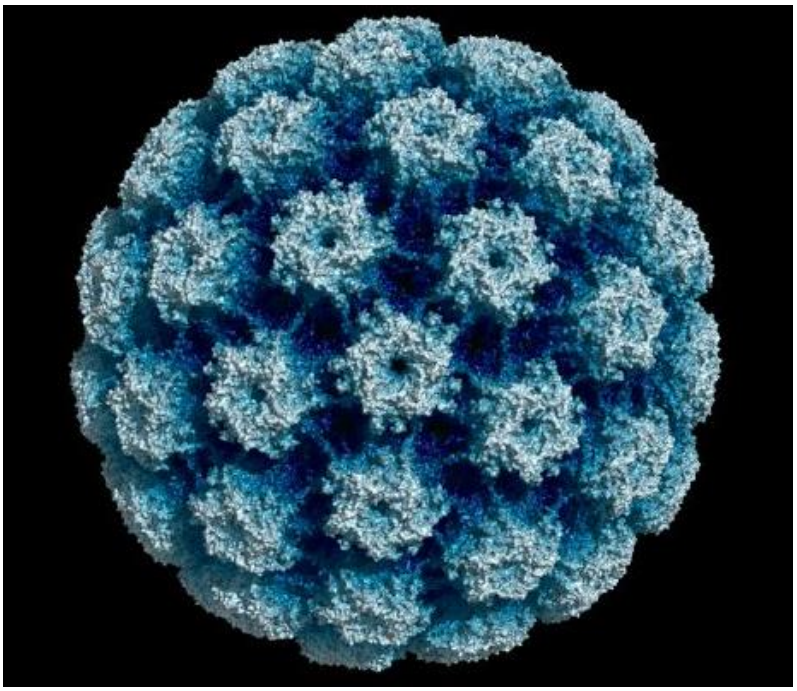
CIDC
Consortium for
Infectious Disease Control

Counselling Patients About HPV

Test Results, Prevention and Vaccination



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Abbreviations Used in This Document

AGW - Anogenital warts

ASC-US - Atypical Squamous Cells of Undetermined Significance

CIDC - Consortium for Infectious Disease Control

CIN - Cervical intraepithelial neoplasia

HR-HPV - High-risk Human Papillomavirus (high risk genotype or 'type' of the human papillomavirus for development of neoplasia)

HPV - Human papillomavirus

HSIL - High-grade squamous intraepithelial lesion

LR-HPV - Low-risk Human Papillomavirus (low risk genotype or 'type' of the human papillomavirus for development of neoplasia)

LSIL - Low grade squamous intraepithelial lesion

Pap Test - Papanicolaou cervical cancer screening test

TOC – Test of Cure

Introduction

The science of screening for cervical cancer has evolved for almost one hundred years since Papanicolaou's original research. Cervix screening is appropriate for all people with a cervix eligible for screening, including women and those who do not identify as women. For the purposes of this document, we will refer to women, but note the information in this document can be used for all people with a cervix who are eligible for screening. Screening programs have varied around the world, reflecting changes in science, technology, epidemiology, and policy. Within Canada, under the jurisdiction of the provinces and territories, there has been a variety of programs, which continue to undergo periodic change. There are differences across Canada in schedules for screening (e.g., age of first screen, screening intervals, and algorithms; and of descriptive words for follow-up of abnormal test results). These are often based on reference publications or guidelines established in Canada and other countries. In addition to screening schedule differences, there are now differences in test methods: conventional cytology on glass slide (Pap smear), liquid-based cytology (Pap LBC), and, most recently, tests for the presence of human papillomavirus (HPV) nucleic acid - either high-risk (HR-HPV) and low-risk (LR-HPV), or HR-HPV only - the cause of most, if not all squamous or adenomatous cervical cancers. There have also been developments in the interpretation of test results and the options for preventive or curative action. Also recently, we have seen the very successful introduction of HPV vaccines, initially for females, and now, increasingly, for males.

The WHO has published a Global strategy* to accelerate the elimination of cervical cancer as a public health problem. This strategy proposes the screening of women with a high-performance test. And for Canada, this high-performance test is the detection of HR-HPV, commonly referred to as HPV testing.

This transition to HPV testing has changed the focus of the screening from looking for cellular changes to finding the necessary cause of cervical cancer - the presence of HR-HPV infection. This has produced many new clinical scenarios and case presentations, resulting in many new questions for patients and care providers alike. HPV testing introduces a new aspect of counselling since HPV testing is testing for a sexually transmitted infection, which was not the case when screening patients for pre-cancerous changes. This resource has been produced to meet the need for relevant information to answer questions about HPV testing and the interpretation and response to test results.

The experts who have contributed to this resource have provided relevant facts and opinions that can be used by all health-care providers and counsellors to inform and advise their patients about HPV issues including HPV testing, prevention, vaccination and treatment in a variety of clinical situations. It is hoped that the information contained in this resource serves a useful purpose as a non-prescriptive reference before, during or after a discussion with patients regarding HPV. Although this resource is intended for health care providers, some of the explanations in the scenarios use wording for communicating with the patient. It is not intended to replace or to contradict national or provincial guidelines or programs. Nor is it intended to promote any type of product or program.

The Consortium for Infectious Disease Control (CIDC) is pleased to offer this resource to health care professionals across Canada. CIDC is very appreciative of the involvement of the expert contributors,

advisors, reviewers and sponsors that enabled this resource to be produced. CIDC is particularly grateful to the authors of the sections which were reviewed and edited through a team effort. Each author has taken responsibility for the content of their sections. CIDC is responsible for the coordination, editing and organization of the overall document.

We hope that you find this booklet useful in your work.

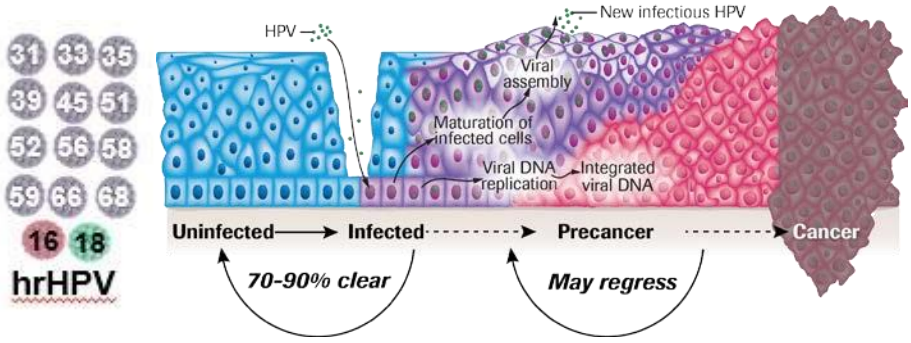
* https://www.who.int/publications/i/item/9789240014107

HPV and Cervical Cancer Screening
General Information

Cervical Cancer Screening in Canada

Decreases in cervical cancer incidence and mortality over the past several decades can largely be attributed to the availability of programmatic cervical cancer screening. Cervical cancer is almost entirely preventable through HPV vaccination and regular screening. Through screening, those at risk for cervical pre-cancer and cancer are identified early, so that treatment can occur to prevent further progression to cervical cancer. Most cases of invasive cervical cancer occur in Canadian women who have never been screened or who have had long intervals between screens[1]. Until recently, the only tool available for cervical cancer screening has been cytology testing (the Pap smear).

