Prevention of HPV-Associated Cancers

Understanding the Current Environment to Maximize Protection

This activity is supported through an independent educational grant from Merck & Co., Inc., Rahway, NJ, USA.

Jointly provided by Center for Independent Healthcare Education and Vemco MedEd

Activity Description

Target Audience

This activity is designed as a comprehensive approach to address the practice needs of primary care providers, including primary care physicians, osteopathic physicians, physician assistants, nurse practitioners, and allied healthcare professionals, who are at the forefront of caring for patients eligible for immunizations and/or at risk for vaccine-preventable diseases.

Learning Objectives

At the conclusion of the educational activity, the learner should be able to:

- Explain the current incidence of human papillomavirus (HPV)-associated cancers in men and women and how the incidence has changed since the availability of HPV vaccination
- Recognize how patient barriers to HPV vaccination can differ depending on age, gender, and other patient factors
- Utilize communication strategies designed to educate vaccine-eligible patients in an age-appropriate and gender-neutral manner about the risks of HPV infection and benefits of vaccination

Faculty and Disclosure

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Chicago, IL

Dr. Rachel Caskey does not have any relevant financial relationships with ineligible companies to disclose. *Dr. Caskey does not discuss any off-label use.*

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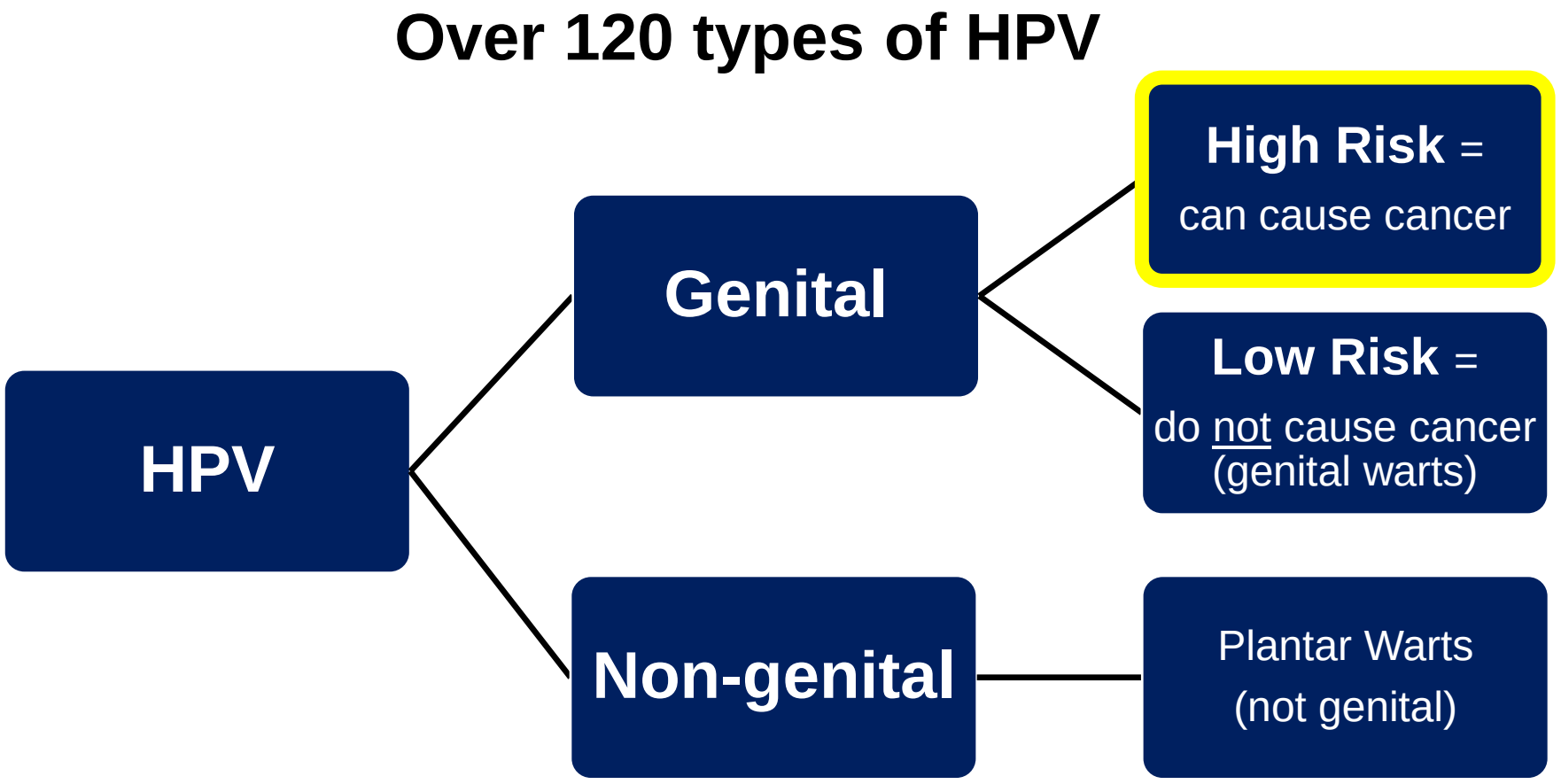
Incidence & Prevalence

- 77.3 million persons in the United States with HPV infection (2018)
  - 42.5 million with a disease-associated HPV infection
    - Anogenital warts
    - Cancer
      - Oropharyngeal: 14.3 per 100,000 persons
      - Cervical: 6.1 per 100,000 persons
      - Anal: 1.7 per 100,000 persons

Lewis RM, et al. *Sex Transm Dis*. 2021;48(4):273-277.
Zhang Y, et al. *JAMA Oncol.* 2021;7(10):e212907.
Available at: NIH SEER Program (2020 stats) https://seer.cancer.gov/statfacts/.

Human Papillomavirus (HPV) in the United States



HPV Durability

- Induce persistent infection without early complications to host
  - Infects where epidermis is disrupted
  - Evades acute immune system response
  - Minimal inflammation, no cell death, no blood viremic phase, infection only epithelial
- HPV cannot self-replicate, uses host DNA polymerases
- Sheds virions through epithelial desquamation
  - Direct contact and vertical transmission

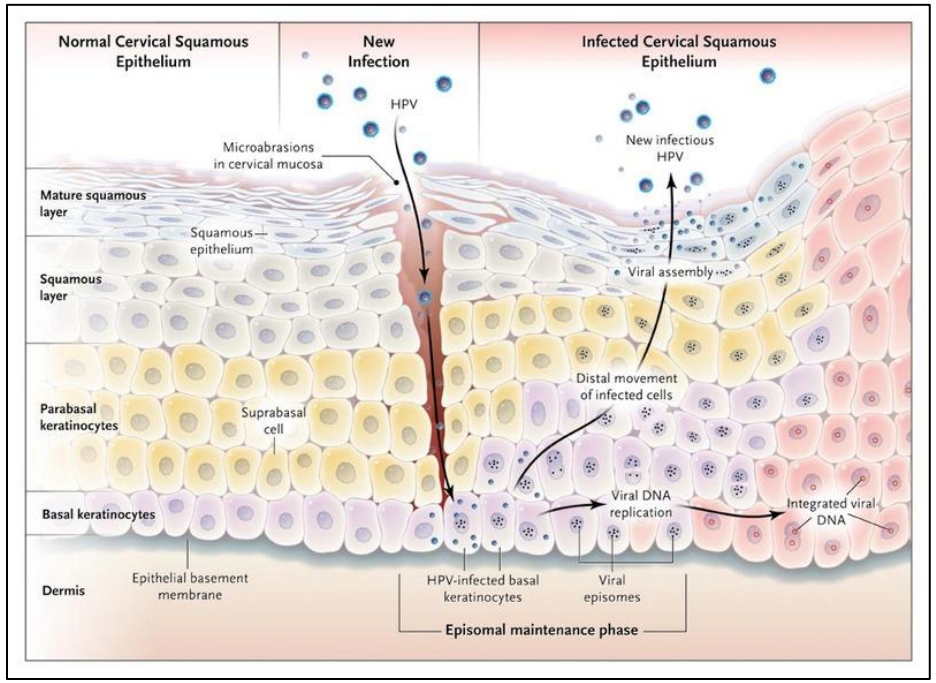


Image: Kahn JA. *NEJM.* 2009;361:271-8.

Araldi RP, et al. *Biomed Pharmacother*. 2018;106:1537-1556.

HPV Infection

- Approximately 90% of those infected ultimately mount an innate and humoral immune-mediated viral clearance
- Some neutralizing antibodies are produced, but are inefficient and will not prevent future infection in many
- Persistent infections (~10%) are at risk for cancer
  - HPV oncoproteins E5, E6, E7

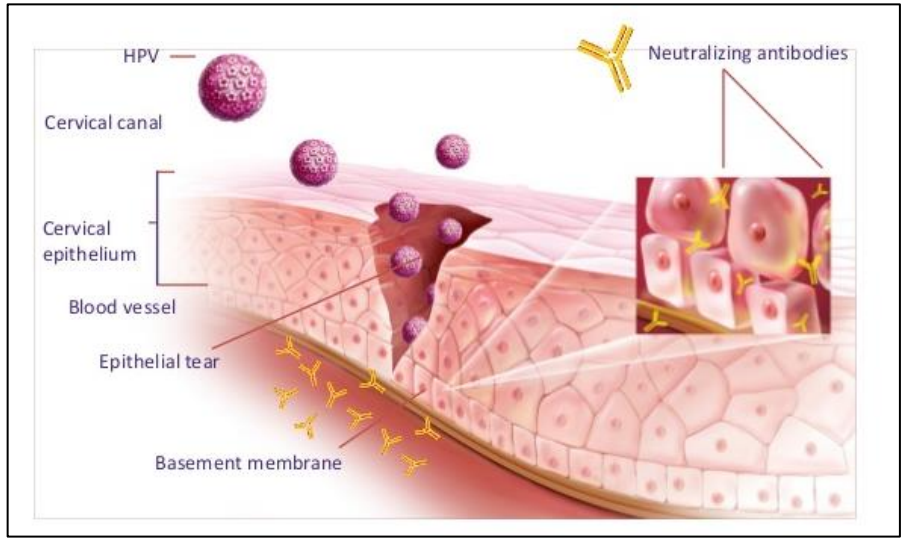


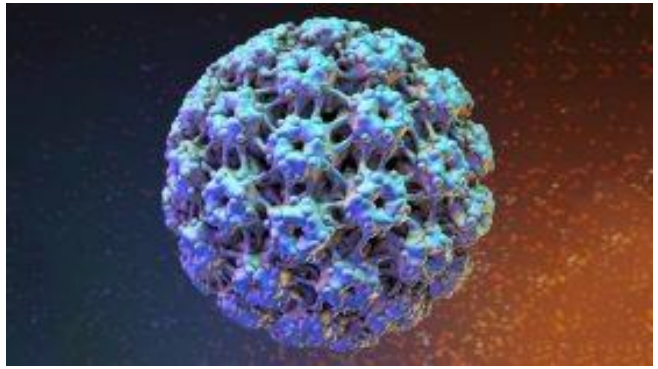
Image: J. Bently. Dalhousie University 2015.

