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HPV vaccine is now routinely indicated for males

ACIP recommends vaccinating all males ages 11 to 21 years and men ages 22 to 26 years who have sex with men or are HIV positive.

At its October 2011 meeting, the Advisory Committee on Immunization Practices (ACIP) recommended to the CDC that quadrivalent human papilloma virus vaccine (HPV4, Gardasil) be routinely given to all males ages 11 to 21 and to men ages 22 to 26 who have sex with men or who are HIV positive, if they have not been previously vaccinated. This replaces a 2009 recommendation that stated HPV4 vaccine could be used in males to prevent genital warts, but stopped short of advocating routine use for all males.¹

There were 3 reasons the previous recommendation did not include HPV4 for routine vaccination of males:

1. The vaccine had been shown to be effective only for prevention of genital warts.
2. The cost effectiveness of the vaccine for use in boys was poor and, in modeling, it yielded less benefit as more females were vaccinated.
3. It was thought that a more effective approach to preventing HPV disease would be to emphasize high rates of vaccination of females.

The new recommendation takes into account recent evidence demonstrating that the vaccine prevents anal intraepithelial neoplasia (AIN) in males, in addition to genital warts. Moreover, vaccination rates in females remain low, which makes vaccinating males more cost effective and additionally protective for females.

Female vaccination rates lower than expected

Despite its effectiveness and safety record, HPV vaccination has had a slow rate of acceptance among females ages 13 to 17 years. Coverage for this group documented in the last national vaccine survey was 48.7% for one dose and 32% for the recommended 3 doses.²

The vaccine is effective in preventing cervical intraepithelial neoplasia (TABLE 1),³ condyloma, and vaginal intraepithelial neoplasia in women ~15 to 26 years of age. Large studies of vaccine safety have documented no serious adverse reactions, other than syncope, which could occur as frequently as 17.9/10,000 females and 12.5/10,000 males.⁴ Another study that involved post-licensure safety data from >600,000 HPV4 doses found no increased risk for a variety of outcomes, including Guillain-Barré syndrome, stroke, venous thromboembolism, appendicitis, seizures, syncope, allergic reactions, and anaphylaxis.^{5,6}

HPV-associated disease in males

HPV causes anal, penile, and oropharyngeal cancers in males, with about 7500 cancers occurring each year in the United States.³ In addition, about 1% of sexually active males in America have genital warts at any one time.⁷ HPV types 6 and 11 cause about 90% of cases.¹

The HPV4 vaccine—when all 3 doses are given—is 89.3% effective in preventing genital warts related to HPV types 6 and 11. Even a single dose is 68.1% effective (95% CI,

TABLE 1

HPV vaccine efficacy against HPV type-related CIN2+ in females ages ~15 to 26 years³

Vaccine/HPV type	Vaccine		Placebo		Efficacy	
	N	CIN cases	N	CIN cases	%	CI*
Bivalent						
HPV 16/18	7344	4	7312	56	93	80-98
HPV 16	6303	2	6165	46	96	83-100
HPV 18	6794	2	6746	15	87	40-99
Quadrivalent						
HPV 16/18	7738	2	7714	100	98	93-100
HPV 16	6647	2	6455	81	98	91-100
HPV 18	7382	0	7316	29	100	87-100

CI, confidence interval; CIN, cervical intraepithelial neoplasia; HPV, human papillomavirus.
 *Confidence interval for bivalent results was 96.1%, and for quadrivalent results was 95%.

TABLE 2

A look at the human papillomavirus vaccines³

	Quadrivalent (Gardasil)	Bivalent (Cervarix)
Manufacturer/VLP types	Merck/6, 11, 16, 18	GlaxoSmithKline/16, 18
Date of US licensure	2006, females 2009, males	2009, females
Dose of protein	20/40/40/20 µg	20/20 µg
Producer cells	<i>Saccharomyces cerevisiae</i> (yeast)	Baculovirus-infected <i>Trichoplusia ni</i> (insect cell line)
Adjuvant	AAHS: 225 µg amorphous aluminum hydroxyphosphate sulfate	AS04: 500 µg aluminum hydroxide; 50 µg 3-O-desacyl-4'-monophosphoryl lipid A
Schedule (IM)	3-dose series	3-dose series

VLP, virus-like particle; IM, intramuscular.

