HPV and Men

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HPV

- Non-enveloped double-stranded DNA virus
- More than 100 different types
- More than 30 are sexually transmitted
- “High-risk” types (e.g. 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58) are associated with cervical and other anogenital cancers, as well as some oropharyngeal cancers
  - Necessary but not sufficient cause of cancer
- “Low-risk” types (e.g. 6, 11, 42, 43, 44) are associated with genital warts, mild cervical dysplasia, recurrent respiratory papillomatosis, but not cancer

- High-risk types are the most common genital HPV infections
HPV and Anogenital Warts

- HPV 6 and 11 most often associated\(^1\)
- Peak prevalence\(^2\)
  - Women 20-24 years (6.2/1000 person years)
  - Men 25-29 years (5/1000 person years)
- Infectivity >75\(\%\)\(^3\)
- Up to 40\(\%\) spontaneously remit\(^1\)

\(^1\)Wiley et al. *CID* 35:S210-24, 2002
\(^3\)Soper DE. In Novak’s Gynecology 13\(^{th}\) ed., Berek JS ed., 2002
Risk Factors for Women

- Young age
- Sexual behavior
  - Risk increases with increasing lifetime number of male sex partners
  - Early age of first sexual intercourse
- Sexual behavior of male sex partners–risk increases for women whose sex partners have multiple sex partners
- Immune status–HPV more likely to be detected in immune-suppressed women
Risk Factors for Men

- Greater lifetime number of sex partners
- Greater number of recent sex partners
- Being uncircumcised
- Immune status
Genital Warts: Appearance

- **Condylomata acuminata**
  - Cauliflower-like appearance
  - Skin-colored, pink, or hyperpigmented
  - May be keratotic on skin; generally non-keratinized on mucosal surfaces

- **Smooth papules**
  - Usually dome-shaped and skin-colored

- **Flat papules**
  - Macular to slightly raised
  - Flesh-colored, with smooth surface
  - More commonly found on internal structures (i.e., cervix), but also occur on external genitalia

- **Keratotic warts**
  - Thick horny layer that can resemble common warts or seborrheic keratosis
Genital Warts: Location

- Warts commonly occur in areas of coital friction.
- Perianal warts do not necessarily imply anal intercourse.
  - May be secondary to autoinoculation, sexual activity other than intercourse, or spread from nearby genital wart site.
- Intra-anal warts are seen predominantly in patients who have had receptive anal intercourse.
- Patients with visible warts can be simultaneously infected with multiple HPV types.
Genital Warts: Symptoms

- Genital warts usually cause no symptoms other than the warts themselves.
- Vulvar warts—dyspareunia, pruritis, burning discomfort
- Penile warts—occasional itching
- Urethral meatal warts—occasional hematuria or impairment of urinary stream
- Vaginal warts—usually asymptomatic; occasional discharge/bleeding, obstruction of birth canal (secondary to increased wart growth during pregnancy)
- Perianal warts—usually asymptomatic; pain, bleeding on defecation, itching
- Most patients have fewer than 10 genital warts, with total wart area of 0.5-1.0 cm².
Treatment Regimens

- Patient-applied and provider-administered therapies are available.
- Providers should be knowledgeable about and have available at least 1 patient-applied and 1 provider-administered treatment.
- Choice of treatment should be guided by:
  - The preference of the patient
  - The available resources
  - The experience of the healthcare provider
Factors Influencing Treatment Selection

- Wart size
- Number of warts
- Anatomic site of wart
- Wart morphology
- Patient preference
- Cost of treatment
- Convenience
- Adverse effects
CDC-Recommended Regimens For External Genital Warts (Patient-Applied)

- **Podofilox 0.5% solution or gel***
  - Patients should apply solution with cotton swab or gel with a finger to visible warts twice a day for 3 days, followed by 4 days of no therapy.
  - Cycle may be repeated as needed up to 4 cycles.
- OR

- **Imiquimod 5% cream***
  - Patients should apply cream once daily at bedtime, 3 times a week for up to 16 weeks.
  - Treatment area should be washed with soap and water 6-10 hours after application.