Araldi RP, et al. *Biomed Pharmacother*. 2018;106:1537-1556.

HPV in the United States

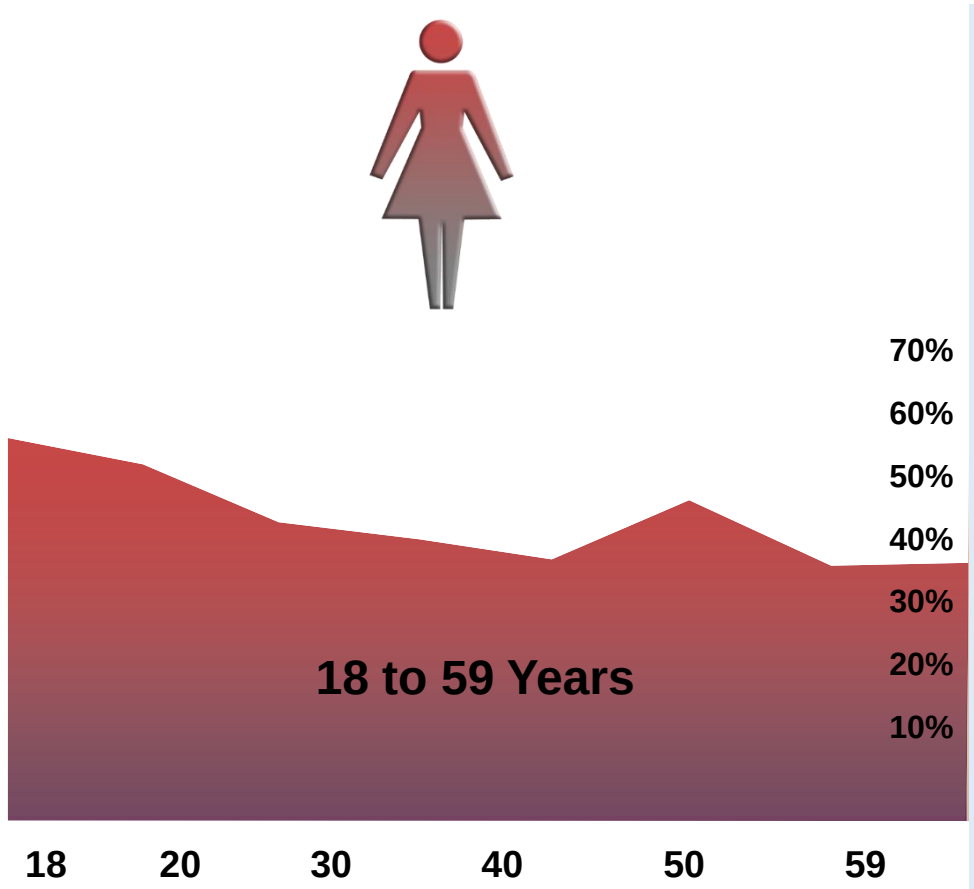
HPV is the most common *sexually transmitted infection* in the U.S.

Over 6.2 million new genital infections annually



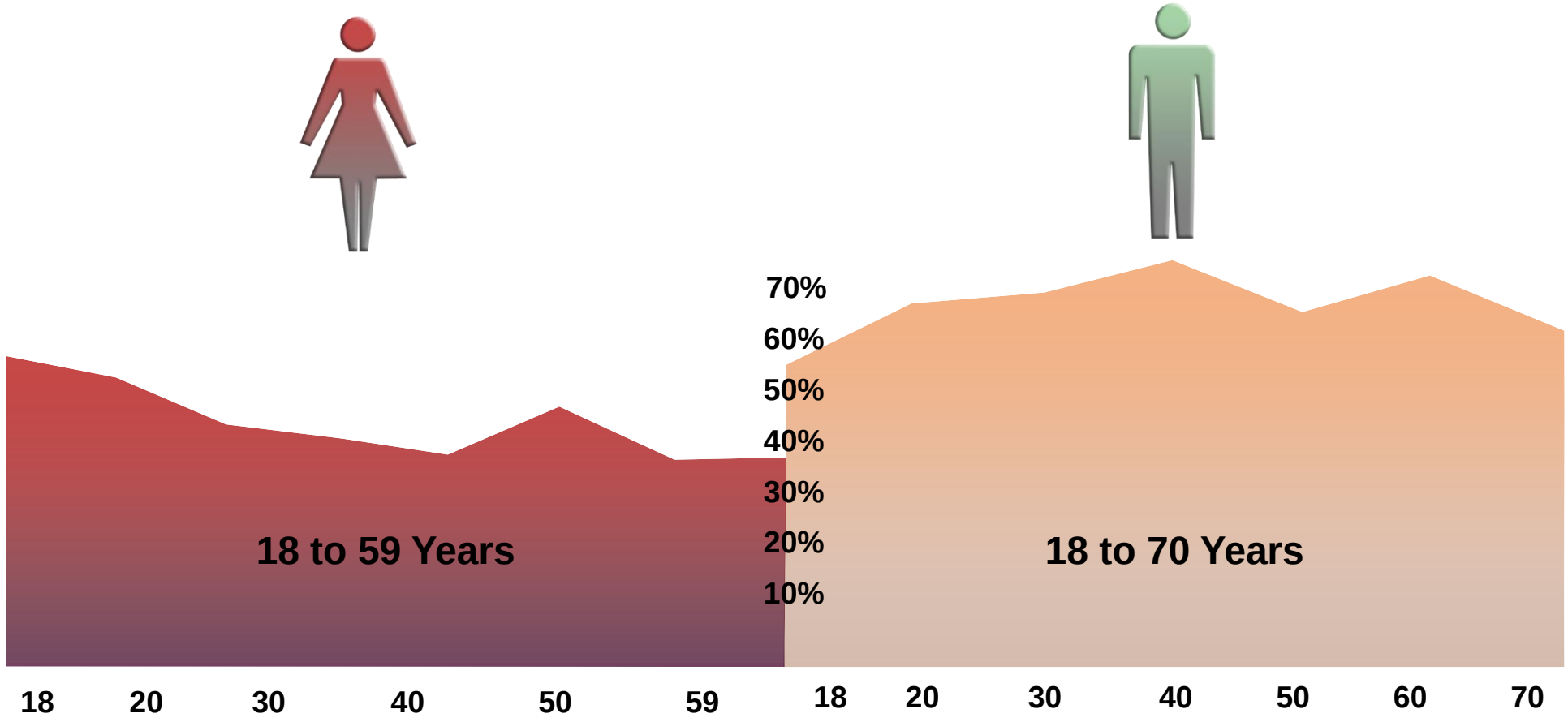
Dunne EF, et al. *JAMA*. 2007;297:813-819.

Genital HPV Prevalence Among Females



Shi R, et al. *BMC Res Notes*. 2014;7:544. Giuliano AR, et al. *Cancer Epidemiol Biomarkers Prev*. 2008;17(8):2036-2043.

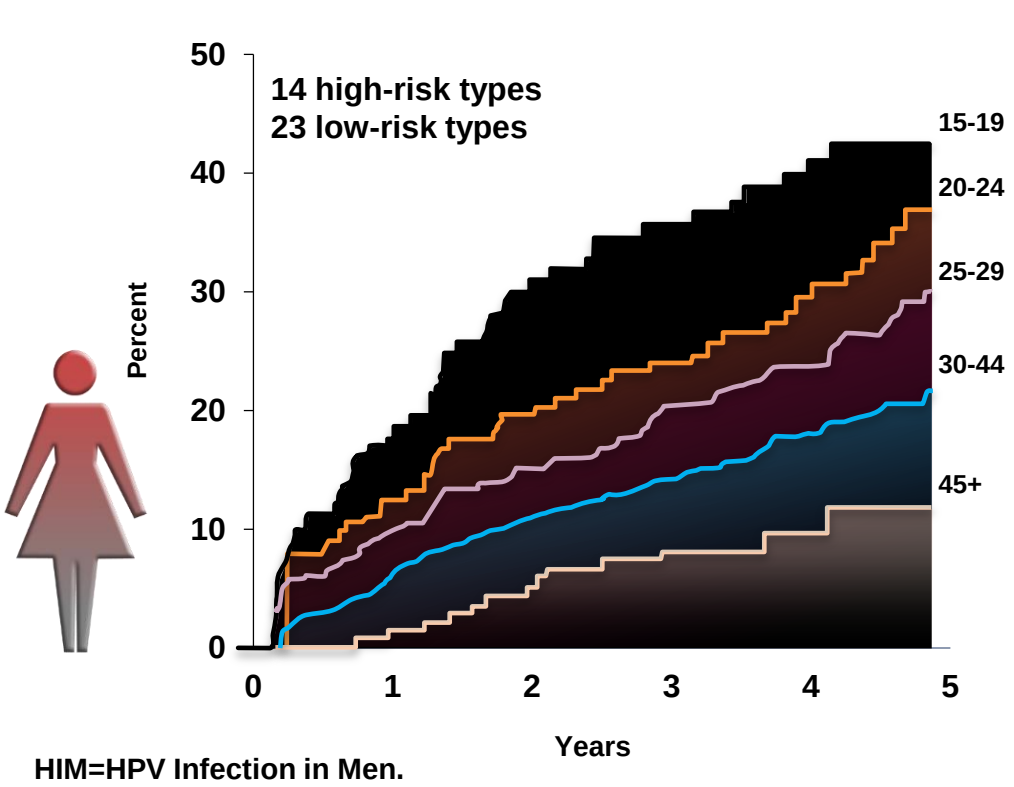
Genital HPV Prevalence Higher Among Males

