Chapter 3: Cervical Cancer Screening Guidelines

Learning Objectives	On completion of this section, the learner will be able to: 1. Identify who should participate in cervical cancer screening and how frequently. 2. Identify who should not participate in cervical cancer screening. 3. Identify who should have increased surveillance.

The cervical cancer screening guidelines in Manitoba are based on the most recent epidemiological data on human papillomavirus (HPV) and cervical cancer and aim to maximize the benefits of screening while minimizing the harms.

Effective March 14, 2022, HPV Triage testing was implemented in Manitoba. Cervical cytology labs in Manitoba began automatically perform high-risk human papillomavirus (hrHPV) testing on the Pap test specimens of women:

- 30 years of age and older with ASCUS Pap test results, and
- 50 years of age and older with LSIL Pap test results.

HPV Triage is used to detect hrHPV genotypes on the Pap test results listed above to determine which patients require colposcopy versus those who can return to routine screening.

Cervical Cancer Screening Eligibility and Interval[1]

It is important to be familiar with the timing and frequency of cervical cancer screening. The following section outlines the cervical cancer screening guidelines for eligible clients in Manitoba.

General Guidelines	
Initiation of screening	• All women and transgender or non-binary individuals with a cervix who are, or have ever had sexual contact (wanted and unwanted) including sexual intercourse, oral and digital skin-to-skin contact involving the genital and/or anal area, or sex with sex toys, should begin screening at 21 years of age. • Women and transgender or non-binary individuals with a cervix who have not had sexual contact by age 21 should delay screening until sexually active.
Routine screening/screening interval	• Every 3 years.
Cessation of screening	• Screening can be discontinued if the client is 70 years and older and has had 3 negative Pap test results in the past 10 years. • Unscreened and/or underscreened clients 70 years of age and older should have 3 consecutive Pap tests, each one year apart. If the results are reported as negative, screening may be discontinued. • Screening can be discontinued after a total hysterectomy as per the guidelines below.

INITIATION OF SCREENING

Background

Infection with human papillomavirus (HPV) is the main risk factor for cervical cancer and is the most prevalent sexually transmitted infection in Canada.[2] 80% of Canadians will have at least one HPV infection within their lifetime. Persistent HPV infections with the same HPV genotype may cause cervical dysplasia, and if left untreated over time, can progress to invasive cervical cancer. Almost all cervical cancers can be traced to oncogenic HPV types; 70% of invasive cervical cancers are caused by HPV types 16 and 18.

The peak incidence of HPV occurs in women under 25 years of age.[3] However, over 90% of HPV infections regress within 24 months without symptoms or intervention.[2 4] It is not clear if "viral clearance" means that an individual's immune system completely eliminates HPV infection or reflects "viral latency" where the amount of virus is reduced to levels undetectable with current diagnostic methods. HPV infections are very common in the lifespan of any individual with a lifetime probability of over 80%.[5] Persistent infection with the same HPV genotype is a necessary risk factor to develop a high-grade cervical precancer abnormality.[6]

It is not clearly understood why HPV infections "resolve" in certain individuals and disease (cervical abnormalities) develops in others. Disease is a rare consequence of this common infection.

When progression occurs, it happens over a long period of time. One study showed that the mean time for progression from LSIL to HSIL was as long as seven years.[7] Approximately 15% of Pap tests in women under the age of 21 in Manitoba will be reported as either low-grade squamous intraepithelial lesion (LSIL) or atypical squamous cells of undetermined significance (ASCUS).[8]

High-grade squamous intraepithelial lesions (HSIL) represent less than 4% of Pap tests in women under the age of 21 in Manitoba.[5] Cervical cancer in young women is very rare. Since 1980, 0.18% of invasive cervical cancers were diagnosed in women under 21.[5] As well, there is a long latent period between exposure to HPV infection and the development of precancerous lesions and invasive cervical cancer. Therefore, delaying the onset of screening young women will still provide the opportunity to detect and treat these lesions if they occur.

