

HPV Transmission

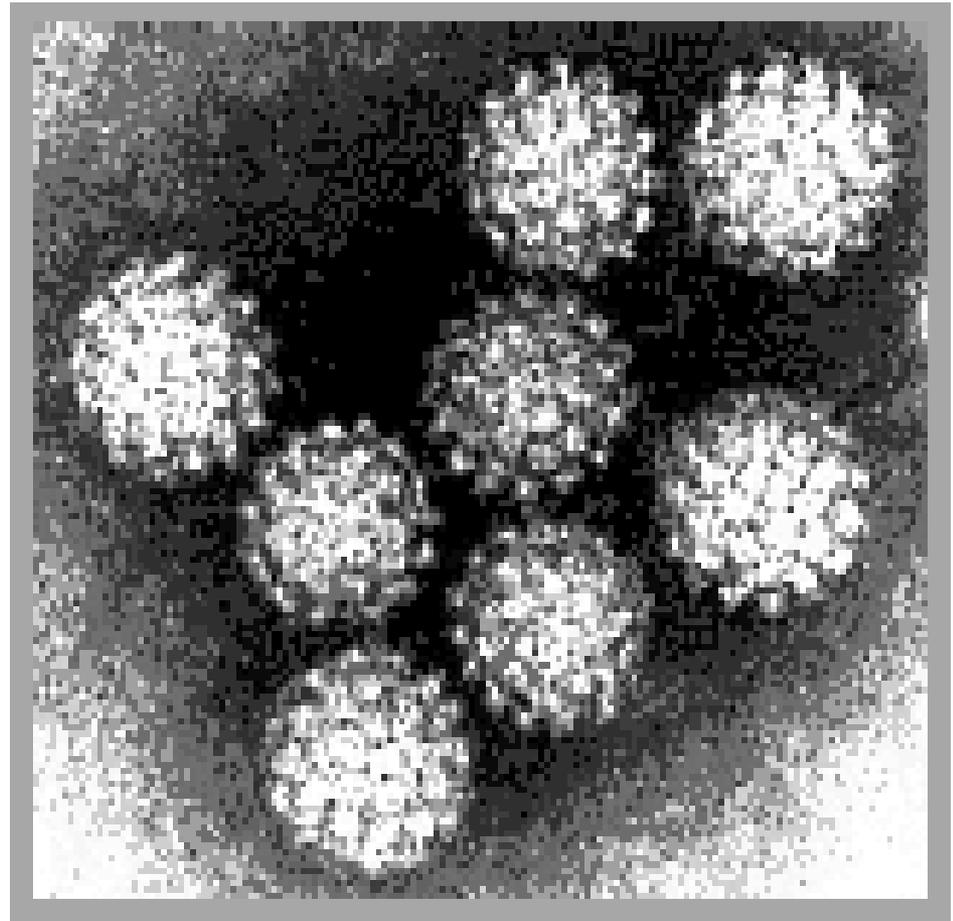
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Disclosure Information

I have no financial relationships to disclose.

Human Papillomavirus (HPV)

- DNA virus
- Over 100 HPV types
- ≥ 40 genital HPV types



Genital/Mucosal HPV Types

<u>HPV TYPE</u>	<u>CLINICAL FINDINGS</u>	<u>CANCER POTENTIAL*</u>
6, 11	genital warts, low grade lesions, recurrent respiratory papillomatosis (RRP)	Low (negligible)
40, 42, 54, 55/44, 61, 70, 72, 81, CP6108	low grade lesions	Low (negligible)
16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82/IS39	low grade lesions, high grade lesions, cancer	High
Uncertain cancer potential: HPV 57, 62, 64/34, 67, 69, 71, 83, 84		

* Cancer potential: Muñoz et al.,
Vaccine 2006;24S3:S3/1

Modes of Transmission

- SKIN contact, not blood or bodily fluids
- Sexual
 - Intercourse (vaginal or Anal) – (most common route)
 - Genital (non-penetrative), oral, digital contact
- Non-sexual
 - Mother to newborn (vertical transmission - rare)
- Auto-innoculation
 - probably important for site-to-site transmission

