National Cancer Institute

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Epidemiology of HPV infection in males

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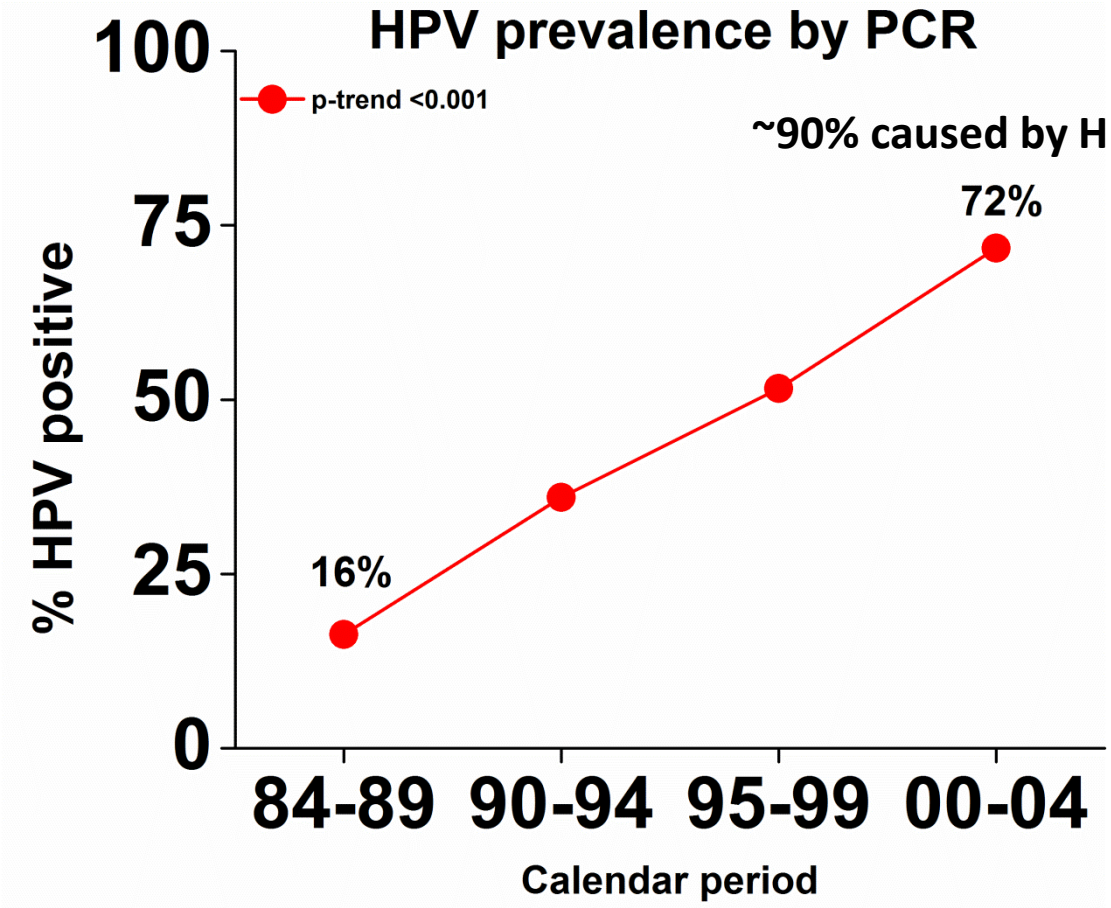
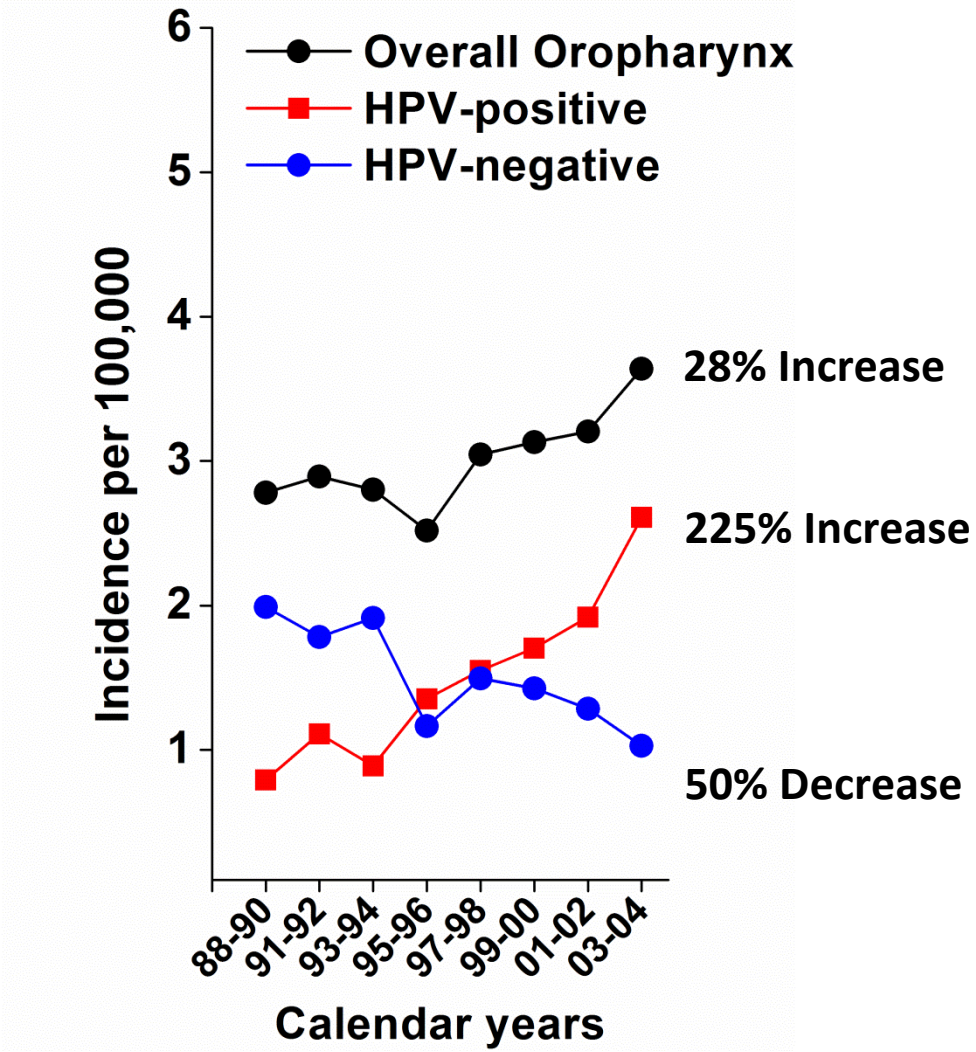
Outline

