HPV: Where Are We Now?
An Update on Screening and Vaccination

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Disclosure

I have no disclosures
Cervical Cancer

- Cervical cancer is one of the leading causes of cancer death in females worldwide
  - 530,000 cases and 275,000 deaths annually
  - 3rd leading cause of cancer death in women worldwide

Rates of HPV-Associated Cancer and Median Age at Diagnosis Among Females in the United States, 2004–2008

- **Cervix**
- **Vulva**
- **Vagina**
- **Anus**
- **Oropharynx**

Age-adjusted to the 2000 U.S. standard population.

*The vaginal cancer statistic for women between the ages of 20 and 39 is not shown because there were fewer than 16 cases.*

Data from population-based cancer registries participating in the CDC-supported National Program of Cancer Registries and/or the National Cancer Institute-supported Surveillance, Epidemiology and End Results Program, meeting criteria for high data quality, and covering 100% of the population. Published in: Watson et al. Human papillomavirus-associated cancers—United States, 2004–2008. MMWR 2012;61:258–261.
Impact of U.S. Screening Programs

Wright TC et al Blaustein’s Pathology of the Female Genital Tract. 5th ed. 2002
Trends in Cervical Cancer Diagnosis

[Graph showing trends in cervical cancer diagnosis rates per 100,000 population over time for different age groups.]

National Cancer Statistics
SEER database
HPV is also known as the Human Papilloma virus, affects both men and women. Over 80 types of HPV have been identified. Some strands have been found to cause cervical cancer, oral cancer, penile cancer and anal cancer. There is a definitive link between oral sex and oral cancer. Studies show that men are 35% more likely to develop HPV-related oral cancer than women. Between 1973 and 2004, the incidence of HPV-related oral cancers among people in their 40s nearly doubled.

Doctors estimate that HPV is the primary cause of the estimated 5,600 cancers that are found each year in the tonsils, lower tongue and upper throat. The American Cancer Society estimates that in 2006, over 9,700 women were diagnosed with cervical cancer, and 3,700 women died from it in the United States. Of an estimated 28,900 cases of oral cancer a year, 18,550 are in men. Studies have shown that among active teens, 80% of oral sex is unprotected.

The prevalence of high-risk genital HPV in women in the U.S. is highest in the 14- to 19-year-old age groups. About 20 million people in the U.S. are currently infected with HPV. Studies show that the Human Papilloma virus is transmitted through direct contact. Each year another 6.2 million people get a new HPV infection. An estimated one million sexually active people in the United States currently have visible genital warts.

It is estimated that 80 percent of all women and 50% of men and women combined will get at least one type of genital HPV. The No. 1 risk factor for getting HPV is a high number of sexual partners.
Human Papilloma Virus

• Most common STI in the United States
  – Prevalence – 79 million
  – Incidence – 14 million/year
  – Most patients do not exhibit clinical disease

• Annual cost $8 billion
  (Dunne EF & Park IU. Infect Dis Clin N Am 27(2013); 767-78)
Human Papilloma Virus

Munoz et al, Vaccine 2006
Initiating Replication

Munoz et al, Vaccine 2006
# Mucosal HPV

<table>
<thead>
<tr>
<th>Anogenital HPV</th>
<th>Low Risk</th>
<th>High Risk (Oncogenic)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV Types</td>
<td>6, 11, 40, 42, 43, 44, 53, 54, 61, 72, 73, 81</td>
<td>16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 82</td>
</tr>
<tr>
<td>Disease Spectrum</td>
<td>Anogenital wart</td>
<td>Cervical cancer</td>
</tr>
<tr>
<td></td>
<td>Recurrent respiratory papillomatosis (RRP)</td>
<td>Oropharyngeal cancer</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anal cancer</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vulvar cancer</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Penile cancer</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vaginal cancer</td>
</tr>
</tbody>
</table>
Natural History of HPV Infection

• Transient infection common
  – Year 1 – 70%
  – Year 2 – 90%

• Persistent infection
  – Necessary for disease progression
  – Oncogenic HPV → dysplasia/cancer
HPV Mediated Cancer in the United States

Total (N = 34 788)
- 9.3% (n = 3242)
- 2.9% (n = 1001)
- 2.1% (n = 734)
- 32.7% (n = 11 388)
- 15.6% (n = 5 434)

