Use of HPV Vaccine in Males and Females

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Summary of the Clinical Problem
Human papillomavirus is highly prevalent. Certain subtypes are oncogenic and many are responsible for a wide range of disease. HPV types 16 and 18 cause about 70% of cervical cancers. Most of the remaining cases of cervical cancer are caused by other types of HPV. HPV types 16 and 18 are also associated with vulvar, vaginal, penile, anal, and oropharyngeal cancers. HPV types 6 and 11 cause approximately 90% of genital warts. The prevalence of infection is high but varies widely across populations. One recent study conducted in the United States, Brazil, and Mexico examined men who have sex with women and men. In this population, with a mean age of 32.5 years, 53.1% were infected with HPV and 30% were infected with oncogenic strains. A larger sample of women in the United States documented an overall prevalence of 26.8%. The highest prevalence was in women aged 20 to 24 years, 44.8% of whom were infected. An estimated 22,000 cancers associated with HPV types 16 and 18 occur annually in the United States.

Characteristics of the Guidelines Source
This guideline was published by the ACIP, which is under the jurisdiction of the US DHHS. The committee consists of 15 voting members who are selected by the secretary of the DHHS. Efforts are made to avoid conflict of interest among panel members by excluding people with "vaccine related interests" (Table). These interests include direct employment of a panelist or an immediate family member by a vaccine manufacturer, holding a patent on a vaccine or related product, or serving on a board of directors of a vaccine manufacturer. The committee members work with outside professional organizations (eg, American Academy of Pediatrics, American Academy of Family Physicians) when developing guidelines. ACIP meetings are open to the public and broadcast via live webcast.

Evidence Base
For the vaccine recommendation for boys and men, efficacy data came primarily from 2 large randomized clinical trials. For the vaccine recommendation for girls and women, efficacy data came from 4 randomized trials, 2 testing the efficacy of each vaccine. Trials assessed vaccine efficacy against anogenital lesions and intraepithelial neoplasia 2+. Vaccine efficacy rates ranged from 97% (95% CI, 79% to 100%) to 100% (95% CI, 94% to 100%) in the per-protocol analyses and 25.7% (95% CI, −1.1% to 45.6%) to 100% (95% CI, 79% to 100%) to 100% (95% CI, 94% to 100%)

Table. Guideline Rating

<table>
<thead>
<tr>
<th>Standard</th>
<th>Rating</th>
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<tbody>
<tr>
<td>1. Establishing transparency</td>
<td>Good</td>
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<tr>
<td>2. Management of conflict of interest in the guideline development group</td>
<td>Good</td>
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<td>3. Guideline development group composition</td>
<td>Good</td>
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<td>4. Clinical practice guideline—systematic review intersection</td>
<td>NA</td>
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<tr>
<td>5. Establishing evidence foundations and rating strength for each of the guideline recommendations</td>
<td>Fair</td>
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<tr>
<td>6. Articulation of recommendations</td>
<td>Good</td>
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<tr>
<td>7. External review</td>
<td>Fair</td>
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<tr>
<td>8. Updating</td>
<td>Fair</td>
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<tr>
<td>9. Implementation issues</td>
<td>Good</td>
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CI, 78.1% to 100%) in the intention-to-treat analyses. All trials were sponsored or cosponsored by the vaccine manufacturers.

Benefits and Harms

Harms of the vaccine appear to be minimal. Adverse effects noted in trials were injection site reactions and postinjection syncope. There has been concern, primarily in the lay media, about increased sexual activity among teens following vaccination. A retrospective cohort study conducted in a managed care organization compared girls who had received the vaccine with those who did not. Sexual activity was inferred from documented pregnancy, sexually transmitted infection testing or diagnosis, and contraceptive counseling. No increase in risk was found in this study.

Most analyses have determined that HPV vaccination of girls and young women is cost-effective. The cost-effectiveness estimates for vaccination of boys and young men varies widely because the outcome is sensitive to multiple factors, including vaccine cost and efficacy, the vaccine coverage of girls and women, and the effect of HPV-associated diseases on quality of life. Estimates in males have ranged from $20,000 to $250,000 per quality-adjusted life-year.

Discussion

The HPV vaccine appears to be highly effective and well tolerated. Existing data demonstrate that the vaccine is highly immunogenic. Trials with clinical end points show a reduction in genital condyoma and precancerous lesions such as cervical and vulvar intraepithelial neoplasia in girls and women and anal intraepithelial neoplasia in men. Effectiveness in reducing rates of cervical cancer and other HPV-associated malignancies (such as head and neck cancers) is expected but has not yet been shown. The vaccine guideline is likely cost-effective for females. There is uncertainty regarding the vaccine’s cost-effectiveness in males.

These guidelines support the use of either quadrivalent or bivalent vaccine in women but only the quadrivalent version in men. Although the bivalent vaccine does cover most oncogenic strains, it would seem that the greater breadth of the quadrivalent vaccine would be preferred given its effectiveness against genital warts. Currently the bivalent vaccine accounts for less than 5% of the market share in the United States.

Areas in Need of Future Study or Ongoing Research

The HPV vaccine and this guideline have both been only recently developed. Adherence to the guideline remains low in the United States. As of 2013, 57% of girls and 35% of boys in the United States had received at least 1 dose of the vaccine. Rates for completion of the series are generally lower. There is greater adherence in children living below the poverty line than in those above. Further study of vaccination rates and disparities in vaccination are necessary. Given the markedly lower efficacy rates in intention-to-treat analyses in the randomized clinical trials and in case-control trials, real-world efficacy data will be useful. There is early evidence that vaccination has positive effects on unvaccinated members of the population through herd immunity. These data will influence cost-effectiveness analyses. Long-term studies of the effects of vaccination on cancers (genital and other) are also needed to extend the data on genital warts and premalignant genital lesions.

REFERENCES