Epidemiology of HPV

- The most common STD in the US and worldwide
- 80% sexually active adults in the US infected with at least one HPV type by age 50¹
- Estimated incidence: 6.2 million per year¹

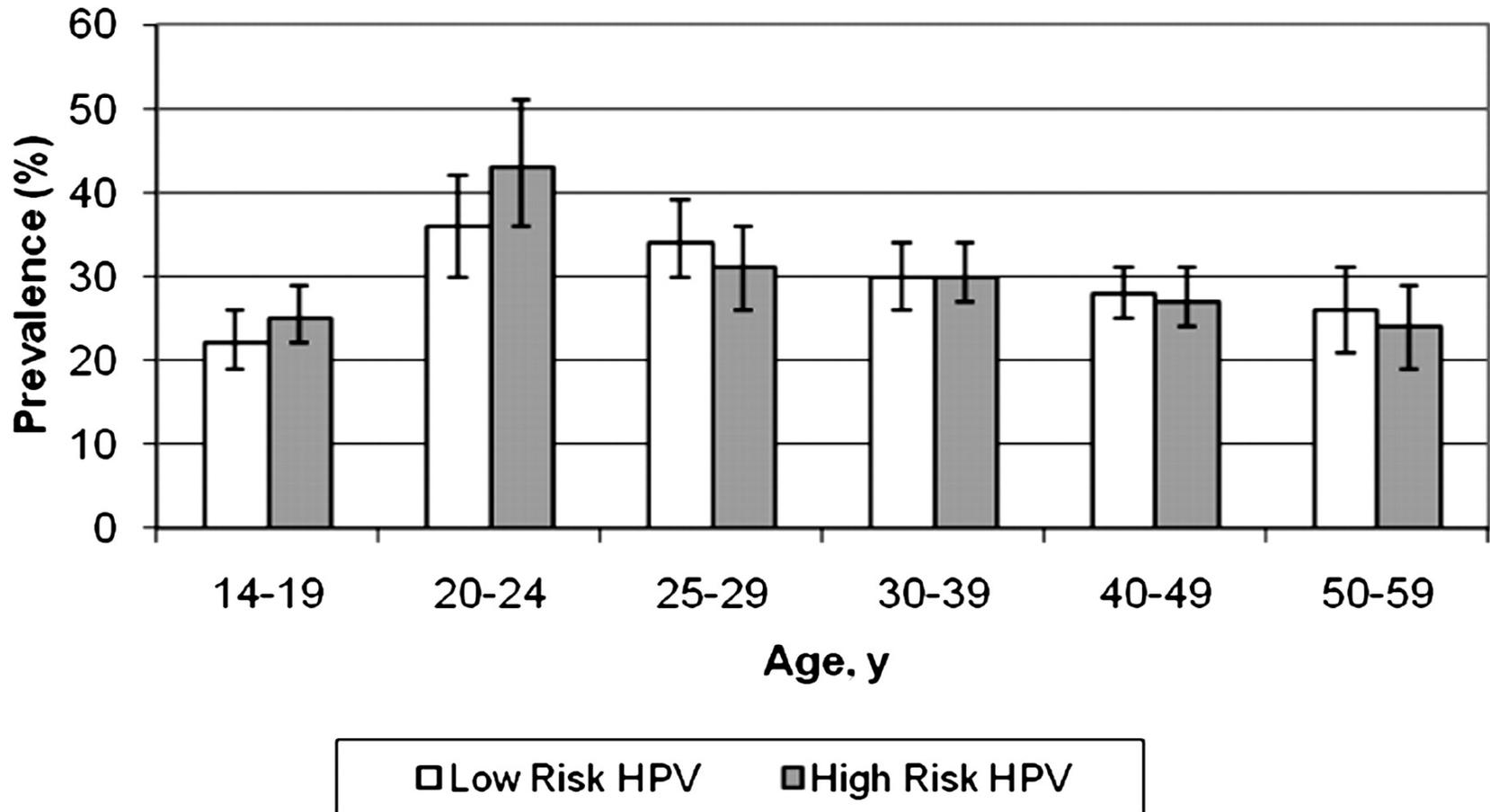
1. Centers for Disease Control and Prevention. Rockville, Md: CDC National Prevention Information Network; 2004

