

# Duty to Advocate: Human Papillomavirus Vaccination

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Despite the excellent benefit-to-risk ratio for human papillomavirus (HPV) vaccination and recommendations for its routine use from the Advisory Committee on Immunization Practices (ACIP), significant controversy surrounding HPV vaccination continues to exist. In light of this controversy and continued low rates of vaccination among U.S. adolescents, the Pediatric Pharmacy Advocacy Group (PPAG) endorses the safety and efficacy of HPV vaccination and agrees with ACIP recommendations for protection of the U.S. population against the potentially severe consequences of HPV. The PPAG recommends that all eligible individuals undergo vaccination. We further recommend that pediatric pharmacists participate in the education of patients and their families and serve as advocates for HPV vaccination. This document serves as an update to the 2008 PPAG position statement.<sup>1</sup>

**ABBREVIATIONS** ACIP, Advisory Committee on Immunization Practices; HPV, human papillomavirus; PPAG, Pediatric Pharmacy Advocacy Group; 2vHPV, bivalent HPV vaccine; 4vHPV, quadrivalent HPV vaccine; 9vHPV, 9-valent HPV vaccine

**KEYWORDS** adolescents; advocacy; awareness, cancer prevention; HPV vaccine; human papillomavirus; pharmacy education; provider recommendation; vaccination

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## Background

Human papillomavirus is the most commonly sexually transmitted disease in the United States, and although most infected individuals remain asymptomatic, infection can lead to cervical, oropharyngeal, and anogenital cancers.<sup>2</sup> Infection is likely to occur soon after onset of sexual activity, with an estimated 14 million new infections per year and a yearly expenditure of approximately \$8 billion.<sup>2</sup> There are currently 3 FDA-approved HPV vaccines: quadrivalent HPV vaccine (4vHPV), bivalent HPV vaccine (2vHPV), and the most recently approved 9-valent vaccine (9vHPV).

As of 2015, ACIP recommends administration of a 3-dose vaccination series (at time frames of 0, 2, and 6 months) for both males and females, to be initiated at ages 11 to 12 years.<sup>3</sup> The series may be initiated as young as age 9 years if desired. The ACIP currently does not provide recommendations to address whether patients who have received some or all of the 2vHPV or 4vHPV vaccine series should complete the series with the 9vHPV vaccine or receive 9vHPV vaccine booster doses. The ACIP recommends catch-up vaccination until age 21 years for males. This is extended to 26 years for high-risk males (immunocompromised or men who have sex with men) and all females.<sup>3</sup> Although the ACIP does not indicate a product preference, the 9-valent vaccine provides protection against the greatest number of cancer and lesion-causing serotypes and may be used in males and females. It is unclear for how much longer Merck will continue to provide both the 4vHPV and

9vHPV vaccines. Details on ACIP recommendations, including product differences and cost-effectiveness, can be found in the 2014 ACIP HPV vaccine recommendations and the 2015 ACIP 9vHPV vaccine update.<sup>3,4</sup>

Although routine use of 4vHPV in females was recommended by the ACIP initially in 2007, vaccination rates have lagged behind those for other adolescent vaccines.<sup>5-7</sup> In 2013, only 37.6% of females and 13.9% of males between ages 13 and 17 years had received all 3 doses of HPV vaccine.<sup>6</sup> This number is far below the Healthy People 2020 initiative's goal of 80% receipt of 3 doses for all individuals ages 13 to 15 years.<sup>8</sup>

## Controversy

In an era of rising public uncertainty regarding vaccines, HPV vaccines have been the subject of controversy beyond the typical vaccine debate.<sup>8</sup> There are many possible reasons for controversy and discomfort with HPV vaccines, including initial recommendation for females only, young age at recommended administration, moral objections, an early push to become mandatory after the initial ACIP recommendations, cost, and uncertainty of supply.