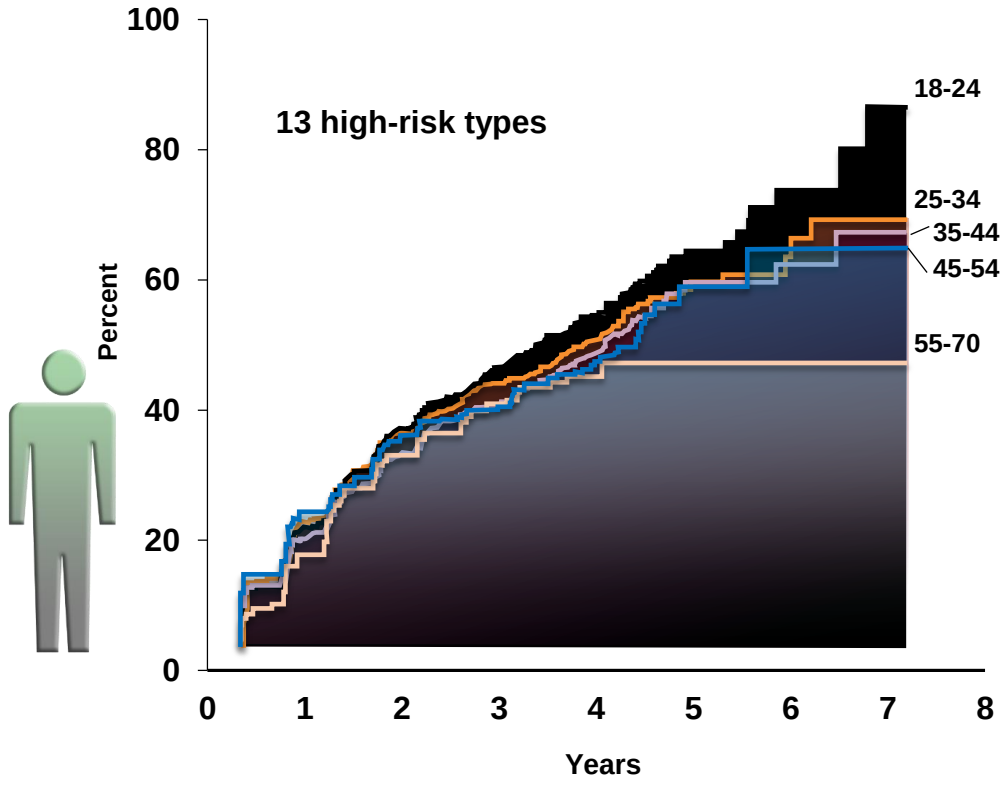


Shi R, et al. *BMC Res Notes*. 2014;7:544. Giuliano AR, et al. *Cancer Epidemiol Biomarkers Prev*. 2008;17(8):2036-2043.

Risk for Acquiring New Genital HPV Infection

Cumulative Risk for New HPV Infections by Age at Baseline

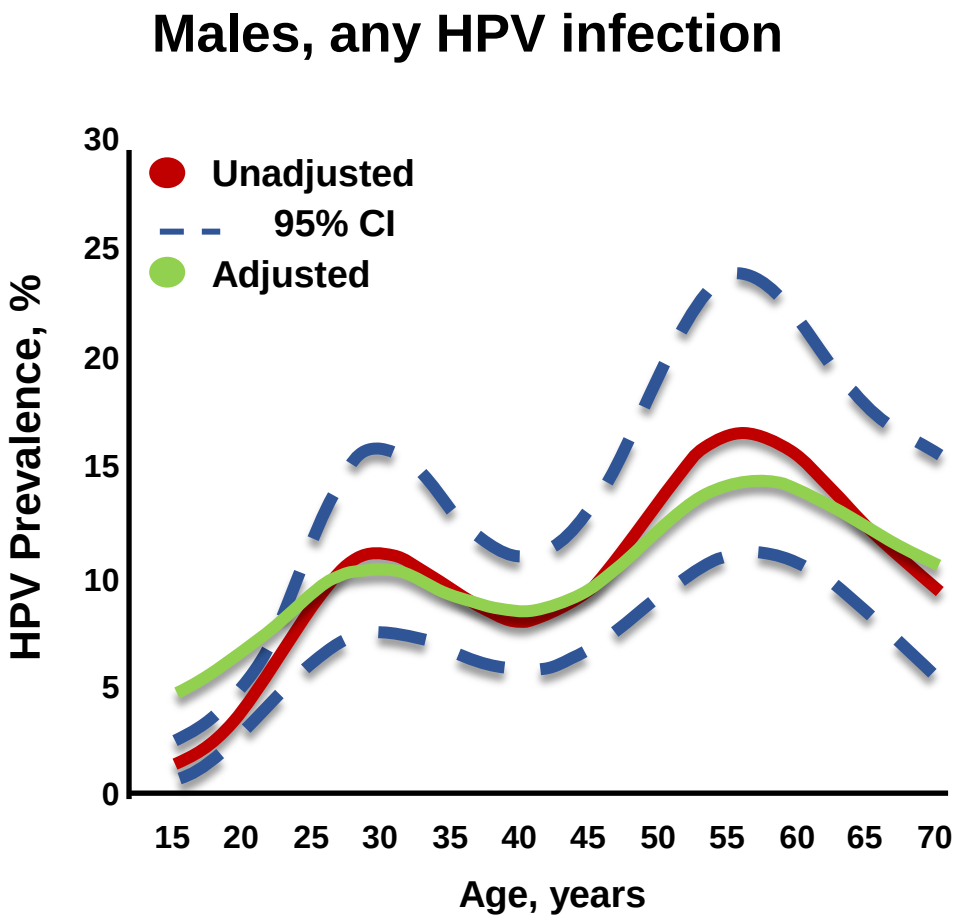


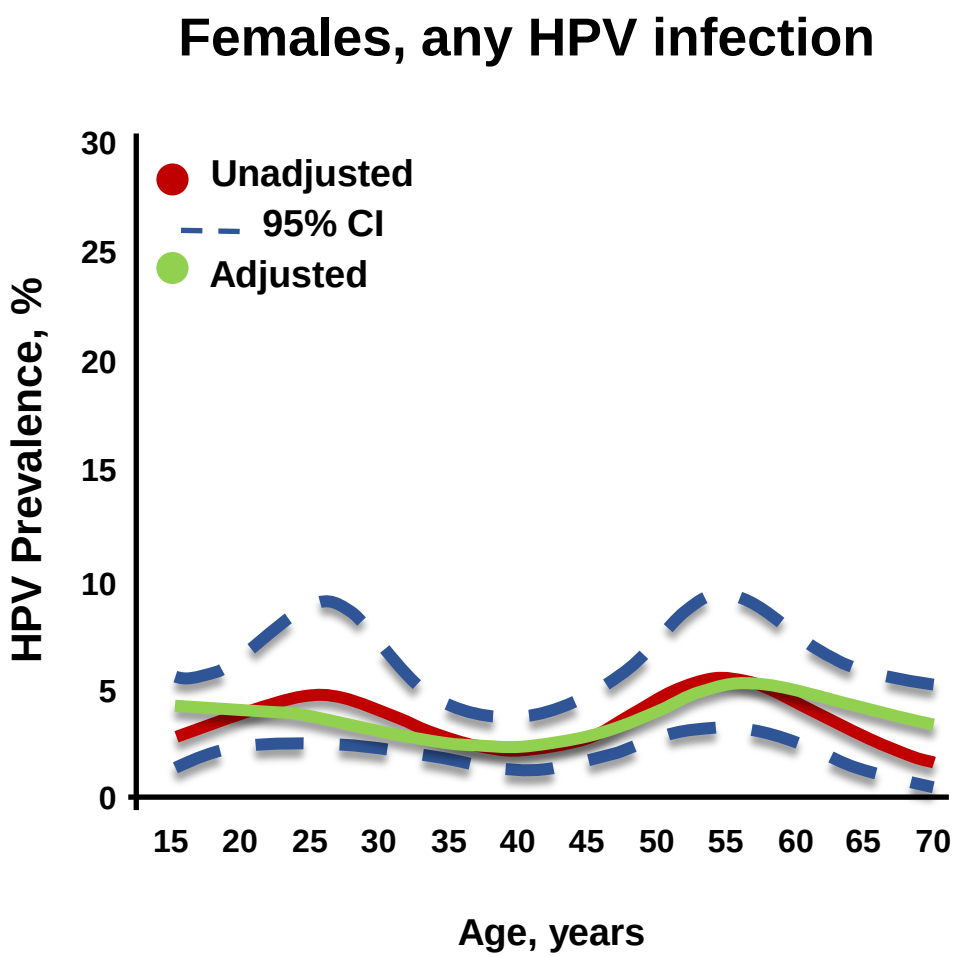


HIM=HPV Infection in Men.

Muñoz N, et al; Instituto Nacional de Cancerologia HPV Study Group. *J Infect Dis.* 2004;190:2077-2087, by permission of Oxford University Press; Adapted from Giuliano AR, et al. *Lancet*. 2011;377(9769):932-940.

Oral HPV Prevalence Is Significantly Higher in Males Than Females





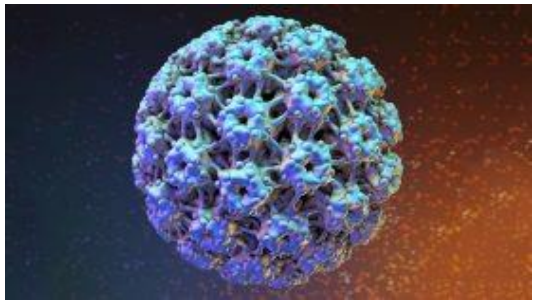
Adapted from Gillison M, et al. *JAMA*. 2012;307(7):693-703.

Transmission of HPV

Surface-to-surface contact!