Recommendation
Screening should be initiated at 21 years of age for all clients who have ever had sexual contact. Transgender males and females may also need regular cervical cancer screening. Healthcare providers should discuss the benefits and potential harms of screening with their patients.

Some sexually active clients may choose to delay onset of screening until 25 years of age as evidence suggests the harms of screening women 21-24 may outweigh the benefits. The decision to delay should take into consideration patients' values, preferences and beliefs.

Rationale
The harms of screening women under 21 years of age outweigh the benefits.

- Pap tests and follow-up procedures expose young women to anxiety and potential harms.
- Treatments such as loop electrosurgical excisions (LEEP) or cone biopsy procedures potentially impact reproductive performance (preterm delivery, low birth weight, increased caesarean section rate, and premature rupturing of membranes)[9], and may be unnecessary in some women.
- "The emotional impact of labeling an adolescent with both a sexually transmitted infection and a potential pre-cancer must be considered because adolescence is a time of heightened concern for self-image and emerging sexuality."[10]
- Cervical cancer in young clients is very rare. Since 1980, 0.18% of invasive cervical cancers in Manitoba were diagnosed in women under 21.[11] Over time, this rate has remained relatively unchanged.
- Most cytological abnormalities in young women are low-grade and non-oncogenic. 90% will spontaneously regress within 24 months.[12,13]
- The latency period between HPV infection and the development of precancerous lesions and invasive cervical cancer is approximately 7 to 10 years.[14] Delaying the start of screening young clients still provides the opportunity to detect and treat lesions.

Although the Canadian Task Force on Preventive Health Care recommends not routinely screening women aged 20-24, a "weak recommendation is assigned due to the uncertainty of the evidence. Screening may still be minimally effective to reduce cervical cancer incidence in this age group.[15] Initiating screening at 21 years of age is consistent with the recommendation made in

most other Canadian provinces and territories, and is also the recommendation made by the U.S. Preventive Services Task Force. CervixCheck will continue to respond to the evolving evidence to support screening guidelines. If patients are interested in deferring initiation of cervical cancer screening, they should have a discussion with their healthcare provider about the potential harms and benefits.

SCREENING INTERVAL (ROUTINE SCREENING)

Recommendation

In the absence of abnormal cytology, routine screening with Pap tests should be performed every 3 years. Healthcare providers (HCPs) should discuss the benefits and harms of screening with patients.

Rationale

Screening every 3 years maintains the benefits of screening while decreasing the harm from over-screening.

- Shorter screening intervals (1-2 years) do not significantly decrease the incidence of cervical cancer more than screening every 3 years.[16 17 18 19 20] Annual screening significantly increases the number of women who are sent for further tests which increase the harms of screening.
- Most countries recommend a 3-5 year interval.

CervixCheck sends recall letters to clients who are overdue for a Pap test.

The greatest reduction in cervical cancer will be achieved by screening eligible women who have not previously been screened, not by screening women earlier or more often.

CESSATION OF SCREENING

The decision to discontinue screening for clients 70 years and older must take into consideration the individual's screening history.

Screening can be discontinued if a client has had 3 consecutive negative Pap tests in the previous 10 years or one negative hrHPV test result in the previous 5 years.

Clients who are 70 years and older who have never had a Pap test, or are underscreened, should have 3 Pap tests one year apart. If these are reported as negative or the patient has a negative hrHPV test result, cervical cancer screening may be discontinued.

The recommendation to discontinue screening in clients 70 years and older is based on evidence that:

- clients with multiple prior consecutive negative cytology or one negative hrHPV result are at low risk for cervical cancer, and
- false positive cytology results incurred from mucosal atrophy in post-menopausal women produces potentially unnecessary follow-up and anxiety in this population.[21]

When providing service to clients 70 years and older, HCPs should:

- obtain a thorough health history to determine whether or not Pap tests are still warranted, and
- provide education about the benefits and risks of continuing to be screened past 69 years of age.

