

Human Papillomavirus (HPV) Testing Frequently Asked Questions (FAQs).

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Overview.

The Ontario Cervical Screening Program (OCSP) will be implementing human papillomavirus (HPV) testing with reflex cytology in cervical screening and as a co-test in colposcopy for screening-related abnormalities. To support this change, FAQs have been developed to give providers offering screening and/or colposcopy information on why, how and when to use HPV testing, and when cytology testing is appropriate. The FAQs also describe forthcoming changes to the OCSP and how these changes are expected to impact providers and the screen-eligible public.

Glossary.

Cervical pre-cancer: Abnormal cell growth in the cervix that is considered moderate or severe. Pre-cancer includes the following histology result types:

HSIL: high-grade squamous intraepithelial lesion; and

AIS: adenocarcinoma in situ

CIN: Cervical intraepithelial neoplasia

CIN3+: Cervical intraepithelial neoplasia grade three or higher

Co-test: A co-test is when a human papillomavirus test and cytology test are performed on a single cervical specimen. The results of these two tests are considered together to inform clinical next steps.

Colposcopy: An examination of the cervix used to rule out the presence of cervical pre-cancer or cancer. If a pre-cancer has been detected, treatment can be performed in colposcopy. Multiple visits in colposcopy may be required over an episode of care, depending on the results of the screening test or initial colposcopy visit, including whether treatment was required.

Cytology test: A test that looks for abnormal cell changes in the cervix

High-grade cytology: High-grade cytology includes the following result types:

- LSIL-H: low-grade squamous intraepithelial lesion, cannot exclude HSIL;
- ASC-H: atypical squamous cells, cannot exclude HSIL;
- HSIL: high-grade squamous intraepithelial lesion;
- AGC: atypical glandular cells;
- AGC-N: atypical glandular cells favours neoplastic;
- AGC-NOS: atypical glandular cells not otherwise specified;
- AEC: atypical endocervical cells;
- AEC-N: atypical endocervical cells favours neoplastic;

- AEC-NOS: atypical endocervical cells not otherwise specified;
- AIS: adenocarcinoma in situ;
- SCC: squamous cell carcinoma;
- ACC: adenocarcinoma;
- ACC-E: endocervical adenocarcinoma; and
- PDC: poorly differentiated carcinoma

Colposcopy: An examination of the cervix used to rule out the presence of cervical pre-cancer or cancer. If a pre-cancer has been detected, treatment can be performed in colposcopy. Multiple visits in colposcopy may be required over an episode of care, depending on the results of the screening test or initial colposcopy visit, including whether treatment was required.

Low-grade cytology: Low-grade cytology includes the following result types:

- ASCUS: atypical squamous cells of undetermined significance; and
- LSIL: low-grade squamous intraepithelial lesion

Negative predictive value: The likelihood that negative test results will correctly identify people who do not have a cervical pre-cancer or cancer and will not develop a cervical cancer in the next five years.

NILM: Negative for intraepithelial lesion or malignancy

Oncogenes: Genes that have the potential to cause cancer

Oncogenic human papillomavirus (HPV) types: Types of HPV that can lead to abnormal cell changes in the cervix and, if left untreated, can lead to cervical cancer over time. Of the over 100 types of HPV, only 13 are known to be oncogenic in the cervix, including types 16, 18 and 45.

Non-oncogenic human papillomavirus (HPV) types: Types of HPV that can only cause low-grade abnormal cell changes in the cervix, and therefore are not associated with an increased risk of cervical cancer. Some non-oncogenic HPV types can contribute to other conditions, such as genital warts. Non-oncogenic HPV types are not detected as part of cervical screening using HPV testing.

Partial genotyping: Partial genotyping is used to identify specific oncogenic types of human papillomavirus (HPV) (i.e., HPV 16, HPV 18 and sometimes HPV 45), which are associated with a higher risk of cervical pre-cancer and cancer. When partial genotyping is performed, the remaining oncogenic HPV types are pooled into a single category known as HPV-positive (other high-risk types). Partial genotyping allows for better risk stratification of screening participants, and avoids over-investigation and overtreatment.

Reflex test: A test performed by a laboratory when the results of a previous test indicate that additional testing is required. The additional test is performed without requiring another order from a health care provider. For the purposes of this document, a reflex test refers to cytology performed on a screening specimen that tests positive for oncogenic human papillomavirus.

About the human papillomavirus test and why it has been introduced into the Ontario Cervical Screening Program.

1. What is the link between human papillomavirus (HPV) and cervical cancer?

- Persistent infection with oncogenic types of HPV is required for almost all cervical cancers to develop (1).
- HPV infections are common and it is estimated that up to 80 per cent of sexually active people will have at least one infection in their lifetime (2, 3).
- However, not all HPV infections are oncogenic. Of the over 100 types of HPV, only 13 are considered oncogenic in the cervix, including types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68 (4). Among these types, 16, 18 and 45 are detected in almost 75 per cent of all squamous cell carcinomas and 94 per cent of adenocarcinomas (4).
- Most HPV infections go away on their own without causing any harm, but a small proportion of infections persist. Persistent infections with oncogenic types of HPV can lead to abnormal cell changes in the cervix which, if left untreated, can lead to cervical cancer over time (1, 5).
- Among oncogenic HPV types, the risk of high-grade abnormal cell changes in the cervix varies and is particularly high for type 16. One study estimated that the cumulative seven-year risk of pre-cancer and cervical cancer is 22 per cent for infections with HPV type 16, compared to a less than five per cent risk for type 51 (4). Pre-cancer and cervical cancer was defined in the study as cervical intraepithelial neoplasia grade three or higher.
- Other types of HPV, including those that cause genital warts (e.g., types 6 and 11), are considered non-oncogenic (6). While infections with non-oncogenic types of HPV can lead to low-grade cell changes in the cervix, they never progress to cancer.

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2. Why is the cervical screening test changing from the cytology test (also known as the Pap test) to the human papillomavirus (HPV) test?

- There are several advantages to using HPV testing for cervical screening instead of cytology testing.
 - Providers can be more confident that people with a negative HPV test do not have a cervical pre-cancer than people with a negative cytology test because the HPV test is a more sensitive screening test, as shown in Table 1.
 - The improved performance of HPV testing over cytology testing allows for longer intervals between screens for people who test negative for HPV.
 - HPV testing is objective, which means results are highly consistent and reproducible. In contrast, cytology testing relies on subjective interpretation of results, which may identify cell changes that are not linked to cervical cancer and therefore do not need to be followed up with further testing.
 - Randomized controlled trials conducted in organized screening programs have shown that the HPV test can reduce the incidence of invasive squamous cell carcinoma and adenocarcinomas in the cervix (1). Cervical screening with HPV testing results in a significant reduction in adenocarcinoma of the cervix compared to screening with cytology testing alone. The HPV test is also better at preventing cervical adenocarcinomas than a cytology test because the HPV test can more effectively identify people with a glandular pre-cancer (2,3).
- HPV testing detects oncogenic types of HPV (i.e., strains containing oncogenic RNA or DNA). HPV testing does not detect low-risk (non-oncogenic) HPV types, such as those that cause genital warts. Therefore, a positive HPV test result means that oncogenic types of HPV were detected and a negative HPV test result means that oncogenic types of HPV were not detected.
- HPV testing in the Ontario Cervical Screening Program (OCSP) includes partial genotyping, which identifies the type of oncogenic HPV infection as 16, 18, 45 or other. Partial genotyping allows people with oncogenic types of HPV to be managed appropriately. For more information about partial genotyping, see question #46 How and why is human papillomavirus (HPV) partial genotyping being used in the Ontario Cervical Screening Program for HPV test interpretation?

- Cytology testing will be used alongside HPV testing in the OCSP as a reflex test for results
 that are positive for oncogenic types of HPV or as a co-test in colposcopy. The OCSP is
 combining cytology testing with HPV testing as using the two tests has a higher chance of
 correctly identifying whether a cervical pre-cancer or cancer exists than HPV testing alone.
 The reflex cytology test will be performed on the same specimen that is submitted to the
 laboratory for HPV testing.
- Primary screening with the HPV test is increasingly considered to be the standard of care for organized cervical screening programs internationally and many jurisdictions have already transitioned from cytology testing to HPV testing (4–7).

Table 1. Selected characteristics of the HPV test and the cytology test for cervical screening

| Characteristic | HPV test | Cytology test |
|--|--------------------------------------|-------------------------------------|
| One-time sensitivity* in detecting cervical pre-cancer and cancer (defined in the study as CIN2+) | 96% (8)*** | 53% (8)*** |
| One-time specificity** in detecting cervical pre-cancer and cancer (defined in the study as CIN2+) | 91% (8)*** | 96% (8)*** |
| What it detects | Oncogenic types of HPV in the cervix | Abnormal cell changes in the cervix |
| Interpretation of test (9) | Objective and reproducible (9) | Subjective (9) |

CIN = cervical intraepithelial neoplasia

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^{*}Sensitivity is the effectiveness of a cervical screening test in detecting cervical pre-cancer and cancer in people who have cervical pre-cancer and cancer (i.e., 96.1 per cent of people with cervical pre-cancer and cancer will be identified with an HPV-positive test).

^{**}Specificity is the effectiveness of a cervical screening test in indicating a normal result in people who do not have cervical pre-cancer and cancer (i.e., 90.7 per cent of people without cervical pre-cancer and cancer will receive a negative test result).

^{***}Sensitivity and specificity estimates shown here are drawn from performance data in the context of cervical screening programs across Europe and North America. However, specific estimates are expected to vary according to the test used and the screening population.

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- 3. What will happen to cytology testing (also known as Pap testing) once human papillomavirus (HPV) testing is introduced?
 - Although HPV testing will replace cytology testing as the primary screening test, cytology testing will continue to play a role in cervical screening.
 - HPV testing will test for oncogenic types of HPV types. Therefore, a positive HPV test result
 means that oncogenic types of HPV were detected and a negative HPV test result means
 that oncogenic types of HPV were not detected.
 - For people who test positive for oncogenic types of HPV, partial genotyping will be used to determine whether they are HPV-positive (types 16, 18/45) or HPV-positive (other high-risk types).
 - For people who test positive for oncogenic types of HPV, the laboratories will automatically
 perform a cytology test on the same specimen (called reflex cytology) to see if the HPV
 infection has caused any cell changes in the cervix.

- If someone has a result that is HPV-positive (other high-risk types), the reflex cytology test
 result will help determine the person's next steps because it can help to identify their
 immediate and subsequent risk of developing pre-cancer (high-grade abnormal cell
 changes) and cervical cancer.
- If someone has a result that is HPV-positive (types 16, 18/45), they should be referred to colposcopy regardless of their reflex cytology test result. However, a reflex cytology test will still be performed because the result will be used by the colposcopists to help them triage and determine the appropriate risk-based management in colposcopy.
- Standalone cytology testing will only be used if a reflex cytology test is unsatisfactory.

4. How much does the human papillomavirus (HPV) test cost for screening participants?

• The HPV test (and reflex cytology, as appropriate) will be available for all eligible people in Ontario at no cost as part of the Ontario Cervical Screening Program. For eligibility criteria, refer to question #9 - Who is eligible for the Ontario Cervical Screening Program?

5. Is the human papillomavirus (HPV) test cost-effective?

- The cost-effectiveness of cervical screening with the HPV test is influenced by the costs of
 cervical screening, treatment and follow-up, as well as which screening and colposcopy
 algorithms are used (e.g., HPV testing with cytology co-testing vs. HPV testing and
 genotyping with reflex cytology performed on positive results vs. HPV testing alone vs.
 cytology testing alone). Cost-effectiveness will also vary depending on how many people
 get HPV vaccination over time in a given population.
- While these factors vary by jurisdiction, studies suggest that cervical screening with HPV
 testing is associated with a lower cost for every quality-adjusted life-year gained (1, 2, 3),
 life-year gained (2, 4) and high-grade cervical lesion detected (5) than cytology-based
 screening strategies.
- While these studies do not exactly mirror the Ontario context, they suggest that implementing HPV testing in the Ontario Cervical Screening Program will be cost-effective.