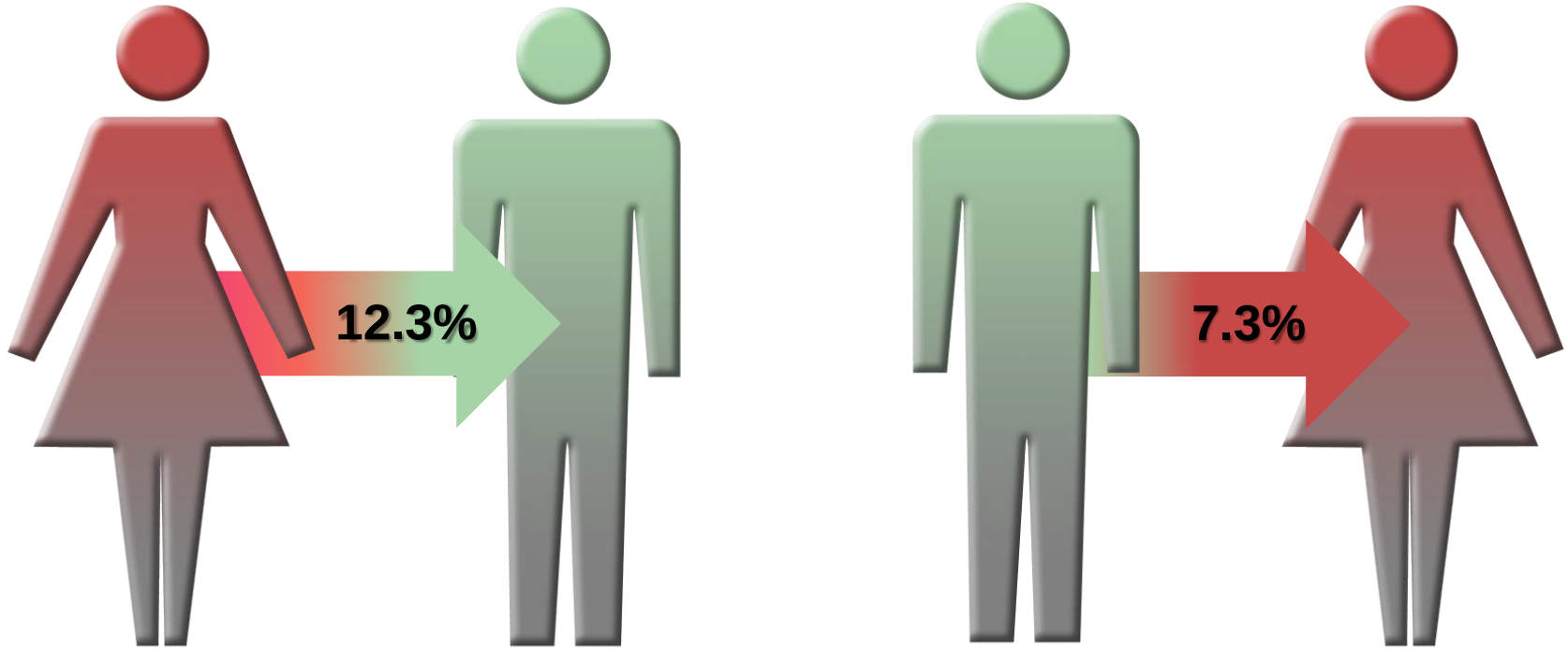
HPV can spread through anogenital region

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



Shew ML, et al. *J Infect Dis*. 2013;207:1012-5.

Genital HPV Transmission From Females to Males Is Higher Than From Males to Females

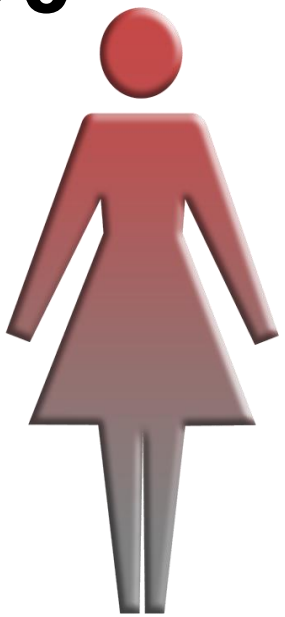


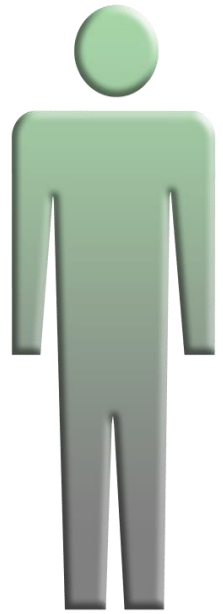
Nyitray AG, et al. *J Infect Dis*. 2014;209:1007-1015.

Few Adults Have Natural Antibodies to HPV Types in the HPV9 Vaccine

SEROPOSITIVE TO
2+ OF THE 9 VACCINE HPV TYPES
(NHANES 2005-2006,
ages 14-59 years)

18%

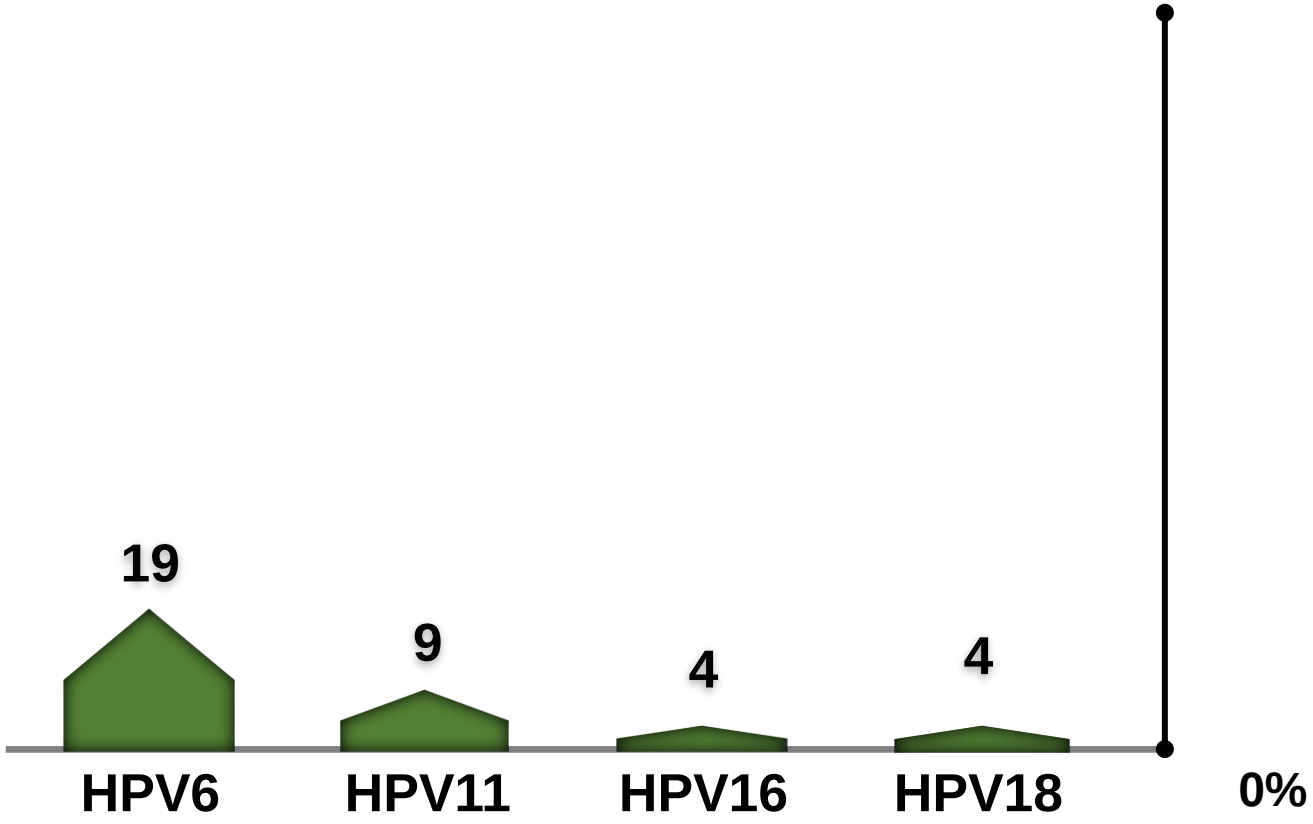




5%

NHANES, National Health and Nutrition Examination Survey.
Liu G, et al. *J Infect Dis.* 2016;213(2):191-198.

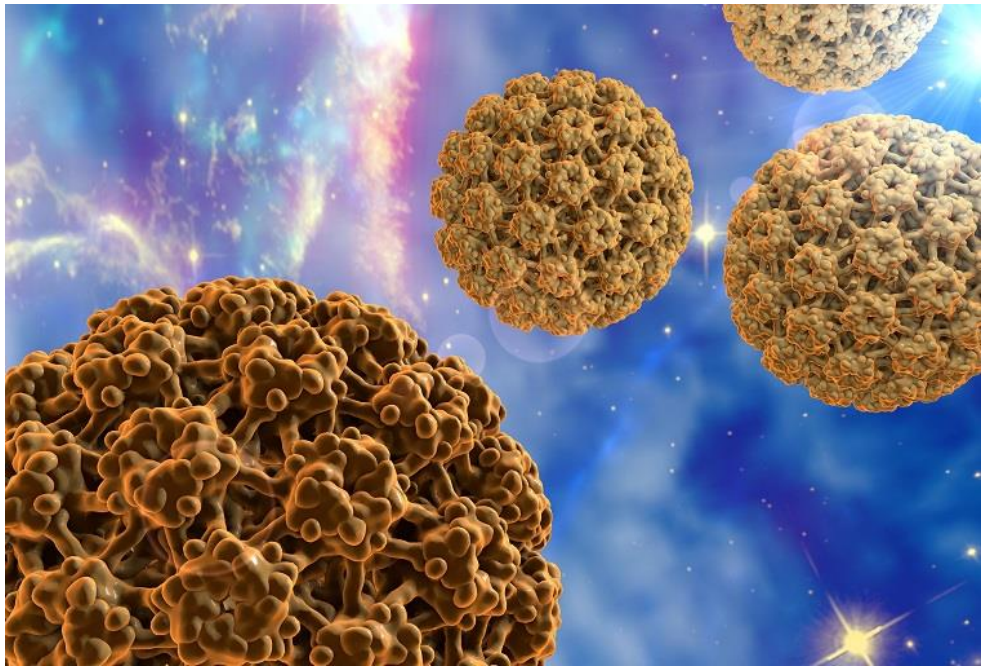
Males Have a Low Rate of Seroconversion Following Infection…



Seroconversion rates within 36 months following genital, anal, or oral infection

Giuliano AR, et al. *Papillomavirus Res*. 2015;1:109-115.

