Updates on Cervical Cancer, HPV Cancers and HPV Vaccine

Nita Karnik Lee, MD MPH
CME Accreditation Statement

The Illinois Chapter, American Academy of Pediatrics is accredited by the Illinois State Medical Society (ISMS) to provide continuing medical education for physicians.

The Illinois Chapter, American Academy of Pediatrics designates each live webinar activity for a maximum of 1 AMA PRA Category 1 Credit(s)™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Nurses and Nurse Practitioners can submit Certificates of Attendance to their accrediting board for credit for participation in the live webinars.
**CME Disclosure Grid**

No disclosures.

* Honorarium for education material review for National Ovarian Cancer Coalition

<table>
<thead>
<tr>
<th>Name and Credentials</th>
<th>Role in Activity</th>
<th>Was there a relevant Financial Disclosure</th>
<th>List of Mitigated Disclosures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Megan Kane Towle, MMS, PA-C</td>
<td>Planning Committee Member</td>
<td>No</td>
<td>N/A</td>
</tr>
<tr>
<td>Craig Batterman, MD</td>
<td>Planning Committee Member</td>
<td>No</td>
<td>N/A</td>
</tr>
<tr>
<td>Caroline Werenskjold, MPH</td>
<td>Staff</td>
<td>No</td>
<td>N/A</td>
</tr>
<tr>
<td>Laura Buthod, MD</td>
<td>Planning Committee Member</td>
<td>No</td>
<td>N/A</td>
</tr>
<tr>
<td>Magale Avitia MPH, CHES</td>
<td>Staff</td>
<td>No</td>
<td>N/A</td>
</tr>
<tr>
<td>Joseph Hageman, MD</td>
<td>CME Reviewer</td>
<td>No</td>
<td>N/A</td>
</tr>
<tr>
<td>Sarah Parvinian, MD</td>
<td>CME Reviewer</td>
<td>No</td>
<td>N/A</td>
</tr>
<tr>
<td>Nita K Lee, MD, MPH</td>
<td>Faculty/Presenter</td>
<td>No</td>
<td>N/A</td>
</tr>
<tr>
<td>Sharon Hovey, MD</td>
<td>Planning Committee Member</td>
<td>No</td>
<td>N/A</td>
</tr>
<tr>
<td>Kathleen Sanabria</td>
<td>Planning Committee Member</td>
<td>No</td>
<td>N/A</td>
</tr>
<tr>
<td>Stephanie Atella</td>
<td>Staff</td>
<td>No</td>
<td>N/A</td>
</tr>
<tr>
<td>Erin Moore</td>
<td>Staff</td>
<td>No</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Funding for this webinar is provided by the Office of Disease Control, through the Illinois Department of Public Health.
Join Us February 15th

At 12pm for Pediatric Travel and Vaccinations with Jen Burns, ANP

Register at illinoisap.org/events
Nita Karnik Lee
Associate Professor, Dept Ob-Gyn, Section of Gynecologic Oncology
Assistant Director, Community Outreach and Engagement.
Objectives

• Review and understand current burden of cervical cancer including vulnerable populations and screening recommendations
• Review and understand current burden of other HPV related diseases and cancers
• Review indications and recommendations for HPV Vaccination
• Review updates in research on the effects of HPV vaccine on pre-cancer and cancer
Review and understand current burden of cervical cancer including vulnerable populations
Estimated age-standardized incidence rates (World) in 2020, cervix uteri, all ages

ASR (World) per 100 000

≥ 25.2
16.7-25.2
11.7-16.7
7.0-11.7
< 7.0

Not applicable
No data

All rights reserved. The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization / International Agency for Research on Cancer concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate borders for which there may not yet be full agreement.

Data source: GLOBOCAN 2020
Graph production: IARC
(https://gco.iarc.fr/)
World Health Organization
WHO’S ELIMINATION STRATEGY 3 Pillars*

1. Prevention through vaccination
   HPV vaccination offers long-term protection against cervical cancer.

2. Screening and treatment of precancerous lesions
   can prevent pre-cancer from developing into cancer.

3. Timely treatment and palliative care for invasive cervical cancer
   can save lives and palliative care can greatly reduce pain and suffering.