* Safety not established in pregnancy
CDC-Recommended Regimens For External Genital Warts (Provider-Administered)

- Cryotherapy with liquid nitrogen or cryoprobe
  - Repeat applications every 1-2 weeks, OR
- Podophyllin resin 10%-25% in compound tincture of benzoin
  - Apply a small amount to each wart and allow to air dry
  - Treatment may be repeated weekly if needed, OR
- Trichloroacetic acid (TCA) or bichloroacetic acid (BCA) 80%-90%
  - Apply small amount only to warts and allow to dry
  - Treatment may be repeated weekly if needed, OR
- Surgical removal--tangential scissor excision, tangential shave excision, curettage, or electrosurgery
- CDC recommended alternatives
  - Intralesional interferon
  - Laser surgery
Treatment of Visible Warts

- Goal is to remove symptomatic wart
- Current treatment does NOT impact the natural history or eradicate infection
- Removal may not decrease infectivity
- Without treatment: warts may resolve, be unchanged, or increase
- Treatment is not likely to influence the development of cervical cancer
HPV Disease Burden in the United States

- Anogenital HPV is the most common sexually transmitted infection in the US
  - Estimated 20 million currently infected
  - 6.2 million new infections/year
- Common among adolescents and young adults
- Estimated 80% of sexually active women will have been infected by age 50
- Infection also common in men
- The American Cancer Society estimates that in 2008
  - 11,070 new cervical cancer cases
  - 3,870 cervical cancer deaths
- Almost 100% of these cervical cancer cases will be caused by one of the 40 HPV types that infect the mucosa
Weighted Percentage of Sexually Active Persons Aged 18 to 54 Years Who Reported Ever Having a Diagnosis of Genital Warts


Overall: 5.6%
Women: 7.2%
Men 4.0%
Correlates of HPV Infection
Multiple Studies

❖ Gender
❖ Race/ethnicity
❖ Number of lifetime sex partners
❖ Substance use
❖ Educational attainment and socio-economic status
Correlates of Clearing HPV Infection in Men

- Circumcision
Weighted Seroprevalence of HPV Types, Age 14-59 Years, NHANES 2003-04

- HPV 6
- HPV 11
- HPV 16
- HPV 18
- Any

Percent Seropositive

Chart showing seroprevalence for males and females of different HPV types.
Seroprevalence of HPV Types Among Females and Males
NHANES 2003-04

Females

Males

All Four Types
Weighted Seroprevalences of HPV Types in Males, 14-59 y.o., NHANES, 2003-2004, by Race/Ethnicity
HPV Prevalence, Incidence and Duration
Males, 18-44 y.o., Tucson, HPV Identification
Giuliano, et al. JID 2008; 198: 857

- **Prevalence = 30%**
  - Oncogenic = 16.6% (51, 39, 16, 52, …)
  - Non-oncogenic = 13.5% (84, 6, 53, 54, …)

- **Incidence = 29.4 per 1,000/person-months**
  (42.3 in negative at enrollment)
  - Oncogenic = 15.5 per 1,000/person-months
    (16, 52, 51, 39, …)
  - Non-oncogenic = 15.4 per 1,000 person-months
    (84, 62, 53, 6, …)

- **Median time to clearance = 5.9 months**
  ~75% by 12 months
  - Oncogenic = 5.8 months
  - Non-oncogenic = 6.0 months
Anal HPV Infection in Men

- **Men who have sex with men** (Chin-Hong, et al. JID 2004; 190:2070-76)
  - Prevalence: 57%
    - 45% had an oncogenic type
  - Independent risk correlates
    - Receptive anal intercourse
    - Number of partners during preceding six months

- **Men who have sex with men, HIV+ & HIV-** (Palefsky, et al. JID 1998; 177:361-7)
  - Prevalence: HIV- = 61%; HIV+ = 93%
    - Oncogenic types: HIV- = 29%; HIV+ = 80%