Natural history of cervical cancer



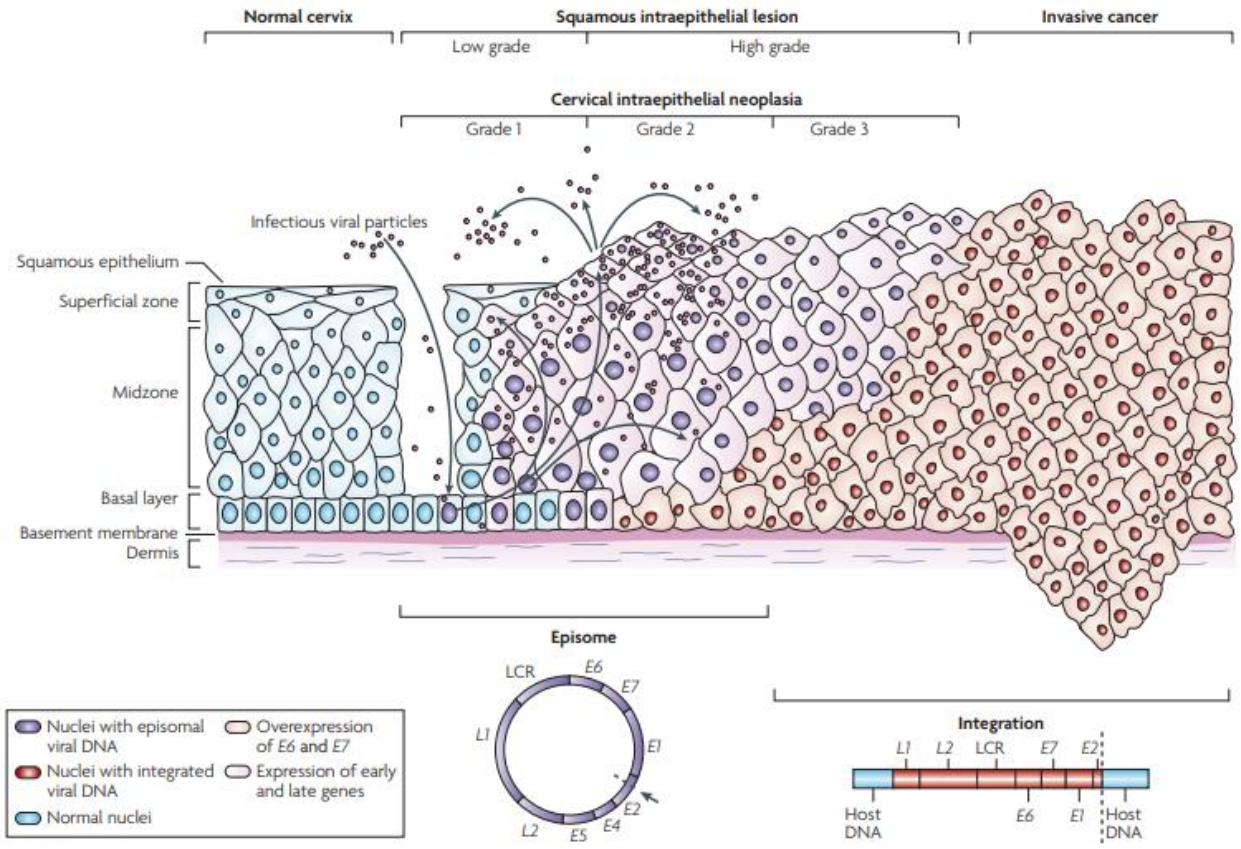
It is well-established that persistent infection with one of approximately 14 high-risk (HR) genotypes of HPV is necessary for the development of cervical cancer[2]. There are approximately 130 HPV genotypes, of which about 40 infect the anogenital tract in both men and women. HPV genotypes are classified as either low-risk (LR) or high-risk (HR). LR-HPV types are associated with anogenital warts (AGW), respiratory papillomatosis and low-grade intraepithelial lesions. HR-HPV genotypes are associated with anogenital cancers and their immediate precursor, high-grade intraepithelial lesion[3]. High-risk HPV types 16 and 18 contribute to approximately 25% of low-grade lesions of the cervix (CIN1), 65% of high-grade lesions (CIN2&3), and 70% of invasive cervical cancer[4,] with the remaining HR-HPV types being associated with approximately 30% of invasive cervical cancer cases. Overall, HPV types covered by the nonavalent HPV vaccine (types 16, 18, 31, 33, 45, 52 and 58) cause 87.1% of invasive cervical cancers in Canada. For the purposes of this document, when referring to HPV testing or HPV associated with cervical cancer, we are referring to testing for HR-HPV infections.

HPV is the most common sexually transmitted infection in the world and most sexually active individuals will have an HPV infection at some point in their lives[3],[5]. It is transmitted via skin-to-skin sexual activity, mostly through vaginal or anal intercourse, but it can also be transmitted through oral sex, mutual masturbation, and the sharing of sex toys [Section 2: Ref 3-11]. Transmission is more likely to happen when HPV

viral load is higher or a lesion/wart is present. Condom use for vaginal and anal intercourse offers some protection, albeit incomplete, against the initial transmission of HPV as well as re-infection between partners. There is some evidence that, among condom users, HPV infection clears more quickly Section 2: Ref 12-15 and CIN is less likely to recur Section 2: Ref 16.

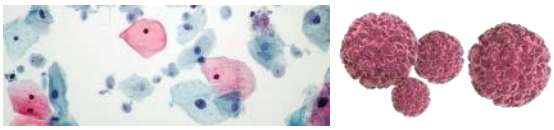
HPV is highly prevalent in women under 30 years of age. The majority of HPV infections are asymptomatic, and regress spontaneously within about 2 years. Approximately 10-15% of women develop a persistent HPV infection, and it is these women who are at risk for progression to cervical cancer[6, 7, 8].

HPV infects cervical basal membrane cells through micro-abrasions of the cervical epithelium. A transient HPV infection may result in either no visible lesion, or low-grade lesions (such as low grade squamous intraepithelial lesion [LSIL] on cytology smear or CIN1 histopathology results). These kinds of lesions extend to less than 1/3 of the epithelium and spontaneously regress through cell mediated immunity. A persistent infection with a high-risk HPV genotype is identified when this HPV genotype is detected in consecutive samples over a period of 6 to 12 months. This can result in high-grade intraepithelial lesion (HSIL on cytology smear/CIN2+ on biopsy) involving full thickness of the epithelium. Regression of high-grade lesion is less likely and if not detected and treated, it could lead to invasive cervical cancer[3, 9].



From: Woodman, C., Collins, S. & Young, L. The natural history of cervical HPV infection: unresolved issues. *Nat Rev Cancer* **7**, 11–22 (2007). https://doi.org/10.1038/nrc2050

HPV Testing compared to cytology testing:



Cytology identifies changes to the cells on the cervix after they have begun to occur. Cytology has low sensitivity to detect high-grade lesions, with the result that it misses nearly half of cervical high-grade lesions[10], giving false negative results. However, given how long cervical cancer takes to develop, and the fact the cytology testing has been recommended every 2 to 3 years, many cervical pre-cancer cells can be identified through regular screening before they develop into cervical cancer. Although successful at decreasing rates of squamous-cell carcinomas, cytology screening has not had success decreasing rates of adenocarcinoma[11].

Unlike cytology testing, HR-HPV testing detects the presence or absence of HR-HPV genotypes and can therefore identify women at risk for cervical abnormalities, earlier and better than cytology, sometimes before dysplasia occurs. With HPV testing a sample of cells from the squamocolumnar junction is not necessarily required. Since HPV testing evaluates for the presence of HPV infection, HPV testing can be conducted on samples collected vaginally, or cervically, which offers opportunities for cervical self-screening (whereby, the person being screened can collect the sample themselves vaginally). The sensitivity of HPV testing as an indicator for the presence of high-grade cervical intraepithelial lesions has been estimated at approximately 95%[10]. Randomized trials have demonstrated that a negative HPV test provides earlier, greater and longer reassurance that the woman is at a very low risk of developing cervical pre-cancer, and as a result the interval between screens for HPV negative women can be extended in a setting where primary HPV testing is implemented[12-15]. In addition, HPV testing has been shown to be more effective than cytology testing for the prevention of adenocarcinomas (by detecting precursor lesions)[16].

Although highly sensitive, HPV testing has somewhat lower specificity, as not all detected HPV infections are predictive of high-grade intraepithelial lesion, or indicative of cervical disease, especially in younger women who are frequently infected transiently by HPV [Section 1: Ref 1]. The majority of HPV infections are transient HPV and do not cause cervical or other cancers. When HPV testing is used in primary screening for cervical cancer, not all HR-HPV positive women should be immediately referred to colposcopy. Instead, a positive HPV test would ideally be followed by a "triage" test to ensure that only higher risk women are referred for further diagnostics. Triage testing occurs when additional testing (a second test) is performed immediately after HR-HPV positive results are obtained to further stratify higher risk women with positive primary test results. In the case of HR-HPV testing, cytology (either liquid-based or a Pap smear) or partial HPV genotyping for detection of HPV 16 or 18 can be used as a triage test. HR-HPV positive women with abnormal cells of any degree identified by cytology (atypical cells of undetermined significance [ASC-US] or greater) can then be referred to colposcopy to assess the presence of histologically confirmed cervical disease. In other words, the highly sensitive test (HPV test) is conducted first, if HR-HPV is detected, a second, more specific test (for example, cytology or HPV 16 and 18 genotyping) is then performed. Cytology testing is only one option that

can be used as the triage test. Other triage testing options are being explored with the use of primary HPV testing. At this time, testing algorithms have not yet been established in Canada.

HPV infection peaks and is high in women under 30 years of age, and starts to rapidly decline after the age of 30[3]. In addition, since most infections in young women are transient[17], it is not recommended that HPV testing be offered to women under the age of 25. HPV testing in women under 25 could lead to the identification and treatment of HPV infections that would otherwise have spontaneously regressed. Over-screening and treatment could potentially cause harm due to anxiety and distress and increase the risk of reproductive sequelae due to unnecessary biopsies and endocervical curettage due to transient HPV infection in young women[18, 19].

The HR-HPV tests currently approved are for cervical screening only; they are not approved nor validated for screening for HPV related cancers in men or for detection of anogenital warts. In some Canadian jurisdictions, HPV testing has been implemented as triage for women with ASCUS cytology results for women 30 years old and above and in some cases after treatment of high-grade lesions before returning to normal screening. Jurisdictions across Canada are in various stages of planning for implementation of primary HPV testing for cervical screening. It is anticipated that over time, HPV testing will replace cytology as the primary tool for screening given the increasing evidence to support the use of HPV testing for cervical cancer prevention.

HPV Vaccination and Cervical Screening:

A number of HPV vaccines have been approved for use in Canada. HPV vaccines do not contain live viruses, rather, they contain a single HPV protein from the surface of the virus. HPV vaccines do not alter effectiveness of HPV testing, as they detect nucleic acids and not virus-specific proteins [Section 1: Ref 6].

Although HPV vaccination has been available through school-based programs in Canada for since 2007, it is not anticipated that screening programs will see large population effects of HPV vaccination on invasive cervical cancers for years to come. In Sweden, quasi disappearance of cervical cancer has been noted in women vaccinated before the age of seventeen. However, there is already evidence that HPV vaccination does decrease the incidence of cervical dysplasia in those who have begun cervical screening and received HPV vaccination in a school-based program[20]. Despite the fact that the two HPV vaccines approved for use in Canada (9vHPV vaccine and 2vHPV vaccine) protect against the HPV types responsible for most cases of cervical cancer, the vaccines do not protect against all types of HPV. Therefore, it is important that women vaccinated against HPV follow the guidelines for cervical cancer screening established in their regions.