*To eliminate cervical cancer, all countries must reach and maintain an incidence rate below four per 100,000 women.
Facts: Cervical Cancer

- Cervix is the opening to the uterus or womb
- Anyone with a cervix is at risk
- 2nd most common cancer death for women 20-29
- Most common age at diagnosis -- 35-44 yo
- Most at risk if no pap or no pap in 5 years
- 14,000+ women in US, 4200 die each year
- Due to HPV infection with a high-risk type
- Precancer can be caught/treated early

PREVENTABLE and TREATABLE
Eradication of Cervical Cancer

• Primary Prevention: HPV Vaccine
• Screening and Secondary Prevention:
  • Pap test and HPV test
• Early Detection
• Improved Diagnostics
  • Better Follow up and Navigation; Better access
• Equitable treatment
• Novel treatments
Screening Saves lives: 1950-2000

Who is still getting cervical cancer in the US?
- People who miss screening completely
- Get Screening but not follow up.
- Uninsured or Underinsured
- Disabled women
- Immigrant communities
- Rural communities
- Hispanic women have higher rates of diagnosis
- Black women have higher cervical cancer mortality
US
<7 new cases/100,000

By State
4.3–9.6/100,000

Black Women
5.6–11.5/100,000

Hispanic
6.5–14.3/100,000
**Rate of New Cancers by Race/Ethnicity, Female**

Cervix, United States, 2013-2017

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Rate per 100,000 women</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>7.5</td>
</tr>
<tr>
<td>Black</td>
<td>8.8</td>
</tr>
<tr>
<td>American Indian/Alaska Native</td>
<td>6.3</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>6.1</td>
</tr>
<tr>
<td>Hispanic</td>
<td>9.5</td>
</tr>
</tbody>
</table>


**Number of New Cancers by Age Group (years), All Races, Female**

Cervix, United States, 2013-2017

Rate of New Cancers by Sex and Race/Ethnicity

Cancer, Illinois 2016

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>7.7</td>
</tr>
<tr>
<td>Black</td>
<td>11.9</td>
</tr>
<tr>
<td>American Indian/Alaska Native</td>
<td>Suppressed</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>4.0</td>
</tr>
<tr>
<td>Hispanic</td>
<td>10.3</td>
</tr>
</tbody>
</table>

Rate per 100,000 people

Cervix Uteri
SEER 5-Year Age-Adjusted Incidence Rates, 2014-2018
Female By Race/Ethnicity, All Ages, All Stages

Rate per 100,000

All Races (includes Hispanic)  Asian / Pacific Islander (includes Hispanic)  Black (includes Hispanic)  Hispanic (any race)  White (includes Hispanic)

Illinois Chapter
INCORPORATED IN ILLINOIS
American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN
Cervix Uteri
U.S. 5-Year Age-Adjusted Mortality Rates, 2015-2019
Female By Race/Ethnicity, All Ages
HPV stands for human papillomavirus

- There are more than 200 types HPV

- HPV can be harmless and often goes away by itself, but some types of HPV can lead to genital warts or certain types of cancer.

- Two types of HPV (types 6 and 11) cause most cases of genital warts

- HPV (types 16 and 18), high-risk HPV, lead to the majority of cancer cases
HPV Review

• Currently most common sexually transmitted infection

• Highest prevalence within 2-5 years of initiation of sexual activity
  • 2nd peak in the 4-5th decade

• ~10% of infections are not cleared within 2 years
How is HPV transmitted?

- Skin to skin contact
- HPV types that are specific to genital areas are transmitted by skin to skin contact in the genital area
- Considered a sexually transmitted disease
- Mixed feelings about this classification and associated stigma
HPV is extremely common – nearly 80 million Americans are currently infected (~1 in 4)

New cases per year, as estimated by the CDC

- Gonorrhea: 820,000
- Chlamydia: 2.86 million
- HPV: 14 million

Illinois Chapter
INCORPORATED IN ILLINOIS
American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN
Increased Risks If:
Smoking
Immune system issues
- HIV
- Transplant

Slow progression from persistent hrHPV infection to CIN to cancer
Clinically significant persistent infections = last at least 2 years
Cervical Cancer Screening

When to start? When to stop?