- Rising incidence rates of oropharynx cancers
- Epidemiology of oral HPV infection
- Opportunities for prevention of HPV-positive oropharynx cancers

Rising oropharynx cancer incidence in the United States caused by HPV

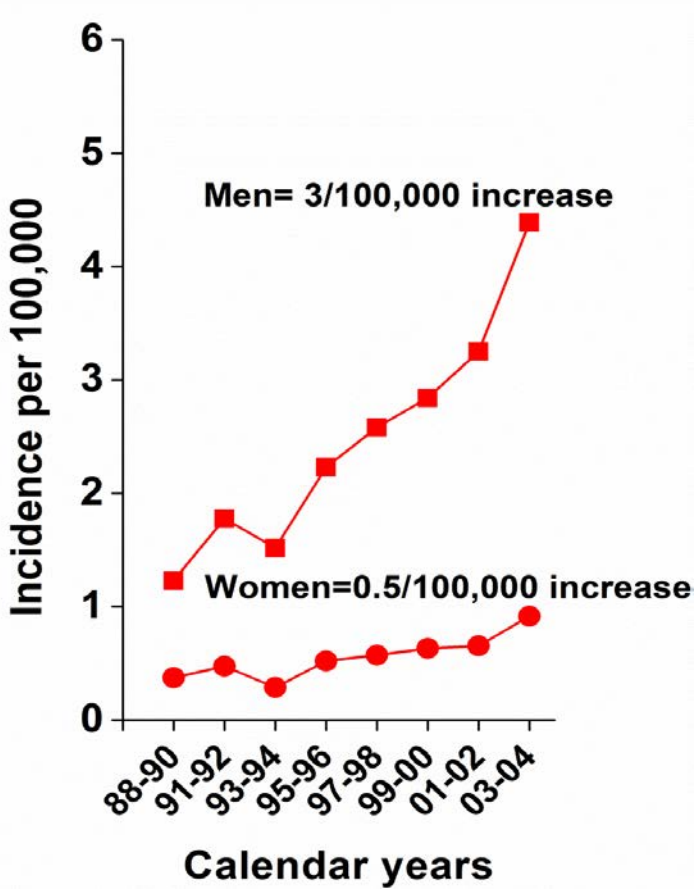




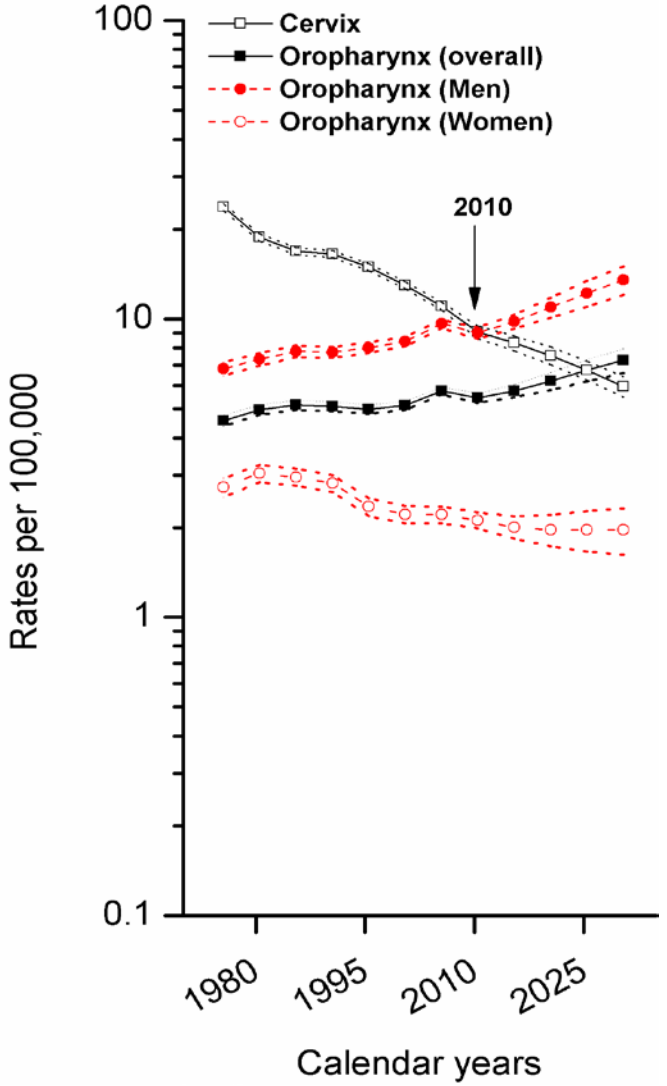
Chaturvedi, JCO 2011

Predominance of oropharynx cancers in males