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Objectives and Scenarios

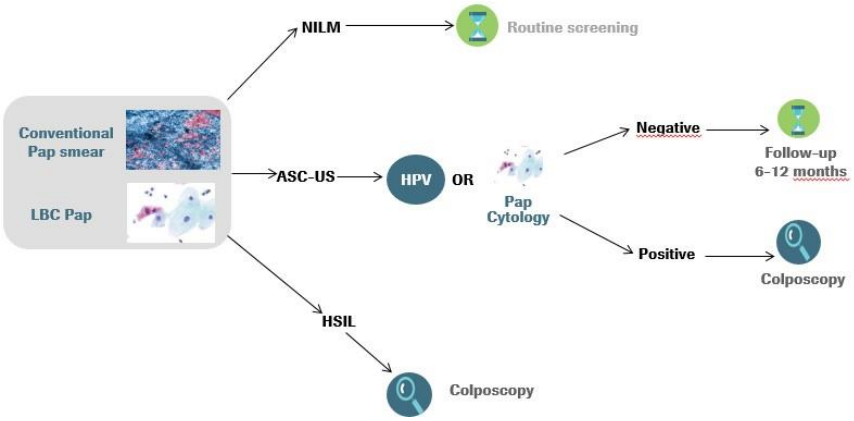
Section 1

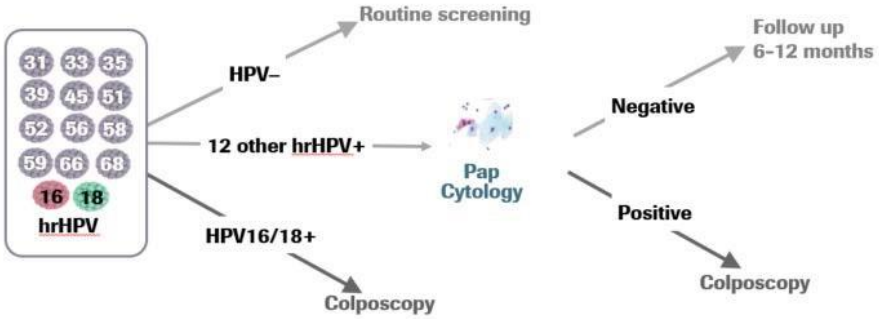
HPV Testing and Screening

Author: Francois Coutlée, MD

Objectives:

1. To understand the clinical meaning of a positive HPV test
2. To delineate the differences between HPV testing and Pap cytology testing
3. To understand the difference between HPV testing for primary screening and HPV testing used in triage in the case of abnormal cytology results





Scenario 1.1: HPV testing in young women

Clinical situation:

A sexually active 22-year-old female attends a medical clinic for a checkup. She has read that HPV is transmitted sexually and causes genital cancer and warts. She also learned that HPV testing is now available. She fears she could be infected with HPV and has cancer or warts. Since she recently completed HPV vaccination, she wonders if HPV testing is preferred for her over a Pap test.

Relevant information which can be shared with the patient:

NOTE: Cervical cancer screening program guidelines and algorithms differ between provinces. See appendix 1.

- HPV testing is not indicated in young women under the age of 25 due to the high rate of transient HPV infections in this age group [13]. Primary HPV testing is not widely available in Canada at the time of this publication. The age at which HPV screening will eventually be done instead of Pap still needs to be determined and will possibly vary from province to province. This age limit will likely be set between ages 25 to 30[1,2,4,5]. (Note: some provinces – and the Canadian Task Force on Preventive Health Care - do not recommend Pap testing under the age of 25). Testing younger women with transient HPV infections will result in unnecessary investigation and potential increase in harm due to biopsies and treatment.
- Most HPV infections are transient and will be controlled by the body's natural immune system within about 2 years. However, in some cases, an HPV infection persists and can evolve into high-grade cell changes (or intraepithelial lesions) and subsequently, for a fraction of cases, to cervical cancer. Transient HPV infections are frequent in many women including young women.
- It is expected that Pap tests will eventually be replaced by HPV testing for older women because of a lower rate of transient HPV infections and lower rate of positive HR-HPV tests in those over the age of 25.
- The currently approved HR-HPV tests are intended to screen for cervical cancer and do not indicate the presence of, or exposure to, genital warts. Genital warts are usually diagnosed upon observation by the health care professional.
- Cervical cancer screening is recommended in vaccinated and unvaccinated women. Available HPV vaccines do not protect against every HPV type; therefore, it is important that women receive cervical cancer screening according to the guidelines in their province.
- Cervical cancer screening results should not influence a woman's decision to receive the HPV vaccine or not.
- Despite the fact that HPV testing is not recommended in women under 25, routine STI/HIV screening is recommended for sexually active women, to screen for other sexually transmitted infections. HPV testing for cervical cancer screening is not part of routine STI screening.

Scenario 1.2: HPV triage for abnormal Pap cytology results

Clinical situation:

A 52-year-old woman has had several normal Pap tests in the past. However, the last Pap test showed an ASC-US result. A second cervical sample was collected and sent for HPV testing. She is referred to you because the laboratory reported the presence of HR-HPV (high risk HPV virus type that indicates increased risk for the development of neoplasia). She has many questions. What is the meaning of 'high-risk' HPV? Does she have, or will she have, cancer? Why was HPV not detected with the Pap test and why was a second sample required? Since she is in a monogamous relationship, does a positive HPV test mean that her husband has had extramarital relationships? How will she be investigated or treated?

Relevant information which can be shared with the patient:

- HPV infection could have been transmitted decades before testing and before the current relationship. Also, exposure to HPV may have occurred without sexual intercourse (meaning non-penetrative sex such as oral sex or genital rubbing).
- Since HPV is very common and may persist for many years, it is impossible to determine how and when it was transmitted. Issues on transmission of HPV are further discussed in section 2.
- HPV testing is not required for her partner since transmission may have been established in their early sexual activities. Penile and anal cancer risk may be extremely low but oropharyngeal cancers are possible.
- In the absence of a wart or lesion, no treatment is available or needed.
- HPV infection will be controlled in most men by the immune system.
- Her male partner can be offered vaccination. The vaccine is indicated in the product monograph for men between 9 to 45 years of age as well as for men having sex with men.
- The use of vaccine is authorized by the National advisory committee on immunization in Canada for individual > 45 years of age who desires to be protected against new infection by HPV. There is some evidence showing reduced transmission and infection of the partner.
- 40 types of HPV infect the genital tract but only those at high-risk for cancer are detected in the current diagnostic HR-HPV tests[6]. HR-HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68 and sometimes 66, are detected in most current HR-HPV tests[13].
- A cytology test (Pap) is reported to be an ASC-US when the pathologist and cytotechnologist cannot determine if the exfoliated cells collected from the cervix are normal or showing intraepithelial lesion. Thus, an ASC-US cytology can be obtained in women without or with actual cervical disease.
- In the conventional Pap test, cervical cells are immediately put on a slide. These cells fixed on a slide cannot be tested for HPV. Then a new sample needs to be obtained for HPV testing. If the sample is collected in a liquid that preserves cells (liquid cytology), then that sample can be utilized for both cytology and HPV testing. Several Canadian laboratories use conventional cytology, explaining why a

second sample was collected in this woman. Had she been tested initially with liquid cytology for her Pap smear, the laboratory could have done directly on the first sample a Pap test followed by HPV testing. Liquid cytology is more expensive than conventional cytology but saves a repeat visit for testing.

- HR-HPV positive women with any abnormal cervical cell changes (which are called intraepithelial lesions – and previously called dysplasia) that are identified on cytology smears are at a higher risk for histologically confirmed cervical high-grade intraepithelial lesions[8,17].
- High-grade cervical intraepithelial lesions are the immediate precursor lesions to squamous cell cervical cancer.
- A woman with ASC-US and a positive HR-HPV test should be referred to colposcopy to assess and grade cervical disease[7,9]. If a high-grade intraepithelial lesion is found at colposcopy, treatment will then be discussed with the patient.
- High-grade intraepithelial lesions can be treated to reduce risk of progression to cancer.
- There is no treatment specifically aimed at eradicating HPV infection itself.
- While there are HPV vaccines available to prevent infection, there is no available treatment against HPV infection itself. Moreover, not everyone infected with HPV will develop cancer. Most HPV infections are asymptomatic and will be controlled by the body's natural immune system. However, in some cases, if HPV infection persists and is left undetected, it can evolve into high-grade intraepithelial lesion and subsequently to squamous cell cancer or adenocarcinoma.

Scenario 1.3: HPV screening for cervical cancer

Clinical situation:

A 40-year-old woman has been returning regularly for cervical cytology for the past two decades. Her sister has been screened with an HPV test in a private laboratory and was told this novel test is more sensitive than Pap cytology. She would like to know if the HPV test is better than a Pap test for cancer screening, and if it is available in Canada from a public medical laboratory. She also wants to know how frequently she should be tested and if the test will identify the HPV type involved, as she read that HPV16 is the most dangerous.

