BC CANCER CERVIX SCREENING
Provincial Health Services Authority

BC Cancer Cervix Screening Program Overview

O

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Cervix Screening Program

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About BC Cancer

BC Cancer provides a comprehensive cancer control program for the people of B.C. BC Cancer is committed to providing all patients with access to a full range of quality cancer services, regardless of where in B.C. they live.

Vision

A world free from cancer

Mission

To reduce the burden of cancer in British Columbia.

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1. Introduction

British Columbia implemented the first population based cervix screening program in the world in 1955 and from 1955 to 1985 cervical cancer incidence decreased by 70%.[1] The primary goals of the Cervix Screening Program are to detect and remove cervical cancer precursors to prevent the development of cervical cancer and to detect asymptomatic cervical cancer at an early clinical stage to decrease mortality. There were 185 new cervical cancer cases in B.C. in 2017.[1] In the same year, 66% of individuals with squamous carcinoma and 46% of individuals with adenocarcinoma had no screening history or were screened more than five years ago.[2]

Cervix screening tests have a potential for false negative and false positive results. If your patient has any clinically suspicious lesions, abnormal bleeding or other relevant symptoms, further evaluation is required even if a screening test result is normal.

2. Roles for Cervix Screening in B.C.

2.1 Screening Partnership Framework

Cancer Screening in B.C. is organized under a partnership framework with regional health authorities, community imaging, laboratory services and primary care providers. BC Cancer provides oversight for organized cancer screening in B.C., and supports:

- development of provincial policies, guidelines and standards,
- strategies to increase public and health care provider awareness, including both benefits and limitations of screening,
- correspondences to eligible British Columbians about results, follow-up and rescreening,
- quality assurance and quality improvement, and
- reporting and monitoring of system performance and screening outcomes.

In B.C., regional health authorities (RHAs) are responsible for the planning and delivery of healthcare services within their geographic areas. RHAs and community health service providers work with BC Cancer Screening to provide high quality screening and diagnostic investigation services.

In addition, as part of the Indigenous Cancer Strategy, BC Cancer Screening is working collaboratively with the First Nations Health authority (FNHA), Métis Nation British Columbia and the BC Association of Aboriginal Friendship Centres to improve cancer screening access and participation of Indigenous people.

Data is collected and analyzed on an ongoing basis to monitor the program's effectiveness and to identify areas for improvement. The program publishes program results anually.[3]

2.2 Cervical Cancer Screening Laboratory

Pap tests are reviewed and results are provided by the Cervical Cancer Screening Laboratory (CCSL) which is operated by PHSA Laboratories. CCSL processes and interprets approximately 325,000 Pap tests annually. The laboratory distributes cervix screening test sampling supplies to health care providers at no cost.

CCSL demonstrates an ongoing commitment to providing quality patient care by following internationally recognized standards of excellence in laboratory practices. The laboratory is accredited by the College of American Pathologists and by the Diagnostic Accreditation Program of College of Physicians and Surgeons of BC.

Please visit the laboratory website for further information about the laboratory.

2.3 Primary Care Providers

Primary care providers play a key role in:

- Identifying people eligible for cervix screening.
- Educating people about the benefits and limitations of screening.
- Educating people about the importance of regular cervix screening.
- Informing people of the signs and symptoms of cervical cancer.

The following licensed health care providers are able to submit cervical samples for screening in British Columbia:

- Members of the BC College of Physicians and Surgeons,
- Members of the BC College of Nursing Professionals who meets the additional competency criteria for pelvic exams and cervix screening,
- Members of the BC Naturopathic Association and
- Members of the College of Midwives of BC.

Health care providers are responsible for ensuring that a report is received for each cervix screening test submitted and are responsible for:

- Informing screening participants of screening test results,
- Ensuring screening participants are referred for specialist assessment and investigation when required, and that ongoing care is coordinated.

2.4 Colposcopy Services

If a cytology result recommends colposcopy follow-up, the Cervix Screening Program will facilitate a referral to the patient's nearest colposcopy clinic with certified colposcopists.

In B.C., colposcopy is a non-core competence for gynecologists and gynecological oncologists. Credentialing and Privileging for colposcopy occurs at the Health Authority level for those who provide this service at a B.C. hospital. Gynecologists interested in providing colposcopy are encouraged to participate in the B.C. Colposcopy Training program facilitated by BC Cancer. The training includes course work with an exam and participation in colposcopy clinics with a trained colposcopist. An annual education event is provided for colposcopists in B.C. and participation in ongoing education activities, submission of quality indicator data and meeting indicator benchmarks is expected. See the Cervix Screening Program Colposcopy Standards for further information on colposcopy.

Most colposcopy services in B.C. are provided in hospitals operated by the regional health authorities. Some colposcopy is provided out of private offices. Colposcopists are responsible for providing colposcopy and treatment reports to the primary care provider.

2.5 Pathology

Pathology laboratories in each health authority are responsible for reporting results on cervix related biopsy and excisional samples. Laboratories are expected to endorse and implement the Cervix Screening Program Pathology Standards.