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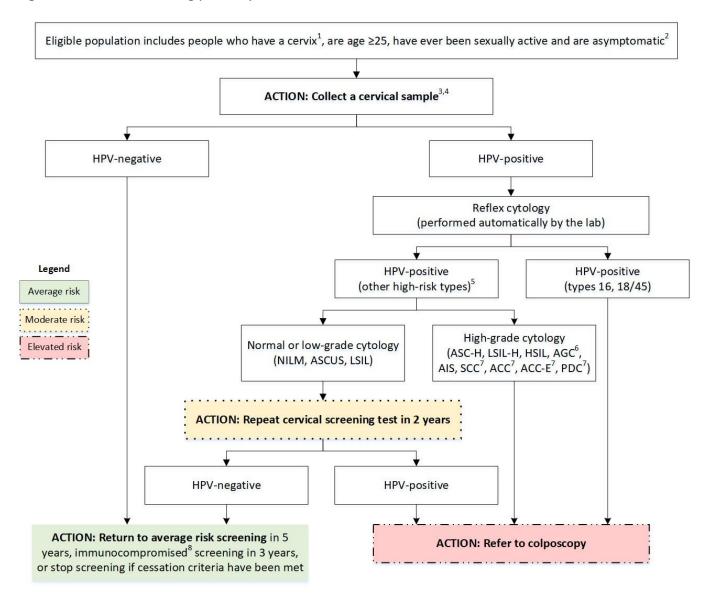
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- 6. When will human papillomavirus (HPV) testing be available in screening and colposcopy as part of the Ontario Cervical Screening Program (OCSP)?
 - Ontario Health (Cancer Care Ontario) is working with the Ministry of Health on changes to the OCSP that are required before implementing HPV testing. Once these changes are complete, HPV testing with reflex cytology testing (also known as Pap testing) will replace cytology testing as the primary cervical screening test in Ontario. In the colposcopy setting, HPV and cytology co-testing will be used instead of standalone cytology testing.
 - When they are available, additional details, including the launch date, will be communicated to providers offering cervical screening and/or colposcopy.
 - To ensure providers are well prepared for the launch of HPV testing, additional resources and supports will be provided on the HPV testing implementation resource hub at <u>ontariohealth.ca/hpvhub</u>

Changes to the Ontario Cervical Screening Program and screening recommendations

- 7. Where can providers offering cervical screening and/or colposcopy find a graphical summary of the new screening pathway?
 - See Figure 1 for a graphical summary of the Ontario Cervical Screening Program (OCSP) screening pathway for human papillomavirus (HPV) testing.
 - A graphical summary of the OCSP screening pathway can also be found on the HPV testing implementation resource hub at <u>ontariohealth.ca/hpvhub</u>

Figure 1: Cervical screening pathway



ACC = adenocarcinoma; ACC-E = endocervical adenocarcinoma; AGC = atypical glandular cells; AIS = adenocarcinoma in situ;

ASC-H = atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion;

ASCUS = atypical squamous cells of undetermined significance; HPV = human papillomavirus;

HSIL = high-grade squamous intraepithelial lesion; LSIL = low-grade squamous intraepithelial lesion;

LSIL-H = low-grade squamous intraepithelial lesion, cannot exclude HSIL;

NILM = negative for intraepithelial lesion or malignancy; PDC = poorly differentiated carcinoma; SCC = squamous cell carcinoma

- Including women, Two-Spirit people, transmasculine people, nonbinary people, pregnant people, post-menopausal people, people who have undergone a subtotal hysterectomy and retained their cervix and people who have had the HPV vaccine. Routine screening is not recommended for people who have had their cervix removed as a result of a hysterectomy. For more information, refer to the OCSP's Vaginal Vault Testing Guidance that can be found on the HPV testing implementation resource hub at ontariohealth.ca/hpvhub
- 2. Any visible cervical abnormalities or abnormal symptoms must be investigated, regardless of age. If a lesion is found during a routine cervical screening test, complete the test and refer the participant to colposcopy or a regional cancer centre. Do not wait for the cervical screening test results to refer someone for next steps.
- 3. The cervical screening test does not test for non-oncogenic types of HPV, such as those that cause genital warts, or other sexually transmitted infections.
- 4. If the HPV test component of the cervical screening test is invalid, repeat sample collection at the participant's earliest convenience, within 3 months. If the repeat HPV test is invalid, refer to colposcopy.
- 5. If the test is HPV-positive (other high-risk types) with unsatisfactory cytology, repeat the cytology test only (i.e., do not repeat the HPV test) at the participant's earliest convenience, within 3 months. If the repeat cytology test is unsatisfactory, refer to colposcopy. After an unsatisfactory cytology result, a course of intravaginal estrogen therapy should be considered for people using transition-related hormone therapy (i.e., androgen therapy) or in post-menopausal people).
- 6. Includes AGC-N/NOS, AEC-N/NOS (AGC-N = atypical glandular cells, favour neoplastic; AGC-NOS = AGC, not otherwise specified; AEC-N = atypical endocervical cells, favour neoplastic; AEC-NOS = AEC, not otherwise specified).
- 7. If someone has SCC, ACC, ACC-E or PDC results, refer them urgently to colposcopy or if they have an obvious lesion, consider referral to gynecologic oncology.
- 8. The following immunocompromised populations may be at a higher risk of cervical pre-cancer and cancer, and should screen every three years if their last HPV test was negative: people living with HIV/AIDS, regardless of CD4 cell count; people with congenital (primary) immunodeficiency; transplant recipients (solid organ or allogeneic stem cell transplants); people requiring treatment (either continuously or at frequent intervals) with medications that cause immune system suppression for three years or more; people who are living with systemic lupus erythematosus (SLE), regardless of whether they are receiving immunosuppressant treatment; and people who are living with renal failure and require dialysis.
- 8. How were the new Ontario Cervical Screening Program (OCSP) human papillomavirus (HPV)-based screening and colposcopy recommendations developed?
 - The primary consideration in developing the new OCSP screening and colposcopy recommendations was that clinical next steps should be based on someone's risk of precancer and cervical cancer (according to their screening and colposcopy results, as well as their immune status), as well as careful balancing of benefits and potential harms.

- Other key considerations were that the recommendations should be:
 - Guided by the evidence;
 - Feasible to implement;
 - Practical for screening participants and for providers to adopt;
 - Acceptable to the public, providers and the screening program; and
 - Integrated well with the planned program design and infrastructure for screening and colposcopy.
- The process for developing the new recommendations included the following inputs:
 - Rapid reviews of the primary literature conducted by Ontario Health (Cancer Care Ontario);
 - Analyses of Ontario screening and colposcopy data, where available and appropriate;
 - Evidence-based screening and colposcopy pathways from organized screening programs in other jurisdictions and recommendations from professional associations; and
 - Expert opinion from a multidisciplinary, international expert panel.
- The expert panel included Ontario, Canadian and international experts in gynecology, gynecologic oncology, pathology, primary care (including primary care providers with experience caring for Indigenous populations), research and the general public. To compliment the expertise of the panel, people with specific areas of expertise (i.e., vaginal vault testing, testing for transmasculine and nonbinary people, testing in immunocompromised populations and colposcopy) provided input as ad hoc panel members.
- The recommendations were also shared with relevant partners and multi-disciplinary subject matter experts in Ontario, Canada and internationally for input before finalizing.

Who should be screened as part of the Ontario Cervical Screening Program.

- 9. Who is eligible for the Ontario Cervical Screening Program (OCSP)?
 - Someone is eligible for cervical screening as part of the OCSP if they:

- Have a cervix^a including women, Two-Spirit people, transmasculine people and nonbinary people, as well as people who have undergone a subtotal hysterectomy and retained their cervix;
- Are age 25 to 69 (some people may screen until age 74)^b;
- Have ever been sexually active^c;
- Have Ontario Health Insurance Plan (OHIP) coverage^d; and
- Have no symptoms suggestive of cervical cancer, such as abnormal vaginal bleeding or discharge, bleeding after sexual activity^c and pelvic pain.
- People immunized for human papillomavirus (HPV), pregnant people and menopausal people who meet the OCSP eligibility criteria listed above still require cervical screening.

^aScreening is not recommended for people born without a cervix and transfeminine people with a neovagina because it may not be clinically or scientifically indicated (1). Routine screening is not recommended for people who have had their cervix removed as a result of hysterectomy; for more information refer to the OCSP's Vaginal Vault Testing Guidance that can be found on the HPV testing implementation resource hub at ontariohealth.ca/hpvhub

^bPeople with one negative HPV test result from age 65 to 69 can stop cervical screening, with a few exceptions. The following people should screen until age 74: people who were not screened from age 65 to 69, immunocompromised populations, and people who have been discharged from colposcopy, but who have not yet met the criteria to return to routine cervical screening by age 69.

^cSexual activity is defined as any sexual contact with another person's genitals (private parts). This contact can be with the hands, mouth or genitals, and includes the sharing of sex toys. Providers should define what is meant by sexual contact so their patients understand that it includes people who have had sexual contact with only one person, have had the same sexual partner for a long time, have not had sexual contact in a long time or have had sexual contact with someone of the same sex.

^dTo help someone get OHIP coverage, visit ontario.ca/page/apply-ohip-and-get-health-card, call Service Ontario toll-free at 1-800-267-8097 or text toll-free TYY at 1-800-268-7095 for more information.

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10. What are the cervical screening recommendations for people who are immunocompromised?

- Most cases of cervical cancer are caused by persistent infection with oncogenic types of human papillomavirus (HPV). Immunosuppression may impair someone's ability to clear an HPV infection. In addition, it may enhance the speed that cervical cellular changes occur and the progression to cervical cancer. Therefore, people who are immunocompromised may be at higher risk of pre-cancer and cervical cancer (1).
- There is limited evidence available to inform age of initiation and screening interval for people who are immunocompromised. Therefore, the recommendations for people who are immunocompromised are based on expert opinion, practices in other jurisdictions and the precautionary principle (i.e., when there are potential harms, scientific uncertainty must be resolved in favour of prevention of harms).
- The Ontario Cervical Screening Program (OCSP) recommends that people who are immunocompromised screen at an interval of three years (as long as their HPV testing results are negative), which is more often than the five-year interval for people in the general screening population.
- The OCSP screening recommendations for people who are immunocompromised apply to people who meet the program <u>eligibility criteria</u> and the OCSP's definition of being immunocompromised. People who are immunocompromised include:
 - Those who are living with human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS), regardless of CD4 cell count;
 - Those with congenital (primary) immunodeficiency;
 - Those who have received transplants (solid organ or allogeneic stem cell transplants);
 - Those requiring treatment (either continuously or at frequent intervals) with medications that cause immune suppression for three or more years;
 - Those who are living with systemic lupus erythematosus, regardless of whether they are receiving immunosuppressant treatment; and
 - Those who are living with renal failure and require dialysis.

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- 11. If people who are immunocompromised are at increased risk of pre-cancer and cervical cancer, why does the Ontario Cervical Screening Program (OCSP) recommend screening them at age 25 and not sooner?
 - There is no primary literature and no Ontario data on the incidence of pre-cancer and cervical cancer in immunocompromised populations under age 25 or on the appropriate age of initiation for cervical screening for these populations. However, cervical cancer among all people under age 25 is extremely uncommon. In Ontario, from 2014 to 2018, only 29 new cases of cervical cancer were diagnosed in people under age 25 (1). Given the low rate of cervical cancer, it is likely that screening under age 25 has no significant benefit and may do more harm than benefit.
 - Abnormal cervical cell changes in people under age 25 tend to be transient and are less likely
 to progress to pre-cancer and cervical cancer (3). In addition, given the long natural history of
 cervical cancer, instances of progression to pre-cancer and cancer are likely to be detected
 through regular screening after age 25.
 - Allowing time for transient abnormal cervical cell changes to resolve among people under age 25 helps to avoid unnecessary follow-up investigation or treatment in colposcopy, which has associated potential harms such as anxiety, discomfort, pain and in some cases, problems with future pregnancies (4).
 - Based on input from the expert panel and jurisdictional scan data, the OCSP recommends
 that people who are immunocompromised as defined by the OCSP should start cervical
 screening at age 25. This recommendation is in alignment with some other cervical screening
 programs that have recently implemented human papillomavirus testing, such as those in
 Australia and England (2, 5).

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12. Are the Ontario Cervical Screening Program (OCSP) screening recommendations different for Two-Spirit, transmasculine and nonbinary people with a cervix?

- Cervical screening recommendations are not different for Two-Spirit, transmasculine and nonbinary people with a cervix.
- Two-Spirit, transmasculine and nonbinary people with a cervix who meet the OCSP eligibility criteria^{a,b} and are due or overdue for screening should be offered cervical screening.
- If someone is considering transition-related surgical removal of the cervix, cervical screening should be offered before the cervix is removed.
- Two-Spirit, transmasculine and nonbinary people who do not meet the OCSP eligibility criteria (e.g., have not been sexually active^b) before undergoing transition-related surgical removal of the cervix do not need cervical screening.
- The use of transition-related hormone therapy (i.e., androgen therapy) in transmasculine and nonbinary people has been associated with a higher rate of unsatisfactory cytology test results. If someone is using transition-related hormone therapy, a course of intravaginal estrogen therapy should be considered after an unsatisfactory cytology test result (1).
- For more information, refer to the Overarching Policy for the Screening of Trans People in the Ontario Breast Screening Program and the Ontario Cervical Screening Program at cancercareontario.ca/en/guidelines-advice/types-of-cancer/61546

^aTo be eligible for screening in the OCSP, someone must be age 25 to 69 (some people may screen to age 74), have a cervix (including Two-Spirit, transmasculine and nonbinary people), have ever been sexually active and have no symptoms suggestive of cervical cancer. For more details, see questions #9 and #10.

^bSexual activity is defined as any sexual contact with another person, including any time someone has contact with another person's genitals (private parts). This contact can be with the hands, mouth or genitals, and includes the sharing of sex toys. Providers should define what is meant by sexual contact so their patients understand that it includes people who have had sexual contact with only one person, have had the same sexual partner for a long time, have not had sexual contact in a long time, or have had sexual contact with someone of the same sex.

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13. Are the Ontario Cervical Screening Program (OCSP) screening recommendations different for people without a cervix?

- People who were born without a cervix (including transfeminine people with a neovagina)
 are unlikely to benefit from cervical screening and are therefore not eligible for screening in
 the OCSP.
- People who have had their cervix removed, including women, Two-Spirit people, transmasculine people and nonbinary people, are ineligible for screening in the OCSP. However, vaginal vault testing may be appropriate if someone has had their cervix removed. For more information, refer to question #23 and the OCSP's Vaginal Vault Testing Guidance that can be found on the HPV testing implementation resource hub at ontariohealth.ca/hpvhub

14. Are screening recommendations different for people who have had human papillomavirus (HPV) immunization?

- The cervical screening recommendations are not different for people who have had HPV immunization.
- HPV vaccination does not protect against HPV infections that were acquired before the vaccine was administered and does not protect against all oncogenic HPV types (1, 2).
- This recommendation will be reviewed over time.

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15. Are the Ontario Cervical Screening Program (OCSP) colposcopy recommendations different for people who have had human papillomavirus (HPV) immunization?

 The OCSP's colposcopy recommendations are not different for people who have had HPV immunization.

16. Where can providers offering cervical screening and/or colposcopy get more information about human papillomavirus (HPV) immunization?