Relevant information which can be shared with the patient:

- The HR-HPV test is considered more sensitive than cytology to indicate the presence of high-grade cervical lesions (95% versus 55%) [1,2,4,5,17,18]. Since HR-HPV test results are objective, highly consistent, reproducible and can be utilized easily for quality assurance programs, HR-HPV testing is considered more reliable by some jurisdictions [2,9,13].
- Primary HPV testing is slowly becoming available in Canada at the time of this publication.
- HR-HPV tests may be available with the appropriate prescription from private laboratories that provide collection kits.
- A clinical trial conducted in Canada did not report a difference in detection of high-grade precancerous lesions between HR-HPV tests detecting HPV DNA or HPV RNA[19].
- Among women undergoing cervical cancer screening, HR-HPV testing compared with cytology testing resulted in a significantly lower likelihood of CIN3+ after a follow-up of 48 months[5].
- Some laboratories report HPV testing results as HPV positive or negative. This is not an adequate reporting strategy and these laboratories should report if HR-HPV is detected or not.
- The lower sensitivity of Pap tests requires more frequent testing than HR-HPV testing[5,13].
- However, the woman in this clinical situation should be reassured since she regularly attended Pap testing and is thus at low risk to have undetected disease.
- The performance of co-testing (HR-HPV test combined with cytology) for primary screening is almost equivalent to HR-HPV testing alone.
- The high reliability of HR-HPV testing (as shown by a high negative predictive value) could allow extending screening visits with HR-HPV testing to at least five years[3, 5,6,13,16].
- Women who are HR-HPV negative are significantly less likely to have high-grade precancerous disease in the next 4 years compared to women with normal cytology[5]. Thus, a negative HR-HPV test result is a good indicator of the absence of high-grade intraepithelial lesion[1-5].
- A positive result for HR-HPV in women over 25 to 30 years old indicates a higher risk for cervical cancer but does rarely indicates the presence of cancer itself[17].
- Invasive cancer arises from high-grade precancerous lesions. Colposcopy with cervical biopsies helps in detecting these lesions and treating them before cancer develops. For some women, treatment is not instituted immediately and they are instead followed up closely.

- The cervical sample collected in a special collection media can be used for both HR-HPV testing and Pap testing. If the sample tests positive for HR-HPV, then a Pap test can be done on the same sample to screen for the presence of abnormal cells. HR-HPV positive women with abnormal cells in the Pap test can then be referred to colposcopy to assess the presence of cervical disease. This strategy is designated as HPV testing with cytology triage of HR-HPV positive samples.
- Only a subset of genital HPV types cause cancer[8,10,11, 13]. They are designated as HR-HPV types. HPV 16 and 18 carry a higher risk of progression to high-grade disease of the cervix and cancer than the other HR-HPV types[8]. The other HR-HPV types cause cancer less frequently and less rapidly than HPV 16 or 18. HPV 45 is considered by many as being as oncogenic as HPV16 and 18, however.
- Although HR-HPV are associated with cervical cancer, HR-HPV types can be detected in women that do not have, and will never have, high grade lesions or cancer.
- Some of the currently available HR-HPV tests report separate results for HPV16 and HPV18 but pool together in one or more pools the other HR-HPV genotypes (including frequently types 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68). These other HPV genotypes combined with HPV16 and 18 are responsible for over 95% of cervical cancers in Canada[11].
- The presence of HR-HPV in women does not necessarily indicate the presence or future occurrence of cancer. Referring all women positive for HR-HPV would lead to an increased number of unnecessary colposcopies and treatment with potential adverse event on reproduction in younger females. Different strategies can help to decide if a woman who is positive for HR-HPV should be referred to colposcopy to avoid unnecessary procedures in a woman with a transient HPV infection or without lesions. These strategies, which may vary between countries and provinces/territories, are designated “triage of HR-HPV positive women”.

  Triage with colposcopy: Triage of HR-HPV positive women to colposcopy can be done with a Pap test and/or HPV 16/18/±45 testing.

  - **HR-HPV positive, HPV16/18/±45 positive:** In one triage strategy, HR-HPV positive women are also tested for HPV16/18/±45[14,15]. Women positive for HPV16/18/±45 are referred to colposcopy. Colposcopy will assess the presence of lesion, grade and treatment options[9, 10].
  - **HR-HPV positive, HPV16/18/±45 negative**: HR-HPV positive women but negative for HPV16/18/±45 can then be tested with a Pap test. Referral to colposcopy is planned if the Pap is abnormal[10,14].
  - **HR-HPV positive, HPV16/18/±45 negative, Pap negative:** Finally, those who are HR-HPV positive with a normal Pap test and negative for HPV16/18/±45, could be retested 6 to 12 months later for HR-HPV and be referred to colposcopy if still positive for HR-HPV (persistent HR-HPV infection).
  - **HR-HPV positive, Pap negative**: In another triage strategy, a Pap test is done when a woman tests positive for HR-HPV. Referral to colposcopy is planned if the Pap is abnormal[10,15]. Those with a normal Pap test could have a repeat cytology testing at 6 and 12 months or be tested for HPV16/18/±45. Women are referred to colposcopy if they are positive for these types or have an abnormal Pap on repeat testing.

*Note: at the time of this publication, some jurisdictions in Canada are considering different triage strategies for primary HPV testing.

Follow-up procedures have to adhere to local recommendations where and when they exist.

Scenario 1.4: HPV testing after treatment of high-grade cervical disease.

Clinical situation:

Finally, the woman in scenario 1.3 tested positive for HR-HPV and triage showed infection with HPV16. She was then referred as indicated in the laboratory report to colposcopy. A high-grade precancerous lesion was demonstrated at colposcopy and was excised. Follow-up by the gynecologist to ensure that treatment was successful was planned with cytology and HR-HPV testing 6 months after treatment. She is now concerned by the delay between testing and the value of HR-HPV tests and meets you for reassurance about these delays.

Relevant information which can be shared with the patient:

- Post-treatment follow-up testing, frequently known as Test of Cure (TOC), using cytology and/or HR-HPV assay allows to determine whether a high-grade precancerous lesion has been cleared or persisted after a surgical procedure. The objectives of posttreatment follow-up testing are to confirm whether treatment was effective, to prevent invasive cancer, and to reassure women [25].
- HR-HPV testing is more sensitive than cytology in detecting high-grade cervical disease after treatment and is the most accurate predictor of treatment outcome[9,12,25].
- A European study showed that the 5-year risks of high-grade cervical lesion associated with negative cytology, negative HR-HPV and a negative co-test at 6 months post treatment was 5.8%, 4.4% and 3.0%. Negative co-tests at 6 and 24 months resulted in a 5-year risk of high-grade lesion similar to that of women within routine screening supporting 6- and 24-month follow-up visits [25].
- Thus, some recommend to perform both HR-HPV tests and cytology in the follow-up of treated women to increase the likelihood of residual or recurrent lesions[21,24,25], explaining why she will have during follow-up both cytology and HR-HPV testing.
- The ability of HR-HPV testing to predict persistent or recurrent high-grade cervical disease is over 90%[9]. HR-HPV persistence represents the main risk factor for recurrence that is not always dependent on margin status.
- Persistence of HR-HPV infection post-excision of high-grade cervical lesion is a risk factor for residual or recurrent disease and will be detected with HR-HPV testing. On the contrary, clearance of HR-HPV infection is an indicator of successful surgical treatment[9,22,23].
- HR-HPV infection persists in approximately 20% of treated women. However, only half of these women will have recurrent or persistent precancerous high-grade lesions [9,22].
- Women with HR-HPV + who had a treatment for a high-grade cervical lesion can be retested at the post-treatment assessment visit. A negative test signals a lower risk of recurrence for the high-grade lesion. A woman with a positive test is at greater risk of recurrent disease.

- Current guidelines recommend testing with HR-HPV detection 6 months after the procedure and not before. If the HR-HPV test is positive, then repeat colposcopy and treatment of any lesions could be performed [9]. After this initial testing, HR-HPV testing will be scheduled each year until consecutive tests are negative, allowing eventually to increase the interval of testing to three years[9]. The risk of developing a recurrent high-grade cervical lesion is less than 1% after three negative HR-HPV tests[20].

Section 1 References: HPV Test and Screening

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Section 2

Sexual Transmission of HPV

Author: Ann N. Burchell, PhD

Objectives:

1. To clarify issues regarding the risks of sexual transmission of HPV
2. To provide information on the natural history of HPV infections
3. To advise on ways to reduce the chances of transmitting HPV

Scenario 2.1: A woman in her first sexual relationship receives a positive HPV test result – how was HPV transmitted?

Clinical situation:

A woman receives a positive result for high-risk HPV. She has had only one sexual partner and they have been sexually active for about one year. She is on oral contraceptives and they are currently not using condoms. Her questions include:

a) What is the possibility this was contacted from a fomite, such as a toilet seat or another non-living object,t rather than from her boyfriend?

b) Should her partner have a test to see if he is still infected with this HPV?

c) Should she encourage her partner to wear a condom even though she herself is not concerned about pregnancy as she is on oral contraceptives?

d) How will she know when she is no longer infectious for possible future sexual contacts?