Observed incidence of HPV-positive oropharynx cancer



Projected incidence of oropharynx cancer



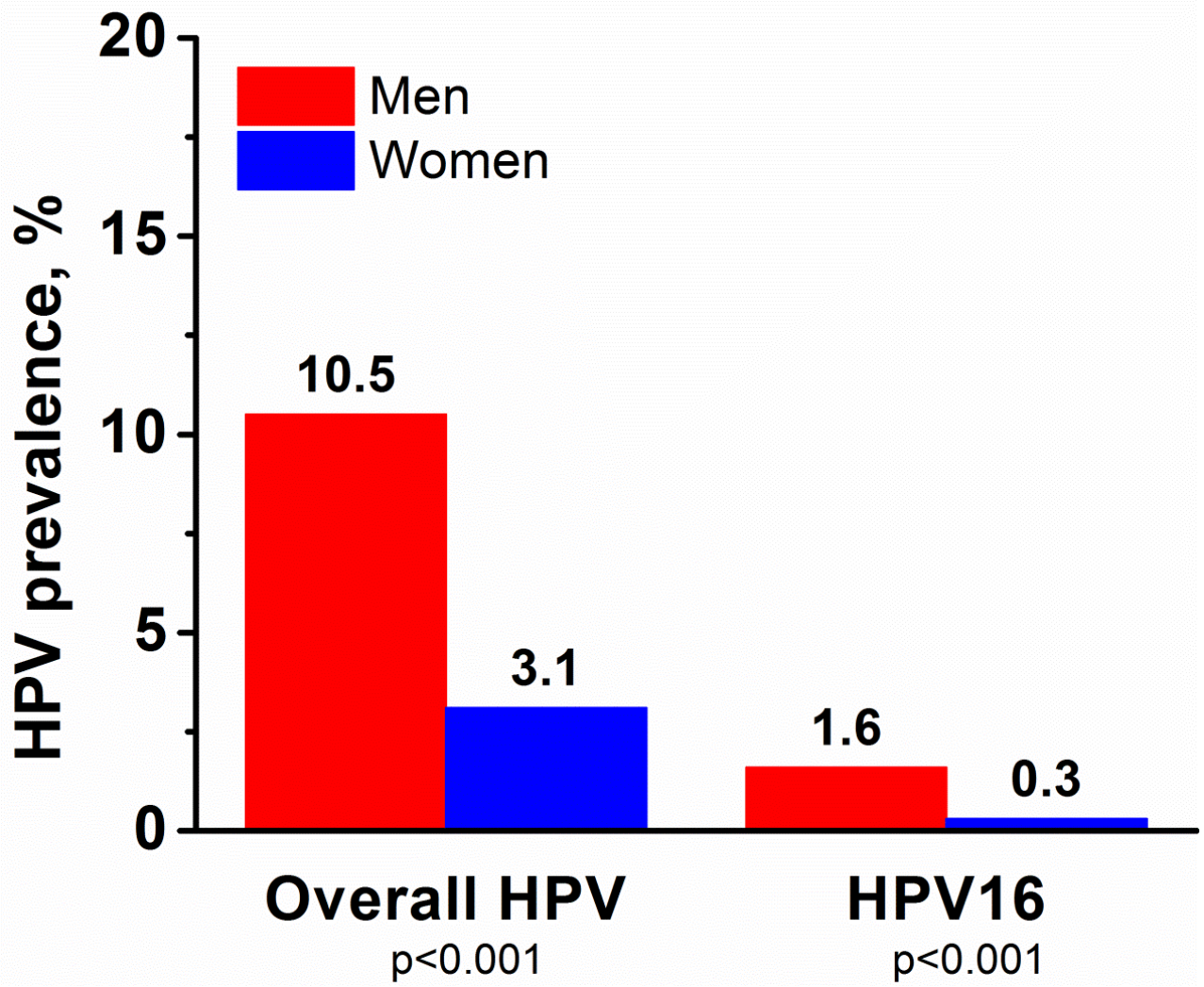
Projected incidence rates

- **Most common HPV+ cancer**
- **2030: Most common head and neck cancer**
- **Majority among men**

Chaturvedi, JCO 2011

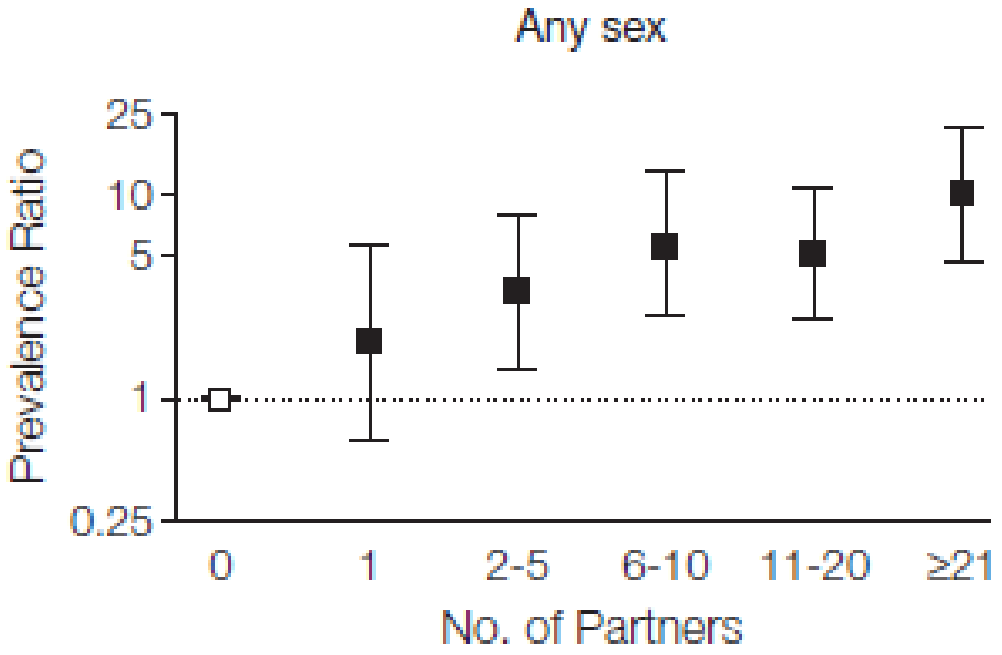
Oral HPV epidemiology in the U.S. population

