Cervical Cancer Prevention and Screening

DRAFT FOR EXTERNAL REVIEW
Questionnaire Available Here: https://shorturl.at/UBzMj
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Scope

This guideline provides recommendations for the primary care prevention, screening and initial investigation for cervical cancer in asymptomatic patients aged 25-69 who are or have been sexually active. The guideline applies to individuals with a cervix, equally to women and TTGD (Two-Spirit, Transgender, Gender-diverse) people and refers to all eligible individuals as "patients". This guideline does not address investigation or management beyond colposcopy, nor does it address other HPV-related cancers in sites outside the cervix.

This guideline was developed to align with BC Cancer Cervix Screening Program information and in consideration of the BC Lifetime Prevention Schedule, In Plain Sight Report, and Truth and Reconciliation Commission of Canada Calls to Action.

Key Recommendations

- All eligible patients should be immunized against the human papillomavirus (HPV).
- All eligible asymptomatic patients aged 25-69 should be screened for cervical cancer every 3-5 years.
- Provide patient education regarding cancer screening, including implications of test results.
- Choose a sample collection method based on patient scenario and preferences.
- Incorporate a trauma informed and culturally safe approach for all patients.
- Screening during pregnancy is not necessary as a routine part of pre-natal screening and is only indicated if due or overdue. If screening *is* to be done during pregnancy, HPV self-collection is not recommended and instead a cervical sample should be collected for liquid-based cytology (LBC).
- While all patients should be screened according to program guidelines, particular attention should be paid to patients with risk factors or those facing barriers to participation to encourage optimal alignment with screening protocols.
- Ensure appropriate longitudinal care interactions for patients who were previously accustomed to having a pap appointment every three years. Consider options for engaging with patients to

identify/address other health and wellness issues, including other preventative care.

- All symptomatic patients should be investigated/managed following best practices, including a speculum examination by someone with experience in gynecologic exams and collection of a LBC sample for co-testing (i.e., HPV and cytology) and identification of presenting symptoms. Appropriate referral should not be delayed pending results of the co-test, if collected. A vaginal sample for HPV screening is not appropriate for symptomatic patients, as it is only for asymptomatic individuals.

Background

BC Cancer leads cancer screening programs for asymptomatic individuals across BC. Historically, the Cervix Screening Program used a conventional Papanicolaou (PAP) smear to detect precancerous lesions. While very specific (96.8%), PAP smears suffer from low sensitivity (55.4%).[1,2] BC Cancer transitioned to a liquid-based cytology (LBC) collection process in 2022 to facilitate timely reporting of results and the ability to test for HPV as well as cytology on a single sample (co-testing).

In 2024, BC Cancer began transitioning to an HPV primary population-based screening program. Research indicates that when HPV testing is used alone or in combination with cytology, there is earlier and enhanced detection of pre-cancerous lesions and a reduction in subsequent cancerous lesions.[3,4] HPV testing is also more reliable, can be done less frequently, and has options for patients to collect their own samples at home. This makes program participation more accessible and convenient for patients across BC, particularly when access to a primary care provider to collect a cervical sample can be a challenge. This represents a significant change for health care providers and patients.

Regular screening reduces the incidence of stage 1A cervical cancer by 67% and stage 3 or worse by 95%.[5] In BC, 66% of patients with squamous cell carcinoma and 46% of patients with adenocarcinoma cervical cancer cases had either never been screened or did not receive timely screening.[6] Unfortunately, only 68% of eligible patients participate in the BC Cervix Screening Program, far less than the 90% target.[7]

Epidemiology

Cervical cancer is the third most frequently identified cancer and fourth leading cause of cancer-related fatalities in females globally.[8,9] One in 170 BC females is expected to develop cervical cancer, while one in 530 will die from it.[7,10] Most are diagnosed before the age of 50.[11]

Studies in BC have shown there are higher rates of invasive cervical cancer in patients who are: Indigenous; current smokers; from rural areas of the province; or who self-identify as visible minorities.[12] Cervical cancer incidence rates are 1.6x in First Nations peoples in BC compared to non-First Nations peoples.[13,14]

Etiology

A persistent infection with a high-risk HPV virus (hr-HPV), accounts for >99% of invasive cervical cancer. [15,16] Among the more than 100 known HPV genotypes, 15 are categorized as high-risk (hr-HPV).[14] The remaining HPV genotypes are categorized as low-risk (lr-HPV), often causing non-

cancerous conditions such as warts. See Table 1: High and Low Risk HPV Types.

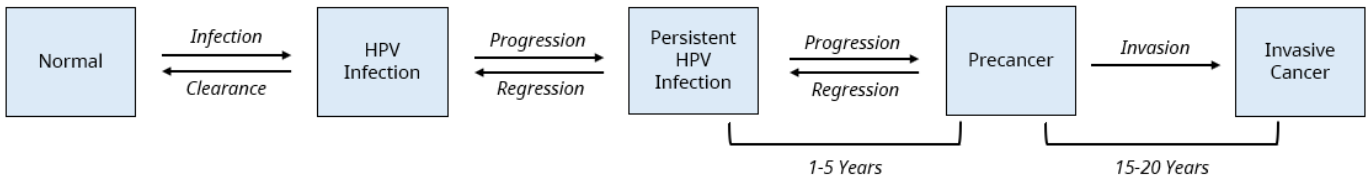
Table 1. High and Low Risk HPV Types[17]

High Risk HPV (hr-HPV)	Low Risk HPV (lr-HPV)
- Associated with cervical cancer, as well as anal, oropharyngeal, penile, vaginal, and vulvar cancers and certain cancers of the head/neck. - *Hr-HPV 16 and 18 are associated with* ***~70%*** *of cervical cancers.* - less common hr-HPV types are 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68.[7]	- Not associated with cervical or other cancers. - Associated with anogenital warts. - 6 and 11 are the most common lr-HPV types.

HPV is transmitted through epithelial-to-epithelial (skin or mucosa) sexual contact.[9] Though less common, it can also be transferred to newborns before or during childbirth.[8,9] Some evidence suggests that HPV infections acquired perinatally may persist atypically.[18] These infections have the potential to cause juvenile recurrent respiratory papillomatosis (RRP), a condition that is rare but particularly morbid.[18]

90% of HPV infections resolve on their own within two years.[19,20] Persistent infections with hr-HPV, lasting for more than two years, can result in cervical dysplasia and subsequent cervical cancer if left undetected and untreated.[19,20] See Figure 1: Cervical Cancer Progression.