3. Screening Program Eligibility

Screening seeks to balance the benefits of screening while limiting the potential harms. The current Cervix Screening Program policy was implemented in 2016 and incorporates evidence from review of the literature, the B.C. Lifetime Prevention Schedule and the Canadian Preventative Services Taskforce.[4, 5]

Screening is recommended for people with a cervix ages 25-69 who are or have been sexually active. Sexual activity includes intercourse, as well as digital or oral sexual activity involving the genital area with a partner of any gender. Further details about eligibility and the rationale are as follows.

For individuals with significant co-morbidities that are likely to limit life expectancy, the need for screening should be assessed on an individual basis and discussed with the individual.

3.1 Frequency of Screening for Average Risk Individuals

Screen by cervical cytology every three years.

The current Canadian Task Force on Preventative Health Care cervical cancer screening guidelines recommends a three year screening interval as the best balance between the small incremental benefit from shorter intervals against the potential harm of overtreatment because of more frequent screening.[4] Screening every three years with cervical cytology is also recommended as an acceptable strategy for cervical cancer prevention by the United States Preventative Services Task Force. [6] Modeling data from eight countries (1,381 people with squamous cell carcinoma of the cervix and 2,259 age-matched controls), estimated the effect of different screening intervals on cervical cancer rates in people ages 20-64 (see table below). [7] Annual screening from ages 20-64 produced the greatest reduction in cervical cancer incidence (93%). Screening every three years was only marginally less protective at 91%, or 90% if screening commences at age 25. [7] Many cervical abnormalities regress within two years of diagnosis [8-10], and therefore a three year screening interval limits over diagnosis while still providing almost identical protection. A modeling study of 938,576 people with biopsy proven cervical neoplasia estimated the excess risk of progression to cervical carcinoma to 3 per 100,000 in people who were screened every three years compared to those screened annually. [11]

Table 1: Effect of different screening intervals.

Effect of Different Screening Policies on Cervical Cancer Incidence, ages 20-64

Age Range	Interval (years)	Lifetime tests	% Reduction in Incidence of Cervical Cancer	Test per Cervical Cancer Prevented
20-64	1	45	93%	3,030
20-64	3	15	91%	1,042
25-64	3	13	90%	917

Adapted from IARC working group evaluation. [7]

3.2 Age to Start Screening

Initiate screening at age 25.

The recommendation to initiate screening at age 25 is based on several factors.

Cervical cancer is rare in people under age 25. Analysis of B.C. data of cervical cancers diagnosed between 1986 and 2009 showed an incidence of 0.5 per 100,000 in people at age 20 and 1.35 per 100,000 in people aged 20 to 24.[12] This incidence is the same as the incidence of breast cancer in men.

Cervix screening appears to be less effective in younger people. A case control study from the United Kingdom showed no significant difference in cervical cancer incidence in people aged 25 to 29 who were screened at ages 20 to 21 or ages 22 to 24 versus people of the same age who were not so screened. [13]

Comparisons of cancer incidence in jurisdictions with different screening commencement ages did not show significant differences in outcomes. In the north-east of England, the screening initiation age increased from age 20 to age 25 in 2004. Cervical cancer incidence in 20 to 25 year old people from north-east England aged 25 increased annually by 10.3% between 2000 and 2009, but also increased by 3.5% annually in people aged 30 to 39.[14] A similar increase was seen in 20 to 25 year people in Wales, where screening of people between the ages of 20 and 24 continued.[14] The incidence and stage data of cervical cancer in people under age 30 in the United Kingdom was evaluated in more detail in 2018.[15] The analysis again showed an increase in the incidence of cervical cancer in 20 to 24 year olds, both in England where the screening 20 to 24 years olds was phased out between 2004 and 2009 but also in Scotland and Wales where screening of this age group continued. Increases in cervical cancer in England in 20 to 24 year olds after 2012 was as a result of screen detected cancers in 24.5 to 25-year old groups, when the age of invitation to screening was changed from age 25 to age 24.5 in 2012. FIGO Stage IA and IB cancers decreased in the 20 to 24.5 years age group and increased in the 24.5 to 25 and 25 to 25.5-year olds age groups. This was explained as the effect of detection of prevalent cervical cancer in the first round of screening. There was no increase in Stage II cancers.[15] The overall picture is reassuring as it points to a slight delay in screen detected disease without evidence that this delay is leading to stage progression at detection.

Only a small subset of cervical cancers in this age group is detected by a screening test, even in jurisdictions where routine organized screening is offered from age 20. In a population based study, only 26% of cervical cancers in people between ages 20 and 25 were detected with a screening test, while 38% were detected as a result of symptoms.[16]

The target abnormalities of cervical cancer screening often undergo spontaneous resolution in young people. Approximately 60 to 70% of biopsy proven cervical intraepithelial neoplasia grade 2 (CIN 2) will regress in younger people over a period of one to three years. [8-10, 17]

Excisional treatments for cervical intraepithelial neoplasia are associated with an increase in premature labour and perinatal mortality (see table 1).[18]

Table 2: Reproductive risk of excisional treatments.