- HPV vaccination is offered free of charge to Grade 7 students in Ontario and may be available through individual public health units as a catch-up program.
- People can get HPV vaccination by prescription and through pharmacies in Ontario.
- For more information, visit <u>ontario.ca/page/getting-hpv-vaccine/</u> and https://health.gov.on.ca/en/pro/programs/immunization/immunization tool.aspx.
- For information on Canada's recommendations on the use of the HPV vaccine, visit the National Advisory Committee on Immunization at <u>canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci.html</u>

17. Do screening recommendations differ based on sexual history or sexual activity?

- Cervical screening should start at age 25 for people with a cervix who have ever been sexually active. Cervical screening is not recommended for people under age 25, even if sexually activity occurred, and is not recommended for people aged 25 and older who have never been sexually active.
- People who have never been sexually active do not need cervical screening because they
 have not been exposed to human papillomavirus (HPV).
 - Sexual activity includes any time someone has contact with another person's genitals (private parts). This contact can be with the hands, mouth or genitals, and includes the sharing of sex toys.
- Screening recommendations are the same for all people with a cervix (including Two-Spirit, transmasculine and nonbinary people) who have ever been sexually active, regardless of their sexual orientation or age of onset of sexual activity.
- Screening interval recommendations are the same for people who have had sexual contact
 with only one person, have had the same sexual partner for a long time, have not had sexual
 contact in a long time or have had sexual contact with someone of the same sex.
- People who are not currently sexually active, but who have been sexually active in the past still need screening because HPV can be present for many years without causing any symptoms. Cervical screening is the only way to find an HPV infection.

18. Should human papillomavirus (HPV) testing be performed as part of sexually transmitted infection screening?

 No. HPV testing should only be used for cervical screening and should not be used as a sexually transmitted infection test (e.g., to determine if someone has contracted an HPV infection from a new sexual partner) for two reasons:

HPV tests only detect certain types of HPV

- Of the over 100 types of HPV, the HPV test only checks for 13 types of HPV that are considered **oncogenic** (i.e., types that cause cervical cancer).
- The HPV test does not check for non-oncogenic types of HPV, such as those that cause genital warts.
- A negative HPV test does not necessarily mean that someone does not have an HPV infection. It only means that an oncogenic HPV infection was not detected.

Screening more frequently does not provide extra protection and can cause harm

- Most oncogenic HPV infections clear on their own, but it can take several years. Almost 80 per cent of infections clear within three years (1).
- Only persistent oncogenic HPV infections cause cervical cancer, which takes many years to develop (15 to 20 years in people who are immunocompetent) (2).
- There is no treatment for oncogenic HPV. Only the pre-cancer and cancer that can develop as a result of a persistent oncogenic HPV infection can be treated.
- Screening more frequently is not beneficial and increases the risk of harm by detecting transient HPV infections. Detecting a transient infection (one that is likely to resolve spontaneously) leads to unnecessary referral, colposcopy, biopsies and possibly treatment. For some people, colposcopy is associated with anxiety, discomfort and pain, and it should only be performed when the benefit of cancer prevention outweighs the risk of harm (3). Furthermore, some treatments used in colposcopy, particularly when they are repeated, have been associated with pregnancy complications, such as preterm labour and cervical stenosis (4).

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19. Do genital warts caused by human papillomavirus (HPV) increase the risk of cervical cancer?

• The types of HPV that cause genital warts (e.g., types 6 and 11) are non-oncogenic and are not known to cause cervical cancer (1, 2).

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20. Should providers perform an human papillomavirus (HPV) test on someone with cervical cancer symptoms?

- HPV testing should not be used to investigate signs or symptoms of cervical cancer.
- An HPV test may still be completed during a routine cervical screening appointment if the
 patient discloses signs or symptoms of cervical cancer, such as abnormal vaginal bleeding or
 discharge, bleeding after sexual activity^a or pelvic pain. However, clinical work-up of the
 symptoms is also required.
- If a lesion is found during a routine HPV test, the patient should be referred immediately to a colposcopist or a regional cancer centre, regardless of whether an HPV test is completed.

^aSexual activity is defined as any sexual contact with another person's genitals (private parts). This contact can be with the hands, mouth or genitals, and includes the sharing of sex toys. Providers should define what is meant by sexual contact so their patients understand that it includes people who have had sexual contact with only one person, have had the same sexual partner for a long time, have not had sexual contact in a long time or have had sexual contact with someone of the same sex.

21. What should providers do if a cervical lesion is found during a routine human papillomavirus (HPV) test?

- If a lesion is found during a routine HPV test, complete the test and refer the patient to colposcopy or a regional cancer centre.
- It is not necessary to wait for the results of the screening test to make the referral. Given the risk of false-negative screening test results, screening test results should not influence the decision to refer to colposcopy if someone has a cervical lesion.
- If reflex cytology testing (also known as Pap testing) has already been completed and is suggestive of cancer, referral to colposcopy or a regional cancer centre is recommended. If the reflex cytology test results are normal, someone with a cervical lesion should still be referred to colposcopy.

22. Should providers screen people who have had a trachelectomy?

- No. People who have had their entire cervix removed, as in a trachelectomy, are not eligible for cervical screening or vaginal vault testing.
- Monitoring following a trachelectomy should be guided by the surgeon who performed the procedure.

23. Do people with a history of abnormal cervical cell changes who have had a hysterectomy need to have vaginal vault testing?

- Only people in the following two groups should have vaginal vault testing with an human papillomavirus (HPV) test after a hysterectomy^a:
 - People with evidence of any of the following histologies in their cervix at hysterectomy (i.e., in the hysterectomy specimen), regardless of margin status or known HPV status:
 - Low-grade squamous intraepithelial lesion (LSIL)
 - High-grade squamous intraepithelial lesion (HSIL)
 - Adenocarcinoma in situ (AIS)
 - People with a history of early cervical cancer (microinvasive cervical cancer, stage 1A1 only), regardless of whether there is still evidence of cancer or pre-cancer at hysterectomy (i.e., may have been excised with a LEEP or cone prior to hysterectomy).
- If the first vaginal vault HPV test is negative, no more HPV tests are needed.

- If someone's HPV test is positive, refer them to colposcopy, regardless of HPV type or reflex cytology test result.
- For details, refer to the Ontario Cervical Screening Program Guidance for Vaginal Vault Testing document available on the HPV testing implementation resource hub at ontariohealth.ca/hpvhub

The use of the HPV test is approved by Health Canada for health care provider-collected cervical samples but has not been reviewed or authorized by Health Canada for use in the vaginal vault. HPV test performance has not been specifically evaluated for detecting vaginal precancer/cancer in relevant populations, therefore risks to the patient may include, but are not limited to, a decrease in testing accuracy. The Ontario Cervical Screening Program Guidance for Vaginal Vault Testing has been developed by Ontario Health in consultation with a multidisciplinary, international expert panel. Other Canadian and international jurisdictions also provide guidance on using the HPV test in the vaginal vault. The information provided by Ontario Health is not intended to serve as a substitute for a clinician's professional experience, independent judgment and decision making. Ontario Health assumes no liability whatsoever for any errors or omissions associated with the information provided herein and furthermore assumes no liability for any decision or action taken by the clinician or others in reliance on the information contained in these materials.

Age of screening initiation and cessation.

24. Why does the Ontario Cervical Screening Program (OCSP) not recommend cervical screening for people under age 25?

- Cervical cancer incidence in people under age 25 is extremely low (1). From 2014 to 2018, the incidence rate for cervical cancer in people under age 25 in Ontario was 0.3 per 100,000, compared to 8.1 per 100,000 for all ages (1).
- Abnormal cervical cell changes in people under age 25 tend to be transient and are less likely
 to progress to pre-cancer and cervical cancer (2). In addition, given the long natural history of
 cervical cancer, instances of progression to pre-cancer and cancer are likely to be detected
 through regular screening after age 25.
- An Ontario study found that cervical screening with cytology testing (also known as Pap testing) did not prevent invasive cervical cancer in people ages 20 to 25 when it was performed three to 36 months before their diagnosis (3).
- Allowing time for transient abnormal cervical cell changes to resolve among people under age 25 helps to avoid unnecessary follow-up investigation or treatment in colposcopy, which has associated potential harms such as anxiety, discomfort, pain and in some cases, problems with future pregnancies (4).
- Therefore, screening in people under age 25 has no significant benefit and has potential for harm.

 The OCSP's recommendations to start cervical screening at age 25 align with those from the Canadian Task Force on Preventive Health Care (5), as well as screening programs in British Columbia, Alberta, Nova Scotia and other programs internationally (6-9).

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25. When should eligible people stop cervical screening? UPDATED APRIL 2025

- Anyone who had previously met the cytology-based cessation criteria (i.e., stop screening at age 70 if they have had 3 negative cytology results in routine screening in the previous 10 years) prior to HPV testing implementation does not need to screen with HPV testing.
- People can stop cervical screening if they have had one negative human papillomavirus (HPV) test result from age 65 to 69, with the following exceptions:
 - People who were not screened from age 65 to 69 should be screened up to age 74.

- Immunocompromised people should continue screening until age 74. Refer to question #10 - What are the cervical screening recommendations for people who are immunocompromised?
- People who have been discharged from colposcopy, but have not yet met the criteria to return to routine cervical screening by age 69 should continue to screen until age 74 (see colposcopy pathways and post discharge table for more information).
- People with an HPV-positive test result from age 65 to 69 should follow the appropriate screening and colposcopy pathways until they have a negative HPV test result or until they are age 74, whichever occurs first.
- People with an HPV-positive test result (regardless of HPV type or reflex cytology test result)
 from age 70 to 74 should be referred to colposcopy. In colposcopy^a:
 - People with high-grade squamous intraepithelial lesion detected at colposcopy should follow the appropriate treatment pathway.
 - People with a negative colposcopy (i.e., histology is low-grade squamous intraepithelial lesion or no biopsy taken) can be discharged from colposcopy and no further screening is required in primary care.

^aDue to potential discomfort and atrophy (which causes visual inspection issues), use of intravaginal estrogen therapy can be considered if someone has no medical contraindications.

26. Why does the Ontario Cervical Screening Program (OCSP) not recommend screening people over age 74?

- The natural history of cervical cancer is very long. Typically, it takes 15 to 20 years for oncogenic human papillomavirus (HPV) infections to progress to cervical cancer in people who are immunocompetent (1).
- As people get older, it is generally accepted that the benefits of screening begin to decrease and the potential harms increase (e.g., burden of additional testing if someone is HPVpositive) (2).
- This approach is aligned with other organized cervical screening programs. The OCSP is not aware of any organized cervical screening program that recommends screening people over age 74.

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Screening interval.

27. How will cervical screening intervals change with human papillomavirus (HPV) testing?

- Before the launch of HPV testing, the Ontario Cervical Screening Program (OCSP)
 recommended cervical screening with cytology testing (also known as Pap testing) three
 years after each normal cytology test result.
- The OCSP now recommends that most eligible people screen with an HPV test five years after each negative HPV test result.
- There are a few exceptions:
 - People who are immunocompromised.
 - The screening interval for people who are immunocompromised is three years after a negative HPV test result.
 - People who are HPV-positive (other high-risk types) with normal or low-grade reflex cytology test results.
 - People who are positive for oncogenic types of HPV other than types 16, 18 and 45 (i.e., HPV-positive [other high-risk types]) with normal or low-grade reflex cytology test results should return to screening in two years.
 - If they remain HPV-positive at their subsequent screening test, they should be referred to colposcopy, regardless of their HPV type or reflex cytology test result.
 - People who have been discharged from colposcopy.
 - People who have been discharged from colposcopy should screen in two years, three years or five years, depending on their cytology test results at referral, immune status, histology and cytology test results, HPV status at discharge and whether treatment was required before discharge from colposcopy.
 - Refer to the Ontario Cervical Screening Program colposcopy pathways and post-discharge table for details, which can be found on the HPV testing implementation resource hub at ontariohealth.ca/hpvhub

28. Should people with genital warts be screened more often for human papillomavirus (HPV)?

- No. Only oncogenic types of HPV can lead to cervical cancer, whereas the types of HPV that cause genital warts are non-oncogenic and are not known to cause cervical cancer (1, 2). Therefore, if someone has genital warts, it will not impact their cervical screening intervals.
- Screening more often does not provide extra protection and can cause harm.
 - Most oncogenic HPV infections clear on their own, but it can take several years.
 Almost 80 per cent of infections clear within three years (3).
 - Only persistent oncogenic HPV infections cause cervical cancer, which takes many years to develop (15 to 20 years in people who are immunocompetent) (4).
 - There is no treatment for oncogenic HPV infections. Only the pre-cancer and cancer that can develop as a result of a persistent oncogenic HPV infection can be treated.
 - Screening more frequently is not beneficial and increases the risk of harm by detecting transient HPV infections. Detecting a transient infection (one that is likely to resolve spontaneously) leads to unnecessary referral, colposcopy, biopsies and possibly treatment. For some people, colposcopy is associated with anxiety, discomfort and pain, and should only be performed when the benefit of cancer prevention outweighs the risk of harm (5). Furthermore, some treatments used in colposcopy, particularly when they are repeated, have been associated with pregnancy complications, such as preterm labour and cervical stenosis (6).

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29. Why is the screening interval increasing from three to five years for people with negative human papillomavirus (HPV) test results?

- Because it takes many years for cervical cancer to develop, someone has a very low risk of
 developing pre-cancer and cervical cancer (1–7) if they get an oncogenic HPV infection in the
 five years after a negative HPV test result. Furthermore, providers can be confident that a
 negative HPV test result correctly identifies people without a pre-cancer or cancer (i.e., the
 HPV test has a high negative predictive value) (1,8).
- Published evidence shows that the risk of high-grade abnormal cervical cell changes five
 years after a negative HPV test result is lower than the risk three years after a normal
 cytology test (also known as a Pap test) result, which provides reassurance that the five-year
 cervical screening interval will not result in additional cancers (1).
- More frequent screening with the HPV test is not supported by evidence, which shows that the potential harms of shorter screening intervals outweigh the benefits (9). More frequent screening can result in greater detection of false-positives and more referrals to colposcopy (9), which causes unnecessary anxiety, discomfort and pain (10).
- The five-year screening interval has been widely adopted internationally among populations that are similar to Ontario.

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30. What if someone asks to be screened more often than the Ontario Cervical Screening Program (OCSP) recommends?