Figure 1. Cervical Cancer Progression (adapted from the World Health Organization's International Agency for Research on Cancer)[4]



Risk Factors

Over 99% of cervical cancer is related to a persistent infection with high-risk HPV, with HPV-16 and HPV-18 responsible for 70% of these cancers.[8,15] HPV is the most common sexually transmitted infection (STI) and affects >70% of sexually active Canadians.[9] Individuals are at greatest risk for an HPV infection in the 5-10 years following their first sexual experience.[21]

Other risk factors for cervical cancer include immunosuppression, including human immunodeficiency virus (HIV) infection, smoking commercial tobacco products, multiparity, becoming sexually active at a young age, having many sexual partners or a partner with a history of many sexual partners, history of other sexually transmitted infections, and Diethylstilbestrol (DES) exposure in-utero (Note: DES not commonly used in Canada after 1980).[6,8,9,22] Oral contraceptive use >5 years also increases the risk of cervical cancer, though this risk decreases after discontinuing use and is neutralized within 10 years.[22,23]

While all patients should be screened according to program guidelines, particular attention should be paid to patients with risk factors or those facing barriers to screening program participation to

encourage optimal alignment with screening protocols. Providers should provide education and support to encourage maintenance of healthy behaviours that impact risk.

Prevention

Cervical cancer is best prevented through HPV immunization. Another way to reduce the risk of cervical cancer is to avoid an HPV infection through safe sexual behaviours, including correct condom use.

Early detection through screening programs and early treatment for pre-cancerous lesions are highly effective secondary prevention measures.

Immunization

HPV vaccines are extremely safe and highly effective in preventing HPV infections and cervical cancer.[21,24] Immunization is strongly recommended for all eligible patients unless they have had severe allergic reactions to yeast or a previous dose of the HPV vaccine. Immunization is best initiated at younger ages and prior to exposure to HPV.[25] However vaccines are still effective in older populations and in preventing recurrence for patients previously treated for cervical dysplasia.

The HPV9 vaccine is approved for use in Canada for patients 9-45 years.[26] It is not recommended for use during pregnancy and is contraindicated for patients who are allergic or have hypersensitivities to any component of the vaccine or its container.[26] The vaccine protects against nine types of HPV that together cause approximately 90% of cervical cancers (HPV 6, 11, 16, 18, 31, 33, 45, 52, and 58).[27] The HPV9 vaccine also protects against anogenital cancer and genital warts.[27]

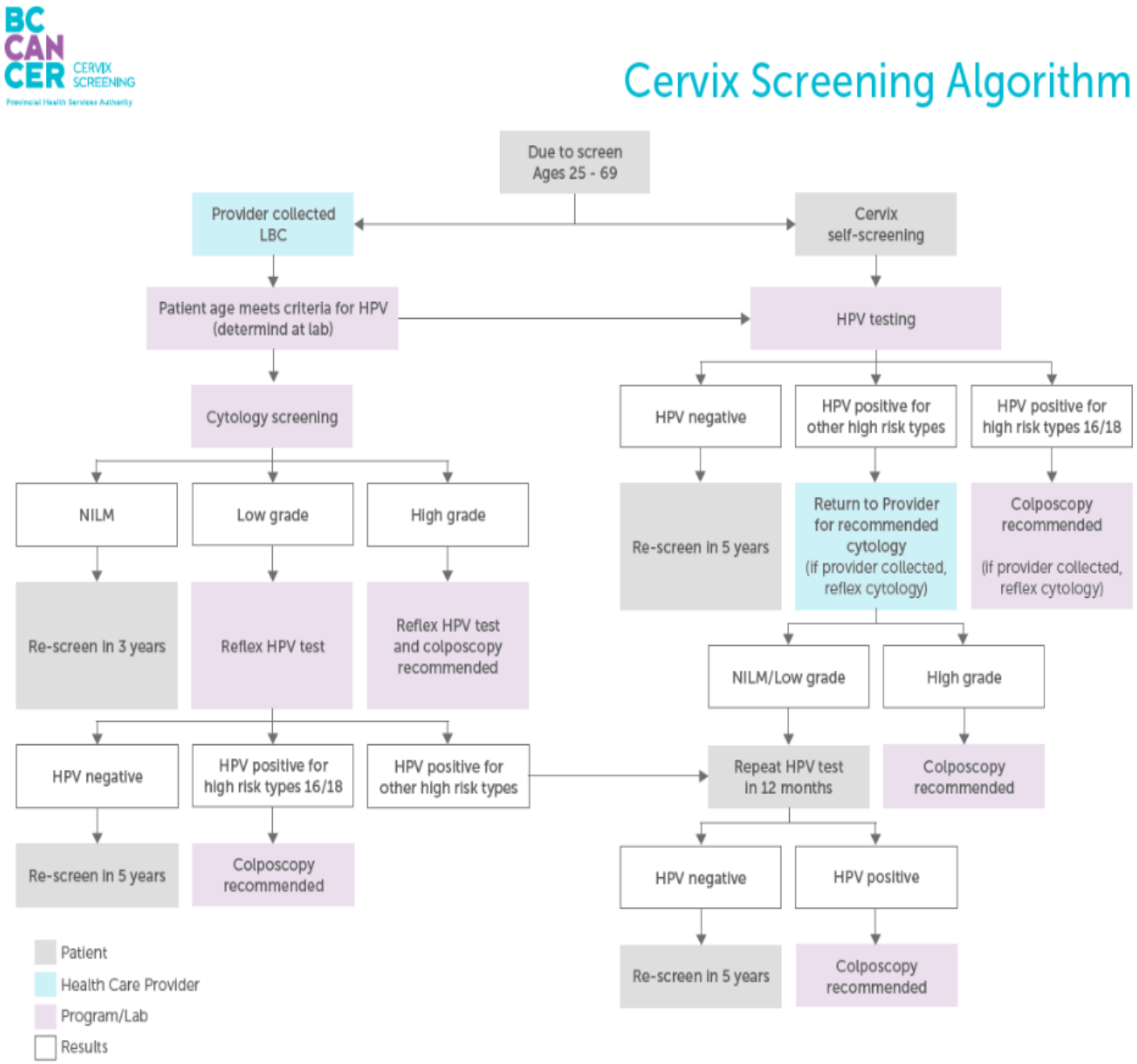
The HPV9 vaccine is publicly funded for BC residents <19 years and specific adult populations at higher risk.[28] It is routinely offered for free to all grade six students through school-based immunization clinics. Those who miss the free vaccine in grade six remain eligible as long as they get their first dose before they turn 19, and their last dose before they turn 26. The vaccine is also recommended but is not publicly funded for adults outside these approved groups. See Appendix A for information on the different types of approved vaccines and their coverage in BC.