Relevant information which can be shared with the patient:

- Reassure her that HPV is very common among both women and men. More than 75% of people get it at least once[1,2,3,4].
- HPV is transmitted through skin-to-skin sexual activity. It is most easily transmitted through vaginal or anal intercourse. Transmission via oral sex occurs,[5,6] and it may also occur via hand-genital touching though this is thought to be far less efficient[7]. Although it is theoretically possible for HPV to transmit via fomites, this is thought to be exceedingly rare compared with sexual activity[3,4,6, 8-13].
- No HPV test is currently approved for men. In the absence of a wart or lesion, no treatment is available or needed. For most men, the body will control an HPV infection on its own and penile cancer is extremely rare[15]. Some head and neck cancers, specifically of the oropharynx, have been on the rise in men and women in high-income countries including in Canada, with greater risk for males[16-18].
- Perfect condom use for vaginal and anal intercourse offers some protection although it is incomplete, usually in the order of a 20% to 70% reduction in risk [20-23]. Using condoms may help to prevent infecting her current and future partner(s). There is also some evidence that consistent use of condom may help to clear HPV infection about 1.7-12 times more quickly and may increase the likelihood of regression of cervical lesions by 3-5 fold[23], compared to non-users or inconsistent users.
- The vast majority of HPV infections last only 1-2 years, and the body controls the infection on its own[1-3]. In most cases, the duration of infectiousness would be short lived, and future HPV-negative tests can provide reassurance. Nevertheless, some HPV infections can go dormant, remain undetectable by current tests, and later reactivate (e.g., during a period of immune suppression)[19], and so it is impossible to state unequivocally that the risk of transmission is zero. As described in more detail in scenario 4.3, the decision to inform future partners is a personal one.
- HPV vaccination could be offered to protect against the HPV types addressed by the vaccine in the future (refer to section 3). Notably, HPV vaccination is now indicated for prevention of oropharyngeal cancers.

Scenario 2.2: Woman with genital warts – can she still have sex?

Clinical situation:

A woman with a new boyfriend presents with genital warts. She is very concerned about these and has questions:

a) Does she need an HPV test to know if she has an oncogenic HPV as well as the one presumably that has caused the genital warts?

b) Is she at increased risk of acquiring an oncogenic HPV or other sexually transmitted infections?

c) Can she still have sex with her boyfriend? Does she need to inform him that she presumably has this virus?

d) How long will the genital warts persist?

Relevant information which can be shared with the patient:

- HPV is very common among both women and men. More than 75% of people will get at least one genital HPV during their life[1-4].
- The HPV types that cause genital warts do not cause cervical cancer. However, people who get one HPV type may have been infected with another HPV type or another sexually transmitted infection. Offer cervical cancer screening tests (see Section 1) if she is due for one, and emphasize the importance of regular cervical cancer screening according to the recommended intervals (refer to Appendix 1, page 49).
- Also, discuss the importance of routine screening for other STIs and HIV and recommend screening for these[1-3].
- HPV is transmitted through skin-to-skin sexual activity. It is most easily transmitted through vaginal or anal intercourse. Transmission via oral sex occurs[5], and it may also occur via hand-genital touching though this is thought to be far less efficient[7]. Transmission is more likely to happen when a lesion/wart is present. It is likely that the boyfriend has HPV too[3,4,6,8-13].
- Condom use for vaginal and anal intercourse offers some protection although it is incomplete, usually in the order of a 20% to 70% reduction in risk[20-23]. Using condoms may help to prevent infecting her current and future partner(s). There is also some evidence that consistent use of condoms may help to clear HPV infection about 1.7-12 times more quickly[23], compared to non-users or inconsistent users. Condom use also helps to prevent transmission of other sexually transmitted infections[1].
- Suggest that she make her partner aware of her genital wart diagnosis out of concern and care for the health of her partner, if she feels comfortable disclosing. Points to emphasize: HPV is extremely common. In the absence of a lesion, no treatment is available or needed, but follow-up may be recommended.
- Regarding how long warts may persist, one option is to wait and see if the they go away on their own. About 50% of warts clear naturally within 4 to 6 months. If the warts persist and/or are bothersome, discuss topical and ablative treatment options[1,2].

- Consider HPV vaccination to protect against other HPV types in the future and prevention of recurrence (refer to section 3 for a discussion about the value of vaccine in similar cases).

Scenario 2.3: Couple with recurring genital warts – who infected whom?

Clinical situation:

A middle-aged male has had recurring but infrequent genital warts since his 20s. He has been married for over 10 years to his wife who had no signs of warts and has had normal cytology results in the past. His wife recently had an extramarital partner and subsequently developed genital warts. The couple wishes to remain together but they have questions:

a) Could they be co-infecting each other with different HPV types? Should she get an HPV test?
b) Is it likely that she got HPV from her extramarital partner rather than her husband since this is the first time she developed warts?
c) Should they use condoms?
d) Should they avoid oral sex?

Relevant information which can be shared with the patient:

- HPV is very common among both women and men. More than 75% of us get it at least once[1-4].
- HPV is transmitted through skin-to-skin sexual activity. It is most easily transmitted through vaginal or anal intercourse. Transmission via oral sex occurs[5,6], and it may also occur via hand-genital touching though this is thought to be far less efficient[7]. Transmission is more likely to happen when an intraepithelial lesion or a wart is present. Repeat infections are possible[6,8-13]. (See section 3 for a discussion about the potential for vaccine to help prevent HPV infection).
- At this time, there is no practical method to find out when one first acquired HPV. Since HPV is so common, and may be detected soon after infection or many years later, it is not helpful, or fair, to blame a sexual partner[1-3].
- The HPV types that cause genital warts do not cause cervical cancer. However, people who get one HPV type may have been infected with another HPV type or a sexually transmitted infection. Recommend cervical cancer screening to the wife, if she is due for one, and emphasize the importance of regular cervical cancer screening according to the recommended intervals (refer to section 1 and see page 49 for guidelines in each province and territory). Recommend screening for other STIs if needed[1-3].
- Condom use for vaginal and anal intercourse offers some protection although it is incomplete, usually in the order of a 20% to 70% reduction in risk[20-23]. Using condoms may help to prevent infecting her current and future partner(s). There is also some evidence that consistent use of condoms may help to clear HPV infection about 1.7-12 times more quickly and may increase the likelihood of regression of cervical lesions by 3-5 fold[23], compared to non-users or inconsistent users.

Section 2 References: Sexual Transmission of HPV

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Section 3

HPV Vaccine as Part of the Pre- or Post-HPV Test Counselling

Author: Marc Steben, MD

Objectives:

1. To state the net benefits of HPV vaccination in sexually active patients with or without HPV test positivity
2. To counsel about the limitations of natural immunity following the clearance of an infection or a lesion
3. To explain the potential benefits of HPV vaccination under different clinical scenarios

Scenario 3.1: Newly single 35-year-old female considering a new relationship

Clinical situation:

A 35-year-old female recently divorced and is now single. She had a negative Pap test 9 months ago. She wants STI screening and an HPV test. From her search on internet and from advice of health professionals in her area she found that she was too old to get the vaccine.

Relevant information that can be shared with the patient about HPV vaccination:

It is important to realize that NACI has recently removed upper limit of age for HPV prophylactic vaccines: "**HPV2, HPV4 or HPV9 vaccine …may be used** in **females over 26 years** of age who have not been vaccinated previously or who have not completed the series"[1].

- Vaccine recommendations made by the manufacturer through the product monograph are prescribed by Health Canada and are more restrictive than professional groups or personalized recommendations of a health worker.
- Women, sexually experienced or not, can benefit from HPV prophylactic vaccination[1,2].
- Most likely she has not been exposed to all HPV genotypes available in the HPV prophylactic vaccines[2], therefore HPV vaccination can still be of benefit to her.
- Women already infected by one of the HPV types available in the vaccines still will get better protection against infection or disease from other vaccine HPV types to which she was not exposed[2,3].
- The protection acquired by naturally eliminating HPV is short-lived, not detectable in a significant proportion of people that clear the infection and does not protect against reinfection or disease[4, 9].
- Women already infected by a vaccine HPV type, presenting with a lesion or not, will get better protection against reinfection and new site lesion or recurrence of the original lesion from the vaccine compared to natural immunity.
- Emphasize the difference between HPV testing for cervical screening and routine STI testing. HPV testing is not a routine part of an STI screen.
- HPV testing is never a prerequisite to HPV prophylactic vaccines and neither pre- nor post-vaccination testing is recommended.
- HPV serology testing is not available outside research laboratories.

Scenario 3.2: Genital warts present in 32-year-old single woman

Clinical situation:

A 32-year-old single female, unvaccinated against HPV, has recently been diagnosed with AGW. She read that HPV vaccines are safe and effective to prevent AGW and wants to know if the HPV vaccine could help her in getting rid of her AGW.
As a primary-care provider, would you give the same counselling for a male patient?

Relevant information that can be shared with the patient about HPV vaccination:

- Anogenital warts are caused by LR-HPV, mostly types 6 and/or 11 and protection against these types is offered only in the 4 and 9 valent vaccines (HPV4, HPV9)[1].
- HPV vaccines have no therapeutic value for her current AGW.
- In patients with external genital lesions, mainly genital warts, the 4-valent vaccine has been found to decrease recurrences of anogenital warts and other external lesions and to help prevent lesions of the cervix if the HPV type in the lesion was one of the vaccine types. Similar findings have been seen for the 9-valent vaccine[3].
- Even if she was already infected by one of the HPV types available in the vaccines, she will receive better protection against disease or re-infection from already exposed HPV types by receiving the 9-valent vaccine if the type she is exposed to is in the vaccine[3].
- The protection acquired by naturally eliminating HPV is short-lived, not detectable in a significant proportion of people that clear the infection and does not protect against reinfection or disease[4].
- Women, sexually experienced or not, can benefit from an HPV prophylactic vaccine[1,2].
- Most likely she has not been exposed to all HPV genotypes available in the HPV prophylactic vaccines[2].
- Condoms offer some protection against transmission for the covered anogenital sites if installed before any sexual contact.
- Timely disclosure to a new partner should allow the time for that partner to start HPV vaccination with the 9-valent HPV vaccine since the 4-valent is not available in Canada anymore; the vaccine would offer better long-term protection than a condom.
- The National advisory committee on immunization has recommended HPV vaccines to persons with AGW[8].

