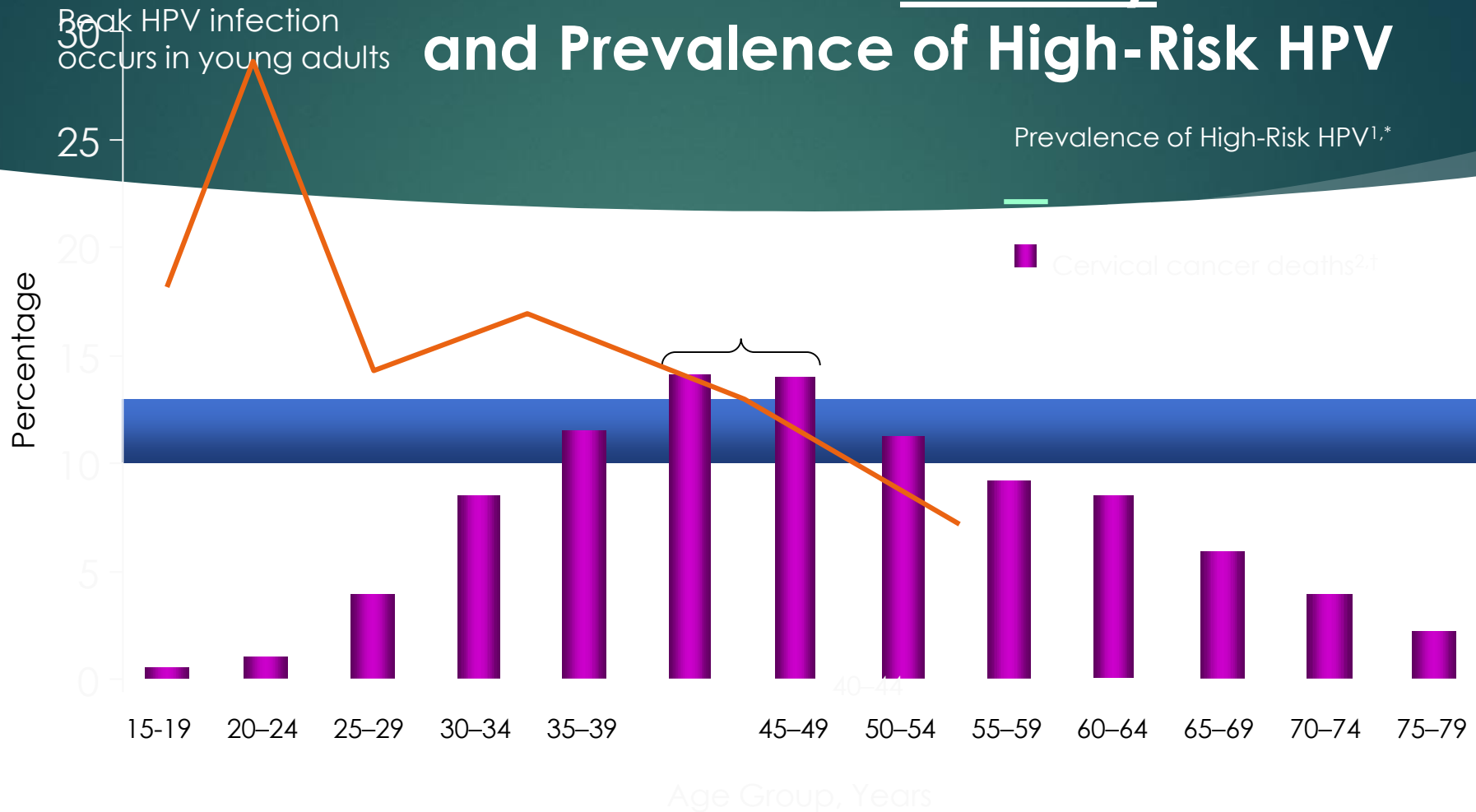
^aPrevalence of cervical HPV infection among 2,356 study participants who complete at least 1 clinical visit. High-risk/oncogenic HPV types included 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 70, 73, 82. Low-risk/non-oncogenic HPV types included 6, 11, 40, 42, 54, 61, 72, 81, 89.

1. Goodman MT et al. *Cancer Res.* 2008;68:8813–8824. Adapted and reprinted by permission from the American Association for Cancer Research: Goodman MT et al, Prevalence, acquisition, and clearance of cervical human papillomavirus infection among women with normal cytology: Hawaii Human Papillomavirus Cohort Study, *Cancer Res*, 2008, vol. 68, issue 21, 8813–8824.