HPV is Ubiquitous



Dunne EF, et al. *JAMA*. 2007;297:813-819.
CDC Pink Book: www.cdc.gov/vaccines/pubs/pinkbook/hpv.html

HPV-Related Cancers in the United States

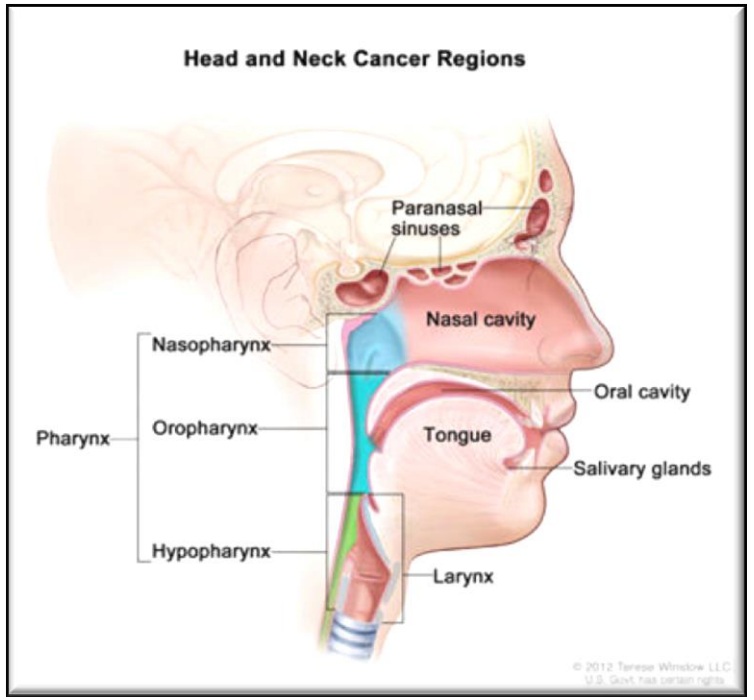
Cancers Caused by HPV in United States
>99% of cervical cancers
>75% of oropharyngeal cancers
91% of anal cancers
75% of vaginal cancers
69% of vulvar cancers
63% of penile cancers

Bailey HH, et al. *J Clin Oncol*. 2016;34(15):1803-1812.
Available at: https://ascopubs.org/doi/pdf/10.1200/JCO.2016.67.2014.

Head and Neck Squamous Cell Carcinomas

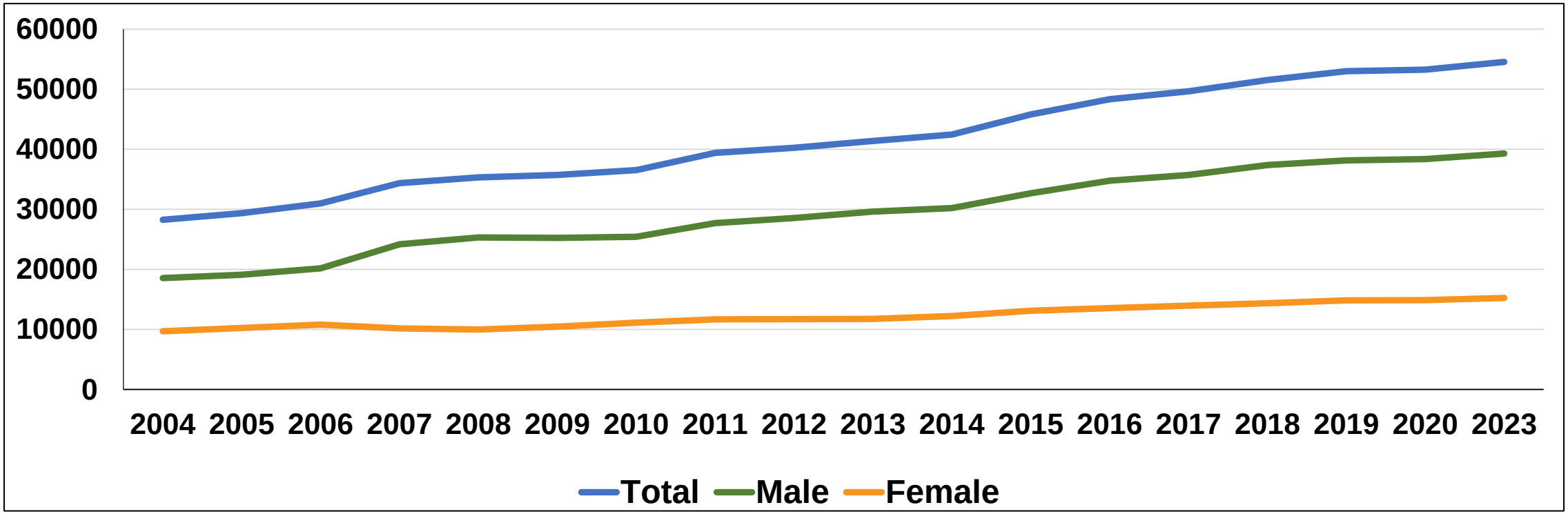
- *Head and neck squamous cell carcinomas* (HNSCC) include cancers of paranasal sinus, nasal cavity, tonsils, oropharynx, oral cavity and larynx
  - 75% due to tobacco and alcohol
  - 25% due to HPV (HPV 16 most prevalent type)

- HPV has been detected in **70-75% of all *oropharyngeal and tonsillar* cancers**
  - Association between HPV and HNSCC is weaker for oral cavity and larynx



Argiris, MV, et al. *Lancet. 2008;*371:1695-1709. 10.1016/S0140-6736(08)60728-X.
Image: NIH National Cancer Institute https://www.cancer.gov/types/head-and-neck/head-neck-fact-sheet.

Incidence of Oropharyngeal Cancers in the United States

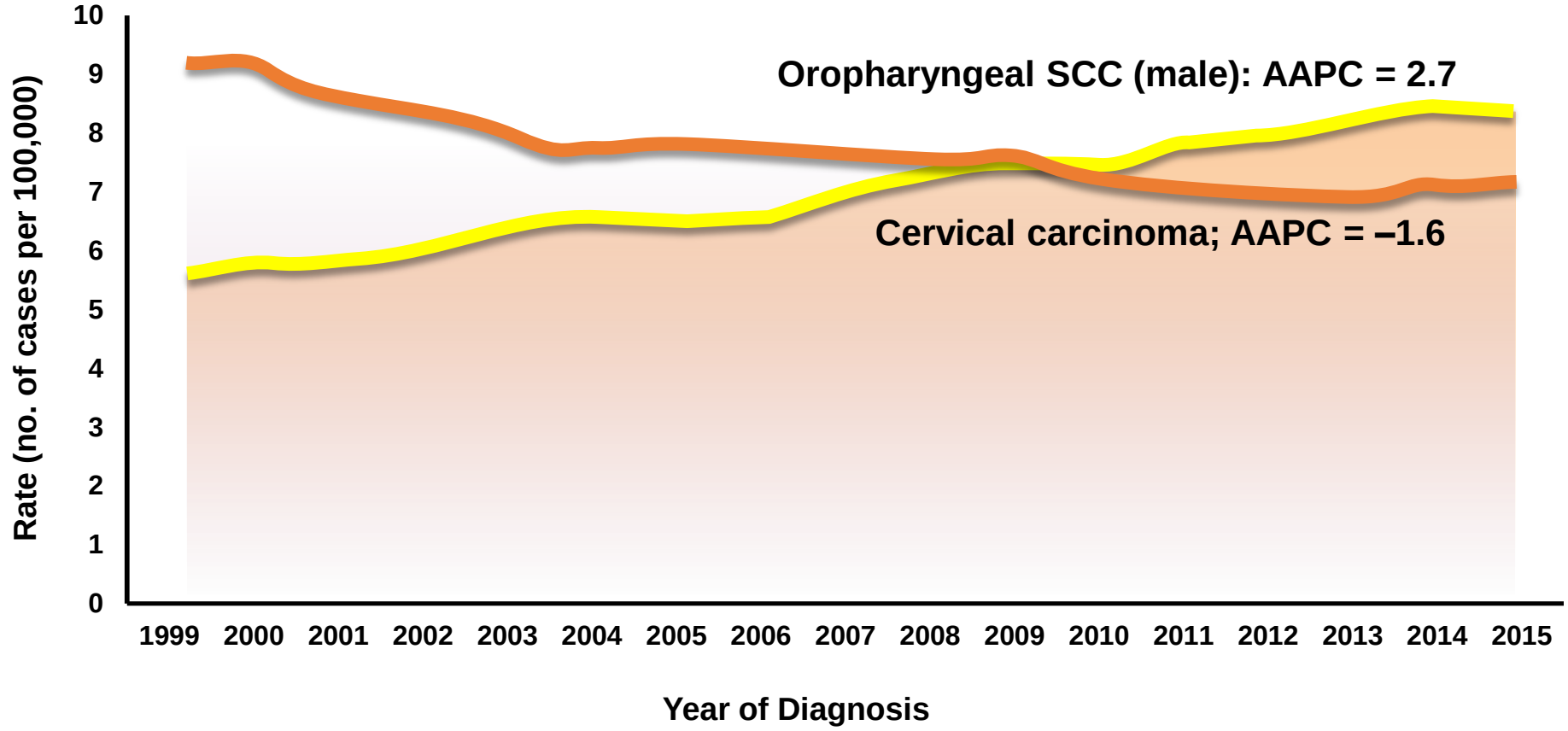


Incidence of HPV-related oropharyngeal carcinomas are **increasing**

- Particularly among <u>males</u> (3× more common)
- 70+% positive for HPV 16

American Cancer Society. *Cancer Facts & Figures. 2004-2023*, www.cancer.org.