- **Heterosexual men** (Nyitray, et al. JID 2008; 197:1675-84)
  - Prevalence: 24.8%
    - 33.3% had an oncogenic type
  - Independent risk correlates
    - Lifetime sex partners
    - Frequency of sex during preceding month
Anal HPV Infection in Men

MSM Prevalent Infection

NHANES
HPV-6, 11, 16, 18 Seropositive

Chin-Hong, et al. JID 2004; 190:2070-76
# HPV Types in External Warts in Men and Women in France

EDiTH Study Data, Aubin, et al. CID 2008; 47:610-615

<table>
<thead>
<tr>
<th>HPV Findings</th>
<th>Men (%)</th>
<th>Women (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 209</td>
<td></td>
<td>N = 214</td>
</tr>
<tr>
<td>One or more low risk types (no high risk)</td>
<td>72.7</td>
<td>52.3</td>
</tr>
<tr>
<td>One or more high risk types (no low risk)</td>
<td>3.8</td>
<td>6.5</td>
</tr>
<tr>
<td>Low and high risk types</td>
<td>21.0</td>
<td>34.1</td>
</tr>
<tr>
<td>Undetermined types</td>
<td>1.9</td>
<td>5.1</td>
</tr>
<tr>
<td>HPV negative</td>
<td>0.5</td>
<td>1.9</td>
</tr>
<tr>
<td>One or more low risk type</td>
<td>93.8</td>
<td>86.4</td>
</tr>
<tr>
<td>One or more high risk type</td>
<td>24.9</td>
<td>40.7</td>
</tr>
</tbody>
</table>

23 genotypes identified, most frequent:  
HPV-6 = 68.3%; HPV-11 = 16.1%; HPV-16 = 9.0%; HPV-51 = 8.0%; HPV-52 = 6.4%; HPV-66 = 5.7%; HPV-53 = 5.0%; HPV-31 = 3.3% HPV-18 = 2.6%; ...

EDiTH Study invasive Cervical cancer:  
HPV-16 = 73%; HPV-18 = 19%  
CIN 2/3: HPV-16 = 62%; HPV-18 = 4%
Clinical Conditions Associated with HPV Types 6,11,16,18

<table>
<thead>
<tr>
<th>Condition</th>
<th>Incidence Per 100,000 U.S.</th>
<th>Estimated Attributable HPV 6,11</th>
<th>Estimated Attributable HPV 16,18</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genital warts</td>
<td>~300</td>
<td>90%</td>
<td>-</td>
</tr>
<tr>
<td>Recurrent respiratory papillomatosis</td>
<td>~1</td>
<td>90%</td>
<td>-</td>
</tr>
<tr>
<td>Low grade cervical abnormalities</td>
<td>~700</td>
<td>10%</td>
<td>30%</td>
</tr>
<tr>
<td>High grade cervical abnormalities</td>
<td>~100</td>
<td>-</td>
<td>50%</td>
</tr>
<tr>
<td>Cervical cancer</td>
<td>9</td>
<td>-</td>
<td>70%</td>
</tr>
<tr>
<td>Vaginal/vulvar cancer</td>
<td>2</td>
<td>-</td>
<td>32%</td>
</tr>
<tr>
<td>Anal cancer</td>
<td>1</td>
<td>-</td>
<td>83%</td>
</tr>
<tr>
<td>Penile cancer</td>
<td>1</td>
<td>-</td>
<td>25%</td>
</tr>
<tr>
<td>Head and neck cancers</td>
<td>1 Woman 5 Men</td>
<td>-</td>
<td>22-31%</td>
</tr>
</tbody>
</table>
Anogenital HPV Implications in Men

- **Self**
  - Anogenital warts
  - Penile and anal neoplasms

- **Others**
  - Transmission to sexual partners
  - Warts and neoplasm in sexual partners
Anal Cancer Incidence and Association With HPV

- Annual incidence among males in the United States is 2,020
- 80% to 90% of cases are HPV related
- 73% of all tumors associated with HPV 16
- Incidence of anal cancer is increasing

