HPV vaccine for cancer and wart prevention

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Clinical question
Is the human papillomavirus (HPV) vaccine effective in preventing cervical lesions or genital warts (condyloma)?

Bottom line
The HPV vaccine prevents advanced cervical lesions (cervical intraepithelial neoplasia [CIN] grades 2 or 3) in 1 in 60 to 125 women and condyloma in 1 in 40 to 50 men and women over 3 to 4 years.

Evidence
Three large international RCTs in females aged 15 to 26 used modified intention-to-treat analysis (including patients with positive test results for HPV at baseline) for all HPV lesions.1-4

• Quadrivalent vaccine (HPV 6, 11, 16, and 18):
  -FUTURE 1 trial following 5455 women for 4 years found decreased external genital lesions (3.8% vs 5.7% placebo; number needed to vaccinate [NNV]=53) and CIN of grade 2 or 3 (6.6% vs 7.1% placebo; not statistically significant).
  -FUTURE 2 trial following 12167 women for 3 years found decreased CIN of grade 2 or 3 (3.6% vs 4.4% placebo; NNV=125).
  -FUTURE 1 and 2 combination trial following women for 4 years found decreased external genital lesions (1.5% vs 4% placebo; NNV=40); CIN of grade 2 or 3 was not reported.
• Bivalent vaccine (HPV 16 and 18 vaccine):
  -Trial following 18644 women for 4 years found decreased CIN of 2 or 3 (3.3% vs 4.9% placebo; NNV=63).
• Smaller studies showed similar effects.5,6
  -All studies excluded those who were pregnant, had previous abnormally Papiconalou test results or genital warts, or had more than 4 to 6 lifetime sexual partners. All studies were funded by vaccine manufacturers. Similar relative efficacy was seen for condyloma in males aged 16 to 26.7

Context
• Worldwide, cervical cancer affects more than 500 000 women per year, mostly in developing countries,8,9 while in Canada about 1500 women per year are diagnosed.10
• About 90% of women with cervical cancer have HPV.8,9
• Women have about a 50% chance of having positive test results for HPV after 3 years of sexual activity.11
• Vaccine serious adverse event rate is similar to placebo.12,4,7
• Future longer-term studies will delineate true effect on cervical cancer and whether a booster is needed.
• In Canada, the quadrivalent vaccine is recommended for females aged 9 to 45 and males aged 9 to 26, and the bivalent vaccine is recommended for females aged 10 to 25.12

Implementation
Primary care clinicians must educate patients and parents about the efficacy and safety of the HPV vaccine. As of May 2013, 111 million doses had been given worldwide.13 Based on postmarketing surveillance (including 700 000 doses in Ontario13), the risk of syncope is 8 per 100 00014 and the risk of anaphylaxis is 0.3 to 3 per 100 000.13,15 Coadministering the HPV and hepatitis B vaccines in schools should improve logistics and uptake,16 although some provinces are using only 2 doses. The larger trials did not find an overall increase in spontaneous abortion or congenital abnormalities,2,4 but the vaccine is not recommended for pregnant women.

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References
3. FUTURE I/II Study Group. Four year efficacy of prophylactic human papillomavirus quadrivalent vaccine against low grade cervical, vulvar, and vaginal intraepithelial neoplasia and anogenital warts: randomised controlled trial. BMJ. 2010;341:c4939.

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