Counselling for a male patient with AGW

- The above counseling also would apply for men
- Only the 4-valent and 9-valent vaccines have been tested in males[1]

Scenario 3.3: Recent diagnosis of high-grade disease of the cervix in a 44-year-old woman

Clinical Situation:

A 44-year-old female has a histologically confirmed high-grade intra-epithelial lesion of the cervix. She is scheduled for a LEEP (Loop Electrosurgical Excision Procedure). After surfing the internet, she wonders if an HPV vaccine could be of use in her case since it seems so effective in preventing high-grade disease. She would also like her husband to receive the HPV vaccine.

Relevant information that can be shared with the patient:

- High-grade disease of the cervix is caused by HR-HPV.
- The HR-HPV types (HPV types 16 and 18) found in the 3 HPV vaccines account for 70% of high-grade disease of the cervix[1,5].
- The HR-HPV types found in the 9-valent HPV vaccine account for nearly 90% of high-grade disease of the cervix[1,5].
- HPV vaccines have no therapeutic value for this patient's *current* high-grade disease of the cervix.
- Even if this patient was already infected by one of the HPV types of the vaccines, she will get better protection against disease or re-infection from already exposed HPV types, or a new vaccine type, by getting the 4-valent or 9-valent vaccine[3].
- Irrespective of the HPV type in the lesion, patients who had received a cervical treatment for high-grade disease of the cervix and had received the 4-valent vaccine (compared to the recipients of the placebo) have been found to benefit through a decrease of all new HPV disease by 46%, all grades of cervical disease by 48%, high-grade disease of the cervix by 65% and all external lesions by 47%. The protection provided by the 9-valent vaccine has also been demonstrated.[14]
- If the lesion is associated with HPV types 6, 11, 16 or 18, it is useful to know that 4-valent vaccine recipients had a reduction of all HPV 6-11-16-18 genital disease by 79%.[3] The protection provided by the 9-valent vaccine has also been demonstrated.[14]
- The vaccine is very effective (women who did not receive the 4-valent HPV vaccine had a hazard ratio [HR] of 2.840 [p<.01] to prevent a recurrence of high-grade disease of the cervix compared to those who had received it)[6,9].
- The protection acquired by naturally eliminating HPV is short-lived and does not protect against reinfection or disease[4,9,10].
- Women, sexually experienced or not, can benefit from the HPV prophylactic vaccine[1,2].
- This patient has most likely not been exposed to all HPV genotypes contained in the HPV prophylactic vaccines[2,10].
- Aside from the benefits of HPV vaccination, it is important to recommend follow-up colposcopies for the woman's high-grade neoplasia.

- Regarding the value of having this patient's husband vaccinated against HPV, the value of the vaccine for him personally is mostly about protection against head and neck cancer[1, 11,12]. There is also no age limit for males to get the 9v HPV vaccine[11,12]. There is data about the higher risk for head and neck cancer in men who have female partners diagnosed with high grade lesion of the cervix and cancers as well as other male malignancies, possibly preventable through immunization if her wife's lesions are caused by an HPV type included in the vaccines.
- Since reinfection is a risk factor for recurrent high-grade disease of the cervix, there might be value for the partner, male or female, to be vaccinated to help prevent further infection or disease in his wife.
- The National advisory committee on immunization has recommended HPV vaccines to women with Pap test anomalies[8].
- There are currently at least 7 studies showing that HPV vaccination in women with cervical disease significantly reduces the rate of recurrence.

Counselling for a male patient with Anogenital Warts (AGW), including men who have sex with men (MSM)

Gardasil 9 is now approved for males 9-45 years[15] but NACI does not limit the age for the vaccine when the vaccine is needed.

- Most of the counselling that is applicable to women about HPV vaccines and high-grade disease of the cervix also would be applicable for men who have sex with men (MSM) and for those who have high-grade disease of the anus.
- Only the 4-valent and 9-valent vaccines have been tested in males[1].
- High-grade disease of the anus is mostly caused by HR-HPV.
- The HR-HPV types found in the 2-valent and 4-valent HPV vaccine account for 50% of high-grade disease of the anus.
- The types found in the 9-valent HPV vaccine account for 90% of high-grade disease of the anus.
- HPV vaccines have no therapeutic value for high-grade disease of the anus.
- HIV negative MSM who had received the 4-valent vaccine had a statistically significant reduction in the rate of recurrence of their high-grade disease of the anus[7].
- The p value at <.06 at 3 years would be due in part due the sharp attrition occurring between the second and third year of the study indicating that protection for men may not be as long as for women[7].
- HIV negative MSM who had received the 4-valent HPV vaccine had lower rates of recurrences for anogenital warts[13].
- The above findings have not been explored yet for the 9 valent vaccine[3].
- Even if MSM were already infected by one of the HPV types of the vaccines, most have not been exposed to all types of the 4-valent or 9-valent vaccine[3].
- The protection acquired by naturally eliminating HPV may be less frequently detected in males than females, short-lived and does not protect against reinfection or disease[4].

- Men, sexually experienced or not, whatever sexual preference or age, can benefit from HPV prophylactic vaccine[1,2]. The 9v HPV vaccine is now approved for males aged 9-45 in Canada in the product monograph but NACI does not recommend an upper age limit [1,15].

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Section 4

HPV Testing:
What do your patients want to know?

Author: Laurie W Smith RN(C) BN MPH

Objectives:

1. To help patients understand the rationale behind HPV testing for cervical screening
2. To provide guidance regarding how to deliver HPV positive results to the patient
3. To provide guidance regarding partner notification of HPV results

Cervical screening is a public health intervention women undergo for the majority of their adult life and the Pap smear is something people are familiar but not necessarily comfortable with. A change in the approach to screening can raise questions, concerns and anxiety[1,2,3]. It is important providers, as trusted sources of information, are prepared to address a variety of concerns and questions. Questions that patients have may surround: the reason for the change in approach to screening; the extended screening interval with HPV testing; and the implications of an HPV positive result. Being armed with key points and messages will be helpful as people start to receive HPV testing and HPV results for cervix screening. Below, are a few key messages the provider may find helpful in conversations with patients.

- HPV is VERY common; most people will be exposed at some point in their lives. This fact helps normalize and de-stigmatize HPV.
- HPV is the necessary cause of cervical cancer----but we haven't always had the technology HPV testing is improved technology allowing us to identify people at risk for pre-cancer, or cancer earlier and better than cytology[1,2,3].
- HPV testing detects the presence of HPV DNA, and can identify women at risk for cervical pre-cancer earlier and better than cytology. Cytology testing detects changes to the cells of the cervix ***after*** they have already changed as a result of an HPV infection. LSIL is mostly acute infection by HPV.
- HPV testing is highly sensitive, and has a high negative predictive value. If someone's HPV test result is negative, it is highly unlikely HPV is present or that they have cervical dysplasia (there is much less of a chance of a false negative with HPV testing than with cytology)
- HPV is the most common sexually transmitted infection in the world. It's reasonable to assume that most people will be exposed to HPV at some point in their lives. However, most HPV infections are transient, and the body's immune system will resolve it without any consequences[4]
- In a smaller number of people, an HR-HPV infection does not clear. It is only this kind of long- term, persistent infection that may lead to cervical pre-cancer and cancer. The timeframe between infection and development of high-grade intraepithelial lesion from a persistent HPV infection can be 10-15 years or longer in immunocompetent people. More rapid development of high-grade lesions might be caused by HPV 16 and/or 18 rather than other HR-HPV or in an immunocompromised state.

The scenarios presented below are a few examples to help guide conversations between the provider and patient.

Scenario 4.1: A 46-year-old woman married to the same partner for 20 years presents for screening and has questions about the differences in tests

Clinical situation:

A 46-yr old, married long-term, presents for cervical screening. She is aware that she is eligible to receive HPV testing but has many questions. She wants to know:

- What are the differences between HPV and Pap testing.
- Why she would benefit from HPV testing vs. her usual Pap smear.
- Why she would not be screened again for 5 years if the HPV test is negative.

Relevant information that can be shared with the patient:

NOTE: Screening program guidelines and algorithms differ between provinces (See Appendix 1)

- HPV has *always* caused squamous or glandular cervical cancer. However, in the past, we haven't had the technology to test for the presence or the integration in the cell of HPV itself. As with many things in our world, technology changes and improves. With the introduction of HPV testing, we now have the ability to offer improved cervical screening
- The Pap smear (cytology testing) identifies cervical cell changes that have already occurred, so that they can be treated prior to progressing to cervical cancer. HPV testing identifies the virus that causes these cell changes, often before they can be seen on the cytology. HPV testing can detect and lead to treatment of cervical pre-cancer earlier, and better than cytology[4,5]
- HPV testing every 5 years is at least as sensitive for detection of abnormalities as Pap screening every 3 years[6]. To the patient, this means one negative HPV test every 5 years is AT LEAST as safe as a negative Pap test every 3 years[7, 8]. Testing more often than necessary may identify transient HPV infections that would otherwise go away on their own and can lead to unnecessary anxiety and or treatment (there are harms to over-screening----more screening does not mean better screening)
- To be at risk for pre-cancer or cancer, one must have a long-term infection for many years (usually 10-15 years or more) with a high-risk HPV type. Historically, cervical screening with cytology has been recommended every 2-3 years because it has the potential for false negatives and screening more frequently, enhances the performance of cytology (not because cell changes occur quickly).