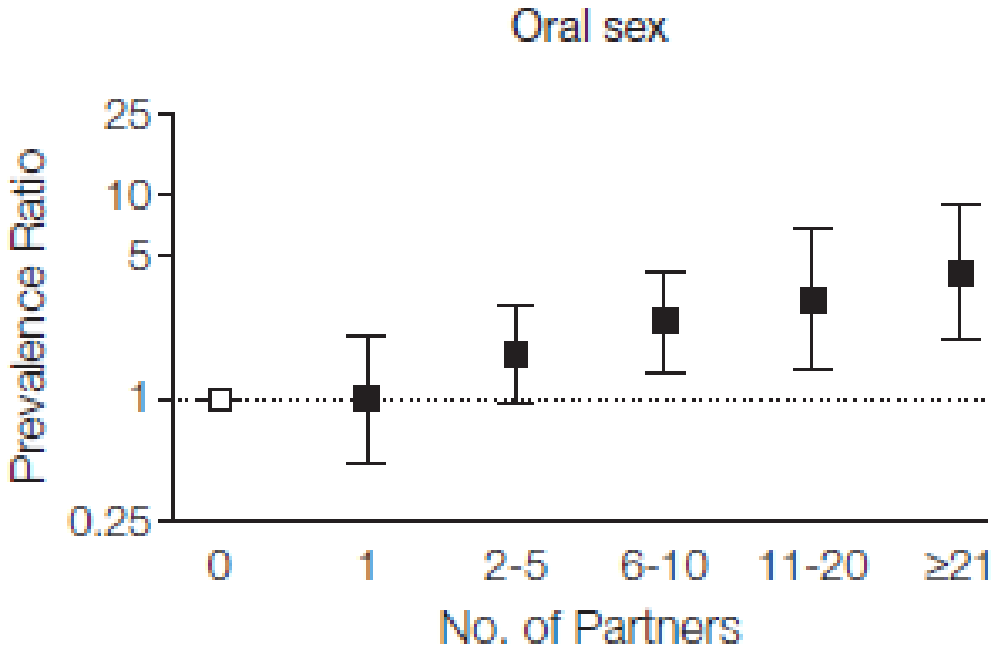
Higher oral HPV prevalence in men than women United States, NHANES 2009-2012



Gillison, JAMA 2012; Chaturvedi, Cancer Res 2015

Association of sexual activity with oral HPV prevalence

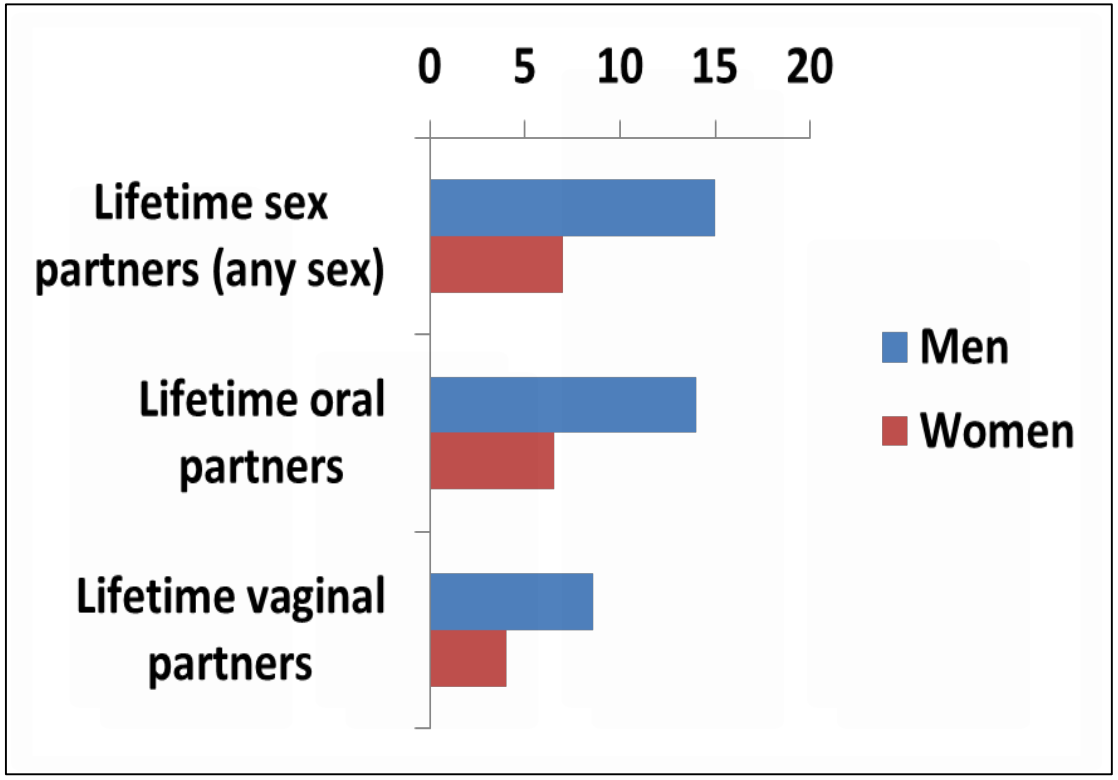




- Oral HPV infection is very rare (<0.3%) in men and women in the absence of sexual activity