Incidence of Anal Cancer by Year

Incidence per 100,000

## Anal Cancer

<table>
<thead>
<tr>
<th>Race</th>
<th>Male Incidence Rate</th>
<th>Male Average Annual Count</th>
<th>Female Incidence Rate</th>
<th>Female Average Annual Count</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
<td>1.0</td>
<td>1,083</td>
<td>1.5</td>
<td>1,935</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>1.0</td>
<td>927</td>
<td>1.6</td>
<td>1,739</td>
</tr>
<tr>
<td>Black</td>
<td>1.2*</td>
<td>124</td>
<td>1.3*</td>
<td>152</td>
</tr>
<tr>
<td>API</td>
<td>0.2*</td>
<td>8</td>
<td>0.4*</td>
<td>19</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>1.0</td>
<td>1,011</td>
<td>1.5</td>
<td>1,796</td>
</tr>
<tr>
<td>Hispanic</td>
<td>0.8*</td>
<td>72</td>
<td>1.5</td>
<td>139</td>
</tr>
</tbody>
</table>

*p < 0.05*
Anal Pap Testing

Can detect anal cancer in early stages when still treatable

No national recommendations
  ▪ Cost effective

Researchers suggest screening
  ▪ Annually if HIV+
  (certain other immuno-compromised patients)
  ▪ Each 2-3 years if MSM
Interest in Anal Pap Tests

Interest is high.

Cost cut interest in testing by more than half

Reed, Reiter, Smith, Palefsky, & Brewer, 2009. In press at AJPH.
Use of Anal Pap Tests

HIV+ men should be tested annually

Less than 1/3 of HIV+ men have ever been tested

Reed, Reiter, Smith, Palefsky, & Brewer, 2009. In press at AJPH.
Squamous Cell Carcinoma of the Penis, U.S., 1998-2003

<table>
<thead>
<tr>
<th>Incidence Rate</th>
<th>Average Annual Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>0.8</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>0.8</td>
</tr>
<tr>
<td>Black</td>
<td>0.8</td>
</tr>
<tr>
<td>API</td>
<td>0.4*</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>0.8</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1.3*</td>
</tr>
</tbody>
</table>

Incidence Rate and Average Annual Count for Squamous Cell Carcinoma of the Penis by Race and Ethnicity.
Circumcision, HPV Infection in Men, Cervical Cancer in Women

- International Multicenter Study (NEJM, 2002), circumcised versus uncircumcised men
  - Penile HPV – adjusted OR = 0.37 (0.16, 0.85)
  - Cervical cancer in monogamous women with male partners with multiple sex partners – adjusted OR = 0.42 (0.23, 0.79)
- Hernandez, et al. (JID 2008; 197: 787-794), uncircumcised men c/w circumcised
  - Penile HPV – adjusted OR = 1.96 (1.02-3.75)
  - Oncogenic HPV – adjusted OR = 2.51 (1.11, 5.69)
- Tobian, et al. (NEJM 2009; 360: 1298-1309), circumcision of HSV-2 seronegative men
  - 2-year prevalence of HPV infection – adjusted RR = 0.65 (0.46, 0.90)
Major Structural Viral Protein L1

- Highly immunogenic

- Can induce neutralizing antibodies (>40-fold higher than after natural HPV infection).

- Self-assemble to form Virus-Like Particles (VLPs)