INDIVIDUALS WHO HAVE NEVER HAD SEXUAL CONTACT

If the HCP determines that an individual has never had sexual intercourse or skin-to-skin contact of the anus, genitals or mouth, the HCP should focus on educating them about the benefits of regular screening once they do become sexually active. The decision to start screening should be mutually agreed upon between the patient and HCP.

HPV transmission occurs through sexual intercourse as well as through skin to skin genital contact. Sexual activity includes oral sex, sex with fingers or hands, genital rubbing and sex with sex toys. HCPs should be sensitive to circumstances where sexual abuse may have occurred and may prevent a client from discussing, remembering or defining sexual activity as such.	Important Information

CLIENTS WHO HAVE HAD THE HPV VACCINE

All clients who have ever been sexually active and have received an HPV vaccine should begin routine screening at age 21. Routine screening should occur every 3 years.

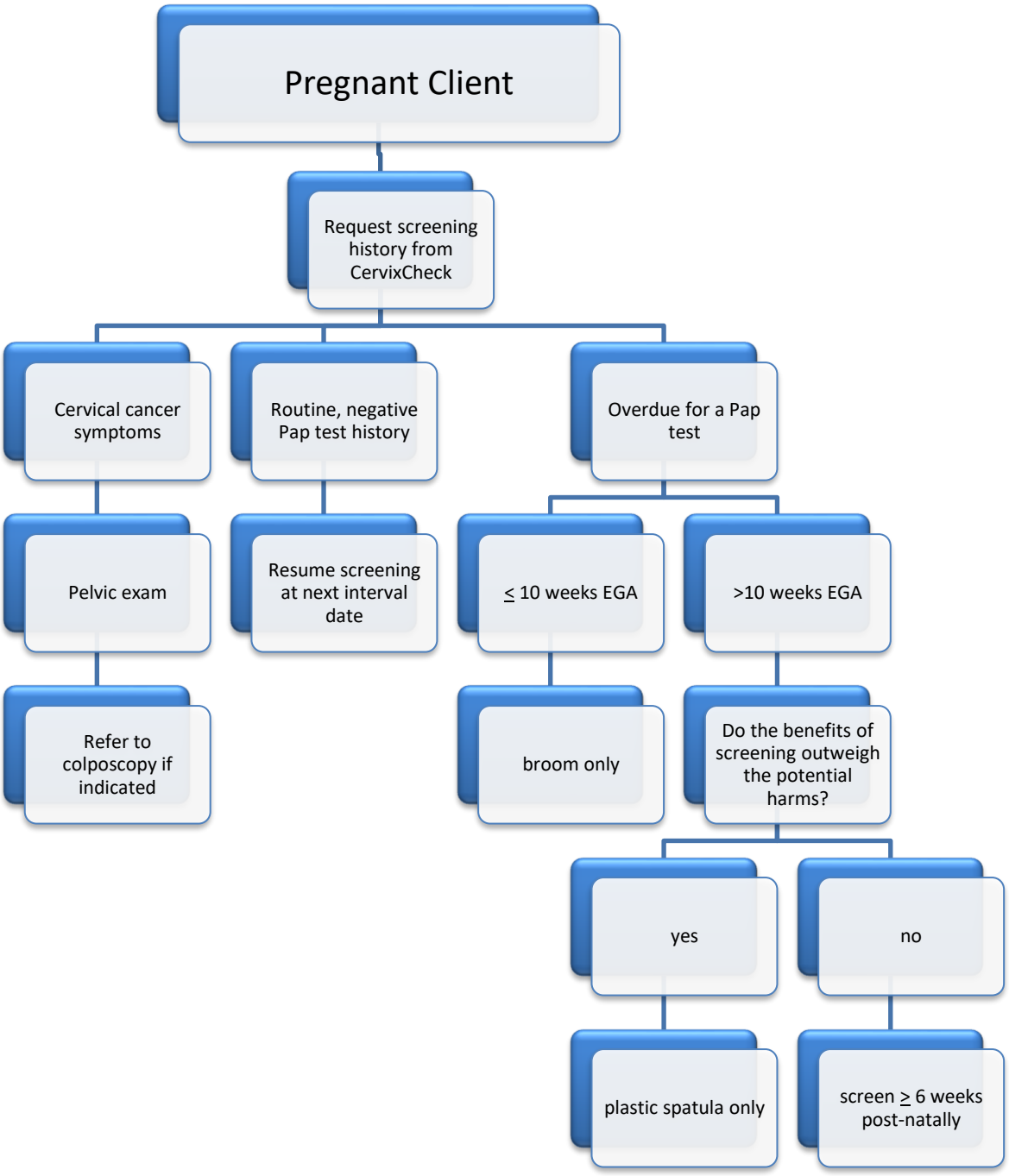
CLIENTS WHO ARE PREGNANT

Screening during pregnancy may produce a significant number of false positive results. Screening pregnant clients is unnecessary if they have had routine negative Pap tests (screening histories can be obtained from CervixCheck). If a pregnant client has any symptoms of cervical cancer, including abnormal bleeding, a speculum exam is appropriate (with or without Pap as indicated). Refer to colposcopy as indicated.

