

Activity Description

Target Audience
 This activity is designed as a comprehensive approach to address the practice needs of pediatricians.

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 and how cancer incidence has been impacted following widespread use of HPV vaccination
- Utilize communication strategies designed to educate vaccine-eligible patients and their parents about the risks of HPV infection and benefits of vaccination
- Identify factors that impact HPV vaccine acceptance and implement approaches to address healthcare disparities among the pediatric population

Faculty and Disclosure

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University of Illinois at Chicago
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.*

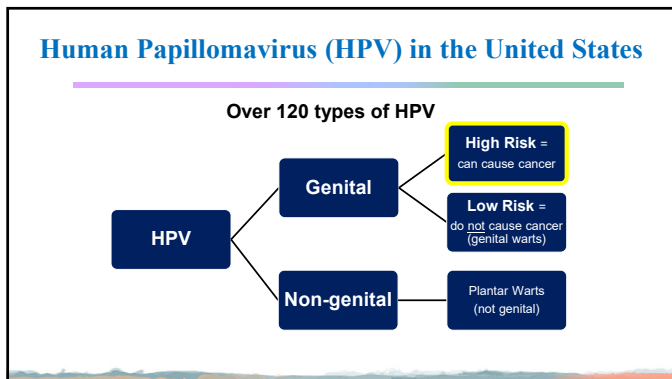
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Incidence & Prevalence

- 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

Levine RM, et al. Sex Transm Dis. 2021;48(4):273-277.
 Zhang Y, et al. JAMA Oncol. 2021;7(10):e212907.
 NIH SEER Program (2020 stats) <https://seer.cancer.gov/statfacts/> (Accessed 9/4/2023).



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 viremia 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. 2019;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

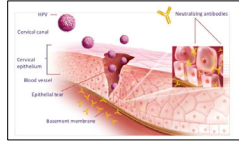


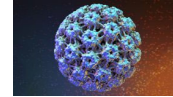
Image: J. Bently, Dalhousie University 2015.

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

HPV in the United States

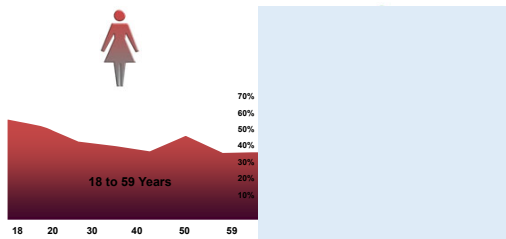
HPV is the most common *sexually transmitted infection* in the U.S.

Over 6.2 million new genital infections annually



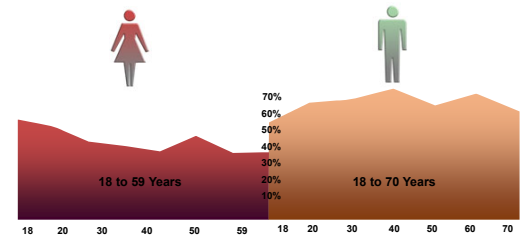
Dunne EF, et al. *JAMA.* 2007;297:813-819.

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.

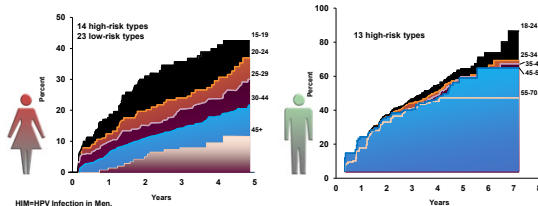
Genital HPV Prevalence Higher Among Males



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

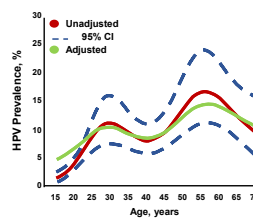
Cumulative Risk for New HPV Infections by Age at Baseline



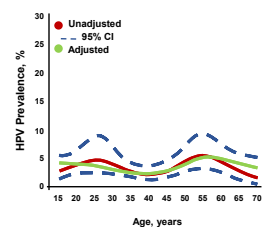
Mulooz N, et al. Instituto Nacional de Cancerologia HPV Study Group. *J Infect Dis.* 2004;190:2077-2087, by permission of Oxford University Press; Adapted from Giuliano AR, et al. *Lancet.* 2011;377(9789):932-940.

Oral HPV Prevalence Is Significantly Higher in Males Than Females

Males, any HPV infection



Females, any HPV infection



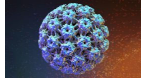
Adapted from Gillison M, et al. *JAMA.* 2012;307(7):693-703.

Transmission of HPV

Surface-to-surface contact!