48.8–80.7).¹ New evidence shows that HPV4 prevents AIN, which can lead to anal cancer.⁸ Effectiveness in preventing AIN 2/3 is 74.9% (95% CI, 8.8–95.4) in those completing 3 doses before onset of infection with one of the HPV types contained in vaccine. Notably, these results were obtained in a subgroup analysis of men who have sex with men. And although the reduction in AIN is expected to lower the incidence of anal cancer, ongoing studies require time to confirm this. If such a reduction is confirmed (and vaccination is started at age 12 in the general male population), the number-needed-to-vaccinate to prevent one case of genital warts would be 18, and to prevent one case of anal cancer, 1581.⁶

No studies have evaluated efficacy of HPV4 in preventing penile or oropharyngeal cancers.

Men who have sex with men at high risk

Men who have sex with men have higher rates of AIN, anal cancers, and genital warts than the general male population.³ Those who are additionally HIV positive have higher rates of genital warts, which are also more difficult to treat.³ AIN is also more common in HIV-infected males.³ The HPV4 vaccine is immunogenic in those who are HIV infected, although the resulting antibody titers are lower than in other populations.

A look at the 2 HPV vaccines

Two HPV vaccines are available (TABLE 2).³

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Do you offer the HPV vaccine to young males?

- Yes, if it is requested
- Yes, but only to those at increased risk
- No, and I don't plan to
- No, but I will now based on ACIP's recommendation
- Other _____

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➤ **New evidence shows that HPV4 prevents anal intraepithelial neoplasia, which can lead to anal cancer.**

ACIP recommendations: HPV vaccine use in males

1. Routinely vaccinate males ages 11 to 12 years with 3 doses of HPV4. The vaccination series can be started at 9 years of age. (A recommendation)
2. Vaccinate males, ages 13 to 21 years, who have not been vaccinated previously or who have not completed the 3-dose series. (A recommendation)
3. Consider vaccinating males ages 22 to 26 years. (B recommendation)
4. Vaccinate men ages 22 to 26 years of age who have sex with men and those in this age group who are HIV positive, if they have not been previously vaccinated. (A recommendation)

Levels of recommendation

- A: Applies to all individuals in an age- or risk factor-based group.
 B: Defers to clinician judgment in determining benefit for individuals.

Source: ACIP meeting; October 25, 2011; Atlanta, Ga.

HPV4 vaccine protects against HPV 6, 11, 16, and 18. Bivalent (HPV2, Cervarix) vaccine contains antigens from HPV 16 and 18. Both vaccines are approved for use in females for the prevention of cervical cancer; HPV4 is preferred if protection against genital warts is also desired. Only HPV4 has been licensed for use in males.

HPV vaccine is effective, but costly

A major consideration with HPV vaccines is their cost. With 3 doses required and each dose costing about \$130,⁹ cost effectiveness is poor when preventing uncommon diseases such as cervical and anal cancer, and a relatively benign disease such as genital warts. Male vaccination at age 12 years, when added to a female vaccination program, costs about

\$20,000 to \$40,000 per quality-adjusted life year (QALY) if all potential HPV morbidity is included, not just that which has been proven to be prevented by the vaccine (assuming oral and penile cancer will also be prevented). Counting only HPV disease demonstrated to be prevented by the vaccine, the result is \$75,000 to \$250,000+ per QALY.⁶ Vaccinating males older than 21 years results in a cost per QALY 2 to 4 times that of vaccinating males younger than 18 years.¹⁰

■ **A final decision.** After considering these factors, ACIP approved a set of recommendations at its October 2011 meeting that will become official once they are published in the *Morbidity and Mortality Weekly Report*. (See “ACIP recommendations for HPV vaccine use in males” above.)

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