Infectious Viral Particles (contain viral DNA)  
VLPs made in Insect Cells (no viral DNA)
<table>
<thead>
<tr>
<th></th>
<th>Gardasil® (Merck)</th>
<th>Cervarix® (GSK)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>U.S. Licensure</strong></td>
<td>June 2006</td>
<td>October 2009</td>
</tr>
<tr>
<td><strong>Antigen</strong></td>
<td>20 mcg HPV6 L1 VLP</td>
<td>20 mcg HPV16 L1 VLP</td>
</tr>
<tr>
<td></td>
<td>40 mcg HPV11 L1 VLP</td>
<td>20 mcg HPV18 L1 VLP</td>
</tr>
<tr>
<td></td>
<td>40 mcg HPV16 L1 VLP</td>
<td>20 mcg HPV18 L1 VLP</td>
</tr>
<tr>
<td></td>
<td>20 mcg HPV18 L1 VLP</td>
<td></td>
</tr>
<tr>
<td><strong>Adjuvant</strong></td>
<td>225 mcg aluminum hydroxyphosphate sulfate</td>
<td>AS04 (500 mcg aluminum hydroxide + 50 mcg 3-deacylated monophosphoryl lipid A)</td>
</tr>
<tr>
<td><strong>Dosing Schedule</strong></td>
<td>0, 2, 6 months</td>
<td>0, 1, 6 months</td>
</tr>
<tr>
<td><strong>Target Groups</strong></td>
<td>9-26 years, males &amp; females</td>
<td>10-25 years, females only</td>
</tr>
<tr>
<td><strong>Efficacy</strong></td>
<td>Comparable against 16/18 X-protection w/ 16 related types?</td>
<td>Comparable against 16/18, no 6/11 X-protection w/ 16 and 18 related types?</td>
</tr>
<tr>
<td><strong>Safety</strong></td>
<td>Comparable (primarily local adverse events)</td>
<td></td>
</tr>
<tr>
<td><strong>Immunogenicity</strong></td>
<td>?Comparable 50x natural immunity</td>
<td>?Comparable 80-100x natural immunity</td>
</tr>
<tr>
<td><strong>Cost</strong></td>
<td>$120-130/dose</td>
<td>$120-130/dose</td>
</tr>
</tbody>
</table>
HPV Vaccine Efficacy

- High efficacy among females without evidence of infection with vaccine HPV types
- No evidence of efficacy against disease caused by vaccine types with which participants were infected at the time of vaccination
- Prior infection with one HPV type did not diminish efficacy of the vaccine against other vaccine HPV types
## Efficacy Study in Adult Women

**HPV 6, 11, 16, 18-Related Persistent Infection, CIN or EGL**

*Per-Protocol Efficacy Population; Mean Follow-Up 2.2 Years*

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Vaccine (N=1910)</th>
<th>Placebo (N=1907)</th>
<th>Efficacy %</th>
<th>Efficacy (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV 6/11/16/18-Related Persistent Infection, CIN or EGL</td>
<td>4*</td>
<td>41</td>
<td>91</td>
<td>(74, 98)</td>
</tr>
<tr>
<td>HPV 16/18-Related Persistent Infection, CIN or EGL</td>
<td>4</td>
<td>23</td>
<td>83</td>
<td>(51, 96)</td>
</tr>
<tr>
<td>HPV 6/11-Related Persistent Infection, CIN or EGL</td>
<td>0</td>
<td>19</td>
<td>100</td>
<td>(79, 100)</td>
</tr>
</tbody>
</table>

*All cases were due to Type 16; 3 were persistent infection, 1 was a CIN 2 co-infection with Type 52 EGL – external genital lesion, CIN – cervical intraepithelial neoplasia*