• After age 21 years old
• Start at age 21 until age 65 years old
• Some can start at age 25 years old with special HPV test
• May test if older than 65 years old if
  • symptoms of bleeding or abnormal discharge
  • have not had regular testing
  • history of abnormal pap smears
Screening Recommendations for Average Risk

2020 Guideline Update some differences with 2018 USPSTF guidelines

Who is average risk? Who is still getting cervical cancer?

- Average risk
  - Not immunocompromised
  - No prior abnormal paps or HR HPV present
- Does not include structural risks of lack of insurance, follow up etc.
- Does not include other barriers to care
Cervix Uteri
U.S. Mortality Rates by Age at Death, 2015-2019
Female By Race/Ethnicity, All Ages

Legend (Race/Ethnicity)
- All Races (includes Hispanic)
- Asian / Pacific Islander (Includes Hispanic)
- Black (includes Hispanic)
- Hispanic
- White (includes Hispanic)

US Mortality Files: National Center for Health Statistics. CDC.
Rates are per 100,000.
For American Indian/Alaska Natives only include cases that are in a Purchased Referral Care Delivery Area (PRCDA).
For more information, see Documentation for American Indian/Alaska Native Data.
[https://seer.cancer.gov/seerstat/documentation/indian_an_index.html]
[https://seer.cancer.gov/seerstat/documentation/indian_an_index.html]
[https://seer.cancer.gov/seerstat/documentation/indian_an_index.html]
[https://seer.cancer.gov/seerstat/documentation/indian_an_index.html]
2020 ACS Guidelines Changes

The ACS 2012 recommendation for co-testing as the preferred test was limited to women aged ≥30 years.

In the new recommendation,

- primary HPV testing is preferred
- both cotesting and cytology alone are included as acceptable transitional screening strategies from age 25 years for all individuals.

The test, the **cobas HPV Test**
- detects DNA from 14 high-risk HPV types
- a positive test for HPV type 16 or 18 is considered an indication for a colposcopy
- a positive test for any of the 12 other high-risk HPV types is considered an indication for a Papanicolaou (Pap) test reflex
- The cobas HPV Test was first approved in 2011 for use in conjunction with or as a follow-up to a Pap test.
<table>
<thead>
<tr>
<th>Age Group</th>
<th>Testing Requirements</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women under 21</td>
<td>No testing</td>
<td>As long as no symptoms</td>
</tr>
<tr>
<td>Women 21-30</td>
<td>Pap test every 3 years</td>
<td>** Some may start at 25 years with special HPV test</td>
</tr>
<tr>
<td>Women 30-65</td>
<td>Pap test every 3 years or Pap and HPV every 5 years</td>
<td>** Some can use primary HPV testing instead</td>
</tr>
<tr>
<td>Women 65 or older</td>
<td>No testing</td>
<td>UNLESS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Symptoms (bleeding, pain)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- No pap for many years prior to age 65 yo</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- History of cervical cancer or abnormal paps</td>
</tr>
<tr>
<td>POPULATION</td>
<td>ACS 2020 (^a)</td>
<td>ACS 2012 (^b)</td>
</tr>
<tr>
<td>-----------------</td>
<td>----------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Aged &lt;25 y</td>
<td>No screening</td>
<td>Cytology alone every 3 y starting at age 21 y</td>
</tr>
<tr>
<td>Aged 25-65 y</td>
<td>Starting at age 25 y, primary HPV test alone every 5 y (preferred)</td>
<td>Cytology alone every 3 y until age 29 y</td>
</tr>
<tr>
<td></td>
<td>Use an FDA-approved HPV test for primary screening</td>
<td>Aged 30-65 y, switch to cotesting (preferred),</td>
</tr>
<tr>
<td></td>
<td>Cotesting every 5 y or cytology alone every 3 y are acceptable options (^b)</td>
<td>cytology alone every 3 y (acceptable)(^b)</td>
</tr>
<tr>
<td></td>
<td>Cotesting or cytology testing alone are acceptable where access to primary HPV</td>
<td>Screening by primary HPV testing alone not recommended for most clinical settings</td>
</tr>
<tr>
<td></td>
<td>testing is limited or not available, as the United States makes the transition</td>
<td></td>
</tr>
<tr>
<td></td>
<td>to primary HPV testing, the use of cotesting or cytology alone for cervical</td>
<td></td>
</tr>
<tr>
<td></td>
<td>cancer screening will not be included in future guidelines (^b)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>For management of positive results and subsequent surveillance, refer to ASCCP 2020</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Risk-Based Management Consensus Guideline (Perkins, 2020) (^c)</td>
<td></td>
</tr>
<tr>
<td>Aged &gt;65 y</td>
<td>Discontinue screening if adequate negative prior screening</td>
<td>No screening after adequate negative prior screening</td>
</tr>
<tr>
<td></td>
<td>Individuals aged &gt;65 y without documentation of prior screening should continue</td>
<td></td>
</tr>
<tr>
<td></td>
<td>screening until criteria for cessation are met</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Adequate negative prior screening is currently defined as 2 consecutive, negative</td>
<td></td>
</tr>
<tr>
<td></td>
<td>primary HPV tests, or 2 negative cotests, or 3 negative cytology tests within the</td>
<td></td>
</tr>
<tr>
<td></td>
<td>past 10 y, with the most recent test occurring within the past 3-5 y, depending on</td>
<td></td>
</tr>
<tr>
<td></td>
<td>the test used</td>
<td></td>
</tr>
<tr>
<td>After hysterectomy</td>
<td>Individuals without a cervix and without a history of CIN2 or a more severe diagno</td>
<td></td>
</tr>
<tr>
<td></td>
<td>sis in the past 25 y or cervical cancer ever should not be screened</td>
<td></td>
</tr>
<tr>
<td>HPV vaccinated</td>
<td>Follow age-specific screening recommendations (same as unvaccinated individuals)</td>
<td>Follow age-specific screening recommendations</td>
</tr>
</tbody>
</table>
The Problem with Screening