- The OCSP strongly discourages screening outside of the recommended intervals. The OCSP's screening intervals are evidence-based and ensure the careful balance between the benefits of screening and the potential harms of over-screening.
 - Most oncogenic human papillomavirus (HPV) infections clear on their own, but it can take several years. Almost 80 per cent of infections clear within three years (1).
 - Only persistent oncogenic HPV infections cause cervical cancer, which takes many years to develop (15 to 20 years in people who are immunocompetent) (2).
 - There is no treatment for oncogenic HPV infections. Only the pre-cancer and cancer that can develop as a result of a persistent oncogenic HPV infection can be treated.
 - Screening more frequently is not beneficial and increases the risk of harm by detecting transient HPV infections. Detecting a transient infection (one that is likely to resolve spontaneously) leads to unnecessary referral, colposcopy, biopsies and possibly treatment. For some people, colposcopy is associated with anxiety, discomfort and pain, and should only be performed when the benefit of cancer

prevention outweighs the risk of harm (3). Furthermore, some treatments used in colposcopy, particularly when they are repeated, have been associated with pregnancy complications, such as preterm labour and cervical stenosis (4).

 For more information about the recommended screening intervals, see question #27 - How will cervical screening intervals change with human papillomavirus (HPV) testing?

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Launching human papillomavirus testing.

- 31. Given the benefits of human papillomavirus (HPV) testing, should providers rescreen someone sooner than their recommended interval when HPV testing is launched?
 - Once HPV testing is launched in the Ontario Cervical Screening Program (OCSP), screening
 participants should have an HPV test when they are next due for screening. Someone's
 screening interval is determined based on their last screening test. Screening earlier than the
 recommended intervals is not necessary.
 - Most people with a negative cytology test (also known as a Pap test) result at their last cervical screen should have an HPV test three years after their last cytology screen.
 - However, people who are screening with cytology at one-year intervals (i.e., people who have been discharged from colposcopy for annual screening, who had a single low-grade cytology test result^a or who are immunocompromised) should have an HPV test one year after their last cytology screen.

- People who had an unsatisfactory cytology test shortly before the launch of HPV testing should repeat their screen with an HPV test.
- After someone has been screened with an HPV test, their next screening interval will be determined based on the OCSP recommendations for HPV testing.
- Ontario Health (Cancer Care Ontario) will continue to send recall letters to people who were previously screened with a cytology test when they are due for their next screening test.

^aPeople who are under age 25 and had a single low-grade cytology result (ASCUS = atypical squamous cells of undetermined significance or LSIL = low-grade squamous intraepithelial lesion) should delay re-screening until they reach age 25. However, if the participant chooses not to delay after a discussion with their health care provider about the limited benefits and potential harms of re-screening before age 25, screening with the HPV test in 12 months is recommended.

32. After human papillomavirus (HPV) testing is implemented, what is the appropriate test indication for people who are currently participating in cytology-based cervical screening? ADDED MARCH 2025

During the transition to HPV testing, the appropriate test indication on the new Ontario
Cervical Screening Program (OCSP) requisition (HPV and Cytology Tests Requisition – For
Cervical Screening) for people currently participating in cervical screening is selected based
on a person's previous cytology test result in primary care, cytology or HPV test result at
discharge from colposcopy, and their immune status.

The following table outlines which test indication to select on the new OCSP requisition:

| Cytology-based risk category and screening interval | When to screen | Recommended test indication on new HPV OCSP requisition |
|---|------------------------------------|---|
| Immunocompetent people at average risk (i.e., screening every three years) History of normal cytology results only Returned to average risk screening after a low-grade cytology result | 3 years after last cytology result | Average risk screening: every 5 years |
| Immunocompromised ^a people at average risk (i.e., screening annually) • History of normal cytology results only | 1 year after last cytology result | Immunocompromised screening: every 3 years |

| Cytology-based risk category and screening interval | When to screen | Recommended test indication on new HPV OCSP requisition |
|---|--|--|
| Returned to average risk screening after a low-grade cytology result | | |
| Immunocompetent and immunocompromised ^a people screening annually due to a history of abnormal results (i.e., a first-time ASCUS/LSIL cytology result or an ASCUS/LSIL cytology result followed by a normal cytology result) | 1 year after last cytology result | HPV-positive (other high-risk types) with normal or low-grade (NILM/ASCUS/LSIL) cytology: 2-year follow-up (moderate risk) |
| Immunocompetent and immunocompromised ^a people screening annually after being discharged from colposcopy with persistent low-grade cytology or an HPV-positive test result | 1 year after last cytology result | HPV-positive (other high-risk types) with normal or low-grade (NILM/ASCUS/LSIL) cytology: 2-year follow-up (moderate risk) |
| Immunocompetent and immunocompromised ^a people discharged from colposcopy to average risk screening | Immunocompetent: 3 years following the last cytology result at discharge; or Immunocompromised: 1 year following the last cytology result at discharge | Immunocompetent: Average risk screening: every 5 years; or Immunocompromised: Immunocompromised screening: every 3 years |
| People with histologic evidence of dysplasia in the cervix at the time of hysterectomy that require a vaginal vault test | 6 – 12 months following hysterectomy | People with histologic evidence of dysplasia in the cervix at the time of hysterectomy and people with a history of early cervical cancer: 1-time posthysterectomy vaginal vault testing |

ASCUS = atypical squamous cells of undetermined significance; LSIL = low-grade squamous intraepithelial lesion; NILM = negative for intraepithelial lesion or malignancy;

^aThe OCSP screening recommendations for people who are immunocompromised apply to people who meet the program <u>eligibility criteria</u> and the OCSP's definition of being immunocompromised. People who are immunocompromised include:

- Those who are living with human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS), regardless of CD4 cell count;
- Those with congenital (primary) immunodeficiency;
- Those who have received transplants (solid organ or allogeneic stem cell transplants);
- Those requiring treatment (either continuously or at frequent intervals) with medications that cause immune suppression for three or more years;
- Those who are living with systemic lupus erythematosus, regardless of whether they are receiving immunosuppressant treatment; and
- Those who are living with renal failure and require dialysis.
- 33. I received a message on my provider report that my patient's test indication for cervical screening was defaulted to average risk screening. How does this impact clinical management of my patient? ADDED MARCH 2025

Why have I received this message?

Laboratories will default the test indication to average risk screening if they are unable to contact the ordering provider to correct the following issues:

- Ontario Cervical Screening Program (OCSP) cervical screening requisition was received with a missing test indication
- OCSP cervical screening request received on incorrect requisition
- OCSP cervical screening requisition received with an inappropriate cytology only request

Why is the test indication important?

The laboratory provides guidance for the clinical management of patients based on the combination of a patient's test indication for cervical screening and the results of their cervical screening test. The combination of this information also determines what correspondence the patient receives about the next steps in their care.

If the defaulted test indication does not align with the appropriate test indication based a patient's screening history, the action required shared in the provider report and correspondence letter could be inaccurate for some test indication and result combinations.

Next steps for providers

If a provider receives a report where it notes a default test indication was applied due to missing information, they should confirm the appropriate action required based on the patient's last screening test result.

Application of the default average risk test indication impacts laboratory clinical management recommendations and correspondence for patients with human papillomavirus (HPV)-positive

(other high-risk types) with low grade or normal cytology if the patient's screening result history includes:

- First-time ASCUS/LSIL cytology result or ASCUS/LSIL cytology result followed by a normal cytology
- Screening annually after discharge from colposcopy with persistent low-grade cytology or an HPV-positive test result

The application of an average risk screening indication for this group would mean that they are incorrectly directed to repeat their cervical screening test in two years, when they should be referred to colposcopy.

Patients with any other result (e.g., HPV-negative, HPV-positive [types 16, 18/45]) will have the correct clinical management recommendation documented in the provider report and correspondence, regardless of their screening history. This includes patients with HPV-positive (other high-risk types) with normal or low-grade cytology results that have a history of normal cytology results only or have returned to average risk screening after a low-grade cytology result or discharge from colposcopy.

- 34. What is the recommended timing for someone's next screening test if they are under age 25 with a normal cytology test (also known as a Pap test) result before human papillomavirus (HPV) testing was implemented?
 - People with normal cytology test results who are under age 25 and immunocompetent should delay their next screen until age 25, or three years after their last test, whichever comes later.
 - People with a normal cytology test result who are under age 25 and immunocompromised should delay their next screening test to age 25, or 12 months after their last test, whichever comes later.
- 35. What is the recommended timing for someone's next screening test if they are under age 25 with an abnormal cytology test (also known as a Pap test) result before human papillomavirus (HPV) testing was implemented?
 - For people under age 25 who had an abnormal cytology test result before HPV testing implementation, recommendations for next steps vary based on their cytology test results, screening history and immune status.
 - For immunocompetent people who had a first-time, low-grade cytology test result before
 the launch of HPV testing, re-screening with an HPV test should be delayed until they reach
 age 25.
 - This recommendation is based on the evidence that HPV infections and related cell changes in the cervix are likely to go away on their own in people under age 25 (1).

- However, if someone chooses not to delay screening after a discussion with their provider about the limited benefits and potential harms of re-screening before age 25, they have the option to re-screen with an HPV test in 12 months.
- Follow-up for people who choose to re-screen before age 25 should be based on the HPV testing recommendations.
- For immunocompromised^a people who had a first-time, low-grade cytology test result before the launch of HPV testing, re-screening with an HPV test should be performed 12 months after their low-grade result, regardless of age.
 - Most cases of cervical cancer are caused by persistent infection with oncogenic types of HPV. Immunosuppression may impair someone's ability to clear an HPV infection.
 - In addition, immunosuppression may increase the speed of the cervical cellular changes caused by an HPV infection, including the progression to cervical cancer.
 - Therefore, people who are immunocompromised with known cervical abnormalities should not delay re-screening to age 25.
- People who had two consecutive low-grade cytology test results and people with highgrade cytology test results before the launch of HPV testing should be referred to colposcopy, regardless of immune status.

^aThe Ontario Cervical Screening Program includes the following groups in its definition of immunocompromised:

- People who are living with human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS), regardless of CD4 cell count;
- People with congenital (primary) immunodeficiency;
- Transplant recipients (solid organ or allogeneic stem cell transplants);
- People requiring treatment (either continuously or at frequent intervals) with medications that cause immune suppression for three years or more;
- People who are living with systemic lupus erythematosus (SLE), regardless of whether they
 are receiving immunosuppressant treatment; and
- People who are living with renal failure and require dialysis.

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- 36. What is the recommended timing for someone's next screening test if they are under age 25 with an unsatisfactory cytology test (also known as a Pap test) result before human papillomavirus (HPV) testing was implemented?
 - The Ontario Cervical Screening Program (OCSP) recommends delaying re-screening until age 25 if someone under age 25 had an unsatisfactory cytology test result before HPV testing was implemented.
 - Unsatisfactory cytology occurs due to specimen collection and processing errors, and not due to an increase in the risk of pre-cancer and cervical cancer.
 - Waiting until age 25 to re-screen is appropriate because the incidence of cervical cancer in people under age 25 is extremely low (1). The risk is lower in this age group because abnormal cervical cell changes in people under age 25 tend to be transient and are less likely to progress to pre-cancer and cervical cancer (2).
 - Given the long natural history of cervical cancer, instances of progression to pre-cancer and cancer are likely to be detected through regular screening after age 25.
 - Allowing time for transient abnormal cervical cell changes to resolve in people under age 25 also helps to avoid unnecessary follow-up investigation or treatment in colposcopy, which has associated potential harms.
 - Therefore, screening in people under age 25 has no significant benefit and has potential for harm.
 - The evidence supports waiting until age 25 to re-screen. However, if after a discussion with their provider about the benefits and risks, someone wants to screen again sooner, the OCSP recommends re-screening with an HPV test at their earliest convenience.

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- 37. How should providers offering colposcopy manage follow-up for people ages 21 to 24 in colposcopy after human papillomavirus (HPV) testing is implemented?
 - For people ages 21 to 24 who are immunocompetent with high-grade squamous intraepithelial lesion (HSIL) histology identified at colposcopy, the Ontario Cervical Screening Program (OCSP) recommends the following:
 - Conservative management with two follow-up colposcopy visits 12 months apart.
 Conservative management can include visual inspection and biopsies without treatment (i.e., no diagnostic excisional procedures, such as a loop electrosurgical excision procedure).

- If HSIL histology persists after two years, treatment is recommended. However, providers may choose to treat during the two-year period of conservative management in some cases.
- For people ages 21 to 24 with adenocarcinoma in situ (AIS) histology identified at colposcopy, the OCSP recommends management according to the AIS colposcopy pathway.
- The OCSP recommends management according to colposcopy pathway 3 for people ages
 21 to 24 who were referred to colposcopy with:
 - Atypical glandular cells, favour neoplastic (AGC-N);
 - Atypical glandular cells, not otherwise specified (AGC-NOS);
 - Atypical endocervical cells, favour neoplastic (AEC-N) or;
 - Atypical endocervical cells, not otherwise specified (AEC-NOS).
- 38. After human papillomavirus (HPV) testing is launched, how should providers offering colposcopy manage people who were referred to them before the launch with only cytology test (also known as Pap test) results? UPDATED MARCH 2025
 - After HPV testing is launched, colposcopy consultations should transition to the new
 Ontario Cervical Screening Program (OCSP) colposcopy pathways. Providers offering
 colposcopy should use these new pathways for all patients, including people who were only
 screened with cytology and are entering colposcopy or are already in colposcopy with
 unknown HPV status.
 - For people <u>entering colposcopy</u> who were referred with only cytology results (HPV status unknown), apply the new OCSP colposcopy pathways based on their:
 - Cytology (Pap test) results at referral, and
 - Histology findings collected at and made available following their first colposcopy visit (i.e., whether a high-grade squamous intraepithelial lesion or adenocarcinoma in situ is detected)
 - The OCSP has developed recommendations on which OCSP colposcopy pathway to follow, as well as when to do HPV-cytology co-testing based on cytology results at referral and colposcopy findings from the first visit. These recommendations are summarized in the tables below.