Gillison, JAMA 2012; Chaturvedi, Cancer Res 2015

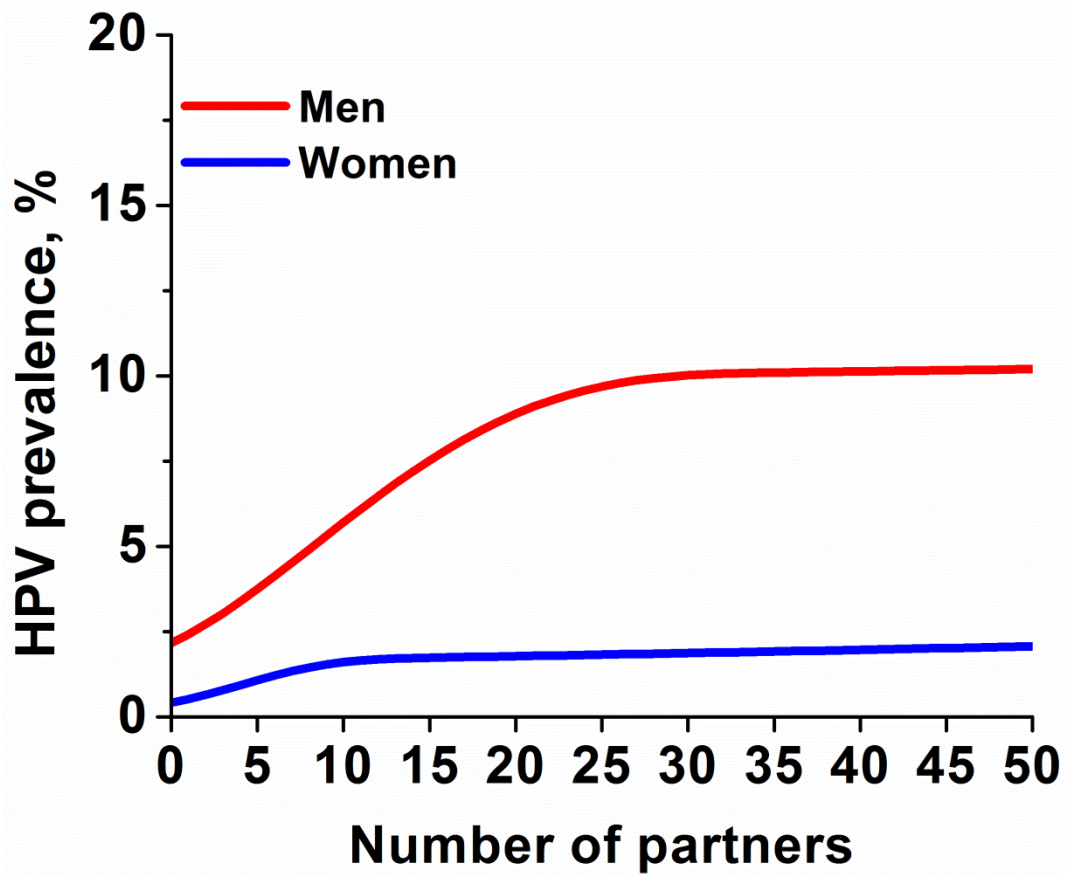
Sexual behavioral differences do not entirely explain higher oral HPV prevalence in men than women



- ~18% of male excess explained by behaviors

Chaturvedi, Cancer Res 2015; D'Souza, PLOS One 2014

Stronger associations of sexual behaviors with oral HPV prevalence in men vs. women