- Stigma
- Other health issues
- Lack of time
- Discomfort with exams
- Lack of knowledge ("Does not apply to me")
- Lack of navigation
- Fear, embarrassment, shame
- Prior abuse or trauma

Understanding Pap Smear Results

Squamous Intra-epithelial Lesion (SIL)

Cervical Changes

Most abnormal paps will not be cancer but need follow up
HPV DNA Testing

• FDA approved for HPV reflex/co-testing
  • Hybrid Capture® 2 (Qiagen)
  • Cervista® (Hologic)
  • APTIMA® (Hologic)
  • Cobas® (Roche)
  • Onclarity® (BD)

• Higher sensitivity than cytology in detecting HSIL
Efficacy of HPV-based screening for prevention of invasive cervical cancer: follow-up of four European randomised controlled trials

Guglielmo Ronco, Joakim Dillner, K-Miriam Elftström, Sara Tunestål, Peter JF Seijdel, Marc Arbyn, Henry Kitchener, Noreen Segnan, Clare Gilham, Paolo Girgop-Rossi, Johannes Boekhoff, Julian Peto, Chris J L Meijer, and the International HPV screening working group
What’s New in Screening Options for Cervical Cancer?

Self – testing vaginal HPV testing
- Tests are not FDA approved yet
- Studies are ongoing on larger scale
- Self test in the office vs Self test at home
- Questions about cost, appropriate follow up and navigation
- Benefits: may be more acceptable, privacy, easy of use, use in underscreened populations
HPV Self Screening

- This study was a crossover randomized clinical trial to evaluate the acceptability of HPV DNA self-sampling compared with that of Pap smears and its impact on the rate of compliance with cervical cancer screening.
- Self Collection was acceptable and preferred
- May be more cost effective

<table>
<thead>
<tr>
<th>Self-collected Samples</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pap Smear Samples</td>
</tr>
<tr>
<td></td>
<td>Positive</td>
</tr>
<tr>
<td>Positive</td>
<td>26 (6.6)</td>
</tr>
<tr>
<td>Negative</td>
<td>4 (1.0)</td>
</tr>
<tr>
<td>Total</td>
<td>30 (7.7)</td>
</tr>
</tbody>
</table>

Abbreviation: HPV, human papillomavirus.