Epidemiology of HPV

- Peak prevalence during adolescence and young adulthood
- In sexually active 15-24 year olds, ~9.2 million are currently infected.¹
 - An estimated 74% of new infections occur in this age group.¹
- Prevalence declines with age

1. Weinstock et al (2004) *Sex Reprod Health*

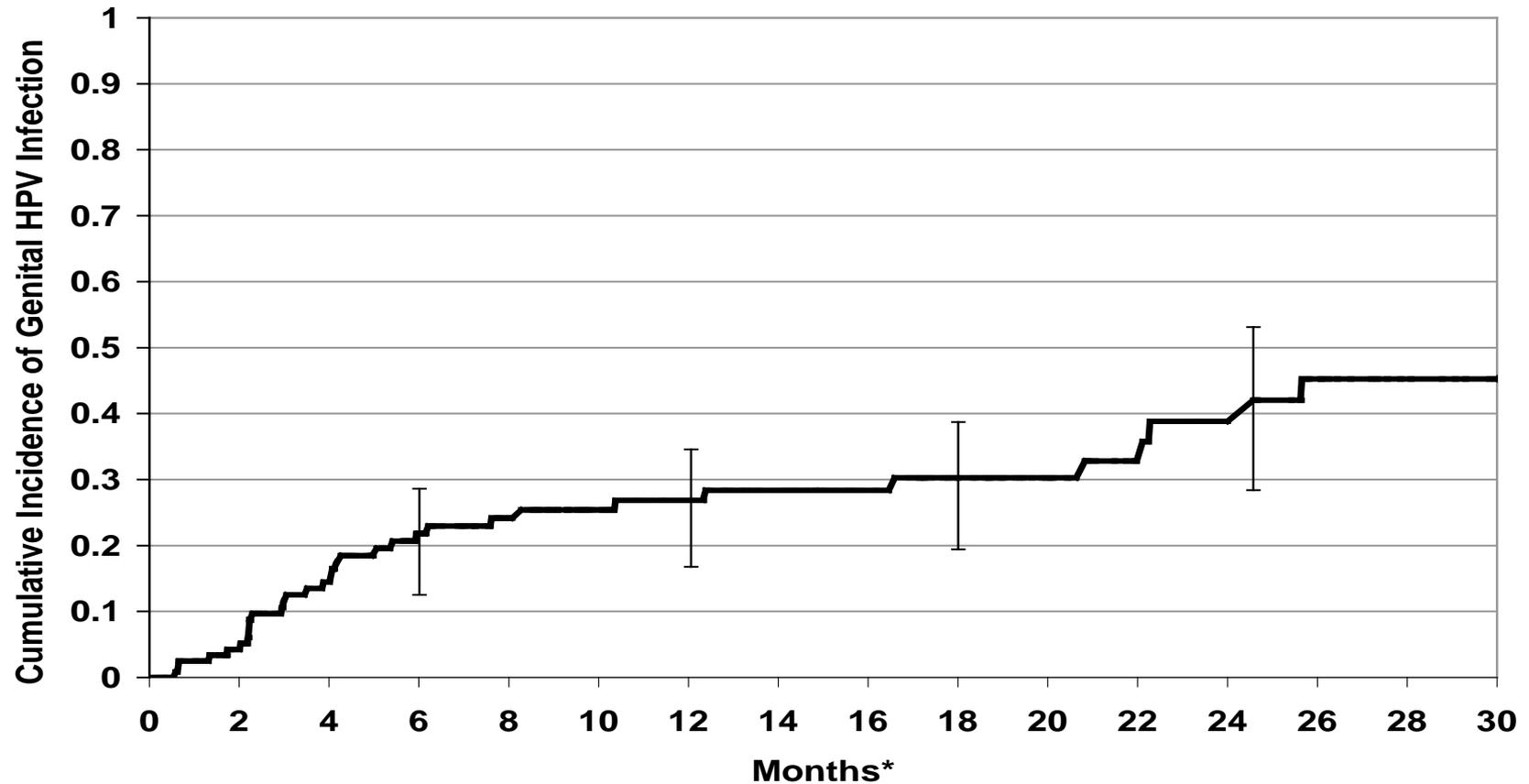
Prevalence of low-risk and high-risk HPV among 4150 14-59 year old females, NHANES 2003-2006