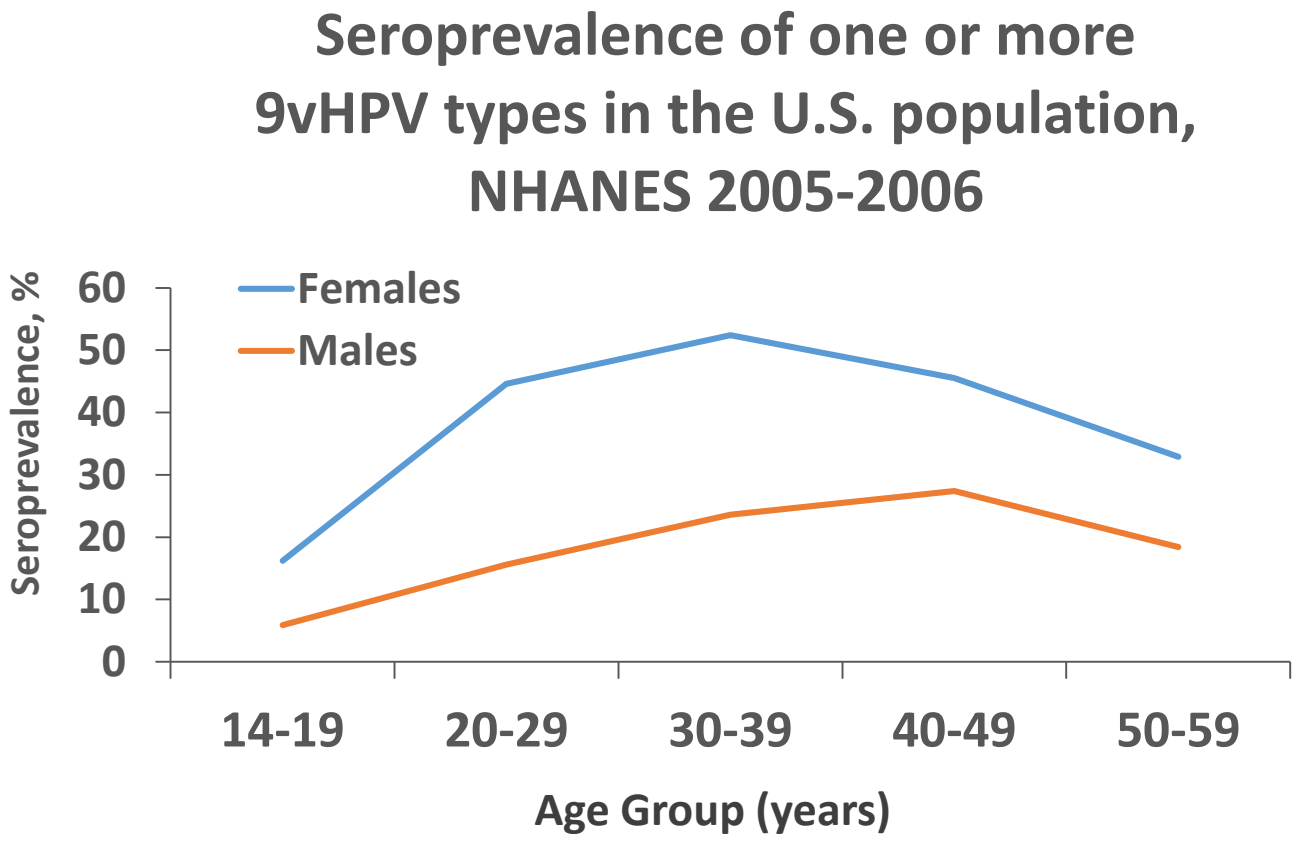


Adjusted for age, race, education, marital status, smoking

- Male susceptibility to oral HPV
  - Steeper increase in prevalence with increasing number of sex partners
  - Later plateau in prevalence with increasing number of sex partners

Chaturvedi, Cancer Res 2015

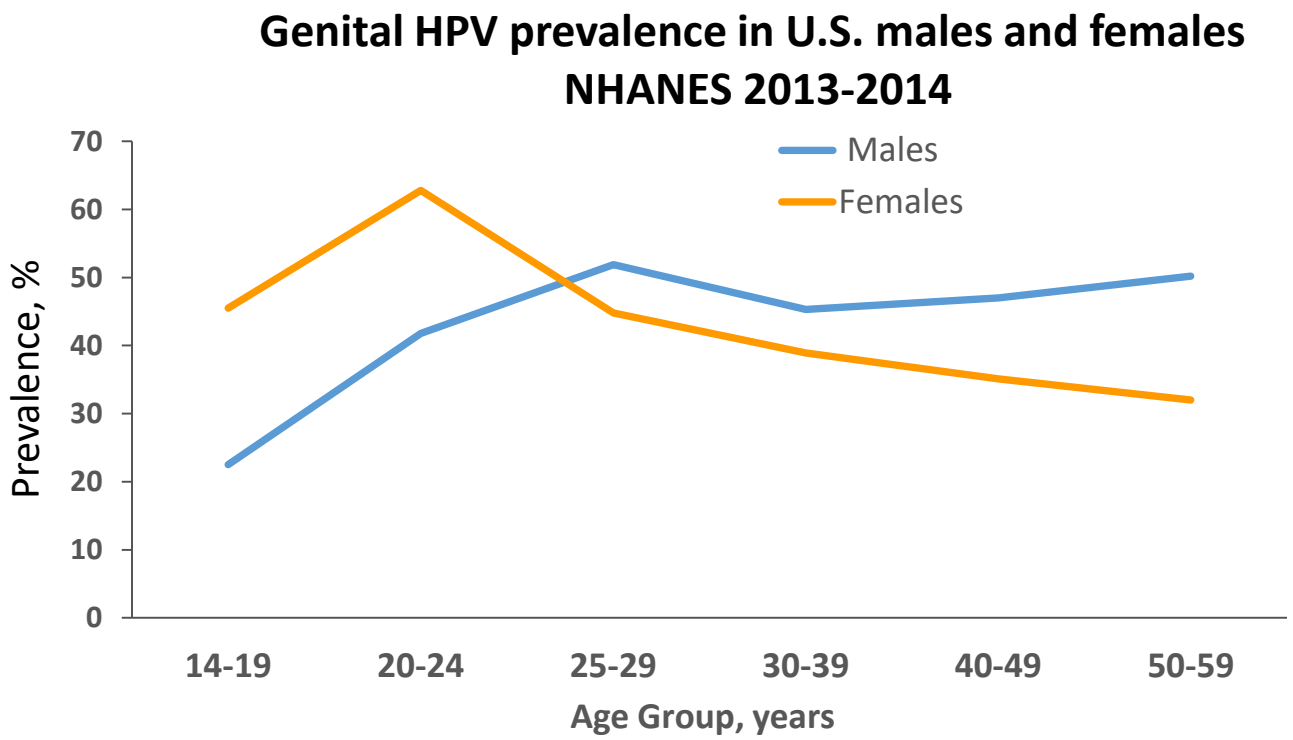
Hypothesis: Immunologic susceptibility in males?



Liu, JID 2016

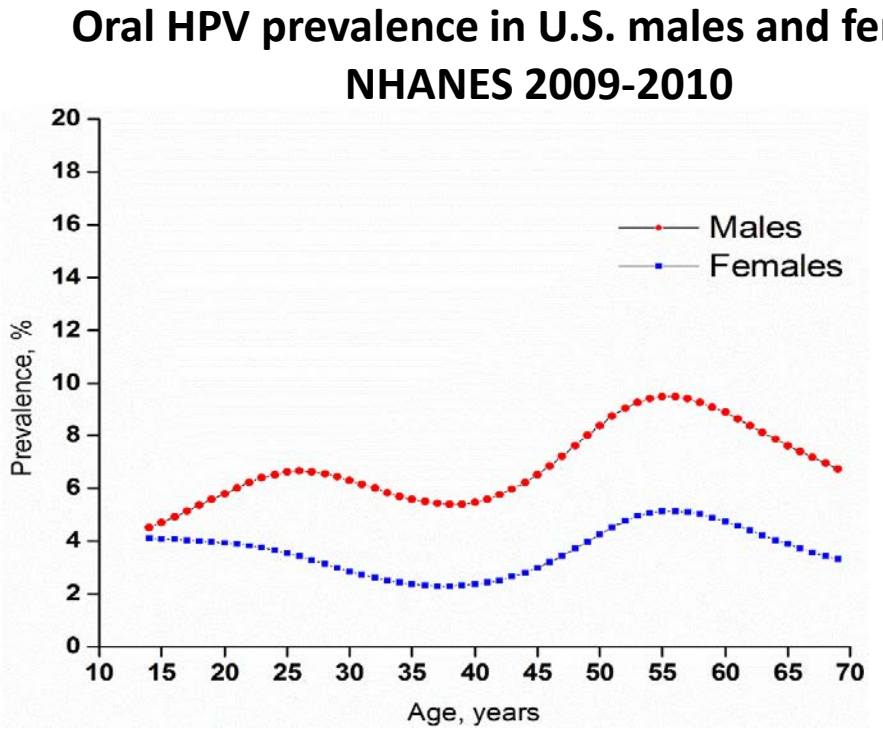
- Lower seroprevalence in males vs. females *(Liu, JID 2016)*
- Lower rates of seroconversion after HPV infection in males vs. females (*Edelstein, JID 2011*)
  - Potentially related to differences in site of infection
    - Females: mucosal epithelium
    - Males: keratinized epithelium
- Oral HPV: Higher oral HPV viral load in males vs. females (*Chaturvedi, JID 2013*)

