



# Addressing HPV-Related Cancer Risk Among Adult Women: A Guide for Health Care Providers

Sex Information and Education Council of Canada (SIECCAN)



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This guide provides health care providers with information on: 1) Human papillomavirus (HPV), HPV-related cancers among adult women, and the importance of HPV vaccination in this population; and 2) how to communicate with women about HPV-related cancer prevention and the HPV vaccine.

## PART 1: THE NEED FOR HPV EDUCATION AND VACCINATION AMONG WOMEN

Human papillomavirus (HPV) is the most common sexually transmitted infection (STI) in Canada (1) and around the world (2, 3). It is estimated that up to 75% of sexually active women and men will acquire at least one HPV infection in their lifetime (4). Most HPV infections are transient and asymptomatic; more than 90% of new HPV infections clear or become undetectable within two years (5). Among women, the prevalence of HPV is typically highest among young adults aged 20- to 24 years (6). However, sexually active women remain at risk for HPV infection throughout their adult years (7, 8).

There are over 100 different types of HPV with more than 40 HPV types that infect the epithelial lining of the anogenital tract and other mucosal areas of the body (1). HPV infections are transmitted by direct sexual contact or skin-to-skin contact. Sexual transmission usually occurs via genital-genital and oral-genital contact, but can also occur through other close skin-to-skin touching during sex (2).

There are approximately 13 cancer causing high-risk HPV types (Table 1) (3). In women, persistent infection with high-risk HPV types is responsible for nearly all cervical cancers and is implicated in cancers of the anus, vulva, vagina, as well as head and neck cancers (9). HPV types 16 and 18 account for approximately 70% of cervical cancers (10, 11, 12, 13). Non-carcinogenic HPV types 6 and 11 cause 90% of anogenital warts in women and men (9, 14).

**Table 1: HPV Types**

Low-Risk HPV	High-Risk HPV
6, 11	16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68
<b>Adverse health outcomes:</b>	<b>Adverse health outcomes:</b>
Anogenital warts	Cancer of the cervix, vulva, vagina, anus, oropharynx, mouth

Source: Trottier, H, Franco, EL. The epidemiology of genital human papillomavirus infection. *Vaccine* 2006; 24, Suppl 1: S4-15 (3).

**The nonavalent HPV vaccine (9vHPV, Gardasil®9) prevents infection with the following HPV types: 6, 11, 16, 18, 31, 33, 45, 52, 58**

## Infection with High-Risk HPV Types is Common Among Adult Women in Canada

- British Columbia: 26% of cervical samples from females aged 15-19 years and 33% of samples from females aged 20-24 years were infected with high-risk HPV types (6).
- British Columbia: 14% of 8,660 cervical samples from females aged 13-86 years were infected with high-risk HPV types (15).
- Northwest Territories: 9% of 5,725 cervical samples from females aged 18-65+ years were infected with high-risk HPV types (16).
- Manitoba: 7% of 592 cervical samples from females aged 14-85 years were infected with high-risk HPV types (17).
- The majority of these high-risk HPV infections are caused by HPV types that are covered in the 9vHPV vaccine.

## HPV-Related Cancers Among Women

### Cervical Cancer

- Among women, cervical cancer is the third most commonly diagnosed cancer and the fourth leading cause of cancer death worldwide (18).
- Although cervical cancer rates have declined in recent years, this decline has reached a plateau and cervical cancer remains an important health concern for women (18, 19).
- Most cases of cervical cancer are caused by persistent infection with a high-risk HPV type, such as HPV 16 or 18 (11, 13, 20).
- In a 2008 international meta-analysis, 94% of 30,848 cases of invasive cervical cancer cases were caused by high-risk HPV types that are covered in the 9vHPV vaccine (11).

### Cervical Screening

Cervical cytology examinations (Pap tests) are used to detect abnormalities (pre-cancerous or cancerous) in the cervix. Screening requirements vary across Canada with most provinces/territories recommending screening every 2-3 years if no abnormalities have been detected. Colposcopy is used to examine abnormalities detected by the pap (1). An abnormal pap is most commonly caused by an HPV infection (21).

HPV DNA testing is approved for use in Canada for women. It is recommended for use in women older than 30 years of age who have cervical lesions or who may show signs of pre-cancerous lesions and may be at risk of developing cervical cancer (22). When testing indicates HPV infection, women will require follow-up and information on HPV natural history and transmission.

Despite routine screening, HPV-related disease can still be missed due to the limitations of the Pap test, such as the low sensitivity of cytology testing and subjectivity of sampling (23). In order to optimize cervical cancer prevention, both HPV vaccination and screening programs are needed (24).