Haupt, presented at Feb 2008 ACIP meeting

<table>
<thead>
<tr>
<th>Incident infection with HPV 16/18</th>
<th>HPV-16/18-AS04 adjuvanted vaccine</th>
<th>Placebo</th>
<th>Vaccine efficacy (%; 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total number of women</td>
<td>Women reporting ≥1 event</td>
<td>Total number of women</td>
</tr>
<tr>
<td>2-2 years</td>
<td>366</td>
<td>2</td>
<td>355</td>
</tr>
<tr>
<td>4-5 years</td>
<td>414</td>
<td>3</td>
<td>385</td>
</tr>
<tr>
<td>5-5 years</td>
<td>401</td>
<td>3</td>
<td>374</td>
</tr>
<tr>
<td>6-4 years</td>
<td>401</td>
<td>4</td>
<td>372</td>
</tr>
<tr>
<td>≥ASC-US</td>
<td>560</td>
<td>2</td>
<td>553</td>
</tr>
<tr>
<td>2-2 years</td>
<td>505</td>
<td>2</td>
<td>497</td>
</tr>
<tr>
<td>4-5 years</td>
<td>505</td>
<td>2</td>
<td>497</td>
</tr>
<tr>
<td>5-5 years</td>
<td>505</td>
<td>2</td>
<td>497</td>
</tr>
<tr>
<td>CIN1+</td>
<td>560</td>
<td>0</td>
<td>553</td>
</tr>
<tr>
<td>2-2 years</td>
<td>481</td>
<td>0</td>
<td>470</td>
</tr>
<tr>
<td>4-5 years</td>
<td>481</td>
<td>0</td>
<td>470</td>
</tr>
<tr>
<td>5-5 years</td>
<td>481</td>
<td>0</td>
<td>470</td>
</tr>
<tr>
<td>CIN2+</td>
<td>560</td>
<td>0</td>
<td>553</td>
</tr>
<tr>
<td>2-2 years</td>
<td>481</td>
<td>0</td>
<td>470</td>
</tr>
<tr>
<td>4-5 years</td>
<td>481</td>
<td>0</td>
<td>470</td>
</tr>
<tr>
<td>5-5 years</td>
<td>481</td>
<td>0</td>
<td>470</td>
</tr>
<tr>
<td>6-4 years</td>
<td>481</td>
<td>0</td>
<td>470</td>
</tr>
</tbody>
</table>
Cross-Protection Against Persistent Infection* in Women with Non-Vaccine Types

<table>
<thead>
<tr>
<th>HPV Type</th>
<th>Quadrivalent HPV Vaccine % (95% CI)</th>
<th>Bivalent HPV Vaccine % (97.5% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV 31</td>
<td>46 (15-66)</td>
<td>36 (1-60)</td>
</tr>
<tr>
<td>HPV 33</td>
<td>29 (-45-66)</td>
<td>37 (-10-64)</td>
</tr>
<tr>
<td>HPV 45</td>
<td>8 (-67-49)</td>
<td>60 (3-85)</td>
</tr>
<tr>
<td>HPV 52</td>
<td>18 (-21-45)</td>
<td>32 (4-52)</td>
</tr>
<tr>
<td>HPV 58</td>
<td>6 (-54-42)</td>
<td>-31 (-132-25)</td>
</tr>
</tbody>
</table>

*detection of same HPV type >=6 months apart in women with at least 1 dose of vaccine

Herrero, *JID* 2009
Higher titers found

- Against HPV16
- In younger patients

Munoz et al. *Lancet* 2009
Haupt, ACIP, June 2009
Routine HPV Vaccination Recommendations

- ACIP recommends routine vaccination of females 11 or 12 years of age, vaccination series can be started as young as 9 years of age
- “Catch-up” vaccination recommended for females 13 through 26 years of age
- An accelerated schedule using minimum intervals is not recommended
- Series does not need to be restarted if the schedule is interrupted
- ACIP recently made a permissive recommendation for vaccinating males with HPV 6 and 11 containing vaccine, 9-26 years old
# HPV-Associated Disease

<table>
<thead>
<tr>
<th>Type</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
</table>
| 16/18 | 70% of Cervical Cancer  
70% of Anogenital Cancer | 70% of Anal Cancer  
Transmission to women |
| 6/11  | 90% of Genital Warts  
90% of RRP lesions | 90% of Genital Warts  
90% of RRP lesions  
Transmission to women |
<table>
<thead>
<tr>
<th>HPV 6/11/16/18 positive to one or more by</th>
<th>Overall (N=4065)</th>
<th>HM (N=3463)</th>
<th>MSM (N=602)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serology</td>
<td>7.6</td>
<td>5.0</td>
<td>22.8</td>
</tr>
<tr>
<td>PCR</td>
<td>12.2</td>
<td>8.8</td>
<td>30.5</td>
</tr>
<tr>
<td>PCR or Serology</td>
<td>17.3</td>
<td>13.3</td>
<td>39.1</td>
</tr>
</tbody>
</table>
### HPV 6/11/16/18-Related EGL Efficacy by Lesion Type