Although parents may feel that ages 9 to 12 years is too young for administration of a vaccine against a sexually transmitted infection, data support vaccination at this age. The peak incident age for both infection and disease has lowered during the past few decades, with approximately 74% of all new HPV infections occurring in the 15- to 24-year-old age group.<sup>2</sup> Vaccination rates

and preventive health visits decline after adolescence, highlighting the importance of providing HPV vaccination to 11- and 12-year-old children who regularly present for health care visits. Additionally, geometric mean antibody titers were significantly higher in recipients of 9vHPV ages 9 through 15 years compared with females ages 16 through 26 years.<sup>3</sup> There may also be some debate about the value of immunizing older patients who may have already been exposed to HPV, but approximately 91% of women ages 18 to 26 years are naive to all 4 serotypes in 4vHPV (6, 11, 16, and 18).<sup>9</sup> In studies evaluating the immunogenicity of HPV vaccines, both females and males ages 16 through 26 years seroconverted >99% to all 9 HPV vaccine types.<sup>3</sup>

Moral objections are typically centered on concerns that vaccination should be unnecessary because premarital sex is immoral, and that vaccination will increase sexual activity among adolescents. In a national survey of high school students, 46.8% of students reported having had sexual intercourse, 5.6% reported having had sexual intercourse before age 13 years, and 34% reported having been sexually active within the past 3 months.<sup>10</sup> An unfortunate additional consideration is that 7.3% of high school students nationwide have reported being forced to have sexual intercourse.<sup>10</sup> A recent insurance database analysis indicated that HPV vaccination in girls ages 12 to 18 years was not associated with increases in sexually transmitted infections, supporting a lack of association between HPV vaccines and unsafe sex practices.<sup>11</sup>

Cost continues to be a concern, because the average wholesale price of 1 dose of 9vHPV vaccine is approximately \$390.<sup>12</sup> A cost-effectiveness model demonstrated that 9vHPV was more cost saving when compared to 4vHPV despite the higher price, because of the avoidance of costs associated with HPV infection management.<sup>3</sup> The acute cost can be significant, particularly for individuals who are uninsured or whose insurance does not cover the HPV vaccine. As of February 2015, federal programs, such as Medicaid and state Children's Health Insurance Programs, must cover the HPV vaccine for both female and male beneficiaries, but there is currently no source of public funding of vaccines for uninsured adults 21 years and older. Merck and GlaxoSmithKline both sponsor assistance programs to provide free vaccines for uninsured low-income adults.

Recipients of 4vHPV and 2vHPV have now been followed for 8 and 9.4 years, respectively, with persistence of antibodies and no newly identified serious adverse events.<sup>13,14</sup> Benefit continues to outweigh risks. Unanswered questions include long-term safety and efficacy, and the potential need for boosters beyond the 9 years of HPV vaccine evaluation, the potential impact of 9vHPV, and the safety and efficacy of a more convenient 2-dose regimen. Vaccine supply has not proven to be an issue, although there is always the potential for this to occur, and the availability of 9vHPV versus 4vHPV

may lead to confusion until the transition is complete.

## Recommendations

The PPAG reaffirms its endorsement of the safety and efficacy of HPV vaccines and recommends that all eligible individuals without contraindications receive HPV vaccination as recommended by ACIP. We stress the importance of vaccine receipt prior to onset of sexual activity. We recommend that pediatric pharmacists participate in the education of patients and their families and serve as advocates for HPV vaccination. We urge adolescents' primary care providers to discuss HPV vaccination with their patients as they would discuss tetanus, diphtheria, and pertussis (Tdap) or meningococcal vaccination.

Steps that can be taken to improve HPV vaccination rates include:

- Local, state, and national pediatric pharmacist advocacy and education, including obtaining pharmacist authority to administer HPV vaccines to adolescents at the state level
- Elimination of overexplanation and differential treatment of HPV vaccines
- Pharmacist-driven adolescent vaccine screening programs
- Use of Merck's outreach program that reminds patients of follow-up visits for the second and third doses of the series <https://www.merckvaccines.com/Products/Gardasil/Pages/seriescompletion/tab/4>
- Assistance for patients unable to afford vaccination with manufacturer-sponsored patient assistance programs: GlaxoSmithKline: <http://www.gsk-vap.com/>; Merck: <http://www.merckhelps.com/GARDASIL>
- Support of HPVANDME.org, a non-profit organization whose aim is to raise awareness of HPV-related throat cancer

## ARTICLE INFORMATION

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