While emerging evidence indicates that a single dose provides excellent protection against HPV,[29–31] Immunize BC currently recommends two doses to anyone who starts the series before their 15th birthday and three doses for anyone who starts the series after their 15th birthday or are immunocompromised. Refer to Immunize BC for program information and recommendations as they may change.

BC Cancer Cervix Screening Program

Refer to Figure 2: BC Cancer Cervix Screening Program Algorithm for an overview.

Figure 2. BC Cancer Cervix Screening Program Algorithm



Notes:

- If colposcopy is indicated, the Cervix Screening Program will automatically refer the patient on behalf of the referring health care provider. Patients will receive a letter advising them that the results of their screening test indicate that further follow-up is needed and that they will be contacted by a colposcopy clinic to arrange an appointment.
- Refer to the Cessation of Screening section below for more information on when patients can safely stop screening based on their previous test results and/or unique scenario.
- Refer to Appendix C for more detailed information on screening program recommendations for patients who are immunocompromised, TTGD, after hysterectomy, during pregnancy, etc.

Eligibility

Patients with a cervix are eligible for cervical cancer screening if they are:

- asymptomatic,
- 25-69 years old (even if they've gone through menopause), and
- have a history of sexual activity (even if not currently sexually active).

Screening is not recommended for patients <25 years, regardless of history of sexual activity. However, patients >69 who have never been screened can still be offered a HPV test.

Pregnancy: Note that screening for cervical cancer is **not** necessary as a routine part of pre-natal screening and can be safely deferred until after pregnancy for those who are up to date. However, pregnancy may represent an opportunity for those who might not regularly access care and are overdue for screening. If screening *is* to be done during pregnancy, self-collection is not recommended and instead a cervical sample should be collected for LBC.

Barriers to Participation

Providers should be aware of systemic and personal barriers that can impact patients' participation in screening programs. The cervical self-screening options serve to reduce some of these barriers and represents an excellent opportunity to increase access to care for patients across BC.

Example of barriers that patients may experience when accessing health care include not having a regular care provider, the impacts of colonization, residing in rural/remote communities, having had few or negative interactions with the health care system, being members of certain groups (e.g., visible minorities, immigrants, low-income, underhoused, trans peoples, history of trauma/violence), certain religious/cultural groups, and those who don't speak the language in which service information/delivery is available.[6,13]

It is critical that providers apply a trauma-informed approach to build trust and best support all patients, including those who experience specific barriers to screening program participation. Refer to the College of Physicians and Surgeons of BC's Indigenous Cultural Safety, Cultural Humility and Anti-racism practice standard, First Nations Health Authority and Health Standards Organization's British Columbia (BC) Cultural Safety and Humility Standard and BC Guidelines Extended Learning Document: Primary Care Approaches to Addressing the Impacts of Trauma and Adverse Childhood Experiences (ACEs) for more information. Note: Additional training is required before administering the ACEs questionnaire.

Frequency

Eligible asymptomatic patients should be screened every 3-5 years, regardless of their HPV immunization status. Follow-up frequency/timing depends on previous screening modality (i.e., cytology versus HPV) and results. Refer to Figure 2: BC Cancer Cervix Screening Program Algorithm for more detail.

Test Types & Sample Collection Methods

The BC Cancer Cervix Screening Program currently uses two tests:

- The HPV test detects a high-risk HPV infection using a vaginal or cervical sample.
- The cytology test detects the presence of precancerous lesions using a cervical sample.

Sample Collection Methods

Asymptomatic patients, often in conversation with their primary care provider, can choose between three sample collection methods. BC and global evidence indicates that screening with a self-collected HPV vaginal sample is as effective as screening with a health care provider-collected cervical sample.[4,8,32–34] Several factors influence what collection method is most appropriate for each patient, including clinical history, comfort with speculum exam, availability for in person visits, and physical aspects like disability, limited motility, etc. Refer to Figure 3: Decision Tree for Sample Collection Method.

1. **Patient Collection: Vaginal Swab for HPV Testing**

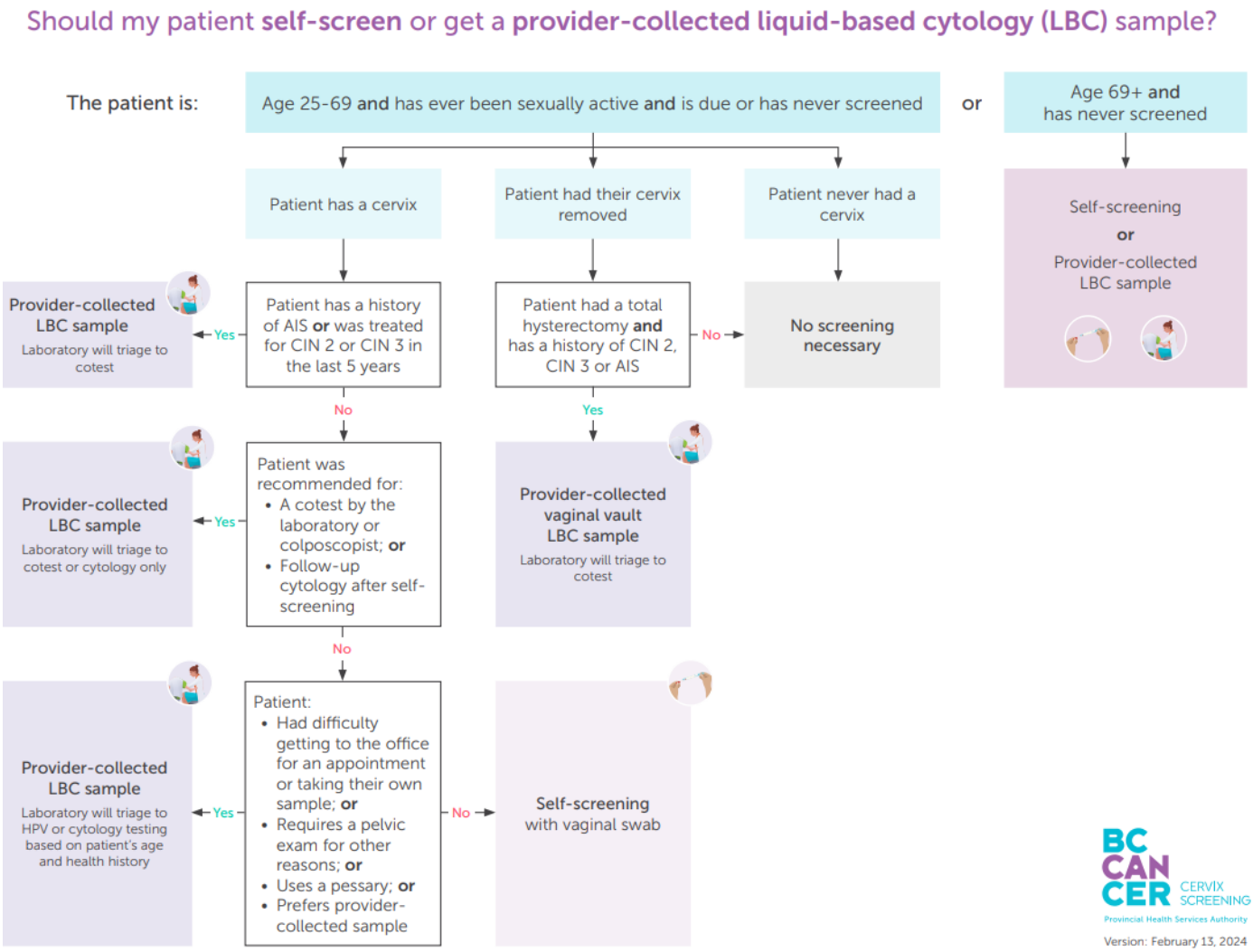
   Patients can take their own vaginal sample using a cervix self-screening kit. Patients can request a kit from BC Cancer online or via telephone, even if they do not have a regular provider. Providers can also request kits to have on hand at their offices. Refer to Appendix B for instructions.