**Table 2: Annual HPV-Related Cancer Diagnosis and Deaths Among Women (Canada)**

	Incidence	Deaths
<b>Cervical</b>	1500	400
<b>Vulva/Vaginal</b>	500	222
<b>Anal</b>	325	63
<b>Oropharyngeal</b>	260	86

*Source (cervical): Canadian Cancer Society estimates for cancer diagnosis and related deaths for 2016. <http://www.cancer.ca/en/cancer-information/cancer-type/see-all/> Accessed 13/12/2016. Canadian Cancer Society's Advisory Committee on Cancer Statistics. Canadian Cancer Statistics 2016. Toronto, ON: Canadian Cancer Society; 2016 (18)*

## Vulvar/Vaginal Cancer

- Invasive vulvar cancer rates have increased in both Canada and the United States in recent years (25).
- In an international study of female anogenital cancers and precancerous lesions, HPV was associated with:
  - 96% of vaginal intraepithelial neoplasia grade 2/3 cases
  - 87% of vulvar intraepithelial neoplasia grade 2/3 cases
  - 74% of vaginal cancers
  - 29% of vulvar cancers
  - 98% of these vaginal cancer cases and 77% of these vulvar cancer cases were caused by HPV types (i.e., 16, 18, 31, 33, 45, 52, 58) that are covered in the 9vHPV vaccine (12).

## Anal Cancer

- In Canada, almost twice as many women are diagnosed with and die from anal cancer compared to men (26).
- Rates of anal cancer among women in Canada and the United States have been increasing for several decades (27, 28).
- In numerous international studies, 75% to 90% of high-grade anal lesions and/or invasive anal cancer cases were associated with HPV 16 (10, 12, 29) which is covered in the 9vHPV vaccine.

## Anal Screening

Screening for anal dysplasia and/or anal cancer is not a routine screening test. However, health care providers can conduct various screening practices to potentially identify early signs of HPV-related anal cancer precursors (e.g., anal dysplasia) (30).

Digital anal exams may detect advanced anal cancer but are unlikely to detect pre-cancerous changes resulting from HPV infection (31). Anal cytologic examinations (anal pap test) can also be performed (32). The standard for the confirmation of high-grade disease is high-resolution anoscopy (HRA) (32).

## Oropharyngeal Cancer

- Oropharyngeal cancer rates have been increasing for the last three decades (33, 34).
- 70% to 80% of oropharyngeal cancers are attributable to HPV infection and rates of oropharyngeal cancer may surpass rates of cervical cancer in the coming years (35).
- Based on data from the 2009-2010 *US National Health and Nutrition Examination Survey* (NHANES), 4% of all women had an oral HPV infection (34).
- Because the vast majority of HPV-related oropharyngeal cancers are associated with HPV types 16 or 18, the HPV vaccine can help to protect women from this increasingly common form of cancer (36).

## Anogenital Warts

- Nearly all cases of anogenital warts are caused by HPV types 6 or 11 (37).
- 7% to 10% of sexually active adult women report having been diagnosed with anogenital warts (38, 39).
- Women who have been diagnosed with anogenital warts often suffer shame and embarrassment, especially when the warts recur and are difficult to treat (37).
- The HPV vaccine covers types 6 and 11 and, therefore, offers protection against anogenital warts.

## Anogenital Warts Screening

Anogenital warts can be diagnosed via a visual inspection of the vulva, vagina, cervix, anus, and surrounding area and then treated (1).

## HPV and HIV

- Women can be immunocompromised for a variety of reasons (e.g., transplantation, chemotherapy, pregnancy, HIV infection) and may be less able to clear an HPV infection (40).
- Anogenital HPV infection in women has been associated with a two-fold increase in the risk of HIV acquisition (41).
- Once co-infected with HIV and HPV, immunosuppression can result in the body being less capable of clearing HPV (42). Immunosuppression can also lead to co-infection with multiple HPV types – including high-risk HPV types that may lead to cancer (43).
- Recurrences of anogenital warts are more likely in individuals who are immunocompromised (37).
- Infection with high-risk HPV type 18 is more common among women with HIV (e.g., 80%) compared to immunocompetent women (e.g., 18%) (30).
- Women who are immunocompromised due to HIV infection are more likely to develop HPV-associated cervical cancer than immunocompetent women (44).
- In a meta-analysis, women with HIV were most commonly infected with high-risk HPV types 18, 33, 51, 52, and 58, as well as types 11, 53, and 61 (45); five of these eight HPV types are covered in the 9vHPV vaccine.

## Recommendations for HPV Vaccination for Women

Public health authorities/organizations, such as Canada's National Advisory Committee on Immunization (NACI) (9) and the US Advisory Committee on Immunization Practices (2) have issued HPV vaccine recommendations for adult women.