If the HCP determines a Pap test may be necessary due to the client's screening history:

- Aim to screen during the first 10 weeks of pregnancy.
- If the client is over 10 weeks pregnant, the benefits of screening should outweigh the potential harms.
- Only the broom should be used in women who are 10 or less weeks EGA.
- Only the plastic spatula should be used in women who are more than 10 weeks EGA.
- The cytobrush is contraindicated in pregnancy.

Where a pregnant client's history is suggestive of cervical cancer the client should be examined. If a visual abnormality is present the client should be referred to colposcopy.



***The cytobrush is contraindicated during pregnancy.**

CLIENTS WHO HAVE HAD A HYSTERECTOMY

Screening of the vaginal vault (broom or spatula) is unnecessary if the client meets all of the following conditions:

- They have had a total hysterectomy (as opposed to a subtotal hysterectomy)
- Hysterectomy was performed for a benign disease (pathology negative for high-grade dysplasia)
- They have had no previous high-grade dysplasia results

If no previous Pap test record is available and/or no pathology is available from the hysterectomy specimen, the client should have 2 consecutive, negative vault results 1 year apart before discontinuing screening.

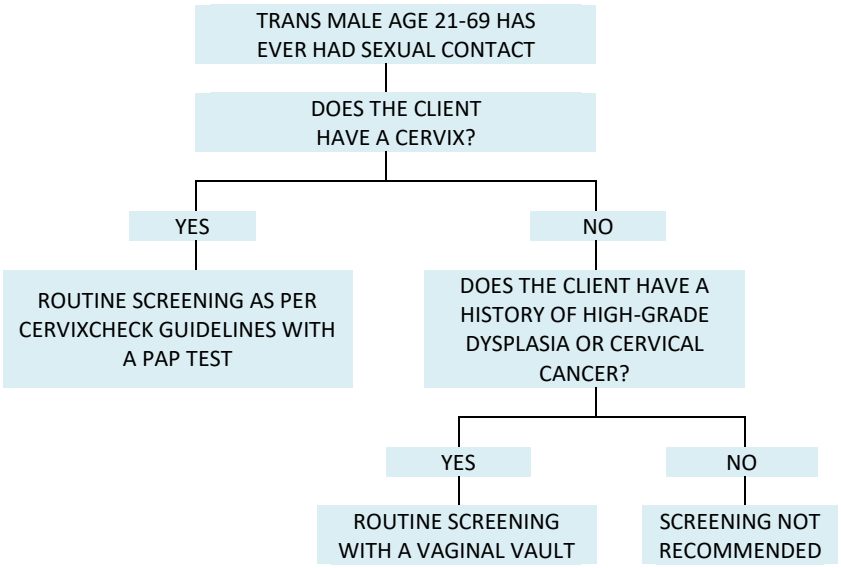
LESBIAN WOMEN OR WOMEN WHO HAVE SEX WITH WOMEN (WSW)

