

September 2022 ~ Resource #380927

HPV Vaccination

modified September 2024

Human papillomavirus (HPV) is the most common sexually transmitted infection in Canada and the US.¹⁻³ Most HPV infections are asymptomatic and resolve without intervention. However, some HPV infections lead to significant morbidity, including precancer and cancer in both females and males.^{2,4} HPV vaccination rates remain low, with just over half of teenagers fully vaccinated for HPV.^{3,5} The FAQ below answers questions about HPV vaccination and includes a few talking points to ease concerns and improve vaccination rates.

Question	Answer/Pertinent Information
<p>Who should be vaccinated against HPV?</p>	<ul style="list-style-type: none"> • <i>Gardasil 9</i> is FDA- and Health Canada-approved in males and females nine to 45 years of age.⁶⁻⁸ • <i>Cervarix</i> (Canada only) is Health Canada-approved in females nine to 45 years of age.⁹ • Ideally start the series between the ages of 11 and 12 years (for females and males).^{10,11} <ul style="list-style-type: none"> ○ Consider starting the series in patients as young as nine years.^{6,10-12} ○ In Canada, age for beginning the HPV series typically depends on provincial/territorial programs (which vary), but most programs are for administration in grade six or seven (i.e., age 11 or 12 years).^{13,14} ○ Routine and catch-up vaccinations are recommended through age 26 years, for males and females.^{12,15} ○ Can consider discussing HPV vaccination with unvaccinated adults between 27 and 45 years, who are most likely to benefit (e.g., patients who anticipate a new sexual partner in the future, especially those with few sexual partners in the past). Though HPV vaccination appears safe in adults over 26 years, benefits are less pronounced than in younger patients.¹² <ul style="list-style-type: none"> ▪ Modeling data suggests that HPV vaccination may prevent more HPV-related cancers in adolescents or young adults (NNT ~ 200) compared to adults vaccinated between 27 and 45 years (NNT ~ 6,500).¹² • Regardless of the original vaccine used to start the series (i.e., previously available <i>Gardasil</i> or <i>Cervarix</i> [Canada only]), feel comfortable using <i>Gardasil 9</i> to complete the series for both females and males.¹⁶ • When possible, use the same vaccine to complete a vaccine series. However, if necessary, any available HPV vaccine can be used to complete the vaccine series. Note that <i>Cervarix</i> (Canada only) is not approved for use in males.² • Per US labeling, <i>Gardasil 9</i> is contraindicated in patients with a severe hypersensitivity to yeast (a component in US and Canadian formulations).⁶
<p>How should HPV vaccine doses be given?</p>	<ul style="list-style-type: none"> • Administer 0.5 mL of the HPV vaccine as an intramuscular injection.² <ul style="list-style-type: none"> ○ <i>Gardasil 9</i> should be given in the upper arm or middle to upper outer thigh.^{6,17} ○ <i>Cervarix</i> (Canada only) should be given in the upper arm (i.e., deltoid).⁹ • Patients should be observed for 15 minutes after administration, due to a risk of fainting.^{2,6}

Question	Answer/Pertinent Information
How many doses of HPV vaccine should be administered?	<ul style="list-style-type: none">• NACI (Canada) recommends a single dose of <i>Gardasil 9</i> for patients nine to 20 years.²• The two-dose series is recommended for immunocompetent patients up to 14 years (US), as an optional alternative to the 1-dose schedule for patients nine to 20 years (Canada), and patients 21 to 26 years (Canada).^{2,6,10}<ul style="list-style-type: none">○ Provides a similar immune response to the three-dose series given to patients 15 years and older.⁶○ <i>Gardasil 9</i> should be given at 0 and six months OR at 0 and 12 months.^{2,6}○ <i>Cervarix</i> (Canada only) should be given at 0 and six months.²○ Ensure a minimum of five months between the two doses.^{6,18}<ul style="list-style-type: none">▪ If the second dose is given less than five months after the first dose, the patient should then be given a third dose. The third dose should be administered six to 12 months after the first dose, and at least three months after the second dose, to ensure response.¹⁶• The three-dose series (doses at 0, 2, and 6 months for <i>Gardasil 9</i>; doses at 0,1, and 6 months for <i>Cervarix</i> [Canada only]) is recommended for:<ul style="list-style-type: none">○ patients 15 years or older starting the vaccine series (US).^{6,10} If the patient received their first dose when they were nine to 14 years, a two-dose schedule (with at least six months between doses) can be used to finish the series.○ patients up to 14 years (US, as an optional alternative to the two-dose series).^{6,8}○ patients with immunocompromising conditions (e.g., cancer, HIV).^{2,18} Note that immunocompromised patients may have a reduced response.^{2,6}○ immunocompetent HIV-infected patients.²• For the three-dose series, there must be at least one month between the first two doses, at least three months between the second and third doses, and at least six months between the first and third doses.²• It is not necessary to restart the two- or three-dose series if more than the recommended time lapses between doses.^{2,18} Complete the vaccination series, starting right where the patient left off.¹⁸
How well is <i>Gardasil 9</i> tolerated?	<ul style="list-style-type: none">• Expect adverse effects to be more common in females compared to males.⁶• Injection-site pain, redness, and swelling are the most common (~90% of females, ~65% of males) adverse effects, but are usually mild.^{2,6,13,17}• Headache is the next most common adverse effect (~10%).⁶• Systemic adverse events (e.g., fatigue, myalgia, fever, nausea) have been reported. However, rates do not seem to differ from the control groups.^{2,6,17}<ul style="list-style-type: none">○ Experts believe fainting with HPV vaccination is the result of getting an injection, not from the vaccine ingredients. Fainting has been reported after administration of almost all vaccines.¹⁹