### **The 2016 NACI recommendations include the following regarding the HPV vaccine:**

- Recommended for females between the ages of 9 and 26 years
- May be used in females over 26 years of age with no upper age limit

Immunocompromised individuals, immunocompetent HIV infected individuals, and individuals who have not received any dose of HPV vaccine by 15 years of age should receive three doses of HPV vaccine.

Women who have been vaccinated with the 2vHPV or 4vHPV vaccine and who want the additional protection provided by the 9vHPV vaccine can receive the 9vHPV vaccine.

Whenever possible, one specific vaccine type should be used for all doses in the three dose series. If a woman has not received all three doses of the vaccine and the specific vaccine used in the previous doses is unknown, 2vHPV, 4vHPV or 9vHPV can be used to complete the series. However, only 4vHPV and 9vHPV protect against HPV types 6 and 11 (genital warts) and only 9vHPV protects against types 31, 33, 45, 52 and 58 in addition to types 16 and 18 which are covered by all 3 vaccines. At this time, studies using a mixed regimen of HPV vaccines have not been conducted for the 9vHPV vaccine.

## Women older than 26 years of age are candidates for the HPV vaccine

### Vaccine efficacy has been demonstrated in adult women

- The most recent NACI recommendations do not identify any upper age limit for the HPV vaccine (9).
- Clinical trials have demonstrated HPV vaccine efficacy (46), as well as sustained immune responses against pre-cancerous and cancerous lesions in women over the age of 26 years (47, 48).

### Sexually active midlife women can have the same risk of HPV acquisition as younger women

- In a study of women aged 25 to 65 years who engage in online dating, HPV infection was correlated with sexual activity – not age (49).
- HPV infection and re-infection is strongly correlated with sexual activity. Midlife women who enter new relationships or have new sexual partners are at risk of acquiring HPV (49).
- In one study, HPV prevalence was highest in two groups of women: those under age 20 and those over age 60 (50).
- In an analysis of 8,469 women aged 18 to 39 years who had been diagnosed with cervical adenocarcinoma, the prevalence of high-risk HPV types 31, 33, 45, 52, and 58 increased with age (51).

### Women with previous HPV-related disease may still benefit from HPV vaccination

- The risk for HPV-related cervical intraepithelial neoplasia (CIN) is higher in individuals previously treated for CIN (52).
- Naturally-acquired antibodies from an HPV infection may not provide protection against subsequent infection with the same HPV types (53).
- Vaccination will not reduce progression to disease from a *current* HPV infection, but may reduce the incidence of subsequent HPV-related disease (54).
- Vaccination after treatment for disease has been shown to reduce the recurrence rate of HPV-related disease (55).
- The vaccine may provide protection from re-infection with HPV types that individuals have been previously exposed to (53, 58).
- NACI recommends vaccination for women with a history of abnormal pap tests or with previous HPV-related disease (9).

### Most women have not been exposed to all 9 high-risk HPV types covered in the HPV 9 vaccine

- It is unlikely that an individual has been exposed to all 9 HPV types contained in the 9vHPV vaccine (9, 11, 12, 20).
- Very few women are infected with multiple HPV types at one time (56, 57).

## Most Adult Women Have Not Been Vaccinated Against HPV

In Canada, HPV immunization rates are measured by two national surveys: 1) the *Childhood National Immunization Coverage Survey* (CNICS) (59) which collects data on females 12-14 years of age and 17 years of age and 2) the *Adult National Immunization Coverage Survey* (ANICS) (60) which collects data on females 18 to 45 years of age.

### According to 2013 CNICS data, national HPV vaccine coverage was:

- 72% for females aged 12-14 years
- 64% for females aged 17 years

### According to 2014 ANICS data, national HPV vaccine coverage was:

- 45% for females aged 18–26 years who received at least one dose (3 doses required).
- 8% for females aged 27–45 years who received at least one dose (3 doses required).

In one study of Canadian female undergraduates (mean age 20 years), only 27% had received the HPV vaccine – despite 93% of the sample being aware of the vaccine’s availability (61).

## Explanations for Low HPV Vaccination Rates Among Adult Women

### *Women’s Lack of Knowledge and Misconceptions about HPV*

Many young adult women lack knowledge about how common HPV is and/or how it can be prevented. For example, when asked why they had not been vaccinated, 73% of female Canadian undergraduates cited reasons, such as low perceived risk of contracting HPV and high perceived behavioural control of not contracting HPV (61).

### *Missed HPV Vaccination in School*

Starting in 2007, provinces and territories in Canada introduced school-based HPV vaccination programs for girls at varying grades (some as early as Grade 4) (62). Even though some provinces offer HPV vaccine catch-up programs at a later grade (63), vaccine uptake rates were very low in the initial years of the program. As a result, many young adult women were not immunized. This issue is further complicated given the differing years and grades at which school-based HPV vaccination programs were introduced across Canada.