^bPrevalence of genital HPV infection among men age 18–44 years in Tucson, Arizona (N = 290). High-risk/oncogenic HPV types included 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66. Low-risk/non-oncogenic HPV types included 6, 11, 26, 40, 42, 53, 54, 55, 62, 64, 67–73, 81–84, IS39, CP6108.

2. Giuliano AR et al. *J Infect Dis.* 2008;198:827–835. Giuliano AR et al, Age-specific prevalence, incidence, and duration of HPV infections in a cohort of 290 US men, *J Infect Dis*, 2008, vol. 198, 827–835, by permission of the Infectious Diseases Society of America.

Cervical Cancer Mortality in the US and Prevalence of High-Risk HPV



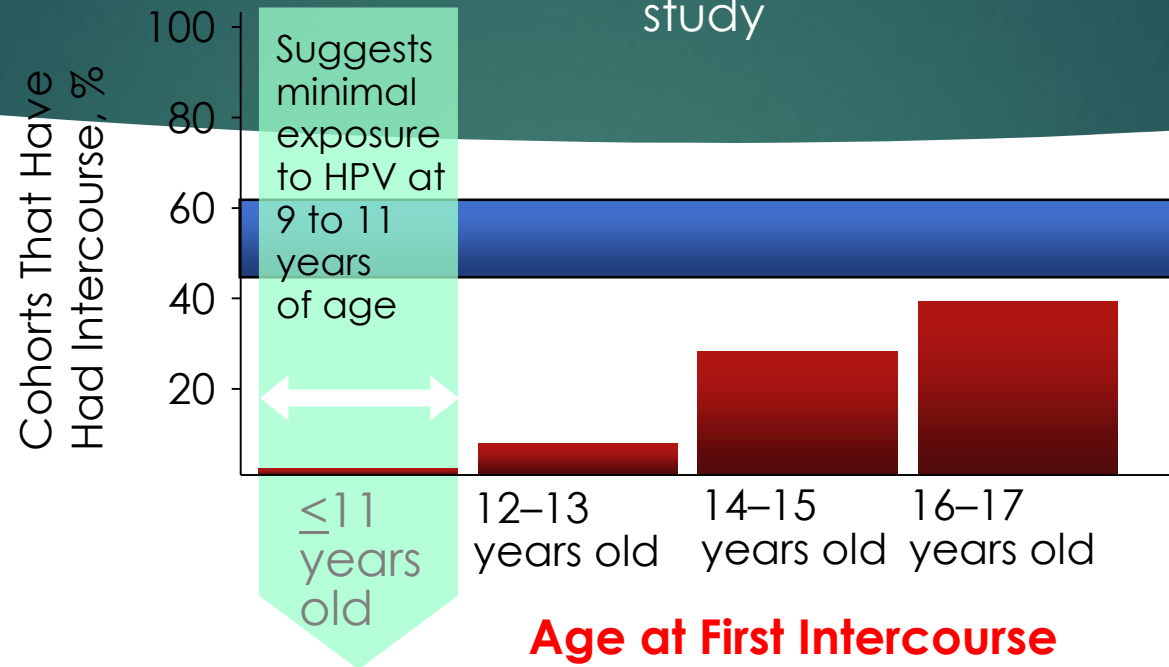
*Population-based prevalence of cervicovaginal HPV in the United States based on self-collected vaginal swabs among females participating in the National Health and Nutrition Examination Survey (NHANES) 2003-2004.¹

†Age distribution of all cervical cancer deaths between 1935 and 2000 in the United States.²

1. Adapted from Dunne EF et al. *JAMA*. 2007;297:813-819. 2. Adapted with permission from Insinga RP. *Womens Health Issues*. 2006;16:236-242.