Hariri S et al. Prevalence of Genital HPV among Females in the United States, the National Health and Nutrition Examination Survey, 2003-2006
J Infect Dis. 2011;204:566-573

Female Risk of Acquiring Genital HPV Infection from her First Male Sex Partner

Winer et al. *J Infect Dis* 2008;197:279-82



*From date of first reported vaginal intercourse with a male partner (Women were censored at reported date of a second sex partner)

HPV in Virgins

- 2-year cumulative incidence of genital HPV in female university students
 - Non-virgins: 38.8%
 - Virgins who initiated vaginal intercourse: 38.9%
 - Virgins who remained virgins: 2.4%
 - Non-penetrative sexual contact was associated with ↑ risk in virgins.

Duration of HPV Infections

- Vast majority of infections resolve spontaneously (90% within 2 years)
- Duration of infections seems to be shorter in men than in women
- Can't be sure whether an infection has "cleared" or become "latent"

Duration of HPV Infections

- In newly sexually active female university students, 90% of new infections cleared within 2 years (half cleared within 9.4 months).¹
 - 19% of “cleared” infections were re-detected within 1 year.

¹Winer et al. Cancer Epi Bio Prev 2011; 20: 699-707

Risk Factors for HPV Infection in Women

- Recent new partners
 - Increased risk with new partners reported in the past year
- Time having known a partner before sex
 - Women knowing their partners for <8 month at greater risk than women knowing their partners for ≥ 8 months
- Sex partner's number of previous partners
 - Increased risk with one or more previous partners
 - Even greater risk if the number of previous partners was unknown!
- Inconsistent condom use with new partners

Association between incident HPV infection and condom use over the past 8 months

(Winer et al. *N Eng J Med* 2006; 354:2645-54)