Question	Answer/Pertinent Information
What does the HPV vaccine protect against?	<ul style="list-style-type: none">• <i>Gardasil 9</i> covers HPV strains 6, 11, 16, 18, 31, 33, 45, 52, and 58.^{6,8}<ul style="list-style-type: none">○ <i>Gardasil 9</i> protects against:^{6,8}<ul style="list-style-type: none">▪ anal and genital warts caused by HPV strains 6 and 11.▪ precancerous or dysplastic lesions caused by vaccine-covered strains.▪ cervical, vulvar, vaginal, anal, oropharyngeal, and other head and neck cancers caused by HPV strains 16, 18, 31, 33, 45, 52, and 58.^{6,8}○ Vaccination with <i>Gardasil 9</i> could prevent more than 90% of HPV-caused cancers.²⁰• <i>Cervarix</i> (Canada only) covers HPV strains 16 and 18.^{9,21}<ul style="list-style-type: none">○ <i>Cervarix</i> is indicated to protect against cervical cancer (squamous cell and adenocarcinoma) by preventing precancerous or dysplasia lesions caused by HPV strains 16 and 18.⁹• Note that the now discontinued <i>Gardasil</i> vaccine covered HPV strains 6, 11, 16, and 18.²¹
What are some suggested talking points with patients and parents? <i>Continued...</i>	<ul style="list-style-type: none">• Discuss the benefits of vaccination with patients and their parents/caregivers. See our <i>Vaccine Adherence: Addressing Myths and Hesitancy</i> algorithm for additional ways to improve vaccination rates and overcome barriers.<ul style="list-style-type: none">○ Vaccination appears most effective (for HPV infection, genital warts, precancerous lesions) when given prior to becoming sexually active in males and females under the age of 26 years.⁶<ul style="list-style-type: none">▪ For older females up to 45 years of age, vaccination may be about 47% effective for HPV infection, genital warts, and precancerous lesions regardless of prior HPV exposure or about 88% effective in those without prior HPV exposure [Evidence Level A-1].²²▪ Modeling data suggests that HPV vaccination may prevent more HPV-related cancers in adolescents and young adults (NNT ~ 200) compared to adults vaccinated between the ages of 27 and 45 (NNT ~ 6,500).¹²• Ask parents/caregivers and/or patients about their concerns.<ul style="list-style-type: none">○ Promote the vaccine as an “anticancer” vaccine.○ Provide vaccine information to parents/patients who request it.○ Useful tools to help communicate the benefits of HPV vaccine to parents and patients include:<ul style="list-style-type: none">▪ CDC’s “Answering Parents’ Questions” at https://www.cdc.gov/hpv/hcp/answering-questions.html.▪ Government of Canada’s “Teens, Meet Vaccines” at https://www.canada.ca/en/public-health/services/publications/healthy-living/teens-meet-vaccines.html?_ga=1.16486706.585774884.1487176194.• Recommend vaccination at a young age to ensure immunity before becoming sexually active.²³<ul style="list-style-type: none">○ Close skin-to-skin sexual touching can spread the virus, making early vaccination important.^{1,13}○ Feel comfortable that HPV vaccination does not increase sexual activity or promiscuity.²⁴• There is insufficient evidence that HPV vaccination causes:<ul style="list-style-type: none">○ anaphylaxis²⁵○ complex regional pain syndrome (CRPS)²⁶

Question	Answer/Pertinent Information
Talking points, continued	<ul style="list-style-type: none"> ○ fertility issues²⁶ ○ Guillain-Barré²⁶ ○ postural orthostatic tachycardia syndrome (POTS)²⁶ ○ syncope²⁵ ○ venous thromboembolism and stroke²⁵ ● Avoid use during pregnancy, due to lack of data.²⁶ <ul style="list-style-type: none"> ○ If a woman becomes pregnant during the vaccine series, delay future injections until after delivery.¹⁸ ● HPV vaccination can be given while breastfeeding.²⁶
How much do the HPV vaccines cost?	<ul style="list-style-type: none"> ● <i>Gardasil 9</i> costs about \$270 (US) or \$185 (Canada) per dose.^a ● <i>Cervarix</i> costs about \$110 (Canada) per dose.^a ● US: Check with insurers to verify coverage. <ul style="list-style-type: none"> ○ Expect vaccinations to be covered for most patients between the ages of nine and 26 years. With updated CDC guidance, reimbursement may include vaccination for males and females up to 45 years.²⁷ ● Canada: All provinces and territories offer HPV vaccines at no cost as part of school vaccination programs. Some insurance providers may cover HPV vaccines.²⁸

Abbreviations: HPV = human papillomavirus, NNT = number to treat.

a. Pricing based on wholesale acquisition cost (WAC). US medication pricing by Elsevier, accessed September 2022.

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

Levels of Evidence

In accordance with our goal of providing Evidence-Based information, we are citing the **LEVEL OF EVIDENCE** for the clinical recommendations we publish.

Level	Definition	Study Quality
A	Good-quality patient-oriented evidence.*	<ol style="list-style-type: none"> High-quality randomized controlled trial (RCT) Systematic review (SR)/Meta-analysis of RCTs with consistent findings All-or-none study
B	Inconsistent or limited-quality patient-oriented evidence.*	<ol style="list-style-type: none"> Lower-quality RCT SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings Cohort study Case control study
C	Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening.	

***Outcomes that matter to patients** (e.g., morbidity, mortality, symptom improvement, quality of life).

[Adapted from Ebell MH, Siwek J, Weiss BD, et al. Strength of Recommendation Taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. *Am Fam Physician* 2004;69:548-56. <https://www.aafp.org/pubs/afp/issues/2004/0201/p548.html>.]

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