Incidence of Cervical Cancer is Declining but the Incidence of HPV-related Oropharyngeal Squamous Cell Carcinomas in Males is Increasing



AAPC, average annual percent change; SCC, squamous cell carcinoma.
CDC's National Program of Cancer Registries; National Cancer Institute's Surveillance, Epidemiology, and End Results program, as cited in Van Dyne EA, et al. *MMWR Morb Mortal Wkly Rep*. 2018;67(33):918-924.

HPV Oropharyngeal Cancers in the United States

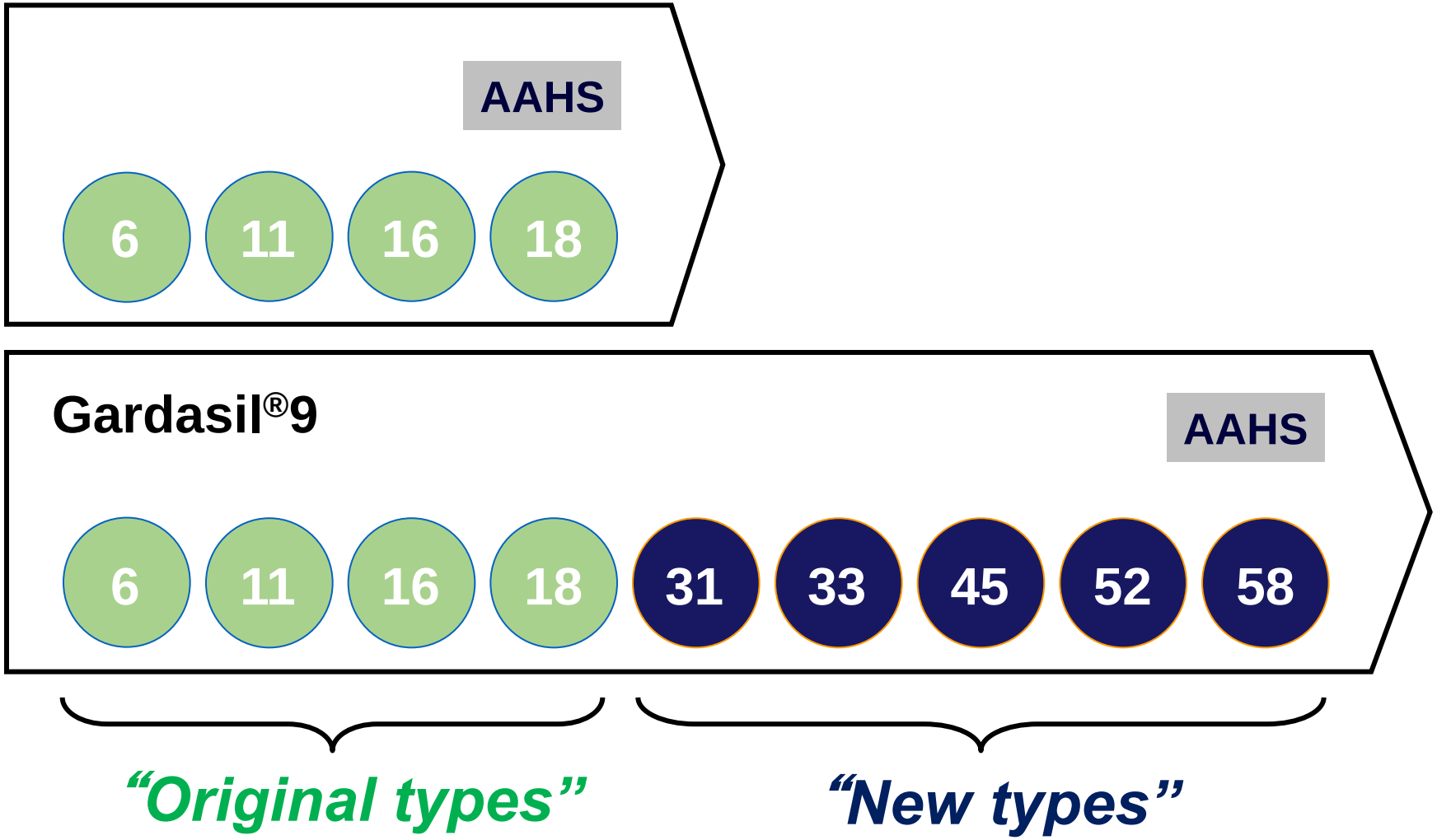
- Transmission is oral sex
  - Though not completely understood
- Why increase in younger individuals?
  - Different sexual norms
  - Oral sex at an earlier age
  - Decrease in other tobacco-related cancers
- Greater prevalence in men?
  - HPV burden in cervix greater than penis

Cancer Facts and Figures 2012, American Cancer Society, www.cancer.org.
Chaturvedi AK, et al. *J Clin Oncol. 2008;*26:612-619.
Annual Report to the Nation of the Status of Cancer, 1975-2009, *JNCI,* 2012.
Marur S, et al. *Lancet Oncol.* 2010;11:781-789.

HPV Prevention: Vaccination

HPV9 – Gardasil 9

9-Valent HPV Vaccine Composition



AAHS, amorphous aluminum hydroxyphosphate sulfate.

12-Year Follow-up on the Long-Term Efficacy of the 4vHPV Vaccine in Females Aged 16-23 Years

100%
Efficacy against CIN2+

12
year follow-up

100%
Efficacy against cervical, vulvar, and vaginal cancer

4vHPV, 4-valent human papillomavirus; CIN,, cervical intraepithelial neoplasia.

Kjaer SK, et al. *Clin Infect Dis.* 2018;66(3):339-345.

6-Year Efficacy of the 9vHPV Vaccine in Females Aged 16-26 Years: A Randomized, Double-Blind Trial

14 15 participants rand mi ed
t receive v n 71 6 r
4v n 71 vaccine

6 year follow-up

High efficacy against certain diseases caused by HPV types

+

Highly efficacious against certain cancers and diseases caused by HPV types

>96% efficacy against:

- High-grade cervical, vulvar, or vaginal disease
- Cervical cancer, CIN2/3, or AIS
- Persistent infection at 12 months

9vHPV, 9-valent human papillomavirus; AIS, adenocarcinoma in situ.

Huh WK, et al. *Lancet*. 2017;390:2143-2159.

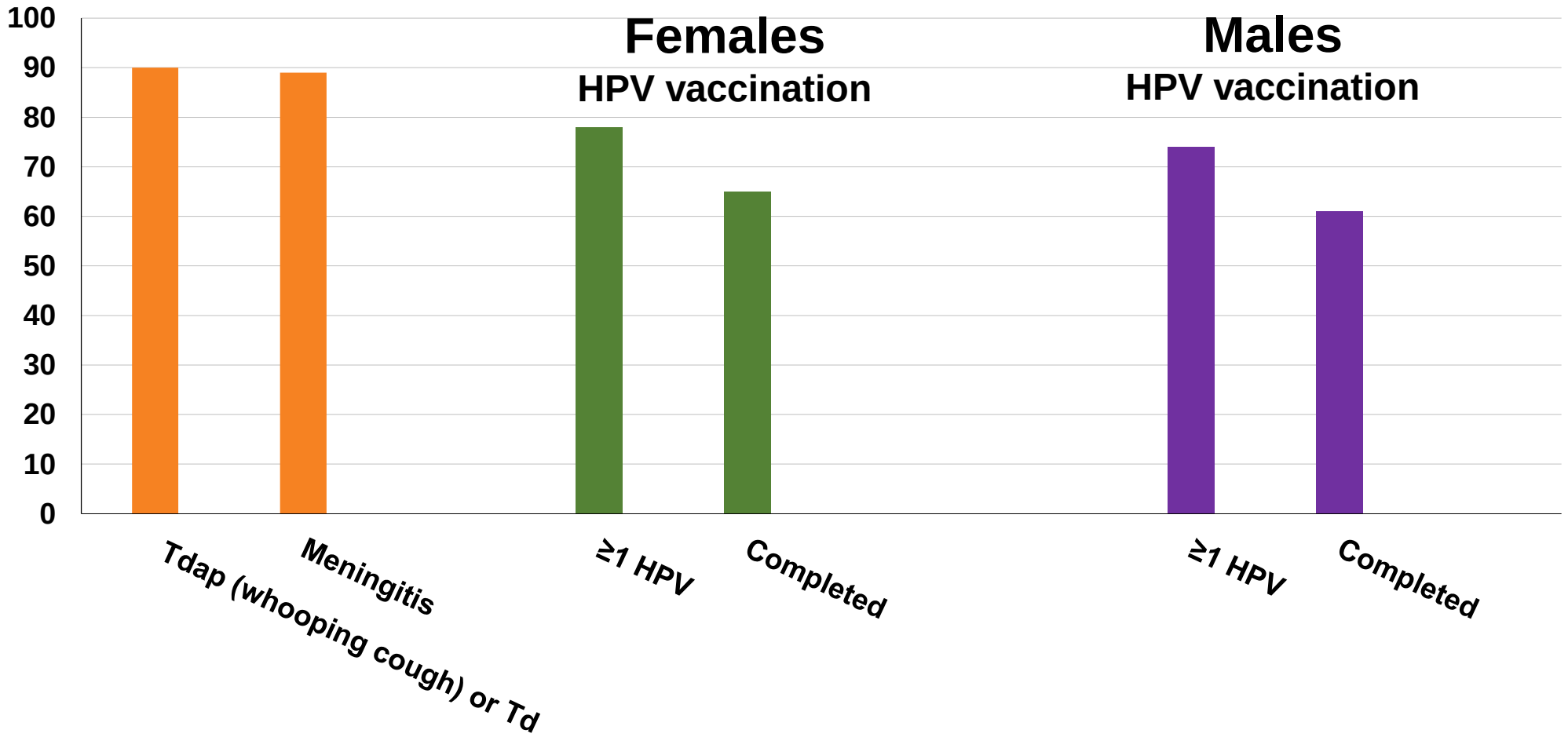
HPV Vaccine Safety

- >350 million doses of HPV vaccine distributed worldwide
- Most common adverse events are mild: Sore arm, myalgias
- Among serious adverse events: **No** patterns to suggest any events related to the HPV vaccine
- Findings similar to the safety of all other adolescent vaccines

Slade BA, et al. *JAMA*. 2009;302(7):750-757; Centers for Disease Control and Prevention. FAQs about HPV safety. CDC. FAQs about HPV safety. Available at: https://www.cdc.gov/vaccinesafety/vaccines/hpv/hpv-safety-faqs.html

Vaccination Coverage in the United States

United States HPV Vaccination Rates



Pingali C, et al. *MMWR Morb Mortal Wkly Rep. 2*023;72(34);912–919.