Lesbian women and WSW have a lower incidence of HPV and invasive cervical cancer. Nevertheless, this population is still at risk. Screening for cervical cancer among lesbian women and WSW should be consistent with screening guidelines for women who have sex with men; screening should occur every 3 years (routine screening).

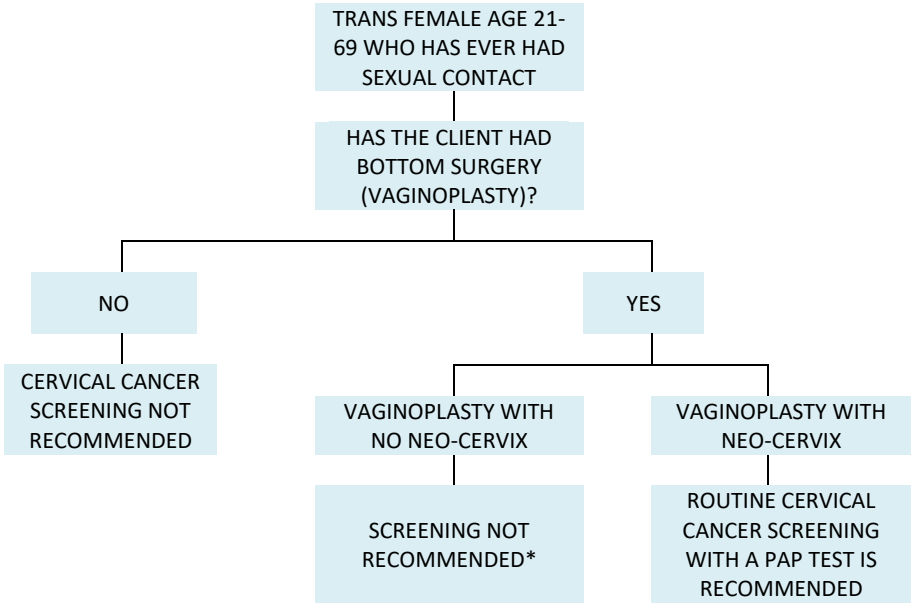
THE TRANSGENDER OR NON-BINARY CLIENT

Screening the transgender client may be necessary. A careful health history should be taken by the HCP to determine if the HCP should proceed with cervical cancer screening, and if so, with a vault smear or a conventional Pap test. Routine screening should occur in the following scenarios:

TRANSGENDER OR NON-BINARY MALE



TRANSGENDER OR NON-BINARY FEMALE



*See the Guidelines for Gender-Affirming Primary Care with Trans and Non-Binary Patients (Sherbourne Health) for more information about visual inspection with speculum.

CLIENTS WHO REQUIRE INCREASED SURVEILLANCE

The following outlines patient characteristics that warrant increased surveillance and provides management recommendations for each of these characteristics.

Patient Characteristics	Management
Recent abnormal Pap test result	Follow up as per the CervixCheck Screening Guidelines "Management of Results"
***Previous high-grade cervical pathology result (≥HSIL/CIN2/moderate dysplasia)**	Screen every year *once discharged from colposcopy*. Screen annually until client meets the criteria to discontinue as per the CervixCheck Screening Guidelines.
Immunosuppressed or HIV positive. Immunosuppression is: ○ CD4 count of < 400 in HIV-positive women, or ○ Transplantation with immunosuppressive therapy > 3 years	Screen every year **All** cytological abnormalities (including low-grade lesions) should be referred to colposcopy
Exposure to diethylstilboestrol (DES)[22] in utero	Screen every year with cytology and colposcopy of cervix and vagina
Previous endometrial cancer	Screening can be discontinued following a complete hysterectomy if patient has no history of high-grade cervical histopathology prior to cancer
Previous ovarian cancer	Screening can be discontinued following a complete hysterectomy if patient has no history of high-grade cervical histopathology prior to cancer
Previous cervical or vaginal cancer	Continue screening annually for as long as the client is biologically healthy