The Most Effective Time to Vaccinate Is Before Exposure¹

Behavior reported in an independent study

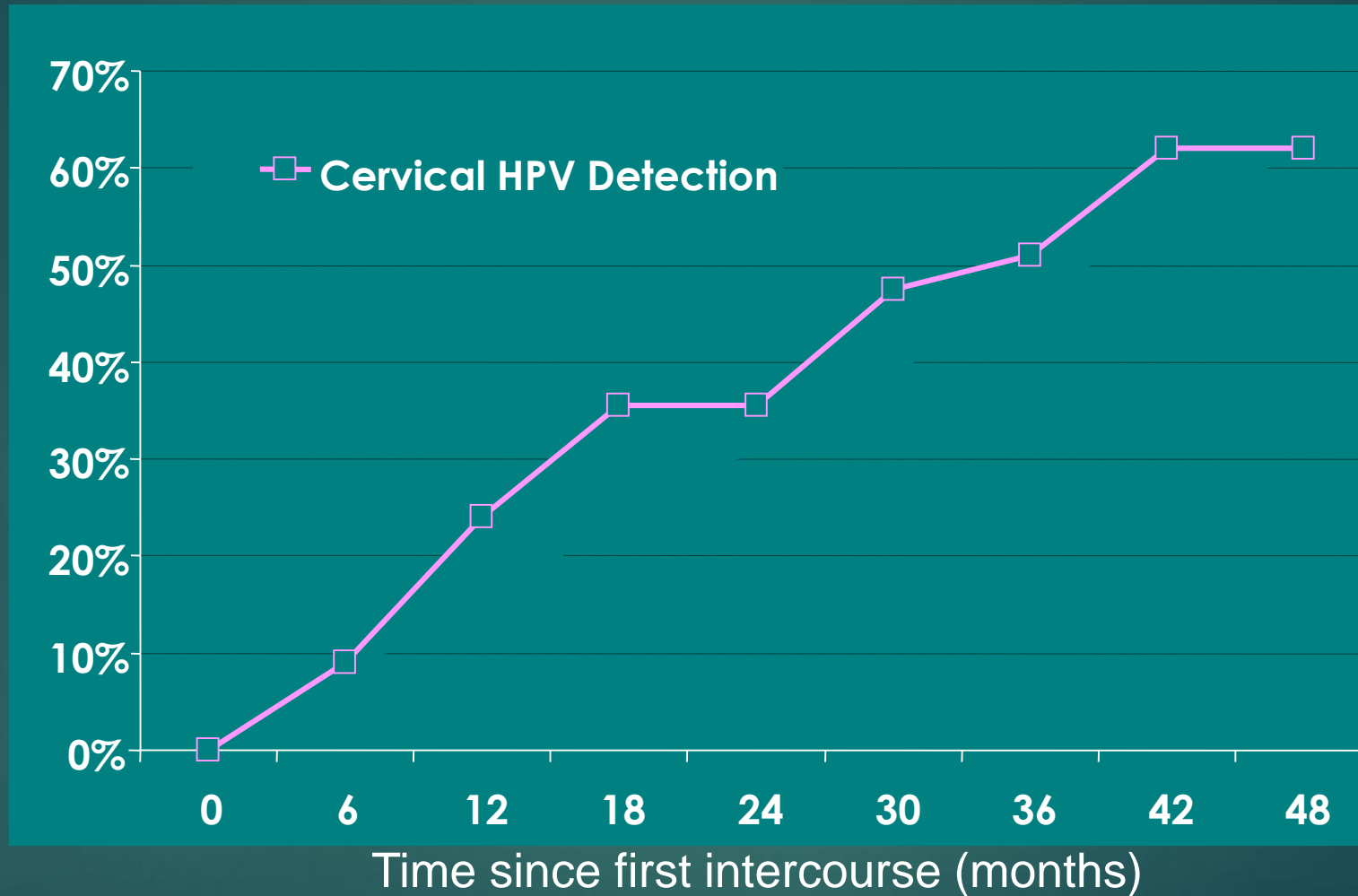


These data suggest minimal risk of exposure to HPV in 9- to 11-year-olds.

In an analysis of 1,552 adolescents and young adults, the subset (n=1,014) featured in this chart reported having engaged in sexual intercourse.²

