


Protecting Against HPV-Related Cancers

Maximizing Opportunities During the COVID-19 Era



 Jointly provided by Center for Independent Healthcare Education and Vemco MedEd

 Supported by an educational grant from Merck & Co., Inc.

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, doctors of osteopathy, 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.

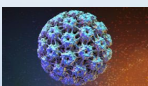
Learning Objectives

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

- Describe the burden of human papillomavirus (HPV) infection in causing anogenital and oropharyngeal cancers in men and women
- Appraise the latest clinical evidence demonstrating the impact of HPV vaccination on the incidence of HPV-related cancers
- Apply communication techniques to address and overcome barriers by healthcare providers and patients on HPV vaccination

Viruses and Cancer

- Globally, viral infections are responsible for 12% of cancers
 - Human Papillomavirus (HPV) is 30% of these cancers
- HPV causes over 610,000 cancer cases and over 250,000 deaths globally
- Evolutionarily conserved – genes have remained nearly unchanged



Bravo IG, et al. Trends Microbiol. 2010;18:432-438.
 Lowy DR. J Clin Invest. 2016;126:5-11.

Human Papillomavirus (HPV) in the United States

Over 120 types of HPV

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  graph LR
    HPV[HPV] --> Genital[Genital]
    HPV --> Non-genital[Non-genital]
    Genital --> HighRisk[High Risk = can cause cancer]
    Genital --> LowRisk[Low Risk = do not cause cancer (genital warts)]
    Non-genital --> PlantarWarts[Plantar Warts (not genital)]
  
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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

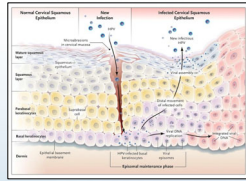


Image: Kahn JA. NEJM. 2009;361:271-8.

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

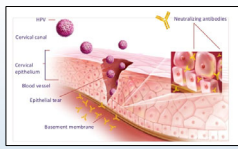


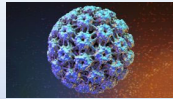
Image: J. Bentley, Dalhousie University 2015.

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

HPV in the United States

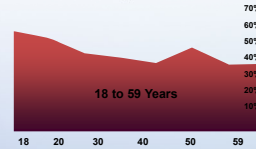
HPV is the most common *sexually transmitted infection* in the U.S.

Over 6.2 million new genital infections annually



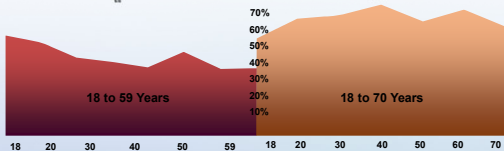
Dunne EF, et al. *JAMA*. 2007;297:813-819.

Genital HPV Prevalence Is Higher in Males Than in Females and Does Not Decrease With Age



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

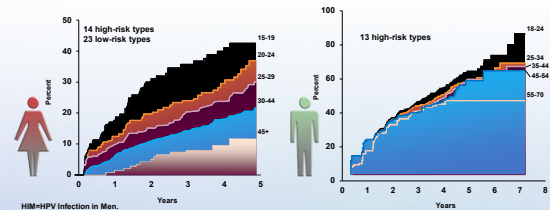
Genital HPV Prevalence Is Higher in Males Than in Females and Does Not Decrease With Age



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

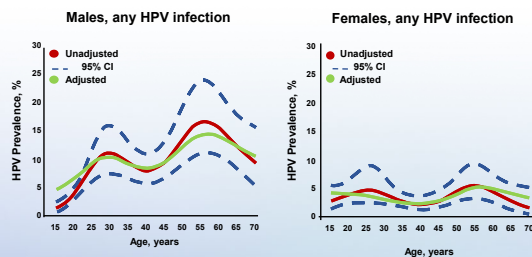
Risk for Acquiring New Genital HPV Infection

Cumulative Risk for New HPV Infections by Age at Baseline



Muñoz N, et al; Instituto Nacional de Cancerología 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(9789):922-940.

Oral HPV Prevalence Is Significantly Higher in Males Than Females



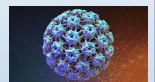
Adapted from Gillison M, et al. *JAMA*. 2012;307(7):693-703.

Transmission of HPV

Surface-to-surface contact!

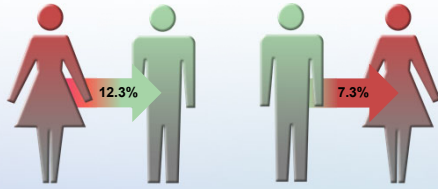
HPV can spread through anogenital region

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



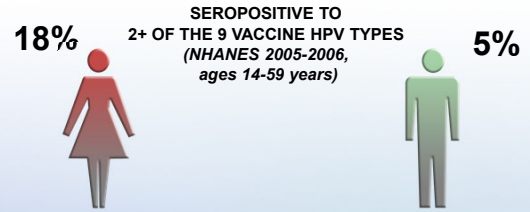
Shew ML, et al. *J Infect Dis*. 2013;207:1012-5.