2. **Provider Collection: Vaginal Swab for HPV Testing**

   Patients who would like support collecting their own vaginal sample may seek assistance from a healthcare provider to gather a vaginal swab.

3. **Provider Collection: LBC Sample for HPV and/or Cytology**
   Providers collect cervical samples using a plastic spatula and cytobrush and transfer the sample into a thin prep LBC medium. The lab triages the sample for either HPV or cytology based on patient and program factors. Refer to BC Cancer for more information on which providers are approved to collect cervical samples.

Figure 3. Decision Tree for Sample Collection Method



Follow Up

Different follow-up is indicated based on screening collection type and result. The Cervix Screening Program uses a combination of partial genotyping and cytology on those who test positive for HPV to help guide subsequent management. Refer to Figure 2: BC Cancer Cervix Screening Program Algorithm for an overview and Appendix C for more detail.

Note: BC Cancer is working in partnership with Divisions of Family Practice and community primary care providers to ensure appropriate and timely follow-up for unattached patients. Similarly, some attached patients may not be able to attend their regular provider's office for follow-up. These patients may elect to see another provider, though screening results will also be sent to the primary clinician if they are identified on the patient record.

Cessation of Screening

Cervical cancer screening program participation can be safely stopped according to the following guidelines. Lab reports will clearly identify when patients can stop screening:

- *Average Risk:* Stop screening at age 69 if no positive HPV screening tests between 65-69 years and under no active surveillance of cervical intraepithelial neoplasia (CIN) 2, CIN 3, or adenocarcinoma in situ (AIS).
- *Immunocompromised:* Stop screening at age 74 if no positive HPV screening tests between 69-74 and under no active surveillance of CIN 2, CIN 3, or AIS.
- If discharged from colposcopy after treatment for CIN 2, CIN 3, or AIS, but have not yet had a 12-month co-test (HPV and LBC) before age 69 (not immunocompromised) or 74 (immunocompromised), complete co-test and discontinue screening after a negative result.

Signs and Symptoms

See Table 2: Symptoms Suggestive of Early-Stage and Advanced Cervical Cancer. Note that none of these symptoms are specific and may be associated with other causes.

Patients presenting with signs and symptoms are not eligible for the screening program. These patients should be investigated/managed following best practices, including a speculum examination by someone with experience in gynecologic exams and collection of LBC samples for co-testing if considered clinically important (i.e., HPV and cytology). A vaginal sample is **not** appropriate for symptomatic patients.

Providers can collect a LBC cervical sample for co-testing, ensuring the requisition includes the presenting symptoms. A referral to a colposcopist is appropriate and may be expedited if the clinical suspicion is high. Note that a cervical sample for HPV and cytology testing is not required for referral and referral should not be delayed pending results of the co-test. Colposcopy and gynecologist exam results will determine if any additional diagnostic testing needed. This is outside the scope of this guideline.

Table 2. Symptoms Suggestive of Early-Stage and Advanced Cervical Cancer.[3]

Early-Stage	Advanced
• Post-coital bleeding • Post-menopausal bleeding • Bleeding between periods • Heavier or longer periods • Vaginal discharge that is watery, contains blood, or has a strong odour and is not otherwise explained by benign causes like infection. • Pelvic pain • Pain during sex	Symptoms of early-stage cervical cancer PLUS any of the following: • Difficult/painful bowel movements • Rectal bleeding during bowel movements • Difficult/painful urination • Bloody urine • Dull backache • Leg swelling • Abdominal pain • Fatigue

Other Clinical / Special Considerations

The benefits of participating in cancer screening programs outweigh potential harms.[5] The new BC Cancer Cervix Screening program options for self-collection help to reduce some barriers and potential harms. Potential harms may include the following:

- False positive or false negative test results.
- Distress leading up to or during sample collection, regardless of collection method.
- Distress or anxiety if the HPV test result is positive even though not all infections develop into dysplasia and not all dysplasia develops into cervical cancer. Similarly, distress or anxiety may arise regarding the stigma associated with sexually transmitted infections, disclosure requirements, and impacts on intimate partner relationships.

There are other clinical and special considerations to keep in mind with HPV self-testing. Previously, screening through provider collected specimens has been an opportunity for those who might not otherwise regularly access care to identify/address "other" health and wellness issues. Providers should consider an approach within their practice to planned, proactive engagement with their patients to review other care needs including but not limited to recommendations from the BC Lifetime Prevention Schedule, STI screening, sexual health education, access to contraception, etc.