	Anticipated Absolute effects		Relative Risk
	Risk (per 1000) [Comparison]	Risk (per 1000) [Intervention] (95% CI)	Intervention/ comparison
Pre term birth (<37 weeks)	54	95 (85 - 106)	1.75 (1.57 - 1.96)
Pre term birth (<37 to 34 weeks)	14	32 (26 - 40)	2.25 (1.79 - 2.82)
Pre term birth (<28 to 30 weeks)	3	7 (5 - 11)	2.23 (1.55 - 3.22)
Low birth weight (<2500 gram)	37	66 (58 - 76)	1.81 (1.58 - 2.07)
Perinatal mortality	7	11 (8 - 14)	1.51 (1.13 - 2.03)

Adapted from Kyrgiou et. al. [18]

3.3 Age to Stop Screening

Stop screening at age 69, provided that there have been at least three negative screening tests in the past ten years and no active surveillance of cervical cancer or pre-cursor abnormalities.

The decision to stop screening is informed by the data on cervical cancer incidence in this age group, the duration of protection against cervical cancer due to prior screening and the life expectancy at the age of discontinuing screening. The Canadian Taskforce for Preventative Healthcare issued a strong recommendation to continue cervical cancer screening till age 69 and a weak recommendation to discontinue screening at age 70.[4] . Cervical cancer incidence rates in B.C. are highest in the age group 40 to 59 (12.2/100,000 in 2015) [19]. Screening is very effective in preventing cervical cancer in people in this age group.[13, 20] There is no evidence that negative screening history, even after three negative screening results, is sufficiently protective at age 45 to 54 to discontinue screening at this age.[21] After age 65 cervical cancer and pre-cancer incidence rates decrease and most people who develop cervical cancer after age 65 have not effectively participated in screening.

3.4 Screening of Immunosuppressed People

Screen people living with HIV and people living with solid organ transplants annually with cervical cytology. Consider commencement of screening at age 21 instead of age 25 and consider continuing screening beyond age 69 depending on life expectancy and comorbidities.

Routine screening using average risk guidelines is recommended for people receiving: chemotherapy for non-gynecologic cancers, estrogen antagonists, and cytotoxic drugs for autoimmune disorders.

People living with HIV and people living with solid organ transplants experience higher rates of HPV infections, cervical pre-cancer and cervical cancer. People living with HIV and with solid organ transplants have prevalence rates of genital oncogenic HPV twice as high as people without either of these. [22, 23] Similar two-fold increases in the rates of squamous intraepithelial lesion (SIL) rates are observed in these people.[24] People living with HIV have a threefold increase in cervical cancer compared to people without HIV. [23] Cervical cancer rates were reported as 16 per 100,000 person years in people living with HIV in a study of combined North American data. [25] In the same study, the cervical cancer rates in people without HIV was five per 100,000 person years. [25] Cervical cancer incidence in people with renal transplants was reported as 14 times the

rates in people without renal transplants. [26] High rates of cervical cancer are reported in recipients of other solid organ transplants, with reported standardized incidence ratios (SIRs) for heart transplants of 14.3 and liver transplants of 30.7 [27, 28] Cervical cytology interpretation appears to have comparable sensitivity in people living with HIV compared to the general population. [29, 30] Based on duration and risk of exposure to HPV infection, screening may be commenced at age 21 instead of age 25.

There is no evidence that people who are receiving chemotherapy, or estrogen receptor antagonists (such as tamoxifen) are at increased risk of cervical abnormalities. [31, 32]

3.5 Same Sex Partners

The recommendations, as outlined in this section, are the same regardless of the sex or gender of the partner. Generally, commence cervix screening at age 25 and screen every three years until age 69.

3.6 Cervix Screening for Transgender, Gender-Diverse and Non-Binary People

For people with a cervix, follow the recommendations outlined in this section. Generally, commence cervix screening at age 25 and screen every three years until age 69.

The screening strategy for transgender, gender diverse and non-binary people is based on the anatomy present and is summarized below. See further information for supporting cervix screening for transgender, gender-diverse and non-binary people in section 4.[33, 34]

Anatomy	Cervix Screening Recommendation
Vagina with cervix	Follow the recommendations for screening for cervical cancer. Generally this means commence screening at age 25 and screen every three years until age 69. Those with a prior high-grade cervical abnormality (i.e. CIN 2, CIN 3, AIS or cancer) are recommended to follow the guidelines outlined in Section 3.9, Table 3.
Vagina with cervix removed	Individuals who have had their cervix removed and with no prior high-grade cervical abnormality (i.e. CIN 2, CIN 3, AIS or cancer) do not need to be screened. Individuals who have had their cervix removed but had a high grade cervical abnormality (i.e. CIN 2, CIN 3, AIS or cancer), are recommended to have vaginal vault screening for 25 years after the most recent high grade diagnosis.[35]

Testosterone induces genital atrophy which can make visualizing the squamocolumnar junction and obtaining a sample more difficult. Topical local estrogen for four weeks can bring down the squamocolumnar junction and make it a more comfortable exam for the patient. Unsatisfactory cytology results and ASC-US results can be more common in this population which unfortunately results in recommendations for repeat testing. Primary HPV screening instead of cytology may be considered for some patients with difficult to obtain samples. Contact the Cervix Screening Program Medical Director to discuss.