Table 1. Colposcopy recommendations for people <u>entering colposcopy</u> with cytology results only (HPV status unknown)

| Cytology test result at referral | Should an HPV- cytology co-test be collected at the first colposcopy visit? | Histology result from first colposcopy visit | What are the recommended next steps following the first colposcopy visit? |
|--|---|---|--|
| Low-grade | Collect an HPV- cytology co-test at the first colposcopy visit ^{a,b} | No high-grade histology detected (no lesion seen or biopsy detected <lsil)< th=""><th>Per OCSP colposcopy pathway 1, discharge from colposcopy and determine interval between discharge and the next cervical screening test in primary care based on the results of the co-test: If cytology is <lsil, (or="" 2="" 3="" 5="" by="" care="" determined="" hpv="" hpv-negative,="" hpv-positive,="" if="" immunocompromised<sup="" in="" interval="" is="" primary="" result.="" return="" screening="" the="" to="" years="">c) If co-test cytology result is high-grade, manage using corresponding OCSP colposcopy pathway based on cytology result.</lsil,></th></lsil)<> | Per OCSP colposcopy pathway 1, discharge from colposcopy and determine interval between discharge and the next cervical screening test in primary care based on the results of the co-test: If cytology is <lsil, (or="" 2="" 3="" 5="" by="" care="" determined="" hpv="" hpv-negative,="" hpv-positive,="" if="" immunocompromised<sup="" in="" interval="" is="" primary="" result.="" return="" screening="" the="" to="" years="">c) If co-test cytology result is high-grade, manage using corresponding OCSP colposcopy pathway based on cytology result.</lsil,> |
| Low-grade | Collect an HPV- cytology co-test at the first colposcopy visit ^{a,b} | High-grade histology detected | Treat and follow pathway 6: Post-treatment management for histology-confirmed HSIL ^d |
| High- grade, excluding AIS | No HPV-cytology co-test required at the first colposcopy visit ^e | No high-grade histology detected | Follow pathway 2: People referred with high- grade cytology (ASC-H, LSIL-H, HSIL) results |
| High- grade, excluding AIS | No HPV-cytology co-test required at the first colposcopy visit ^e | High-grade histology detected | Treat and follow pathway 6: Post-treatment management for histology-confirmed HSIL ^d |
| AGC ^f | No HPV-cytology co-test required at first colposcopy visit ^e | No high-grade histology detected | Follow pathway 3: People referred with AGC or AEC cytology results ^d |
| AIS | No HPV-cytology co-test required at first colposcopy visit ^e | Any | Follow pathway 4: People referred with AIS cytology results |

AIS = adenocarcinoma in-situ; ASC-H = atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion; ASCUS = atypical squamous cells of undetermined significance; HPV = human papillomavirus; HSIL = high-grade squamous intraepithelial lesion; LSIL = low-grade squamous intraepithelial lesion; LSIL-H = LSIL, cannot exclude HSIL; NILM = negative for intraepithelial lesion or malignancy; OCSP = Ontario Cervical Screening Program

^aAn HPV-cytology co-test is recommended during the first colposcopy visit for all people entering colposcopy who were referred with low-grade cytology. The recommended testing indication to use on the <u>HPV and Cytology Tests Requisition – Colposcopy for Follow-up of Cervical Screening Related Abnormalities</u> for people during their first colposcopy visit is: Co-testing 12 months after initial colposcopy where high-grade squamous intraepithelial (HSIL) lesion was not detected.

^bThis co-test is collected at the same time as a biopsy and before histology results from biopsy are available. When no high-grade histology is detected (no lesion seen or biopsy detected <LSIL), the HPV-cytology co-test results can be used to determine the interval between discharge and the next cervical screening test in primary care based on the results of the co-test. If high-grade histology is detected, treatment is recommended.

'The OCSP includes the following groups in its definition of immunocompromised:

- People who are living with human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS), regardless of CD4 cell count
- People with congenital (primary) immunodeficiency
- Transplant recipients (solid organ or allogeneic stem cell transplants)
- People requiring treatment (either continuously or at frequent intervals) with medications that cause immune suppression for three years or more
- People who are living with systemic lupus erythematosus (SLE), regardless of whether they
 are receiving immunosuppressant treatment
- People who are living with renal failure and require dialysis

dOCSP colposcopy pathways can be accessed at ontariohealth.ca/hpvhub

^eHPV-cytology co-tests are used to determine the interval between discharge and next cervical screening test in primary care. As such, co-tests are not recommended when additional visits in colposcopy are required, and discharge is not imminent.

fIncludes AGC-N/NOS, AEC-N/NOS (AGC-N = atypical glandular cells, favour neoplastic; AGC-NOS = AGC, not otherwise specified; AEC-N = atypical endocervical cells, favour neoplastic; AEC-NOS = AEC, not otherwise specified).

- For people <u>already undergoing care</u> in colposcopy who only have cytology screening results (HPV status unknown):
 - Apply the new OCSP colposcopy pathways on their highest-grade cytology test results, and
 - Manage and discharge them based on their HPV-cytology co-test results
- The table below provides recommendations on HPV-cytology co-testing for discharge from colposcopy in several clinical scenarios.

Table 2. Colposcopy recommendations for people <u>already undergoing care</u> in colposcopy who have cytology results only (HPV status unknown)

| Highest grade cytology test result | Recommended OCSP colposcopy Pathway ⁱ | Colposcopy and HPV-cytology co-testing recommendations to determine discharge from colposcopy and when to return to screening in primary care |
|------------------------------------|---|--|
| Low-grade | Follow pathway 1: People referred with normal (NILM) or low- grade cytology (ASCUS, LSIL) results | When entering pathway 1, a single colposcopy visit is required to confirm the absence of high-grade histology and eligibility for discharge from colposcopy. One HPV-cytology co-test is recommended before discharge to determine when to return to screening in primary care ^{g,h} |
| High-grade | Follow pathway 2: People referred with high-grade cytology (ASC-H, LSIL-H, HSIL) results | When entering pathway 2, at least 2 colposcopy visits are required to confirm the absence of high-grade histology and eligibility for discharge from colposcopy. Therefore, if all required investigations from the first colposcopy visit in pathway 2 ⁱ are complete and normal, at least one more visit is needed. One HPV-cytology co-test is recommended before discharge to determine when to return to screening in primary care ^{g,h} |
| AGC ^j | Follow pathway 3: People referred with AGC or AEC cytology results | When entering pathway 3, at least 2 colposcopy visits are required to confirm the absence of high-grade histology and eligibility for discharge from colposcopy. Therefore, if all required investigations from the first colposcopy visit in pathway 3 ⁱ are complete and normal, at least one more visit is needed. One HPV-cytology co-test is recommended before discharge to determine when to return to screening in primary care ^{g,h} |

| Highest grade cytology test result | Recommended OCSP colposcopy Pathway ⁱ | Colposcopy and HPV-cytology co-testing recommendations to determine discharge from colposcopy and when to return to screening in primary care |
|--------------------------------------|---|---|
| | | When entering pathway 6, at least 2 colposcopy visits are required to confirm the absence of high-grade histology and eligibility for discharge from colposcopy. |
| Post-treatment (excluding AIS) | Follow pathway 6: Post-treatment management for histology- confirmed HSIL | It is recommended that 2 HPV-cytology co-tests (each done at different visits) be used to determine when to return to screening in primary care. The only exception is if someone has already had 2 colposcopy visits before the launch of HPV testing and at the third visit no high-grade dysplasia is detected, only 1 HPV-cytology co-test is recommended to determine when to return the person should resume screening in primary care ^{g,h} |
| AIS or post- treatment for AIS | Follow pathway 7: Post-treatment management for histology- confirmed AIS | A minimum of 5 years of follow-up in colposcopy with negative cytology results is recommended to confirm the absence of high-grade or AIS histology or three consecutive negative HPV/cytology co-tests are required before discharging to screening in primary care. For people already undergoing post-treatment care, colposcopists may consider extending follow-up to perform HPV/cytology co-testing. |

AIS = adenocarcinoma in-situ; ASC-H = atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion; ASCUS = atypical squamous cells of undetermined significance; HPV = human papillomavirus; HSIL = high-grade squamous intraepithelial lesion; LSIL = low-grade squamous intraepithelial lesion; LSIL-H = LSIL, cannot exclude HSIL; NILM = negative for intraepithelial lesion or malignancy; OCSP = Ontario Cervical Screening Program

^gDuring the transition to HPV testing, the recommended testing indication to use on the <u>HPV and Cytology Tests Requisition – Colposcopy for Follow-up of Cervical Screening Related Abnormalities</u> will depend on whether a person has been treated in colposcopy.

- For people who have **not been treated** in colposcopy, the recommended testing indication is: Co-testing 12 months after initial colposcopy where high-grade squamous intraepithelial (HSIL) lesion was not detected.
- For people who have been treated in colposcopy, the recommended testing indication is: Co-testing during post-treatment follow-up for HSIL or adenocarcinoma in situ (AIS).

^hPeople who have HPV-negative test results can return to screening with the HPV test in primary care in five years (or three if immunocompromised) and people who have HPV-positive test results can return to screening in two years. The OCSP includes the following groups in its definition of immunocompromised: people living with HIV/AIDS, regardless of CD4 cell count; people with

congenital (primary) immunodeficiency; transplant recipients (solid organ or allogeneic stem cell transplants); people requiring treatment (either continuously or at frequent intervals) with medications that cause immune system suppression for three years or more; people who are living with systemic lupus erythematosus (SLE), regardless of whether they are receiving immunosuppressant treatment; and people who are living with renal failure and require dialysis.

OCSP Colposcopy Pathways can be accessed at ontariohealth.ca/hpvhub

Includes AGC-N/NOS, AEC-N/NOS (AGC-N = atypical glandular cells, favour neoplastic; AGC-NOS = AGC, not otherwise specified; AEC-N = atypical endocervical cells, favour neoplastic; AEC-NOS = AEC, not otherwise specified).

Other questions about changes to program recommendations.

- 39. Will the screening letters that people receive be updated once human papillomavirus (HPV) testing is available in the Ontario Cervical Screening Program (OCSP)?
 - Ontario Health (Cancer Care Ontario) will be updating the cervical screening letters to align
 with changes to the OCSP. The new letters will launch when HPV testing becomes available
 through the OCSP.
 - If someone gets a cytology test (also known as a Pap test) before the implementation of HPV testing, they will still receive a cytology test result letter.
 - Once HPV testing is launched, a notable change to the OCSP screening letters will be the
 availability of physician-linked correspondence. Physician-linked correspondence letters are
 personalized screening invitations, recalls and reminders generated by the OCSP that
 include the name of someone's physician. Evidence shows a positive relationship between
 physician recommendation for screening and participation in colorectal cancer, breast
 cancer and cervical screening (1-5).
 - If a provider has already enrolled in physician-linked correspondence for ColonCancerCheck, their patients will automatically begin to receive physician-linked correspondence for OCSP screening invitation, recall and reminder letters from Ontario Health (Cancer Care Ontario) with the launch of HPV testing.
 - To sign up for physician-linked correspondence, visit <u>cancercareontario.ca/en/physician-linked-correspondence</u>

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- 40. Where can providers offering cervical screening and/or colposcopy find more information about the Ontario Cervical Screening Program (OCSP) cervical screening recommendations and colposcopy recommendations?
 - For more information about the OCSP cervical screening and colposcopy recommendations, please visit:
 - The human papillomavirus (HPV) testing implementation resource hub at ontariohealth.ca/hpvhub for resources before the launch of HPV in the OCSP; and
 - Screening Resources for Healthcare Providers Cancer Care Ontario for resources after the launch of HPV in the OCSP.

Ordering the human papillomavirus test and collecting the specimen.

- 41. How do providers collect a cervical specimen for screening and colposcopy?
 - Step-by-step guidance on how to collect a cervical specimen using the ThinPrep® system is available on the HPV testing implementation resource hub at ontariohealth.ca/hpvhub.
- 42. Can collection devices be left in collection vials during cervical specimen collection using the ThinPrep® system?
 - Unlike some other systems for cervical specimen collection, the ThinPrep® system does not
 allow any part of a collection device to be left in the collection vial. Examples of device
 parts that are not allowed include the head of the broom-like device, the head of the
 endocervical brush and the spatula.
 - Specimens with any part of a collection device left in the collection vial will be rejected by the laboratory.

• Step-by-step guidance on how to collect a cervical specimen using the ThinPrep® system is available on the HPV testing implementation resource hub at ontariohealth.ca/hpvhub.

43. Can providers who offer screening or colposcopy use lubricant when collecting a cervical specimen using the ThinPrep® system?

- Providers who offer screening or colposcopy may use water or small amounts of lubricant gel when collecting a cervical specimen to make the speculum more comfortable for the screening participant.
- Using too much lubricant or using lubricants that contain carbomer or Carbopol® polymers (thickening agents) may cause an invalid test result. To minimize the risk of an invalid test result:
 - Use lukewarm water to warm and lubricate the speculum, or
 - If a lubricant gel needs to be used for participant comfort:
 - Use a dime-sized amount of water-soluble and carbomer-free gel lubricant (1,2) (refer to the ThinPrep® Pap Test Lubricant Compatibility List (3) at hologic.com/thinprep for a list of lubricant brands that have been validated by Hologic, Inc.)
 - Apply the lubricant only to the outer sides of the speculum blades, avoiding contact with the tip and inner sides of the speculum
- Step-by-step guidance on how to collect a cervical specimen using the ThinPrep® system is available on the HPV testing implementation resource hub at ontariohealth.ca/hpvhub.

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44. Will there be a new Ontario Cervical Screening Program (OCSP) requisition form for human papillomavirus (HPV) testing and cytology testing (also known as Pap testing) for screening?

- Yes. There will be a new OCSP-specific screening requisition form for ordering an HPV test with reflex cytology, standalone cytology (where appropriate) or vaginal vault testing (HPV and Cytology Tests Requisition – For Cervical Screening).
- Providers will not be able to order OCSP-funded testing using any other requisition.