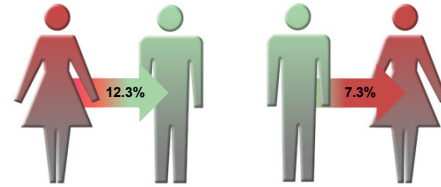
HPV can spread through anogenital region

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



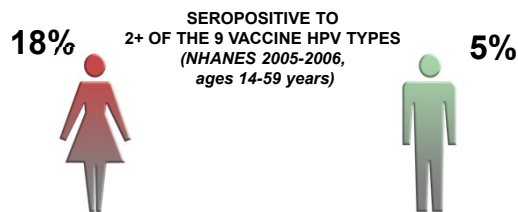
Shew ML, et al. *J Infect Dis.* 2013;207:1012-6.

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



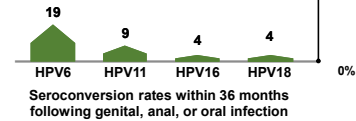
Nytray AG, et al. *J Infect Dis.* 2014;209:1007-1015.

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



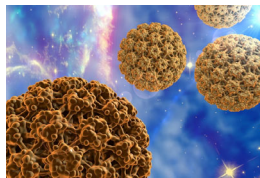
NHANES, National Health and Nutrition Examination Survey.
Liu G, et al. *J Infect Dis.* 2016;213(2):191-198.

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



Giuliano AR, et al. *Papillomavirus Res.* 2016;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

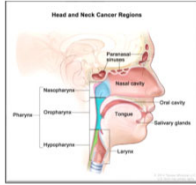
Cancers Caused by HPV in United States

>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(18):1803-1812.
Available at: <https://ascopubs.org/doi/pdf/10.1200/JCO.2016.67.2014>.

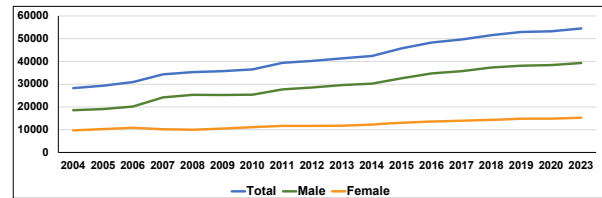
Head and Neck Squamous Cell Carcinomas

- **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>

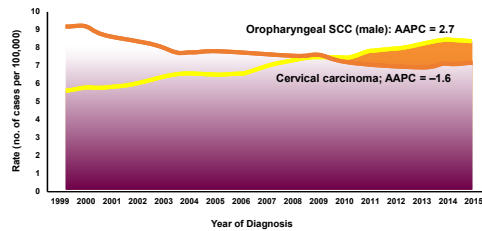
Incidence of Oropharyngeal Cancers in U.S.



- Incidence of HPV-related oropharyngeal carcinomas are **increasing**
- Particularly among **males** (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.

Adults are Unaware of Link Between HPV and Oropharyngeal Cancer

Survey of 288 adults (18 to 45 years) seeking routine outpatient care at an otolaryngology (ENT) clinic in Boston

- 26.6% vaccinated against HPV (10.6% of men)
- Only 23.3% understood the relationship between HPV infection and oropharyngeal cancer
 - Women more likely aware of relationship between HPV and cancer and more likely to be informed about HPV from a healthcare practitioner
- Knowledge of the relationship between HPV infection and cancer was associated with a greater likelihood of being vaccinated

Bloom JC, et al. *JAMA Otolaryngol Head Neck Surg*. 2023:e232073 (Online ahead of print). doi:10.1001/jamato.2023.2073.

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

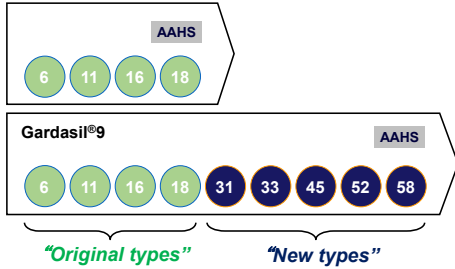
Cancer Facts and Figures 2012, American Cancer Society, www.cancer.org. Chaturvedi AK, et al. *J Clin Oncol*. 2008;26:612-619. Annual Report to the Nation of the Status of Cancer, 1975-2009, *JNCI*. 2012. Marur S, et al. *Lancet Oncol*. 2010;11:781-789.