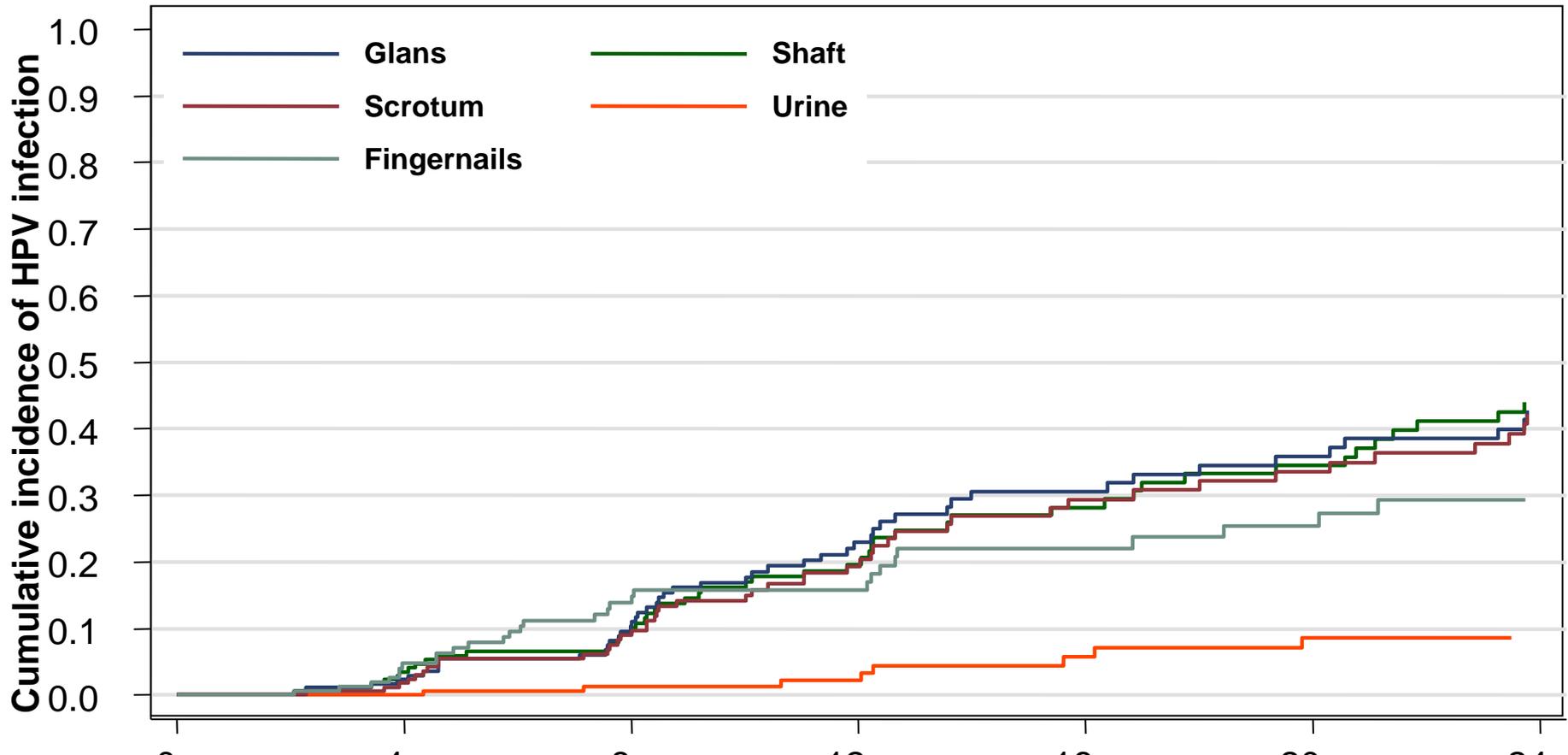
Newly sexually active HPV naïve female university students who used condoms consistently (100% of time) reduced their risk of acquisition by 70%.*

Those who used condoms at least half the time reduced their risk of acquisition by 50%.*

*Compared to those who used condoms <5% of the time, adjusting for numbers of new partners and numbers of partners' new partners.

Incidence of Genital HPV Infection by Anatomic Site Among Sexually Active Male University Students (18-23 Years Old)

(Partridge et al. *JID*, 2007;196:1128-36)



Circumcision and HPV?

- A meta-analysis of 21 studies (including 2 RCTs in Africa) showed that HPV was less prevalent in circumcised than uncircumcised men (OR=0.6, 95% CI: 0.4-0.8)¹
 - No effect on HPV acquisition or clearance
- A longitudinal study in young heterosexual men showed no effect on overall HPV acquisition, but multi-focal genital infection was more common in uncircumcised men.²
- Does it affect men's susceptibility to infection and/or infectivity and persistence?