HPV Vaccine Recommendations: ACIP Update

- HPV vaccination recommended for both males and females through age 26 years
  - Target age 11-12 years
    - Can start as early as age 9
  - If <15 years of age: **2 doses** (6 months apart)
  - If ≥15 years of age: **3 doses** (at 0, 2 and 6 months)
- For ages 27 to 45 years: decision to vaccinate based on *shared decision-making*

Meites E, et al. *MMWR Morb Mortal Wkly Rep*. 2019;68(32):698-702.

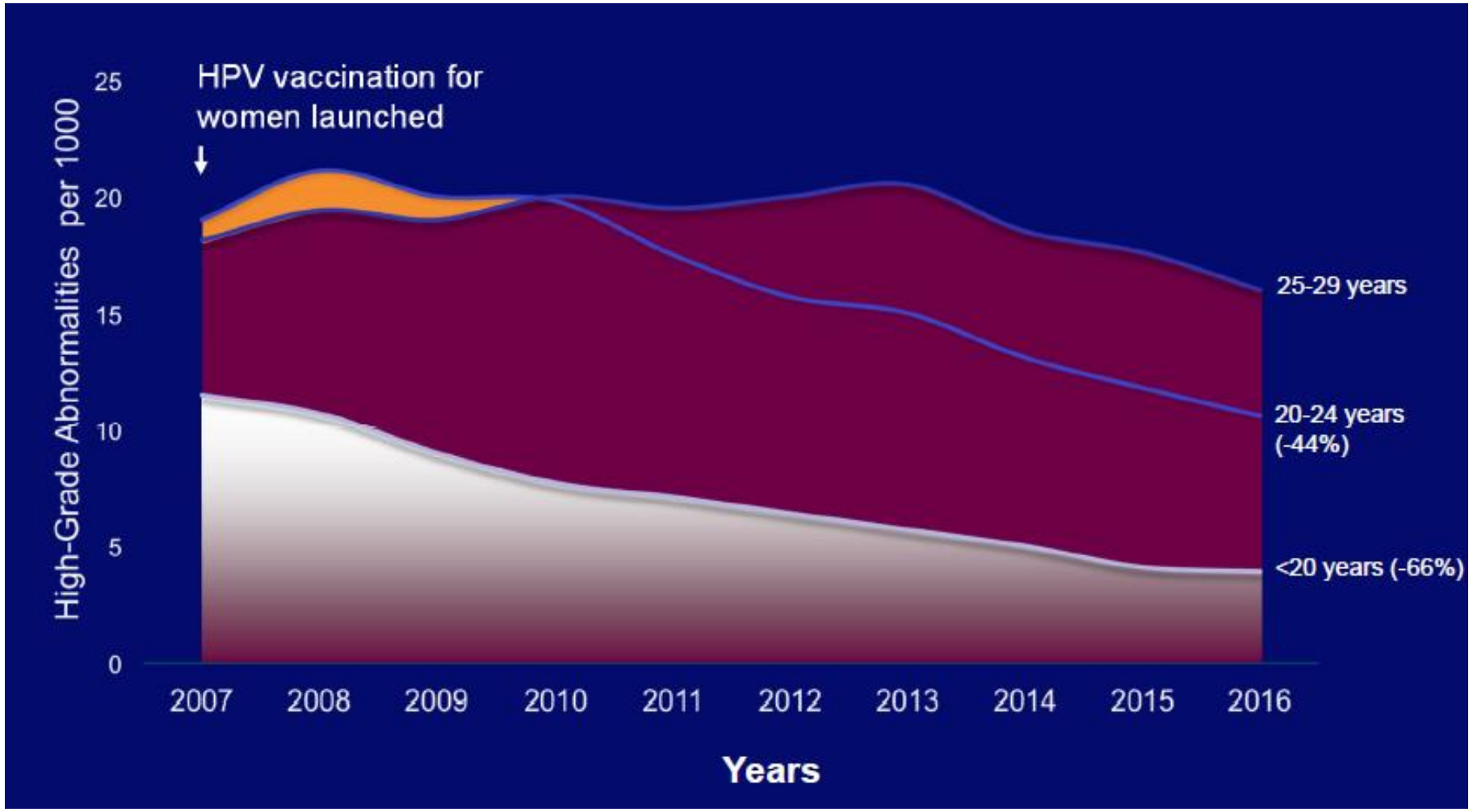
Early Vaccination Is Key

- Population-based cancer registry data from multiple countries support the importance of early vaccination
- Recent studies suggest that HPV vaccination, especially when given at a younger age, is associated with **substantial reductions in the risk of cervical cancer**
- Adult vaccination (27-45yo) has the potential to prevent thousands of cancers per year but many clinicians and patients unaware of vaccine is approved for this age group

Mix JM, et al. *Cancer Epidemiol Biomarkers Prev*. 2021;30(1):30-37.
Liao C-I, et al. *JAMA Netw Open*. 2022;5(3):e222530.
Falcaro M, et al. *Lancet*. 2021;398(10316):2084-2092.
Lei J, et al. *N Engl J Med*. 2020;383(14):1340-1348.
King LM et al. *Open Forum Infectious Disease*. Volume 10, Issue 1, January 2023.

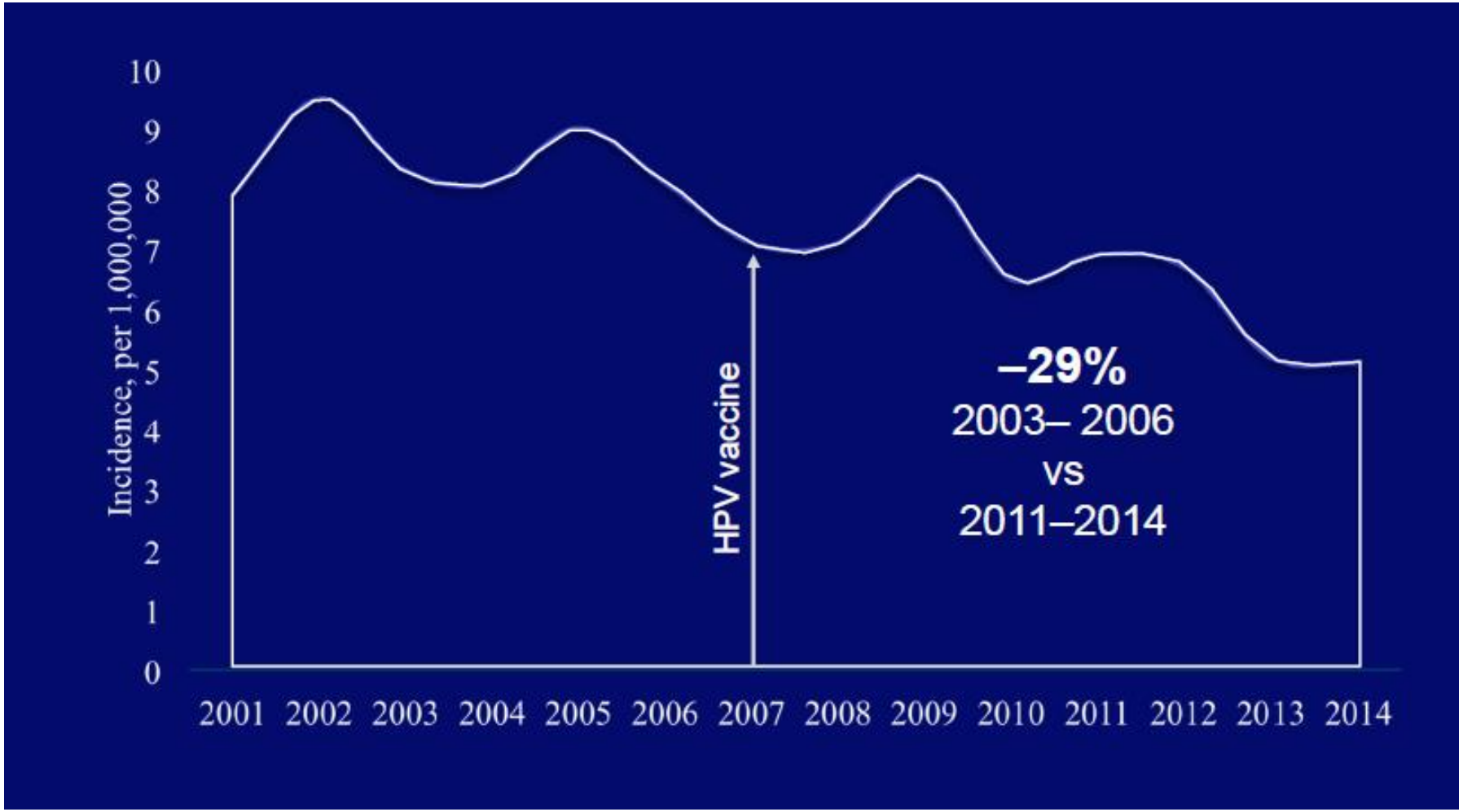
Clinical Outcomes

Australia: Trends in High-Grade Cervical Abnormalities by Age Pre- and Post-Vaccination