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



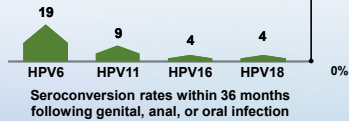
Nyiray AG, et al. *J Infect Dis.* 2014;209:1007-1015.

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



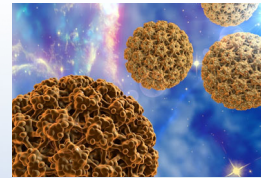
NHANES, National Health and Nutrition Examination Survey.
Liu G, et al. *J Infect Dis.* 2016;213(2):191-198.

Males Have a Low Rate of Seroconversion Following Infection...



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

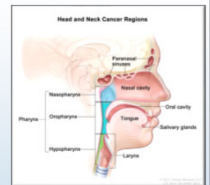
HPV-Related Cancers in the United States

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.
<https://ascopubs.org/doi/pdf/10.1200/JCO.2016.87.2014>. Accessed May 19, 2021.

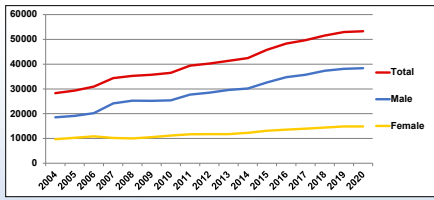
Head and Neck Squamous Cell Carcinomas

- *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>

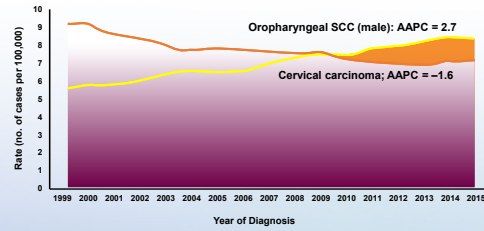
Incidence of Oropharyngeal Cancers



- Incidence of HPV-related oropharyngeal carcinomas are **increasing**
- Particularly among **males** (3x more common)
 - 70+% positive for HPV 16

American Cancer Society, Cancer Facts & Figures, 2004-2020, www.cancer.org.

The incidence of cervical cancer is declining but the incidence of HPV-related oropharyngeal squamous cell carcinomas (SCCs) 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 Yan Dye EA, et al. *MMWR Morb Mortal Wkly Rep.* 2016;65(33):318-324.

HPV Oropharyngeal Cancers in U.S.

- 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. Manor S, et al. *Lancet Oncol.* 2010;11:751-759.

HPV Prevention: Vaccination

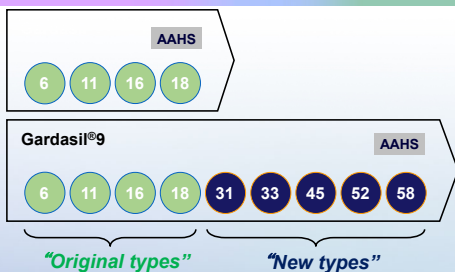


HPV2 — Cervarix (GSK)

HPV4 — Gardasil (Merck)

HPV9 — Gardasil 9 (Merck)

9-Valent HPV Vaccine Composition

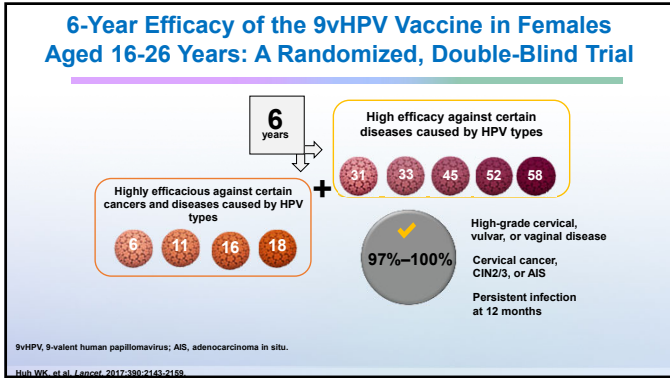


AAHS, amorphous aluminum hydroxyphosphate sulfate

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



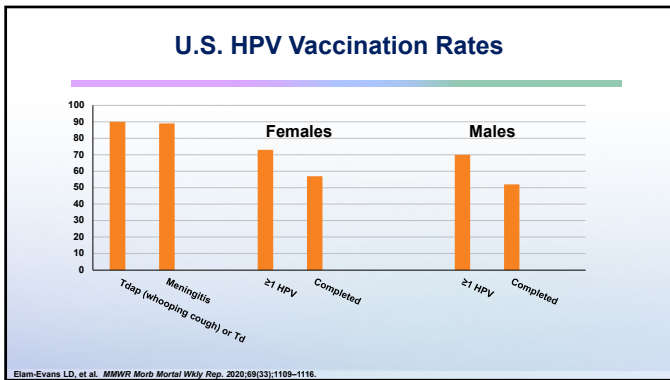
4vHPV, 4-valent human papillomavirus; CIN₂, cervical intraepithelial neoplasia.
 Kjaer SK, et al. *Clin Infect Dis.* 2018;66(3):339-346.



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

Stato BA, et al. *JAMA*. 2009;302(7):780-787; Centers for Disease Control and Prevention. FAQs about HPV safety. <https://www.cdc.gov/vaccinesafety/vaccinesafety/hpv/hpv-safety-faq.html>. Last Reviewed July 15, 2020. Accessed May 19, 2021.