- 45. Where can providers find the new Ontario Cervical Screening Program (OCSP) requisition form for human papillomavirus (HPV) testing and cytology testing (also known as Pap testing) for screening?
 - Leading up to the launch of HPV testing, the HPV and Cytology Tests Requisition For Cervical Screening will be available on the HPV testing implementation resource hub at ontariohealth.ca/hpvhub and as part of an information package sent to providers who offer screening.
 - In addition, Ontario Health (Cancer Care Ontario) is working with OntarioMD (OMD) to make the requisition form available through certified electronic medical records (EMRs).
 - Providers can contact their EMR vendor closer to the launch of HPV testing implementation to explore how the requisition form will be made available in their EMRs.
- 46. Will there be a new Ontario Cervical Screening Program (OCSP) requisition form for human papillomavirus (HPV) testing and cytology testing (also known as Pap testing) for colposcopy?
 - Yes. There will be a new, OCSP-specific requisition form for use as part of a colposcopic episode of care (HPV and Cytology Tests Requisition – For Follow-up of Screening-Related Abnormalities).
 - Providers will not be able to order OCSP-funded testing using any other requisition.
- 47. Where can providers find the new Ontario Cervical Screening Program (OCSP) requisition form for human papillomavirus (HPV) testing and cytology testing (also known as Pap testing) for colposcopy?
 - Leading up to the launch of HPV testing, Regional Cancer Programs will be working with colposcopy facility partners to support the integration of the colposcopy-specific requisition (HPV and Cytology Tests Requisition – For Follow-up of Screening-Related Abnormalities) into electronic medical record systems where appropriate.
 - This requisition will also be available on the HPV testing implementation resource hub at ontariohealth.ca/hpvhub and will be sent as part of an information package of pre-launch materials shared with providers offering colposcopy.
 - For questions, providers can contact their Regional Cancer Program or facility directly.
- 48. Why is "sex as appears on Ontario Health Insurance Plan (OHIP) card" included as a patient identifier in the Ontario Cervical Screening Program (OCSP) screening and colposcopy requisitions?
 - The "sex as appears on OHIP card" patient identifier helps link screening participants to the OCSP correspondence program, which mails participants invitation, result and recall letters.

These letters support patient care by encouraging participation in screening and timely follow-up of abnormal results.

• The sex that appears on someone's OHIP card may not match their sex assigned at birth or gender identity. All people who have a cervix and meet the eligibility criteria for cervical screening should be offered cervical screening. These people include, but are not limited to, Two-Spirit, transmasculine and nonbinary people with a cervix.

^aThe eligible population includes people who have a cervix (including women, Two-Spirit people, transmasculine people, nonbinary people, pregnant people, post-menopausal people, people who have undergone a subtotal hysterectomy and retained their cervix, and people who have had the HPV vaccine), are age 25 or older, have ever been sexually active and are asymptomatic. Routine screening is not recommended for people who have had their cervix removed as a result of a hysterectomy.

- 49. How do providers submit claims for payment to the Ontario Health Insurance Plan (OHIP) for Ontario Cervical Screening Program (OCSP) cervical screening and colposcopy-related tests?
 - The OHIP <u>Schedule of Benefits for Physician Services</u> will be updated to reflect new clinical guidance and standards for HPV testing in cervical screening and colposcopy. The Ministry of Health will provide updates on any changes to fee codes and payment rules before HPV implementation through the publication of an INFOBulletin on the ministry's website.
 - Providers with questions about claims billing and payment can contact the Ministry of Health's Service Support Contact Centre at 1-800-262-6524 or SSContactCentre.MOH@ontario.ca.
- 50. Will cervical screening and colposcopy-related tests in the Ontario Cervical Screening Program (OCSP) be available to people without Ontario Health Insurance Plan (OHIP) coverage? UPDATED APRIL 2025
 - Cervical screening and colposcopy-related tests for people without OHIP coverage are outside of the OCSP.
 - People can pay for cervical screening and colposcopy-related tests if they do not have OHIP
 coverage or only have other types of health insurance coverage (e.g., private insurance
 plans). People who cannot pay for these tests may be able to get tested for free through a
 community health centre or alternative funding.
 - A non-OCSP requisition should be used for ordering tests that are outside of the OCSP.
 - Providers can connect directly with their laboratory service provider for more information on the ordering and billing (if applicable) process for tests that are outside of OCSP.

51. What is the Ontario Cervical Screening Program (OCSP) Declined Referral Letter and when is it used?

- The OCSP Declined Referral Letter can be sent by colposcopists to providers whose colposcopy referrals are not aligned with OCSP recommendations. The decision to refer to colposcopy should be based on the OCSP's cervical screening recommendations. These recommendations are based on someone's immediate risk of pre-cancer and cervical cancer, which is determined by their age, screening results and screening history.
- Colposcopists are encouraged to use a letter template to communicate with the referring provider about the reason for declining a referral. A sample declined referral letter template that reflects the changes to the OCSP screening recommendations for human papillomavirus can be found on the HPV testing implementation resource hub at ontariohealth.ca/hpvhub
- If a provider receives a declined referral letter, but their patient meets the criteria for referral to colposcopy, they should resubmit the referral with additional clinical information.

52. Can providers request sexually transmitted infection (STI) testing on the same specimen used for human papillomavirus (HPV) testing through the Ontario Cervical Screening Program (OCSP)?

- No. The specimen collected for HPV testing cannot be used for STI testing.
- The HPV test checks for the presence or absence of oncogenic types of HPV only. The HPV test does not check for non-oncogenic types of HPV, such as types that cause genital warts.
 As a result, the HPV test is not appropriate for routine STI screening.
- For more information, refer to question #18 <u>Should human papillomavirus (HPV) testing</u> be performed as part of sexually transmitted infection (STI) screening?
- Providers who would like to test for the presence of other STIs, such as chlamydia, gonorrhea or HIV, should collect separate swabs and fill out separate (non-OCSP) requisitions.
- STI testing is not in scope for the OCSP. For more information on recommendations for the screening of sexually transmitted infections, refer to <u>Canadian Guidelines on Sexually</u> <u>Transmitted Infections – Canada.ca</u>.

Screening and colposcopy test results.

53. How will providers who offer screening or colposcopy get results from the laboratory for human papillomavirus (HPV) testing and cytology testing (also known as Pap testing)?

- Laboratories participating in the Ontario Cervical Screening Program (OCSP) will use a
 provider's preferred process (e.g., fax, electronic, mail) to send them results. OCSP
 screening test results, as well as HPV testing and cytology test results from colposcopy, will
 also be available through the Ontario Laboratory Information System.
- Providers who offer screening will get screening results directly from their participating laboratory. These results will include any next steps recommended by the OCSP.
- Colposcopists will get HPV and cytology test results directly from their participating laboratory. Colposcopists are encouraged to keep referring providers informed of their patient's progress throughout colposcopy. The participating laboratories will not send referring providers results of the HPV and cytology tests done in colposcopy, unless the ordering colposcopist requests it on the requisition.
- Colposcopists are encouraged to send discharge letters to referring providers when someone is discharged back into screening in primary care. Discharge letters should indicate whether someone needed treatment and what the recommended risk-based screening interval is post-discharge. OCSP discharge letter templates are available on the HPV testing implementation resource hub at ontariohealth.ca/hpvhub.

54. Why are cervical specimens from human papillomavirus (HPV) tests and cytology tests (also known as Pap tests) sometimes rejected by the laboratory?

- HPV and cytology test specimens are sometimes rejected by the laboratory due to issues with the cervical specimen or requisition.
- Potential reasons that a cervical specimen could be rejected include:
 - Part of the collection device (i.e., broom, spatula or endocervical brush) was left in the collection vial
 - Information on the label is missing, illegible or incomplete
 - Label on the vial and corresponding requisition do not match
 - Missing requisition
 - Not intact (e.g., vial may be leaking)
 - Collected using inappropriate media or collection device

- Collected using an expired collection device or the specimen has expired
- Potential reasons that a requisition could be rejected include:
 - Screening participant is not eligible for cervical screening (e.g., inappropriate age or not due for screening)
 - Incomplete or illegible information
 - Missing cervical specimen
 - Duplicate requisition
 - Inappropriate cytology-only request
 - Multiple indications selected
 - Missing testing indication
- If there are issues with the cervical specimen or requisition, the laboratory will attempt to contact the provider who submitted them at least three times to get the required information. If the laboratory cannot get the information, the specimen and requisition will be rejected.
- Providers have been paired with laboratories that are participating in the Ontario Cervical Screening Program (OCSP) and should contact their laboratory if they have questions about cervical specimens or requisitions:

Dynacare: 1-800-565-5721

LifeLabs: 1-877-849-3637

North Bay Regional Health Centre: 1-888-418-6430

Step-by-step guidance on how to collect a cervical specimen using the ThinPrep® system
and instructions on how to fill out OCSP requisition forms are available on the HPV testing
implementation resource hub at <u>ontariohealth.ca/hpvhub.</u>

55. What are the next steps for people with human papillomavirus (HPV)-negative test results in screening?

- People who are negative for oncogenic types of HPV (and who are immunocompetent) should screen again in five years. They will be sent a recall correspondence letter from Ontario Health (Cancer Care Ontario) at that time, unless they have opted out of correspondence.
- People should be reassured that the risk of high-grade abnormal cell changes in the cervix five years after a negative HPV test result is lower than the three-year risk after a normal

cytology test (also known as a Pap test) result, and that it is appropriate to be screened again in five years, regardless of sexual activity^a (1).

^aSexual activity is defined as any sexual contact with another person's genitals (private parts). This contact can be with the hands, mouth or genitals, and includes the sharing of sex toys. Providers should define what is meant by sexual contact so their patients understand that it includes people who have had sexual contact with only one person, have had the same sexual partner for a long time, have not had sexual contact in a long time or have had sexual contact with someone of the same sex.

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- 56. How and why is human papillomavirus (HPV) partial genotyping being used in the Ontario Cervical Screening Program for HPV test interpretation?
 - All oncogenic types of HPV have oncogenes that, with persistent infection, can lead to precancer and cervical cancer. However, this risk varies by HPV type (1).
 - Partial genotyping allows for the identification of HPV types 16, 18 and 45. Among oncogenic HPV types, types 16, 18 and 45 are detected in almost 75 per cent of all squamous cell carcinomas and 94 per cent of adenocarcinomas (2). Testing for types 16 and 18 is associated with the greatest proportion of cervical cancers and pre-cancers being detected (1, 3-5), and types 18 and 45 are found in a relatively high number of adenocarcinomas^a. People with HPV types 16, 18 and 45 will receive a test result of "HPV-positive (types 16, 18/45)".
 - The remaining oncogenic HPV types are grouped together and labelled "other." These
 "other" oncogenic HPV types can lead to pre-cancer and cervical cancer, but less frequently
 and as such are considered to be lower risk. People with these remaining oncogenic HPV
 types will receive a test result of "HPV-positive (other high-risk types)".
 - In addition to performing partial genotyping, the laboratories will automatically perform
 cytology testing (also known as Pap testing) on all specimens that test positive for
 oncogenic types of HPV (called reflex cytology).
 - By separately identifying HPV types 16, 18 and 45, people can be further risk stratified. This
 information in combination with the reflex cytology test results can be used to determine
 someone's clinical next steps.

^aThe Ontario Cervical Screening Program's recommendations were informed by risk-based data that did not reflect HPV type 45 individually. However, the HPV test platform procured by the OCSP does not differentiate between HPV types 18 and 45. The HPV assay was procured after the recommendation development process was complete.

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57. What are the next steps for people with human papillomavirus (HPV)-positive (types 16, 18/45) test results in screening?

- Among oncogenic HPV types, types 16, 18 and 45 are detected in almost 75 per cent of all squamous cell carcinomas and 94 per cent of adenocarcinomas (1). Types 16 and 18 are associated with the greatest proportion of cervical cancers and pre-cancers being detected (2-5), and types 18 and 45 are found in a relatively high number of adenocarcinomas^a.
- Therefore, people who are HPV-positive (types 16, 18/45) should be referred to colposcopy, even if their reflex cytology test (also known as a Pap test) result is normal.
- Even though people who are HPV-positive (types 16, 18/45) should be referred to colposcopy regardless of the reflex cytology test results, the reflex cytology test is still performed by the laboratories because the result will be used by the colposcopist to determine the appropriate risk-based management in colposcopy.

^aThe Ontario Cervical Screening Program's recommendations were informed by risk-based data that did not reflect HPV type 45 individually. However, the HPV test platform procured by the OCSP does not differentiate between HPV types 18 and 45. The HPV assay was procured after the recommendation development process was complete.

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58. What are the next steps for people with human papillomavirus (HPV)-positive (other high-risk types) test results in screening?

- Partial genotyping allows for the identification of HPV types 16, 18 and 45. Among oncogenic HPV types, types 16, 18 and 45 are detected in almost 75 per cent of all squamous cell carcinomas and 94 per cent of adenocarcinomas (1). Types 16 and 18 are associated with the greatest proportion of cervical cancers and pre-cancers being detected (2-5), and types 18 and 45 are found in a relatively high number of adenocarcinomas^a. The remaining oncogenic HPV types are grouped together and labelled "other."
- In addition to partial genotyping, all specimens that test positive for oncogenic types of HPV
 will have reflex cytology testing (also known as Pap testing) performed on them automatically
 by the laboratories.
- The next step for people with HPV-positive (other high-risk types) test results is based on their reflex cytology test result and their screening interval.
- Recommendations for people being screened every five years (or three years if immunocompromised) include the following:
 - People with HPV-positive (other high-risk types) and low-grade or normal reflex cytology test results should repeat their screening test in two years. This allows time for the HPV infection to clear in over 50 per cent of people (2).
 - People with HPV-positive (other high-risk types) and high-grade reflex cytology test results should be referred to colposcopy.
- Recommendations for people being screened in two years after a previous HPV-positive (other high-risk types) test result include the following:
 - People who are HPV-positive (regardless of HPV type and reflex cytology test result) at the two-year re-screen should be referred to colposcopy because this indicates persistent infection.
 - People who are HPV-negative at the two-year re-screen can return to average risk screening in five years, immunocompromised screening in three years or stop screening if cessation criteria have been met.