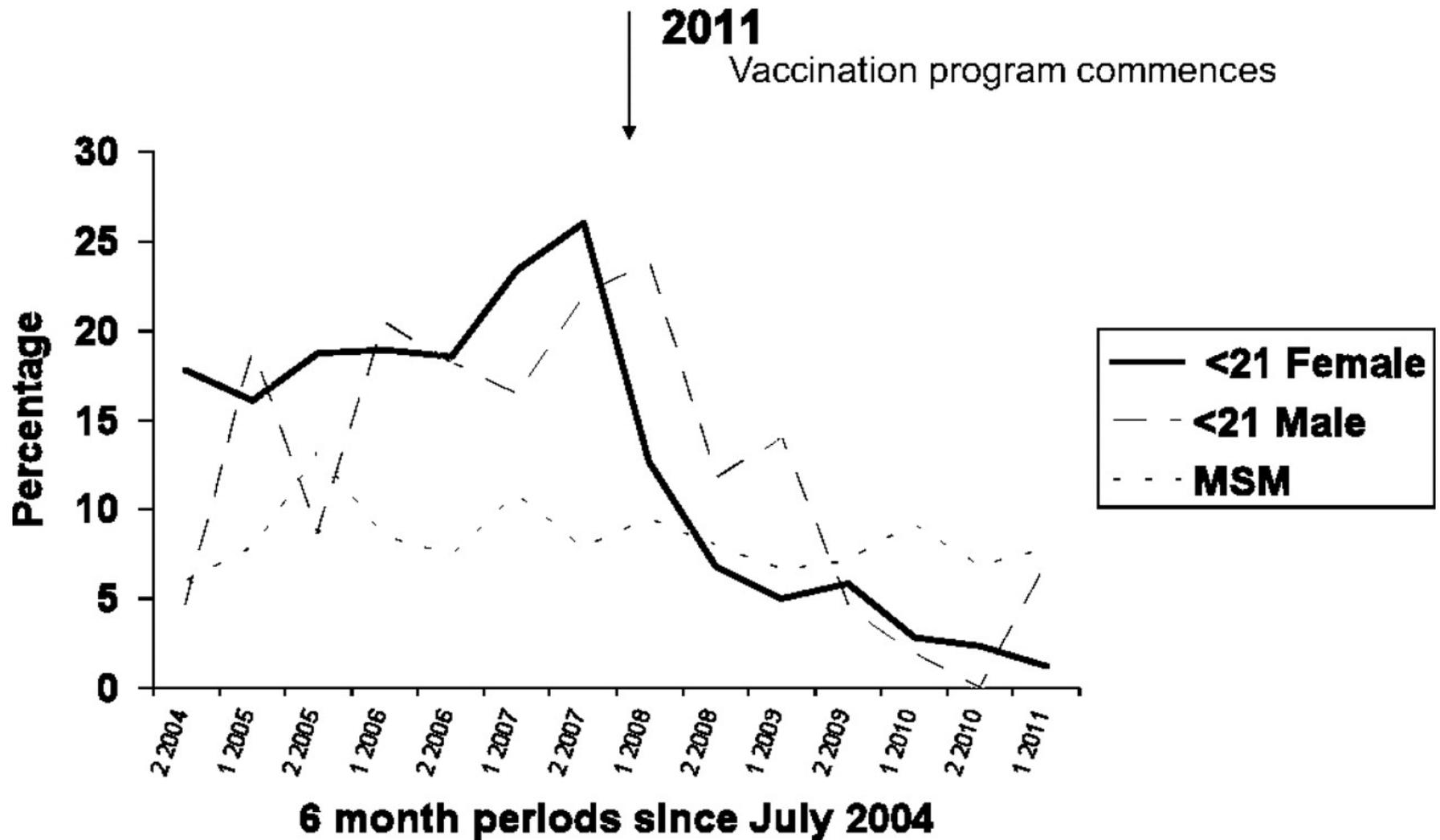
¹Albero et al, Sex Transm Dis 2012; 39:104-113

²Vanbuskirk et al, Sex Transm Dis 2011; 38:1074-81

Transmission Dynamics

- HPV not restricted to “core groups”
- Concurrency and serial monogamy likely increase rate of transmission
- HPV is more transmissible than other viral STDs, but similar to bacterial STDs
- Male-to-female less efficient than female-to-male

Presentations with warts in men and women <21 years, and MSM all ages, July 2004 to end June



Read T R H et al. Sex Transm Infect doi:10.1136/sextrans-2011-050234



HPV in mid-adult women

- Are mid-adult women at risk for new HPV infections, or are the majority of “new” infections due to reactivation or persistence of infections acquired at younger ages?
- It is impossible to distinguish between new infection and reactivation.
- There are no perfect markers of prior infection.