**Per Protocol Efficacy Population**

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>GARDASIL (N=2025)</th>
<th>Placebo (N=2030)</th>
<th>Observed Efficacy (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td># Cases</td>
<td>n</td>
<td># Cases</td>
</tr>
<tr>
<td>HPV 6/11/16/18-Related EGL</td>
<td>1394</td>
<td>3</td>
<td>1404</td>
<td>32</td>
</tr>
<tr>
<td>Condyoma</td>
<td>1394</td>
<td>3</td>
<td>1404</td>
<td>28</td>
</tr>
<tr>
<td>PIN 1 or worse</td>
<td>1394</td>
<td>0</td>
<td>1404</td>
<td>4</td>
</tr>
<tr>
<td>PIN 1</td>
<td>1394</td>
<td>0</td>
<td>1404</td>
<td>2</td>
</tr>
<tr>
<td>PIN 2/3 or Cancer</td>
<td>1394</td>
<td>0</td>
<td>1404</td>
<td>2</td>
</tr>
<tr>
<td>PIN 2/3</td>
<td>1394</td>
<td>0</td>
<td>1404</td>
<td>2</td>
</tr>
<tr>
<td>Cancer</td>
<td>1394</td>
<td>0</td>
<td>1404</td>
<td>0</td>
</tr>
</tbody>
</table>

**Merck Protocol 020 Efficacy Study in Men, Reported by Haupt, ACIP Meeting, 2/24/10**
<table>
<thead>
<tr>
<th>Endpoint</th>
<th>GARDASIL (N=299)</th>
<th>Placebo (N=299)</th>
<th>Observed Efficacy (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV 6/11/16/18-Related AIN</td>
<td>194</td>
<td>208</td>
<td>77.5</td>
<td>40, 93</td>
</tr>
<tr>
<td>AIN 1</td>
<td>194</td>
<td>144</td>
<td>73.0</td>
<td>16, 93</td>
</tr>
<tr>
<td>Condyoma</td>
<td>194</td>
<td>144</td>
<td>100.0</td>
<td>8, 100</td>
</tr>
<tr>
<td>Non-acuminate</td>
<td>194</td>
<td>170</td>
<td>60.4</td>
<td>-34, 91</td>
</tr>
<tr>
<td>AIN 2 or Worse</td>
<td>194</td>
<td>208</td>
<td>74.9</td>
<td>9, 95</td>
</tr>
<tr>
<td>AIN 2</td>
<td>194</td>
<td>208</td>
<td>75.8</td>
<td>-17, 98</td>
</tr>
<tr>
<td>AIN 3</td>
<td>194</td>
<td>208</td>
<td>63.7</td>
<td>-103, 96</td>
</tr>
<tr>
<td>Anal Cancer</td>
<td>194</td>
<td>208</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>
# HPV 16/18-Related AIN 2/3 Efficacy by Lesion Type

**MSM Per Protocol Efficacy Population**

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>GARDASIL (N=299)</th>
<th>Placebo (N=299)</th>
<th>Observed Efficacy (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td># Cases</td>
<td>n</td>
<td># Cases</td>
</tr>
<tr>
<td>HPV 16/18-Related AIN 2/3</td>
<td>192</td>
<td>1</td>
<td>205</td>
<td>8</td>
</tr>
<tr>
<td>By HPV Type</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV 16</td>
<td>167</td>
<td>1</td>
<td>170</td>
<td>6</td>
</tr>
<tr>
<td>HPV 18</td>
<td>173</td>
<td>0</td>
<td>193</td>
<td>2</td>
</tr>
<tr>
<td>By Lesion Type</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AIN 2</td>
<td>192</td>
<td>0</td>
<td>205</td>
<td>6</td>
</tr>
<tr>
<td>AIN 3</td>
<td>192</td>
<td>1</td>
<td>205</td>
<td>4</td>
</tr>
<tr>
<td>Anal Cancer</td>
<td>192</td>
<td>0</td>
<td>205</td>
<td>0</td>
</tr>
</tbody>
</table>

Merck Protocol 020 Efficacy Study in Men, Reported by Haupt, ACIP Meeting, 2/24/10
Effect of Inclusion of Other Health Conditions on the Cost-Effectiveness of Vaccination Strategies

Would He Get an HPV Vaccination to Protect You? Um, No

Friday, 06/12/2009 at 8:04 AM
Willingness

Most heterosexual men were unwilling to get HPV vaccine.