3.7 Screening After Treatment for CIN 2, CIN 3, AIS and Invasive Carcinoma

3.7.1. Endocervical Adenocarcinoma in Situ (AIS)

There are no randomized or pseudorandomized controlled trials to guide management decisions after treatment for AIS. Cohort studies report a risk of recurrent AIS or progression to invasive, or microinvasive adenocarcinoma in 12% to 40% of patients. [36] [37] The best predictors of risk were, completeness of excision and HPV status. [37] [36] Patients should continue with colposcopy follow up unless the AIS has been excised with clear margins and the post treatment HPV test is negative.

There are no long term follow up studies to guide long term follow up, but based on the long term persistence of invasive carcinoma risk for squamous abnormalities, we recommend annual screening with cervical cytology until age 69 or until it has been 25 years since the most recent histologically proven AIS diagnosis. The need for ongoing screening should be considered in view of health conditions that may limit life expectancy of the patient.

3.7.2. Cervical Intraepithelial Neoplasia Grade 2 and 3 (CIN 2 and CIN 3)

The evidence suggests that the risk for invasive carcinoma remains elevated for at least 20 but up to 25 years after excisional treatment for high grade lesions.[38-41] This risk of invasive carcinoma is not significantly altered by hysterectomy.[38] There is acceleration of the risk after age 60, suggesting the need for screening beyond the age at which screening usually ceases.[42] Based on this we recommend to continue screening until age 69 or until it has been 25 years since the most recent histologically proven CIN 2 or CIN 3 lesion. Testing for Human Papillomavirus DNA (HPV Testing) may aid significantly to stratify the risk after treatment for CIN 2 and CIN 3. HPV testing is offered in colposcopy clinics and performed before patients are discharged from colposcopy clinics and is performed at the follow up colposcopy visit 6 months after the excisional treatment. The need for ongoing screening should be considered in conjunction with the overall medical condition of the patient.

3.7.2.1. HPV Status unknown

If the HPV status is unknown, we recommend annual screening for the first five years. The screening interval can be increased to every 36 months after the initial five years, provided that all screening results in this period have been negative and that there have been at least three negative screening tests in the past five-year period.

3.7.2.2. HPV Positive

We recommend continued follow up within the colposcopy clinic until HPV status is negative.

3.7.2.3. HPV Negative

If HPV status is negative at the 6-month colposcopy follow up visit, the patient can be discharged from colposcopy follow up. Cervical cytology collected by the primary care provider 12 months after discharge from the colposcopy clinic is recommended. If cytology at 12 months is negative, the screening interval can be increased to every 36 months. Screening should continue until age 69 or until it has been 25 years since the most recent histologically proven CIN 2 or CIN 3 lesion.

3.7.3. Invasive Carcinoma

3.7.3.1. Superficially Invasive Carcinoma (TNM Stage T1a, FIGO stage IA1 and IA2)

Follow up after treatment for superficially invasive (or microinvasive) squamous carcinoma is identical to follow up after CIN 2 and CIN 3. Data for follow up after superficially invasive adenocarcinoma are lacking. Annual screening until age 69 or until it has been 25 years since the most recent histologically proven adenocarcinoma or adenocarcinoma in situ is recommended.

3.7.3.2. Carcinoma TNM Stage T1b and Higher or FIGO Stage IB or Higher

The patient's oncologist is responsible for the initial post-treatment follow-up. Once discharged from the care of an oncologist, annual screening is recommended for the first five years. The screening interval can be increased to every 36 months after the initial five years, provided that all screening results in this period have been negative and that there have been at least three negative screening tests in the past five-year period. A systematic review found that 89 to 99% of local recurrences of cervical cancer after curative intent treatment occurred in the first five years.[43] Since the vast majority of invasive cervical cancers are caused by HPV there is a risk of developing a second invasive carcinoma of either the cervix or vaginal vault. The magnitude of this risk after treatment for invasive carcinoma is unknown, but based on expert opinion in B.C., screening should continue until age 69 or until it has been 25 years since the most recent histologically proven CIN 2, CIN 3 or invasive carcinoma diagnosis.

3.8 Unscheduled Screening

Other than the history of previous cytological or histological abnormality and immunosuppression (HIV positive or organ transplant recipient), clinical information cannot consistently predict a group of people at higher than average risk for cervical abnormality and it is best to follow average risk guidelines for screening. [44, 45] Healthcare providers play a vital role in preventing over-screening which may lead to screening related harms.

Unless otherwise due for screening, a screening test should not be collected in association with pregnancy (pre- or postpartum), when an intrauterine device is placed or removed, or when oral contraceptive is initiated. There is no reason to commence screening earlier or to screen more frequently as a result of diagnosis of genital warts, multiple sexual partners, new sexual partners, heavy smoking or hormone replacement therapy (HRT).