^aThe Ontario Cervical Screening Program's recommendations were informed by risk-based data that did not reflect HPV type 45 individually. However, the HPV test platform procured by the OCSP does not differentiate between HPV types 18 and 45. The HPV assay was procured after the recommendation development process was complete.

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- 59. What are the next steps for people who have been evaluated in colposcopy, discharged to screening at a two-year interval and now have human papillomavirus (HPV)-positive (other high-risk types) test results in screening?
 - If someone has an HPV-positive test result (regardless of HPV type or reflex cytology test result) at the two-year screening test post-discharge from colposcopy, they should be referred back to colposcopy. This result indicates persistent HPV infection.

60. What are the next steps for people who have an invalid human papillomavirus (HPV) test result?

- Invalid HPV test results can be caused by laboratory processing errors or specimen collection issues.
- After an invalid HPV test result, the HPV test should be repeated at the participant's earliest convenience, within 3 months, to inform clinical management.
- People with two consecutive invalid HPV test results in screening within a 21-month period should be referred to colposcopy.
- Note, reflex cytology will not be performed by the laboratories after an invalid HPV test.

61. What are the next steps for people who are human papillomavirus (HPV)-positive, but who have unsatisfactory reflex cytology test (also known as a Pap test) results?

- Unsatisfactory reflex cytology test results may be caused by laboratory issues, specimen collection issues or participant-related factors.
- In most cases, after an unsatisfactory reflex cytology test result, a repeat standalone cytology test should be performed to inform clinical management. More specific details are summarized below.

In primary care:

- People who are HPV-positive (other high-risk types) with an unsatisfactory reflex cytology test result should have a repeat standalone cytology test at their earliest convenience, within 3 months. If someone has two consecutive unsatisfactory cytology test results within a 21-month period, they should be referred to colposcopy.
- People who are HPV-positive (types 16, 18/45) with an unsatisfactory reflex cytology test result should be referred to colposcopy. The repeat (standalone) cytology test will be performed at the first colposcopy visit.

o In colposcopy:

- People who are referred to colposcopy with unsatisfactory cytology test results (i.e., HPV-positive [types 16, 18/45] and unsatisfactory cytology or a second consecutive HPV-positive [other high-risk types] and unsatisfactory cytology), should have a cytology (i.e., standalone cytology) test performed at the first colposcopy visit to inform best management.
- If an HPV/cytology co-test performed during colposcopy yields an unsatisfactory cytology test result, a repeat (standalone) cytology test should be completed. Standalone cytology tests can be indicated on the requisition form.
- The use of transition-related hormone therapy (i.e., androgen therapy) in transmasculine and nonbinary people has been associated with a higher rate of unsatisfactory cytology test results. Therefore, a course of intravaginal estrogen therapy should be considered after an unsatisfactory cytology test result in transmasculine and nonbinary people (1).
- Intravaginal estrogen therapy can also be considered for post-menopausal people (2).

REFERENCES

 Ontario Health (Cancer Care Ontario). Overarching Policy for the Screening of Trans People in the Ontario Breast Screening Program and the Ontario Cervical Screening Program [Internet].
 Toronto; 2021 [cited 2022 Sep 22]. Available from: cancercareontario.ca/en/guidelines-advice/types-of-cancer/61546 2. Bateson DJ, Weisberg E. An open-label randomized trial to determine the most effective regimen of vaginal estrogen to reduce the prevalence of atrophic changes reported in postmenopausal cervical smears. Menopause. 2009;16(4):765–9.

62. If someone has genital warts, but has an human papillomavirus (HPV)-negative test result, should they still go to colposcopy?

- No. If someone has an HPV test that is negative for oncogenic types, they are not at an elevated risk for pre-cancer and cervical cancer. Therefore, they do not need to be seen in colposcopy.
- The management of genital warts is out of scope for the Ontario Cervical Screening Program.
 Genital warts should be managed by a local practice with appropriate resources (e.g., primary care, sexual health clinic).

63. How should providers offering colposcopy manage people who are ready to be discharged from colposcopy, but who do not have a primary care provider?

- People without a primary care provider can call Health811 at 811 (TTY: 1.866.797.0007) or visit <u>ontario.ca/page/find-family-doctor-or-nurse-practitioner</u>. They can also find Indigenousled health centres at https://iphcc.ca/meet-our-members/.
- Colposcopists can consider transferring people to their (or a colleague's) gynecology practice for cervical screening.
- Colposcopists should not perform ongoing colposcopy on people who are ready to be
 discharged and do not have a primary care provider. For some people, colposcopy is
 associated with anxiety, discomfort and pain, and should only be performed when the benefit
 of cancer prevention outweighs the risk of harm (1).

REFERENCE

- 1. Sharp L. After-effects reported by women following colposcopy, cervical biopsies and LLETZ: Results from the TOMBOLA trial. BJOG An Int J Obstet Gynaecol. 2009 Oct;116(11):1506–14.
- 64. What information about human papillomavirus (HPV) screening test results will be included in the Ontario Health (Cancer Care Ontario) Ontario Cervical Screening Program (OCSP) correspondence letters?
 - Correspondence letters will continue to be sent to screen-eligible people in Ontario (unless they have opted out), but the letters will be updated to reflect the introduction of HPV testing as part of the OCSP.
 - Screening result letters will include high-level information about a participant's cervical
 screening test result (i.e., whether a type of HPV was detected that can sometimes cause
 cervical cancer) and their next steps, if any. Screening result letters will also include some
 frequently asked questions that provide more information about HPV and cervical cancer.

- Given the complexity of communicating result information in these letters, people with HPVpositive test results will not be provided with information about the oncogenic type of HPV detected or results of reflex cytology.
- Providers will receive detailed result information and recommendations for next steps from the laboratories, and are responsible for communicating results to their patients. Providers offering cervical screening will share this information with their patients.
- In alignment with the current state, letters will not be sent by Ontario Health (Cancer Care Ontario) with results from colposcopy visits. Results from colposcopy visits will be reviewed with patients through the colposcopy clinic.
- Ontario Health (Cancer Care Ontario) conducted thorough testing of a subset of the
 correspondence letters in English and French. Screen-eligible people participated in either
 one-on-one interviews or a focus group to review and provide feedback on the letters to
 ensure that they were clear, culturally acceptable, motivating, and actionable. Participant
 feedback was used to revise and improve the letters.

65. Can cervical screening detect abnormalities suggestive of non-cervical malignancies?

- Cytologic abnormalities suggestive of non-cervical malignancies, while rare, can be detected during cervical screening. These abnormalities may include uterine adenocarcinoma, sarcoma and endometrial cells in someone age 45 or older.
- While identification of non-cervical abnormalities is technically not in scope for the Ontario Cervical Screening Program, all clinically relevant findings, including cytologic abnormalities suggestive of non-cervical malignancies, will continue to be shared with providers through provider result reports from the laboratories.
- Correspondence letters will not include reflex cytology test results. However, if potential noncervical abnormalities are identified from a reflex cytology test, screening participants will receive information on their HPV status and will be informed that abnormal cells were detected. The letter will recommend that the screening participant meet with their provider to discuss next steps.

Screening activity report updates

66. When will the introduction of human papillomavirus (HPV) testing be reflected in the *MyPractice* Primary Care Plus (with Screening Activity Report [SAR] data)?

- The MyPractice Primary Care Plus (with SAR data) will be updated to reflect the launch of HPV
 testing in the Ontario Cervical Screening Program effective approximately 3 months after HPV
 testing launches. Until that time, HPV testing will not be reflected in the MyPractice Primary
 Care Plus (with SAR data).
- When HPV testing is launched, the due date in the MyPractice Primary Care Plus (with SAR data) for testing after a cytology screening test will remain unchanged. After screening

- participants get primary HPV testing, their screening status in the *MyPractice* Primary Care Plus (with SAR data) will align with the new recommendations.
- The MyPractice Primary Care Plus (with SAR data) is accessible through ONE ID. For more
 information on how to sign up for the MyPractice Primary Care Plus (with SAR data), please
 visit Primary Care Reports.

Screening and colposcopy during pregnancy

67. Are there different recommendations for cervical screening during pregnancy?

- Cervical screening recommendations and indications for referral to colposcopy are the same, regardless of pregnancy status.
- Cervical cancer can be diagnosed in pregnancy, so providers should ensure that their patients
 are up to date for cervical screening when they come for prenatal care. However, pregnancy
 does not increase someone's risk of developing cervical pre-cancer or cancer, so pregnant
 people do not need to be screened unless they are due or overdue for cervical screening.
- Cervical sampling is safe during pregnancy. However, instruments should not enter the
 cervical canal during sampling, so either use the broom or the plastic spatula without the
 endocervical brush. Screening may be deferred to the postpartum period if there are risk
 factors for preterm labour or bleeding, or if the screening participant would prefer to defer
 testing.

68. Should screening ever be deferred during pregnancy?

• Cervical screening is usually avoided after 24 weeks of pregnancy because it can be uncomfortable, but it can be resumed as early as six weeks postpartum.

69. Are there guidelines for colposcopy during pregnancy?

- Primary care providers should continue to screen people who are pregnant and refer them to colposcopy when appropriate.
- Recommendations for colposcopy in pregnancy are out of scope for the Ontario Cervical Screening Program. For information on this topic, please refer to the 2023 Canadian Colposcopy Guideline: A Risk-Based Approach to Management and Surveillance of Cervical Dysplasia.

Screening and colposcopy for people with a double cervix

70. How do providers who offer screening or colposcopy collect cervical specimens from people with a double cervix (didelphys)?

- When collecting cervical specimens from people with a double cervix, providers should collect one specimen from each cervix.
- A new collection device should be used for each cervical specimen and both specimens should be collected using the same type of device (i.e., using two separate brooms or two separate endocervical brush-spatula combinations).
- Each cervical specimen should be placed in a separate vial. Each vial should be labelled with the required patient information and identify which cervix the specimen is from (i.e., right or left cervix).
- Both cervical specimens should be submitted using a **single requisition form**. Providers should check off the indication for double cervix in the specimen section on the requisition.
- Step-by-step guidance on how to collect a cervical specimen using the ThinPrep® system is available on the human papillomavirus (HPV) testing implementation resource hub at ontariohealth.ca/hpvhub.

71. How do providers who offer screening or colposcopy interpret results for people with a double cervix?

- People with a double cervix will get a result for each cervix. In some cases, there may be a
 different result for each cervix.
- Providers should manage follow-up based on the most severe result and the pathway for the most severe result should be applied to both cervixes. For example, if the result for someone's right cervix is human papillomavirus (HPV)-negative and their left is HPV-positive (other high-risk types) with low-grade cytology, they should follow the pathway for moderate risk screening, which means they would return to screening in two years and a specimen should be collected from both cervixes at that time.

72. How will people with a double cervix find out their results?

People who have a double cervix will get two result letters from the Ontario Cervical
 Screening Program. The program will send a recall letter based on their most severe result.

Changes to the Ontario Cervical Screening Program's colposcopy recommendations.

73. What happens when someone has been discharged from colposcopy back to primary care?

- Providers offering colposcopy are strongly encouraged to send discharge letters to the
 referring provider when a patient is discharged back to primary care. The discharge letter
 should indicate whether the person required treatment and when they should return to
 screening.
- The OCSP is revising the current discharge letter templates for the launch of HPV testing, which will be available on the HPV testing implementation resource hub at ontariohealth.ca/hpvhub.
- Primary care providers are responsible for ensuring that participants screen at the
 appropriate time. People that are discharged from colposcopy for screening sooner than 5
 years will not be sent a recall letter by Ontario Health (Cancer Care Ontario). Screening
 recommendations after discharge from colposcopy are available on the HPV testing
 implementation resource hub at ontariohealth.ca/hpvhub.

74. How have the colposcopy pathways changed with the introduction of human papillomavirus (HPV) testing?

- The colposcopy pathways have been revised to reflect the incorporation of HPV testing in the Ontario Cervical Screening Program and to align with new evidence published since the development of the original pathways in 2016.
- The colposcopy pathways summarize episodes of care and describe next steps, including number of colposcopy visits, necessary interventions, tests, when someone may be eligible for discharge and the recommended interval for screening post-discharge from colposcopy.
- The colposcopy pathways were developed using a risk-based approach, which involved estimating someone's risk of developing pre-cancer and cervical cancer based on their screening results (i.e., at referral) and findings in colposcopy. More information about the development of the colposcopy pathways, including the detailed pathways themselves, can be found on the HPV testing implementation resource hub at ontariohealth.ca/hpvhub
- There are seven colposcopy pathways:
 - Colposcopy pathway 1: Investigation and management for people referred with HPVpositive and normal (NILM) or low-grade cytology (ASCUS, LSIL) results;
 - Colposcopy pathway 2: Investigation and management for people referred with HPVpositive and high-grade cytology (ASC-H, LSIL-H, HSIL) results, excluding AIS;

- Colposcopy pathway 3: Investigation and management for people referred with HPVpositive and AGC or AEC cytology (AGC-NOS, AEC-NOS, AGC-N and AEC-N) results;
- Colposcopy pathway 4: Investigation and management for people referred with HPVpositive and AIS cytology results;
- Colposcopy pathway 5: Investigation and management for people referred with HPVpositive and SCC, ACC, ACC-E or PDC cytology results;
- Colposcopy pathway 6: Post-treatment management for histology confirmed HSIL;
 and
- Colposcopy pathway 7: Post-treatment management for histology confirmed AIS.

ACC = adenocarcinoma; ACC-E = endocervical adenocarcinoma; AEC = atypical endocervical cells; AEC-N = atypical endocervical cells, favour neoplastic; AEC-NOS = atypical glandular cells of endocervical origin, not otherwise specified; AGC = atypical glandular cells; AGC-N = atypical glandular cells, favour neoplastic; AGC-NOS = atypical glandular cells, not otherwise specified; AIS = adenocarcinoma in situ; ASC-H = atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion; ASCUS = atypical squamous cells of undetermined significance; HSIL = high-grade squamous intraepithelial lesion; LSIL = low-grade squamous intraepithelial lesion; LSIL-H = low-grade squamous intraepithelial lesion; NILM = negative for intraepithelial lesion or malignancy; PDC = poorly differentiated carcinoma; SCC = squamous cell carcinoma.