Men (N = 13 446)
- 7.4% (n = 1001)
- 14.4% (n = 1 934)
- 37.3% (n = 12 989)

Women (N = 21 342)
- 11.6% (n = 2 478)
- 15.2% (n = 3 242)
- 3.4% (n = 734)
- 53.4% (n = 11 388)
- 78.2% (n = 10 511)
- 16.4% (n = 3 500)
# Estimated Cancer Statistics - 2014

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Cases</th>
<th>Deaths</th>
<th>% Oncogenic HPV</th>
<th>% HPV16/18</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oropharynx</td>
<td>42,440</td>
<td>8,390</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>Cervix</td>
<td>12,360</td>
<td>4,020</td>
<td>99</td>
<td>70</td>
</tr>
<tr>
<td>Anus</td>
<td>7,210</td>
<td>950</td>
<td>90</td>
<td>75</td>
</tr>
<tr>
<td>Vulva</td>
<td>4,850</td>
<td>1,030</td>
<td>45</td>
<td>45</td>
</tr>
<tr>
<td>Vagina</td>
<td>3,170</td>
<td>880</td>
<td>55</td>
<td>55</td>
</tr>
<tr>
<td>Penis</td>
<td>1,640</td>
<td>320</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>71,670</strong></td>
<td><strong>15,590</strong></td>
<td></td>
<td><strong>44,105</strong></td>
</tr>
</tbody>
</table>

HPV-Associated Cervical Cancer Incidence Rates by State, United States, 2004-2008

*Age-adjusted to the 2000 U.S. standard population.
Data from population-based cancer registries participating in the CDC-supported National Program of Cancer Registries and/or the National Cancer Institute-supported Surveillance, Epidemiology and End Results Program, meeting criteria for high data quality, and covering 100% of the population. Published in: Watson et al. Human papillomavirus-associated cancers—United States, 2004–2008. MMWR 2012;61:258–261.
HPV Types That Cause Squamous-Cell Cervical Cancer Worldwide

- HPV 16: 14%
- HPV 18: 3%
- HPV 16 and 18: 2%
- HPV 31: 5%
- HPV 45: 3%
- HPV 52: 3%
- HPV 58: 3%
- HPV negative: 15%
- All other HPV types: 52%

Prevention of HPV-Mediated Cancer

• Primary Prevention
  – Bivalent vaccine
  – Quadrivalent vaccine

• Secondary Prevention
  – Cervix only
    • Pap smear screening
    • HPV testing
### United States screening guidelines for women at average risk for cervical cancer (2013)

<table>
<thead>
<tr>
<th>Category</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial Screening</strong></td>
<td>Begin at age 21yrs</td>
</tr>
<tr>
<td></td>
<td>Women &lt;21 yrs.. should not be screened regardless of risk factors</td>
</tr>
<tr>
<td><strong>Annual Screening</strong></td>
<td>Not recommended for any age group</td>
</tr>
<tr>
<td><strong>Screening Method and Interval</strong></td>
<td><strong>Age 21-29:</strong> Cytology alone every 3 yrs. (no co-testing)</td>
</tr>
<tr>
<td></td>
<td><strong>Age 30-35:</strong> Cytology alone every 3 yrs. Cytology + HPV co-testing every 5 yrs.</td>
</tr>
<tr>
<td><strong>Cessation of screening</strong></td>
<td>Age &gt; 65 with adequate screening history</td>
</tr>
<tr>
<td><strong>Post-hysterectomy screening</strong></td>
<td>Cervix Removed: No history of dysplasia/cancer – discontinue</td>
</tr>
<tr>
<td></td>
<td>Cervix Retained: Continue per screening guidelines</td>
</tr>
<tr>
<td><strong>Screening in vaccinated women</strong></td>
<td>Continue screening according to age specific recommendations</td>
</tr>
</tbody>
</table>

[www.cdc.gov/cancer/cervical guidelines](http://www.cdc.gov/cancer/cervical guidelines)
## Screening

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytology</td>
<td>31-78%</td>
<td>91-96%</td>
</tr>
<tr>
<td>HPV testing</td>
<td>61-100%</td>
<td>62-96%</td>
</tr>
</tbody>
</table>
The HPV vaccine

- L1 capsid proteins
  - Create “virus-like” particles
- Greater levels of neutralizing antibody than natural infection
  - Durable antibody production
- Non-infectious
- Non-oncogenic
# The HPV Vaccines