People with symptoms or abnormal appearance of the cervix should be referred to a colposcopy clinic for evaluation. A Pap test is not recommended and referral to colposcopy should be arranged as soon as possible, regardless of any Pap test result (see section 4).

3.9 Withdrawal from Screening

The decision to participate in cervix screening is an informed choice and people may choose to voluntarily discontinue screening. Apart from informed personal choice, there may be appropriate medical reasons to discontinue screening, such as severe illness that renders screening of limited or no additional health benefit or severe discomfort and/or anatomic impediment to obtaining a satisfactory sample. In the latter instance, a gynecological referral to directly view the cervix and/or to obtain a screening sample should be offered.

It is important to make sure that screening participants are offered the opportunity to be informed of the benefits of screening and the risk of cervical cancer, before the decision is made to not participate in screening.

3.10 Summary of Screening Recommendations

Table 3: Summary of Recommendations

	Categories	Screening Recommendation	Screening Interval
Average risk	**Age 25-69**		
	With a cervix	Recommended	3 years
	Have received the HPV vaccine	Recommended	3 years
	In same sex relationship	Recommended	3 years
	Trans people with a cervix	Recommended	3 years
	High risk behaviours	Recommended	3 years
	Cervix removed [a]	Not recommended	N/A
	Never had sexual contact [b]	Not recommended	N/A
	Age < 25	Not recommended	N/A
	Age > 69		
	Adequate screening history [c]	Not recommended	N/A
	Inadequate screening history and generally well	Recommended	3 Negative Screens [d]
Higher than aaverage risk	**Immunocompromised**		
	Organ transplant	Recommended	Annual
	HIV Positive	Recommended	Annual
	Other (e.g. autoimmune disease)	Recommended	3 years
	CIN 2 and CIN 3 (treated with ablation, excision or hysterectomy) [e]		
	HPV Status Unknown		
	Diagnosed <5 years ago	Recommended	Annual
	Diagnosed between 5 years and 25 years ago [f]	Recommended	3 years
	Diagnosed ≥ 25 years ago and age ≤ 69	Recommended	3 years
	Diagnosed > 25 years ago and age >69	Not recommended	N/A
	HPV Negative and first annual screen negative		
	Diagnosed < 25 years ago	Recommended	3 years
	Diagnosed ≥ 25 years ago and age ≤ 69	Recommended	3 years
	Diagnosed ≥ 25 years ago and age > 69	Not recommended	
	HPV Positive	Per colposcopist recommendation	

History of Adenocarcinoma in situ (AIS), treated		
Diagnosed < 25 years ago	Recommended	Annual
Diagnosed ≥ 25 years ago and age ≤ 69	Recommended	Annual
Diagnosed ≥ 25 years ago and age > 69	Not recommended	N/A
History of invasive carcinoma and discharged by oncologist or colposcopy clinic [e]		
Diagnosed <5 years ago	Recommended	Annual
Diagnosed between 5 years and 25 years ago [f]	Recommended	3 years
Diagnosed ≥ 25 years ago and age ≤ 69	Recommended	3 years
Diagnosed > 25 years ago and age >69	Not recommended	N/A

(a) No CIN 2, CIN 3, AIS, or carcinoma either in past 25 years or identified in hysterectomy sample.
(b) Sexual contact includes intercourse, as well as digital or oral sexual activity involving the genital area with a partner of any gender.
(c) No CIN 2, CIN 3, AIS, or carcinoma in past 25 years, at least 3 consecutive negative screens in past ten years and last screen between age 67 and 69.
(d) Three consecutive negative screens before discontinuing. May be done annually to shorten period of screening.
(e) Cervical or vaginal vault smear.
(f) Five years since diagnosis and at least three consecutive negative screens within 5 years after treatment.

4. Underserved and Vulnerable Populations

Participation in cervix screening is not evenly distributed across populations or cultures. There are known populations that are less likely to screen and keep up-to-date with screening. Factors contributing to the inequity in care are multifactorial and barriers are both personal and systemic. Within a primary care practice, these populations may need additional services and support to be safely encouraged to participate in screening. Conversations with patients and community service providers who regularly support these populations are needed to assess barriers and determine what approach may be required to engage and support the person for regular screening. Cervix screening rates are known or suspected to be lower for the following populations:[46-52]

- Low-income
- Immigrant
- Indigenous (First Nations, Métis and Inuit)
- Transgender, gender diverse and non-binary
- Not attached to a primary care provider
- Rural and remote communities
- Those less familiar with the BC health system
- Those who do not speak the language in which service information is available
- History of trauma and/or violence (ref needed)

In B.C., cervical cancer incidence is higher amongst First Nations people compared to the non-First Nations population.[53]

Some people may prefer a female provider to complete their screening. The Cervix Screening Program maintains a list of providers across B.C. who are willing to see people for cervix screening and includes information on language spoken at the clinic and whether a female provider is available. Ongoing follow-up and care can continue with a person's usual provider. See the Clinic Locator at www.screeningbc.ca.