75. Should providers offering colposcopy repeat an human papillomavirus (HPV) test at initial colposcopy?

- Routine repeat HPV testing at initial colposcopy is not required because it takes time for HPV infections to clear (less than 50 per cent of infections will clear within one year [1]).
 Therefore, someone's HPV status is unlikely to have changed by the time they get to colposcopy.
- The only instance where repeat HPV testing is required at initial colposcopy is when someone's HPV status is unknown because they were referred to colposcopy after two consecutive invalid HPV tests.

REFERENCE

 Demarco M, Egemen D, Raine-Bennett TR, Cheung LC, Befano B, Poitras NE, et al. A Study of Partial Human Papillomavirus Genotyping in Support of the 2019 ASCCP Risk-Based Management Consensus Guidelines. J Low Genit Tract Dis. 2020;24(2):144–7.

76. Should providers offering colposcopy repeat a cytology test (also known as a Pap test) at initial colposcopy?

 Routine repeat cytology testing at the first colposcopy visit should not be performed if the referral cytology test was done within six months of the colposcopy visit.

- An Ontario data analysis has shown high agreement between results when cytology is repeated within six months of the referral cytology (1). More than 96 per cent of people with a low-grade referral cytology test result had a low-grade or normal result when repeated within six months.
- While there was lower agreement between referral and repeat cytology test results when the referral result was high-grade, optimal management in these scenarios should be based on the highest risk result. Therefore, a lower grade result on a repeat specimen at the first colposcopy visit should not change someone's management in colposcopy.
- However, to help determine appropriate risk-based management in colposcopy, there are two clinical circumstances in which a cytology^a test should be ordered at initial colposcopy within six months of the referral cytology test result:
 - If someone was referred to colposcopy with two consecutive unsatisfactory cytology test results; or
 - If someone was referred to colposcopy with human papillomavirus (HPV)-positive (types 16, 18/45) and an unsatisfactory cytology test result.
- If there has been significant delay (more than six months) from test to referral, repeat cytology should be ordered without an HPV test (i.e., standalone cytology test).
- The use of transition-related hormone therapy (i.e., androgen therapy) in transmasculine and nonbinary people has been associated with a higher rate of unsatisfactory cytology test results. In these circumstances, a course of intravaginal estrogen therapy should be considered after an unsatisfactory cytology test result (2).
- Intravaginal estrogen therapy can also be considered for post-menopausal people (3).

^aCytology test refers to a standalone test, which can be indicated on the requisition. A repeat HPV test is not required.

REFERENCE

- 1. Ontario Health (Cancer Care Ontario). Internal data analysis: Divergence of index cytology and cytology at first colposcopy visit. 2020.
- Ontario Health (Cancer Care Ontario). Overarching Policy for the Screening of Trans People in the Ontario Breast Screening Program and the Ontario Cervical Screening Program [Internet].
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- 3. Bateson DJ, Weisberg E. An open-label randomized trial to determine the most effective regimen of vaginal estrogen to reduce the prevalence of atrophic changes reported in postmenopausal cervical smears. Menopause. 2009;16(4):765–9.

77. How will cytology testing (also known as Pap testing) be used in the colposcopy setting for the management of screening-related abnormalities once human papillomavirus (HPV) testing is introduced?

- Cytology testing will be used in colposcopy as a co-test with HPV testing. A co-test is when an HPV test and cytology test are performed on a single cervical specimen, and both results are considered together to inform clinical next steps.
- Co-testing is used to help inform whether someone can be appropriately discharged to primary care and what their subsequent screening intervals should be once discharged from colposcopy. See colposcopy pathways 2, 6 and 7 for more information.
- In general, a co-test (HPV test and cytology test) should be performed in colposcopy. HPV
 testing with reflex cytology should only be performed in screening. Reflex cytology will help to
 determine whether the HPV infection has caused cell changes in the cervix. The result of the
 reflex cytology test will help determine immediate and subsequent risk of developing precancer and cervical cancer and inform next steps.
- If someone's HPV test result is HPV-positive (types 16, 18/45), they will be referred to colposcopy regardless of their reflex cytology test result. However, the reflex cytology test is still performed automatically by the laboratories because the result will be used by the colposcopist to help inform risk-based management in colposcopy (i.e., which colposcopy pathway to follow).
- Standalone cytology testing (i.e., without HPV testing) will only be used in colposcopy in the following two clinical circumstances. In these cases, the cytology test at initial colposcopy visit is used to determine eligibility for discharge from colposcopy:
 - At the initial colposcopy visit for people who were referred to colposcopy after two
 consecutive unsatisfactory cytology test results, or with HPV-positive 16, 18 and 45
 results and an unsatisfactory cytology test result; and
 - When the referral cytology was performed more than six months ago.
- Standalone cytology testing will also be used when a cytology co-test was unsatisfactory (i.e., result could not be obtained).

78. When should providers order an human papillomavirus (HPV)/cytology (also known as a Pap test) co-test in colposcopy?

- A co-test is when an HPV test and cytology test are performed on a single cervical specimen, and both results are considered together to inform clinical next steps.
- Co-testing is recommended at specific visits in colposcopy pathways 2, 6 and 7. The combined
 results of the HPV and cytology tests will help determine whether someone can be
 appropriately discharged to primary care and what their subsequent screening intervals
 should be once discharged from colposcopy.

• A co-test is ordered using the Ontario Cervical Screening Program requisition form designed specifically for colposcopy.

79. How will the human papillomavirus (HPV) test be used in the colposcopy setting for the management of screening-related abnormalities?

- The HPV test will be implemented in colposcopy as a co-test with cytology testing (also known as a Pap testing). A co-test is when an HPV test and cytology test are performed on a single cervical specimen, and both results are considered together to inform clinical next steps. Co-testing is recommended at specific visits in colposcopy pathways 2, 6 and 7, including:
 - o If a high-grade lesion is not detected in someone with a high-grade cytology; and
 - In the post-treatment population.
- The role of HPV testing as part of the co-test is to determine whether a significant risk of precancer (high-grade abnormal cell changes) remains, which will inform whether someone can be appropriately discharged to primary care and what their subsequent screening intervals should be once discharged from colposcopy.

80. When is human papillomavirus (HPV) testing required following treatment in colposcopy?

- After treatment in colposcopy, HPV testing is recommended as a co-test with cytology testing (also known as Pap testing).
- The HPV and cytology test results are used (along with margin status and histology) to determine the risk of recurrence, eligibility for discharge and the appropriate screening interval once discharged from colposcopy.
- Refer to pathways 6 and 7 for specific recommendations.

81. How should providers offering cervical screening manage people who repeatedly test positive for oncogenic human papillomavirus (HPV) types in screening (i.e., they have a persistent HPV infection), but who have normal cytology test (also known as a Pap test) results?

- People who repeatedly test positive for oncogenic HPV types in screening remain at risk for high-grade abnormal cell changes in the cervix and need to be monitored closely.
- As a result, people in this group will move between cervical screening in primary care and
 follow-up in colposcopy until the infection clears or a high-grade lesion is detected. For
 example, someone referred to colposcopy with HPV-positive and normal reflex cytology test
 results will be discharged to primary care for repeat screening in two years if only low-grade
 lesions or no lesions are detected in colposcopy. If that person remains HPV-positive (with
 normal or low-grade cytology test results) at the next screening episode, they will be referred
 back to colposcopy, regardless of their HPV type or reflex cytology test result. If no lesion is

- detected in colposcopy, they will be discharged again to screening in two years in primary care.
- While it is important to closely monitor people who have a persistent HPV infection with normal cytology test results, a negative colposcopy lowers their risk of pre-cancer and cervical cancer, which means they can be discharged to primary care. Furthermore, people who remain in colposcopy are at risk of overtreatment; some treatments used in colposcopy, particularly when they are repeated, have been associated with pregnancy complications, such as preterm labour and cervical stenosis (1).

REFERENCE

1. Ontario Health (Cancer Care Ontario). Internal data analysis: Divergence of index cytology and cytology at first colposcopy visit. 2020.

Education, resources and communications.

- 82. Will there be educational opportunities for providers offering cervical screening to support the implementation of human papillomavirus (HPV) testing in the Ontario Cervical Screening Program (OCSP)?
 - Yes. For providers who perform cervical screening, Ontario Health (Cancer Care Ontario) will
 offer an accredited continuing professional development module on the implementation of
 HPV testing and the new OCSP cervical screening recommendations. This module will be
 available regionally through face-to-face and virtual presentations hosted by regional clinical
 leads.
 - To learn more about the accredited continuing professional development module presentations, providers should contact their Regional Cancer Program. A list of Regional Cancer Programs can be found at <u>cancercareontario.ca/en/cancer-care-ontario/programs/regional-cancer-programs</u>
 - Closer to the launch of HPV testing, Ontario Health (Cancer Care Ontario) will also offer provincial webinars with details on HPV testing implementation. The webinars will be accessible to providers across Ontario.

83. Will there be educational opportunities for providers offering colposcopy on the implementation of human papillomavirus (HPV) testing in the Ontario Cervical Screening Program (OCSP)?

- Yes. Ontario Health (Cancer Care Ontario) will be supporting the delivery of presentations that provide an overview of the changes to the OCSP's colposcopy recommendations before implementing HPV testing in Ontario. These presentations will be available regionally in person and virtually, and will be hosted by Regional Cervical Screening and Colposcopy Leads.
- Closer to the launch of HPV testing, Ontario Health (Cancer Care Ontario) will also offer provincial webinars with details on HPV testing implementation. The webinars will be accessible to providers across Ontario.
- In addition, Ontario Health (Cancer Care Ontario) will continue to provide updates on the implementation of HPV testing in the OCSP at the Colposcopy Community of Practice (CoP) webinars.
 - The Colposcopy CoP brings together Ontario colposcopists and other members of the colposcopy community (e.g., pathologists, colposcopy nurses) to share, educate and support implementation of evidence-informed best practices for colposcopy through accredited webinars.
 - To participate in the Colposcopy CoP or get access to the CoP Resource Hub (which
 includes previous webinar recordings, clinical tools and more to support best practice
 delivery of colposcopy in Ontario), email colposcopyCoP@ontariohealth.ca.

84. What resources will be available to support providers offering cervical screening talk to screen-eligible people about the human papillomavirus (HPV) test?

- A one-page fact sheet will be developed for screen-eligible people in Ontario that provides more information about cervical screening with the HPV test. Closer to the launch of HPV testing in Ontario, this fact sheet will be made available on the HPV testing implementation resource hub at ontariohealth.ca/hpvhub. The fact sheet can be shared with screen-eligible people and can be used to help answer questions they may have. Our website also provides information for the public about cervical screening. Our website will be updated at the launch of HPV testing to provide information on when to get screened, what cervical screening is, what HPV is and how the HPV test is used, as well as links to additional websites for patients.
- Information for the public about cervical screening is available at <u>ontariohealth.ca/cervical-test</u>.

85. How will the changes to the Ontario Cervical Screening Program (OCSP) be communicated to screen-eligible people in Ontario?

- Screen-eligible people will continue to receive correspondence from the OCSP by mail. This
 correspondence includes invitation and recall letters that let people know they are due for
 screening, as well as result letters with information about their cervical screening test result
 and next steps they need to take. These letters will reflect the implementation of human
 papillomavirus (HPV) testing in screening.
- Our website at ontariohealth.ca/cervical-test provides information for the public about cervical screening. The relevant sections will be updated at the launch of HPV testing to provide information on what cervical screening is, when to get screened, what HPV is and how the HPV test is used.
- A one-page fact sheet for screen-eligible people will be developed that provides more
 information about cervical screening with the HPV test. This fact sheet will also be shared
 with the Regional Cancer Programs and will be available on the HPV testing implementation
 resource hub at <u>ontariohealth.ca/hpvhub</u>. This resource will be translated into 26 different
 languages.
- Ontario Health (Cancer Care Ontario) will work with partners to raise awareness broadly about the launch of HPV testing through stakeholder and public communication activities.

86. Where can providers offering cervical screening find additional supports and resources for cervical screening with human papillomavirus (HPV) testing for First Nations, Inuit, Métis and urban Indigenous people?

- It is important to be aware of the unique needs of First Nations, Inuit, Métis and urban Indigenous people when they try to access screening. Providing care that acknowledges, respects and incorporates cultural and language considerations is an essential part of personcentred care.
- Providers should ensure that the screening participant and their family understand what
 happens during cervical screening, and the types of resources and supports available,
 including access to <u>Indigenous Navigators in the Regional Cancer Programs for those with a
 positive cervical screening result</u>. Providers should also ensure that the participant and their
 family are given sufficient time to process and ask questions about the information shared,
 and that they are given the option to speak to their provider again.
- All First Nations, Inuit, Métis and urban Indigenous people who live in Ontario are eligible for coverage under the Ontario Health Insurance Plan when accessing cervical screening; however, there may be additional barriers to care, such as geographical remoteness, lack of health care providers, racism in the health care system, communication barriers and jurisdictional issues.

- Additional supports and cervical screening resources for First Nations, Inuit, Métis and urban Indigenous people will be available closer to the launch of HPV testing at cancercareontario.ca/en/get-checked-cancer/indigenous-cancer-screening-resources and on the HPV testing implementation resource hub at ontariohealth.ca/hpvhub.
- Some of the tools that will be updated to reflect the implementation of HPV testing and changes to screening recommendations include the Cancer and Screening Toolkit, the Cancer 101 Whiteboard video, cancer screening fact sheets, and cancer screening posters and postcards.

Need this information in an accessible format? 1-877-280-8538, TTY 1-800-855-0511, info@ontariohealth.ca
Ce document est disponible en anglais seulement en raison de son exemption de la traduction en vertu de la Loi sur les services en français.