- Participating in cervical cancer screening as recommended by the guidelines established in each province is one of the best ways to protect against cervical cancer.
- For more information, refer the patient to the additional resources found in Appendix 1.

Scenario 4.2: A 38-year-old single female, receives HPV positive results

Clinical situation:

A 38-yr old, divorced, and dating woman, is concerned about her positive HPV test results. She wants to know next steps, is there a "cure", and if she will develop cervical cancer. She feels it important to convey that she is not promiscuous. She wants to know how to determine who gave her HPV and if she can catch it again.

Relevant information that can be shared with the patient:

- A positive HPV result does NOT mean a person has or will develop cancer. Knowledge of HPV status allows clinicians to determine next steps to manage accordingly in order to detect and treat pre-cancer to prevent cervical cancer. Not all HPV infections lead to pre-cancer but when HPV is detected, a person can have reassurance that they will be followed closely. One of the best ways to prevent cervical cancer is to participate in routine cervical screening.
- HPV testing for cervical screening will identify if a HR-HPV type is present. Follow-up after HPV is detected, often is determined by the type of HPV detected. If HPV types 16 and/or 18 are detected, given the association between cervical cancer risk with either of these genotypes, a person may be immediately referred to colposcopy. If genotypes other than HPV 16 or 18 are detected the next step is often cytology testing to see if any abnormal cervical cells are also present. The results of either colposcopy or a follow-up Pap, of these tests will determine future management and follow-up.
- At the time of publishing this document, primary HPV testing algorithms including triage strategies have not yet been established. However, many jurisdictions across Canada are in various stages of planning for HPV-based screening. It is likely that most jurisdictions will be implementing an HPV-based screening approach with partial genotyping. Partial genotyping can detect HPV 16/18, and "other" high-risks separately so a more tailored triage approach can ensure those at highest risk for dysplasia are managed accordingly.
- There is no specific "cure" for high-risk HPV; however, successful treatment is available for the effects of an HPV infection if it has caused changes to the cells of the cervix (e.g., LEEP if needed for moderate to severe dysplasia) Management or future treatment will be determined based on the combination of HPV results and the cytology and/or colposcopy results.
- It is not possible, nor is it necessary, to determine when HPV was caught or from whom. HPV may be detected soon after infection or not until many years later. HPV is very common in the population. Most people are unaware if they have an HPV infection, and the body usually clears the infection on its own. It is possible to be re-infected again in the future with the same or other HPV types
- It is also possible that a person may have acquired HPV years ago, and it remained "undetectable" or "latent" for many years; as people age, there may be reactivation of a previous HPV infection[9]
- For more information, refer the patient to the resources found in Appendix 1.

Scenario 4.3: A 33-year-old woman in a new relationship with a previous history of genital warts presents with a recent positive HR-HPV test

Clinical situation:

A 33-year-old woman, has tested positive for HR-HPV (non-16 or 18). Her cytology results are normal. She is in a relatively new relationship. She had genital warts 10 years ago, but has not had them since. She wonders if this is why she is HPV positive now, or if her new partner gave her HPV. She wants to know if she should tell her current partner or future partners, about her HPV results.

Relevant information that can be shared with the patient:

- There are many types of HPV, some are called LR-HPV types and some are HR-HPV types. LR-HPV are associated with AGW and they do not lead to cervical cancer. It is only a persistent infection (i.e., many years) with HR-HPV that can lead to cervical cancer.
- HPV testing identifies if an HR-HPV infection is present (HPV testing for cervix screening does not detect if low-risk types are present). A history of AGW will not affect the results of HPV testing for high grade intraepithelial lesion during cervical screening, nor can people receive HPV testing to assess for AGW.
- Extensive HPV genotype testing is available and is useful in research but it is not recommended in screening for the prevention of cervical cancer. Testing might be available through a private lab for a fee but is not recommended.
- It's a personal decision whether or not to notify a partner of the results of a Pap or HR-HPV test. Because HPV is very common, it is likely both partners have been exposed at the time the infection is detected. In addition, HR-HPV could have been contracted years before and it's not possible to determine from whom a person may have caught the HPV infection.
- HPV is not a "reportable" infection, like some other STIs (for example, chlamydia or syphilis) so the same "contact tracing or notification" process for sexual partners, to offer them testing and treatment, is not required with an HPV positive result.
- If choosing to tell a partner, start with the basics: HPV is the most common STI, and one can assume that most sexually active people are exposed at some point in their lives; HPV is not the same as other STIs (i.e., chlamydia/gonorrhea); it's not helpful, or necessary to determine from whom a person got HPV or when; HPV related cancers are less common in men, and there currently is no HPV test for men.
- For more information, refer the patient to the resources found in Appendix 1.

Section 4 References:

HPV Testing: Interpreting the Results to the Patient

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Section 5

HPV Testing and Beyond: Complex Psychosocial Issues

Author: Zeev Rosberger, PhD

Objectives:

1. To understand and assess complex psychosocial - sexual reactions to test results
2. To understand the implications of standard psychoeducational and supportive interventions
3. To provide guidance on when to refer to an experienced psychosocial health professional

Scenario 5.1: A 30-year-old single woman, with several past sexual partners since sexual debut, recently had a positive HPV test and Pap and colposcopy biopsies indicating CIN3

Clinical situation:

A 30-year-old, single woman was offered co-testing including a Pap smear and an HPV test. All of her previous Pap smears were negative. The HPV test was positive and the Pap smear indicated an HSIL. She was called by her physician, given an appointment where they discussed the need for a referral for colposcopy. The colposcopy appointment was made and scheduled in two weeks. During this time, she became severely anxious, with diminished appetite, and sleep disturbance. A LEEP was performed and follow-up was arranged. She returned 6 months later for a colposcopy and a TOC with HPV testing, the results from which all came back negative.

Relevant information that can be shared with the patient:

- Provide information about high-grade disease evolution into cervical cancer, to address severe psychosocial distress and worry about a cancer diagnosis due to delays in initial diagnosis and treatment[1,2,3].
- Provide strong reassurance and emotional support[6].
- During the initial discussion with the patient regarding the results, a rapid psychosocial screening should be performed by standard brief, psychometrically valid questionnaire (e.g., the GAD-7 or PHQ9); and/or specific mental status questions regarding sleep, appetite, excessive worry/fear, attention, changes in activities of daily living, etc[2].
- Provide information regarding the link between HPV, CIN, and cancer and emphasize the fact that the HPV test, since it is more sensitive than Pap has led to earlier intervention and closer follow-up[1].
- Reassure patient as to prognosis, that distress will usually wane with time, but if persistent, referral to an experienced psycho-social-sexual-oncology health professional should be considered[5].

Scenario 5.2: A 35-year-old woman attends her first screening at the urging of her husband and receives a positive result for HR-HPV.

Clinical situation:

A 35-year-old woman, married for 12 years with two children, undergoes HPV testing when her husband discovers she has avoided screening and health care visits in general throughout her life, as she is fearful of receiving 'bad news'. Her screen is positive for HR-HPV but her triage Pap is negative. She had a few partners prior to marriage and assumes this was also her husband's experience, and she is a smoker since high school. She is given an appointment to return in 12 months for follow-up HPV testing and Pap.

Relevant information that can be shared with the patient:

- The woman may be a health care avoider and this suggests a slightly different counselling approach. An informational-only approach may not be enough to help the woman change her healthcare avoidance behavior and cope with her fears. More complex responses may require more sensitive interventions.
- Requires appropriately nuanced information regarding mechanisms of transmission of HPV and associated risk factors and need for surveillance (transmission information available elsewhere in this document. See general information section).
- Requires information about the importance of follow-up as per guidelines due to long term risk if infection does not clear.
- There exist individual differences in information-seeking styles and levels of intolerance of uncertainty that will moderate stress and anxiety and perhaps compromise health behaviour compliance. More health information may not always be effective. On the contrary, more information may increase anxiety and lead to greater avoidance in someone with high health communication avoidance and high intolerance of uncertainty. Consider using alternate approaches (in addition to information) such as motivational, behavioural and social cognitive approaches.
- The patient should be reassured that her particular information-seeking style is 'normal', as there are many in the general population who feel similarly.
- If the patient so desires, then a brief informational sheet or pamphlet could be provided.
- An assessment should be made regarding her history of health care avoidance and as to how much information the patient desires and is willing to tolerate. With the patient's permission, her partner could be invited to participate, receive the detailed information, encourage the patient to quit smoking to reduce the recurrence of HPV infection and ensure she attends follow-up screenings.

Scenario 5.3: A 21-year-old single, unemployed woman attends a community health clinic as she is concerned about a possible STI

Clinical situation:

A 21-year-old, single, unemployed woman presents at a clinic because wants to know if she has an STI. She has a history of multiple partners since sexual debut at age 16, inconsistently using condoms, and has also experienced 2 pregnancies which were terminated with therapeutic abortions. She has a history of smoking, alcohol and drug use, but denies use of IV drugs. Based on her clinical history of non-compliance/loss to follow-up, she is incorrectly, and against current guidelines, offered an HPV screen and the results are positive for HR-HPV. Pap is negative. HIV test is negative and all other STI tests are negative.