<table>
<thead>
<tr>
<th></th>
<th>Bivalent</th>
<th>Quadrivalent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brand Name</td>
<td>Cervarix</td>
<td>Gardasil</td>
</tr>
<tr>
<td>Manufacturer</td>
<td>Glaxo Smith Kline</td>
<td>Merck</td>
</tr>
<tr>
<td>HPV types covered</td>
<td>HPV 16, 18</td>
<td>HPV 6, 11, 16, 18</td>
</tr>
<tr>
<td>Patients studied</td>
<td>&gt;27,000</td>
<td>&gt;25,000</td>
</tr>
<tr>
<td>Inclusion of males</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Dose schedule</td>
<td>3 doses: 0, 1, 6 months</td>
<td>3 doses: 0, 2, 6 months</td>
</tr>
<tr>
<td>Duration of immunity</td>
<td>&gt; 6 years</td>
<td>&gt;5 years</td>
</tr>
<tr>
<td>Cross protection observed</td>
<td>HPV 31, 45, 52</td>
<td>HPV 31, 45, 52</td>
</tr>
</tbody>
</table>
ACIP Recommendations

General Female Population

- Vaccine
  - Bivalent or Quadrivalent

- Recommendation
  - Routine administration
    - Age 11-12 yrs.
  - Accepted age range
    - Age 9-26 yrs.

General Male Population

- Vaccine
  - Quadrivalent

- Recommendation
  - Routine administration
    - Age 11-12 yrs.
  - Accepted age range
    - Age 11-21 yrs.
Are We Vaccinating Appropriately?
Actual and Achievable Vaccination Coverage if Missed Opportunities Were Eliminated: Adolescents 13-17 Years, NIS-Teen 2012

Among girls unvaccinated for HPV, 84% had a missed opportunity

Missed opportunity: Healthcare encounter when some, but not all ACIP-recommended vaccines are given.
HPV-1: Receipt of at least one dose of HPV.

Long Term Implications of Current Vaccination Rates

• 26 million girls < 13 y/o
  – No vaccination
    • 168,400 cervical cancers
    • 54,100 deaths
  – 30% vaccination rate prevents
    • 45,500 cancers
    • 14,600 deaths
  – 80% vaccination rate prevents
    • 98,800 cancers
    • 31,700 deaths
Conclusions

• HPV is a significant cause of cancer nationwide
• Cervical cancer remains the leading HPV-mediated cancer in women
• Prevention strategies are under utilized
References

- CDC. Grand Rounds: Reducing the burden of HPV-associated cancer and disease. MMWR 2014; 63(04); 69-72.
- Stanley M. HPV vaccination in boys. Hum Vac and Immuno 2014; 10(7):
# Screening Guidelines

<table>
<thead>
<tr>
<th>Group</th>
<th>ACOG 2009</th>
<th>USPSTF 2012</th>
<th>ACS 2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women age &lt;21</td>
<td>No screening</td>
<td>No screening</td>
<td>No screening</td>
</tr>
<tr>
<td>Women age 21–29</td>
<td>Cytology every 2 years; HPV testing not recommended</td>
<td>Cytology every 3 years; HPV testing not recommended</td>
<td>Cytology every 3 years; HPV testing not recommended</td>
</tr>
<tr>
<td>Women age 30–85</td>
<td>Cytology every 3 years if three consecutive normal results; addition of HPV testing also appropriate</td>
<td>Cytology every 3 years or cytology plus HPV testing every 5 years</td>
<td>Cytology plus HPV testing every 5 years (preferred) or cytology alone every 3 years; both are regardless of screening history</td>
</tr>
<tr>
<td>Women age &gt;85</td>
<td>Following three normal screening results and no abnormal results in the last 10 years, screening may be discontinued</td>
<td>If adequately screened in the past, screening should be discontinued</td>
<td>If adequately screened in the past, screening should be discontinued</td>
</tr>
<tr>
<td>Women with total hysterectomy and no prior history of high-grade CIN</td>
<td>No need to continue screening if hysterectomy was for benign indication</td>
<td>Screening should be discontinued</td>
<td>Screening should be discontinued</td>
</tr>
</tbody>
</table>

ACOG, American College of Obstetricians and Gynecologists; USPSTF, U.S. Preventive Services Task Force; ACS, American Cancer Society.