Review and understand current burden of other HPV related diseases and cancers
HPV Multiple Impacts on Population Health

• The Problem – HPV Virus

- 2+ Million Abnormal PAP smears for cervical cancer
- 1+ Million Low-grade cervical dysplasia
- 355,000 Genital warts
- 300,000 High-grade cervical dysplasia
- ~35,000 HPV-Attributable Cancers

Source: https://www.cdc.gov/cancer/hpv/statistics/cases.htm
## Cancers Caused by HPV per Year, U.S., 2013-2017

<table>
<thead>
<tr>
<th>Cancer site</th>
<th>Percentage probably caused by any HPV type</th>
<th>Number probably caused by any HPV type</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Cervix</td>
<td>91%</td>
<td>11,000</td>
</tr>
<tr>
<td>Vagina</td>
<td>75%</td>
<td>700</td>
</tr>
<tr>
<td>Vulva</td>
<td>69%</td>
<td>2,800</td>
</tr>
<tr>
<td>Penis</td>
<td>63%</td>
<td>0</td>
</tr>
<tr>
<td>Anus</td>
<td>91%</td>
<td>4,400</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>70%</td>
<td>2,200</td>
</tr>
<tr>
<td>TOTAL</td>
<td>79%</td>
<td>21,100</td>
</tr>
</tbody>
</table>

https://www.cdc.gov/cancer/hpv/statistics/cases.htm
Review HPV and indications and recommendations for HPV Vaccine
Prophylactic HPV Vaccines

• DNA-free virus-like proteins (VLPs)
  • Major capsid antigens L1 and L2

• Serve as immunogens
  • Induce a strong humoral response – neutralizing antibodies
  • Some cellular response

• Non-infectious and non-oncogenic
Virus-like Particle
## Serological Response to HPV

<table>
<thead>
<tr>
<th>natural infection</th>
<th>Vaccination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local cell mediated immunity</td>
<td>Strong humoral immunity</td>
</tr>
<tr>
<td>Seroconversion ~60%</td>
<td>Seroconversion ~100%</td>
</tr>
<tr>
<td>Time to seroconversion: 12 months</td>
<td>High titers</td>
</tr>
<tr>
<td>Delayed and low-titer Ab</td>
<td>Significant cross-protection</td>
</tr>
</tbody>
</table>
## Vaccine Efficacy and Immunogenicity

<table>
<thead>
<tr>
<th>STUDY</th>
<th>PATRICIA</th>
<th>Costa Rica</th>
<th>VIVIANE</th>
<th>HPV-P-007</th>
<th>FUTURE I + II</th>
<th>NCT00543 543</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
<td>Phase 3 randomized controlled</td>
<td>Phase 3 randomized controlled</td>
<td>Phase 3 randomized controlled double blind</td>
<td>Phase 2 randomized multicenter double blind placebo-controlled</td>
<td>Randomized double-blind placebo-controlled</td>
<td>Phase 2b-3 randomized</td>
</tr>
<tr>
<td>Vaccine type</td>
<td>Bivalent</td>
<td>Bivalent</td>
<td>Bivalent</td>
<td>Quadrivalent</td>
<td>Quadrivalent</td>
<td>9-valent</td>
</tr>
<tr>
<td>Age group</td>
<td>15-25</td>
<td>18-25</td>
<td>&gt;25</td>
<td>16-23</td>
<td>16-26</td>
<td>16-26</td>
</tr>
<tr>
<td>Trial size</td>
<td>18644</td>
<td>7466</td>
<td>5778</td>
<td>1158</td>
<td>17622</td>
<td>14215</td>
</tr>
<tr>
<td>End point</td>
<td>CIN3+</td>
<td>CIN2+</td>
<td>CIN1+</td>
<td>Sero+/safety</td>
<td>CIN2+</td>
<td>CIN2+</td>
</tr>
<tr>
<td>Efficacy (seroconversion)</td>
<td>98.2%</td>
<td>89.8%</td>
<td>96.2%</td>
<td>100%</td>
<td>100%</td>
<td>96.7%</td>
</tr>
<tr>
<td>Follow up</td>
<td>34.9 months</td>
<td>8.4 years</td>
<td>7 years</td>
<td>3 years</td>
<td>3.7 years</td>
<td>4 years</td>
</tr>
</tbody>
</table>

Comparison of the Immunogenicity and Reactogenicity of a Prophylactic Quadrivalent Human Papillomavirus (Types 6, 11, 16, and 18) L1 Virus-Like Particle Vaccine in Male and Female Adolescents and Young Adult Women