85% thought it was only for women – or just didn’t know!
Model for Assessing Human Papillomavirus Vaccination Strategies


Cervical Cancer

Warts

Male

Female
Impact of HPV Vaccine Efficacy in Boys on Cost Effectiveness Ratios

Kim & Goldie, BMJ 2009 Oct 8;339:b3884. doi: 10.1136/bmj.b3884
## Incremental Cost-effectiveness Analysis

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Discounted total</th>
<th>Incremental</th>
<th>(\Delta) Costs</th>
<th>(\Delta) QALY</th>
<th>$/QALY (\dagger)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Costs</td>
<td>QALY</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F14</td>
<td>1,657,060,138</td>
<td>49,381,805</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>F11+F14</td>
<td>1,701,890,888</td>
<td>49,383,159</td>
<td>44,830,750</td>
<td>1,354</td>
<td>$33,115</td>
</tr>
<tr>
<td>F14 (80)+M14 (80)</td>
<td>1,966,567,138</td>
<td>49,383,654</td>
<td>309,507,000</td>
<td>1,849</td>
<td>$167,364</td>
</tr>
</tbody>
</table>

\(\dagger\) Incremental to the F14 program

Fawziah Marra, Pharm.D., Pharmacy and Vaccine Services, BC Centre for Disease Control
Conclusions

- Routine vaccination of all boys not cost-effective, especially with high vaccine coverage in females and high levels of cervical cancer screening
- Bringing other morbidity into consideration favors male vaccination more from a cost standpoint
- Certain sub-groups of males at higher risk would benefit from HPV vaccine, especially with the low level of screening
- Would males accept HPV vaccine?
Correlates of HPV Vaccine Acceptability Among Heterosexual Men

- Ever had sex*
- Perceived risk of infection*
- Perceived benefit*
- Perceived risk of side effects (negative)**
- Hassle and cost (negative)*
- Self-efficacy to receive vaccine*
- Perceived as normative behavior*
- Familiarity with HPV vaccine**
- Tobacco use**

* Gerend and Barley, STD 2009; 36: 58-62
** Ferris, et al. JABFM 2009; 22: 34-42
Correlates of HPV Vaccine Acceptability Among Gay and Bisexual Men

- Physician’s recommendation
- ≥5 lifetime sexual partners
- Perceived severity of HPV-related disease
- Perceived effectiveness of HPV vaccine
- Anticipated regret

Estimated 1+ Dose HPV Vaccination Coverage, Females 13-17 Years

National Immunization Survey, 2008
National Coverage = 37%

Massachusetts:
≥1 dose = 53.3% (U.S. = 37.2%)
≥3 doses = 29.1% (U.S. = 17.9%)

Source: CDC. National, state, and local area vaccination coverage among adolescents aged 13-17 years---United States, 2008.
Bach PB. Gardasil: from bench, to bedside, to blunder.

Lancet 2010; 375: 963-964
9 Key Parental Perceptions

- Disease susceptibility,* ability of parent to control this
- Disease danger,* ability of parent to control disease outcome
- Reliability of disease information
- Vaccine danger*
- Would HPV vaccination encourage sex*
- Preference for errors of omission
- “Free ride” (trust in herd immunity)

Disinhibition

**Sex**
6%-12% of parents in the US believe HPV vaccine will make girls have sex.
(Brewer & Fazekas, 2007)

1 in 200 parents said it was the main reason for not vaccinating.
(Gottlieb, Brewer et al., 2009)

**Screening**
5% of females think getting HPV vaccine means they don’t need screening.
(Rodewald & Orenstein, 2009)