*Cervical **histopathology** specimens have historically been reported using a variety of terminology systems. Squamous abnormalities have generally been reported using terms including “dysplasia”, “cervical intraepithelial neoplasia” (CIN) and “squamous intraepithelial lesions”. Recently, the Pan-Canadian Cervical Screening Network (Canadian Partnership Against Cancer) reported on and published Canadian consensus statements for reporting on histopathology specimens from the cervix and vagina[23]. Manitoba cytology labs have adopted these consensus statements. The following table provides the current cervical histopathology nomenclature, and correlates it to previous reporting terminology.

Cervical histopathology nomenclature correlations

Dysplasia terminology	CIN terminology	2014 Consensus Statements (current)
Normal	Normal	Negative
Mild dysplasia	CIN 1	Low-grade squamous intraepitheleal lesion (LSIL)
Moderate dysplasia	CIN 2	High-grade squamous intraepitheleal lesion (HSIL)
Severe dysplasia	CIN 3	
Carcinoma in-situ	CIN 3	
Dysplasia NOS	CIN NOS	Squamous intraepitheleal lesion (SIL), Ungraded
Adenocarcinoma in-situ (AIS)		High-grade adenocarcinoma intraepithelial lesion
Invasive carcinoma	Invasive carcinoma	Superficially Invasive Squamous Cell Carcinoma (SISCCA)
		Invasion

PREVIOUS HIGH-GRADE CYTOLOGY RESULTS: WHAT'S THE RECOMMENDED INTERVAL?

In the colposcopic management of high-grade (ASC-H/HSIL) or persistent low-grade Pap test results, a sample of cervical tissue (biopsy) is typically obtained to confirm the diagnosis. A significant proportion of histology outcomes, however, do not correlate with the cytology result. The following provides management recommendations for Pap test results that were over-called (the cytologic impression was more severe than the histological diagnosis), under-called (the cytologic impression was less severe than the histological diagnosis), not correlated (no histological diagnosis is available), or correlated (the cytological impression correlated with the histological diagnosis).

Once discharged from colposcopy, and in the absence of a history of high-grade histopathology results, patients should be routinely screened every 3 years.

Cytology result (Pap test)	Histology result (biopsy/ECC)	Recommended screening interval
High-grade (ASC-H/HSIL)	≤Low-grade squamous intraepithelial lesion (Negative/LSIL/mild atypia/CIN 1)	Every 3 years once discharged from colposcopy.
High-grade (ASC-H/HSIL)	≥High-grade squamous intraepithelial lesion (HSIL/CIN 2/CIN 3/AIS/SISCCA*)	Every year once discharged from colposcopy. There is no evidence to support how long annual screening should continue. Discontinue screening once the patient reaches the criteria for cessation as per the CervixCheck guidelines.
High-grade (ASC-H/HSIL) that is not necessarily connected to the current biopsy event, i.e. a high-grade result in the past that has no existing biopsy related to the event.	≤Low-grade squamous intraepithelial lesion (Negative/LSIL/mild atypia/CIN 1)	Every 3 years once discharged from colposcopy (the client may have been pregnant and not referred for colposcopy until result was explored post postpartum, the Pap test may have been overcalled).
High-grade (ASC-H/HSIL)	No biopsy/histopathology	There is no evidence to support a recommended interval. A very conservative approach would be to screen every year. The clinician may consider extending the interval after a few years if all results are negative. This decision should be made in consultation with the client and align with their values and preferences.
High-grade (ASC-H/HSIL)	Cervical cancer	After treatment for cervical cancer, clients should continue screening annually as long as they are biologically healthy. The age of screening cessation for those with a history of cervical cancer is not well defined.