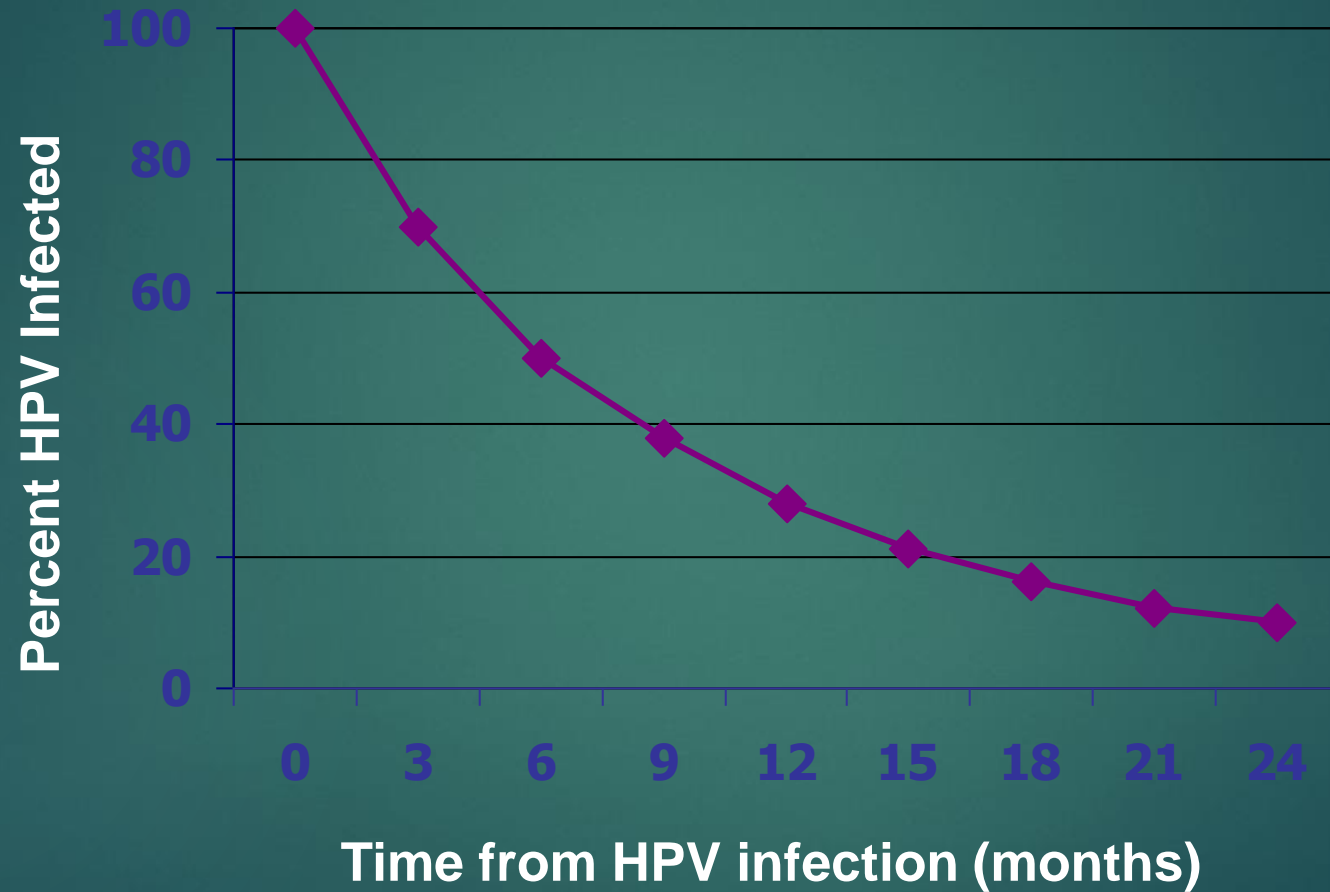
1. Centers for Disease Control and Prevention. *MMWR* 2002;51(No. RR-6):1-80. 2. Hoff T et al. *National Survey of Adolescents and Young Adults: Sexual Health Knowledge, Attitudes and Experiences*. Henry J. Kaiser Family Foundation;2003:14.