Stan L. Block, MD; Tony Nolte, PhD; MBBS; Carlos Sattler, MD; Elinor Bars, MD; Katherine E. D. Giancatiari, MD; Collin D. Marchant, MD; Xavier Castellsagay, MD, PhD, MPPH; Steven A. Ruscha, MS; Susanne Lukac, BS; Janine T. Bryan, PhD; Paul F. Cervavagaugh, Jr., PhD; Keith S. Rettinger, MD, MPH, for the Protocol 016 Study Group

Approval from age 9

Approval for males

End-of-study safety, immunogenicity, and efficacy of quadrivalent HPV (types 6, 11, 16, 18) recombinant vaccine in adult women 24–45 years of age

X Castellsague1; N Muñoz2; P Pinna3; D Ferris4; J Misonou5; H Ackel6; J Luna7; K Myers8; S Hilyary9; OM Boudina10; J Bryan11; S Visco12, BM Haap13 and A Sath14

Approval up to age 45

Approval for 2 dose schedule in young kids
HPV Vaccination Guidelines

Who Gets 2 Doses?

- A 2-dose schedule is recommended for people who get the first dose before their 13th birthday. In a 2-dose series, the second dose should be given 6–12 months after the first dose (0, 6–12 month schedule).
- The minimum interval is 5 months between the first and second dose. If the second dose is administered after a shorter interval, a third dose should be administered a minimum of 5 months after the first dose and a minimum of 12 weeks after the second dose.
- If the vaccination schedule is interrupted, vaccine doses do not need to be repeated (no maximum interval).
- Immunogenicity studies have shown that 2 doses of HPV vaccine given to 9–14 year-olds at least 6 months apart provided as good or better protection than 3 doses given to older adolescents or young adults.

Who Gets 3 Doses?

- A 3-dose schedule is recommended for people who get the first dose on or after their 15th birthday, and for people with certain immunocompromising conditions.
- In a 3-dose series, the second dose should be given 1–2 months after the first dose, and the third dose should be given 6 months after the first dose (0, 1–2, 6 month schedule).
- The minimum intervals are 4 weeks between the first and second dose, 12 weeks between the second and third doses, and 5 months between the first and third doses. If a vaccine dose is administered after a shorter interval, it should be re-administered after another minimum interval has elapsed since the most recent dose.
- If the vaccination schedule is interrupted, vaccine doses do not need to be repeated (no maximum interval).

Start Talking Early
Ages 9-10
2 doses

On Time
Ages 11-12
2 doses

Late
Ages 13-14
2 doses

Late
Ages 15-26
3 doses
Current Indications

• Females
  • Age 9-45 for prevention of cervix, vulvar, vaginal, anal, oropharyngeal/other head and neck cancers (2020)
  • Cervical, vulvar, vaginal, anal precancerous/dysplastic lesions
  • Genital warts

• Males
  • Age 9-45 for prevention of anal, oropharyngeal/other head and neck cancers (2020)
  • Anal precancerous/dysplastic lesions
  • Genital warts
Current CDC Recommendations

• Any licensed HPV vaccine can be used to complete series on same schedule
• No maximum interval (no need to repeat dose if schedule interrupted)
• Minimum intervals
  • 4 weeks b/w 1st and 2nd dose
  • 12 weeks b/w 2nd and 3rd dose
  • 5 months b/w 1st and 3rd dose
  • If 2 dose regimen, 5 months b/w 1st and 2nd dose
Current CDC Recommendations

• Age 27-45: consider for those most likely to benefit
  • Shared decision-making considerations:
    • Adults at risk of new infection (new sexual partner)
    • Change in life circumstances; people living longer
    • No clinical Ab test to determine immunity
    • Prophylactic; does not treat/prevent progression if already infected
    • Cost

• Not recommended in pregnancy (not studied)
• Immunocompromised: 3 doses
Safety

• Most common adverse reactions:
  • Injection site reactions (20-90%)
  • Temp 100F (10-30%)

• Well tracked and monitored
• 270 Million doses worldwide
• 120 Million doses in US
Contraindications/Precautions