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*

Meltes E, et al. *MMWR Morb Mortal Wkly Rep*. 2019;68(32):696-702.

Vaccine Recommendations

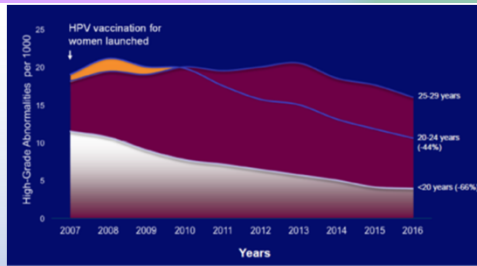
HPV vaccine should be offered to all age-eligible adolescents and adults *regardless* of “risk”

Only potential screening questions:

1. Previously vaccinated against HPV?
2. Currently pregnant?

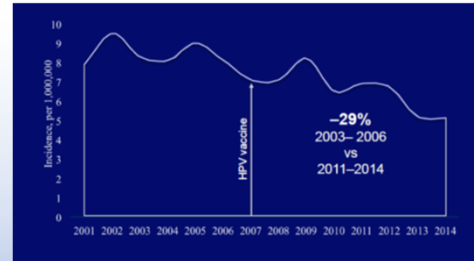
Clinical Outcomes

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



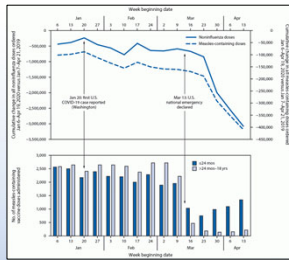
Kirby Institute. HIV, viral hepatitis and sexually transmissible infections in Australia: annual surveillance report 2018. Sydney: Kirby Institute, UNSW Sydney; 2018. <https://kirby.unsw.edu.au/reports/hiv-hepatitis-and-sexually-transmissible-infections-australia-annual-surveillance>. Accessed May 19, 2021.

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.

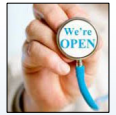
Child and Adolescent Vaccination Rates Declined During the Pandemic



Ackerson BK, et al. *Pediatrics*. 2021; doi: 10.1542/peds.2020-047092. Elam-Evans LD, et al. *MMWR Morb Mortal Wkly Rep*. 2020;69(33):1109-1116. Santoli JM, et al. *MMWR Morb Mortal Wkly Rep*. 2020;69(15):381-383.

First, Need to Get Adolescents Back to Clinic!

- Consider in-person visits vs. telehealth
 - Waiting room size and exam rooms dictate
 - Stagger in-person and telehealth visits
 - Screening process for acute illness or COVID exposure
- Vaccine-only visits vs. clinician visits
- Expansion of hours to accommodate more in-person visits



First, Need to Get Adolescents Back to Clinic!

Outreach

- Reminders, calls, portal messaging, etc.
- Back to school needs
- Reassure safety of coming into healthcare setting



Creative Strategies

- Offering COVID vaccines for family members
- Extended hours for vaccines



WHO. <https://www.who.int/news-room/spotlight/ten-threats-to-global-health-in-2019>. Accessed May 19, 2021.

WHO Threats to Global Health

1. Air pollution and climate change
2. Noncommunicable chronic disease
3. Global influenza pandemic
4. Fragile and vulnerable settings
5. Antimicrobial resistance
6. Ebola and other high-threat pathogens
7. Weak primary health care
8. **Vaccine hesitancy**
9. Dengue
10. HIV



WHO. <https://www.who.int/news-room/spots/10-threats-to-global-health-in-2019>. Accessed May 19, 2021.

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. Accessed at: https://www.aap.org/in-us/Documents/immunization_vaccine-hesitant%20parent_final.pdf. Accessed May 19, 2021.

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

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.

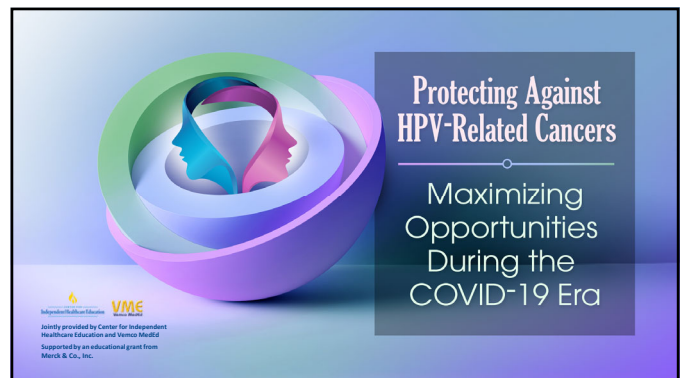
HPV: A Life Course Infection

Prevention during adolescence and adulthood

Disease during adulthood

Infection . . . Anytime!

Your Recommendation Matters!



Protecting Against HPV-Related Cancers

Maximizing Opportunities During the COVID-19 Era

Identified provided by Center for Independent Healthcare Education and Vaccine Model. Supported by an educational grant from Merck & Co., Inc.