Incidence of Cervical HPV Detection in Women from the Time of Sexual Debut



Collins et al. Br J Obstet Gynecol 2002;109:96

Clearance of HPV Infections Over 2 Years

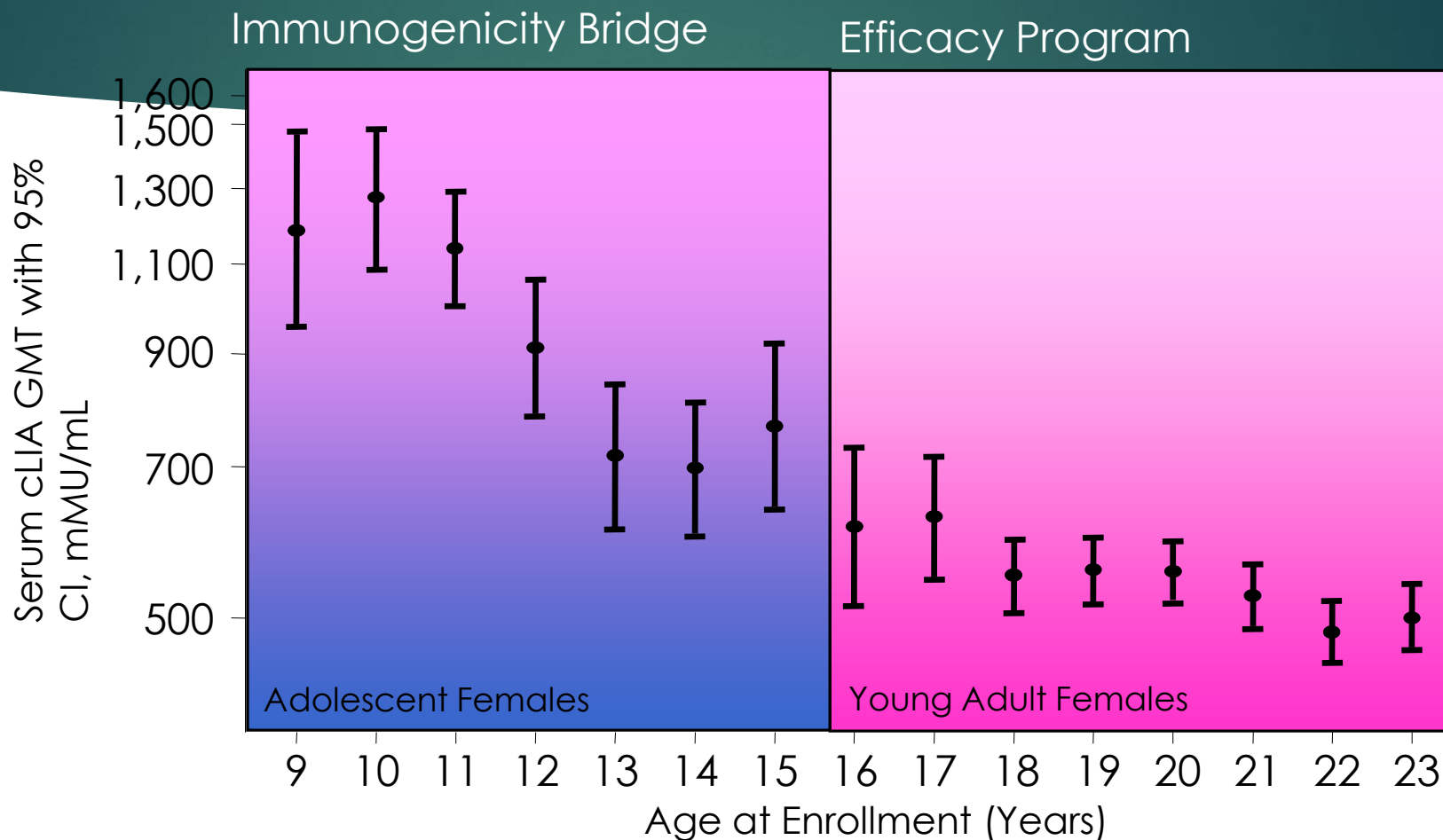


Adapted from Brown et al. JID 2005:191;182

Neutralizing Antibodies by Age at Enrollment

Neutralizing anti-HPV 6 GMTs at Month 7

Per-protocol immunogenicity population (ages 9–26)*



*Inclusive of 5 study protocols; all GMTs measured using cLIA.

cLIA = competitive Luminex® immunoassay.

Data available on request from Merck & Co., Inc. Please specify information package 20652350(1)-HPV.

HPV among “virginal” females



- ▶ Among n=22 virginal adolescent females, 45% had HPV, primarily due to sexual behaviors other than penile-vaginal sex (Shew 2013)
- ▶ Among n=250 college-age women 9% had HPV prior to sexual debut (Winer 2010)

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Does the HPV Vaccine Work?