For transgender, gender-diverse and non-binary people, Trans Care BC has developed several educational resources for providers and patients and are an excellent source for guidance and advice for these populations in B.C. Resources include a document for sexual health screening and pelvic exam.[54] The following information may help with providing cervix screening for this population.

The current trend is an increasing role for the primary care provider in the healthcare of trans people, rather than solely specialist care. This will be facilitated by familiarity with the below terminology, and adoption of pronouns and names used by the patient, which may differ from their identification and medical chart. Provider knowledge of gender-affirming terminology and language can contribute to greater access to services, increased uptake in screening and better health outcomes for trans and gender diverse individuals.

Definitions	
Transgender	People who identify with a gender that is different from the sex they were assigned at birth.
Cisgender	People who have a gender identify that matches the sex they were assigned at birth.
Non-binary	An umbrella term to refer to diverse people whose gender identify is neither male or female
Gender diverse	Gender roles and/or gender expression that do not match social and cultural expectations; gender non-conforming; gender variant.
Two-Spirit	A term used within some Indigenous communities, encompassing cultural, spiritual, sexual and gender identity.

For more information, please visit Trans Care BC: www.phsa.ca/transcarebc

5. Pregnancy, Contraception, Menopause and Hysterectomy

5.1 Pregnancy

Cervix screening tests should only be offered during pregnancy if screening is due or overdue. Screening is not necessary as a routine part of pre-natal screening for those who are up to date with screening.

5.2 Use of Contraceptives

Oral contraceptive use is associated with a small increase in cervical intraepithelial neoplasia (CIN) and cervical cancer, after controlling for HPV infection. There is insufficient evidence to evaluate whether stopping contraception will alter the rate or clearance of CIN and effective contraception should not be discontinued as a result of an abnormal cervical screening test or biopsy proven cervical abnormality. [55]

5.3 Menopause and Use of Hormonal Replacement Therapy

Post-menopause, people generally have lower rates of abnormal cervical cytology results although atrophic changes may cause difficulties with cervical cytology interpretation. Treatment by topical estrogen may occasionally be recommended by the Cervical Cancer Screening Laboratory to aid in interpretation of cervical samples showing atrophic changes. If estrogen is contraindicated a cervical screening test should be repeated at the recommended interval without topical estrogen treatment.

A limited number of studies reported no increase in the risk of cervical cancer or abnormal cervical screening results due to hormonal replacement therapy [56, 57].

5.4 Hysterectomy

People who had a total hysterectomy (i.e. cervix removed and with no past or present high-grade cervical abnormality (i.e. CIN 2, CIN 3, AIS or cervical carcinoma) can discontinue screening.

People who had a subtotal hysterectomy with conservation of the cervix and with no past or present high-grade cervical abnormality (i.e. CIN 2, CIN 3, AIS or cervical carcinoma) should continue to follow average risk guidelines.

People who had a total hysterectomy and with current or past high-grade cervical abnormality (i.e. CIN 2, CIN 3, AIS or cervical carcinoma) should annually screening for the first five years after treatment for the high grade abnormality. The screening interval can be increased to every 36 months after that, provided that there have been at least three consecutive negative screening results in the preceding five years.

In the absence of a history of CIN 2, CIN3, AIS or invasive carcinoma, the risk of vaginal abnormalities or vaginal cancer is low after hysterectomy. In a large cohort study of 10,595 vaginal smears from 6,265 people after hysterectomy, a total of 0.5% of all smears showed atypical squamous cells of undetermined significance, 0.5% showed low grade squamous intraepithelial lesion and 0.1% showed high grade squamous intraepithelial lesion. Subsequent biopsies revealed high vaginal intraepithelial neoplasia in three instances (0.05%) and no vaginal carcinomas.[58]

In contrast, the risk of invasive squamous carcinoma of the vaginal vault remains elevated for up to 20 years after treatment for CIN 2 or CIN 3. This risk is increased, even after hysterectomy. [38]

6. Symptoms or Abnormal Clinical Findings

6.1 Abnormal Cervix

It is very important to directly visualize the cervix when obtaining the sample. If any suspicious abnormality is noticed during speculum examination, please refer for colposcopic evaluation. Do not wait for the cervix screening result and refer even if the screening result is reported as normal.