• Anaphylaxis to vaccine component
• Anaphylactic allergy to latex (bivalent)
• Immediate hypersensitivity to yeast
• Moderate or severe acute illness (precaution—defer until sx improve)
• Minor acute illness is NOT a reason to defer vaccination
Review updates in research on the effects of HPV vaccine on pre-cancer and cancer
Efficacy of HPV Vaccine

• Australia was the first country to implement a national HPV vaccination program in 2007

• Other European countries have also reached the 10-year post-HPV vaccination program implementation period

• Data on the efficacy of vaccination published
# Efficacy of HPV Vaccine

Estimates of genital HPV prevalence among sexually active women aged 18–24 years, by HPV type, Australia, 2005–2012 (n = 1,260)

<table>
<thead>
<tr>
<th>HPV type</th>
<th>Pre-vaccination era (2005–07)</th>
<th>Post-vaccination era (2010–12)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall population prevalence</td>
<td>Overall population prevalence</td>
<td>Prevalence in vaccinated</td>
</tr>
<tr>
<td>Overall</td>
<td>5.5%</td>
<td>0.9%</td>
<td>0.2%</td>
</tr>
<tr>
<td>HPV 6</td>
<td>1.5%</td>
<td>0.4%</td>
<td>0%</td>
</tr>
<tr>
<td>HPV 11</td>
<td>21.3%</td>
<td>4.2%</td>
<td>1.5%</td>
</tr>
<tr>
<td>HPV 16</td>
<td>8.4%</td>
<td>1.9%</td>
<td>0.6%</td>
</tr>
<tr>
<td>HPV 18</td>
<td>5.0%</td>
<td>4.0%</td>
<td>2.7%</td>
</tr>
<tr>
<td>HPV 31</td>
<td>4.0%</td>
<td>1.5%</td>
<td>1.4%</td>
</tr>
<tr>
<td>HPV 33</td>
<td>1.0%</td>
<td>2.6%</td>
<td>1.7%</td>
</tr>
<tr>
<td>HPV 45</td>
<td>7.4%</td>
<td>8.2%</td>
<td>6.9%</td>
</tr>
<tr>
<td>HPV 52</td>
<td>5.5%</td>
<td>3.4%</td>
<td>3.9%</td>
</tr>
<tr>
<td>HPV 58</td>
<td>6.9%</td>
<td>1.3%</td>
<td>0.2%</td>
</tr>
<tr>
<td>HPV 6/11</td>
<td>26.2%</td>
<td>5.4%</td>
<td>2.1%</td>
</tr>
<tr>
<td>HPV 31/33/45</td>
<td>9.4%</td>
<td>7.8%</td>
<td>5.6%</td>
</tr>
<tr>
<td>4vHPV types</td>
<td>28.7%</td>
<td>6.5%</td>
<td>2.3%</td>
</tr>
<tr>
<td>High-risk HPV types</td>
<td>47.0%</td>
<td>34.9%</td>
<td>34.4%</td>
</tr>
<tr>
<td>All HPV types</td>
<td>59.9%</td>
<td>48.8%</td>
<td>40.4%</td>
</tr>
</tbody>
</table>

---

**Euro Surveill. 2018;23(41)**
Efficacy of HPV Vaccine

• Additional findings
  • Substantial decrease in genital condylomas
  • Decrease in HPV prevalence among heterosexual men
    • Herd immunity effect

• Mathematical models
  • Reduction in other HPV-associated cancers (anal, vulvar, vaginal, oral, oropharyngeal)

* Euro Surveill. 2018;23(41)
HPV Vaccination Reduces Cervical Pre-Cancers

- Women have seen dramatic decreases in high-grade cervical lesions in the U.S.

Slide from National HPV Roundtable
Duration of Protection

• Continued protection against high grade cervical, vaginal, vulvar neoplasia observed through at least 10 years after vaccination
• Persistent antibody levels and protection against infection also reported up to 10 years after vaccination
• Additional data as followed over time
• No current evidence that booster/revaccination is necessary

Prevention of Cervical Cancer


• Cross-sectional SEER study
• Compared 4 year average annual incidence of cervix cancer in 2003-2006 and 2011-2014 (pre and post vaccine)
• 4 year average annual incidence rates (age 15-24)
  • 29% lower post vs pre vaccine (6.0 vs 8.4 per 1,000,000 people)
  • No significant decrease for age 25-34
Prevention of Cervical Cancer