1. **HPV Prevalence and Immunity after HPV Vaccination Program (starting in 2008) in Scotland.** *Emerging Infectious Diseases* Jan. 2016. **Major Decrease in recovering Vaccine serotypes and some cross-protection and herd immunity during the next 5 years**
2. **Prevalence of HPV After Introduction of the HPV Vaccine in US.** *Pediatrics*, March 2016. **Within 6 years of Initiating HPV Vaccination Program 64% decrease in the vaccine serotypes in 14-19 year olds and 34% decrease 20-24 year olds. Compared to non-vaccinated, efficacy 89%**

HPV Vaccination Initiation in a Southern California Private Pediatric Practice

Harry Pellman, MD and Brandon Brown, PhD

- **Private practice, mostly middle class, most have some kind of insurance**
- **202 consecutive children (ages 11-19) that were recommended to receive their 1st HPV vaccine in appropriate type OVs**
- **After the OV was concluded and parents either agreed or refused the HPV vaccine, a nurse requested that they fill out a very short questionnaire about their views on HPV vaccination**
- **Acceptors and refusers received different questionnaires**
- **No personal info requested, only age and sex**

HPV Vaccination Initiation in a Southern California Private Pediatric Practice

Harry Pellman, MD and Brandon Brown, PhD

Results:

1. Opportunity to vaccinate 124 males (61.4%) vs. 78 females (38.6%)
2. Male acceptance rate 88.7% and female acceptance rate 70.5% ($p < 0.001$)
3. Most common acceptance reasons were doctor recommendation (84.2%). 2nd most important reason “publicity” about importance of the vaccine (63.6%). Belief in importance of vaccines and recommendations by AAP, CDC, etc. 3rd most important (44.9%).
4. Most important refuser reason “I want to research the vaccine more” was (55.6%), then “my child is too young for the vaccine”(24.3%).
5. Fears that the vaccine would encourage sexual behaviors only 11%

PROS HPV Vaccine Study

Suellen Hopper, PhD and Harry Pellman, MD, and PROS Central

Purpose of study: How do practitioners communicate with parents and their family about HPV vaccination?

#1 factor influencing HPV vaccination is whether practitioner explicitly and strongly recommends

PROS HPV Vaccine Study

Suellen Hopper, PhD and Harry Pellman, MD, and PROS Central

Survey sent to PROS
members via Qualtrics
February 18 2016

Survey closed March
31, 2016

N=470 responded “yes” to currently providing well child care to 11-12 year olds

Randomized to receive one of two versions of 5 vignettes (describing hypothetical clinic visits)

PROS HPV Vaccine Study

Suellen Hopper, PhD and Harry Pellman, MD, and PROS Central

Vignettes: varied by:

- Parental reaction**
- Age**
- Gender**
- Ethnicity**
- #shots in clinic visit**

Outcomes:

- Strength of recommendation**
- Urgency**
- Communication strategies used**
- Peer norms (descriptive)**
- Peer norms (injunctive)**
- Sexual maturity judgment**

Participant Demographics

N=470 participated; 31% response rate

62% women practitioners

Mean years in practice 22 years (SD=9.8)

Mean age 53 (ranged from 27-79)

42% practice in suburban; 26% urban, not inner city; 19% rural; 13% urban inner city

47 states participated (plus Puerto Rico)

20% practitioners estimate that >75% of their patients have public insurance

26% practitioners estimate that 26-50% of their patients have public insurance

TRENDS

- **Strongly recommend 64-67%;**
 - For boys drops to 45%
 - Among 11 year olds, drops to 38%
 - Equally likely to strongly recommend by race, #shots
- **Urgency (recommending today)**
 - More likely with age 15 (85%) than age 11 (66%)
 - Gender, ethnicity, # shots equally likely
- **Sexual Maturity Judgment**
 - Practitioners 45% likely to make maturity judgment with boys (18% with girls)
- **Communication strategies used**
 - Emphasizing cancer prevention (81-89%)
 - Normalizing (79-82%)
 - Enthusiastic tone (55-65%)
 - Antibody response (42-57%) less used communication strategy
 - Preventing warts (50-57%) less used communication strategy

PROS study on Provider Attitudes About HPV Vaccine: Suellen Hopper, PhD and Harry Pellman, MD, and PROS Central

- **Question: Rank the usual 11 y/o vaccines in perceived importance to you (389/488 responded):**
- **218/389 (56%) Prioritized Tdap**
- **86/389 (24%) prioritized MCV4**
- **37/389 (9.5%) prioritized HPV**
- **39/389 (10%) prioritized Influenza**



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"The Sign of the Cross"




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**Thank ya, thank
ya vera much!!!**