Resources

Abbreviations & Definitions:

- AIS: Adenocarcinoma in situ
- CIN: Cervical intraepithelial neoplasia
- Co-Test: When a sample undergoes both HPV and cytology testing.
- DES: Diethylstilbestrol
- HPV: Human papillomavirus
- HPV Test: When the sample is assessed for high-risk (oncogenic) HPV genotypes.
- hr-HPV: High risk HPV
- Liquid-Based Cytology: Cells from the cervix are collected using a spatula and/or cytobrush that are then transferred into a container containing an alcohol-based fixative. The liquid-based sample is submitted to the laboratory for testing and can be used for cytology, HPV testing or both, depending on the indication and testing algorithm.
- lr-HPV: Low risk HPV
- NILM: Negative for intraepithelial lesion or malignancy
- Provider-Collected Sample: When the provider collects a vaginal sample for HPV testing or a cervical sample for LBC and/or HPV testing.
- Reflex Test: When the result of the primary test necessitates secondary testing. For example, when a sample was first assessed for HPV and, due to an HPV-positive test result, is then sent for cytology assessment.
- Self-Screening Kit: A kit that has everything a patient needs to collect a sample from their vagina for HPV testing.
- TTGD: Two-Spirit, Transgender, Gender-diverse

Practitioner Resources

- BC Cancer Screening Program Practitioner Resources
    - Practitioners can also order BC Cancer educational materials for their offices.
- FNHA Health Benefits Program Overview: Outlines six benefit areas: dental, medical supplies and equipment, medical transportation, mental health, pharmacy, and vision.
- RACE (Rapid Access to Consultative Expertise): A phone consultation line for physicians, nurse practitioners and medical residents. Contact your local RACE line for the list of available specialty areas. If your local RACE line does not cover the relevant specialty service or there is no local RACE line in your area, or to access Provincial Services, please contact the Vancouver/Providence RACE line.
- Pathways: An online resource that allows FPs, NPs, and their office staff to quickly access current and accurate referral information, including wait times and areas of expertise, for specialists and specialty clinics. Login required.
- Health Data Coalition: An online, physician-led data sharing platform that can assist you in assessing your own practice in areas such as chronic disease management or medication prescribing. Data can graphically represent patients in your practice with chronic diseases, allowing for reflection on practice and tracking improvements over time.
- Family Practice Services Committee
    - Practice Support Program: Offers focused, accredited training sessions for BC physicians to help them improve practice efficiency and support enhanced patient care.
- Doctors of BC: Supports BC's doctors to be leaders in delivering and improving patient care.
- BC Family Doctors: Provides resources for Family Physicians to support efficient practice management and appropriate compensation for the provision of primary care services.
- Public Health Agency of Canada: Provides resources to help patients make wise choices about healthy living, including increasing physical activity and eating well.
- British Columbia Centre of Disease Control
- BC Women's Hospital

Patient, Family and Caregiver Resources

- HealthLinkBC: Patients can call HealthLinkBC at 8-1-1 toll-free in B.C., or for the deaf and the hard of hearing, call 7-1-1. They will be connected to an English-speaking health-service navigator, who can provide health and health-service information and connect patients with a registered dietitian, exercise physiologist, nurse, or pharmacist.
- FNHA Health Benefits Program Overview: Outlines six benefit areas: dental, medical supplies and equipment, medical transportation, mental health, pharmacy, and vision.
- Travel and Accommodations Assistance Program: Available to residents of BC who must travel from their homes to access medical care.

ICD-9 Diagnostic Codes

- 180.0 – Malignant neoplasm of endocervix
- 180.1 – Malignant neoplasm of exocervix
- 180.8 – Malignant neoplasm of other specified sites of cervix
- 180.9 – Malignant neoplasm of cervix uteri, unspecified site
- 233.1 – Carcinoma in situ of cervix uteri

- 079.4 – Human papillomavirus in conditions classified elsewhere or unspecified site
- V76.2 – Screening for malignant neoplasms of cervix.

Billing Codes

Description	Fee for Service Model	LFP Model (LFP practitioner/Locum)
Vaginal swab done in by FP	Visit fee (00100 age series)	Interaction code (98031/98061)
Cervical Sample for LBC (with speculum)	Visit fee (00100 age series) plus Office Vaginal Speculum exam (14562) plus Mini Tray fee (00044)	In-person Interaction with a Standard Procedure (98021/98051)

Appendices

- Appendix A: HPV Vaccine Information
- Appendix B: HPV Test Collection Instructions
- Appendix C: BC Cancer Cervix Screening Program Summary

Associated Documents

The following documents accompany this guideline:

- List of Contributors

References

1. Delpero E, Selk A. Shifting from cytology to HPV testing for cervical cancer screening in Canada. *CMAJ*. 2022;194(17):E613-E615. doi:10.1503/cmaj.211568
2. Mayrand MH, Hanley J, Franco EL. Human Papillomavirus DNA versus Papanicolaou Screening Tests for Cervical Cancer. *n engl j med*. Published online 2007.
3. Ogilvie GS, van Niekerk D, Krajden M, et al. Effect of Screening With Primary Cervical HPV Testing vs Cytology Testing on High-grade Cervical Intraepithelial Neoplasia at 48 Months: The HPV FOCAL Randomized Clinical Trial. *JAMA*. 2018;320(1):43-52. doi:10.1001/jama.2018.7464
4. Bouvard V, Wentzensen N, Mackie A, et al. The IARC Perspective on Cervical Cancer Screening. *The New England Journal of Medicine*. Published online 2021.
5. Landy R, Pesola F, Castañón A, Sasieni P. Impact of cervical screening on cervical cancer mortality: estimation using stage-specific results from a nested case–control study. *Br J Cancer*. 2016;115(9):1140-1146. doi:10.1038/bjc.2016.290
6. Proctor L. *BC Cancer Cervix Screening Program: Program Overview*.; 2024:1-54. http://www.bccancer.bc.ca/screening/Documents/Cervix-Program-Overview.pdf
7. *BC Cancer Cervix Screening: 2018 Program Results*. BC Cancer; 2020:1-28. http://www.bccancer.bc.ca/screening/Documents/Cervix-Program-Results-2018.pdf
8. World Health Organization. *Comprehensive Cervical Cancer Control: A Guide to Essential Practice*. 2nd ed. World Health Organization; 2014. Accessed November 17, 2023. https://iris.who.int/handle/10665/144785
9. Canada PHA of. Human Papillomavirus (HPV). October 12, 2007. Accessed June 13, 2024. https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/human-papillomavirus-hpv.html
10. *Statistics by Cancer Type - Cervix*. BC Cancer; 2021:2. Accessed November 15, 2023. http://www.bccancer.bc.ca/statistics-and-reports-site/Documents/Cancer_Type_Cervix_2018_20210305.pdf
11. Risk Factors for Cervical Cancer. Canadian Cancer Society. Accessed June 13, 2024.