- N = 1,672,983
  - 527,871 vaccinated; 1,145,112 unvaccinated
  - Among vaccinated, 83.2% initiated before 17 y/o

- Cervical cancer cases
  - 19 in vaccinated
    - 2 if vaccinated before 17 y/o
    - 17 if vaccinated age 17-30 y/o
  - 538 in unvaccinated
Prevention of Cervical Cancer

HPV Vaccination and Risk of Invasive Cervical Cancer

Lei et al. NEJM 2020;383:1340-1348

• Incidence rate ratio vaccinated/unvaccinated adjusted for age at f/u = 0.51
  • Adjusted for other covariates = 0.37
  • Adjusted for all covariates
    • 0.12 if vaccinated <17 y/o
    • 0.47 if vaccinated age 17-30 y/o

• Risk of cervical cancer in those vaccinated before 17 y/o was 88% lower than those never vaccinated
The estimated relative reduction in cervical cancer rates by age at vaccine offer were 34% (95% CI 25–41) for age 16–18 years (school year 12–13), 62% (52–71) for age 14–16 years (school year 10–11), and 87% (72–94) for age 12–13 years (school year 8), compared with the reference unvaccinated cohort. The corresponding risk reductions for CIN3 were 39% (95% CI 36–41) for those offered at age 16–18 years, 75% (72–77) for age 14–16 years, and 97% (96–98) for age 12–13 years. These results remained similar across models. We estimated that by June 30, 2019 there had been 448 (339–556) fewer than expected cervical cancers and 17 235 (15 919–18 552) fewer than expected cases of CIN3 in vaccinated cohorts in England.
Figure 2 shows the model 3 estimates of cumulative incidence for age 20 years to younger than 30 years for cohorts 4 to 7.
Oral Health and HPV Vaccine

HPV Vaccine Limitations

• Perception issues regarding efficacy and safety

• Incomplete protection against all oncogenic HPV types

• Effect on cervical cancer screening
  • 96% patients aware of pap need after vaccination

• Vaccine cost
  • 9-valent full schedule $360-$580

• Low provider recommendation (72.6%)
  • Safety concerns, personal attitudes and beliefs, limited knowledge of HPV carcinogenesis and vaccine benefits, concerns about reimbursement
HPV Vaccine Fall due to COVID-19

- Monthly routine vaccination use per 1000 vaccine-eligible children and adolescents enrolled in Louisiana Medicaid in the years before (2017-2019) and during the COVID-19 pandemic (2020)

- Compared to the 2017-2019 average vaccination rates, we found a 28% reduction in measles, mumps, and rubella (MMR), a 35% reduction in human papillomavirus (HPV), and a 30% reduction in tetanus, diphtheria, pertussis (Tdap) vaccinations in 2020

- Vaccine uptake was lower in April 2020 after the declaration of a state of emergency and in late summer when back-to-school vaccinations ordinarily occur, little evidence of recovery in later months

Opportunities to Leverage due to COVID-19

“The lessons learned and the technical, logistical and human resources which have been established to combat COVID-19 by vaccination and testing”

Engaging Communities and Tailoring Messaging

- Immigrant community education and outreach
- Language and literacy choices
- Lay leader engagement

HPV Vaccine: Opportunities for Childhood Cancer Survivors

- Higher disease burden of HPV related diseases and cancer
- Lower HPV Vaccine rates
How Can We Ensure Vaccination?
CDC Strategies

• Bundle your recommendation
• Ensure a consistent message
• Use every opportunity to vaccinate
• Provider person examples
• Effectively answer questions
Summary

• HPV vaccine is safe, effective, and durable
• Recent evidence for cervical cancer prevention in addition to dysplasia is maturing
• Vaccination rates are improving but still not at goal
• COVID pandemic continues to significant negative impact on preventive care
• Implementation of strategies to ensure routine vaccination coverage urgently needed
Other Resources

• Hpvroundtable.org
• ACS (cancer.org)
• HPV VACs (Vaccinate Adolescents against Cancers) Program
• Mission: HPV Cancer Free
• CDC.gov
Please feel free to reach out!

THANKS!

nlee@bsd.uchicago.edu