Different age-specific HPV prevalence patterns in females vs. males



Female: Decline in prevalence at older ages

Male: No decline in prevalence at older ages



Female and male: Bimodal pattern

- New acquisition?
- Reactivation of latent infection?
- Birth cohort effect?

- No age-related decline in prevalence in males at any site
- Disease-relevance of infections acquired at older ages is unknown

Lewis, JID 2017; Gillison, JAMA 2012

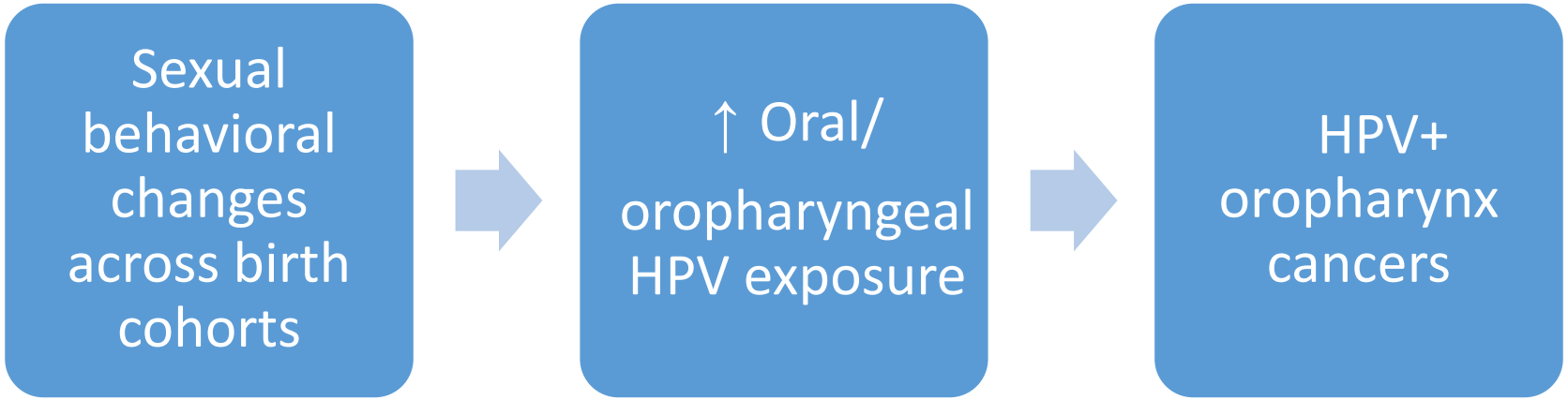
Natural history and pathogenesis of oral HPV infection

- Very few natural history studies
- Steps between oral HPV acquisition and development of HPV-positive oropharynx cancer are unknown

Knowns
Risk factors for oral HPV infection and HPV+ oropharynx cancer
Good estimates of oral HPV prevalence
Limited estimates of oral HPV incidence and persistence

Unknowns
HPV-induced precancerous lesion in the oropharynx
Time from acquisition of infection to development of cancer
Disease-relevance of infections acquired at older ages

Hypothesis for the increase in HPV-positive oropharynx cancers in recent years in the United States



Screening and prevention

Secondary prevention through screening

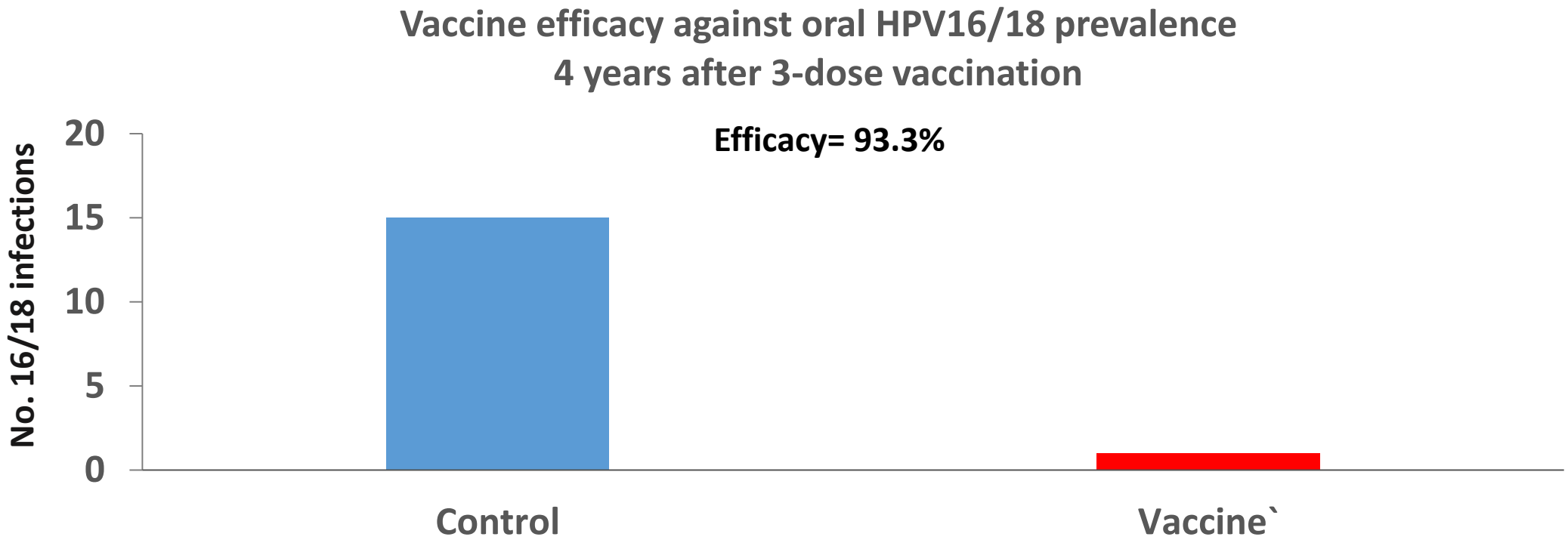
- Not feasible at this time because an HPV-induced precancerous lesion has not yet been identified