Health care providers should also be aware that women who have immigrated to Canada are, depending on their country of origin, unlikely to have received the HPV vaccine.

### *Lack of Health Care Provider Recommendation*

In Canada, low adult vaccination rates may be due to health care providers not recommending vaccines to their patients/clients (64). In a national survey of US pediatricians and family physicians, the majority of health care providers recommended the HPV vaccine inconsistently, behind schedule, and/or without urgency (65). Women who receive a HPV vaccine recommendation from their health care provider are more likely to be vaccinated (61, 65, 66, 67, 68).

*The Society of the Gynecologic Oncology of Canada* suggests that health care providers be mindful of their role in influencing clients’ decisions regarding HPV vaccination and recommend the HPV vaccine as appropriate (20).

**A recommendation from a health care provider is the most important factor in a woman getting the HPV vaccine.**



## PART 2: COMMUNICATING WITH WOMEN ABOUT HPV AND HPV-RELATED CANCER PREVENTION

All sexually active women are at risk for HPV infection and HPV-related cancers. It is important for health care providers to make women aware of these risks and discuss steps that women can take to lower their risks of HPV infection and the subsequent development of HPV-related cancers and genital warts. The companion fact sheet to this guide (*HPV-Related Cancers Among Women: What You Need to Know to Reduce Your Risk*) provides basic information for women.

### Steps for HPV-Related Cancer Prevention

#### Cervical Screening

- Periodic cervical screening (pap test) based on provincial/territorial guidelines will help identify cervical cancer before the development of symptoms, thereby increasing the chances of successful treatment (69).
- Since the vaccine does not protect against all HPV types, health care providers should remind patients that even with HPV vaccination, other prevention strategies, such as regular cervical screening, should continue (69).

#### Condom Use

- Using condoms correctly and consistently can help reduce the transmission of HPV (70, 71).
- HPV can still be transmitted from skin-to-skin contact (from areas not covered by a condom) even if using condoms (72).
- HPV is commonly transmitted via oral sex. Oral HPV infections can subsequently lead to oropharyngeal cancer (73, 74).

#### HPV Vaccination

- Health care providers should inform female clients that the HPV vaccine is the most effective way to prevent HPV and HPV-related cancers.
- The most current HPV vaccine (9-valent) protects against the main HPV strains that cause genital warts (types 6, 11) and high-risk HPV strains that cause cancer (types 16, 18, 31, 33, 45, 52, 58) (2, 9).



## HPV Vaccination Practices

### Standard of Care: Vaccination

The US Center for Disease Control and Prevention's *Standards for Adult Immunization Practice* (75) recommends that health care providers should:

- **ASSESS** immunization status of all patients at every visit.
- **RECOMMEND** vaccines that patients need.
- **ADMINISTER** needed vaccines or REFER to a provider who can immunize.
- **DOCUMENT** vaccines received by patients (or refusal of vaccine).

### The US Center for Disease Control and Prevention also recommends a **SHARE** approach to recommending vaccines (76):

- **S**hare the reasons why the recommended vaccines are right for the patient's given age, health status, lifestyle, job, or other risk factors.
- **H**ighlight positive experiences with vaccines (personal or in practice) to reinforce the benefits and strengthen confidence.
- **A**ddress patient questions and any concerns about vaccines (side effects, safety, vaccine effectiveness) in plain and understandable language.
- **R**emind patients that vaccines protect them and their loved ones from many common and serious diseases.
- **E**xplain the potential costs of getting the disease, including serious health effects, time lost (missing work, family obligations), and financial costs

## Potential Opportunities for Health Care Providers to Initiate Discussions about HPV Vaccination with Adult Women Clients

There are numerous opportunities during routine medical care that are conducive for health care providers to initiate discussions about the HPV vaccine with female clients. Many of these opportunities are related to discussions with clients regarding their recent sexual activity and/or ongoing sexual health.

### Below are some potential consultation opportunities for health care providers to address HPV vaccination:

- Contraception (e.g., IUD, oral contraception)
- Urinary tract infections (UTIs), yeast infections
- STI prevention/history related to HPV or other STI
- Pre-conception counseling (mother-child transmission)
- Travel/general vaccination check-ups
- Divorce and new sexual partnerships

## Strong versus Weak Recommendation for HPV Vaccination

### Strong recommendation:

Health care provider's words or tone clearly suggest that the patient should get the vaccine. Ownership of recommendation is conveyed by the use of personal pronouns ("I" or "we") and adverb/verb choice "recommend." (77)

### Sample statement:

*"I recommend that you get the HPV vaccine."*

### Weak recommendation:

Worded in third person, in a passive voice, or is coupled with a qualification (e.g., disclaimer, reason for opting out) (77).

### Sample statement:

*"When they learn that HPV can cause cancer, some women decide to get the vaccine."*

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