https://cancer.ca/en/cancer-information/cancer-types/cervical/risks
12. Simkin J, Smith L, Van Niekerk D, et al. Sociodemographic characteristics of women with invasive cervical cancer in British Columbia, 2004–2013: a descriptive study. *cmajo*. 2021;9(2):E424-E432. doi:10.9778/cmajo.20200139
13. *Sacred and Strong: Upholding Our Matriarchal Roles - The Health and Wellness Journeys of BC First Nations Women and Girls*. First Nations Health Authority, Office of the Provincial Health Officer; 2021.
14. McGahan CE, Linn K, Guno P, et al. Cancer in First Nations people living in British Columbia, Canada: an analysis of incidence and survival from 1993 to 2010. *Cancer Causes Control*. 2017;28(10):1105-1116. doi:10.1007/s10552-017-0950-7
15. Walboomers JMM, Jacobs MV, Manos MM, et al. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. *J Pathol*. 1999;189(1):12-19. doi:10.1002/(SICI)1096-9896(199909)189:1<12::AID-PATH431>3.0.CO;2-F
16. Gates A, Pillay J, Reynolds D, et al. Screening for the prevention and early detection of cervical cancer: protocol for systematic reviews to inform Canadian recommendations. *Syst Rev*. 2021;10(1):2. doi:10.1186/s13643-020-01538-9
17. Cervical Cancer Symptoms. National Cancer Institute. https://www.cancer.gov/types/cervical/symptoms
18. Khayargoli P, Niyibizi J, Mayrand MH, et al. Human Papillomavirus Transmission and Persistence in Pregnant Women and Neonates. *JAMA Pediatrics*. 2023;177(7):684-692. doi:10.1001/jamapediatrics.2023.1283
19. Kjaer SK. Type specific persistence of high risk human papillomavirus (HPV) as indicator of high grade cervical squamous intraepithelial lesions in young women: population based prospective follow up study. *BMJ*. 2002;325(7364):572-572. doi:10.1136/bmj.325.7364.572
20. Kjaer SK, Frederiksen K, Munk C, Iftner T. Long-term Absolute Risk of Cervical Intraepithelial Neoplasia Grade 3 or Worse Following Human Papillomavirus Infection: Role of Persistence. *JNCI Journal of the National Cancer Institute*. 2010;102(19):1478-1488. doi:10.1093/jnci/djq356
21. *Human Papillomavirus (HPV) Vaccines: Canadian Immunization Guide*. Health Canada Accessed November 15, 2023. https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-9-human-papillomavirus-vaccine.html#p4c8a2
22. Asthana S, Busa V, Labani S. Oral contraceptives use and risk of cervical cancer—A systematic review & meta-analysis. *European Journal of Obstetrics & Gynecology and Reproductive Biology*. 2020;247:163-175. doi:10.1016/j.ejogrb.2020.02.014
23. Gadducci A, Cosio S, Fruzzetti F. Estro-progestin Contraceptives and Risk of Cervical Cancer: A Debated Issue. *Anticancer Res*. 2020;40(11):5995-6002. doi:10.21873/anticanres.14620
24. Palmer T, Wallace L, Pollock KG, et al. Prevalence of cervical disease at age 20 after immunisation with bivalent HPV vaccine at age 12-13 in Scotland: retrospective population study. *BMJ*. Published online April 3, 2019:l1161. doi:10.1136/bmj.l1161
25. St Sauver JL, Finney Rutten LJ, Ebbert JO, Jacobson DJ, McGree ME, Jacobson RM. Younger age at initiation of the Human Papillomavirus (HPV) vaccination series is associated with higher rates of on-time completion. *Prev Med*. 2016;89:327-333. doi:10.1016/j.ypmed.2016.02.039
26. *An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI): Updated Recommendations on Human Papillomavirus (HPV) Vaccines*. Public Health Agency of Canada; 2024.
27. *Gardasil 9 Product Monograph*. Merck Canada Inc; 2024. https://www.merck.ca/en/wp-content/uploads/sites/20/2021/04/GARDASIL_9-PM_E.pdf
28. HPV. Immunize BC. June 11, 2024. Accessed June 13, 2024. https://immunizebc.ca/vaccines/HPV
29. Watson-Jones D, Changalucha J, Whitworth H, et al. Immunogenicity and safety of one-dose human papillomavirus vaccine compared with two or three doses in Tanzanian girls (DoRIS): an open-label, randomised, non-inferiority trial. *The Lancet Global Health*. 2022;10(10):e1473-e1484. doi:10.1016/S2214-109X(22)00309-6
30. Batmunkh T, Dalmau MT, Munkhsaikhan ME, et al. A single dose of quadrivalent human papillomavirus (HPV) vaccine is immunogenic and reduces HPV detection rates in young women in Mongolia, six years

after vaccination. *Vaccine*. 2020;38(27):4316-4324. doi:10.1016/j.vaccine.2020.04.041
31. Barnabas RV, Brown ER, Onono MA, et al. Efficacy of Single-Dose Human Papillomavirus Vaccination among Young African Women. *NEJM Evidence*. 2022;1(5). doi:10.1056/EVIDoa2100056
32. Ronco G, Dillner J, Elfström KM, et al. Efficacy of HPV-based screening for prevention of invasive cervical cancer: follow-up of four European randomised controlled trials. *The Lancet*. 2014;383(9916):524-532. doi:10.1016/S0140-6736(13)62218-7
33. Perkins RB, Guido RS, Castle PE, et al. 2019 ASCCP Risk-Based Management Consensus Guidelines for Abnormal Cervical Cancer Screening Tests and Cancer Precursors: *Journal of Lower Genital Tract Disease*. 2020;24(2):102-131. doi:10.1097/LGT.0000000000000525
34. Arbyn M, Castle PE, Schiffman M, Wentzensen N, Heckman-Stoddard B, Sahasrabuddhe VV. Meta-analysis of agreement/concordance statistics in studies comparing self- vs clinician-collected samples for HPV testing in cervical cancer screening. *Intl Journal of Cancer*. 2022;151(2):308-312. doi:10.1002/ijc.33967

Appendix A: HPV Vaccine Information

Vaccine	Protects Against	Immunize BC Coverage

HPV9 (Gardasil 9)	• HPV Types: 6, 11, 16, 18, 31, 33, 45, 52, 58
	• Anogenital cancers
	• Genital warts
		Recommended and publicly funded for:
		• All students in grade 6 to 12. Routine program in Grade 6, with catch-up in other grades and a variety of community-based settings.
		• Individuals who get their first dose before they turn 19 and get their last dose before they turn 26.
		• HIV positive people 9-26 years of age.
		• Cisgender males 19-26 years of age who:
		  ○ Have sex with other men.
		  ○ Are not yet sexually active but are questioning their sexual orientation.
		  ○ Are street-involved.
		• Two-Spirit, transgender, and non-binary individuals 19-26 years of age (inclusive) at the time of series commencement.
		