6.2 Symptoms

Cervix screening is appropriate for those who are age eligible and asymptomatic. People with symptoms including post coital bleeding, persistent intermenstrual bleeding and/or a persistent vaginal discharge that cannot be explained by benign causes such as infection should have a speculum examination by someone with experience in cervical disease. Referral to a colposcopist is appropriate and may be expedited if the clinical suspicion is high. A screening test is not required for referral. Contact bleeding at the time of sample collection, in the absence of other concerning symptoms need not be referred. [59]

7. Conventional Cytology

7.1 Conventional Cytology

The current screening test in British Columbia is the conventional cervical smear. For further information on submitting cervical samples and obtaining supplies, please consult the online documentation of the Cervical Cancer Screening Laboratory (CCSL). [60]

Cervix screening in British Columbia, using conventional cervical cytology, has decreased invasive cervical cancer rates by 70%.[61] Liquid based cytology LBC has not been shown to have higher sensitivity for detecting cervical cancer precursor abnormalities. A meta-analysis of 56 studies showed no difference in detection of high grade cervical abnormalities between LBC and conventional cytology, when only high quality studies were evaluated.[62] In a large randomized trial, LBC showed no improved detection of CIN 2 or more severe abnormality compared to conventional cytology.[63]

8. Cervix Screening Results

The CCSL uses the 2001 Bethesda System for result reporting. Please refer to the CCSL website and documentation for further information regarding reporting format and terminology. Please contact CCSL for any laboratory related concerns. [60]

A table with the positive predictive values (PPVs) for cytology results is outlined below in section 8.13.

8.1 Unsatisfactory and Rejected Samples

In accordance with accreditation standards CCSL has strict specimen labeling requirements and will not process specimens if specimen identification cannot be confirmed. Samples which are inadequate for interpretation due to poor preservation or obscuring elements will be reported as unsatisfactory for interpretation and should be repeated within 6 months.

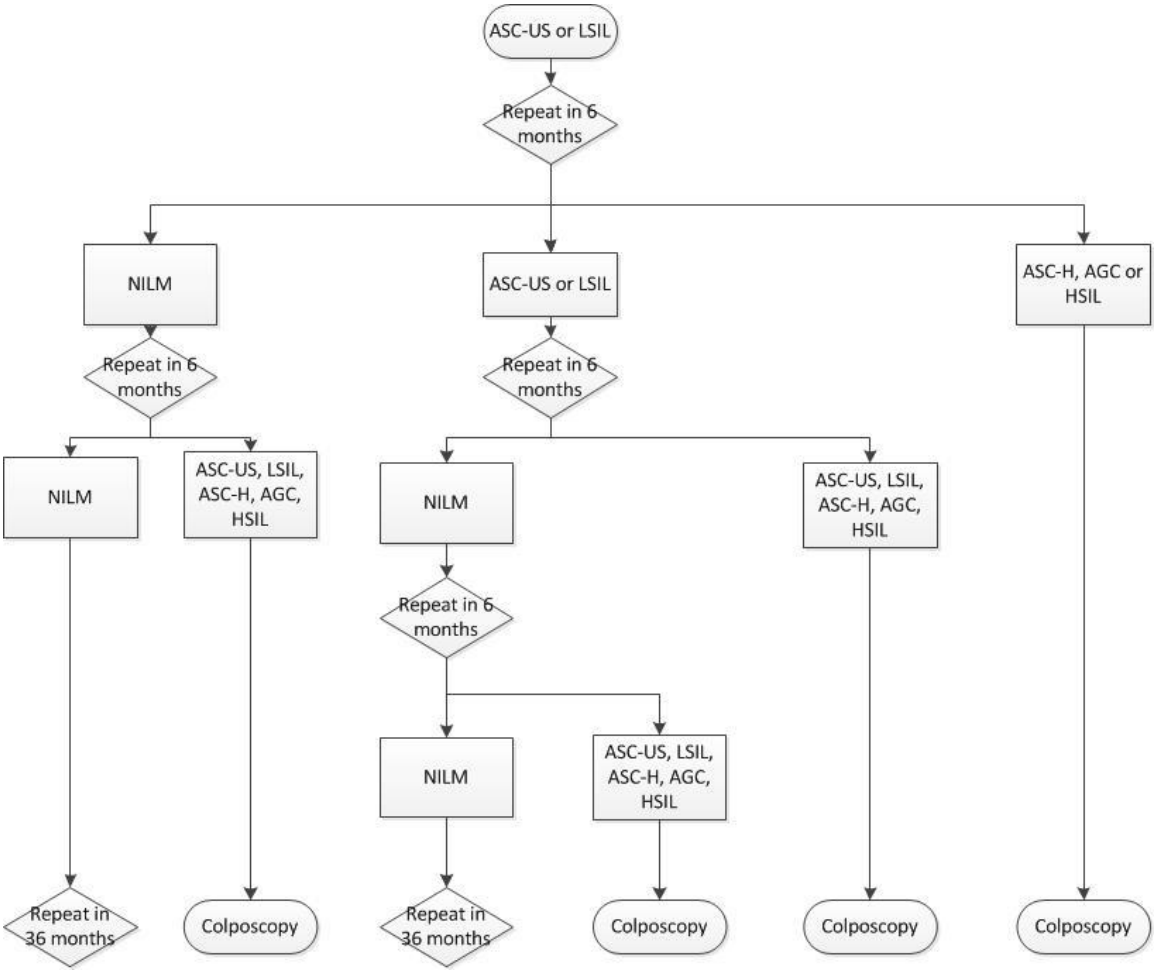
8.2 Negative for intraepithelial neoplasia and malignancy (NILM)

These are screening tests that show no significant abnormality and would generally receive a recommendation to repeat cervix screening in 36 months. Shorter screening intervals are recommended for individuals with immunosuppression, in active follow up for low grade abnormality and after treatment for CIN 2, CIN 3, endocervical adenocarcinoma in situ or cancer. People with significant symptoms including post coital bleeding, persistent intermenstrual bleeding and/or a persistent vaginal discharge that cannot be explained by benign causes such as infection should have a speculum examination by someone with experience in cervical disease. Referral to a colposcopist is appropriate and may be expedited if the clinical suspicion is high. Screening results may be negative in the presence of carcinoma.

