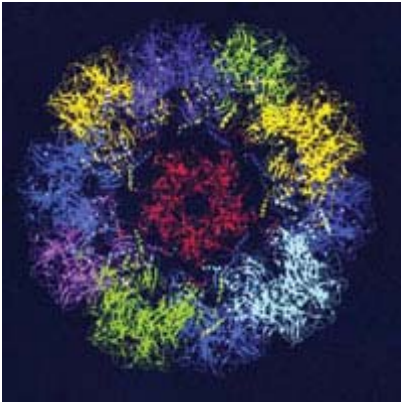




## Human Papillomavirus (HPV)

### HPV Vaccine Information for Clinicians - Fact Sheet



Virus-like particles (VLPs) assembled from the L1 protein of human papillomavirus 16

CDC and partners, including the American Academy of Pediatrics, recommend HPV vaccination of both girls and boys at ages 11 or 12 years and suggest that clinicians strongly recommend HPV vaccination for preteens and teens who have not yet been fully vaccinated.

### Background

Approximately 20 million people are currently infected with genital human papillomavirus (HPV) in the United States (U.S.). As many as half of these infections are among adolescents and young adults, ages 15 through 24 years of age. HPV is so common that most sexually active adults become infected at some point in their lives.

Of the more than 40 HPV types that infect human mucosal surfaces, most infections are asymptomatic and transient. However, certain oncogenic types that persist can cause cervical cancer and other, less common cancers, including cancers of the anus, penis, vulva, vagina, and oropharynx (back of throat including base of tongue and tonsils). Other, non-oncogenic HPV types can cause genital warts and, rarely, respiratory tract warts in children which is a condition called juvenile-onset recurrent respiratory papillomatosis (RRP).

Every year, about 12,000 women are diagnosed with cervical cancer, and about 4,000 women die from this disease in the U.S. About 1% of sexually active men and women in the U.S. have genital warts at any given time.

Two HPV vaccines are licensed by the Food and Drug Administration (FDA). The bivalent HPV vaccine (Cervarix) prevents the two HPV types, 16 and 18, which cause 70% of cervical cancers. The quadrivalent HPV vaccine (Gardasil) prevents four HPV types: HPV 16 and 18, as well as HPV 6 and 11, which cause 90% of genital warts. Quadrivalent vaccine has also been shown to protect against cancers of the anus, vagina and vulva. Only quadrivalent vaccine is licensed in use for males.

Both vaccines are administered as a 3-dose series. HPV vaccines are routinely recommended for 11 and 12 year old girls and boys. The vaccine series can be started beginning at age 9 years. Vaccination is also recommended for 13 through 26 year-old females, and 13 through 21 year-old males who have not completed the vaccination series. Males aged 22 through 26 years may be vaccinated. HPV vaccine is also recommended for gay and bisexual men (or any man who has sex with men) and persons with compromised immune systems (including HIV) through age 26, if they did not get fully vaccinated when they were younger.

These vaccines have no therapeutic effect on HPV-related disease, so they will not treat existing diseases or conditions caused by HPV. The vaccines are made from non-infectious HPV virus-like particles (VLPs) and do not contain thimerosal or mercury as a preservative.

The two vaccines use different adjuvants. The quadrivalent vaccine uses alum (225 µg amorphous aluminum hydroxyphosphate sulfate) adjuvant, while the bivalent vaccine uses ASO4 (500 µg aluminum hydroxide 50 µg 3-*O*-deacyl-4'-monophosphoryl lipid A).

## HPV Vaccine Recommendations

**Either HPV vaccine is routinely recommended for 11- or 12-year-old girls. Quadrivalent HPV vaccine is routinely recommended for 11- or 12-year-old boys. The vaccine series can be started beginning at age 9 years. Vaccination is also recommended for 13- through 26-year-old females and 13- through 21-year-old males who have not completed the vaccine series.**

**Quadrivalent HPV vaccine may be given to 22- through 26-year-old males. Vaccination is routinely recommended for both men who have sex with men (MSM) and immunocompromised persons aged 22 through 26 years.** Vaccination with either the bivalent HPV vaccine or the quadrivalent vaccine is recommended for protection against HPV types 16 and 18, for the prevention of cervical cancers and precancers in females. Vaccination with the quadrivalent HPV vaccine is recommended for protection against HPV types 16, 18, 6 and 11, for the prevention of cervical, vulvar, vaginal cancers and precancers in females, as well as anal cancers and precancers and genital warts in both females and males.

Ideally, patients should be vaccinated before onset of sexual activity, when they may be exposed to HPV. Patients who have been infected with one or more HPV types still get protection from the vaccine types they have not acquired.

HPV vaccines can be given to the following:

- Lactating women.
- Patients with minor acute illnesses, such as diarrhea or mild upper respiratory tract infections, with or without fever.
- Women who have had an equivocal or abnormal Pap test, a positive HPV test, or genital warts. However, these patients should be advised that data do not indicate that the vaccine will have any therapeutic effect on existing Pap test abnormalities, HPV infection or genital warts.
- Patients who are immunocompromised, either from infection, disease or medication. However, the immune response to vaccination and vaccine efficacy might be less in immunocompromised people.

HPV vaccines should **not** be given to:

- Patients with a history of immediate hypersensitivity to any vaccine component. Quadrivalent HPV vaccine is contraindicated for persons with a history of immediate hypersensitivity to yeast. Bivalent HPV vaccine in prefilled syringes is contraindicated for persons with anaphylactic latex

allergy.