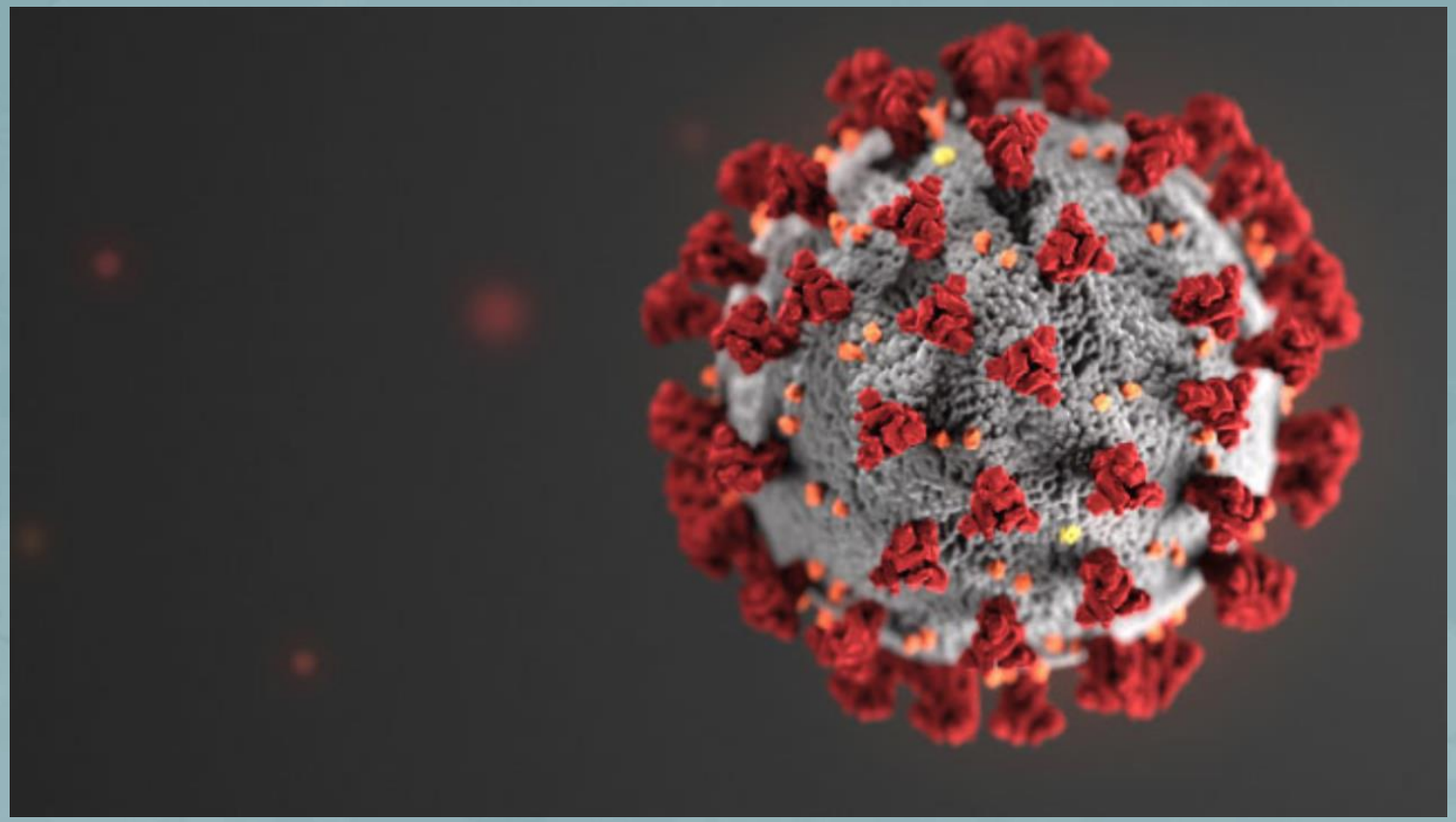


Kirby Institute. HIV, viral hepatitis and sexually transmissible infections in Australia: annual surveillance report 2018. Sydney: Kirby Institute, UNSW Sydney; 2018. https://kirby.unsw.edu.au/report/hiv-viral-hepatitis-and-sexually-transmissible-infections-australia-annual-surveillance.

USA: Trends in Cervical Cancer Incidence Among 15- to 24-Year-Old Females

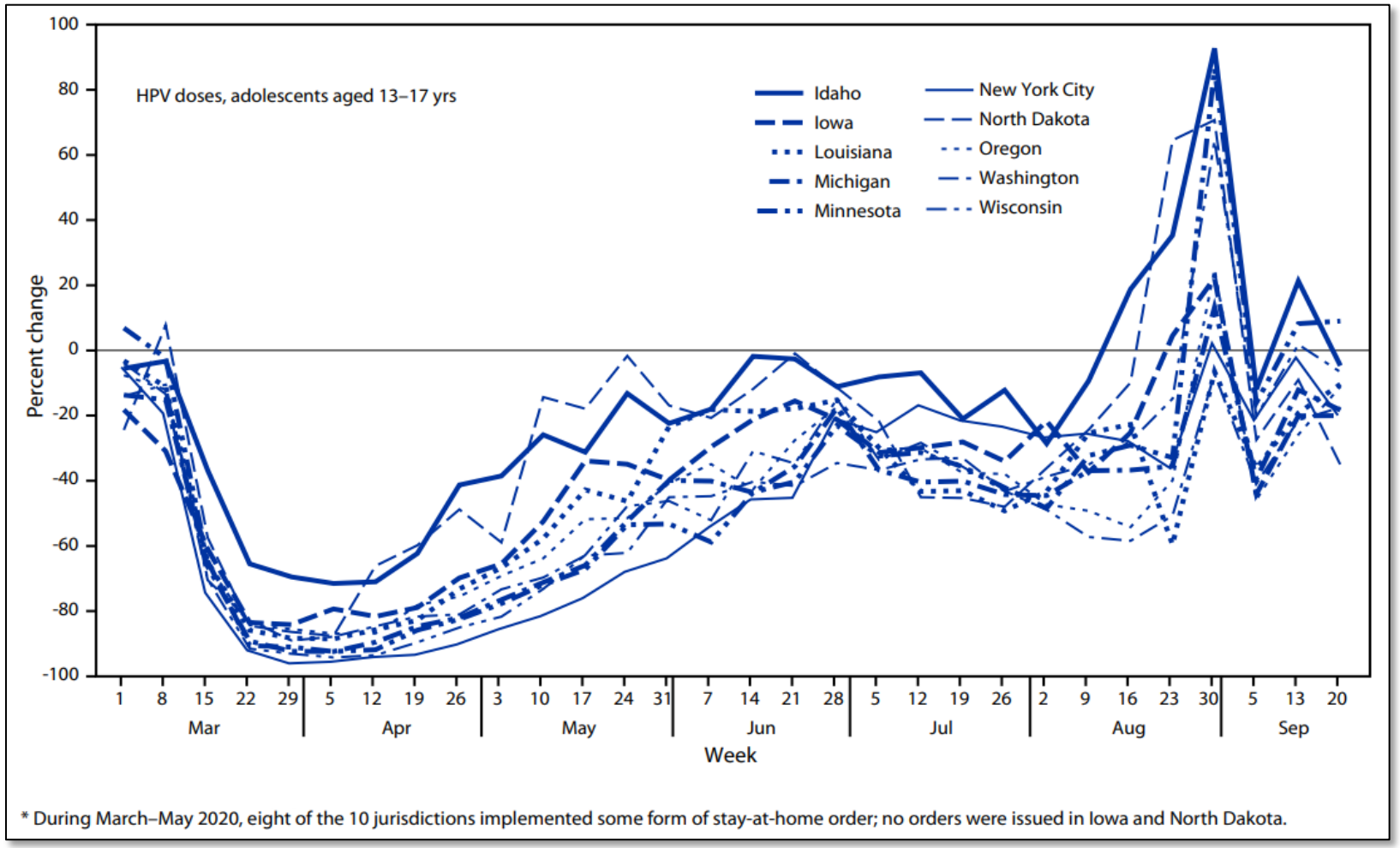


Guo F, et al. *Am J Prev Med*. 2018;55:197-204.



Impact of COVID-19 Pandemic on HPV Vaccination Rates?

- ercent change in vaccine d ses administered t 1 -17 arch-Sept
- mpared ith the average d ses administered same peri d 18 1



Murthy BP, et al. *MMWR Morb Mortal Wkly Rep.* 2021;70(23):840-845.

Strategies to Improve Vaccination

Things That Provoke Doubt in Patients

- Follow invalid contraindications to immunization
  - Low-grade fevers
  - Mild illness
- Providing reading material rather than recommending
- Equivocating on recommendations or answers
- Clinical team providing different recommendations
- **Not giving a strong and clear recommendation**

American Academy of Pediatrics: Addressing Common Concerns of Vaccine-Hesitant Parents.
Available at: https://www.aap.org/en-us/Documents/immunization_vaccine-hesitant%20parent_final.pdf.

How We Present the Vaccine: Considerations

"Sex is for other people's kids"

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

#2: Immunization 101: Vaccines prevent, they don't treat

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

How We Present the Vaccine

Potential Solutions

Approach to *Avoid*: Mode of Transmission

"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 16.

Do you want this vaccine for your daughter?"

Approach to Consider: *Less is More*

"Today your son is due for three routine vaccines which include HPV, meningitis vaccine, and Tdap. 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?”

Reminder, for the Majority of People

Start with a strong, consistent *presumptive* recommendation

"I recommend you receive the HPV vaccine."

Rather than the *participatory approach*

"Do you want to get a HPV vaccine?"

Opel DJ, et al. *Pediatrics*. 2013;132:1037-1046.

Vaccine Hesitant

Vaccine hesitant individuals are likely to become *more* entrenched in belief if confronted directly

- Transition to a supportive discussion

- **Avoid** lecturing with facts, science or logic

Consider micro-motivational interviewing:

Open Questions: What are your concerns

Affirming Statements: Many people share your concern

Summarize with autonomy: As discussed, vaccines are held to high safety standards. HPV vaccine is a serious infection. I recommend your son receive the HPV vaccine, but it is important for you to make that decision.

Amin AB, et al. *Nature Human Behaviour. 2017;*1:873–880. doi:10.1038/s41562-017-0256-5.

HPV: A Life Course Infection

Prevention during adolescence and adulthood

Disease during adulthood

Infection . . . Anytime!

Your Recommendation Matters!

Open Forum: Q&A

Evaluation Link:

https://www.surveymonkey.com/r/FOMA-HPV