		Recommended but not publicly funded for the following groups. These individuals can access the vaccine at most pharmacies, travel clinics, and some sexual health clinics. Private pay is approximately $200 per dose.
		• Females 19-45 years of age (unless noted above).
		• Males 19-26 years of age (unless noted above).
		• Males 27 years of age and older who have sex with men.

HPV2 (Cervarix)	• HPV Types: 16, 18 • Cervical cancer • Anal cancer	Is only approved for use in females. Is not publicly funded in BC. Private pay is approximately $100 per dose.
HPV4 (Gardasil)	• HPV Types: 6, 11, 16, 18 • Cervical cancer • Anogenital warts	No longer available in Canada. Approved for: • Females 9-45 years of age • Males 9-26 years of age

Appendix B: HPV Test Collection Instructions

Patients can order a test kit HERE or by calling 1-877-702-6566.

Providers can order test kits for their offices HERE (login required).

INSTRUCTIONS

BEFORE USING THIS KIT:

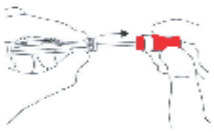
- Read through these instructions or watch the step-by-step video: screeningbc.ca/cervix

DO NOT USE THIS KIT:

- When you are on your period. Wait until your period is over.
- If you are pregnant or use a pessary. Talk to a health care provider about your screening options.
- If you've had your cervix removed (e.g., total hysterectomy). Talk to a health care provider to see if cervix screening is still required.

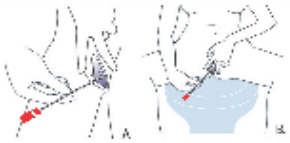
1. Wash your hands. Get undressed from the waist down.

2. **Prepare the swab**: Hold the red cap to remove the swab from the tube. Put the tube on a clean surface. **Do not touch the soft end of the swab.**



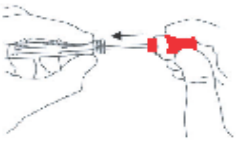
3. Hold the swab at the red line.

4. **Collect your sample**: Stand (A) or sit (B) with your legs apart. Using your other hand, hold back the folds of skin.



5. Gently insert the swab into your vagina, where you would normally put your tampon, until your fingers touch your external genitals (vulva). Rotate the swab as you **slowly count to 20**, then remove the swab.

6. Slide the swab into the plastic tube and close firmly.



IF COMPLETING KIT AT THE CLINIC:

7. Double check the health care provider has labelled the collection date on your tube. Place the tube into the plastic bag. Seal the bag.

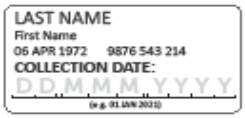
8. Return the sealed bag containing your collection device to the health care provider.

9. The health care provider will complete your lab requisition and submit your sample to the lab for you.

OR

IF COMPLETING KIT AT HOME:

7. **CLEARLY** write your collection date on the tube label **AND** the lab requisition. Place the tube into the plastic bag. Seal the bag.



8. Put the sealed bag and your lab requisition into the prepaid return envelope.

9. Drop off the envelope today at a Canada Post office or post box.

The test shouldn't hurt. If you feel any pain while collecting your sample, please ask a health care professional for help.

Appendix C: BC Cancer Cervix Screening Program Summary

Refer to the BC Cancer for full details on the Cervix Screening Program here. Summary below, excerpted from pages 36-42.

Age to Start Screening	• Initiate screening at age 25. Cervical screening is not recommended for those over age 25 who have never been sexually active.
Cessation of Cervical Screening	• Average Risk: Stop screening at age 69, provided that there has been a negative HPV screening test between the ages of 65 and 69 and under no active surveillance of pre-cursor abnormalities. • Immunocompromised: Stop screening at age 74 provided there has been a negative HPV screening test between the ages of 65 and 69 and under no active surveillance of pre-cursor abnormalities. • Those who have been discharged from colposcopy, but have not yet completed the post discharge 12 month cotest (HPV and cytology testing) before age 69 (average risk) or 74 (immunocompromised), should continue with screening until they have had a negative cotest. After this, screening can be discontinued.
Management of Those over age 69 with HPV Positive Results	• Refer to colposcopy directly. • If colposcopic evaluation is negative, discharge to primary care for a repeat HPV test in 12 months. If patients continue to be HPV positive, refer back to and follow in colposcopy until HPV negative or aged 79. • At age 79 and the colposcopic examination is negative, HPV positive patients can be discharged with no further need for screening.

Screening of Immunosuppressed	• Immunosuppressed patients to initiate cervix screening with an HPV test starting at age 25 if they are or have ever been sexually active. • Immunosuppressed patients who are HPV negative to screen every 3 years with an HPV test. • Immunosuppressed patients can stop screening at age 74, provided that there has been a negative HPV screening test between the ages of 69 and 74 and they are under no active surveillance of pre-cursor abnormalities. • Immunosuppressed patients who are positive for high risk HPV, regardless of genotype or cytology results, refer directly to colposcopy.
Screening of Transgender, Gender-Diverse and Non-Binary People	Cervix Present • Follow the recommendations for average risk screening for cervix screening. Cervix Removed • No prior CIN 2, CIN 3 or AIS, cervix screening not recommended. People who have had a total hysterectomy with history of CIN 2, CIN 3 or AIS should have a cotest (HPV and cytology testing) on a sample from the vaginal vault at 12 months post hysterectomy. Any positive HPV test or a high grade or glandular cytology result should be referred directly to colposcopy. After a negative cotest, screening can be discontinued. Neovagina, No Cervix • Individuals who had a vaginoplasty or surgically created vagina, screening is not recommended.
Screening of DES-Exposed Patients	• Annual colposcopic examination of both the cervix and vagina with cotest (HPV and cytology testing) is recommended until age 69.