- Patients with moderate or severe acute illnesses. In these cases, patients should wait until the illness improves before getting vaccinated.
- Pregnant women. Although the vaccine has not been causally associated with adverse pregnancy outcomes or adverse events to the developing fetus, data on vaccination in pregnancy are limited. Any exposure to vaccine in pregnancy should be reported to the appropriate HPV vaccine pregnancy registry:
  - The toll-free number for Gardasil is 800-986-8999
  - The toll-free number for Cervarix is 888-452-9622

## HPV Vaccine Safety

HPV vaccines were studied in thousands of people in many countries around the world, including the United States. These studies showed no serious safety concerns and found that both HPV vaccines were safe. Common, mild adverse events reported during these studies include pain where the shot was given, fever, dizziness, and nausea. More than 46 million doses of HPV vaccine have been distributed in the United States as of June 2012. Most doses distributed have been Gardasil.

Syncope can occur after any medical procedure, including vaccination. Recent data suggest that syncope after any vaccination is more common in adolescents. Adolescents and adults should be seated or lying down during vaccination. Providers should consider observing patients in seated or lying positions for 15 minutes after vaccination.

For each of the vaccines, a detailed post-licensure safety monitoring plan, coordinated by the FDA and CDC, is in place. For more information about the Vaccine Adverse Event Reporting System (VAERS) visit [www.vaers.hhs.gov](http://www.vaers.hhs.gov) (<http://www.vaers.hhs.gov>) <http://www.cdc.gov/Other/disclaimer.html>

## HPV Vaccine Efficacy Studies and Antibody Response

The main efficacy study of the bivalent vaccine was conducted in young women aged 15 through 25 years. Among women who had not been previously exposed to a targeted HPV type, the clinical trials demonstrated 93% vaccine efficacy in preventing cervical precancers due to HPV 16 or 18. In all studies of the bivalent HPV vaccine, more than 99% of females developed an HPV 16 and 18 antibody response 1 month after completing the 3-dose series.

The main efficacy studies of the quadrivalent vaccine were conducted in young women and men (16 through 26 years of age). Among persons not previously exposed to a targeted HPV type, the trials demonstrated nearly 100% vaccine efficacy in preventing cervical precancers, vulvar and vaginal precancers, and genital warts in women caused by the vaccine types, as well as 90% vaccine efficacy in preventing genital warts and 75% vaccine efficacy in preventing anal precancers in men.

In women already infected with a targeted HPV type, the vaccines do not prevent disease from that HPV type but protect against other vaccine types. Immunogenicity studies of both vaccines have been conducted in girls, ages 9 to 15 years of age. Over 99% of vaccinated girls in these studies developed antibodies after vaccination.

HPV vaccines offer a promising new approach to the prevention of HPV and associated conditions. However, they do not replace other prevention strategies, such as regular cervical cancer screening using the Pap test, since the vaccines will not prevent all HPV types.

## Duration of Vaccine Protection

Studies suggest that vaccine protection is long-lasting. Current studies (with up to about six years of follow-up data) indicate that the vaccines are effective, with no evidence of waning protection. This

information will be updated as additional data regarding duration of protection become available.

## HPV Vaccine Administration

**Both brands of HPV vaccine should be delivered through a series of 3 intra-muscular injections over a 6-month period. The second and third doses should be given 2 and 6 months after the first dose.**

The vaccines can be administered at the same visit as other age-appropriate vaccines, such as tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine, quadrivalent meningococcal conjugate vaccine (MCV4), influenza vaccine, and hepatitis B vaccine.

Providers should consider a 15-minute waiting period for vaccine recipients following vaccination.

Cervical cancer screening recommendations have not changed for females who receive the HPV vaccine.

## Why is HPV vaccination only recommended through age 26?

HPV vaccines are licensed for females and males through age 26 years. Vaccination would have the greatest benefit when administered to girls and boys, aged 11 or 12 years.

As in trials in younger women, a clinical trial of quadrivalent vaccine in women >26 years found the vaccine to be safe. This study also showed that the vaccine was effective in women without evidence of existing or past infection with HPV vaccine types. However, the study demonstrated limited or no protection against disease in the overall study population. Neither vaccine is licensed in the United States for use in women over the age of 26 years. Although women over age 26 years are not recommended to receive HPV vaccination, they should have cervical cancer screening as currently recommended.

## Covering the Cost of the Vaccine

The Vaccines for Children (VFC) program helps families of eligible children who might not otherwise have access to vaccines. The program provides vaccines at no cost to doctors who serve eligible children. Children younger than 19 years of age are eligible for VFC vaccines if they are Medicaid-eligible, American Indian, or Alaska Native or have no health insurance. "Underinsured" children who have health insurance that does not cover vaccination can receive VFC vaccines through Federally Qualified Health Centers or Rural Health Centers. Doctors can charge a fee to give each shot. However, VFC vaccines cannot be denied to an eligible child if a family can't afford the fee.

State and private programs offering no- or low-cost vaccines may also be available for eligible persons. Contact your State Health Department (<http://www.cdc.gov/mmwr/international/relres.html>) to see if your state has such a program.

Vaccine providers should notify patients that:

**CDC and partners, including the American Academy of Pediatrics, recommend HPV vaccination of females and males at ages 11 or 12 years and suggest that clinicians strongly recommend HPV vaccination for preteens and teens who have not yet been fully vaccinated.**

- It is important to get all 3 doses of HPV vaccine to get the full benefits.
- Vaccinated females will still need regular cervical cancer screening, beginning by age 21, since vaccination will protect against most, but not all, of the HPV types that cause cervical cancer.
- All vaccinated patients should continue to practice abstinence or protective sexual behaviors (i.e.,