*Superficially Invasive Squamous Cell Carcinoma

PREVIOUS HIGH-RISK HPV TEST RESULT:
WHAT'S THE RECOMMENDED INTERVAL?

The screening interval is dependent on the histopathology result, not the high-risk HPV result or the Pap test result.

Key Messages for Healthcare Providers

- 90% of HPV infections will spontaneously regress within 2 years.
- High grade lesions and cervical cancer are very rare in young clients under 21 years of age.
- There is a long latent period between exposure to the HPV infection and the development of precancerous lesions and invasive cervical cancer.
- Annual screening offers little benefit over screening performed at 2 to 3 year intervals and exposes clients to unnecessary risks and anxieties.
- Pap test sensitivity is 51% and specificity is 98%.
- High-risk HPV testing is 89.9% sensitive and 89.9% specific for CIN2+ results.[24]

Benefits & Potential Harms of Cervical Screening: Facilitating Informed Decision-Making

The CervixCheck screening guidelines aim to ensure clients receive the greatest benefit from cervical cancer screening and avoid unnecessary tests. This balance is achieved when we can identify cervical cancer precursors likely to progress to invasive cancer (**maximizing the benefits)**, and avoid the detection and unnecessary treatment of transient HPV infection and its associated benign lesions that are not destined to become cancerous (**minimizing the potential harms**).

HCPs should facilitate a discussion with clients about the benefits and harms of screening with Pap tests. The goal of the client-HCP discussion is to:

- foster an **understanding** of the Pap test, its benefits and potential harms, and
- support **client participation** in the clinical decision; one that is **informed** and consistent with the individual's **preferences and values.**

For example, a 21 year-old female who only recently became sexually active is very anxious about her first Pap test. After reading a brochure about cervical cancer, she realizes her risk for developing cervical cancer at her age is very low. She wonders if she needs to be screened this year given that this is the recommendation, but her fear about the test continues to make her very anxious.

A discussion between the HCP and the patient would highlight the individual's fears and anxieties about the Pap test, as well as the individual's recent onset of sexual activity. With these factors under consideration, and after a discussion about the benefits and harms of screening with the Pap test, the HCP and client decide together to delay screening for another year. In the meantime, the HCP provider will continue to educate and counsel them about the Pap test, ensuring that when the time comes for the first Pap test, they are informed and feel ready to perform the procedure.

CervixCheck can support you to discuss the benefits and harms of Pap tests with patients. See the Manitoba Cancer Screening Guidelines for more information about benefits and potential harms.

The following chart outlines the benefits and potential harms of screening with the Pap test.

Benefits	Potential Harms
• Observational data have shown declines of up to 80% in cervical cancer mortality following introduction of organized screening with Pap tests • Cervical dysplasia can be removed with procedures during colposcopy • Detecting cancer at an early stage may result in simpler treatment, more treatment options, and less need for chemotherapy	• False positives • False negatives • Screening and follow up may cause anxiety • Discomfort or bleeding may result from the Pap test or colposcopy • Treatment with cold knife conization and large loop excision of the transformation zone (LLETZ) may increase a woman's risk for pre-term delivery, low birth weight, caesarean section, and premature rupturing of membranes during future pregnancies

	Recommended Reading

CervixCheck Resources (cancercare.mb.ca/screening/resources)
CervixCheck Screening Guidelines
HPV Triage – Information for Healthcare Providers
Human Papillomavirus (HPV) Frequently Asked Questions (for patients)

1. Who should have a Pap test and how frequently? 2. Describe the screening guidelines for pregnant women. 3. What are the requirements for not screening the vaginal vault after a hysterectomy? 4. Who should be excluded from Pap tests? 5. Who should be screened with increased surveillance?	Chapter 3 Self-Test

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