8.3 Atypical squamous cells of undetermined significance (ASC-US) and low grade squamous intraepithelial lesion (LSIL)

ASC-US and LSIL are followed by repeat cervix screening at six months and 12 months after the initial ASC-US or LSIL interpretation. Referral to colposcopy is recommended if the abnormality progresses to a higher-grade abnormality (see below) or if either ASC-US or LSIL is still present at 12 months. Return to 36 monthly screening is recommended after two consecutive screening tests reported as NILM. A table with the positive predictive values (PPVs) for cytology results is outlined below in section 8.13.

FIGURE 1: FOLLOW UP DIAGRAM FOR ASC-US AND LSIL



8.4 Atypical Squamous Cells of Undetermined Significance (Cannot Rule Out High Grade Lesion) (ASC-H)

Immediate colposcopy referral is recommended for an interpretation of ASC-H. A table with the positive predictive values (PPVs) for cytology results is outlined below in section 8.13.

8.5 High-Grade Squamous Intraepithelial Lesion (HSIL), moderate dysplasia

Immediate colposcopy referral is recommended for any interpretation of HSIL, moderate dysplasia. A table with the positive predictive values (PPVs) for cytology results is outlined below in section 8.13.

8.6 High-Grade Squamous Intraepithelial Lesion (HSIL), severe dysplasia

Immediate colposcopy referral is recommended for any interpretation of HSIL, severe dysplasia. A table with the positive predictive values (PPVs) for cytology results is outlined below in section 8.13.

8.7 Atypical Endocervical Glandular Cells Not Otherwise Specified (AGC-NOS).

Immediate colposcopy referral is recommended for an interpretation of AGC (NOS). A table with the positive predictive values (PPVs) for cytology results is outlined below in section 8.13.

8.8 Atypical Endocervical Glandular Cells Favour Neoplasia (AGC –FN) and Endocervical Adenocarcinoma In Situ (AIS).

Immediate colposcopy referral is recommended for an interpretation of AGC-FN and AIS. A table with the positive predictive values (PPVs) for cytology results is outlined below in section 8.13.

8.9 Potential Invasive Squamous Cell Carcinoma and Potential Endocervical Adenocarcinoma

Referral for these two categories should be expedited as a matter of urgency. A table with the positive predictive values (PPVs) for cytology results is outlined below in section 8.13.

8.10 Benign Endometrial Cells in Cervical Samples

Benign endometrial cells are a normal finding in the first half of the menstrual cycle. Finding benign appearing endometrial cells in the second half of the menstrual cycle may indicate dysfunctional endometrial bleeding, especially if accompanied by menorrhagia, metrorrhagia or irregular menstrual cycles. Endometrial carcinoma is rare before the age of 45 years, as such, endometrial biopsy or referral for further investigation is generally reserved for those over the 45 years of age. The need for referral should be based on a general assessment of endometrial carcinoma risk inclusive of cytological findings and clinical signs and symptoms. Cervical cytology examination has poor sensitivity for endometrial carcinoma and should not be used as a screening test to either rule in or rule out an endometrial abnormality.

8.11 Atypical Endometrial Cells or Endometrial carcinoma

Patients with these findings should be referred to colposcopy or a general gynecologist for further evaluation. Cervical cytology examination has poor sensitivity for endometrial carcinoma and should not be used as a screening test to either rule in or rule out an endometrial abnormality.

8.12 Possible Extrauterine Carcinoma or Rare Malignancies

These should be dealt with on a case by case basis and may need a multidisciplinary team approach for management. Contact the Cervical Cancer Screening Laboratory for clarification of the results if needed.

8.13 Summary of Positive Predictive Values of Cytology Results

Table 4: Positive Predictive Value of Cytology Result

Cytology Result	PPV for CIN 2, CIN3 or Cancer	PPV for CIN 3 or Cancer	PPV for Cancer
ASCUS	20.20%	9.02%	0.08%
LSIL	27.25%	11.99%	0.05%
ASC-H	53.99%	35.19%	0.90%
HSIL (moderate dysplasia)	67.00%	39.16%	0.42%
HSIL (severe dysplasia)	88.36%	75.35%	4.18%
AGC-NOS	18.60%	14.14%	2.42%
AGC-FN	70.13%	66.23%	23.12%
AIS	81.82%	81.82%	36.36%
Squamous cell carcinoma	90.79%	90.79%	34.21%
Adenocarcinoma	67.86%	67.86%	42.86%

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