HPV Prevention: Vaccination



HPV9 – Gardasil 9

9-Valent HPV Vaccine Composition



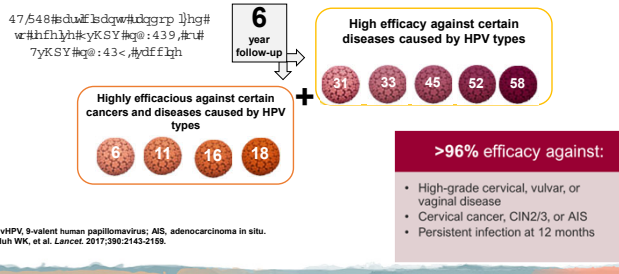
AAHS, amorphous aluminum hydroxyphosphate sulfate

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



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



HPV Vaccine Safety

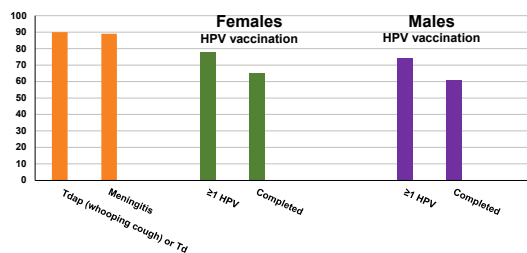
- >350 million doses of HPV vaccine distributed worldwide
- Most common adverse events are mild: Sore arm, myalgias
- Among serious adverse events: **No** patterns to suggest any events related to the HPV vaccine
- Findings similar to the safety of all other adolescent vaccines

Stade BA, et al. *JAMA*. 2009;302(7):760-767; 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 U.S.



U.S. HPV Vaccination Rates



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):698-702.

Early Vaccination Is Key

- Srsxawirg0edvng#Edqfhu#hjl lwa| #gdvd#urp #p x0sd0#frxqvlv# vxssru#k#h#p srudqf#h# #hdud#ydf#f#qdw#r#
- Uhf#q#v#x#j#h#v#k#d#K#S#Y#y#d#f#f#q#d#w#r#/#v#s#h#f#d#0# #k#q# #j#y#h#q#d#w#d# #r#x#q#j#h#d#j#h#/#d#v#r#f#d#w#g# #l#k#x#e#v#d#q#w#d#d# #u#h#g#x#f#w#r#q#v#q# #k#h#d#v#n# #i#f#h#y#l#f#d#q#E#d#q#f#h#u
- D#g#x#0#y#d#f#f#q#d#w#r#q# #5 : 078 |r, #k#d#v#k#h# #r#w#q#w#d#k#r# #s#u#y#h#q#w# #w#r#x#v#d#q#v#r# #f#d#q#f#h#u# #h#u# #h#d# #e#x#w#p# #q# | #f#d#q#l#d#q#v#d#q#g# #d#w#h#q#w# #x#q#d#z# #d#h# #i#y#d#f#f#q#h# #v#h#s#s#u#r#y#h#g# #r#u#k#l#v#d#j#h# #j#u#r#x#s# #

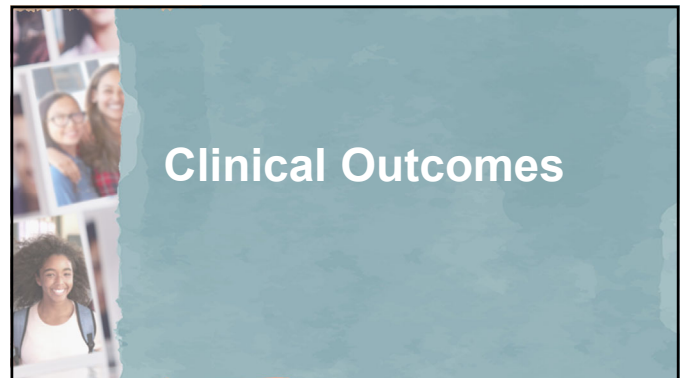
Mix JM, et al. *Cancer Epidemiol Biomarkers Prev.* 2021;30(11):20-37; Liao C-L, et al. *JAMA Netw Open.* 2022;5(3):e222530; Falcato M, et al. *Lancet.* 2021;398(10316):2084-2092; Lai J, et al. *N Engl J Med.* 2020;383(14):1340-1348; King LM, et al. *Open Forum Infectious Disease.* Volume 10, Issue 1, January 2022

Vaccine Recommendations

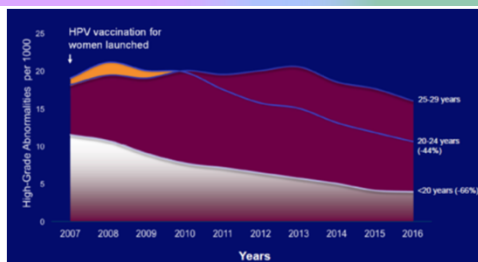
HPV vaccine should be offered to all age-eligible adolescents and adults *regardless* of “risk”

Only potential screening questions:

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

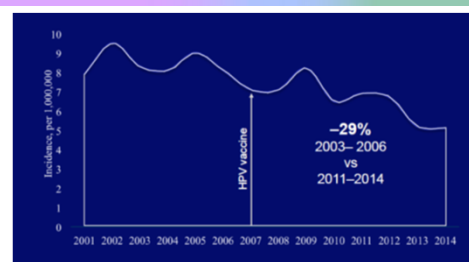


Australia: Trends in High-Grade Cervical Abnormalities by Age Pre- and Post-Vaccination

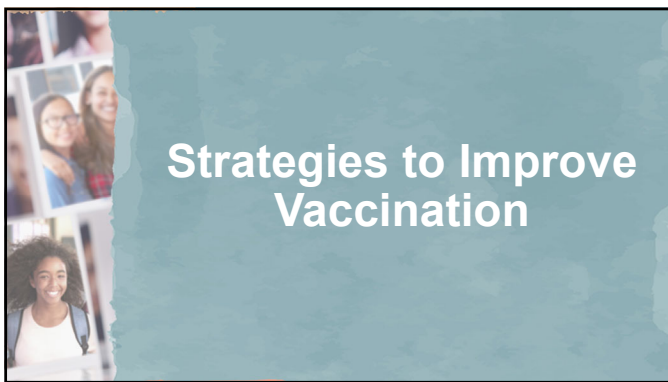
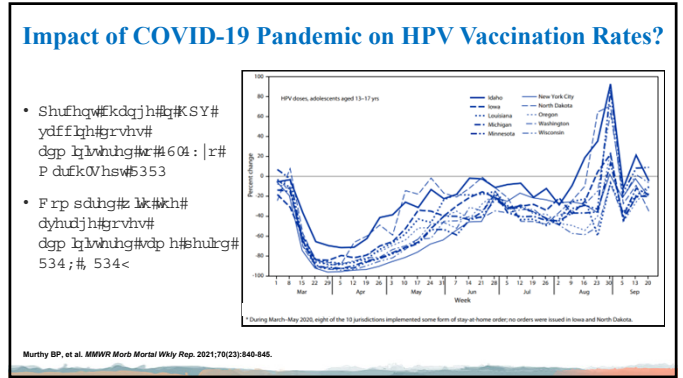
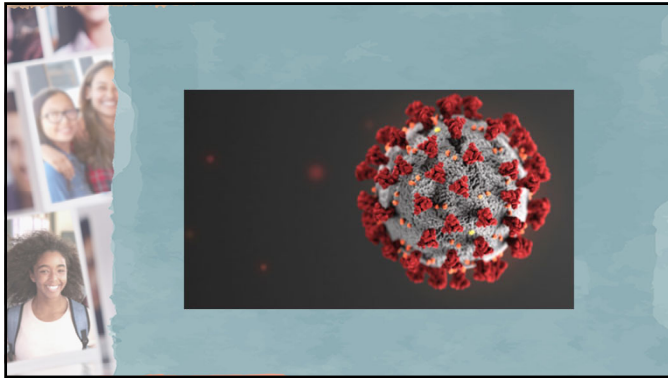


Kirby Institute. HIV, viral hepatitis and sexually transmissible infections in Australia: annual surveillance report 2018. Sydney: Kirby Institute, UNSW Sydney; 2018. <https://kirby.unsw.edu.au/report/hiv-viral-hepatitis-and-sexually-transmissible-infections-australia-annual-surveillance>.

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.



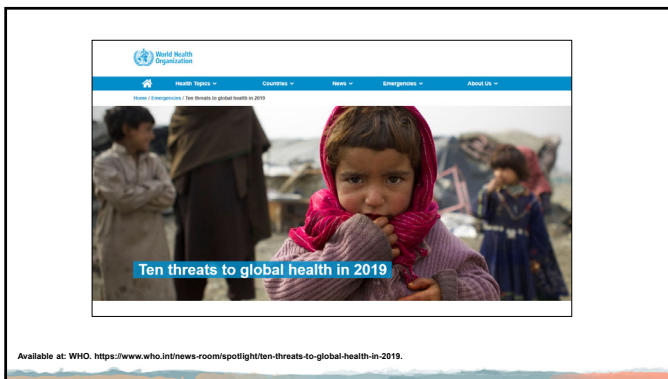
Need to Get Adolescents Back to Clinic!

Outreach

- Reminders, calls, portal messaging, etc.
- Back to school needs

Creative Strategies

- Extended hours for vaccines
- Standing orders for vaccines



WHO Threats to Global Health

- Air pollution and climate change
- Noncommunicable chronic disease
- Global influenza pandemic
- Fragile and vulnerable settings
- Antimicrobial resistance
- Ebola and other high-threat pathogens
- Weak primary health care
- Vaccine hesitancy**
- Dengue
- HIV

Available at: <https://www.who.int/news-room/spotlight/ten-threats-to-global-health-in-2019>.

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/MIAAP-HPV>