Screening in Pregnancy	• Screening is not necessary as a routine part of pre-natal screening for those who are up to date with screening. Screening can be delayed in patients who are expected to continue to engage with the health system until they are postpartum. • Provider-collected cervix screening can be offered during pregnancy if screening is due or overdue. • Use prenatal care as an opportunity to engage under or never screened patients in the screening program.
Screening after 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 have had a total hysterectomy with current or past high-grade cervical abnormality (i.e. CIN 2, CIN 3 or AIS) should have a cotest (HPV and cytology testing) on a sample from the vaginal vault at 12 months post hysterectomy. Any positive HPV test or if cytology shows ASC-H, HSIL or AGC, refer to colposcopy. If HPV is negative and cytology is NILM, ASCUS or LSIL, screening can be discontinued.
Screening after Excisional Treatment for High Grade Cervical Intraepithelial Neoplasia (CIN)	• After discharge from colposcopy, cotest (HPV and cytology testing) at 12 months through their primary care provider. • If HPV is negative and cytology is NILM, ASCUS or LSIL they can transition back to routine HPV-based screening at 3 year intervals (average risk) or 1 year interval (immunocompromised). • If at the 12 months cotest (HPV and cytology testing), high risk HPV is positive or if cytology shows ASC-H, HSIL or AGC, re-refer to colposcopy. • Screening can be discontinued at age 69 (average risk) or 74 (immunocompromised) provided the patient has had a negative cotest (HPV and cytology testing) and they are under no active surveillance of pre-cursor abnormalities.

Screening after Excisional Treatment for Endocervical Adenocarcinoma in Situ (AIS)	• After discharge from colposcopy, cotest (HPV and cytology testing) at 12 months through their primary care provider. • If HPV is negative and cytology is NILM, ASCUS or LSIL they can transition back to a cotest (HPV and cytology testing) at 3 year intervals (average risk) or 1 year interval (immunocompromised). • If High risk HPV is positive or if cytology shows ASC-H, HSIL or AGC, re-refer to colposcopy. • Screening for HPV negative patients can be discontinued at age 69 (average risk) or 74 (immunocompromised) provided that there has been a negative cotest (HPV and cytology testing) at last screen and they are under no active surveillance of pre-cursor abnormalities.
Screening after Cervical Cancer Treated with Surgery or Radiation	• The patient's colposcopist or oncologist is responsible for outlining the post-treatment follow-up of a patient diagnosed with cervical cancer for the first 5 years. • Once discharged from the care of the colposcopist/oncologist, screening is no longer recommended. Ongoing surveillance for recurrence by someone experienced in cervical disease is recommended.
Cervical Evaluation in Those Exhibiting Signs and Symptoms of Cervical Cancer	• Cervix screening is only appropriate for those who are age eligible and asymptomatic. • People with symptoms eg. post coital bleeding, abnormal bleeding and/or a persistent vaginal discharge should have a speculum examination by someone with experience in gynecologic exams. • Providers can perform a cotest (HPV and cytology testing) and referral to a colposcopist is appropriate and may be expedited if the clinical suspicion is high. • A cotest (HPV and cytology testing) is not required for referral and referral should not be delayed pending results of the cotest.
HPV Invalid	• Repeat HPV testing. Unless a cotest (HPV and cytology testing) was recommended, a self-screening test will be sent to the patient at the time of the invalid result notification. • If repeat test is invalid, refer to colposcopy.

Rejected Samples	• CCSL will reject and will not process specimens if specimen identification cannot be confirmed. • Unless a cotest (HPV and cytology testing) was recommended, a self-screening test will be sent to the patient at the time of the invalid result notification.
Unsatisfactory Samples	• Samples which are inadequate for interpretation due to poor preservation or obscuring elements. • Unless a cotest (HPV and cytology testing) was recommended, a self-screening test will be sent to the patient at the time of the invalid result notification.
High Risk HPV Negative	• Repeat cervical screening in 5 years. • Shorter screening interval recommendation for immunocompromised patients and after treatment for CIN 2, CIN 3 or AIS.
High Risk HPV 16/18 Positive	• Refer to colposcopy. • If screening is performed with a provider-collected sample, the CCSL will perform a cytological evaluation to aid in the colposcopist's decision. • If screening is performed by self-sampling, colposcopist will collect a cytology sample to aid with management decisions.
High Risk HPV Other Positive with ASC-H, HSIL or AGC Cytology	• Refer to colposcopy.
High Risk HPV Other Positive with Unknown or Unsatisfactory Cytology Result	• Follow-up cervical screening with primary care provider. • If cytology samples are reported as unsatisfactory on two different occasions, colposcopy referral is recommended.

High Risk HPV Other Positive with Cytology Negative (NILM), ASCUS or LSIL	• Repeat HPV in 12 months.
	• If repeat HPV test is negative, return to routine screening (e.g. every 5 years for average risk patients).
	• If repeat HPV test is positive for any HPV type; refer to colposcopy.
	  ○ If screening is performed with a provider-collected sample, the CCSL will perform a cytological evaluation to aid with colposcopist's decision.
	  ○ If screening is performed by self-screening, colposcopist will collect a cytology sample at the time of colposcopy to aid with management decisions.

ASCUS and LSIL	• Pap test will be triaged by reflex HPV testing.
	  ○ If HPV test is positive for HPV other than 16 or 18; HPV testing is recommended in 12 months.
	  ○ If HPV test is positive for HPV 16 or 18; colposcopy referral is recommended.
	  ○ If HPV test is negative; return to routine screening (e.g. every 5 years for average risk patients).

ASC-H, HSIL, Moderate Dysplasia and Severe Dysplasia	• Refer to colposcopy.
Atypical Glandular Cells	• Refer to colposcopy.
Benign Endometrial Cells in Cervical Sample	• 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.
Atypical Endometrial Cells or Endometrial Carcinoma	• Refer to colposcopy or a general gynecologist for further evaluation which should include an endometrial biopsy.
Possible Extrauterine Carcinoma or Rare Malignancies	• Features of possible extrauterine carcinoma or rare malignancies may be identified in cytology samples collected from participants who are HPV positive. • These should be dealt with on a case-by-case basis and may need a multidisciplinary team approach for management. Contact the CCSL for clarification of the results if needed.