Risk of incident high-risk HPV infection in female mid-adult online daters (n=421)¹

Sexual activity in prior 6 months	Hazard Ratio
Not sexually active with male partners	1.0
Sex with 1 male partner who was not new	1.2 (0.7-2.3)
Sex with new partner(s) or multiple partners	3.0 (1.7-5.2)

¹Winer et al. Abstract presented at IPV 2011 conference, Berlin, Germany.

HPV Reactivation from Latency

- In HIV+ women who were not recently sexually active, low CD4+ T-cell count was associated with increased HPV incidence.¹
- Age-related / post-menopausal immune senescence may contribute to increased persistence or reactivation of latent infections.

¹Strickler et al. J Natl Cancer Inst 2005;97:577-586.

Does Re-infection Occur?

- Neutralizing antibodies likely protect against re-infection with the same HPV type.
- Difficult to distinguish re-infection from re-activation.
- Limited epidemiologic data for and against.

HPV in non-genital sites

HPV in Fingers

- HPV detected on fingers of 38% of women and 64% of men with genital warts.¹
- The 2-year cumulative incidence of HPV in fingernail tips was 32% in male university students.²
- 14% of fingernail tip samples from female university students were HPV+.³
 - The same HPV type was concurrently detected in 60% of vaginal samples.
 - Re-detection at the next visit was less common in fingernail tip samples (15%) than in vaginal samples (73%).

¹Sonnex et al. *Sex Transm Infect* 1999;75:317-9.

²Partridge et al. *J Infect Dis* 2007;196:1128-36.

³Winer et al. *Cancer Epi Bio Prev* 2010;19: 1682-5.

HPV in Fingers

- True infection?
- Deposition?
- Autoinnoculation?

Autoinnoculation

- In a small study of 25 heterosexual couples, the rate of autoinnoculation (between genitals, anus, hands) in men was comparable to the rate of female-to-male transmission.¹
- In female university students, vaginal HPV infections tended to precede cervical infections.²

¹Hernandez et al. Emerging Infectious Diseases 2008;14:888-94.

²Winer et al. AJE 2003;157:218-26.

Oral HPV

Oral HPV

- HPV linked to oropharyngeal squamous cell carcinomas (OSCCs) (~90% due to HPV16)¹
- Incidence of OSCCs is increasing and expected to surpass that of cervical cancer by 2020²

¹D'Souza et al. N Engl J Med 2007;356(19):1944-56

²Chaturvedi et al. J Clin Oncol 2011;29(32):4294-301

Oral HPV Prevalence

- National survey of healthy individuals aged 14-69 years¹:
 - Any HPV: 6.9%
 - HPV16: 1%
 - Prevalence higher in men (10.1%) than in women (3.6%)
 - Bimodal age distribution (peak prevalence in adults aged 30-34 and 60-64 years)

¹Gillison et al. JAMA 2012; 15(307):693-703

Oral HPV Transmission

- Oral HPV is predominantly sexually transmitted.
 - Oral HPV prevalence 8-fold higher in sexually experienced individuals, and associated with lifetime numbers of sex partners.¹
- Link between oral sex behaviors/open mouth kissing partners and oral HPV is inconclusive.
- Smoking, immunosuppression, and genital HPV infection have also been associated with oral HPV.
- Data on oral HPV acquisition and natural history are lacking.

¹Gillison et al. JAMA 2012; 15(307):693-703