Relevant information that can be shared with the patient:

- Ensure patient is aware that a positive HPV test result in patients under age 30 (25 in some jurisdictions), does not signify an increased risk for cervical cancer, nor have implications for her partners. HPV testing in patients under age 25 is inappropriate.
- A detailed sexual, STI/HPV, drug and personal history will contextualize the patient's current and ongoing life issues, especially as they affect sexual activity and possibly impulse control.
- A further assessment of the person's psychosocial history and the social determinants of health (housing situation, existing support network, etc.), and suggesting community supports and referrals, may be appropriate.
- Detailed written, website and other educational materials regarding the mechanisms of transmission of HPV, specific risks regarding HIV and HPV (as well as Hepatitis C), the short- and long-term risks of other STIs as well, should be given in conjunction with opportunities for questions and discussion[1,2].
- Provide information regarding regular follow-up for retesting at current guideline specified intervals, detailed feedback regarding preventive practices, i.e., condom use, where to find needle and syringe programs (if applicable), and the option of STI testing and/or cervical cancer screening (e.g., HR-HPV testing results) and communication with sexual partners.
- Future appointments should be made for retesting with telephone reminders if possible.
- If appropriate and with consent, the opportunity should be taken to refer the patient for drug counselling and/or rehabilitation[6] and/or to ensure she has access to information about local needle and syringe programs, if available.

Section 5 References:

HPV Testing and Beyond: Complex Psychosocial Issues

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Appendix 1

Additional Resources – General (in alphabetical order)

1. **Canadian Cancer Society:**
   https://cancer.ca/en/cancer-information/cancer-types/cervical/screening
2. **Centres for Disease Control Atlanta:** www.cdc.gov/hpv/index.html
3. **Cervical Cancer Screening Guidelines Across Canada:**
   https://s22457.pcdn.co/wp-content/uploads/2021/01/cervical-cancer-screening-environmental-scan-2019-2020-Jan132021-EN.pdf (see pages 10-11)
4. **GOC – The Society of Gynecologic Oncology of Canada:**
   https://gyneoncology.ca/gynecologic-cancers/cervical-cancer/
5. **Government of Canada:**
   https://www.canada.ca/en/public-health/services/diseases/human-papillomavirus-hpv.html
6. **HealthLink BC:**
   https://www.healthlinkbc.ca/illnesses-conditions/cancer/cervical-cancer
7. **HPV Information - Society of Obstetricians and Gynaecologists of Canada (SOGC):** www.hpvinfo.ca
8. **Immunize Canada: www.immunize.ca/en/diseases-vaccines/hpv.aspx**
9. **National Institutes of Health: https://www.cancer.gov/types/cervical**
10. **PHAC - Public Health Agency of Canada:**
    www.phac-aspc.gc.ca/std-mts/hpv-vph/hpv-vph-vaccine**eng.php**
11. **SOGC - Society of Obstetricians and Gynaecologists of Canada: www.sogc.org**

Additional Resources – For Clinicians (in alphabetical order)

BC Centre for Disease Control. HPV: A Patient's Guide
https://smartsexresource.com/resources/hpv-a-patients-guide/

BC Centre for Disease Control. Sexual Health Information for Everyone.
https://smartsexresource.com/wp-content/uploads/resources/bccdc-hpv-provider-guidebook-2021-screen.pdf

BC reference guide for Healthcare Professionals (FAQs):
http://www.bccancer.bc.ca/screening/health-professionals/cervix

Canadian Partnership Against Cancer (professional): (Evidence-based cancer system tools):
http://www.cancerview.ca/preventionandscreening/cervicalcancercontrolincanada/

Canadian Task Force on Preventive Health Care (CTFPHC): Website included recommendation algorithm, Clinician FAQ:
http://canadiantaskforce.ca/ctfphc-guidelines/2013-cervical-cancer/clinician-algorithm/

Cervical Cancer Screening Guidelines by Province/Territory

For Canadian Provincial and Territorial cervical screening programs and guidelines:

Canadian Cancer Survivor Network:
https://survivornet.ca/cancer-type/cervical-cancer/screening-programs/cervical-cancer-screening-and-clinical-guidelines-across-canada/

Canadian Partnership Against Cancer. January, 2021. Cervical Screening in Canada: Environmental Scan (https://s22457.pcdn.co/wp-content/uploads/2021/01/cervical-cancer-screening-environmental-scan-2019-2020-Jan132021-EN.pdf (see pages 10-11)

AB: https://screeningforlife.ca/for-health-providers/cervical-screening-information/?d=1#clinical_practice_guidelines

BC: http://www.bccancer.bc.ca/screening/Documents/Cervix-Program-Overview.pdf
www.bccancer.bc.ca/screening/health-professionals/cervix

MB:https://www.cancercare.mb.ca/export/sites/default/screening/.galleries/files/getcheckedmb/g-hcp-guidelines.pdf (see page 5)

NB: https://www2.gnb.ca/content/dam/gnb/Departments/h-s/pdf/en/Cancer/screening/CervicalCancerScreeningGuidelines.pdf

NL: https://www.nlma.nl.ca/FileManager/Documents/docs/2016/Cervical_Screening_Guidelines-2016.pdf

NS: https://library.nshealth.ca/Cancer/Screening#s-lg-box-15620653

ON:
https://www.cancercareontario.ca/sites/ccocancercare/files/assets/OCSPScreeningGuidelines.pdf

PE: https://www.princeedwardisland.ca/en/information/health-pei/pap-screening-and-cervical-cancer-prevention
https://www.princeedwardisland.ca/en/information/health-pei/pap-and-cervical-screening-clinics

QC: https://www.inspq.qc.ca/en/publications/1371
https://www.inesss.qc.ca/fileadmin/doc/INESSS/Rapports/Oncologie/INESSS_Cancer_col_uterus_Avis.pdf

SK: http://www.saskcancer.ca/health-professionals-article/cancer-screening-guidelines-and-resources/cervical-cancer-screening
http://www.saskcancer.ca/images/pdfs/health_professionals/clinical_resources/cancer_screening_guidelines_and_resources/Cervical%20Cancer%20Screening%20Guidelines.pdf

NU: **www.gov.nu.ca/sites/default/files/fillpdf/cervical_cancer_screening_guidelines-final.pdf**

NWT: **https://www.cancernwt.ca/services/d%C3%A9pistage-et-d%C3%A9tection-pr%C3%A9coce/cervical-cancer-screening**

YK: https://survivornet.ca/cancer-type/cervical-cancer/screening-programs/cervical-cancer-screening-and-clinical-guidelines-across-canada/

Additional Resources – For Patients (in alphabetical order)

1. **Canadian Medical Association Journal – cervical screening recommendations**
   https://www.cmaj.ca/content/185/1/35.full
2. **Canadian Task Force on Preventive Health Care (CTFPHC): Website included recommendation algorithm for patient, patient FAQ**
   https://canadiantaskforce.ca/guidelines/published-guidelines/cervical-cancer/
   http://canadiantaskforce.ca/tools-resources/cervical-cancer-2/cervical-cancer-patient-algorithm/
3. **BC Screening patient information:**
   http://www.bccancer.bc.ca/screening/cervix/get-screened
4. **Canadian Partnership Against Cancer (patient and families)**
   https://www.partnershipagainstcancer.ca/topics/cervical-cancer-screening-in-canada-2021-2022/programs/
5. **HPV FOCAL Study for patient (FAQs)**:
   http://www.bccancer.bc.ca/our-research/participate/cervical-screening#HPV--&--testing--FAQs
   A comprehensive list of FAQs surrounding HPV, HPV testing and HPV positive results

Cervical Screening Programs by Province/Territory

AB - www.screeningforlife.ca/cervical

BC - www.bccancer.bc.ca/screening/cervix

MB - https://www.cancercare.mb.ca/screening/cervix#clinics

NB - www2.gnb.ca/content/gnb/en/departments/health/NewBrunswickCancerNetwork/content/NewBrunswickCervicalCancerPreventionScreeningProgram.html

NL –
https://cancercare.easternhealth.ca/prevention-and-screening/cervical-screening-program/
https://www.centralhealth.nl.ca/cervical-screening-initiatives
https://westernhealth.nl.ca/index.php/programs-and-services/services-a-z/provincial-cervical-screening-initiatives-program

NS – https://www.nshealth.ca/service-details/Cervical%20Cancer%20Prevention%20Program
https://cdha.nshealth.ca/nova-scotia-cancer-care-program-5

ON - https://www.cancercareontario.ca/en/types-of-cancer/cervical/screening

PE - https://www.princeedwardisland.ca/en/information/health-pei/pap-screening-and-cervical-cancer-prevention

QC - https://www.msss.gouv.qc.ca/ministere/lutte-contre-le-cancer/depister-le-cancer/#col-uterus
https://www.inesss.qc.ca/fileadmin/doc/INESSS/Rapports/Oncologie/INESSS_Cancer_col_uterus_Avis.pdf

SK - http://www.saskcancer.ca/screening-article/screening-programs-for-cervical-cancer

NT - The Pap test can be done at any health centre or primary care clinic. Book an appointment with your primary care provider to be screened.

NU - appointments for Pap tests can be made through a health care provider or a community clinic

YK - appointments for Pap tests can be made through a health care provider or a community clinic