- Additional unanswered questions
  - Methods for screening
  - Treatments for risk-mitigation in screen-positives
  - Cost-effectiveness

- Screening with oral HPV tests is not recommended by the American Dental Association*

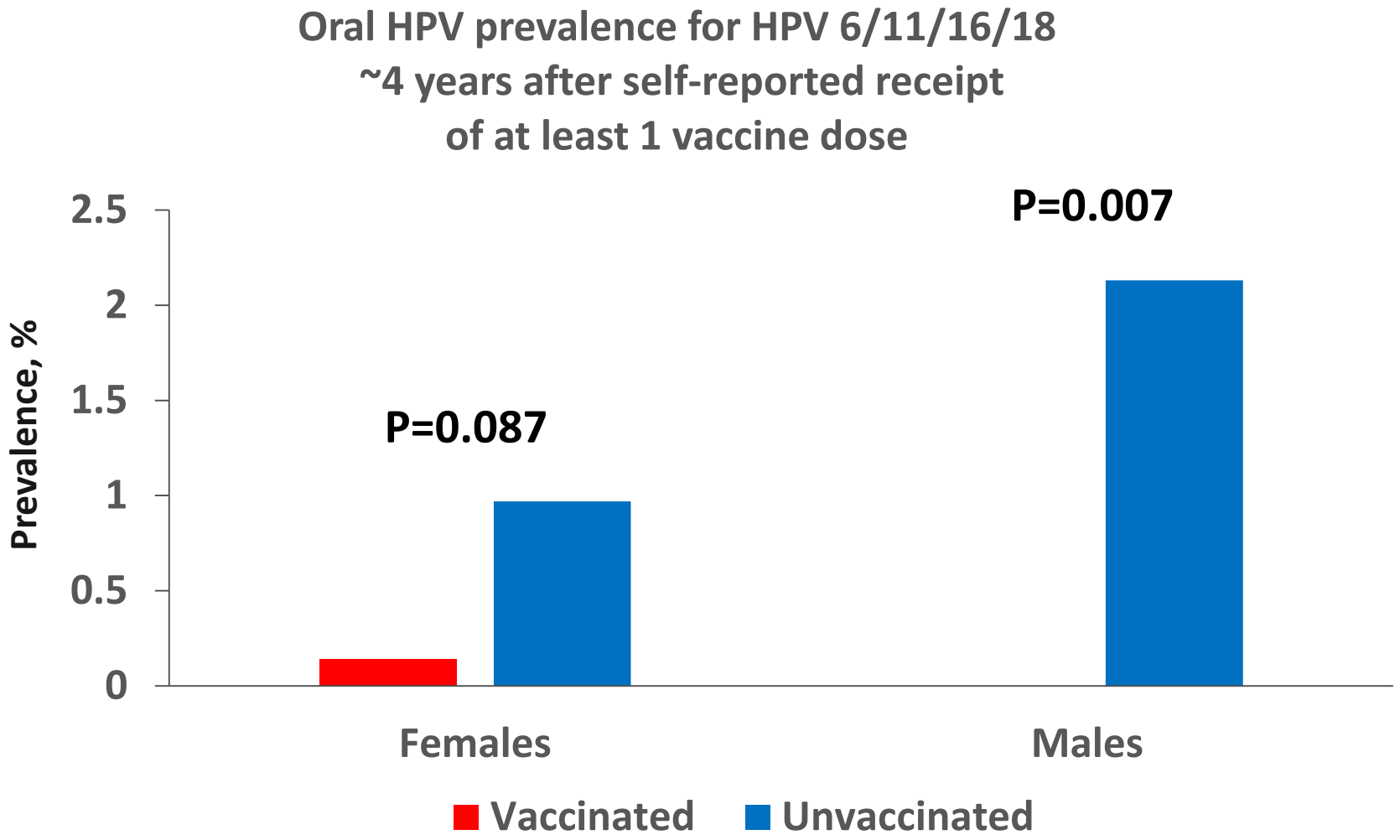
**Lingen, J Am Dent Assoc 2017*

NCI Costa Rica Vaccine Trial in young women: Reduced prevalence in vaccinated women



Herrero, PLOS One 2013

U.S. population of young adults (ages 18-33 years): Lower oral HPV prevalence in vaccinated men and women



Chaturvedi, JCO 2017

Summary

- HPV is the cause of rising oropharynx cancer incidence in recent years in the United States
- Male predominance of oral HPV infection and HPV-positive oropharynx cancer in the United States
- Screening and early detection of HPV-positive oropharynx cancer is not currently feasible
- HPV vaccination of young individuals is the most promising prevention strategy